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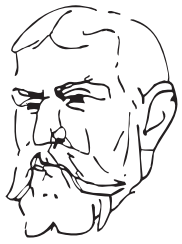

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ORIGINAL ARTICLES

ORIGINAL ARTICLE

IMPLEMENTATION OF QUANTITATIVE ELECTROENCEPHALOGRAPHY TO IMPROVE EFFICACY OF DIAGNOSIS AND TREATMENT MANAGEMENT OF CHRONIC CEREBRAL ISCHEMIA

DOI: 10.36740/WLek202211101

Tatiana V. Chernii, Volodymyr I. Cherniy, Daria O. Fokina
STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

The aim: To improve the effectiveness of diagnosis and treatment of chronic cerebral ischemia through the use of quantitative electroencephalography in civil servants on the outpatient and hospital stage.

Materials and methods: A total of 150 patients (59 males and 91 females) aged from 40 to 69 years were examined. The patients were divided into three groups statistically correlated with the main disease - chronic cerebral ischemia (CCI), degree of severity - CCI level 2, age and statistical status. Registration of brain biopotentials was performed using a computerized electroencephalograph of «TredexExpert» series. The total spectral power capacity - ASP (μV/√Hz), relative power capacity - RSP (%) were studied in the investigated frequency ranges.

Results: The study of three groups of patients with CCI of different genesis, an increase in ASP of all studied ranges, but of varying degrees of severity, was found: first, delta and theta ranges, then beta ranges, and finally, to a lesser extent, ASP of the alpha1 range and alphaS range. Therefore, the RSP of alpha1- and alphaS-bands significantly decreased in all studied groups.

Conclusions: 1. In all studied groups, the relative spectral power of the alpha 1 and alphaS bands decreased significantly. An increase in the relative spectral power of the beta-frequency rhythm in all leads was established. 2. The identified neurophysiological differences in the formation and course of dyscirculatory encephalopathy of various genesis are used to monitor the effectiveness of treatment of chronic brain ischemia.

KEY WORDS: chronic cerebral ischemia, quantitative electroencephalography, integral quantitative analysis

Wiad Lek. 2022;75(11 p1):2565-2568

INTRODUCTION

Cerebrovascular diseases (CVD) are one of the most important medical and social problems of modern neurology and occupy leading positions in terms of prevalence, mortality and disability in almost all countries of the world. The most common clinical form of cerebrovascular pathology is chronic cerebral ischemia (CCI), one of the leading syndromes of which is cognitive impairment. International literature uses the term "mild cognitive impairment" (MCI) [1]. The development of chronic ischemia of the brain is caused by a slowly progressive dysfunction that occurs as a result of diffuse or small focal damage to brain tissue in conditions of long-standing insufficiency of cerebral blood supply [2]. Moderate cognitive impairment develops in 12-20% of cases, severe - in 5-6%, however, about 50-80% of dementia cases remain undiagnosed, which negatively affects the effectiveness of treatment and social adaptation of patients [3]. Computed tomography (CT) or magnetic resonance imaging (MRI) in such patients visualize multiple ischemic foci, leukoareosis, atrophy of the brain substance with expansion of the cerebrospinal fluid spaces. Quantitative electroencephalography is an adequate and productive method for characterizing the current functional state of patients with CCI, predicting the outcome of the disease and the success of recovery [4].

THE AIM

The aim was to improve the effectiveness of diagnosis and treatment of chronic cerebral ischemia through the use of quantitative electroencephalography in civil servants on the outpatient and hospital stage.

MATERIALS AND METHODS

A clinical and neurological examination was carried out according to a fragment of the scientific study: "Improving diagnostics and methods of personalized comprehensive treatment and rehabilitation of civil servants with chronic brain ischemia and comorbid pathology". A total of 150 patients aged from 40 to 69 years were examined. The patients were divided into three groups statistically correlated with the main disease - chronic cerebral ischemia (CCI), degree of severity - CCI of level 2, age and statistical status. The first group consisted of 50 patients with CCI without concomitant hypertension, the second group consisted of 50 patients

with CCI and hypertonic disease, the third group consisted of 50 patients with CCI and a history of stroke or transient ischemic attack (TIA). The number of patients examined was 59 males and 91 females. The diagnosis was confirmed by clinical, neurological and neuropsychological examination. Control group of healthy volunteers - 20 persons.

Registration of brain biopotentials was performed using a computer electroencephalograph of the «TredexExpert» series [2]. The commutation scheme was 8-channel, Cup-shaped chlorosorbic electrodes were used, which were applied according to the international «10-20» system. A monopolar biopotential injection with a reference electrode on the lobe of the ipsilateral ear was used. EEG recording was performed mainly at an EEG channel sensitivity of 50 μV/cm. The time constant was 0.3 s and the high frequency filter was 50 Hz, which corresponds to a restored waveform of 0.5-50 Hz.

Particular attention was paid to the preparation of the output electroencephalographic signal for further computer processing. Visually, the most representative pattern of the artifact-free EEG was selected, the duration of which, in most cases, was 4 seconds. The following EEG recording protocol was followed: quiet inactivity. The software consisted of the fast Fourier transform function and computation of power and coherence spectra averaged for the following EEG frequency ranges: delta (1-4 Hz), theta (5-7 Hz), alpha S (8-12 Hz), alpha 1 (9-11 Hz), beta1 (13-20 Hz), beta 2 (20-30 Hz). The total spectral power capacity - ASP (μV/√Hz), relative power capacity - RSP (%) were studied in the investigated frequency ranges. The evaluation of EEG quantitative indicators was carried out by means of integral quantitative analysis [5]. The EEG study was conducted during the course of treatment of patients with CCI. Statistical processing of the research results was carried out on a PC using the Microsoft Excel software package. Mathematical processing was performed using standard statistical packages STATISTICA 6.0.) [6].

RESULTS

Investigation of the absolute and relative spectral potency of all the studied ranges on the whole brain in discirculatory encephalopathy of different etiology showed the following (Table I).

In conditions of CCI without concomitant hypertension (group 1) there was an increase of ASP of all studied ranges, except for ASP-alpha S-diapazon. The RSP of the alpha1- and alpha S-band was significantly decreased, and the RSP of the beta1-band was increased. The total spectral power of the EEG-pattern increased.

Under the conditions of CCI with a history of stroke (group 3) there was a similar increase in ASP of all studied ranges, including ASP of alpha1-diapasone and alpha S-diapasone. At the same time, the RSP of the alpha1- and alpha S-bands was significantly decreased. There was a clear tendency for the RSP of beta1-band to increase. The total spectral power of the EEG band increased. There were no significant differences in the absolute (μV/√Hz) and relative (%) spectral power between the first and second groups.

In conditions of hypertensive dyscirculatory encephalopathy (2nd group), an increase in ASP of all studied ranges, including ASP of the alpha1-range and alpha S-range, was also established. At the same time, the RSP of the alpha1- and alpha S-bands significantly decreased, and the RSP of the beta1- range increased. The total spectral power of the EEG pattern increased, which was significantly different from the indicators in the 1st and 3rd groups.

The study of three groups of patients with CCI of different genesis showed, an increase in ASP of all studied ranges, but of varying degrees of severity: first, delta- and theta-ranges, then beta-ranges, and finally, to a lesser extent, ASP of the alpha1- range and alpha S- range. Therefore, the RSP of alpha1- and alpha S-bands significantly decreased in all studied groups. A characteristic feature is also the increase in the total spectral power of the EEG parameter in all groups studied. These changes in spectral power were reflected in the values of integral coefficients.

When studying the zonal distribution of RSP in patients with CCI of various genesis, bilateral activation of "pathological" delta-wave activity and suppression of the alpha-frequency rhythm in the frontal cortex was established. The maximum decrease in the level of the spectral power of the alpha rhythm was noted bilaterally in the frontal, central and occipital regions. An increase in the RSP of the beta-frequency rhythm due to the activation of the β1-wave range throughout the brain and the activation or tendency to activation of the β2-rhythm across all leads. No significant changes in theta-band RSP were found in all investigated regions - frontal, central, occipital and temporal (F1, F2, C3, C4, O1, O2, T3, T4).

Thus, an increase in kfc_1 = (δ + θ + β1) / (α + β2) in patients with discirculatory encephalopathy of different genesis was established, which reflects impairment of functional intermodality between the diencephalic, brain stem, thalamo-hypothalamic structures, and basal lobe of the frontal cortex (Table I). Similarly, kfc_2 = (δ + θ) / (α + β2 + β1) on both sides, which also reflects the mechanism and degree of disorganization of electrical activity of the brain. The change in kfc_5a (β1 / β2) reflects a uniform increase in the ASP of the beta-band, and the change in kfc_11 (δ / θ) reflects a uniform increase in the ASP of the delta- and theta-bands (Table I). The tendency to decreasing of kfc 5 = (β1 / β2) - reflects disorder of the ratio of total cortical activity to activation level of cognitive processes.

The decrease of kfc_15 = (α / β2) for all groups under study demonstrates impaired cortical-cortical, cortical-talamic, cortical-limbic relations. Kfc20 = (δ / β2) tends to decrease, reflecting decreased reticulo-cortical influences on cortical tone and decreased normal cortical tone (Table I).

DISCUSSION

It should be noted that the lowest level of total spectral power of the EEG pattern was found in group 1 of the study, which is primarily due to the prevalence of low-amplitude

Table I. The value of integral coefficients (kfc) in patients with chronic cerebral ischemia

Groups	Control group	Patients with CCI		
		Without hypertension	With hypertension	History of stroke
Parameters	Median (95 %CI)	Median (95 %CI)	Median (95 %CI)	Median (95 %CI)
kfc_1a (D)	0,94 (0,9 – 0,99)	2,51 (1,71 - 3,59) #	2,16 (0,91-3,71) #	2,02 (1,45-3,71) #
kfc_1a (S)	0,93 (0,9 – 0,97)	2,16 (1,47 - 4,77) #	1,33 (0,83-2,1) #	1,52 (1,11-3,33) #
kfc_2 (D)	0,69 (0,67 – 0,71)	1,54 (0,95-1,8) #	1,05 (0,44-1,71) #	0,87 (0,67-1,61)
kfc_2 (S)	0,7 (0,68 – 0,72)	1,51 (1,25-3,99) #	0,98 (0,58-1,6) #	1,21 (0,89-2,61) #
kfc_5a (D)	2,04 (1,95–2,14)	1,5 (1,0-2,09)	1,92 (1,57-2,94)	1,88 (1,29-3,33)
kfc_5a (S)	1,53 (1,50 - 1,58)	0,64 (0,39-0,84) #	0,78 (0,46-1,94) #	0,57 (0,38-2,3) #
kfc_11 (D)	1,23 (1,23-1,28)	2,86 (2,45-4,96) #	2,74 (2,24-3,76) #	2,34 (0,55-4,96) #
kfc_11 (S)	2,19 (1,77-2,2)	2,72 (2,09-6,17)	2,84 (2,13-4,23)	2,69 (1,47-5,29)
kfc_15 (D)	7,85 (7,8 – 7,9)*	1,65 (1,35-4,14)* #	2,94 (1,6-8,54)*#	1,72 (0,92-7,55)*#
kfc_15 (S)	7,69 (7,65 – 7,74) *	2,22 (1,5-5,89)*#	2,38 (1,29-3,91)*#	3,77 (0,94-9,84)*#
kfc_20a (D)	5,81 (3,96-5,82)	5,44 (2,83-7,85)	5,67 (3,05-8,02)	4,37 (1,32-6,23)
kfc_20a (S)	6,47 (5,85-6,47)	5,26 (3,47-13,09)	4,09 (3,17-7,28)	5,31 (1,59-10,46)

NOTE: # - agreement of differences between the groups (Wilcoxon T-test; $p < 0.05$, (T-W)); * - agreement of differences between the groups (Wilcoxon W-test; $p < 0.05$ (W -W)).

and medium-amplitude electroencephalograms in the patients of this group.

The 1st group was characterized by a significant level of disorganization of the EEG pattern due to the minimum - in comparison with the other study groups - the level of ASP in the αlfa-, αlfa1- and beta1-ranges with the maximum values of the ASP in the beta- and beta 2-ranges. At the same time, in patients of the 1st group in the left hemisphere, the highest levels of the 1st and 2nd integral coefficients were recorded, which reflected the prevalence of the influence of the structure of the reticular formation of the upper trunk level of nonspecific regulation and the functionally related structures of the left hemisphere on the formation of a complete bioelectric picture of the brain [7]. It is important to note the detected bilaterally minimal (significantly reduced compared to the indicators in other research groups) values of the integral coefficients of the 15th and 20th due to the pronounced dominance of the high-frequency beta 2 rhythm (the maximum level of RSP beta2 - range), which reflected significant cortical irritation [7].

In this study, it was proved that patients of the 2nd group of the study recorded the maximum (compared to other groups) indicators of the total power spectrum of the EEG pattern, which is associated with the prevalence of high- and medium-amplitude electroencephalograms in this category of patients. This should be regarded as prognostically favorable signs of the absence of hypoperfusion and the so-called "energy deficiency", that is, predictors of the preservation of compensatory mechanisms of the CNS in conditions of chronic brain ischemia. Neurophysiologically, these predictors are manifested by a less pronounced level of disorganization of the EEG pattern with a maximum level of αlfa S- and αlfa 1-activity against the background of minimal activation in the delta - and beta 2-bands of the EEG, which should be considered as manifestations of a high level of tension. in the systems of nonspecific regulation of the CNS at the thalamic level with moderate insufficiency of the upper trunk level of nonspecific regulation. Therefore, the levels of the 1st and 2nd integral coefficients in both hemispheres were as close as possible to the indicators of the control group and were significantly lower ($p \leq 0.05$) than in the patients of the 1st and 3rd study groups. And the indicators of the 20th and 15th kfc bilaterally exceeded the values in the 1st and 3rd groups. All this was combined in patients of the 2nd group with the highest, compared to other groups, indicators of systolic and diastolic blood flow velocity in the basin of the left internal carotid artery, which indicated the absence of significant hypoperfusion, energy and mitochondrial insufficiency.

Interesting changes in the EEG pattern were found in the patients of the 3rd group of the study. Thus, the values of the total spectral power had no significant differences from the levels in the 1st and 2nd groups, as they varied widely. It should be noted the highest level of absolute and relative spectral power in the β1-rhythm range, which should be considered as manifestations of excessive tension in non-specific brain structures located outside the cortex when removing the effects of the reticular formation of the trunk and increasing the influence on the cortex from the side of the thalamus and, especially, the caudate nuclei, which should be regarded as manifestations of excessive activation of subcortical structures, primarily basal nuclei (basal ganglia, nuclei basales) [8].

CONCLUSIONS

1. In the study of three groups of patients with CCI of different genesis, an increase in the absolute spectral power of all studied ranges, but of varying degrees of severity, was found, first, in the delta and theta ranges, then in the beta ranges, and finally, to a lesser extent, in the power of the alpha1 range and alphaS -range and the total spectral power of the EEG pattern increased.

2. In all studied groups, the relative spectral power of the alpha 1 and alpha S bands decreased significantly. An increase in the relative spectral power of the beta-frequency rhythm due to the activation of the beta1-wave range, activation or tendency to activation of the beta 2-rhythm in all leads was established.
3. The 1st group (patients with AMI without hypertensive disease) was characterized by a significant level of disorganization of the EEG pattern due to the minimum level of absolute spectral power of the αlfa S -, αlfa1-, and beta1- bands at the same time as the maximum values of the relative spectral power of the delta- and beta 2-bands, the highest levels of the 1st and 2nd integral coefficients, which reflected the predominance of the influence of the structure of the reticular formation of the upper trunk level of nonspecific regulation and the functionally related structures of the left hemisphere on the formation of a complete bioelectrical picture brain.
4. In the patients of the 2nd group of the study (patients with hypertensive dyscirculatory encephalopathy), a less pronounced level of disorganization of the EEG pattern with the maximum level of alfa- and αlfa1-activity against the background of minimal activation in delta- and beta 2- bands of the EEG, which should be considered as manifestations of a high level of tension in the systems of the thalamus with a moderate insufficiency of the upper trunk structures of non-specific regulation of the CNS.
5. The identified neurophysiological differences in the formation and course of dyscirculatory encephalopathy of various genesis are used to monitor the effectiveness of treatment of chronic brain ischemia, carrying out differentiated intensive therapy.

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ORCID and contributionship:
Tatiana V. Chernii: 0000-0002-0095-6091 [A,D]
Volodymyr I. Cherniy: 0000-0002-9885-9248 [E,F]
Daria O. Fokina: 0000-0003-1244-3792 [B,C]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Tatiana V. Chernii
State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department
5 Verkhnya st., 01014 Kyiv, Ukraine
tel: +38050-577-13-37
e-mail: tatiana.cherniy@gmail.com

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ORIGINAL ARTICLE

POSSIBILITIES OF USING PERIOPERATIVE ENERGY MONITORING IN INTENSIVE CARE IN PATIENTS WITH ACUTE CALCULOUS CHOLECYSTITIS

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Anatolii I. Denysenko, Volodymyr I. Cherniy
STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

The aim: To study possibilities of using perioperative energy monitoring in intensive care in patients with acute calculous cholecystitis (ACC).

Materials and methods: 131 patients with ACC, who underwent laparoscopic cholecystectomy (LC) under general anesthesia were studied. Risk of ASA II-IV. Group I (n = 63) - intensive care aimed at maintaining vital functions. Group II (n = 68) - additional use of indirect calorimetry data.

Results: At the stages of the reverse position of Trendelenburg, pneumoperitoneum and the beginning of the operation, a decrease in hemodynamic, a violation of the oxygen status and metabolism were observed with more pronounced manifestations in the I group, where there was a longer recovery. In patients of group II, on the background of enhanced infusion therapy and administration of glucocorticoids, their recovery was more intense, they woke up faster and were transferred to the ward. These patients had 2,4 times less nausea and vomiting, and less postoperative pain upon awakening ($p<0,05$).

Conclusions: In patients with ACC, correction of hemodynamic, oxygen status and metabolism, makes LC safer.

KEY WORDS: acute calculous cholecystitis, laparoscopic cholecystectomy

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INTRODUCTION

According to the updated recommendations of the World Society of Emergency Surgery WSES (World Society of Emergency Surgery, 2020), the overall prevalence of gallstone disease with the presence of gallstones is 10-15% of the general surgical patient population, with some differences between countries. 20-40% of them have complications associated with gallstone disease with an annual incidence of 1-3%, and acute calculous cholecystitis (ACC), which occurs in 10-15% of cases and is their first clinical manifestation. The authors point to early laparoscopic cholecystectomy as the standard of care for ACC, even in the most severe patients, especially the elderly, patients with serious concomitant pathology (cardiovascular, hepatic, and renal) and patients who are at high risk of surgical intervention [1]. At the same time, subtotal cholecystectomy is proposed as the safest surgical option in cases of complicated gallbladder removal. Peculiarities of laparoscopic technologies, the use of carboxyperitoneum, specific "steep" positions of the patient's body on the operating table put forward their requirements for their anesthetic support and perioperative intensive therapy [2,3]. Literary data indicate the great importance of energy processes in the body of patients and their influence on the perioperative course of surgical interventions[4-6]. However, in our opinion, questions regarding safe (target) values of metabolism, its disturbances, and therefore the choice of appropriate perioperative technologies of intensive therapy during laparoscopic cholecystectomy for ACC remain unanswered. Taking into account all of the above, anesthetic support and perioperative intensive therapy in patients with ACC require a thorough study of perioperative changes in hemodynamics, gas exchange, metabolism and determination of methods of their correction.

THE AIM

The aim was to study possibilities of using perioperative energy monitoring in intensive care in patients with acute calculous cholecystitis.

MATERIALS AND METHODS

The study was prospective, not randomized. The authors adhered to the principles contained in the 1964 Declaration of Helsinki and their latest amendments. All the patients gave oral and written voluntary informed consent for examination, tests, treatment, operation, analgesia and data processing. The work with patients was prepared and carried out in accordance with the principles of ethics. The permission to conduct the study and the study protocol were approved of by the bioethics committee of the institution. The study group included 131 patients with ACC, who underwent laparoscopic cholecystectomy, (m-59, w-72). The age of the patients is 34–87 years, the functional severity class according to the ASA is II–IV. The average duration of the operation was 74,5 minutes. Operative interventions were performed under general anesthesia using the inhaled anesthetic sevoflurane and the narcotic analgesic fentanyl under conditions of low-flow artificial ventilation of the lungs. Induction of

anaesthesia was by propofol. Atracurium was used as a muscle relaxant. Monitoring of ventilation indicators, gas composition of the respiratory mixture, mean blood pressure, (MBP, mmHg), body temperature, neuromuscular conduction, and depth of anesthesia was performed with the built-in monitor of the Dräger Fabius Tiro anesthetic breathing apparatus and the Infinity Delta biomonitor (Dräger, Germany). In the course of the study, cardiac index (CI, $l \times min^{-1} \times m^{-2}$) were determined by the continuous calculation method esCCO biomonitor Life Scope PVM – 2701, NIHON KONDEN (Japan, Europe GmbH), gas composition and acid-alkaline state of blood - analyzer Cobas b 221 (Roche Diagnostics GmbH, Germany, Austria). Oxygen mode indicators were calculated, using a computer algorithm on a special device for Android 5: oxygen delivery (DO_2, $ml \times min^{-1} \times m^{-2}$), oxygen consumption ($VO_2$, $ml \times min^{-1} \times m^{-2}$), oxygen extraction ratio (O_2ER, %) and respiratory quotient (RQ, unit). In addition, all patients underwent energy monitoring using indirect calorimetry (special device for Android 5) and determination of the metabolic rate (MR, $cal \times min^{-1} \times m^{-2}$), basal metabolic rate (BMR, $cal \times min^{-1} \times m^{-2}$), target metabolic rate (TMR, $cal \times min^{-1} \times m^{-2}$) and metabolic disorders (MD, %) [7-8]. Patients were divided into two groups. Group I (n=63) consisted of patients in whom perioperative intensive therapy was aimed at maintaining and correcting the main indicators of vital functions according to the "International Standards of Safe Anesthesiology Practice" (WFSA 2010). Group II (n=68) - patients who, in addition to maintaining and correcting the main indicators of vital functions (WFSA 2010), underwent perioperative intensive therapy taking into account energy monitoring indicators. In them, from the moment of reverse Trendelenburg position, imposition of pneumoperitoneum and before the removal of the gallbladder, infusion therapy with balanced salt solutions was intensified and 125 mg of prednisolone was administered intravenously under the control of current and target metabolism, with subsequent determination and assessment of the level metabolic disorders. In cases of a decrease in MR and an increase in TMR relative to baseline values, especially with values of current metabolism close to the basal level and below, i/v hydrocortisone 125-250 mg was additionally administered. The basis for the appropriate correction of metabolism was the maintenance of normal oxygen status, normovolemia, normocardia, and optimal values of the acid-base status. The obtained results were compared with the initial values, and the MR - with BMR. Examination stages: initial data before surgery - 1st stage, induction of anesthesia - 2nd stage, reverse Trendelenburg position of the patient's body on the operating table, pneumoperitoneum and the beginning of the operation - 3rd stage, gallbladder removal - 4th stage, suturing the postoperative wound and restoring the horizontal position of the body - the 5th stage, the end of the operation - the 6th stage, awakening and transportation to the ward - the 7th stage). In the postoperative period, in all patients, the rate of awakening after the end of the operation was assessed by time (in minutes): beginning of eye opening (BEO), recovery of consciousness (RC), tracheal extubation (TE) and readiness for transfer to the ward (RTW) at 10 points according to the postoperative recovery scale of Aldrete (1970), the incidence of postoperative nausea and vomiting. Evaluation of postoperative analgesia was performed according to Visual Analog Pain Scale (VAS, Huskisson 1974) immediately after awakening (stage 1), after 3 hours (stage 2), after 6 hours (stage 3), after 12 hours (stage 4) and after 24 hours (stage 5). Statistical processing of the results was carried out using the STATISTICA v.64 software package (license number 12334567). Using the specified software package, the obtained quantitative parameters were checked and confirmed their compliance with the Gaussian normal distribution law according to the Shapiro-Wilk test. Having a normal distribution of parameter values, the arithmetic mean value (M) and its standard error (m) were determined. The significance of the differences in indicators was assessed using the Student's test (t). For all types of analysis, the critical level of significance (p) was <0,05.

RESULTS

The initial indicators of metabolism, in both groups, were without disturbance significantly (MD - 3,7±0,2% in group I, and 3,9±0, 4% in group II) and the value of metabolism was close to the TMR, which testified to the same conditions of their energy generation and energy supply, which corresponds to the absence of differences in the level DO_2 and VO_2, with the reference values of the O2ER ($p<0,05$, table I-II).

At the stages of induction of anesthesia, the reverse Trendelenburg position of the patient's body on the operating table, pneumoperitoneum and the beginning of the operation, a decrease in hemodynamic indicators, a violation of the oxygen regime and metabolism was observed, with the advantage of changes in group I (table I-II). In group I, at the time of induction, MBP decreased by 17,4% and reached a value of 90±5 mmHg and continued to decrease until the end of the pneumoperitoneum application stage and the beginning of the operation to 83±6 mmHg. ($p<0,05$). CI, at the time of induction, decreased by 16,1%, the reverse Trendelenburg position of the patient's body and the imposition of pneumoperitoneum - by 35,5%, and at the time of the start of the operation, it became 2,0±0,1 $l \times min^{-1} \times m^{-2}$ ($p<0,05$). DO_2 and VO_2, in the reversible Trendelenburg position, imposition of pneumoperitoneum and the beginning of the operation, decreased synchronously with the hemodynamic parameters. Thus, compared to the initial values, DO_2 decreased by 24,8%, and VO_2 - by 14,6%, with increased oxygen extraction indicators up to 31,6±0,3% at the beginning of the operation ($p<0,05$). In group II, changes in hemodynamics and oxygen status at these stages were less significant. CI, at the stage of the reverse Trendelenburg position of the body, application of pneumoperitoneum and the beginning of the operation, it decreased by 16,7% and had a value of 2,5 $l \times min^{-1} \times m^{-2}$), which was higher by 25% at the same stage of group I ($p<0,05$). Changes DO_2 and VO_2 at these stages were significantly smaller than in group I, while maintaining the reference values O_2ER (27,4±0,4%). Metabolism in both groups, at these stages of the study, decreased with a preference for changes in group I. Thus, in this group, at the induction stage, it decreased by 13,6%, and in the group II - by 8,1%. At the same time, metabolic disorders increased, respectively, in group I – by 4 times (14,6±1,3%) and in group II – by 2,6 times (10,1±1,2%) ($p<0,05$). At the stage of reverse Trendelenburg position, imposition of pneumoperitoneum and the beginning of the operation, the metabolism in both groups

Table I. Dynamics of indicators of hemodynamics, oxygen regime and metabolism of patients of group I (n=63, M±m)

Indicators/ research stages	1	2	3	4	5	6	7
MBP (mmHg)	109 ±6	90* ±5	83*# ±6	94 ±6	98 ±5	104 ±6	108 ±5
CI (l×min^{-1}×m^{-2})	3,1 ±0,1	2,6* ±0,1	2,0*# ±0,1	2,2* ±0,1	2,5* ±0,1	2,7# ±0,1	3,0# ±0,1
DO_2 (ml×min^{-1}×m^{-2})	464 ±12	440* ±11	349*#ϰ ±11	473*#ϰ ±11	512*#ϰ ±13	523*# ±10	534*# ±10
VO_2 (ml×min^{-1}×m^{-2})	123 ±5	112 ±5	105 ±6	127* ±4	136* ±4	144* ±5	148* ±4
O_2ER (%)	26,4 ±0,2	26,1 ±0,2	31,6* ±0,3	28,4 ±0,2	27,4 ±0,3	27,3 ±0,2	27,4 ±0,2
RQ (unit)	0,83 ±0,01	0,82 ±0,02	0,85 ±0,02	0,86 ±0,03	0,84 ±0,02	0,83 ±0,01	0,83 ±0,01
MR (cal×min^{-1}×m^{-2})	752φ ±11	650*#φ ±14	480*#ϰφ ±12	548*#φϰ ±11	585*#φϰ ±11	621*# ±10	646*#φ ±10
TMR, (cal×min^{-1}×m^{-2})	781 ±10	761 ±12	832 ±11	859 ±12	763 ±10	742 ±12	739 ±11
BMR (cal×min^{-1}×m^{-2})				579±10			
MD (%)	3,7 ±0,2	14,6* ±1,3	42,3*#ϰ ±2,4	36,2 ±2,3	23,3 ±2,2	16,3 ±1,6	12,6 ±1,2

* – the difference is significant in comparison with the original data (p<0,05).
\# – the difference is significant in comparison with the similar stage of group II (p<0,05).
ϰ – the difference is significant in comparison with the previous value (p<0,05).
φ – the difference is significant in comparison with the basal level of metabolism (p<0,05).

Table II. Dynamics of indicators of hemodynamics, oxygen regime and metabolism of patients of group I (n=68, M±m)

Indicators/ research stages	1	2	3	4	5	6	7
MBP (mmHg)	108 ±5	99* ±6	94*# ±7	96 ±8	106 ±4	109 ±4	115 ±3
CI (l×min^{-1}×m^{-2})	3,0 ±0,1	2,8 ±0,1	2,5*# ±0,1	2,6 ±0,1	2,8 ±0,1	3,3#ϰ ±0,1	3,6*# ±0,1
DO_2 (ml×min^{-1}×m^{-2})	456 ±11	449* ±13	417*# ±14	541*#ϰ ±12	549*# ±11	569*#ϰ ±11	585*# ±12
VO_2 (ml×min^{-1}×m^{-2})	125 ±4	116 ±4	111* ±5	135* ±5	146* ±4	152* ±4	154* ±4
O_2ER (%)	26,7 ±0,5	26,4 ±0,5	28,4 ±0,4	28,1 ±0,6	27,5 ±0,5	26,5 ±0,4	26,3 ±0,5
RQ (unit)	0,84 ±0,01	0,83 ±0,02	0,83 ±0,02	0,85 ±0,02	0,84 ±0,02	0,84 ±0,01	0,83 ±0,01
MR (cal×min^{-1}×m^{-2})	755φ ±12	694*φ# ±13	655*#φϰ ±13	716*#φϰ ±11	742*#φ ±14	751#ϰφ ±13	767#φ ±12
TMR, (cal×min^{-1}×m^{-2})	784 ±12	763 ±15	792 ±13	827ϰφ ±12	821ϰφ ±13	819*ϰφ ±14	804ϰφ ±12
BMR (cal×min^{-1}×m^{-2})				585±12			
MD (%)	3,9 ±0,4	10,1* ±1,2	17,1*#ϰ ±2,1	13,4*# ±1,3	9,6*ϰ ±1,2	8,3* ±0,3	4,6* ±0,2

* – the difference is significant in comparison with the original data (p<0,05).
\# – the difference is significant in comparison with the similar stage of group I (p<0,05).
ϰ – the difference is significant in comparison with the previous value (p<0,05).
φ – the difference is significant in comparison with the basal level of metabolism (p<0,05).

approached the basal level, and its disturbances were more significant with the predominance of changes in group I. Thus, in group I, the metabolism was below the basal level by 17,1%, the initial value by 36,2%, and the value of the previous stage - by 26,2%(p<0,05). Disturbance of metabolism, at this stage, was the most significant in both groups. In group I, it had a value of

Table III. Dynamics of indicators of the awakening and visual analog pain scale

Group	BEO	RC	TE	RTW	visual-analog pain scale (cm)				
					Examination stages				
					1	2	3	4	5
I	14,1±1,3	16,3±1,5	20,4±2,1	22,3±2,3	1,5±0,2	4,5±0,4	3,9±0,3	3,2 ±0,3	2,0±0,3
II	8,6±1,2*	9,7±1,5*	13,1±2,7*	15,2±2,8*	1,4±0,3	3,6 ±0,2	2,8±0,3*	2,1±0,4*	1,3±0,2

*- the difference is significant in comparison with the similar stage of group I ($p < 0,05$)

42,3±2,4% and, against the background of a decrease MR and growth TMR, it exceeded the similar indicator of group II by 2,5 times (p<0,05), which, against the background of a growing energy-oxygen deficit, posed a threat occurrence of perioperative complications. Changes in metabolism and its disturbances in group II were less significant: metabolism exceeded the basal level by 12%. At the same time, its violations were significantly smaller than those of group I – 17,1±2,1% (p<0,05). Since the removal of the gallbladder, stabilization and steady growth of hemodynamic indicators, restoration of oxygen regime and metabolism was observed in both groups (table I-II). In group I, the recovery of hemodynamic parameters to the level of initial values was slower than in group II and lasted until the end of the operation and awakening. In group II, from the moment of restoration of the horizontal position of the patients and suturing of the wound, a faster growth of CI was observed, compared to group I. Thus, in this group, at the end of the operation, CI exceeded the corresponding values of the gallbladder removal stage by 26,9%, suturing wounds - by 17,9% and had a value of 3,3±0,1 l min^{-1} m^{-2}, and at the stage of awakening it exceeded the initial values by 20%. DO_2 and VO_2, at these stages of the study, they steadily increased, with the advantage of changes in group II. Thus, at the time of awakening, compared to the initial values, DO_2 increased in group I by 15,1%, and in group II by 28,3%, while a corresponding increase in VO_2 was observed: in group I - by 20,3%, and in group II - by 23,2% (p<0,05), while maintaining the reference values of O_2ER. The metabolism also increased. Thus, in group I, at the time of removal of the gall bladder and restoration of the horizontal position of the body, the MR increased, compared to the previous stages, respectively, by 14,2% and 6,8%, remaining below the initial value, until awakening (p<0,05). In group II, a more intensive growth of MR was observed and the corresponding values of group I were exceeded (p<0,05). At the stage of awakening, there was a complete recovery of MR to the level of the initial value, where it had a value of 767±12 cal×min^{-1}×m^{-2}. At the same time, the target value of metabolism and the degree of its violations remained not high, not significantly different from the initial values. Regarding the awakening of patients, it is noteworthy that in group II, they woke up faster after anesthesia and were transferred from the operating room to the ward after the end of the surgical intervention. Thus, spontaneous eye opening, recovery of consciousness, extubation of the trachea and readiness for transfer to the ward were faster in them than in group I, respectively, by 39,0%, 40,5%, 35,8% and 31,8 % ($p < 0,05$). At the same time, postoperative pain, according to VAS, in group II, 6 and 12 hours after waking up, was lower, respectively, by 28,2% and 34,4%, than in group I (table III, $p < 0,05$). Cases of postoperative nausea and vomiting, in group II, occurred 2,4 times less frequently: 5 (7,4%) versus 11 (17,5%) in group I, which required additional administration of the selective $5HT_3$ serotonin receptor antagonist (ondansetron) in the total dose 8-16 mg (p<0,05).

DISCUSSION

In both groups, the initial metabolism was balanced and had minimal disturbances (MD in group I – 3,7±0,2%, in group II – 3,9±0,4%). In both groups, at the stages of induction of anesthesia, reverse Trendelenburg position, application of pneumoperitoneum and the beginning of the operation, a decrease in hemodynamic indicators, a violation of the oxygen condition and metabolism was observed with more pronounced manifestations in group I, where perioperative intensive therapy was aimed only at maintaining and correcting the main indicators vital functions, not taking into account the current, target metabolism and the amount of metabolic disturbances, which depend on the stage of the operation, conditions and possibilities of energy production, its energy supply relative to individual levels of energy demand (target metabolism), at a given specific moment in time. Of course, many factors influence all this. These are the initial state of volemia, the patient's weight, his position on the operating table, hemodynamic and oxygen indicators, the acid-base state of the blood, and the amount of intra-abdominal pressure of carbon dioxide. This explains the decrease of the current metabolism in group I, at these stages, below the basal level and its slow recovery, which lasted, practically, until the stage of the end of the operation and awakening, remaining, at the same time, below the initial values. The use of intensive therapy in group II, taking into account the indicators of energy monitoring, strengthening of infusion therapy with balanced salt solutions and i/v drip administration of glucocorticoids under the control of current and target metabolism, determination of its violations, prevented long-term hypometabolism, made the perioperative course stable and predictable, which contributed to rapid restoration of hemodynamics, oxygen status and metabolism [4]. This may be due to the faster awakening of patients of the group II after anesthesia and transfer from the operating room to the ward, a lower frequency of postoperative nausea and vomiting compared to the I group, and, possibly, a lower intensity of postoperative pain.

CONCLUSIONS

1. Patients with ACC, during laparoscopic interventions, have significant disorders of hemodynamics, oxygen status, and metabolism, especially at the stage of the reverse Trendelenburg position, application of pneumoperitoneum, and

the beginning of the operation, where the metabolism decreased almost to the basal level, which is the justification for the need to use perioperative energy monitoring.
2. The necessity of strengthening infusion therapy with balanced salt solutions and intravenous drip administration of 125-250 mg of prednisolone under the control of current and target metabolism, with the subsequent definition and assessment of metabolic disorders from the moment of reverse Trendelenburg position, imposition of pneumoperitoneum, the beginning of surgical intervention and the removal of the gallbladder, has been proven.
3. Timely correction of hemodynamics, oxygen status, and metabolism in patients with ACC, due to increased infusion therapy, optimization of ventilation, gas exchange, hemodynamics, and use of glucocorticoids, taking into account the dynamics of changes in metabolism and determining the severity of its disorders, makes perioperative intensive care of ACC safer.

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ORCID and contributionship:
Anatolii I. Denysenko: 0000-0002-9057-0327 [A-D]
Volodymyr I. Cherniy: 0000-0002-9885-9248 [E,F]

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CORRESPONDING AUTHOR
Anatolii I. Denysenko
State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department
5 Verkhnya st., 01014 Kyiv, Ukraine
tel: + 380672840995
e-mail: anatolyden@gmail.com

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ORIGINAL ARTICLE

ANALYSIS OF INDICATORS OF THE DYNAMICS AND PREVALENCE OF THE MAIN CLASSES OF CHRONIC NON-INFECTIOUS DISEASES (ON THE EXAMPLE OF THE ANALYSIS OF THE WORK INDICATORS OF A MULTIPROFESSIONAL HEALTH CARE FACILITY)

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Dmytro D. Diachuk, Anna S. Zdelova, Yurii B. Yashchenko, Rimma P. Tkachenko, Volodymyr Y. Burko
STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

The aim: To conduct an analysis of the dynamics and prevalence of the main classes of chronic non-infectious diseases of the population contingent attached to a multidisciplinary health care institution, to determine the main predictive trends of morbidity for the formation of a strategy for the prevention of the development of these pathologies and their complications.

Materials and methods: We used methods of structural and logical analysis, bibliosemantic. In the course of the research, we analyzed individual indicators of the health status of patients over 18 years of age, who are attached for medical care to the SIS «Research and Practical Center of Preventive and Clinical Medicine» SAD, and constructed predictive trends for 5 years.

Results: The conducted retrospective analysis made it possible to state that the health of the adult population, which is attached for medical care to the SIS RPCPCM SAD during 2009-2021, is stable, without negative dynamics and a forecast expectation of deterioration over the next 5 years, which is confirmed by the analysis of forecast trends of dynamic changes in indicators of general and primary morbidity, as well as the prevalence of diseases.

Conclusions: The stability of the dynamics of indicators of the total incidence of the most common nosological forms of diseases of the main rating classes of diseases indicates the effectiveness of preventive measures, detection of bridges and early diagnosis of diseases among the attached contingent.

KEY WORDS: morbidity of the population, classes of diseases, chronic non-infectious diseases, diseases of digestive organs, endocrine pathology, retinal pathology

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INTRODUCTION

The health of the population is one of the determining factors in the development of the economy of any country, an indicator of its well-being, and an indicator of the effectiveness and efficiency of social reforms.

A number of domestic and foreign authors note that the search for ways to reduce the prevalence of non-communicable diseases (NCDs) is an urgent medical and social problem and a strategic vector of national health policy in the vast majority of countries of the world. In the WHO European Region, NCDs are also the most common cause of death, accounting for 86% of all cases and 77% of the global disease burden [1–3].

According to the Institute of Health Measurement and Evaluation, about 40% of people aged 15 to 49 years and 80% of 50-69-year-olds in the world die from diseases of the circulatory system and respiratory diseases, malignant neoplasms and diabetes, which have received the general name of non-communicable diseases diseases (NCDs). In Ukraine, in the mentioned age groups, the share of deaths caused by NCDs is significantly higher than in European countries and amounts to 60% and 90%, respectively [4].

In the National report «Sustainable Development Goals: Ukraine», in particular within the scope of goal 3, the priority task is to reduce premature mortality from non-communicable diseases. In the context of the above issues, the National Action Plan for Non-Communicable Diseases to achieve the global goals of sustainable development, adopted as part of the implementation of the Agreement on the Association of Ukraine and the EU in the direction of reforming the public health system, is directed [5-8].

The main group of indicators with which it is possible to assess the health of the population is formed by statistical data on the level of morbidity of the population, its dynamics, structure, etc. After all, the study of trends in the incidence and prevalence of diseases among different age groups is the basis for strategic reform of the health care system, both at the level of the health care institution and at the national level. That is why, in the course of the research, first of all, the analysis of morbidity indicators was carried out in order to understand the extent of their prevalence, including primary morbidity.

THE AIM

The purpose of our work is to conduct an analysis of the dynamics and prevalence of the main classes of chronic non-infectious diseases of the population attached to a multidisciplinary health care institution, to determine the main predictive trends of morbidity in order to form a strategy to prevent the development of these pathologies and their complications.

Table I. The load factor of the working-age population by persons of retirement age in the SIS RPCPCM SAD and the city of Kyiv for the period 2011-2021 (per 100 people)

Years	SIS RPCPCM SAD	Kyiv
2011	118,8	34,5
2012	117,5	34,6
2013	120,5	28,6
2014	127,6	29,5
2015	135,7	30,6
2016	131,6	40,3
2017	158,5	41,3
2018	154,5	33,5
2019	154,1	34,4
2020	151,6	35,1
2021	154,9	36,0
In average (M±m)	138,64±3,8	34,4±0,8

MATERIALS AND METHODS

The methods of structural and logical analysis, bibliosemantic analysis were used. In the course of the research, we analyzed individual indicators of the health status of patients over the age of 18, who are attached for medical care to the State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department (hereinafter - SIS RPCPCM SAD) (form No. 12) from 2009 to 2021 inclusive, their dynamics and projected trends for 5 years are constructed. The structure of morbidity by classes of diseases and the main nosological forms was studied with a comparative analysis with the corresponding indicators for the city of Kyiv based on the data of official statistics [8].

RESULTS

As of 01.01.2022, 33,698 adults are receiving medical care at the SIS RPCPCM SAD, of which 20,483 (60.8%) are over 60 years old. Such a feature of the age structure of the attached contingent is characteristic of SIS RPCPCM SAD, which distinguishes it according to the distribution of the permanent population of the city of Kyiv by age, in which, according to official statistics, the specific weight of persons of retirement age is up to 30% (Table I).

In connection with the peculiarities of the demographic burden on the attached population, the morbidity indicators and its structure in the SIS RPCPCM SAD have peculiarities compared to the corresponding indicators in the city of Kyiv.

In the structure of the prevalence of diseases (Fig. 1) in 2021, the first five ranking places were occupied by diseases

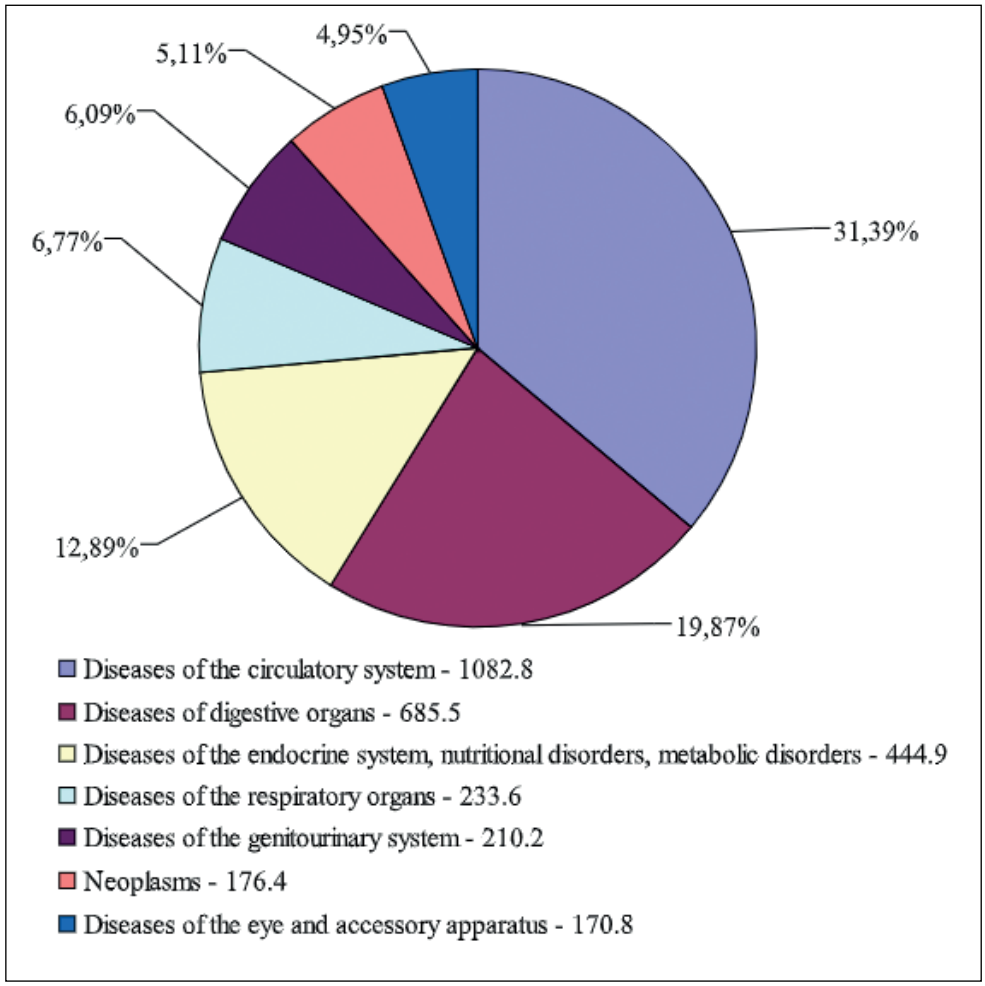

Fig. 1. The structure of the prevalence of diseases among the adult population attached for medical services to the SIS RPCPCM SAD (per 1,000 adult population)

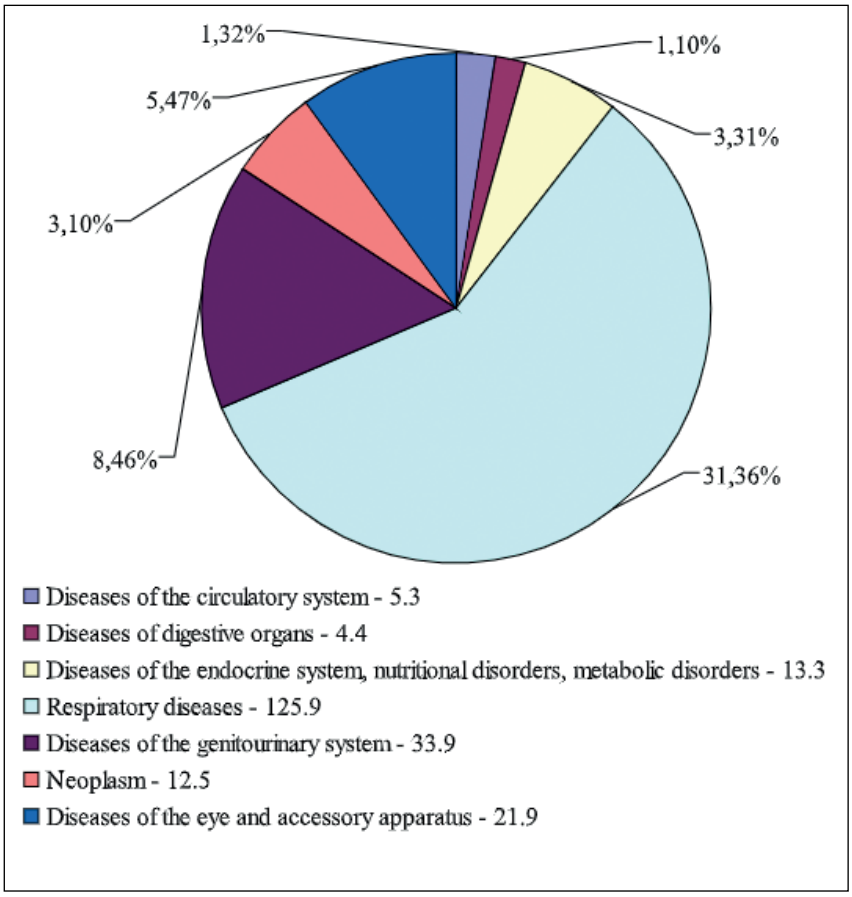

Fig. 2. Morbidity structure of the adult population attached for medical care to the SIS RPCPCM SAD (per 1,000 adult population)

Table II. Primary incidence of diseases of the circulatory system in the adult population of Kyiv and patients treated at the SIS RPCPCM SAD (per 10,000 population over 18 years of age)

	2017	2018	2019	2020	2021	The rate of change in the indicator from 2017 to 2021, %
Kyiv	560,6	504,9	437,6	354,8	333,9	- 40,4
SIS RPCPCM SAD	200,8	176,1	129,3	107,1	53,42	- 73,4

of the circulatory system (1082.8 per 1000 population), digestive organs (685.5 per 1000 population), endocrine system, nutritional disorders, metabolic disorders substances (444.9 per 1000 population), respiratory organs (233.6 per 1000 population), genitourinary system (210.2 per 1000 population).

In the structure of morbidity (Fig. 2) in 2021, the first five ranking places were occupied by diseases of the respiratory system (125.9 per 1000 population), genitourinary system (33.9 per 10000 population), eye and its accessory apparatus (21.9 per 1000 population), endocrine system, nutritional disorders, metabolic disorders (13.3 per 1000 population), neoplasms (12.5 per 1000 population), circulatory system (5.3 per 1000 population).

The conducted retrospective analysis made it possible to state that the health of the adult population, which is attached for medical care to the SIS RPCPCM SAD during 2009-2021, is stable, without negative dynamics and a forecast expectation of deterioration over the next 5 years (Fig. 3), which is confirmed by the analysis of forecast trends of dynamic changes in indicators of general and primary morbidity, as well as the prevalence of diseases using logarithmic approximation and confidence levels (R2).

Over the past five years, there has been a clear trend in the SIS RPCPCM SAD, as well as in the city of Kyiv, to decrease the level of primary morbidity of diseases of the circulatory system, which may indicate the effectiveness of preventive work among the population or the insufficient level of detection of cardiovascular diseases vascular system among the population.

Taking into account the preventive orientation of the medical support of patients at the DNU SIS RPCPCM SAD, the higher rates of coverage of the attached contingent by dispensary supervision, the indicators of primary morbidity of the main nosological forms of the class of diseases of the circulatory system at the SIS RPCPCM SAD are significantly lower compared to the corresponding indicators in the city Kyiv (Table II).

Diseases of the digestive organs occupy the second place in the structure of the overall incidence of patients over the age of 18 at the SIS RPCPCM SAD (6,854.7 per 10,000 adult population). The prevalence of the main nosological forms

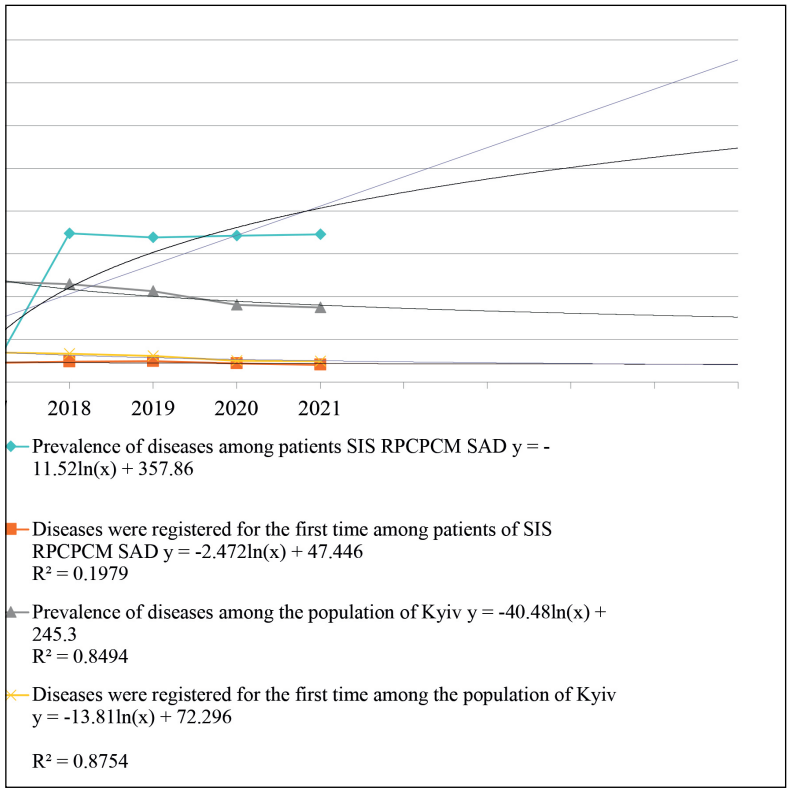

Fig. 3. Dynamics of indicators of prevalence of diseases and morbidity of the population of Kyiv and patients of SIS RPCPCM SAD (per 1000 population) for the period 2017-2021 and forecast trends

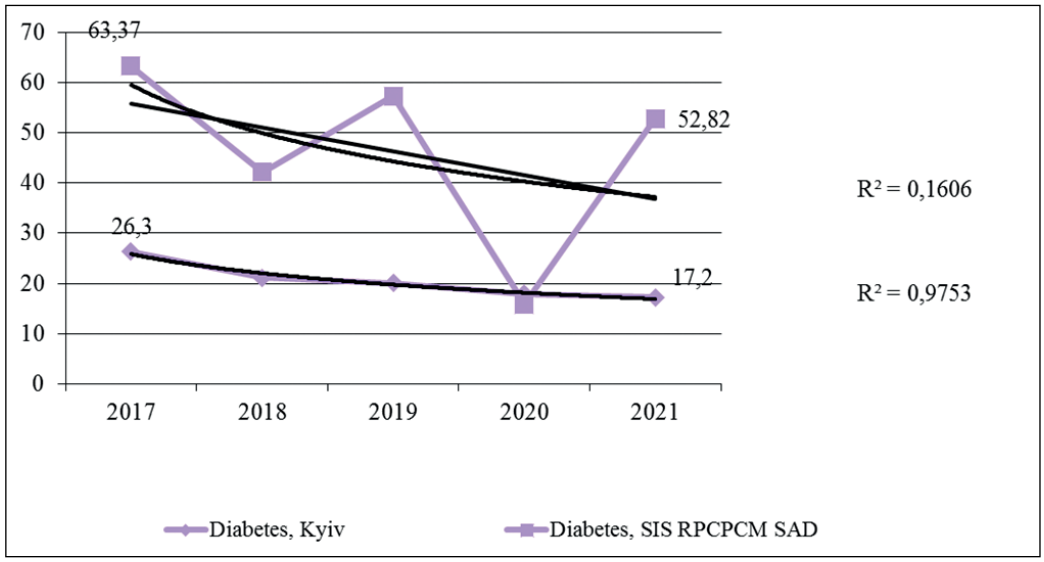

Fig. 4. Primary incidence of diabetes among the population over 18 years of age attached for medical care to the SIS RPCPCM SAD and among the adult population of the city of Kyiv (per 10,000 adult population)

of the class of diseases of the digestive organs among the adult contingent attached to the SIS RPCPCM SAD is significantly higher compared to the adult population of Kyiv.

The analysis of the dynamics of the above indicators over the past five years indicates a clear decrease in the prevalence and primary incidence of the most common diseases of the stomach and duodenum among the population of Kyiv (the approximation probability indicators are quite high, more than 0.8 for the trend of disease prevalence, and more 0.9 for the trend of primary morbidity indicators), which may indicate a decrease in the population's receptivity or low detectability of this pathology. However, the stability of the prevalence of these nosological forms among patients of the SIS RPCPCM SAD with a simultaneous significant decrease in the levels of primary morbidity (approximation probability indicators more than 0.8) indicates a sufficient level of dispensary monitoring of patients of this group and the effectiveness of preventive interventions to prevent the development diseases The level of coverage of patients with peptic ulcer disease, gastritis and duodenitis by dispensary supervision is 92.1%.

When analyzing the dynamics of the above indicators over the past five years, a similar situation is observed as with the indicators of stomach and duodenal morbidity - a clear decrease in the prevalence and primary morbidity among the population of Kyiv (the approximation probability indi-

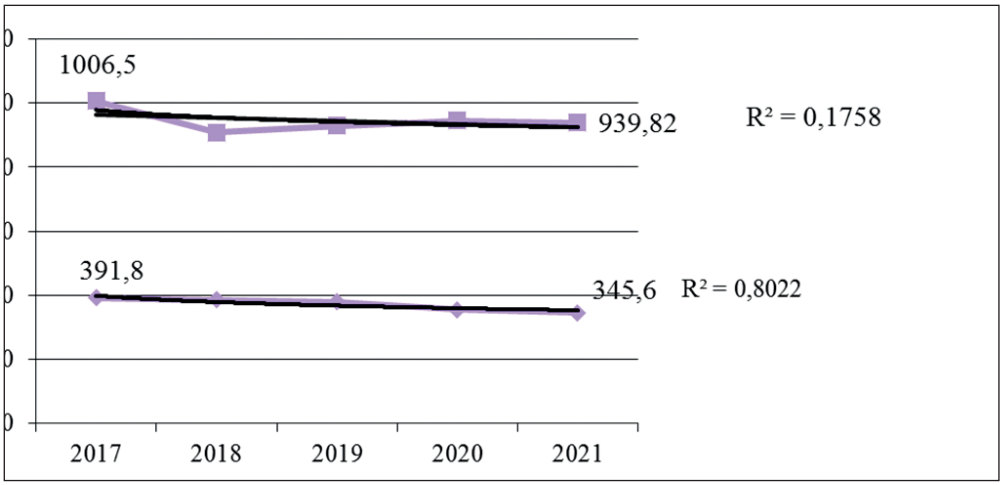

Fig. 5. Prevalence of diabetes mellitus among the population over 18 years of age attached for medical care to the SIS RPCPCM SAD and among the adult population of the city of Kyiv (per 10,000 adult population)

cators are quite high, more than 0.8 for the trend prevalence of diseases, and more than 0.9 for the trend of indicators of primary morbidity) and the stability of indicators of the prevalence of these nosological forms among patients of the SIS RPCPCM SAD with a simultaneous significant decrease in the levels of primary morbidity (indicators of the probability of approximation more than 0.8). The level of coverage by dispensary supervision of patients with cholecystitis and cholangitis is 94.3%, and for pancreatic diseases - 94.6%.

Diseases of the endocrine system, nutritional disorders, metabolic disorders in the structure of the general morbidity of patients over 18 years of age of SIS RPCPCM SAD occupy the third place. The level of their prevalence among the attached contingent is almost 5 times higher than the overall incidence of diseases of this class of diseases (according to statistics of 2021, the prevalence rate of diseases of the endocrine system, nutritional disorders, and metabolic disorders among patients of the SIS RPCPCM SAD was 4449.2 per 10,000 adult population, and among the population of Kyiv in the corresponding group — 938.7). The primary incidence rate of diseases of the endocrine system, nutritional disorders, and metabolic disorders among patients of the SIS RPCPCM SAD also exceeds the corresponding indicator among the population of Kyiv (according to the statistics of 2021 - 132.95 and 60.2 per 10,000 adult population, respectively).

In the structure of diseases of the endocrine system, nutritional disorders, and metabolic disorders among the adult population, diabetes is the most common pathology.

Among the patients of the SIS RPCPCM SAD patients with diseases of the endocrine system, nutritional disorders, metabolic disorders with diabetes, one in five. Among the population of Kyiv - 36.8%. The dynamics of the primary incidence of diabetes among the adult population of Kyiv and the population over 18 years of age attached for medical services to the SIS RPCPCM SAD is presented in Fig. 4.

The analysis of the dynamics of the general and primary incidence of diabetes (Fig. 4, Fig. 5) over the past five years indicates a clear decrease in the primary and general incidence of diabetes among the population of Kyiv (the approximation probability indicators are quite high - 0.97 and 0.8, respectively), which may indicate a decrease in the turnability of the population and/or low detectability of this pathology.

Among the patients of the SIS RPCPCM SAD, the dynamics above the indicated indicators are relatively stable, the trend of changes during the years 2017-2021 is unreliable (approximation probability indicators 0.16 and 0.17, respectively), which may indicate a sufficient level and effectiveness of preventive interventions to prevent the development of the disease, as well as the development of complications.

The most common eye complications of diabetes are diabetic retinopathy (DR), cataracts, and glaucoma.

DR is a microangiopathy manifested by occlusion of small vessels and their pathological permeability. Among adult patients, vision loss due to DR occurs in 8-15% of cases. In patients with insulin-dependent diabetes mellitus, 5-7 years after the onset of the disease, clinically significant symptoms appear in 15-20% of cases, after 10 years - in 50-60%, and after 30 years in almost all patients. With non-insulin-dependent diabetes, due to late diagnosis, DR is detected in 15-30% of cases, after 10 years - in 50-70%, and after 30 years in almost 90% of patients.

Therefore, when conducting an analysis of the main health indicators of the population of the age group older than 18 years of age assigned by the decree for medical services to the SIS RPCPCM SAD, there is a high burden of the working population by persons of retirement age. Compared to the adult population that receives medical assistance in health care institutions of Kyiv, the load factor of the working-age population by persons of retirement age in the SIS RPCPCM SAD is 4 times higher (average for 10 years, 2011-2021 - 34.4 ±0.8 and 138.64±3.8 per 100 people).

As a result of the peculiarities of the age structure of the attached contingent, the structure of the general morbidity of patients receiving medical care at the SIS RPCPCM SAD has peculiarities, in particular, in 2021, the first five ranking places were occupied by diseases of the circulatory system (1082.8 per 1000 population), digestive organs (685.5 per 1000 population), endocrine system, nutritional disorders, metabolic disorders (444.9 per 1000 population), respiratory system (233.6 per 1000 population), genitourinary system (210.2 per 1000 population).

DISCUSSION

In the National report «Sustainable Development Goals: Ukraine», in particular within the scope of goal 3, the priority task is to reduce premature mortality from non-communicable diseases. In the context of the above issues, the National Action Plan for Non-Communicable Diseases to achieve the global goals of sustainable development, adopted as part of the implementation of the Agreement on the Association of Ukraine and the EU in the direction of reforming the public health system, is directed [5-8].

As a number of researchers note in their publications, the key role in the implementation of primary prevention, timely detection, and dispensary monitoring of people with NCDs belongs to the outpatient and polyclinic link of the health care system. Monitoring the prevalence of NCDs is the basis for planning treatment and prevention measures, development of organizational forms and methods of work of outpatient polyclinic institutions, as well as control the effectiveness of their activities in preserving the health of the population. [9, 10].

In addition, as noted in the research of Tkachenko V.I., chronic non-communicable diseases cause global socio-economic losses of the population of many countries of the world, including Ukraine. It is they who determine the level of total mortality of the entire population of our country by 82.8% and by 62.4% – the mortality of the population of working age [11-13]. That is why, following the recommendations of the WHO, in each country, the determination of the most significant risk factors for NCDs, their targeted correction, as well as control of their dynamics are the basis of NCD prevention.

Over the past 10-15 years, the main cause of mortality and disability in Ukraine is a large group of non-infectious diseases, such as cardiovascular pathology, neoplasms, various external causes of death, and others. Currently, there are regulatory and legal acts in Ukraine that prescribe the list of preventive examinations and the list of occupational diseases and the corresponding procedures and necessary actions to combat them, but they need to be revised and updated following the new challenges of today.

CONCLUSIONS

The stability of the dynamics of indicators of the total incidence of the most common nosological forms of diseases of the main rating classes of diseases (trend changes for the approximation reliability indicators are close to 1.0) indicates the effectiveness of measures for prevention, detection of bridges and early diagnosis of diseases among the attached contingent. The levels of coverage of dispensary supervision of patients of SIS RPCPCM SAD are quite high (more than 90%).

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ORCID and contributionship:
Dmytro D. Diachuk: 0000-0003-4583-4909 [E, F]
Anna S. Zdelova: 0000-0003-2436-176X [A-D]
Yurii B. Yashchenko: 0000-0003-1790-6725 [A, C, F]
Rimma P. Tkachenko: 0000-0003-3775-8002 [B, D, E]
Volodymyr Y. Burko: 0000-0002-4174-9566 [B, D]

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CORRESPONDING AUTHOR
Anna S. Zdelova
State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department
5 Verhnya st., 01014 Kyiv, Ukraine
tel: +380674456909
e-mail: loriann2005vs2017@gmail.com

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ORIGINAL ARTICLE

FINE-NEEDLE ANGIOGRAPHY IN CHRONIC LIMB-THREATENING ISCHEMIA DIABETIC PATIENTS

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Sergii N. Didenko[1], Andrii V. Ratushniuk[2], Oleksandr V. Liksunov[2], Oleksandr M. Orlych[3], Yurii M. Hupalo[4], Dmytro A. Makivchuk[4]

[1] CLINICAL HOSPITAL «FEOFANIYA» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

[2] STATE INSTITUTION "NATIONAL INSTITUTE OF SURGERY AND TRANSPLANTOLOGY N.A. O. SHALIMOV NATIONAL MEDICAL SCIENCES ACADEMY OF UKRAINE", KYIV, UKRAINE

[3] KYIV CITY CLINICAL HOSPITAL № 1, KYIV, UKRAINE

[4] STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

The aim: The features and efficiency of performing fine-needle angiography for Chronic Limb-Threatening Ischemia (CLTI) in Diabetic Patients diagnosis.

Materials and methods: From 2015-2020, a total of 180 angiography procedures were performed in below-the-knee (BTK) arterial disease diabetic patients with CLTI (Rutherford category 4 to 6). Relative contraindications such as severe heart failure, myocardial infarction (MI), arterial hypertension, impaired renal function, allergy to contrast media and intolerance to antiplatelet therapy we carefully evaluated and compared with the major amputation risks. Patients were selected with adequate inflow to the common and popliteal arterys, as defined by presence of normal ipsilateral femoral and popliteal pulse, biphasic or triphasic Doppler waveform. Ultrasound controlled fine-needle angiography, by retrograde puncture of the superficial femoral artery (SFA) was performed with an 18G-70mm angiographic needle in 96 patients (1st group). Antegrade angiography using femoral sheath in 84 patients (2nd group).

Results: We have obtained adequate visualization BTK vessels by administering "Omnipak 300" 70% solution 9 mL with a power injector at a 3 mL/sec rate through the needle. Through the sidearm of the femoral sheath a total of contrast 15 mL, administered at 5 mL/sec rate. Fine-needle angiography 2.16 times reduces the injected contrast amount in patients. The hemorrhagic events frequency in the 1st group was significantly lower.

Conclusions: Fine-needle angiography is recommended for CLTI Diabetic Patients diagnosis.

KEY WORDS: heart failure, myocardial infarction (MI), arterial hypertension, impaired renal function, antiplatelet therapy intolerance

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INTRODUCTION

Foot ulcerative-necrotic lesions in diabetic patients are one of the common CLTI complications. The main reason for which is an infraction of the limb arteries patency [1]. Open, endovascular and hybrid operations on arteries are performed for limb revascularization, [2]. Since DUS and CT do not provide complete information about distal arterial lesion for determining the tactics of surgical BTK SOD treatment in diabetic patients it is necessary to perform angiography [3]. However, Femoral sheath angiography has certain deficiencies and can lead to complications. Most contrast agents are nephrotoxic. Because some patients have heart failure, myocardial infarction (MI), arterial hypertension, impaired renal function, allergy to contrast media and intolerance to heparin or antiplatelet therapy diabetic nephropathy, the contrast infusion can degrade their renal function thus dose-dependent effect is observed [4]. Using femoral sheath insertion to perform angiography can cause superficial and deep hematomas, destruction of atherosclerotic plaque with arterial thrombosis or distal embolization [5,6]. The study was designed to improve the technique of arteriography in diabetic patients with CLTI.

THE AIM

To examine the features and efficiency of performing fine-needle angiography in chronic limb threatening ischemia (CLTI) diabetic patients caused by below-the-knee (BTK) arterial segment steno-occlusive lesion (SOL).

MATERIALS AND METHODS

We analyzed performing fine-needle angiography features in 180 chronic limb threatening ischemia (CLTI) type II diabetes mellitus patients (Rutherford category 4 to 6). All patients were treated in 2015-2020, among them 104 male, 76 female, mean age (67.3 ± 6.5) years, the diabetes history was (13.4 ± 3.8) years. Patients had below-the-knee (BTK) arterial segment steno-occlusive lesion (SOL) with a passing ilio-femoral arterial segment. Patients were selected

Table I. Femoral arterial segment blood flow duplex ultrasound measurements

Artery	Measurements			
	Diameter, mm	PSV, m/s	PI	VFR, ml/min
Common femoral artery (CFA)	11,6 ± 0,9	0,86 ± 0,22	8,1 ± 1,4	719,6 ± 41,3
Superfacial femoral artery (SFA) proximal segment	7,2 ± 0,5	0,81 ± 0,25	7,2 ± 1,1	441,9 ± 47,2
Superfacial femoral artery (SFA) distal segment	5,8 ± 0,4	0,73 ± 0,19	8,4 ± 2,2	418,5 ± 41,7
Profunda	4,6 ± 0,4	0,61 ± 0,09	3,9 ± 0,8	258,8 ± 42,1

Table II. Contrast volume used during single limb angiography

Group of patients	«Omnipak 300»	
	Contrast volume, ml	Active contrast substance iod/ioheksol, g
1st	9 (70% solution)	2,7/5,82
2nd	15	4,5/9,71

Table III. Post angiography hemorrhagically complications

Group of patients	Complications					
	Subcutaneous hematoma		Femur soft tissues hematoma		Pseudoaneurysm	
	Abs. numb.	%	Abs. numb.	%	Abs. numb.	%
1st (n=96)	8	8,3	4	4,2	–	–
2nd (n=84)	12	14,3	7	8,3	2	3,9

with adequate inflow to the common and popliteal artery, as defined by presence of normal ipsilateral femoral and popliteal pulse, biphasic or triphasic Doppler waveform in the ipsilateral common femoral and popliteal artery.

Patients were divided into two groups. The 1st group included 96 patients who underwent fine-needle angiography method using 9 mL "Omnipak 300" 70% solution with a power injector at a 3 mL/sec rate. The 2nd group included 84 patients who underwent angiography method using 15 mL contrast medium through femoral sheath, administered at 5 mL/sec rate.

We conducted angiography results analysis in 180 patients with CLTI type II diabetes mellitus. BTK arterial segment SOL with a passing ilio-femoral arterial segment was patients inclusion criteria of the study.

Fine-needle angiography method was performed using Euroampli ALIEN (EUROCOLUMBUS SRL, Italy) mobile angiographic system, femoral sheath angiography was performed using the Philips Integris Allura (Netherlands) angiographic system.

60 minutes before and after angiography all patients were hydrated with 10 ml/kg Ringer's solution.

After ilio-femoral arterial segments patency in the 1st group patients was confirmed (arterial stenosed by less than 30% according to DUS were considered to be patent), angiography was performed due to the proposed method. Under ultrasound control, a fine-needle SFA retrograde puncture was performed 1-2 cm below its ostium with an 18G-70mm needle without a mandrel. Angiography was performed punctured site to the foot with the "Omnipak 300" 70% solution injection. The mobile angiographic system was installed in an oblique projection at an 45° angle for better visualization. During the distal BTK arteries examination the foot was rotated from the direct to the lateral projection. 2nd group patients underwent antegrade CFA puncture femoral sheath arteriography by installing 6F introducer. During angiography "Omnipak 300" was administered from the puncture site to the foot.

After angiography we determined Lee-White coagulation time in the operating room according to which hemostasis was performed for 20 minutes manual compression and a bandage was applied for 24 hours.

The study was providing with compliance of Council of Europe Convention on Human Rights and Biomedicine principles, World Medical Association Declaration of Helsinki on the ethical principles for medical research involving human subjects, and current regulations of the Ministry of Health of Ukraine. All patients signed an informed consent to participate in the study. The study protocol was approved by the local ethics committee.

RESULTS

CFA blood flow was distributed into SFA and Profunda in 2:1 ratio. Descending genicular artery is one significant branch of passing SFA blood flow. Practically the entire SFA blood volume reaches the popliteal artery and flows further to tibial and pedal arterial segments. Using DUS we examined the femoral segment arteries blood flow (CFA, SFA and Profunda) along with the detection of the arteries diameter, peak systolic velocity (PSV), pulsatility index (PI) and volumetric flow rate (VFR) in 32 patients of the 1st and the 2nd group (Table I).

According to our data, in BTK arterial segment SOL diabetic patients with CLTI 63.1% of the blood volume from the CFA is distributed to SFA, 36.9% is distributed

to Profunda. It confirms the contrast agent injected into the CFA is distributed in the same way.

Therefore, when injecting a contrast agent directly into SFA, its amount can be reduced by 2 times. Since the contrast in CFA is less blood soluble, a 70% "Omnipak 300" solution was used in the 1st group patients (Table II).

Thus, performing fine-needle technique aniography allowed to reduce the injected contrast active substance amount to the 1st group patients by 2.16 times. This method reduced the contrast-induced nephropathy risk, which is especially important for impared renal function diabetic patients.

An artery puncture size is 1.86 times smaller after 18G (1.4 mm) fine-needle compared to 6F (2.6 mm) femoral sheath insertion, which allows to reduce the number of hemorrhagic complications (Table III).

DISCUSSION

Fine-needle technique superiority is particularly clear in the ability to visualize the artery wall structure and determine atherosclerotic plaques and calcifications localization using DUS. It allows to punctuate the SFA mouth precisely within the least changed artery wall, which reduces the risk of atherosclerotic plaque rupture causing artery valve formation, the plaque with thrombosis, and distal embolization [7].

During femoral sheath through artery wall insertion, artery spasm often appears in the puncture, which, along with the introducer in the artery lumen can lead to transient acute lower limb ischemia. No such complication was observed after the 18G fine-needle artery wall puncture. When the contrast agent was injected selectively into the SFA, better contrast of the distal arterial third and foot arteries was observed, which increased the accuracy of determining indications for surgical revascularization.

In other previous publications, it is noted that the frequency of hemorrhagic complications after CFA and SFA puncture is the same [7]. However, in our study, the use of fine-needle puncture, specifically SFA, resulted in a lower rate of hematomas or pseudoaneurysm formation compared with stealth puncture. In particular, due to the fact that the patients in our study have diabetus mellitus and mainly femoropopliteal arterial segment lesions.

Since after performing fine-needle angiography, the frequency of hemorrhagic complications in patients of the 1st group was significantly lower compared to the 2nd group patients, we consider hemostasis by manual compression for 20 minutes and applying a pressure bandage for 24 hours to be sufficient, which reduces the research cost, as there is no need to use an artery suturing device.

CONCLUSIONS

1. Performing the fine-needle angiography suggests by 1.67 times reducing the contrast active substance amount. This significantly reduced the contrast-induced nephropathy risk, especially in impaired renal function diabetic patients.
2. The hemorrhagic complications frequency in the group of patients who underwent fine-needle angiography was significantly lower compared to the group of patients who underwent femoral sheath angiography.

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ORCID and contributionship:
Sergii N. Didenko: 0000-0002-3115-7524 [C,F]
Andrii V. Ratushniuk: 0000-0003-0806-3973 [D,E]
Oleksandr V. Liksunov: 0000-0002-2239-1060 [B,C]
Oleksandr M. Orlych: 0000-0002-0538-9858 [A,B]
Yurii M. Hupalo: 0000-0002-4856-1398 [D,E]
Dmytro A. Makivchuk: 0000-0002-5894-6355 [C, E]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Sergii N. Didenko
Clinical Hospital «Feofaniya» State Administrative Department
21 Zabolotnogo St., 03143, Kyiv, Ukraine
tel.: +38 (044) 259–65–74
e-mail: hirurgdidenko@gmail.com

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ORIGINAL ARTICLE

FEMOROPOPLITEAL ANGIOPLASTY *VS* OPEN SURGERY FOR CHRONIC LIMB-THREATENING ISCHEMIA

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Oleksandr A. Holyachenko[1], Anatolii M. Kravchenko[1], Andrii O. Golyachenko[2], Vitaliy G. Gurianov[3], Ivan V. Karol[4,5]
[1]STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE
[2]I. HORBACHEVSKY TERNOPIL NATIONAL MEDICAL UNIVERSITY, TERNOPIL, UKRAINE
[3]BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE
[4]SHUPYK NATIONAL HEALTHCARE UNIVERSITY OF UKRAINE, KYIV, UKRAINE
[5]CNE «BROVARY MULTIDISCIPLINARY CLINICAL HOSPITAL», BROVARY, UKRAINE

ABSTRACT

The aim: To compare the results of femoro-popliteal PTA vs open surgery in chronic limb-threatening ischemia (CLTI) and analyze clinical efficacy long-term results.

Materials and methods: Between 2018 – 2019, 145 patients with CLTI who underwent femoro-popliteal arterial segment steno-occlusive lesions (SOL) unilateral revascularization. Open surgery were performed for – 48 (33, 1%), percutaneous transluminal angioplasty (PTA) for – 73 (50.3%), and were treated with hybrid surgical interventions for – 24 (16.6%).

Results: During the analysis, no statistically significant difference was found among the three groups patients indicators. According to the diabetes patients indicator, the differences among the groups are statistically significant ($p<0.001$), diabetes was present in only 16.7% of open surgical intervention group patients, 45.8% of PTA group patients, 54.8% of the hybrid surgery group patients. In the overall comparison 2-year limb preservation after open surgery 93.8%, after PTA 91.7%, and after hybrid surgery 91.6%; amputations: open surgery – 6.2% PTA- 8.2 %, hybrid surgery -8.3%; exemption from surgical re-intervention: open surgery - 68.7%, PTA- 58.9%, hybrid surgery – 75%. There were no differences in limb preservation and amputation between open surgery, hybrid intervention, and PTA. A difference was found only in reintervention tactic among the open surgery and PTA groups as opposed to the hybrid surgery.

C**onclusions:** Limb salvage and CLTI patients survival after open surgery and PTA who were not performed major amputation in 2 years term after revascularization were comparable regardless of treatment method.

KEY WORDS: percutaneous transluminal angioplasty (PTA), steno-occlusive lesions, duplex ultrasound scan

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INTRODUCTION

Femoro-popliteal arterial segment atherosclerosis leads to ischemia, which threatens the limb. The surgical tactics choice for the femoro-popliteal segment steno-occlusive lesions (SOL) treatment remains open. One of the newest techniques is femoro-popliteal percutaneous transluminal angioplasty (PTA)[1-3]. Open surgery is more traumatic for patients.

Infralingual bypassing has traditionally been considered the treatment of choice for chronic limb-threatening ischemia (CLTI) to avoid major amputation. However, there is more data on the femoro-popliteal segment endovascular revascularization efficiency and achieving good limb salvage rates. Endovascular procedures performing has increased rapidly over the past decade. BASIL is a randomized controlled trial that has compared two critical limb ischemia treatment methods: open surgery or X-ray endovascular angioplasty [2].

Surgical and endovascular techniques comparison in randomized controlled trials is difficult due to forming comparison groups problems.

THE AIM

The aim was to compare the results of femoro-popliteal PTA and femoro-popliteal segment open surgery in CLTI and analyze clinical efficacy long-term results.

MATERIALS AND METHODS

Between 2018–2019, 145 patients with CLTI who underwent femoro-popliteal arterial segment SOL unilateral revascularization. 48 (33, 1%) patients were performed open surgery, 73 (50.3%) patients were performed PTA and 24 (16.6%) patients were treated with hybrid surgical interventions. The study was providing with compliance of Council of Europe Convention on Human Rights and Biomedicine principles, World Medical Association Declaration of Helsinki on the ethical principles for medical research involving human subjects, and current regulations of the Ministry of Health of Ukraine. All patients signed an informed consent to participate in the study. The study protocol was approved by the local ethics committee.

Among the patients 50 (34.5%) female and 95 (65.5%) male, the patients age ranged from 51 to 97 years. X-ray

Table I. The characteristics of patients divided by three groups

Characteristic		Type of operation			Difference between groups significance level, p
		Open surgery interventions (n=48)	PTA (n=73)	Hybrid surgery interventions (n=24)	
Age		72,7±8,8	71,7±7,8	73,8±8,1	0,528
Gender	F	15 (31,2)	4 (16,7)	31 (42,5)	0,059
	M	33 (68,7)	20 (83,3)	42 (57,5)	
Chronic limb ischemia class (Rutherford)	II	5 (10,4)	1 (4,2)	4 (5,5)	0,521
	III	13 (27,1)	6 (25,0)	15 (20,5)	
	IV	15 (31,2)	5 (20,8)	17 (23,3)	
	V	15 (31,2)	11 (45,8)	36 (49,3)	
	VI	0 (0,0)	1 (4,2)	1 (1,4)	
TASK II class	A	10 (20,8)	2 (8,3)	9 (12,3)	0,622
	B	9 (18,8)	6 (25,0)	22 (30,1)	
	C	9 (18,8)	4 (16,7)	10 (13,7)	
	D	20 (41,7)	12 (50,0)	32 (43,8)	
Smoking	+	22 (45,8)	8 (33,3)	37 (50,7)	0,334
	-	26 (54,2)	16 (66,7)	36 (49,3)	
Diabetes	+	8 (16,7)	11 (45,8)	40 (54,8)	<0,001
	-	40 (83,3)	13 (54,2)	33 (45,2)	
Arterial hypertension	+	19 (39,6)	14 (58,3)	39 (53,4)	0,214
	-	29 (60,4)	10 (41,7)	34 (46,6)	
Angiosomal trophic disorders	-	16 (33,3)	11 (45,8)	37 (50,7)	0,168
	+	32 (66,7)	13 (54,2)	36 (49,3)	

Notes: for quantitative characteristics, the indicator is presented through the mean value ( ) and standard deviation (±SD), for qualitative characteristics - through absolute and relative frequency (%). ANOVA criterion was used for comparing quantitative characteristics, the Chi-square criterion was used for qualitative characteristics.

endovascular interventions were performed according to the TASC II recommendations [4,5].

X-ray endovascular intervention patients were divided into: male - 42 (%), female - 31 (%),open surgical interventions: male - 33 (%), female - 15 (%), hybrid interventions: male- 20 (%), female – 4 (%). The treatment result was estimated after 30 days and after 2 years.

Exclusion criteria: below-the-knee (BTK) artery lesions, popliteal artery aneurysm, and non-atherosclerotic peripheral artery disease patients.

The surgical intervention algorithm planning for CLTI patients examination included segmental pressure measurement using the Heaco Sonoline C device, the ischemic rest pain indicators with knee level pressure ‹ 40 mm Hg. or tissue necrosis ‹ 60 mm Hg. a duplex ultrasound scan (DUS) was also performed using Mindray M5 and Samsung Medison R3 devices, blood flow velocity and femoro-popliteal arterial segment SOL extent were considered, a linear sensor with a variable ultrasound frequency of 9-15 MHz was used, patients also underwent diagnostic angiography using a Philips Alura X-per F920.

In patients with SOL less than 15 cm length and according to DUS results the method of choice was PTA (Endvascular first) [4]. Stenting was selectively performed in patients with intimate media detachment or SOL rigidity after ballon-angioplasty. In primary interventions 3% was stenting. Before the endovascular procedure we performed intra-arterial heparin injection (5000 IU).

After PTA, the patients were treated with 5000 IU heparin every 6 hours per day and received long-term supportive therapy: Aspirin 100 mg per day and Rivaroxaban 2.5 mg per day. Standard follow-up examination's included DUS 1 month and 2 years after the intervention.

Open surgical revascularization was performed in cases with ≥ 15 cm SOL length, mostly autovenous bypassing. In 23.7% patients was used allobypass due to non-suitable veins. Patients were treated with 5000 IU heparin every 6 hours during hospitalization and Aspirin 100 mg per day and Rivaroxaban 2.5 mg twice a day on an outpatient basis long-term therapy. Standard follow-up examination's included DUS 1 month and 2 years after the intervention.

RESULTS

Clinical characteristics, intervention and post-operative patients data were collected from primary medical records. Data on early and late amputations and reinterventions data were retrospectively collected. Study included atherosclerotic femoro-popliteal arterial segment SOL and diabetic patients. The characteristics of patients divided by three groups are shown in Table I

Table II. The comparative analysis results of CLTI femoro-popliteal segment SOL patients who underwent PTA and open surgery

Characteristic	Type of operation			Significance difference level among groups, p
	Open surgery interventions (n=48)	PTA (n=73)	Hybrid surgery interventions (n=24)	
Amputation	1 (2,1)	2 (8,3)	4 (5,5)	0,473
Re-intervention	8 (16,7)	4 (16,7)	19 (26,0)	0,389

Notes: for qualitative characteristics, the indicator is presented through absolute and relative frequency (%). When comparing quantitative features, the chi-square test was used for qualitative features.

During the analysis, no statistically significant difference was found among the three groups patients indicators (Table I, p>0.05 for all indicators except the diabetes frequency). According to the diabetes patients indicator, the differences among the groups are statistically significant (p<0.001), diabetes was present in only 16.7% of open surgical intervention group patients, 45.8% of PTA group patients, 54.8% of the hybrid surgery group patients.

The Rutherford classification was used according to the limb ischemia damage clinical severity category degree, patients who underwent PTA with category 2-4 - 36 (%), category 5-6 - 37 (%), open surgery patients with 2-4 category - 32 (%), 5-6 category - 16 (%), hybrid surgeries patients with 2-4 category - 12 (%), with 5-6 category - 12 (%).

The comparative analysis results of CLTI femoro-popliteal segment SOL patients who underwent PTA and open surgery are shown in Table II.

During the analysis, no statistically significant difference between the groups was found (Tab. II) either in the limb amputation risk (p=0.473) or re-intervention risk (p=0.389).

Reintervention because of thrombosis or restenosis within 1 month of observation was performed in 7 (14.5%) patients after open surgery, operated limb high amputation in 1 (2%) patient, reintervention was performed in 18 (24.6%) patients, high amputation in 4 (5.4%) patients, after hybrid surgical intervention reintervention were performed in 4 (16.6%) patients and amputations were not performed. In 2 years follow-up reoperation was performed in 12 (16.4%) patients after PTA, high amputation of the operated limb was performed in 5 (6.8%) patients, after open surgery reoperation was performed in 8 (16.6%) patients, high amputation of the operated extremity in - 2 (4.1%) patients, reintervention after hybrid surgery in - 2 (8.3%) patients and amputations were performed in - 2 (8.3%) patients.

2 (1.3%) patients died due to concomitant diseases with a preserved limb, 8 (5.5%) after operated limb high amputation.

In the overall comparison 2-year limb preservation after open surgery 93.8%, after PTA 91.7%, and ater hybrid surgery 91.6%; amputations: open surgery- 6.2% PTA- 8.2 %, hybrid surgery -8.3%; exemption from surgical re-intervention: open surgery- 68.7%, PTA- 58.9%, hybrid surgery - 75%. There were no differences in limb preservation and amputation between open surgery, hybrid intervention, and PTA. A difference was found only in reintervention tactic among the open surgery and PTA groups as opposed to the hybrid surgery.

Overall survival, lower extremity amputation, limb preservation without amputation, reintervention, pain relief at rest and intermittent claudication absence, healing of ulcers and wounds of the affected lower extremity were considered the main results of this study. The duration average of was 1.5 ± 2.2 years. The limb preservation rate for all surgeries types in 2 years is 90.3%.

DISCUSSION

Comparing X-ray endovascular, hybrid, and surgical revascularization is difficult because patient groups tend to differ in risk factors as well as arterial lesions requiring treatment. As shown by previous studies, only 4–29% of lesions were considered to be equally amenable to treatment by any method [1,6], which impairs the general validity of the study results in CLTI. Limb preservation is considered the most important CLTI treatment result. After group adjustment, there was no significant difference in limb preservation between treatments, but open surgery was associated with better limb preservation without reintervention.

This study results suggest hybrid surgery (open surgical methods combined with angioplasty) is better for saving the limb without repeated surgical interventions in the long term, as opposed to open surgery combined with PTA, when treating significantly larger femoro-popliteal SOL. In the analysis we also observed that open surgery and PTA had no differences in 2 years term after revascularization without limb reintervention. Open surgery was associated with a significant increase in subsequent overall survival and a trend toward improvement without amputation.

The reintervention score was significantly higher in diabetic patients after PTA, open surgery, and hybrid surgery. This is largely due to our general practice: if the symptoms of CLTI do not improve after the surgical intervention, the surgical reintervention with PTA success rate is relatively higher than with open surgery.

All patients were treated until the symptoms subsided or wounds healed. Routine clinical examination was performed for the PTA group, the hybrid intervention group, and the open surgery group. Previously, no resources were directed to therapy patients long-term routine follow-up because of a lack of its advantages evidence compared with the strategy we followed. Our data registry includes all

patients who underwent revascularization, endovascular, hybrid, or surgical for femoro-popliteal segment SOL.

CONCLUSIONS

Limb salvage and CLTI patients survival after open surgery and PTA who were not performed major amputation in 2 years term after revascularization were comparable regardless of treatment method.

Limb salvage without performing surgical reintervention were significantly better after open surgery, but survival without amputation was similar in all study groups. PTA can be considered a first-line tactic before performing open surgery in patients with femoro-popliteal segment SOL if technically appropriate. PTA should be performed according to The Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease (TASC II).

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ORCID and contributionship:

Oleksandr A. Holyachenko: 0000-0003-1583-0894 [A,B,D]
Anatolii M. Kravchenko: 0000-0001-6863-0197 [E,F]
Andrii O. Golyachenko: 0000-0003-2695-0023 [E,C]
Vitaliy G. Gurianov: 0000-0001-8509-6301 [C]
Ivan V. Karol: 0000-0003-3684-0127 [B]

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CORRESPONDING AUTHOR

Oleksandr A. Holyachenko
State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department
5 Verkhnya st., 01014 Kyiv, Ukraine
tel.: +380961329593
e-mail: holyachenko92@gmail.com

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ORIGINAL ARTICLE

PERCUTANEOUS TRANSLUMINAL ROTARY ATHERECTOMY IN PATIENTS WITH ATHEROSCLEROTIC LESIONS OF BELOW THE KNEE ARTERIES

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Yurii M. Hupalo[1], Sviatoslav Y. Denysov[2], Anton M. Kutsyn [1,2], Yelizaveta O. Lebedieva[2], Mykhailo M. Grusha[3]

[1]STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

[2]CLINICAL HOSPITAL «FEOFANIYA» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

[3]BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE

ABSTRACT

The aim: To determine the effectiveness of the combination of the percutaneous transluminal rotational atherectomy (PTRA) techniques with plain old balloon angioplasty (POBA) and POBA monotherapy (POBA-mono) in endovascular treatment (ET) of patients with occlusive-stenotic lesions below the knee (BTK) arteries.

Materials and methods: We studied two groups, the main included patients (n=9) aged who underwent PTRA and POBA of BTK arteries, and the comparative group (POBA-mono) of patients (n=24) who underwent POBA monotherapy of BTK arteries.

Results: Thrombosis of the reconstructed segments in the target arteries after 12 months was diagnosed in 95% of patients of the control and 1 – main groups (Ft, p=0.00001). Healing of trophic ulcers of the foot in the first month after ET was observed in 78% (n=7) of patients of the main group and in 13% (n=3) of the control group ($\chi 2$ (1, n=33) = 10.2961; p=0.0013), and after 3 months – in 100% (n=9) and 83% (n=20) of patients in the respective groups.

Conclusions: The combination of PTRA with POBA reduces the probability of repeated violations of the patency of the target artery. In addition, it increases the healing efficiency of trophic ulcers of the LE compared to POBA monotherapy.

KEY WORDS: endovascular treatment, thrombosis, occlusive-stenotic lesions, trophic ulcer, cardiovascular

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INTRODUCTION

Cardiovascular disease (CVD) is a major cause of disability and mortality worldwide. Despite significant achievements over the past decades in the diagnosis, treatment, and prevention of such diseases, occlusive-stenotic lesions of the arteries of the lower extremities (LE) leads the second place in the structure of CVD due to their contribution to the development of critical ischemia (35.0-64.7%). Furthermore, treatment of such patients is difficult due to the frequency of development of thrombosis and restenosis in them (6.0-42.0%) and the need for repeated surgical interventions in 1/3 of patients [1].

Clinical recurrence of critical limb ischemia (CLI) is associated with a high rate of nonhealing ulcer recurrence, major amputation, and death. Patients witch undergoing reinterventions than patients without reinterventions had lower rate of healing (28.5% vs. 71.9% p = 0.0001) higher rate of ulcer recurrence (20% vs. 10.3% p = 0.03), major amputation (24.3% vs. 4.3% p = 0.0005), and death (33.3% vs. 7.9% p = 0.002) [2].

A novel alternative to standard angioplasty and stenting is the excision of the obstructing arterial plaque using a minimally invasive technique, the atherectomy, to improve outcomes and lower r intervention rate [3]. Atherectomy is a competing technique that uses a rotating cutting blade or burr to excise the atheroma [4]. Thus, the problem of treatment of occlusive and calcified lesions of BTK arteries remains relevant and requires further study.

THE AIM

The aim was to determine the effectiveness of the combination of the percutaneous transluminal rotational atherectomy (PTRA) techniques with plain old balloon angioplasty (POBA) and POBA monotherapy (POBA-mono) in endovascular treatment (ET) of patients with occlusive-stenotic lesions below the knee (BTK) arteries.

MATERIALS AND METHODS

A comparative analysis of the results of ET of 33 patients (10 women and 23 men; mean age 69.6±8.9 years) of the BTK atherosclerotic occlusive-stenotic lesions with trophic ulcers in the foot was performed (2020-2022). Depending on the application of the percutaneous transluminal angioplasty (PTA) method, 2 groups of patients were distinguished: the main group (PTRA+POBA) included 27% of patients (n=9), who underwent PTRA+POBA of BTK

Table I. Characteristics of atherosclerotic lesions of the BTK arteries in the studied groups of patients, n / %.

LESION LOCALIZATION	Main group (n=9)	Control group (n=24)
Anterior tibial artery	2 / 22	6 / 25
Posterior tibial artery	5 / 56	4 / 17
Peroneal artery	0	2 / 8
Anterior+Posterior tibial artery	1 / 11	5 / 21
Anterior+Posterior tibial+Peronea artery	0	2 / 8
Posterior tibial+Peronea artery	1 / 11	1 / 4
Anterior tibial+Peronea artery	0	4 / 17
Calcification	9 / 100	15 / 63*

Note: * – p=0,039 (Ft)

arteries, and the comparative group (POBA-mono) – 73% of patients (n=24), who underwent POBA monotherapy of BTK arteries. Diabetes mellitus was diagnosed in 28 (85%) patients, arterial hypertension – 33 (100%), coronary heart disease – 22 (67%), and atrial fibrillation – in 8 (24%) cases. Six (18%) patients demonstrated the decline of estimated glomerular filtration rate <35 ml/min/1.73 m^2.

Patients were studied for the primary patency of the target artery and other vessels by preoperative ultrasound. The wound healing, limb amputation, and the development of cardiovascular events during the year were analyzed every 3 months after ET. All patients got optimal medical treatment before and after ET.

PTA was performed by POBA and PTRA with POBA. Rotablation was performed by standard coronary technique, and burr size was selected by Burr/Artery ratio 0,75-0,85/1 [5].

The study was conducted by the principles of the Council of Europe Convention on Human Rights and Biomedicine, the World Medical Association Declaration of Helsinki on the ethical principles for medical research involving human subjects, and current regulations of the Ministry of Health of Ukraine. The study not used new medications, biologics, or devices. Additional risks associated with scientific research, apart from those possible against the background of surgical intervention for lower limb ischemia, are not expected. Examinations and medical procedures were performed in the inpatient department under a doctor's supervision. All patients signed informed consent to participate in the study.

The Mann-Whitney U-test (for quantitative variables), and the Pearson`s agreement test ($\chi^2$ test) with Yates correction or Fisher`s exact test (Ft) (for qualitative variables) were used to assess the statistical significance of differences between the studied groups. A p-value <0.05 was considered as statistically significant.

RESULTS

The studied groups were comparable by age, sex, and the profile of associated conditions.

According to the data from preoperative ultrasound, which determined the target vessels for endovascular intervention the groups had differences in the topography of the lesions of the BTK arteries and the amount of endovascular intervention (Table I).

In particular, all the patients from the main group presented with the calcification of the BTK arteries, compared with 63 % of the cases in the control group (Ft, p=0,039). The studied groups did not differ significantly by the number of affected BTK arteries (Figure 1).

Mortality among 24 patients in the control group was 8% (n=2) during the first 6 months. In 1 patient of the control group, within 3 months, a limb was amputated, on which an endovascular intervention was previously performed. The frequency of cardiovascular events during the year of observation after endovascular treatment in patients of the main group was 11% (n=1) and in patients of the control group - 8% (n=2) which includes ACS and Stroke. The frequency of preservation of the limb during 12 months in patients of the main group was 100% (n=9) and in patients of the comparison group - 96% (n=21).

Thrombosis or reocclusion of the reconstructed segments of the BTK arteries occurred in 4% (n=1) of control group patients in the first month, in 25% (n=6) - after 3 months, in 44% (n=10) - after 6 months and in 86% (n=18) - after 9 months after ET. After 12 months of ET, occlusion in the target artery was diagnosed in 95% of patients in the control group and only 1 in the main group (Ft, p=0.00001) (Figure 2).

At the same time, no statistically significant differences between the groups were found in the rate of repeated endovascular interventions during the year, which was performed in 1 patient of the main and 9 of the control groups (Ft, p=0.20351).

Healing of trophic ulcers of the foot in the first month after ET was observed in 78% (n=7) of patients of the main group and in 13% (n=3) of the control group (χ2 (1, n=33) = 10.2961; p=0.0013), and after 3 months – in 100% (n=9) and 83% (n=20) of patients in the respective groups (Figure 3).

Despite the fact that calcification of BTK arteries in 100% (n=9) of patients in the main group technical success rate was achieved in 100% of cases.

The complication was 11% (n=1) in the main group: the distal part of the rotawire has been damaged and separated

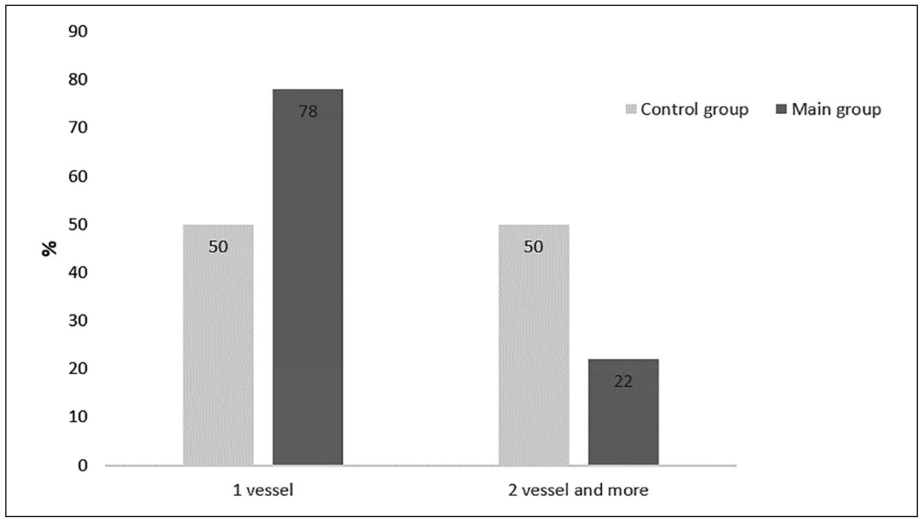

Fig. 1. The number of affected BTK arteries in the studied groups of patients (%) ($\chi 2$ (1, n=33) = 1.0868; p=0.297)

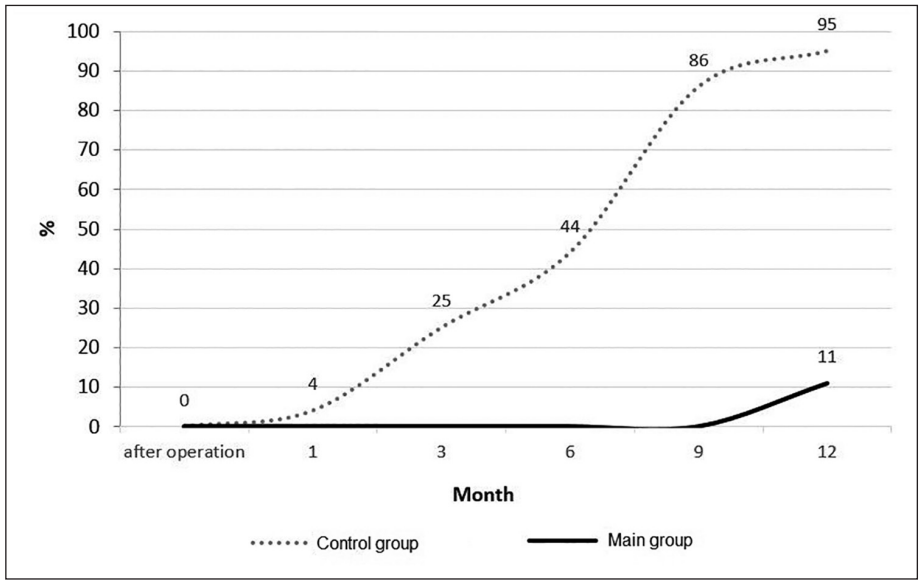

Fig. 2. The frequency (%) of impaired patency of the target artery in the studied groups of patients with BTK lesions (month). The total number of patients in the main group (n=9) was 100%. At 1 and 3 months of observation, the total number of patients in the control group (n=24) was taken as 100%. At six months, 23 patients were accepted as 100%, and at 9 and 12 months - 21 patients of the control group. (Ft, p=0.00001)

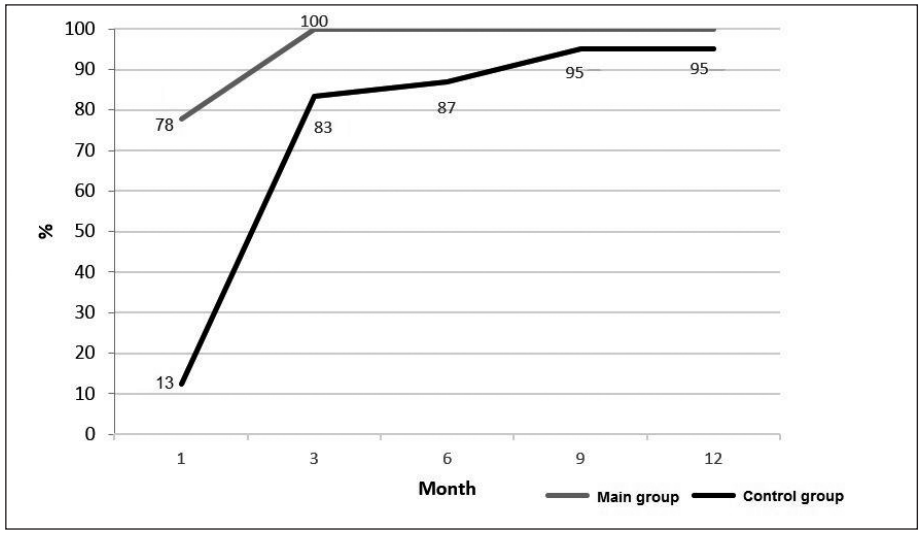

Fig. 3. The frequency (%) of foot trophic changes among patients of the study groups with BTK lesions (month). The total number of patients in the main group (n=9) was 100%. At 1 and 3 months of observation, the total number of patients in the control group (n=24) was taken as 100%. At six months, 23 patients were accepted as 100%, and at 9 and 12 months - 21 patients of the control group. At 3 months (p=0.0013).

from the main body of the wire. The damaged part of the wire was snared and successfully reviewed from the vessel without compromising distal lumen flow. In the control group complications were observed in 13% (n=3): 1 case – vessel perforation of the anterior tibial artery, treated by long-time balloon inflation; 2 cases – bleeding complication of puncher site from the common femoral artery, all treated by prolonged manual compression.

DISCUSSION

Transluminal atherectomy appears to be an effective, predictable, and safe method for removing occlusive atheromatous deposits from peripheral arteries [6]. While established treatments have a solid evidence base and guidelines for their use [7], the outcomes for atherectomy are less well understood [8]. However, unfortunately, there are few high-quality comparative data to guide the choice of a specific endovascular approach [9]. In addition, the PTRA requires a more significant number of observation objects to optimize the performance of the intervention.

Using Rotablation before POBA in calcified BTK lesions in most cases gives the opportunity to reach adequate inflation of the balloon in target arteries for maximum expansion of balloon surface with minimal additional vessel wall trauma [10].

In previous quite old studies where Rotablation used as a stand-alone procedure for ET of BTK lesions reported big complication amount 25-50% of all treated patients. Complications were quite typical for Rotablation atherectomy: arterial spasm, thrombosis, dissection, vessel perforation, distal embolism, and no-reflow [11,12]. That is why new studies and concepts have been performed over the last decades and aim investigators to find new treatment algorithms and methods to reduce complication rates. RESCUE-BTK trial showed that Rotablation was used as an adjunctive device for balloon angioplasty when POBA was unsuccessful. This concept gave a high technical success rate of 94.5% in BTK lesion treatment and much lower complication rates of 1.8% [13]. Our results were almost the same in the technical success rate of 100%, but the complication rate was higher in the main group – at 11%, in the control group – at 13%.

In the last few years, new debulking and plaque modification devices have been developed for endovascular treatment in BTK arteries, such as shockwave balloons, directional atherectomy, laser atheroablation, orbital atherectomy that can tell about the ongoing search for optimal treatment algorithm and optimal devices for BTK lesions.

CONCLUSIONS

Reconstructive endovascular interventions are an effective treatment method for patients with occlusive-stenotic lesions of BTK arteries because they facilitate the healing of trophic ulcers and allow preserving LE with a low risk of developing cardiovascular events. At the same time, using the PTRA technique improves the treatment results of patients with calcified lesions of the BTK arteries. The probability of target vessel occlusion increases when using POBA-mono compared to combining PTRA with POBA. In addition, healing trophic ulcers occur more actively in patients with atherosclerosis of BTK when PTRA is combined with POBA.

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ORCID and contributionship:
Yurii M. Hupalo: 0000-0002-9467-115X [A]
Sviatoslav Y. Denysov: 0000-0002-3214-8208 [A,B,D]
Anton M. Kutsyn: 0000-0001-9421-8032 [A,B,D]
Yelizaveta O. Lebedieva: 0000-0002-7582-8406 [A,B,D]
Mykhailo M. Grusha: 0000-0001-6003-7970 [C,E,F]

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The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Sviatoslav Y. Denysov
Clinical Hospital «Feofaniya» State Administrative Department
21 Zabolotnogo str., 03143 Kyiv, Ukraine
tel: +380507518542
e-mail: Denisovsu84@gmail.com

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ORIGINAL ARTICLE

ASSESSMENT OF THE EFFICIENCY OF PIEZOELECTRIC AND CLASSIC OSTEOTOMY WHEN PERFORMING SEPTORHINOPLASTY

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Oleksandr O. Karchynskyi, Tetiana O. Karchynska, Andriy V. Lupyr
KHARKIV NATIONAL MEDICAL UNIVERSITY, KHARKIV, UKRAINE

ABSTRACT

The aim: Comparison and analysis of the main intraoperative and postoperative results of piezoelectric and traditional osteotomy in septorhinoplasty.

Materials and methods: Examination and treatment were carried out in 40 patients who were divided into two groups. The first included patients who underwent septorhinoplasty using a traditional osteotomy - 20 people (control group). In the second group of patients, piezoelectric surgery was used for septorhinoplasty. This research group consisted of 20 people. All patients of both groups underwent only primary septorhinoplasty by closed and open methods. Piezoelectric surgery was performed using a Japanese VarioSurg3 NSK piezotome.

Results: The research was conducted on the first day after surgery, 3 days and a week after treatment. The following indicators were evaluated: intraoperative complications (mucosa damage), postoperative complications: (swelling of the eyelids,periorbital ecchymoses, nasal secretion activity, inflammatory reaction of the nasal cavity, postoperative pain)**.** Significantly fewer cases of mucosal damage were detected in the second study group compared to the first. And the severity of postoperative complications in the second group of patients who underwent septorhinoplasty with the help of a piezotome was statistically significantly ($p<0.05$) lower than in patients of the control group.

Conclusions: Piezoelectric surgery has a number of advantages over traditional osteotomy techniques, such as selectivity of impact on soft tissues, accuracy of bone destruction. Piezoelectric osteotomy during septorhinoplasty can reduce intra- and postoperative complications with statistical reliability.

KEY WORDS: piezotome, rhinoplasty, osteotomy

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INTRODUCTION

Piezoelectric surgery is a new method commonly used during osteotomy, which uses ultrasonic piezoelectric vibrations to reduce the severity of diseases [1]. In recent decades, piezosurgery has become quite popular for clinical applications in various surgical fields due to its ability to minimize tissue trauma and complications associated with it [2]. This method is considered a relatively new alternative to bone operations in craniofacial surgery. [3].

In rhinoplasty surgery, processing of the bone vault and side walls is most often performed with mechanical tools: saws, chisels, osteotomes, and rasps [4].

Electric rasps, burs and files have been designed specifically for use in rhinoplasty surgery to achieve good results. However, there are limitations such as increased operative time, risk of soft tissue damage, greater impact and difficulty in performing lateral osteotomies. Recently, surgeons have begun to use ultrasonic instruments with a piezoelectric drive for the treatment of bony vault and lateral osteotomies. [5,6].

Piezoelectric technology has been around for several years as a surgical tool for precise removal of soft tissues and bones [7]. Although several studies have compared the difference in postoperative complications between piezoelectric and conventional osteotomies, none of them has clearly concluded that one method is superior to the other. [8-14]. This issue remains poorly studied, therefore, an in-depth analysis and comparison of traditional techniques and piezoelectric osteotomy when performing septorhinoplasty is quite relevant.

THE AIM

Comparison and analysis of the main intraoperative and postoperative results of piezoelectric and traditional osteotomy in septorhinoplasty.

MATERIALS AND METHODS

Examination and treatment were carried out in 40 patients who were divided into two groups. The first included patients who underwent septorhinoplasty using a traditional osteotomy - 20 people (control group). In the second group of patients, piezoelectric surgery was used for septorhinoplasty. This research group consisted of 20 people.

The age of the patients ranged from 23 to 52 years. The gender and age distribution in both groups was approximately the same.

The study was conducted at the clinical base of the Department of Otorhinolaryngology of KhNMU in the Department of Head and Neck Surgery in the period 2020-2022.

All patients of both groups underwent only primary septorhinoplasty by closed and open methods.

Piezoelectric surgery was performed using a Japanese VarioSurg3 NSK piezotome.

Statistical data processing was performed on a personal computer using Microsoft Excel spreadsheets. The median (Me), 95% confidence interval was determined for each quantitative parameter. Student's t-test, Spearman's correlation test were used to compare numerical data. Differences at $p<0.05$ (95% significance level) were considered statistically significant. Assessment of study quality was based on a double-blind randomized controlled trial.

The trial was conducted in accordance with the ethical principles of the Declaration of Helsinki, Good Clinical Practice guidelines from the International Conference on Harmonisation, and any applicable countryspecific regulatory requirements. All patients provided written informed consent before study initiation. The study was approved by local ethics review boards at the participating sites.

RESULTS

When comparing the results of septorhinoplasty in both groups of patients, we studied and evaluated the following indicators:

- intraoperative complications (mucosa damage)
- postoperative complications:
- swelling of the eyelids
- periorbital ecchymoses
- nasal secretion activity
- inflammatory reaction of the nasal cavity
- postoperative pain

Symptoms were assessed on the first day after surgery, 3 days and one week after treatment.

The obtained results were compared with the results of other authors [8-14].

Postoperative pain was assessed using a pain scale (VAS - visual analogue scale). The remaining symptoms were evaluated separately using graduated scales.

The results of the study were as follows.

Intraoperative complications (mucosal damage) were assessed only three days after surgery by endoscopic examination. Significantly fewer cases of mucosal damage were detected in the second study group compared to the first. Student's t-test value: 11.15. The critical value of the Student's t-test = 2.024 at the level of significance $\alpha = 0.05$. Spearman's correlation coefficient (ρ) is 0.536. The connection between the investigated features is direct, the closeness (strength) of the connection according to the Chaddock scale is noticeable.

The critical value of Spearman's test = 0.447. ρ observation > ρ critical, the dependence of signs is statistically significant ($p<0.05$).

Swelling of the eyelids was noted in both groups, increasing on the first day after surgery. At the same time, in the control group, this indicator was significantly higher on the third day with statistical significance ($p<0.05$). Student's t-test value: 6.59. The critical value of the Student's t-test = 2.024 at the level of significance $\alpha = 0.05$. By the seventh day, the difference in signs did not acquire a statistically significant difference ($p>0.05$) and had approximately the same distribution.

The next sign studied is periorbital ecchymoses. In the first group of patients, this indicator was higher than in the second with statistical significance throughout the study period (1, 3, 7 days) ($p<0.05$).

The distribution of the indicator of the activity of the nasal secretion of the two groups was as follows: during the first day, the nasal secretion in the patients of the control group was higher than in the patients of the second group, but the indicator did not reach a statistically significant difference ($p>0.05$), on the third day, the severity of the symptom was significantly decreased in the second study group, compared to the first, and by the seventh day of observation, the level of secretion was approximately the same.

The inflammatory reaction of the nasal cavity in the second group was less pronounced compared to the first group with statistical significance ($p<0.05$) on the first and third day of observation. By the seventh day, the severity of this symptom in both groups significantly decreased and had no statistically significant difference ($p>0.05$).

Postoperative pain was assessed by patients using a visual analog scale (Fig. 1)

At the same time, in the first group, complaints about the severity of pain were significantly higher than in the second group, which underwent septorhinoplasty using a piezotome with statistical significance ($p<0.05$) on the first,

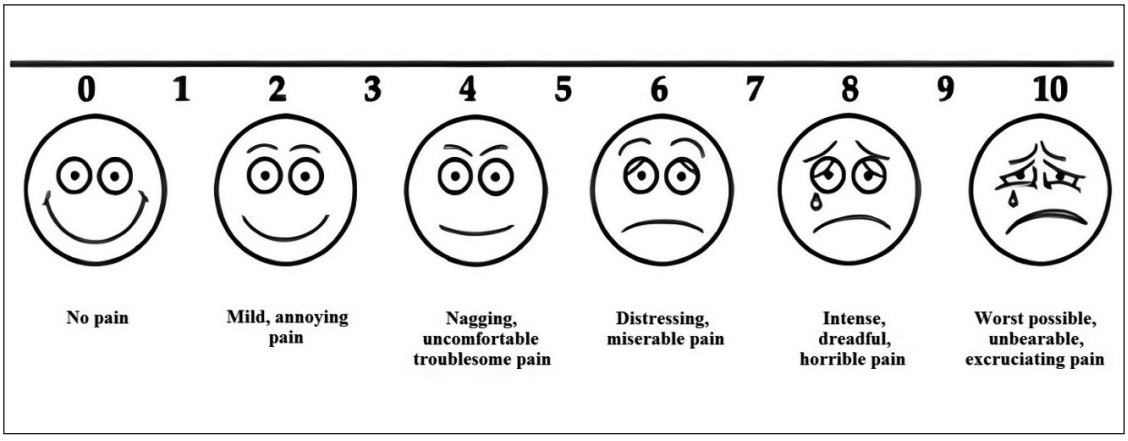

Fig. 1. Visual-analog pain assessment scale

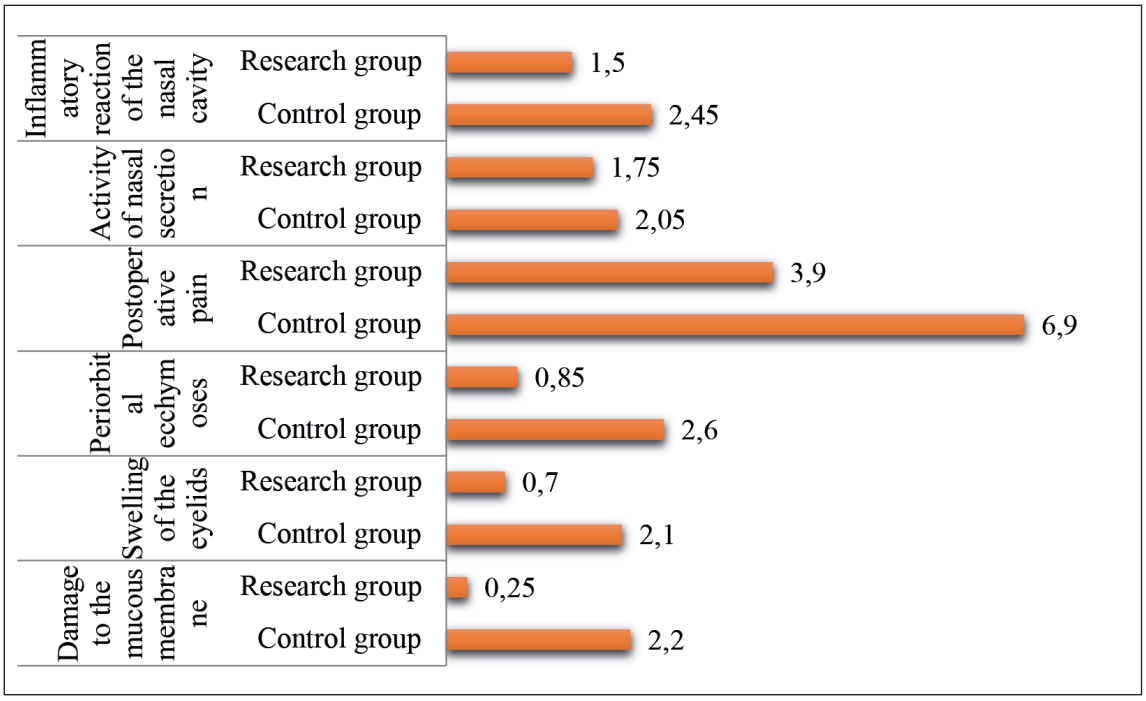

Fig. 2. Distribution of indicators between two groups at the third day

third and seventh days of observation. Student's t-test value: 5.26. The critical value of the Student's t-test = 2.024 at the level of significance α = 0.05 (the first day of observation).

In general, when evaluating all symptoms, we obtained the following distribution of indicators on the third day of observation between the control group, in which septorhinoplasty was performed using the traditional method, and the second group, in which piezoelectric osteotomy was used (Fig. 2)

DISCUSSION

Compared to traditional head and neck surgery, piezoelectric surgery is a relatively new method and requires a qualitative analysis of its effectiveness. Meller C. [7] studied the advantages of piezoelectric devices compared to traditional instruments and came to the conclusion of the advantages of the former in terms of less "wear and tear", better selectivity in relation to tissues and technical differences such as ease of use, short learning curve, better visibility.

The conducted research revealed several advantages of this method. These include the ability to perform surgery on bony structures in a more controlled manner, with fewer comminuted and radiating accidental bone fractures, especially when working on thin bony structures. At the same time, the possibility of avoiding damage to adjacent soft tissues increases, and the risk of osteonecrosis and damage to the periosteum and cartilage located under bone structures decreases. In addition, reducing the time of surgical intervention gives the ability to increase control over nasal bleeding, its speed, and power, and the congruent alignment of new fragments of the bones of the pyramid makes it possible to form a stable structure of the external nose, which in the following makes it possible to obtain the expected result.

Previous studies have assessed the severity of early postoperative symptoms, such as eyelid swelling and ecchymosis [8-14], postoperative pain [14], and mucosal damage [8,11]. At the same time, the results obtained using the ultrasound technique were significantly lower compared to traditional osteotomy, which does not contradict the data obtained by us. The assessment of the effectiveness of the piezotome during septorhinoplasty showed a lower incidence of intra- and postoperative complications, such as swelling of the eyelids, periorbital ecchymoses, nasal discharge, inflammatory reaction of the nasal cavity, postoperative pain, as well as intraoperative damage to the mucous membrane, which is positively reflected in the postoperative recovery and overall well-being and patient satisfaction.

CONCLUSIONS

1. Piezoelectric surgery has a number of advantages over traditional osteotomy techniques, such as selectivity of impact on soft tissues, accuracy of bone destruction.
2. Piezoelectric osteotomy during septorhinoplasty can reduce intra- and postoperative complications with statistical reliability.

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ORCID and contributionship:
Oleksandr O. Karchynskyi: 0000-0001-5356-9987 [A, B, D, F]
Tatiana O. Karchynska: 0000-0002-0053-207X [C, D]
Andriy V. Lupyr: 0000-0002-9896-163X [E]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Oleksandr O. Karchynskyi
Kharkiv National Medical University
4 Nauky Ave, 61022 Kharkiv, Ukraine
tel: +380950068809
e-mail: oo.karchynskyi@knmu.edu.ua

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ORIGINAL ARTICLE

ESTIMATION OF PREDICTORS AND DEVELOPMENT OF PROGNOSTIC MODEL FOR COMORBID COURSE OF DIABETES MELLITUS AND ISCHEMIC HEART DISEASE

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Marharyta V. Koshkina, Volodymyr D. Babadzhan, Olga I. Kadykova
KHARKIV NATIONAL MEDICAL UNIVERSITY, KHARKIV, UKRAINE

ABSTRACT

The aim: To determine predictors and develop the model of prognosis of comorbidity of ischemic heart disease and type 2 diabetes mellitus.

Materials and methods: 126 patients were involved in the study and divided into three groups. Main group involved 70 patients with comorbid T2DM and IHD; comparison group included 36 IHD-only patients; 20 patients were included into control group.

Results: Predictors of comorbid T2DM and IHD included titin (OR = 0.001 [95.0 % CI 0.001–0.105], p = 0.021); I and II grade hypertension (respectively OR = 28.993 [95.0 % CI 1.595–526.940], p = 0.023 and OR = 19.050 [95.0 % CI 1.078–336.620], p = 0.044); left ventricle hypertrophy (OR = 3.169 [95.0 % CI 1.103–3.108], p = 0.032); very low density cholesterol level (OR = 49.032 [95.0 % CI 4.155–578.644], p = 0.022); and stenocardia symptoms in significant physical load (OR = 6.199 [95.0 % CI 1.129–34.039], p = 0.036).

Conclusions: developed model can be used in prediction of comorbid course of T2DM in patients with IHD for early diagnosis of cardiovascular complications in such patients.

KEY WORDS: prediction, comorbidity, type 2 diabetes mellitus, ischemic heart disease

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INTRODUCTION

According to International Diabetes Federation, worldwide prevalence of diabetes is 415 million cases, of which 91.0 % is Type 2 diabetes mellitus (T2DM) [1]. By 2040 it is expected that prevalence of T2DM will rise to 642 million cases [1,2].

Among all cases of T2DM more than 50 million cases are in Europe [3]. In recent decades incidence of the disease increased almost three times and will additionally double in next decades [4].

Frequently T2DM triggers development of various cardiovascular diseases [5]. The most frequent of them is chronic insufficiency of coronary blood stream (leads to hypoxia and violations of contractility and relaxation of myocardial) [6]. Moreover T2DM the development of the diastolic dysfunction (up to 75% of cases), which relates to excessive weight, violation of glucose metabolism and development of ischemic heart disease (IHD) [7], which burdens the course of T2DM [8].

According to data, T2DM decreases live duration on more than 10 years [9], mostly due to cardiovascular diseases which are the common causes of morbidity and mortality in T2DM [10]. To date, comorbidity, accompanied with aging, and deterioration of overall health, is significant medical burden [10-21]. According to meta-analysis [1] weighted mortality rates in T2DM 9.9% [95% CI 8.6–11.3%], and comparison causes of death for IHD, stroke or cerebrovascular diseases (respectively 29.7 % [95.0% CI 25.1–34.4 %] and 11.0 % [95.0 % CI: 8.8–13.3 %]).

Data show that T2DM is the comparison risk factor of IHD [11]. According to the study in China 52.9% of hospitalized patients with IHD had diabetes mellitus, and 25.1% of patients with diabetes had IHD [10].

To date significant researchers are trying to study various clinical, instrumental, and epidemiological characteristics of patients with comorbid course of T2DM and IHD in order to provide early diagnosis and treatment for prophylaxis of possible complications. Among biochemical markers, one of the most promising is assessment of titin levels in blood serum, which was shown to have good prognostic possibility.

Titin is large sarcomere protein and is responsible for strength of cardiomyocytes. According to database (Universal Protein Resource, 2017), titin relates to various cardiovascular processes: contraction of heart muscle, development of heart muscle, hemostasis, heart hypertrophy, production of heart myofibrils etc. [12]. Several researchers found that violations of regulation titin are closely connected with different cardiovascular diseases (heart failure (HF), IHD, hypertension etc.) [13]. It was also found in other researchers [12], that titin has high prognostic value, as activity of myocardial exone N2B (cardiac titin) patients with cardiovascular diseases could serve as myocardium damage marker [14].

Thus, assessment of titin levels in blood serum of patients with T2DM and ischaemic heart disease and finding of associations with additional clinical and anamnestic parameters is actual task of modern medicine.

Table I. Frequency analysis of comparison and co-existent pathology (no., %)

Index		Control (n = 20)	IHD (n = 36)	IHD+T2DM (n = 70)	p_1	p_2
HF stage	I	0 (0.0)	14 (38.9)	20 (28.6)	< 0.001	0.503
	II A	0 (0.0)	20 (55.6)	47 (67.1)		
HTN stage	No	20 (100.0)	6 (16.7)	1 (1.4)	< 0.001	0.011
	2	0 (0.0)	21 (58.3)	47 (67.1)		
	3	0 (0.0)	9 (25.0)	22 (31.4)		
Functional classes						
Significant load (I functional grade)		0 (0.0)	29 (80.6)	67 (95.7)	< 0.001	0.011
Walking with regular speed > 500 m (II functional grade)		0 (0.0)	19 (52.8)	40 (57.1)	< 0.001	0.668
Walking with regular speed < 500 m (III functional grade)		0 (0.0)	11 (30.6)	14 (20.0)	0.023	0.225
Any physical load or rest (IV functional grade)		0 (0.0)	4 (11.1)	3 (4.3)	0.173	0.180

Note: p_1 – significance of differences between all groups; p_2 – significance of differences between main and comparison groups

Table II. Lipid metabolism and titin levels in studied patients, M ± SD

Index	Control (n = 20)	IHD (n = 36)	IHD+T2DM (n = 70)	p_{1-2}	p_{1-3}	p_{2-3}
TC, mmol/L	4.50 ± 0.32	4.93 ± 1.10	5.21 ± 1.51	0.087	0.083	0.443
HDL, mmol/L	1.42 ± 0.16	1.27 ± 0.30	1.34 ± 0.25	< 0.001	0.039	0.045
TG, mmol/L	0.80 ± 0.11	1.41 ± 0.47	1.88 ± 0.81	< 0.001	< 0.001	0.005
LDL, mmol/L	2.89 ±0.27	2.80 ± 1.26	2.90 ± 1.40	0.784	0.763	0.889
VLDL, mmol/L	0.40 ± 0.01	0.65 ± 0.19	0.91 ± 0.38	< 0.001	< 0.001	< 0.001
AC	2.53 ± 0.17	2.97 ± 1.06	2.96 ± 1.35	0.266	0.337	0.684
Titin, ng/ml	0.37 ± 0.05	0.24 ± 0.05	0.22 ± 0.04	< 0.001	< 0.001	0.05

Note: p_{1-2} – significance of differences between control group and isolated IHD; p_{1-3} – significance of differences between control group and common orbit IHD+T2DM; p_{2-3} – significance of differences of differences between isolated IHD and comorbid IHD+T2DM.

THE AIM

The aim was to investigate predictors and develop the modal of prognosis of comorbidity in IHD and T2DM.

MATERIALS AND METHODS

The study included 126 patients. Main group included 70 patients with comorbid IHD and T2DM (28 (40.0%) of men and 42 (60.0%) of women); comparison group included 36 patients with isolated IHD (21 (58.3%) of men and 15 (41.7%) of women). Control group included 20 individuals (11 (55.0%) of men and 9 (45.0%) of women.

The ethical approval was obtained from Bioethics Committee of the Kharkiv National Medical University. All the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008, as well as the national law.

RESULTS

Distribution of patients by heart failure stage showed non-significant (p=0.503) prevail of heart failure of I functional class in comparison compared to main group (respectively 38.9% and 28.6%). In comorbid IHD+T2DM group there were more patients with heart failure of IIA functional class then in comparison group (respectively 67.1% and 55.6%) — table I.

Regarding the presents and stage of hypertension (HTN) the results show to the next data. Significantly (p=0.011) comparison group compared to main group had more patients with no hypertension (16.7% and 1.4%). Hypertension of II and III grade was observed frequently in IHD+T2DM group than in IHD-only group (respectively 67.1% vs. 58.3% and 31.4% vs. 25.0%) — table I.

Analysis of limitations of physical activity showed that patients with comorbid T2DM developed symptoms under significant load more frequently than patients with IHD+T2DM: respectively 95.7 % and 80.6 % (p = 0.011). Symptoms development during walking in regular speed > 500 m was equal in both groups (p = 0.668) and during walking with regular speed < 500 m was also similar (p = 0.225). 11.1 % of patients of comparison group and 4.3 % of patients of main group (p = 0.180) developed cardiac symptoms during any physical load or at rest — table I.

Total cholesterol (TC) levels were lower in control group (4.5±0.32 mmol/L) than in comparison (4.93±1.10

Table III. Associations of clinical-anamnestic and clinical-instrumental parameters with presence of T2DM (univariate analysis)

Index	OR	95.0 % CI	p
Clinical and anamnesis parameters			
Gender (female)	1.556	0.586–4.133	0.375
Age, years	1.018	0.961–1.079	0.543
No HF	Reference		0.708
I grade HF	0.817	0.105–6.322	0.846
II grade HF	1.279	0.156–10.456	0.819
No hypertension	Reference		0.199
I stage hypertension	8.088	0.755–86.640	0.084
II stage hypertension	8.889	0.770–102.671	0.080
Obesity	1.665	0.301–9.093	0.562
Current smoker	0.603	0.141–2.577	0.495
Duration of IHD	1.355	0.635–2.888	0.432
Heart morphology			
Left ventricle hypertrophy	2.661	1.113–6.359	0.028
No cardiosclerosis	Reference		0.609
Anterior wall cardiosclerosis	1.375	0.225-8.411	0.730
Posterior wall cardiosclerosis	0.378	0.146–2.074	0.378
Lipid metabolisms parameters			
TC, mmol/L	0.407	0.162–1.023	0.056
HDL, mmol/L	12.109	1.450–101.120	0.021
TG, mmol/L	1.156	0.390–3.426	0.793
LDL, mmol/L	1.976	0.846–4.613	0.115
VLDL, mmol/L	112.065	4.509–2785.087	0.004
Stenocardia functional class			
Significant load (I functional grade)	6.300	1.358–29.235	0.019
Walking with regular speed > 500 m (II functional grade)	1.204	0.411–3.525	0.735
Walking with regular speed < 500 m (III functional grade)	0.484	0.141–1.663	0.249
Any physical load or rest (IV functional grade)	0.477	0.081–2.807	0.413
Titin levels			
Titin, ng/ml	0.001	0.001–0.138	0.018

mmol/l) and main group (5.21±1.51 mmol/L). However, high density lipoproteins (HDL) in control group were significantly lower than in comparison ($p<0.001$) and main ($p = 0.039$) group and patients with comorbid IHD+T2DM had significantly higher levels of HDL ($p = 0.045$) than in isolated IHD. The lowest level of triglycerides (TG) was found in control group (0.80±0.11 mmol/L), which was significantly ($p<0.001$) higher than in comparison and main groups. Noteworthy that low density lipoproteins level did not differ significantly between all study groups. On the other hand, very low-density lipoproteins (VLDL) were significantly lower in control group ($p<0.001$) than in comparison and main group. Despite being higher atherogenicity coefficient (AC) in control group, parameter did not differ significantly between groups — table II.

Titin levels were the highest in control and significantly ($p<0.001$) prevailed over comparison (0.24±0.05 ng/ml) and main group (0.22±0.004 ng/ml) — table II.

Non-significant associations were found with age and gender (respectively OR = 1.556 [95.0 % CI 0.586–0.375], $p = 0.375$ and OR = 1.018 [95.0 % CI 0.961–1.079], $p = 0.543$); of I grade HF and II grade HF (respectively OR = 0.817 [95.0 % CI 0.105–6.322], $p = 0.846$ and OR = 1.279 [95.0 % CI 0.156–10.456], $p = 0.819$) with presence of T2DM. Moreover, presence of obesity, current smoking and IHD duration were also associated with T2DM non-significantly in univariate analysis (respectively OR = 1.665 [95.0 % CI 0.301–9.093], $p = 0.562$, OR = 0.603 [95.0 % CI 0.141–2.577], $p = 0.495$ and OR = 1.355 [95.0 % CI 0.635–2.888], $p = 0.432$) — table III.

Trend to significant association was found with I and II grade hypertension: OR = 8.088 [95.0 % CI 0.755–86.650],

Table IV. Association of clinical-laboratory and clinical-instrumental parameters with comorbidity of IHD and T2DM (multivariate backward Wald analysis)

Predictor	B-coefficient	OR	95.0 % CI	p
Titin, ng/ml	-14.843	0.001	0.001–0.105	0.021
No hypertension		Reference		0.074
I grade hypertension	3.367	28.993	1.595–526.940	0.023
II grade hypertension	2.947	19.050	1.078–336.620	0.044
Left ventricle hypertrophy	1.153	3.169	1.103–3.108	0.032
VLDL	3.892	49.032	4.155–578.644	0.002
Stenocardia under significant load (I functional grade)	1.824	6.199	1.129–34.039	0.036
Constant	-2.007	0.134		

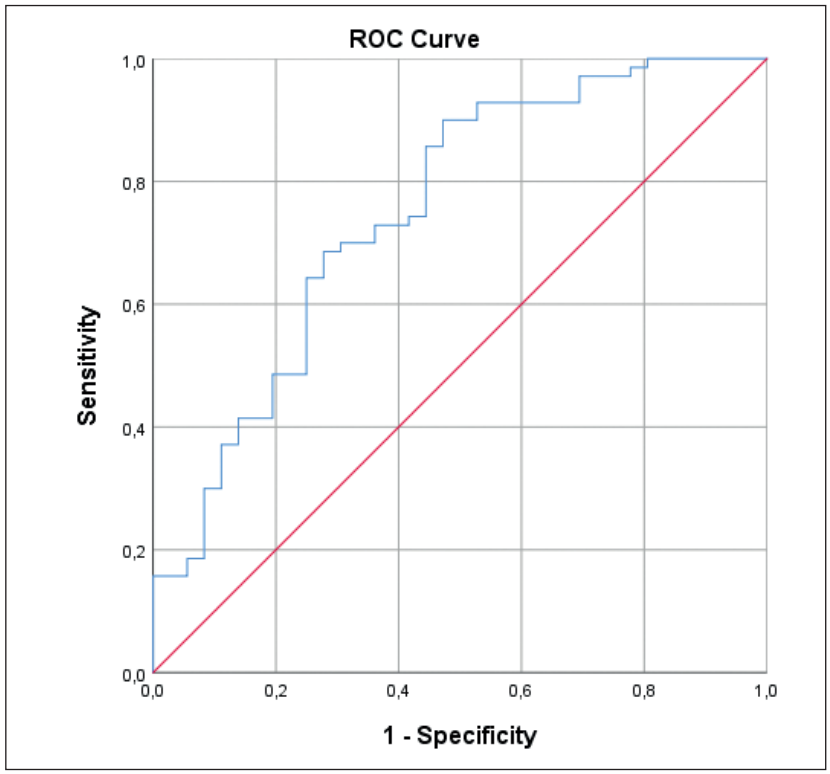

Fig. 1. ROC-analysis of developed prognostic model (AUC = 0.751 [95.0 % CI 0.649–0.852], p < 0.001).

p = 0.084 and OR = 8.889 [95.0 % CI 0.770–102.671] (p = 0.080) — table III.

Among morphological parameters of heart, it was found that left ventricle hypertrophy was significantly (p = 0.028) associated with comorbid T2DM (OR = 2.661 [95.0 % CI 1.113–6.359]). Cardiosclerosis of different localization was associated with T2DM non-significantly: anterior wall — OR = 1.375 [95.0 % CI 0.225–8.411] (p = 0.730) and posterior wall –– OR = 0.378 [95.0 % CI 0.146–2.074] (p = 0.378) –– table III.

Noteworthy, that total cholesterol was inversely associated with comorbid T2DM (OR = 0.407 [95.0 % CI 0.162–1.023], p = 0.056) and direct association was found with HDL and VLDL: respectively OR = 12.109 [95.0 % CI 1.450–101.120] (p = 0.021) and OR = 112.065 [95.0 % CI 4.509–2785.078] (p = 0.004). Non-significant associations were found with TG and LDL (respectively OR = 1.156 [95.0 % CI 0.390–3.426], p = 0.793 and OR = 1.976 [95.0 % CI 0.846–4.613], p = 0.115) –– table III.

Only limitations under significant load were significantly associated with T2DM: OR = 6.300 [95.0 % CI 1.358–29.235], p = 0.019, other parameters showed non-significant associations. Titin showed reverse association with T2DM comorbidity: OR = 0.001 [95.0 % CI 0.001–0.138], p = 0.018 –– table III.

Multivariate analysis (table IV) revealed that significant predictors of comorbid course of IHD and T2DM are titin levels (OR = 0.001 [95.0 % CI 0.001–0.105], p = 0.021); I and II grade hypertension (respectively OR = 28.993 [95.0 % CI 1.595–526.940], p = 0.023 and OR = 19.050 [95.0 % CI 1.078–336.620], p = 0.044); left ventricle hypertrophy (OR = 3.169 [95.0 % CI 1.103–3.108], p = 0.032); VLDL (OR = 49.032 [95.0 % CI 4.155–578.644], p = 0.022) and presence of stenocardia under significant load (OR = 6.199 [95.0 % CI 1.129–34.039], p = 0.036).

Next step was to develop and test prognostic model for prediction of comorbid IHD+T2DM:

IHD+T2DM = -2.007 – (14.843 × titin, ng/ml) + (3.367, if I grade HNT) + (2.947, if II grade HTN) + (1.153, if has

LV hypertrophy) + (3.892 × VLDL, mmol/L) + (1.824, if has stenocardia under significant load)

Classification parameters of developed model were estimated using ROC-analysis (fig.). Cut-off point is = -2.0312, with sensitivity of 85.7 % and specificity of 55.6 %.

DISCUSSION

Significant associations of titin levels were determined (OR = 0.001 [95.0% CI 0.001–0.105] with the comorbidity of T2DM and IHD. It should be noted that Rahim M. et al. [12] established a high sensitivity of the heart-specific N2B fragment of titin to cardiomyocyte damage in myocardial infarction (MI) with comorbidity of T2DM compared to controls (patients with T2DM without MI): patients with MI STEMI and T2DM –– OR = 0.60 [95.0% CI 0.38–0.83)], p < 0.0001 and with MI NSTEMI and T2DM — OR = 0.46 [95.0% CI 0.22–0.70)], p < 0.0001.

Another study (2781 patients with atrial fibrillation and 4959 patients of the control group) [15] also determined the significant sensitivity of titin levels in the blood serum in CVD and found a statistically significant relationship between loss-of-function variants of the gene that encodes the sarcomere titin protein (TTN) and atrial fibrillation (OR = 1.76 [95.0% CI 1.04–2.97].

Also, high sensitivity of titin levels to cardiomyocyte damage was recorded by Kötter S. et al. [16], who established a significant decrease in the relative phosphorylation of N2B-taitin in the tissues of patients with heart failure with dilated and hypertrophic cardiomyopathy: respectively by 35±5% and by 38±6% –– under the condition of using Ser4010 polyclonal antibodies; respectively by 27±3% and 27±5% –– when using Ser4099 and by 23±7% and 26±8% –– when using Ser4185. These results indicated an excessive compensatory activation of the β-adrenergic system, which provokes an increase in the passive stiffness of the myocardium during the progression of HF.

Moreover, we obtained significant associations of stage I and II hypertension (respectively OR = 28.993 [95.0% CI 1.595–526.940], p = 0.023 and OR = 19.050 [95.0% CI 1.078–336.620], p = 0.044) with comorbidity of T2DM and IHD, corresponding to the results obtained by Sun C. D. et al. [17], who found a high association of genetically determined T2DM with the risk of developing hypertension (OR = 1.07 [95.0% CI 1.04–1.10], p = 0.34) in patients with coronary artery disease.

Moreover, significant associations were found within lipid metabolism parameters. Thus, increased VLDL was directly associated with T2DM (OR = 49.032 [95.0 % CI 4.155–578.644], p = 0.022). Patsouras A. et al. [18], who ascertained the marker properties of LDL cholesterol in predicting the development of coronary artery disease in patients with T2DM. It was reliably determined that patients with T2DM are characterized by a more severe course of IHD and have a significantly higher risk of developing cardiovascular complications (relative risk = 3.197 [95.0% CI 1.171–8.730], p = 0.023); and the risks of IHD in patients with T2DM significantly increased with increasing LDL levels (OR = 4.97 [95.0% CI 1.96–12.57], p = 0.001).

Other studies [19] also proved the interdependence of LDL levels and increased risks of IHD and T2DM. It was determined that a genetically determined increase in LDL levels by 38 mg/ml increased the risk of IHD (OR = 1.68 [95.0% CI 1.51–1.87) and T2DM (OR = 0.79 [95.0% CI 0.71–0.88].

CONCLUSIONS

According to the obtained results, the comorbid course of IHD and T2DM is associated with a significant decrease in titin levels, which pathogenetically can be an early predictor of abnormalities in the morphology, contractile and dilatation function of the heart, and of the development of HF. The presence of concomitant T2DM in patients with coronary heart disease is also associated with hypertension of both stage I and II, which confirms the involvement of T2DM in the pathogenesis of increased systemic blood pressure and deterioration of the course this disease. In such patients, LV hypertrophy, as one of the morphological manifestations of both hypertension and HF, and increased concentrations of VLDL cholesterol are more often determined. and the occurrence of angina symptoms during significant physical exertion (OR = 6.2, p = 0.036). The proposed prognostic model has high classification qualities and can be used in predicting the comorbid addition of T2DM in patients with CAD with the aim of early diagnosis of cardiovascular complications of this comorbidity.

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ORCID and contributionship:
Marharyta V. Koshkina: 0000-0003-3392-9599 [A-D]
Volodymyr D. Babadzhan: 0000-0002-3939-4209 [E, F]
Olga I. Kadykova: 0000-0002-0108-0597 [A, E, F]

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CORRESPONDING AUTHOR
Marharyta V. Koshkina
Kharkiv National Medical University
4 Nauki ave, 61000 Kharkiv, Ukraine
tel: +380501854123
e-mail: maiorovarita2393@gmail.com

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ORIGINAL ARTICLE

RESULTS OF RESEARCH OF PERSONAL HYGIENE PRODUCTS FOR SUITABILITY FOR SPECIAL PROCESSING IN ZONES OF CHEMICAL, RADIOACTIVE CONTAMINATION AND IN COMBAT CONDITIONS

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Natalia V. Kurdil[1], Olga O. Khudaikulova[1], Borys I. Palamar[2], Oleksandr V. Yushchenko[3], Lyudmila A. Ustinova[4], Artur O. Zulfigarov[5], Yevhen V. Gavrylko[5]

[1]L.I. MEDVED'S RESEARCH CENTER OF PREVENTIVE TOXICOLOGY, FOOD AND CHEMICAL SAFETY OF THE MINISTRY OF HEALTH OF UKRAINE, KYIV, UKRAINE
[2]BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE
[3]SARAYA CO., LTD, HIGASHISUMIYOSHI-KU, OSAKA, JAPAN
[4]UKRAINIAN MILITARY MEDICAL ACADEMY, KYIV, UKRAINE
[5]IHOR SIKORSKY KYIV POLYTECHNIC INSTITUTE, KYIV, UKRAINE

ABSTRACT

The aim: Research of personal hygiene products with detoxification properties by evaluating their formulation composition, emulsifying and complexing ability to heavy metal ions and radionuclides.

Materials and methods: The complex-forming ability of raw materials with heavy metal ions was determined in vitro, the content of heavy metals was determined by the method of atomic emission spectrometry with inductively coupled plasma (BS EN 13805:2014); determined the content of ^{137}Cs, ^{232}Th, ^{40}K, ^{226}Ra, ^{90}Sr in washings from the surface of the skin of hands treated with personal hygiene products. The means were tested for compliance with the standard on scintillation spectrometers of gamma radiation energy «SEG-001» «AKP-S» and beta radiation (SEB-01-70); methods used: MI 12-04-099 and MI 12-05-099.

Results: A high complexing ability of the pectin-containing «Liana» shampoo was found in relation to heavy metal ions ($Co^{2}+$, $Cu^{2}+$, $Zn^{2}+$, $Cd^{2}+$, $Pb^{2}+$), as well as in their combined presence. It was established that the effectiveness of removing fatty impurities from the surface of the skin of the «Liana» product was 10.1 times higher than that of liquid soap ($p<0.001$). A high level of deactivating, degassing and antibacterialproperties of the personal care products «Bastion» and «Bastion-M» was revealed.

Conclusions: Today, there is significant potential in the creation of formulations for special (sanitary) skin and hair surface treatment, containing natural complexing agents as detoxicants, and can be used in special professional activities associated with the risk of exposure to CBRN factors.

KEY WORDS: special treatment, sanitary treatment, heavy metals, radionuclides

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INTRODUCTION

In the conditions of increasing endogenous and exogenous pollution of the environment, which is a consequence of the Chornobyl disaster, hostilities, inundations caused by floods and other disasters, special processing of the terrain, defense structures, weapons, equipment, uniforms, shoes, personal protective equipment become important, medical and sanitary property, personnel and places of temporary residence and mass stay of the population[1-4].A component of special processing is degassing, detoxification and disinfection. Special processing consists in removing radioactive substances, chemical and biological agents from the uniforms and skin of personnel of military units [5].An element of special processing is sanitary processing.

The analysis of scientific research in the field of special treatment products has shown that promising products for the sanitary treatment of skin and hair are deactivating shampoos for hair and body and personal hygiene with deactivating, degassing and antibacterial action, which, thanks to their balanced composition, are detoxifiers for external use and have deactivating, degassing and antibacterial properties and can be used as intended in hazardous conditions in the CBRN.

THE AIM

Study of suitability for use in CBRN contamination zones and combat conditions of personal hygiene products with deactivating, degassing, detoxification properties by evaluating their formulation composition, emulsifying and complexing ability in relation to heavy metal ions, and ability to remove radionuclides from skin and hair surfaces.

MATERIALS AND METHODS

The complex-forming ability of pectin (raw material), shampoo and hygiene products (Liana, Bastion, Bastion-M) in relation to heavy metal ions was found in vitro. The effectiveness

Table I. Complexing ability of pectin solution in relation to heavy metal ions

Object of study	Complexing ability of pectin, mg met/g pectin				
	Co^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}
Apple pectin	260	203	200	195	254

*The presence of globules is observed.

Table II. Complexing ability of pectin-containing shampoo «Liana» in relation to heavy metal ions in their combined presence

Object of study	Complexing ability, %				
	Co^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}
Pectin-containing deactivating shampoo «Liana»	25	20	18	15	22

*The presence of globules was observed. The presence of sediment in the form of globules indicates pectin/metal complexation.

Table III. Complexing ability of shampoo – control No. 1 in relation to heavy metal ions in their combined presence

Object of study	Complexing ability, %				
	Co^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}
Shampoo – control *	0,9	1,1	0,2	0,02	4,2

* Absence of globules was observed, there is a small sediment.

Table IV. Complexing ability of shampoo – control No. 2 in relation to heavy metal ions in their combined presence

Object of study	Complexing ability, %				
	Co^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}
Shampoo – control *	0,8	0,2	0,02	0,01	0,5

* Absence of globules was observed, there is a small sediment.

of removing heavy metal ions from the surface of the skin was determined in washings from the hands of employees of JSC «State Joint-Stock Company «Automobile Roads of Ukraine» of the subsidiary «KhmelnytskyiOblavtodor» branch of «Rusanivnisky Special Quarry». Determination of the content of heavy metals was carried out by the method of atomic emission spectrometry with inductively coupled plasma (sample preparation according to BS EN 13805:2014) [6]. Washes from the surface of the skin of hands treated with hygiene products were examined for the content of ^{137}Cs, ^{232}Th, ^{40}K, ^{226}Ra, ^{90}Sr (Basic sanitary rules for ensuring radiation safety of Ukraine, 2005, DSP 6.177-2005-09-02.). Determination of radionuclide content was performed on scintillation energy spectrometers of gamma radiation (SEG-001 «AKP-S») and beta radiation (SEB-01-70) [7, 8]. Measurements were carried out according to the MI 12-04-099 method using the SEG-002 «AKP-P» semiconductor type gamma radiation energy spectrophotometer and the MI 12-05-099 method using the SEB-01 scintillation type beta radiation energy spectrophotometer. The relative measurement error ranges from ±10% to ±50% at $p < 0.05$. Pectin was used (brand SWEJ-1 manufactured by PEKTOWIN Sp.zo.o.), obtained from apple pomace by acid-thermal hydrolysis of raw materials.

RESULTS

It is known that products containing pectins are effective detoxification, as studies have shown. Pectins, due to their gel- and structure-forming properties and the ability to bind heavy metal ions, have shown themselves well as hygienic preventive means for removing heavy metal salts and radionuclides from skin and hair surfaces. Salts of heavy metals, primarily lead, zinc and oil, are quite widely available in the metalworking, glass, textile, porcelain and earthenware and other industries, as well as as a result of hostilities, where there is catastrophic damage to the environment by factors of various origins, harmful effects on which. human health largely depends on solubility in water and fats, duration and ways of entering the body. It is indisputable that the creation of external detoxification agents, which creates natural complexing agents of plant origin, is an actual direction in the field of cosmetics, food industry, and medicine and should have a scientific basis.

As part of the research work, some characteristics of the deactivating shampoo for hair and body «Liana» were studied. «Liana» was manufactured in accordance with technical requirements: U 24.5-2859920992-001:2006 «Shampoos for hair and body with deactivating properties. Technical conditions» for use as a personal hygiene product for workers in heavy metallurgy, nuclear power plants, mining and chemical industry; everyday life (including for use in emergency situations). Manufacturer: Ukrainian-Bulgarian LLC «Pirana» (Kharkov), by order and according to the technology of IE"Shokur A.A." and packaged by «BARA» LLC.

On the basis of the L.I. Medved's Research center of preventive toxicology, food and chemical safety of the Ministry of Health of Ukraine studies were conducted on the complexing

Table V. Test results of deactivating shampoo for hair and body «Liana» according to physical and chemical indicators

Indicator name	Requirements for documentation	Actual value	The unit of measurement	Regulatory requirements for research methods	The relative error of the tests
Kinematic viscosity at a temperature of 20^{0}C	-	698	мм^2	State Standard GOST 33	0,35 %**

**The permissible relative difference between two consecutive determinations should not exceed the given value.

Table VI. Results of studies of model environments No.1 (combined sample)

Indicator	Actual value, mg/dm3	Regulatory requirements for research methods
Lead	0,602	State Standard GOST 30178-96
Cadmium	not revealed	
Copper	2,806	

Table VII. Results of studies of model environments No. 2 (combined sample)

Indicator	Actual value, mg/dm3	Regulatory requirements for research methods
Lead	0,010	State Standard GOST 30178-96
Cadmium	not revealed	
Copper	0,050	

ability of apple pectin, pectin-containing shampoo «Liana», control shampoos No.1 and No.2 (which contained all components of the pectin-containing deactivating shampoo formulation, except for pectin), with heavy metal ions. Heavy metal ions were determined in washings by atomic absorption method (tables I-IV).

A test of the emulsifying ability of a pectin-containing shampoo in relation to fatty impurities was carried out. The pectin-containing deactivating shampoo «Liana» was 10.1 times ($p<0.001$) higher than this indicator for liquid soap in terms of its effectiveness in removing fatty impurities from the surface of the skin.

The product was checked for microbiological safety indicators, the mass fraction of surfactant (according to the stated method for determining – Standard SEB 2542), kinematic viscosity at a temperature of 20^{0}C (table 5), as well as washes from the surface of hands treated with pectin-containing deactivating shampoo for hair and body «Liana», and washed from the surface of hands treated with liquid soap, according to radiological indicators (Table V).

The obtained data indicate that with the available mass fraction of surfactant and given kinematic viscosity, uniform application of the product to the skin and its subsequent washing off are ensured. Radiological studies have shown that deactivating shampoo for hair and body "Liana" has the ability to remove radionuclides from the surface of the skin, namely: ^{137}Cs 1.06 times, ^{232}Th by 1.12 times, ^{40}K by 26.19 times and ^{90}Sr by 2.52 times more effective than liquid soap ($p<0.001$).

In cooperation with «Shokur A.A.» LLC additional studies were carried out at the Institute of Geochemistry, Mineralogy and Ore Formation them. M.P. Semenenko, National Academy of Sciences of Ukraine (an act of research on the complex-forming ability of pectin with respect to heavy metals, the pectin-containing deactivating shampoo «Liana», control shampoos No.1 and No.2, which contained all components of the pectin-containing deactivating shampoo recipe, except for pectin, and the effectiveness of the pectin-containing deactivating shampoo «Liana». The obtained results confirmed the effectiveness of the «Liana» shampoo in removing heavy metal ions.

Therefore, according to the results of review of accompanying documents (test reports of shampoo for hair and body with deactivating properties "Liana", issued by SE "KhmelnytskyiRegional Center for Standardization, Metrology and Certification" and protocol of radiological control of products issued by DU "Khmelnytskyi Regional Laboratory Center of the Ministry of Health of Ukraine"), risk assessments for public health, namely (no more, in points): skin irritation index – 0; acute toxicity index when applied to the skin – 0; index of chronic toxicity when applied to the skin – 0; index of irritating action on the mucous membrane of the eyes – 2; acute toxicity index when administered into the stomach – 1; index of sensitizing effect – 0; bacteria genus Enterobacteriaceae, in 1 cubic cm – are not allowed; S. aureus, in 1 cm^3- are not allowed; Pseudomonas aeruginosa in 1 cubic cm – are not allowed; yeast and mold fungi, CFU/g – no more than 100; the total number of MAFAM, CFU/g – no more than 1000; hydrogen index – within 3.5-8.5 units. pH, mass fraction of surface-active substances – no more than 15.0% and the efficiency tests of the product, deactivating shampoo for hair and body "Liana" meets the requirements of "State sanitary rules and safety standards of products of the perfumery and cosmetics industry – standards: DSanPiN 2.2.9.027-99 and TU 24.5-2859920992-001:2006, and can also be used in the declared field: "Personal hygiene product for workers in heavy metallurgy, nuclear power plants, mining and chemical industry; daily life (including for use in emergency situations)".

A study of the effectiveness of removing heavy metal ions from the skin of employees of OJSC "State Joint Stock Company "Automobile Dorogy of Ukraine" of the subsidiary "Khmelnytskyi Oblavtodor" of the branch "Rusanivniskyi Special Quarry" showed that "Liana" shampoo was able to remove lead from the surface of the skin in 60, 2 times, copper is 56.12 times more effective than liquid soap. In addition, washings of dirt from the surface of the skin treated with liquid soap contained more non-emulsified fatty phase than washings of dirt from the surface of skin treated with pectin-containing deactivating shampoo for hair and body "Liana", while, according to the observations of the doctor of the sanitary department of the branch, the condition of the skin was determined as unsatisfactory, as the presence of fuel oil residues and other organic and inorganic contaminants was visually recorded in the pores of the skin.

The washes of dirt from the surface of the skin treated with pectin-containing deactivating shampoo "Liana" (model environment No.1) and the washes of dirt from the surface of the skin treated with liquid soap (model environment No.2) are presented in the tablesVI-VII.

Personal hygiene product «Bastion» produced by «Energochem Scientific and Production Association» LLC was tested for compliance with domestic legislation and technical conditions of U 20.4-31454306-014:2014 «Bastion personal hygiene products (deactivating, degassing, antibacterial, detoxifying). Studies on determining the complex-forming ability in relation to heavy metal ions and radionuclides of the personal care product «Bastion» revealed that the product not only has a high complex-forming ability in relation to heavy metals, but also prevents contamination of the skin by microorganisms from the yeast family (Malassezia furfur and Pityrosporum oval).

DISCUSSION

The obtained data demonstrate that the means «Bastion» and «Bastion M» are expedient to use not only in production conditions associated with the use of salts of heavy metals and radioactive metals, but also as a dermatological protective agent for daily cleaning and protection of the skin and its appendages from exogenous pollution. The experimentally established effective amount of the products for the body and its appendages is calculated from 15 cm^3 to 20 cm^3: contact time with the surface of the skin (exposure) of the body and its appendages is 2 minutes, taking into account the application and uniform distribution of the means on the treated body surface.

Previous studies of personal hygiene products containing pectin allow us to conclude that pectin improves the functional state of the epidermis in vitro and the physical state of hair, neutralizes the harmful effects of surface-active substances, prevents the disorganization of lipids in the stratum corneum of the skin and the loss of transepidermal moisture. The studies of low- and high-esterified pectins mainly relate to various aspects of their use in the production of food products [9, 10], however, data on the effectiveness of pectins in the composition of hygiene products (shampoos) are practically absent. Based on the results of our research, we received a Ukrainian patent for the invention [11].

Given that an important and rather complex aspect of special treatment is the sanitary treatment of skin and hair, it is advisable to increase the availability of the above means for use by rescue and military units, as well as their use along with skin disinfection means, which can be solved, for example, by developing kits from disinfectants and personal hygiene products with deactivating, degassing, detoxifying and/or antibacterial properties (according to State classifier of products and services: code 20.2 and code 20.4).

CONCLUSIONS

In conditions of high risk of radioactive, chemical and biological contamination of the human environment, there is a high need for sanitary treatment products that have deactivating, degassing and detoxifying properties due to the content of safe and effective detoxification-complexing agents of plant and/or chemical origin in the formulation. In peacetime or outside the combat zone, individual sets of such tools together with disinfectants were useful for use by the population in everyday life and agriculture(on farms, vineyards, etc.), in the Chornobyl zone and other areas of potential CBRN contamination.

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ORCID and contributionship:
Natalia V. Kurdil: 0000-0001-7726-503X[A,B,D]
Olga O. Khudaikulova: 0000-0003-3156-8208[A,B,D]
Borys I. Palamar: 0000-0003-2510-0713[A,B,E]
Oleksandr V. Yushchenko: 0000-0003-0563-2819[A,D,F]
Lyudmila A. Ustinova: 0000-0002-6582-7231[E,F]
Artur O. Zulfigarov: 0000-0003-2840-0607[A,C,D]
Yevhen V. Gavrylko:0000-0001-9437-3964[E,F]

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CORRESPONDING AUTHOR
Borys I. Palamar
Bogomolets National Medical University
13 Taras Shevchenko Blvd, 01601 Kyiv, Ukraine
tel: +380672387654
e-mail: palamar.bi@ukr.net.

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ORIGINAL ARTICLE

RADIOFREQUENCY DENERVATION OF THE FACET JOINTS AND LOCAL PERIARTICULAR ADMINISTRATION OF ANAESTHETICS IN FACET SYNDROME TREATMENT

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Mykola V. Kvasnitskyi
STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

The aim: To determine the effectiveness of radiofrequency denervation of the facet joints in combination with periarticular administration of local anaesthetics in patients with facet syndrome.

Materials and methods: The early and long-term results of treatment patients with facet syndrome were analysed. The Visual Analogue Scale of pain and the Oswestry Disability Index were used. The 47 patients underwent radiofrequency denervation of the facet joints in combination with periarticular administration of local anaesthetics (the main group). The 136 patients underwent only radiofrequency denervation of the facet joints (control group).

Results: Immediately after the treatment as well as in 3 months and in 1 year after it, a reliable results of treatment of facet syndrome in both the main and the control groups was attained. At the same time, there were significant differences between the main group and the control group immediately after treatment. But in 3 months and in 1 year after it there were no such differences that proved a significantly higher efficiency of high radiofrequency denervation of facet joints in combination with periarticular administration of local anaesthetics in the early postoperative period.

Conclusions: The radiofrequency denervation of the facet joints has proved to be an effective method of treatment of patients with spondyloarthritis both in the short and long term outcomes. Periarticular administration of local anaesthetics enhances the effectiveness of radiofrequency denervation of the facet joints only for the short term outcomes.

KEY WORDS: spondyloarthritis, radiofrequency denervation of the facet joints, periarticular blockades

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INTRODUCTION

A clinical significance of spondyloarthritis was first mentioned in the early twentieth century [1,2]. With the development of the discogenic theory of back pain, less attention has been paid to concomitant spondyloarthritis. Spondyloarthritis was first reported as a cause of pain by J.E. Goldthweit [3]. Much interest to this pathology was paid in the 1970s because of successful treatment of back pain by denervation of the intervertebral joints. [4]. Thus, a concept of facet syndrome was established and a large number of research on various methods of joint denervation, ways of selecting patients for this procedure and a comparative analysis of different treatments were developed [5-8]. In about 40% of cases, facet syndrome is the cause of chronic pain in the lower back; this amount is higher in the elderly population [9].

In the recent literature, much attention is paid to clinical manifestations and treatment methods of facet syndrome [10-12]. However, some researchers reject clinical significance of spondyloarthritis [13, 14], and other authors assign it very nearly a major role in the genesis of lower back pain [15, 16]. Pain in persons suffering from spondyloarthritis has a remitting course, and episodes of pain with each exacerbation tend to prolong. Over time, pain becomes constant. It is usually located at the lumbosacral region above the affected joints; it can irradiate to the buttocks and upper thighs. Facet pain is dull, but at maximum it can be radicular (pseudoradicular pain). A morning short-term pain is typical, it reduces after walking. The pain is stronger when stretching the spine, especially if combined with tilts or rotation towards pain side. Neurological disorders are absent. Palpation reveals muscle tension and soreness in the affected joints. Significant structural changes of the spine are considered to be the main cause of back pain, although no direct relationship between the degree of morphological changes and pain is evidenced.

Non-steroidal anti-inflammatory drugs, chondroitin sodium sulfate, glucosamine have the greatest evidence for effectiveness [17]. The authors do not agree on the effectiveness of facet joints radiofrequency denervation. Targeted works concerning the combined use of radiofrequency denervation of facet joints with periarticular injection of anesthetic are practically absent. Due to contradictory data on the effectiveness of interventional therapy, in routine clinical practice it is recommended to use invasive techniques only with accurate verification of the source of pain and in cases of pharmacotherapy failure.

THE AIM

The aim of the study was to determine the effectiveness of radiofrequency denervation of the facet joints in combination with periarticular administration of local anaesthetics to eliminate pain in the patients with facet syndrome.

MATERIALS AND METHODS

The early and long-term results of treatment of 47 patients (25 male and 22 female aged from 56 to 77 years) (the main group) with facet syndrome were analysed. The patients underwent high-frequency denervation of the facet joints (using RFG-1A/RFG-1B device, produced by Radionics) in combination with periarticular administration of local anaesthetics (2% lidocaine, 6-10 ml).

The control group consisted of 136 patients (73 male and 63 female aged from 44 to 81 years) with a lower lumbar pain with dominating spondyloarthritis. These patients underwent only radiofrequency denervation of the facet joints.

Two methods of treatment of degenerative disorders of the spine with a predominant damage of the facet joints accompanied by chronic lower lumbar pain were compared: radiofrequency denervation of the facet joints in combination with periarticular administration of local anaesthetics (facet anaesthesia) (the main group) and radiofrequency denervation of facet joints only (the control group).

The study was conducted in accordance with the principles of the Council of Europe Convention on Human Rights and Biomedicine, World Medical Association Declaration of Helsinki on the ethical principles for medical research involving human subjects, and current regulations of the Ministry of Health of Ukraine. The study protocol was approved by the local ethics committee. All patients signed an informed consent to participate in the study.

In all cases clinical and neurological manifestations of degenerative spinal cord damage correlated with the results of imaging methods of investigation: spondylography, MRI and CT of the lumbar spine. Assessment of pain is the basis of clinical examination of patients with degenerative damage of the spine. As this syndrome is purely subjective, the special pain evaluation scales and questionnaires were used. The pain Visual Analogue Scale (VAS) is a simple but demonstrative indicator of health and quality of life. The Oswestry Low Back Pain Disability Questionnaire (Oswestry Disability Index) was used to assess the quality of life in cases of spondyloarthritis; it allows minimizing the impact of other diseases on the results of the study and better assessing the impact of pain on the daily activities of the patients. Examination and evaluation by these questionnaires and scales were performed four times in both groups of patients: the first time before radiofrequency denervation (or before conservative treatment), the second time after minimally invasive treatment (or conservative), in 3 months and in one year after treatment. The results of treatment were analysed by assessment of the dynamics of pain decrease using the VAS, as well as of the functional state by the Oswestry Disability Index.

Radiofrequency denervation of the facet joints is performed under local anaesthesia in the position of the patient on the abdomen. Under the control of the electron-optical transducer (EOT), a puncture was performed around the affected intervertebral joints at specific points: target points of radiofrequency destruction. The needle was inserted into the outer-lateral surface of the facet joint, in the area of anatomical localization of the medial branch of the posterior spinal nerve (primary dorsal branch). Then, the needle mandrel was replaced by an active electrode, which was connected to a radiofrequency generator producing a high-frequency pulse current, which was conveyed through the electrode to the target points of radiofrequency destruction. Radiofrequency destruction is a technologically high-frequency electric current from the active electrode to the passive plate with destruction of the tissue around the active electrode. Electric current heats the tissue passing through it. The intensity of tissue heating depends on its electrical resistance (impedance). As a result of thermal heating of the tissue, the proteins of nerve structures are denaturated (nerve tissue enters a state of parabiosis) in the immediate vicinity of the electrode. Destruction is carried out at a temperature of 70 degrees for up to 1 minute. To identify the correct position of the needle, electrical stimulation of the facet nerves with a frequency of 50 Hz was performed by the radiofrequency generator RFG-1A/RFG-1B by Radionics company. Patients usually experience tingling in the area of the relevant facet joint. Then the frequency is decreased to 2 Hz and the state of the limb muscles is evaluated. The absence of muscle contractions in the extremities indicates a correct position of the electrode.

The duration of radiofrequency denervation of the facet joints did not exceed 30 minutes. In most cases, there were slight short-term tingling and tingling during the manipulation. After micro-intervention, patients felt well, no complications were evidenced. After the intervention, bed rest for one hour was recommended to the patients and they were discharged from the hospital two hours later.

Clinical features of the main and control groups of patients are presented in Table I. According to clinical manifestations, the patients of the main and control groups were regarded as by pain in the lower back and/or corresponding sclerotomes, symptoms of paravertebral muscle tension at this level, limited movement in the absence of symptoms of tension or neurological dysfunctions. The duration of the disease ranged from three to 39 years.

There was no significant difference between the studied groups (Table 1). Preliminary selection of patients by sex, age, clinical course of the disease, anatomical and morphological changes of the spine was not performed.

The division of patients according to the level of damage of the intervertebral joints is presented in Table II.

The attained data were statistically processed using the methods of parametric analysis of biometric indicators (according to the Student's T test, the differences were considered statistically significant at $p \leq 0.05$, a tendency at $0.1 > p > 0.05$, the differences were considered statistically insignificant at $p > 0.1$). The analysis of the results was performed using the X2 agreement criterion. The statistical analysis was performed on a personal computer using Microsoft Excel 2000, Microsoft Access 2000 of the Windows 98 operating system.

RESULTS

Before surgery, the average rate of pain in the main group according to the VAS was 7.6 points. Taking into account the results of treatment in the early postoperative period, the patients were divided into the following groups according to the VAS: excellent – no pain (32 patients), good – pain

Table I. Clinical features of the main and control groups of patients

Clinical features and indicators	Main group n=47	Control group n=136
Males	25 (54.4±4.6%)	73 (53.7±3.1%)
Females	22 (51.6±6%)	63 (46.3±3.1 %)
Average age	61.1±2.8	66.2±2.3
Average disease duration (years)	13.7±2.9	16.4±2.1
Average duration of acute condition (months)	3.1±0.5	2.8±0.4
Average number of affected intervertebral joints	2.6±0.4	3.2±0.3
Average size of intervertebral protrusion (mm)	3.8±0.6	3.4±0.7
Spondylolisthesis	4 (8.4%)	6 (4.4%)
Spinal stenosis	2 (4.0%)	4 (2.9%)
Spondyloarthritis	47 (100%)	136 (100%)

Table II. Division of patients of the main and control groups according to the level of dominant damage of the functional spinal unit (FSU)

Level of FSU damage	Main group	Control group
L3-L4	4%	9%
L4-L5	57%	69%
L5-S1	66 %	52%

Table III. Average parameters of pain syndrome of the main and control groups of patients (according to VAS)

Groups of patients	Before treatment	After treatment	In 3 months	In one year
Main	7.6±0.21 (n=47)	1.8±0.19* (n=47)	4.3±0.16 (n=38)	4.6±0.20 (n=31)
Control	8.1±0.16 (n=136)	2.8±0.22 (n=136)	3.9±0.24 (n=110)	4.2±0.34 (n=84)

Notes: * – $p<0.05$, significant difference of the results only immediately after treatment between the main and control group according to the VAS.

Table IV. Average parameters of functional state of the main and control groups of patients (according to the Oswestry Disability Index, points)

Groups of patients	Before treatment	After treatment	In 3 months	In one year
Main	43±0.5 (n=47)	10±0.7* (n=47)	29±0.6 (n=38)	32±0.5 (n=31)
Control	44±0.5 (n=136)	18±0.6 (n=136)	28±0.7 (n=110)	30±0.8 (n=84)

Notes: * – $p<0.05$, significant difference of the results only immediately after treatment between the main and control group according to the Oswestry Disability Index.

relieved to 2 points (9 patients); satisfactory – pain relieved to 4 points (5 patients), unsatisfactory – pain relieved to 6 points and more (1 patient). In 3 months after treatment (38 patients were examined), the patients were divided into the following groups according to the VAS: excellent – no pain (21 patients), good – pain relieved to 2 points (9 patients); satisfactory – pain relieved to 4 points (6 patients), unsatisfactory – pain relieved to 6 points and more (2 patients). In one year after treatment, 31 patients were examined. The patients were divided into the following groups according to the VAS: excellent – no pain (10 patients), good – pain relieved to 2 points (7 patients); satisfactory – pain relieved to 4 points (11 patients), unsatisfactory – pain relieved to 6 points and more (3 patients). Similar results of treatment according to the VAS were attained in the control group (in order to facilitate the perception of the material without overloading it with numbers, only the average parameters of this group of patients are presented in Table III).

Before surgery, the average pain rate in the main group according to the Oswestry Disability Index was 45 points. Taking into account the results of treatment in the early postoperative period, the patients were divided into the following groups according to the Oswestry Disability Index: excellent – pain revealed to 5 points (34 patients), good – pain revealed to 15 points (10 patients); satisfactory – pain revealed to 25 points (3 patients), no unsatisfactory results (pain revealed to 35 points). In 3 months after treatment (38 patients were examined), the patients were divided into the following groups according to the Oswestry Disability Index: excellent – pain revealed to 5 points (23 patients), good – pain revealed to 15 points (10 patients); satisfactory – pain revealed to 25 points (4 patients), unsatisfactory – pain revealed to 35 points (1 patient). In one year after treatment, 31 patients were examined. The patients were divided into the following groups

according to the Oswestry Disability Index: excellent – pain revealed to 5 points (11 patients), good – pain revealed to 15 points (8 patients); satisfactory – pain revealed to 25 points (10 patients), unsatisfactory – pain revealed to 35 points (2 patients). Similar results of treatment according to the Oswestry Disability Index were attained in the control group (in order to facilitate the perception of the material without overloading it with numbers, only the average parameters of this group of patients are presented in Table IV).

Estimation of average parameters of pain syndrome and functional state of patient follow-ups in the main and control groups are presented in Table III and Table IV, respectively.

As seen in the Tables III and IV, immediately after treatment and in 3 months as well as in 1 year after it (both according to the Oswestry Disability Index and the pain Visual Analogue Scale) reliable results of treatment of facet syndrome were attained in the main group as well as in the control groups that proved the effectiveness of both treatment methods. However, there was a significant difference between the main and control groups immediately after treatment that proved a higher efficiency of radiofrequency denervation of the facet joints in combination with periarticular administration of local anaesthetics only in the early postoperative period (the first week after treatment). However in the late postoperative period (in 3 months and in 1 year after treatment) there was no significant difference between the main and control groups.

DISCUSSION

In the recent literature, much attention is paid to clinical manifestations and treatment methods of facet syndrome [18, 19].

The authors do not agree on the effectiveness of facet joints' radiofrequency denervation. The studies of the effectiveness of radiofrequency denervation of facet joints, which were controlled by simulation techniques, have proved minor advantages of radiofrequency denervation [20, 21]. Some authors argue about the effectiveness of the method [22,23] while others deny it [24]. Hence, it leads to various clinical recommendations. Injection therapy and denervation procedures are commonly used in the management of chronic low-back pain (LBP) despite uncertainty regarding their effectiveness and safety. To provide an evaluation of the current evidence associated with the use of these procedures, a systematic review was performed. Existing systematic reviews were screened, and the Cochrane Back Review Group trial register was searched for randomized controlled trials fulfilling the inclusion criteria. Overall, there is only low to very low-quality evidence to support the use of injection therapy and denervation procedures over placebo or other treatments for patients with chronic LBP. However, it cannot be ruled out that in carefully selected patients, some injection therapy or denervation procedures may be of benefit [25]. A Kaye et al. [26] published a meta-analysis of 52 controlled trials comparing injections of glucocorticoids, topical analgesics, and placebo in chronic back pain associated with intervertebral disc herniation of the cervical, thoracic, and lumbar spine, and stenosis. This study confirmed the advantages of interventional methods: for all localizations of the damage, a high level of evidence (II), in which the effectiveness of active therapy exceeded the effect of "pacifiers".

Paraarticular blockade of the facet joint with an anesthetic (with or without steroid) is not only of diagnostic significance. Paraarticular blockades are a common and safe method of back pain treatment in facet arthropathy. In the United States, this method is the 2nd among all interventions to relieve pain [27]. As an interventional procedure, it has a very low risk of complications, including infectious or nerve trunks damage. However, other researchers do not recommend intra-articular facet injections [28]. Due to contradictory data on the effectiveness of interventional therapy, in routine clinical practice, it is recommended to use invasive techniques only with accurate verification of the source of pain and in cases of pharmacotherapy failure.

The conducted research was precisely aimed at clarifying the results of the combined treatment of radiofrequency denervation of facet joints with periarticular injection of anesthetic and showed the effectiveness of such treatment in the early postoperative period in patients with facet syndrome.

CONCLUSIONS

The radiofrequency denervation of the facet joints has proved to be an effective method of treatment of patients with spondyloarthritis both in the short and long term outcomes. Periarticular administration of local anaesthetics enhances the effectiveness of radiofrequency denervation of the facet joints only for the short term outcomes.

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ORCID and contributionship:
Mykola V. Kvasnitskyi: 0000-0001-5271-0213 [A-F]

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CORRESPONDING AUTHOR
Mykola V. Kvasnitskyi
State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department
5 Verkhnya st., 01014 Kyiv, Ukraine
tel: +380503395408
e-mail: kvas1954s@gmail.com

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ORIGINAL ARTICLE

THE METHOD OF ATOMIC FORCE MICROSCOPY AS A POSSIBLE TOOL FOR TESTING THE BIOCOMPATIBILITY OF IMPLANTS IN TRAUMATOLOGY AND ORTHOPEDICS PRACTICE

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Hlib O. Lazarenko, Igor V. Boiko
STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE», KYIV, UKRAINE,
STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

The aim: To establish the possibility of using the atomic force microscope (AFM) to predict the body's reaction to the implant.

Materials and methods: A total of 32 patients, 22 men and 10 women, the average age of the patients was 55±6 years, were included in the study. They performed pre- and post-operative testing of the biocompatibility of orthopedic implant materials with the patient's body with the help of AFM.

Results: According to the research, an increase in pro-inflammatory factors was found, which may indicate a constant inflammatory process, which is probably related to the presence of the implant.

Conclusions: On the basis of atomic force spectroscopy, an express method of testing biomaterials for compatibility with the body of a specific recipient and studying the effect of the reactions of recipient tissues on the surface of various implants has been developed. The obtained results can be useful in planning further clinical studies.

KEY WORDS: biocompatible materials, rejection reaction, implant losing, hypersensitivity reaction, aseptic losing

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INTRODUCTION

In recent years, the number of surgical interventions for joint endoprosthetics has increased in the world. Orthopedic doctors use a wide range of implants (hip, knee, shoulder, elbow, ankle and small joints of the feet and fingers). However, each of these implants is a foreign body for our body. A rejection reaction or a manifestation of increased sensitivity to the implant material is observed in 6-30% of cases after surgical intervention [1-3]. With the rapid growth of the number of biomedical materials, there is an urgent need to develop methods for diagnosing individual biocompatibility *in vitro* and *in vivo*. As a result, the number of studies aimed at the development and experimental clinical application of biocompatible materials of natural and artificial origin with specified properties has increased dramatically.

In our opinion, only by considering each living organism and its tissue reactions to any foreign body as an individual reaction to a specific stimulus, it is possible to approach predicting the degree of biocompatibility of implant materials at the preoperative stage with a high degree of probability.

Unlike natural materials, artificial materials do not have certain receptors on their surface that are recognized by the protective immune system of a living organism.

A certain electronic heterogeneity of the surface of these materials plays the role of binding centers for protective proteins [4-8]. Persistent uncontrolled adsorption of blood plasma proteins activates the local immune response, which can subsequently lead to inflammation with the formation of a fibrous capsule around them and the loss of their functional properties [8-11].

A certain electronic heterogeneity of the surface of these materials plays the role of binding centers for protective proteins. Persistent uncontrolled adsorption of blood plasma proteins activates the local immune response, which subsequently can lead to inflammation with the formation of a fibrous capsule around them and the loss of their functional properties. The latter, in turn, demonstrate a metal-antigen complex for T cells, which leads to further activation of CD4 +, CD8 + cells and macrophages, with the subsequent release of pro-inflammatory cytokines [12, 13], which (such as: tumor necrosis factor (TNF- α), interferon-γ (IFN-γ), interleukin (IL-1, IL-2, IL-6), receptor-activating nuclear factor-kappa B ligand (RANK-L)) lead to an immune response that causes tissue inflammation with subsequent damage to periprosthetic tissues [14-16]. This process leads to the selective dissolution of the components of the implant and its destruction. The products of this dissolution affect the absorption or accumulation of proteins on the surface of toxic substances, as well as the formation of a dense layer of the extracellular matrix around the material. Adhesion of proteins on the surface of the implant depends on the chemical properties of the material, as well as on its physical characteristics.

The study of protein-surface interactions is important for the improvement of biomaterials, and, in particular,

for achieving biocompatibility of implants, for minimizing undesirable effects such as biological contamination [17]. At the same time, the fact that protein adsorption is a complex process and controlled by a large number of parameters [18] limits our ability to accurately predict the behavior of proteins, even when they interact with surfaces under certain conditions. To overcome this limitation and to understand the fundamentals of protein-material interaction, it is necessary to emphasize the research of the molecular level of the interaction.

Atomic force microscopy (AFM) has become a powerful tool for measuring molecular forces, which extends from determining the strength of ligand–receptor binding [19] to describing the mechanical properties and extensibility of larger biomolecules [20] or reproducing recognition maps of biological surfaces [21]. All these applications are based on the competence of AFM to manipulate single molecules and monitor their sensitive interactions. A prerequisite for their success is knowledge of the structural properties, both geometric and biophysical, of the molecular system being experimented on, so that desired measurements can be distinguished from artefacts.

These methods cover the range from entropic forces of several femto-Newtons to covalent bond breaking values of several nano-Newtons.

With the help of AFM, it is possible to effectively study both the ligand-receptor interaction (intermolecular forces) and the structures of individual macromolecules. To study the specific binding between biomolecules, an increasing force is applied to the ligand-receptor complexes and the time dependences of the dissociation process are recorded. There are a number of controlled specific bimolecular interactions, which creates real prerequisites for successfully solving a number of applied diagnostic problems with the help of nanobiosensor technologies, which can be implemented using the hardware and software base of atomic force microscopes (AFMs).

THE AIM

The aim of this study was to establish the possibility of using the atomic force microscope (AFM) to predict the body's reaction to the implant.

MATERIALS AND METHODS

We and our colleagues proposed individual prediction of the compatibility of materials with the recipient's body based on atomic force spectroscopy of IgG bioadhesive interactions with the surface of implants [22-26].

The diagnostic method consists in measuring the strength of adhesion when testing the contact of IgG with biomaterial for stretching and tearing. In addition to the strength of this testing of the contact of dissimilar biomaterials for breaking includes a wide range of volumetric viscoelastic processes with different relaxation times, as well as highly elastic deformation characteristic of a number of polymers and the destruction of the formed biobridge between the probe and the surface. Adhesion of each of the materials to the substrate and to the probe, respectively, plays a certain role here.

In order to carry out quantitative assessments, we analyzed in detail the various mechanisms involved in the rupture process, built appropriate physical and mathematical models of this phenomenon [25, 26].

Modeling of the features of the interaction between the pure probe and the sample was carried out, without the presence of biological samples on them. The nature of the interaction here is determined by capillary forces generated by water menisci that condense from the air. Although the characteristic dimensions of the water meniscus and the biopolymer bridge are significantly different, the model of the water meniscus was taken as a starting point. Theoretical models describing viscoelastic processes during deformation of biopolymers are generalized and adapted. A model describing AFM bioadhesion testing of materials is formulated.

Prediction of biocompatibility of different materials based on the magnitude of their interaction forces under conditions when one object is planted on the surface and the other is attached to the edge of the AFM probe.

AFM studies of bioadhesive detachment force were performed on a scanning probe microscope NANOSCOPE IIIa (VEECO Corp.) both in air (at a temperature of 22°C and relative humidity of 30%) and in a liquid medium (0.9% sodium chloride solution). The speed of vertical movement of the probe was chosen in the range from 20 to 20,000 nm/sec. Contact probes made of Si3N4 DNP-20 (VEECO Corp.) with a V-shaped cantilever were used for measurements. The average radius of the tip of the probe was 30 nm, the stiffness of the cantilever was 0.06 N/m. The control of the form of the tip was performed before and after measurements using the «blind reconstruction» method using the test grid TGT-1 (NT-MDT). The value of the stiffness of the cantilever was specified by analyzing the spectrum of its temperature noise. The typical shape of the top of the probe is the top of a quadrangular pyramid. The tip itself has an elliptical shape, the top of the tip is well approximated by a circle up to a height of about 25 nm. This allows us to use the spherical probe model in theoretical calculations. In order to avoid the effect of a possible modification of the investigated surfaces and to minimize the influence of the topography, a series of force curves was taken with a step of 100 nm on the surface, covering a 1x1 μm area (100 curves in one area of the surface).

The scheme of measurements of the bioadhesive detachment force is presented in Fig. 1. At the initial moment, the probe modified by antibodies (AT) is far from the surface of the sample (Fig. 2, point 1) and the strength of the surface-AT (antigen (AG)) interaction is zero. Next, the AFM system of vertical movement of the probe brings the probe to the surface, controlling the distance with angstrom accuracy. At some minimum probe-surface distance, the modified probe is «captured» by the surface under the action of attraction forces (Fig. 2, point 2). When the probe and the surface are brought closer together, repulsive forces begin to act, preventing the probe from penetrating the surface. After reaching the maximum value of the repulsive force (set by the operator based on the conditions of the experiment) (Fig. 2, point 3), the reverse vertical movement

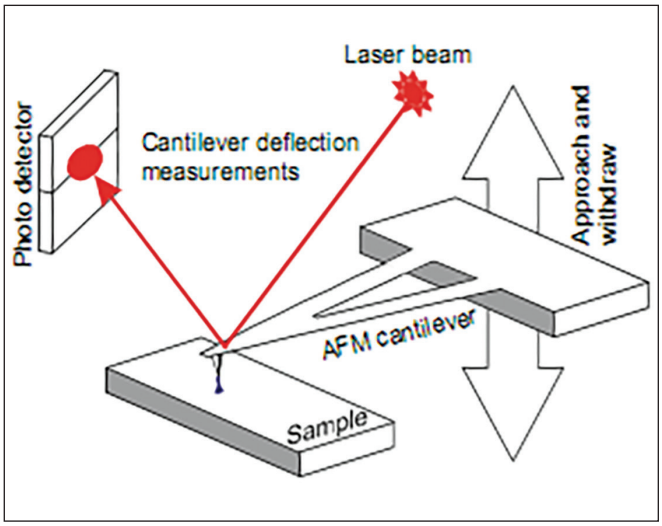

Fig. 1. Scheme of measurement of «probe-surface» interaction forces in atomic force spectroscopy (AFS) mode.

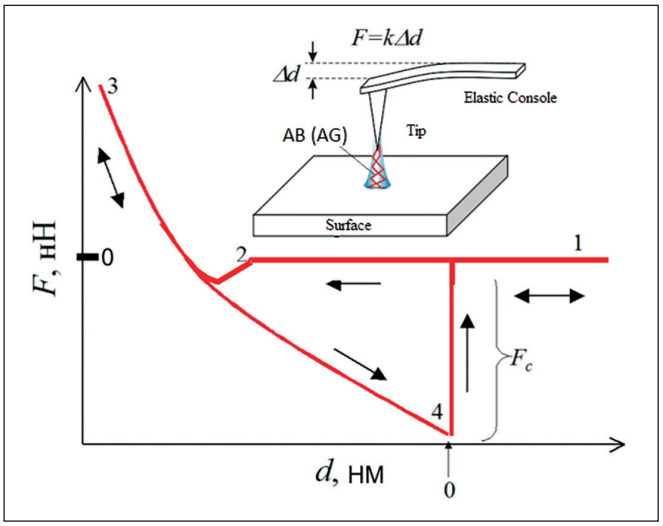

Fig. 2. Scheme of measurements of the bioadhesive detachment force F by the ACC method. The strength of bioadhesion is determined by the measured AFM value of the elastic deformation of the probe cantilever d as F = kd, where k is the elastic constant of the cantilever.

Table I. Physical characteristics of the implant base alloy

Material	Processing method	Young's modulus (GPa)	Compressive strength limit (MPa)	Ultimate tensile strength (MPa)
Ti6Al4V	Cold	100–110	830–1070	920–1140

Note: the average holding force of the clean probe on the surface of the implant ranges from 5 to 8 nN.

Table II. Average values of C-reactive protein (CRP), clinical parameters of the blood formula, IgG concentration in blood serum and data on the holding power of the surface of the titanium sample Ig (F)

Parameters Time point	CRP (0-5 mg/l)	Gran % (47-75 %)	Lym % (19-37 %)	Mon % (3-10 %)	IgG g/l (5,5-18,5 g/l)	AFM F nN (5-8 nN)
Before operation	3,1	66,0	31,2	4	7,8	56,3
14 days after operation	5	58,1	30,4	4	7,9	50,1
1 month after operation	34,5	68,2	23,2	5	11,2	48,7
4 month after operation	39,1	68,0	43,1	7	14,3	51,8

of the probe begins. At the same time, the net effect of all the forces holding the modified probe near the surface is balanced by the force of the elastic deformation of the probe console at point 4, at which separation from the surface occurs. Thus, the maximum value of the force of bioadhesive interaction corresponds to the value of the force of separation of the probe from the surface (Fig. 2, point 4), which is equal to the force of elastic deformation of the probe console, by the measuring system of AFM detection by the value of its deflection *d*.

Functionalization of the probe is carried out by applying an antibody (AT). Total IgG isolated from the patient's blood serum was used as AT. IgG will make it possible to measure the strength of interaction between the surface and the immunoglobulin fixed on the AFM probe and thus determine the compatibility of this material with a living organism. AT probe was applied from a solution with a concentration of 0.1 μg/ml. (solution - 0.9% NaCl).

Measurements were carried out both in air and in water in order to check the difference between the obtained data, whether it is significant for conducting assessments of bioadhesion forces. During measurements in the atmosphere, a so-called capillary bridge is formed on the surface of the sample due to the presence of capillary forces, which makes a significant contribution to the magnitude of adhesive forces. Thus, the values of the pull-off force when measured in air are greater than when measured in water. However, as it was established, the qualitative relationships between the values of the separation forces for different samples are preserved. The method is described in more detail in our previous works [25-26].

RESULTS

In the clinic of the State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department, pre- and post-operative testing for the biocompatibility of orthopedic implant materials with the patient's body was carried out with the help of AFM, with the prior consent of the patients.

A total of 32 patients, 22 men and 10 women, the average age of the patients was 55±6 years, were included in the study. All patients were examined before surgery according to a standard protocol, and allergic anamnesis to the components of the implant was also collected. The main material for the implant was titanium alloy Ti6Al4V (Table I).

Previously, patients had 5 ml of venous blood sampled before surgery, 14 days after surgery, 1 and 4 months after surgery. Total Ig was isolated from the serum using a standard method [27]. After purification and dilution to the appropriate concentration, 2 μg/ml. According to the previously described method, Ig G was applied to the AFM probe, then the implant material (titanium component of the latter) was tested for compatibility with the patient's body. The value of the holding force of the probe with the recipient's Ig on the surface of the implant was considered as an assessment of the compatibility of the material with the patient's body. The higher the value of the retention force, the more likely was the development of a reaction to the implant by the recipient's body. Listed in the Table. II data indicate that in one of the patients, the level of CRP and the number of segmented neutrophils only increase over time. And the results of testing with the help of AFM remain at the level of 49-56 nN, which indicate a stable reaction of the body to the implant. The tension of the immune system is constantly maintained by the presence of a foreign body (implant), and the specificity of Ig to the material of the prosthesis remains very high.

DISCUSSION

Adsorption of blood plasma proteins controls the reaction of the human body to the implant material.

When implants (artificial materials) are introduced into a complex biological environment like blood, nonspecific protein adsorption is the first surface-mediated event impacting later biological processes [28]. On the other hand, nonspecific protein adsorption determines the subsequent series of interactions that can lead to surface biofouling, an inflammatory reaction, and device failure [29].

Therefore, measuring non-specific protein adsorption on surfaces is important for predicting and optimizing material performance in biological applications. Understanding the nature of protein-surface interactions be- yond measuring the amount of adsorbed protein may be critical to developing advanced surfaces and, in particular, for achieving biocompatibility of implants, for minimizing undesirable effects such as biological contamination.

Undoubtedly, a more accurate understanding of the protein–biomaterial interaction mechanisms, on a nanoscopic level, is a prerequisite to finding general rules governing such processes. With AFM, it is possible to effectively study both the ligand-receptor interaction (intermolecular forces) and the structures of individual macromolecules. AFM has already been used to visualize and investigate conformation and morphologic changes of serum proteins adsorbed. In this case development of optimal conditions for nano biosensor testing of implants using AFM and the study of the effect of reactions of the recipient's tissues on the surface of the implants, which can significantly increase the effectiveness of surgical treatment of diseases of the musculoskeletal system through the selection/selection of optimally compatible implants with the recipient's body [10].

CONCLUSIONS

The main problem solved by researchers is the biocompatibility of artificial and natural materials. Undoubtedly, all the problems, gaps and shortcomings that arise in this field emphasize the need for new, clinically useful diagnostic and prognostic tests to determine the probability of a pathological response caused by an implant before implantation and to adequately assess the entire spectrum of possible reactions after implantation, focusing on the processes that are formed at the cellular level levels. Thus, AFM can be one of the effective tools for observing and analyzing processes that operate inside or between biomolecules. On the basis of atomic force spectroscopy, when correlating the intermolecular interaction of biomolecules (on an AFM probe) and conformational changes of proteins adsorbed on implant materials, a promising express method of testing biomaterials for compatibility with the body of a specific recipient has been developed. Currently, we are conducting further clinical studies on experimental animals.

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The study was conducted in compliance with the basic principles of the World Medical Association Declaration of Helsinki on the ethical principles for medical research involving human subjects, current Ukrainian regulations, and the Interdisciplinary Principles and Guidelines for the Use of Animals in Research, Testing, and Education, developed by The New York Academy of Sciences` Ad Hoc Committee on Animal Research in conjunction with an Advisory Panel. The study protocol was approved by the local ethics committee. All the patients provided written informed consent regarding the participation in the study and surgical treatment.

The study performed as a fragment of the complex scientific project of the Scientific Department of Minimally Invasive Surgery (State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department) «Surgical treatment optimization based on multimodal fast recovery program using nanobiosencoric technologies and anaesthesiological providing» (state registration number 0122U000233; term: 2022-2024).

ORCID and contributionship:
Hlib O. Lazarenko: 0000-0001-8585-5355 [A-E]
Igor V. Boiko: 0000-0002-2929-5549 [E, F]

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The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Hlib O. Lazarenko
State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department
5 Verkhnia St., 01014 Kyiv, Ukraine
tel: +380977964483
e-mail: lazarenkog@gmail.com

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ORIGINAL ARTICLE

PRACTICAL ASPECTS AND RESULTS OF COGNITIVE THERAPY IN THE EARLY RECOVERY PERIOD OF ISCHEMIC STROKE

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Olga G. Morozova, Anna N. Kosheleva, Bogdan S. Fedak, Volodymyr I. Ponomaryov, Aleksandr A. Yaroshevskiy, Iryna M. Kravchenko, Inna V. Reminiak

EDUCATIONAL AND SCIENTIFIC MEDICAL INSTITUTE OF THE NATIONAL TECHNICAL UNIVERSITY «KHARKIV POLYTECHNIC INSTITUTE», KHARKIV, UKRAINE

ABSTRACT

The aim: To determine the impact of cognitive training on the degree of cognitive functions recovery and quality of life in the early recovery period of ischemic stroke.

Materials and methods: 108 patients with cerebral infarction were examined outpatiently, follow-up from 1 to 3 months from the onset of the disease. Basic assessment methods: screening index of cognitive disorders according to the Montreal Cognitive Assessment Scale (MoCA), SF-36 questionnaire.

Results and Conclusions: Comprehensive rehabilitation measures for the early recovery period of ischemic stroke achieve improvement of the cognitive sphere: a significant increase in the average score on the Montreal scale of cognitive functions assessment (MoCA scale) in both observation groups.

KEY WORDS: cerebral infarction, cognitive disorders, rehabilitation treatment, cognitive therapy, cognitive functions assessment scale of MoCA, SF-36 questionnaire

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INTRODUCTION

According to the Ministry of Health of Ukraine, every year in Ukraine there are about 130 thousand cases of stroke: 30-40% of stroke patients die within the first 30 days and up to 50% - within 1 year from the onset of the disease, 20-40% - need outside help (12.5 % of primary disability), and only about 10% return to full life [1]. Each subsequent stroke impairs the quality of life and complicates the comorbidities course. Ischemic stroke is a severe form of cerebrovascular disease. Two thirds of patients after stroke have disorders of attention, memory, gnosis, praxis, speech, thinking, which significantly affects everyday activity and reduces quality of life [2, 3]. Cognitive dysfunctions after stroke often have peculiarities of formation and course, which are differ from the peculiarities of cognitive deficits development in Alzheimer's disease. That is why the results of a brief examination of cognitive function (Mini-Mental State Examination, MMSE) in patients with stroke may be inaccurate. The Montreal Cognitive Assessment (MoCA) scale has been proposed as a screening test sensitive to vascular cognitive impairment [4]. This scale in a relatively short time (8-13 minutes) evaluates attention and concentration, executive functions, memory, speech, visual and constructive skills, abstract thinking, arithmetic, time and place orientation . The result of 26-30 points is considered normal. Restoration of cognitive functions is most effective in the early recovery period (from 21 days to 6 months after stroke) [5].

THE AIM

The aim was to determine the cognitive training impact on the degree of cognitive functions recovery and life quality in the early recovery period of ischemic stroke.

MATERIALS AND METHODS

The study of 108 patients with cerebral infarction was conducted in an outpatient conditions, the follow-up period was from 1 month from the onset of the disease to 3 months. The average age of the subjects was 54.6 ± 3.4 years. The main group: 58 patients with ischemic stroke in the early recovery period, patients had being received drug therapy, physical therapy, therapeutic massage, cognitive training (including speech therapy if indicated). The principles of speech disorders restoration are formulated in our work [6]. In particular, part of the methodological approaches to cognitive training for the executive functions correction is borrowed from the next authors [7, 8]. Control group: 50 patients with ischemic stroke in the early recovery period, who received an identical course of treatment without cognitive therapy.

Criteria for inclusion in the study: patients in the early recovery period of cerebral infarction, MoCA scale from 20 to 25 points inclusive, aphatic disorders of mild severity, outpatient rehabilitation. Exclusion criteria: NIHSS (National Institutes of Health Stroke Scale) from 13 to 34, afferent motor aphasia, hemorrhagic stroke.

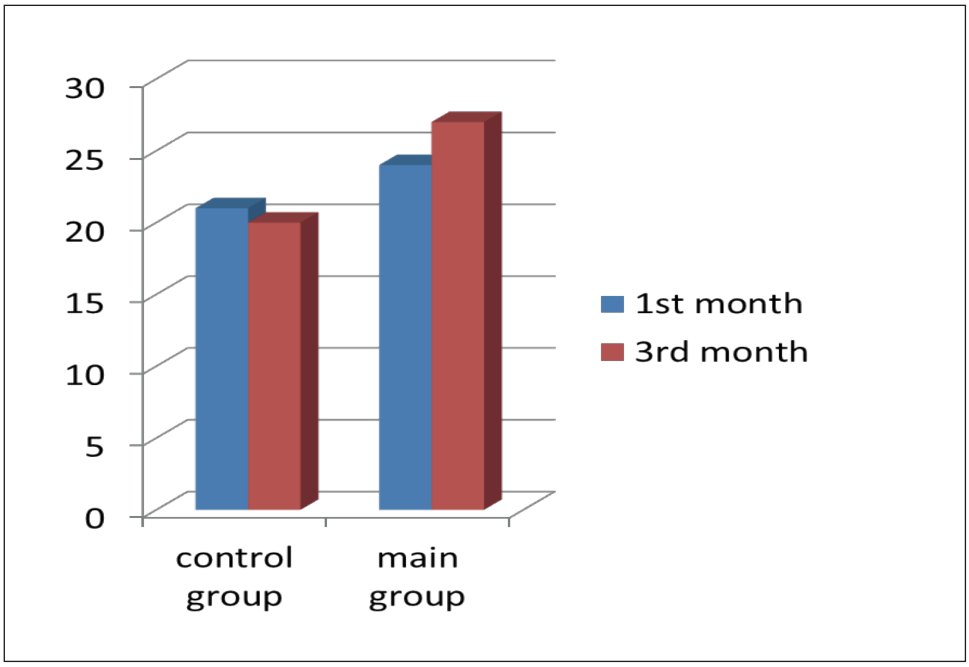

Fig. 1. The MoCA scale average score.

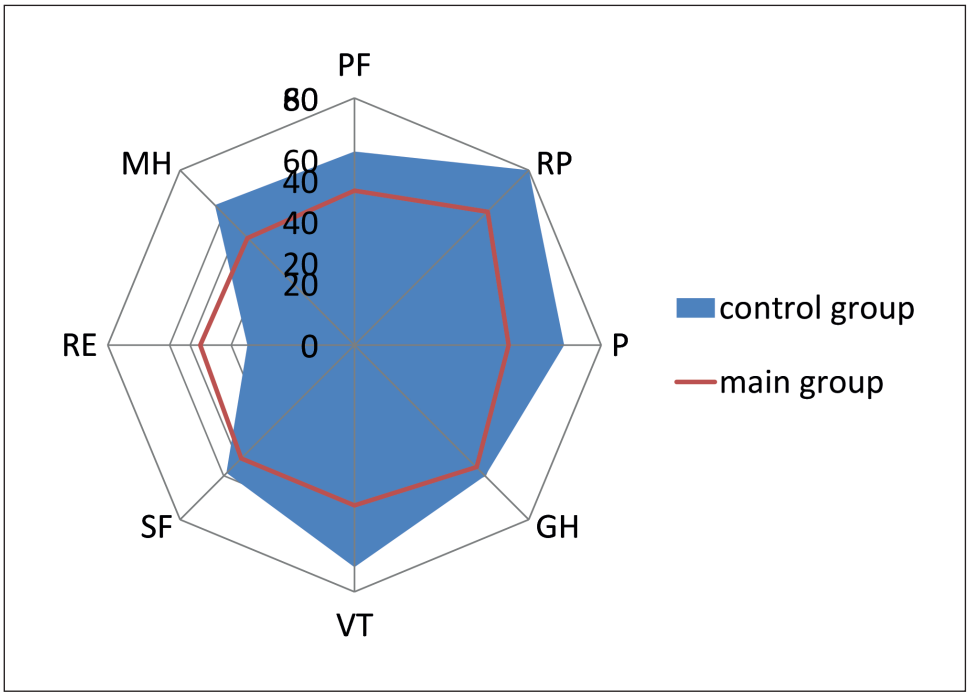

Fig. 2. Dynamics of life quality parameters according to the SF-36 questionnaire, 3 months.

The following assessment methods were used as criteria for the effectiveness of treatment, along with general clinical and instrumental studies: screening index of cognitive disorders according to the Montreal Cognitive Assessment Scale (MoCA) [9], quality of life questionnaire (MOS SF-36).

One of such a questionnaire is the Medical Outcomes Study Short Form 36 (MOS SF-36). It was developed at the Center for the Study of Medical Outcomes (USA) in 1992 by Jonh E. Ware and Cathy Donald Sherbourne, and translated by IQOLA (The International Quality of Life Assessment, Boston, USA) under the direction of Dr. JE Ware and B. Gandek [10]. According to the questionnaire 8 parameters are calculated which are responsible for physical and psycho-emotional functioning [11].

Cognitive training gradually under the condition of systematic repetitions includes restoration of adequate reactions and orientation of the patient in personality, time and space, restoration of separate cognitive functions and integrative-functional skills, and at the later stages - learning strategies for cognitive-behavioral compensation of residual cognitive deficit and training of integrative-functional skills in everyday life. Classes are held individually or in a group depending on patient condition severity. The transition from individual to group classes occurs when the patient is able to communicate with others. In

Table I. The average score according to the MoCA scale during dynamic observation in the ischemic stroke early recovery period.

Terms of evaluation	Control group	Main group	The statistical significance (p-value) between the groups
1st month	21,07 ± 1,12	20,84 ± 1,32	p>0,05
3rd month	24,64 ± 1,90	27,08 ± 1,33	p<0,05
The statistical significance (p-value) within the group in dynamic observation	p<0,05	p<0,05	

Table II. Dynamics of life quality parameters according to the SF-36 questionnaire

SF-36 indexes	Control group	p_1	Main group	p_2
Physical functioning (PF)	25,44 ± 2,37 / 47,18 ± 2,11	<0,05	24,09 ± 1,68 / 50,97 ± 1,90	<0,05
Role-playing physical functioning (RP)	15,47 ± 3,29 / 60,04 ± 2,13	<0,05	13,31 ± 3,04 / 61,88 ± 1,68	<0,05
Body pain (P)	50,02 ± 2,11 / 51,04 ± 3,27	>0,05	48,04 ± 3,75 / 50,02 ± 4,90	>0,05
General health (GH)	33,46 ± 2,90 / 45,67 ± 4,98*	<0,05	31,30 ± 2,40 / 56,44 ± 1,68*	<0,05
Viability (VT)	28,30 ± 4,96 / 54,56 ± 3,94	<0,05	29,40 ± 1,60 / 52,46 ± 5,16	<0,05
Social functioning (SF)	42,10 ± 2,97 / 44,46 ± 2,95*	>0,05	44,09 ± 3,37 / 52,44 ± 1,97*	<0,05
Role-playing emotional functioning (RE)	24,35 ± 3,37 / 26,47 ± 2,17*	>0,05	23,04 ± 4,81 / 50,48 ± 2,09*	<0,05
Mental health (MH)	41,42 ± 2,10 / 48,56 ± 2,72	<0,05	40,06 ± 3,47 / 49,48 ± 0,95	<0,05

Note: numerator - observation period of 1 month, denominator - observation period of 3 months, p_1 - probability of differences pre- and post treatment indexes in the control group, p_2 - probability of differences pre- and post treatment indexes in the main group, * - probability of differences p <0.05 in the control and main groups compared.

addition, he has the opportunity to complete the exercises and control their own behavior. Restorative work is carried out on all impaired cognitive functions. The peculiarities of each case are taken into account, namely the individual characteristics of the patient's personality, the severity of somatic status, living conditions, level of education and so on. Restorative cognitive training is carried out according to a specially developed program, certain tasks and goals are formulated, methods of work are chosen. The duration of an individual lesson is about 45 minutes, a group lesson - 1 hour. In the early recovery period classes were held 3 times a week.

Cognitive rehabilitation of patients from the main group included measures to reorganize the environment. This allows the patient to act successfully despite functional disorders. Modification of the environment included: physical environment (rearrangement of furniture, organization of sleeping, living, eating places, etc.), schedule (establishing a clear schedule, schedule of therapeutic activities for the patient and others), work organization of medical staff and the patient's relatives (providing recommendations for communication with a patient with aphatic disorders, for communication with a patient in the early recovery period).

All studies were performed at the beginning of follow-up (1st month of illness) and after 3 months from the beginning of the disease. Statistical processing of the obtained data was performed using the program Statistica 6.0 with the determination of the Mean (M), the standard error of the mean (m), the t-test of Student's reliability, the statistical significance of results (p-value). Differences in indicators were considered statistically significant at p <0.05.

RESULTS

During the observation, the assessment of cognitive functions conditions dynamics of the patients with cerebral infarction was performed at the 1st and 3rd month from the onset of the disease according to the inclusion and exclusion criteria (Table I).

At the beginning of the observation, the MoCA scale average score did not differ between the examined groups (p> 0.05). When tested in the dynamics after the 3rd month of observation there was a significant increase in the total score in both groups. The average score on the MoCA scale was significantly higher in the main group, which was underwent measures for cognitive training, in this group the average score reached normal values (Fig. 1).

The SF-36 questionnaire has particular importance ensuring in scientific research diverse information of the physical, emotional and social patient functions in the environment. This questionnaire gives an opportunity to compose a picture of the health general state, but it is quite time consuming and can't be used by health care providers. Elderly stroke patients had difficulties in completing the questionnaire and were elucidated to provide instructions how to complete. In the SF-36 test, no significant differences between groups were registered at the beginning of the observation (Table II).

In general, low life quality indexes were revealed in physical functioning (PF), role-playing physical functioning (RP), general health (GH), viability (VT), social functioning (SF), emotional functioning (RE), and mental health (MH). These test components correspond to motor and cognitive deficits, emotional disorders of acute and recovery periods of the disease, ie limitation of the patient's life and functioning. After the rehabilitation treatment course there was a positive trend in life quality in both groups in physical and emotional sphere, but some dissimilarities between the groups were observed.

Significant differences between the control and main groups when compared on the 3rd month from the disease onset were observed for general health parameters (main group 56.44 ± 1.68 points, control group 45.67 ± 4.98 points; $p < 0.05$), social functioning (main group 52.44 ± 1.97 points, control group 44.46 ± 2.95 points; $p < 0.05$) and role emotional functioning (main group 50.48 ± 2.09 points, control group 26.47 ± 2.17 points; $p < 0.05$). It should be underlined that 5 of the 8 parameters of life quality in the control group acquired positive changes during the restorative treatment of the ischemic stroke early recovery period, which is the time when the sanogenesis processes are most active and effective (Fig. 2).

The main group that received cognitive therapy gains improving 7 of 8 life quality parameters (Fig. 2), the cognitive strategy demonstrates the most significant results in the role-playing emotional functioning, i.e. there was an improvement in emotional state in everyday life, patients have got the ability to perform more than before treatment.

DISCUSSION

The revealed low levels of quality of life indicators in patients after ischemic stroke behind the scales PF, RP, GH, VT, SF, RE, and MH are consistent with the results of other studies [12, 13]. So, Prost A. et al defined, that the lowest QoL was found for the role limitations due to physical problems, general health, and vitality subscales in patients after ischemic stroke [12]. Jung S. H. et al. determined significant improvement in BBS, MBI, and PCS of the SF-36 component after the 4-week rehabilitation therapy in patients after ischemic stroke [13].

Our results are also confirmed by Cheiloudaki E. and Alexopoulos E. C. [14], who determined that patients after an ischemic stroke have rather low levels of their quality of life (the overall assessment of the quality of life according to the SS-QoL questionnaire was an average of 4.3 ± 0.7 range from 2.0 to 4.9) with lower values for subscales: Personality (3.4 ± 1.1), Social roles (3.9 ± 1.0), Energy (3.9 ± 1.2), Work/Productivity (4.1 ± 1.0), Thinking (4.2 ± 1.0) and Mood (4.3 ± 0.7). At the same time, using univariate analysis, they established that work/productivity-related quality of life was inversely associated with compliance (OR – 0.44; 95.0 % CI: 0.23–0.82).

Another study (Ramos-Lima M. J. M. et al [15]) determined that the average quality of life score (SS-QoL questionnaire) after an ischemic stroke was 151, indicating a rather low quality of life. The most vulnerable subscales after a stroke are probably defined for the following subscales: Work/Productivity, Social Roles, Personality, Energy, and Family Roles. Yes, it was determined to be probable ($p < 0.001$) that the lowest score of the quality of life according to the SS-QoL questionnaire after an ischemic stroke was obtained for the subscales: Work/Productivity (7.66 ± 4.78), Personality (8.24 ± 4.49), Energy (8.56 ± 4.82), Family Roles (8.56 ± 4.20), Thinking (9.26 ± 3.95) and Social Roles (11.71 ± 7.02). Also, probably ($p < 0.001$) lower quality of life was established in patients with worse functional status and greater clinical severity of stroke (Spearman's rank correlation coefficient for the modified Rankin scale -0.6843 and for the scale NIHSS – -0.5103).

CONCLUSIONS

1. Comprehensive rehabilitation measures in the early recovery period of ischemic stroke lead to the cognitive sphere advance in both groups as evidenced by a significant increase in the score of the Montreal Cognitive Assessment Scale (MoCA scale). It should be noted that in the main group underwent cognitive training treatment the effectiveness of therapy was probably higher, as proved by the average MoCA scale score reaching normal values.
2. Physical and emotional disorders of the acute period of ischemic stroke have a significant impact on quality of life: we observed low rates in physical functioning (PF), Role-playing physical functioning (RP), general health (GH), viability (VT), social functioning (SF), role-playing emotional functioning (RE), mental health (MH).
3. Cognitive rehabilitation affects the dynamics of life quality as evidenced by life quality increasing according to the SF-36 questionnaire in the main group (7 of 8 parameters), in the control group (5 of 8 parameters), corresponding to the return of patients to everyday environment.
4. Cognitive therapy has certain advantages in achieving positive dynamics of vital parameters, social functioning and emotional functioning, improving patients' cognitive sphere in the early recovery period of ischemic stroke. The study of cognitive training regimes peculiarities, in particular of patients with more severe deficient conditions in the late recovery period of ischemic stroke, can be considered as a research prospect.

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The ethical approval was obtained from Bioethics Committee of the Kharkiv National Medical University. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008, as well as the national law. Informed consent was obtained from all the patients included in the study.

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ORCID and contributionship:

Olga G. Morozova: 0000-0002-3088-624X [A, D-F]
Anna N. Kosheleva: 0000-0001-9923-8841 [D, E]
Bogdan S. Fedak: 0000-0003-2898-2141 [D, E]
Volodymyr I. Ponomaryov: 0000-0003-2513-3187 [D, E]
Aleksandr A. Yaroshevskiy: 0000-0002-2720-9985 [D]
Iryna M. Kravchenko: 0000-0003-4052-7045 [A-F]
Inna V. Reminiak: 0000-0003-1084-9203 [D]

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Volodymyr I. Ponomaryov
Educational and Scientific Medical Institute of the National Technical University «Kharkiv Polytechnic Institute»
79 Pushkinska St., 61022 Kharkiv, Ukraine
tel: +380637486769.
e-mail: ponomaryov_VI@ukr.net

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ORIGINAL ARTICLE

STUDY OF NEUROTICISM AND EXTRAVERSION AS PREDICTORS OF THE SYNDROME OF EMOTIONAL BURNOUT (EBS) IN STUDENTS

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Svitlana P. Palamar[1], Tetiana S. Gruzieva[2], Liudmyla L. Nezhyva[1], Viktor Y. Yelenskyi[3], Nina M. Rudenko[1], Mykola M. Khomik[4], Yuriy Y. Savchenko[1]

[1]BORYS GRINCHENKO KYIV UNIVERSITY, KYIV, UKRAINE
[2]BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE
[3] STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE
[4]THE NATIONAL DEFENSE UNIVERSITY OF UKRAINE NAMED AFTER IVAN CHERNIAKHOVSKYI, KYIV, UKRAINE

ABSTRACT

The aim: To investigate internal factors – neuroticism and extroversion, which can be predictors of emotional burnout syndrome and their prevalence among student youth.

Materials and methods: Used a complex of methods: theoretical – theoretical analysis, synthesis, systematization; sociological method of questioning; empirical: observation, testing-Eysenck's methods for assessing the impact of neuroticism and externality; statistical. The object of the research is the process of influence of personal characteristics (individual factors) on the development and spread of EBS among students. Subject – personal characteristics (individual factors) of students – extraversion and neuroticism. The number of respondents was 610 students.

Results: A study of the personal characteristics of neuroticism and extraversion, which can be predictors in the genesis of EBS, was conducted. It has been established that several negative internal factors influence students. The significant prevalence of internal risk factors of EBS indicates the need for a comprehensive approach to its prevention and the need for the development and application of modern adequate methods, forms, and methods of prevention.

Conclusions: The presence and influence of internal factors on the development of EBS have been theoretically proven. It has been established that there is a significant propagation of personal characteristics that may have signs of negative internal factors. The need for preventive measures for the development of EBS among students has been revealed.

KEY WORDS: emotional burnout syndrome (EBS), internal factors, neuroticism, extraversion, introversion

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INTRODUCTION

Burnout syndrome is a medical problem worldwide. It is based on mental and behavioral changes [1,2]. This problem is characterized by significant destructive consequences both for family and professional relationships and for society as a whole. EBS is widespread in the society of various countries. Thus, the syndrome is noted in up to 40% of patients working in the public sector of Canada and the USA. The percentage of diseases among doctors, nurses, and teachers varies between 51-57%.

Based on the multifactorial theory of the disease [3, 4], three components are inherent in EBS: emotional exhaustion, depersonalization, and reduction of personal achievements. With emotional exhaustion, patients experience emotional tension and overstrain, indicating a feeling of exhaustion of their resources, which is followed by a feeling of emptiness. As a result, all emotions are muted and lose their brightness. Depersonalization is characterized by a callous attitude towards acquaintances, relatives, partners, clients, and patients. A person affected by EBS shows a lack of empathy and formal and impersonal communication [5, 6, 7]. The reduction of personal achievements is characterized by the devaluation of personal activity and dissatisfaction with one's activities and successes. As a result, patients complain of a sense of meaninglessness in life and apathy [8, 9].

It is known that EBS depends on the activity (education, work) of a person. At the same time, a feeling of disappointment appears, which can have a pronounced character up to despair [10]. Patients point to the difference, which acquires a sense of dissonance, between personal contribution and the received award [11].

THE AIM

To investigate internal factors – neuroticism and extroversion, which can be predictors of emotional burnout syndrome and their prevalence among student youth.

MATERIALS AND METHODS

Used a complex of methods – theoretical (theoretical analysis, synthesis, systematization) – for generalization theoretical approaches to determining the essence and characteristics of the impact of neuroticism and manifestations of externality on the personality; sociological method of questioning (in order to obtain information about the feelings and motives of a person's behavior); empirical (observation, testing-Eysenck's methods for assessing the impact of neuroticism and e externality); statistical (method of mathematical statistics to determine the validity and reliability of the results obtained, comparison of experimental data with the initial ones). The object of the research is the process of influence of personal characteristics (individual factors) on the development and spread of EBS among students. Subject – personal characteristics (individual factors) of students – extraversion and neuroticism. The number of respondents was 610 students. At the same time, the results of the questionnaires of 54 respondents were not considered due to insincerity in the answers. Insincerity in answers was determined by the scale of lies according to the Eysenck method (EPI, option B). The research considered the results of a survey of 556 people, of which 228 people study at the Bogomolets National Medical University and 328 at the Borys Grinchenko Kyiv University, which is 41.01% and 58.99% respectively.

RESULTS

EBS develops more often in people who communicate a lot in their profession. This category includes doctors, nurses, teachers, social workers, etc. Scientists note a high percentage of EBS, up to 50%, among doctors and students, in particular doctors [12, 13]. The existence of the problem of EBS, 45-52% among students, is confirmed by many domestic and foreign scientists [5-7, 12].

Many factors contribute to the development of EBS among students. They are classified as external or professional and individual. It is known that motivational factors are the leading factors for the successful adaptation of students to study and that high motivation to study is a safeguard against emotional burnout. Therefore, it can be argued that individual factors are leading. These include age, gender, education, marital status, work experience, and personal characteristics (endurance, locus of control, resistance style, self-esteem, anxiety, neuroticism, and extraversion). Many researchers prefer personal characteristics (low self-esteem, high neuroticism, anxiety, externality) in the development of EBS [14].

Neuroticism is a personality trait characterized by emotional instability, anxiety, fear, rapid mood swings, low self-esteem, and sometimes vegetative disorders. In a broad sense, neuroticism is defined as the inability to effectively regulate negative emotions [14, 15]. Neuroticism is one of the strong predictors of the development of mental disorders. Scientists Clark & Watson, Costa & McCare, Tellegen, Warr et al., Watson & Clark indicate a strong dependence on the presence of neuroticism and negative affect. According to Elliot and Thrash, neuroticism, negative emotionality and behavioral inhibition form a factor in a person, which the authors called "avoidance temperament". Scientists have found a strong positive relationship between neuroticism and stress during exams in students. It is believed that the components of neuroticism are excitement, insecurity, and emotionality. Neurotic individuals often have discomfort and a feeling of anxiety during social and communicative stress. Such people are focused on their emotional experiences, and a high level of neuroticism negatively affects personal everyday and professional life. A high level of neuroticism prevents the creation of a pleasant atmosphere of communication, which is unacceptable for professions where communication is a tool and has a negative impact during training.

Personal characteristics of a person in the theory of personality also include introversion and extroversion. Extroverts are a type of personality that focuses on the outside world and the people that surround this personality. Extroverts like to communicate with people and attract people's attention wherever they are – whether at public speeches or informal events. Inactivity and loneliness deprive them of a sense of the meaning of life. According to Leonhard, an extrovert is a person without free will, subject to external influence, and an introvert is a strong-willed person. Introverts are characterized by restraint, pedantry, punctuality, and few words. It must be remembered that Leonhard's typology is psychiatric, not psychological, it is used to determine pathology. In psychology, for characterizing the personality, but not for the definition of pathology, such psychological terms as the locus of control (internal and external), externalism, and internalism (Akoff and Emery), etc., are close to Leonhard's interpretation.

The terms "extraversion" and "introversion" are also used in the Myers-Briggs typology, in socionics, in psychosophy, and in other modern questionnaires and diagnostic methods, where their interpretation has its specificity.

Why do young people, who are students, lose interest in learning? Why does the motivation to learn a profession, which should become the basis of all life, the foundation of well-being, become less than some other circumstances? Explanations may be different. Psychologists, more often than not, explain this with the development of EBS and indicate that anyone can suffer from this ailment.

To study this phenomenon, its possible development and spread among students, we conducted a study of the personal characteristics of neuroticism and extraversion, which can be predictors in the genesis of EBS.

An anonymous questionnaire survey was conducted among students of the third and fourth years of medical faculties studying at the Bogomolets National Medical University and among students of the first, second, third, fourth, and fifth courses of faculties of the Borys Grinchenko Kyiv University. The data are presented in Table I.

Analyzing the received data, by processing the questionnaires, according to the Eysenck method regarding the indicators of extroversion/introversion among all respondents, the result was obtained, according to which the

Table I. Number of respondents

№	Respondents	Quantity	Percentage
1	O.O. Bogomolets National Medical University	228	41,01%
2	Borys Grinchenko Kyiv University	328	58,99%
3	The total amount	556	100,00%
4	Total amount of surveyed by the questionnaire method	610	
5	Answers not considered	54	

Table II. Indicators of extraversion and introversion

	Deep introvert		Introvert		Ambivert		Extravert		Bright extravert	
	Amount	%	Amount	%	Amount	%	Amount	%	Amount	%
O.O. Bogomolets National Medical University	---	---	28	12,28% ±2,17%	161	70,61% ±3,02%	34	14,91% ±2,36%	5	2,19% ±0,97%
Borys Grinchenko Kyiv University	8	2,44% ±0,85%	35	10,67% ±1,7%	183	55,79% ±2,74%	88	26,83% ±2,45%	14	4,27% ±1,12%
Total	8	1,44% ±0,5%	63	11,33% ±1,34%	344	61,87% ±2,06%	122	21,94% ±1,76%	19	3,42% ±0,77%

Table III. Indicators of neuroticism

	Very high level		High level		Average level		Low level	
	Amount	%	Amount	%	Amount	%	Amount	%
Bogomolets National Medical University	36	15,79% ±2,41%	92	40,35% ±3,25%	87	38,16% ±3,21%	13	5,7% ±1,54%
Borys Grinchenko Kyiv University	41	12,5% ±1,83%	104	31,71% ±2,57%	158	48,17% ±2,76%	25	7,62% ±1,46%
Total	77	13,85% ±1,46%	196	35,25% ±2,03%	245	44,06% ±2,11%	38	6,84% ±1,07%

Table IV. Intensive rate and extensive indicator

Students	Intensive rate (number of cases per 100 students)		Extensive indicator, %	
	Extraversion	Neuroticism	Extraversion	Neuroticism
NMU of O.O. Bogomolets	37.500	49.460	33.243	39.913
Borys Grinchenko Kyiv University	31.098	25.360	27.568	20.464
Total	44.207	49.101	39.189	39.623

largest number of surveyed students were ambiverts – 344 people, which is 61.87%. Introverts and deep introverts – 63 students (11.33%) and 8 (1.44%), respectively, which makes a total of 71 (12.77%). Extroverts and bright extroverts – 122 (21.94%) and 19 (3.42%), respectively, which together makes 141 (25.36%). So, the research established that there are 70 more people (12.59%) with extroversion, who have a higher risk of emotional burnout, than with introversion, who have a reduced risk of developing SEV (Table II, Fig. 1).

When comparing the extroversion/introversion index (Fig. 1) among students of two universities, it was found that there are fewer extroverts among medical students, the index is 14.91% versus 26.83% among Borys Grinchenko Kyiv University students. This also applies to bright extroverts. The indicator is 2.19% among medical students, against 4.27% among Borys Grinchenko Kyiv University students (Fig. 2).

Manifestations of the personal characteristic – extroversion are less among medical students by 14%. The number of people with introversion is almost the same, according to the study, medical students have less by only 0.83% (Fig. 3 and Fig. 4).

The results of the study of the level of neuroticism, high indicators of which in an individual are a prerequisite for the occurrence of emotional burnout, indicate a very high level – in 77 students (13.85%) and a high level in 196 students (35.25%) (Table III, Fig. 5).

Among the respondents, 245 (44.06%) had an average level of neuroticism and 38 (6.84%) had a low level of neuroticism. A very low level was not detected. So, in 273 people (49.1%), which is almost half of all respondents, an increased risk of emotional burnout associated with a high level of neuroticism was found.

Research has established that the prevalence rate of a high level of neuroticism among students at different universities is different. So, at Bogomolets National Medical University

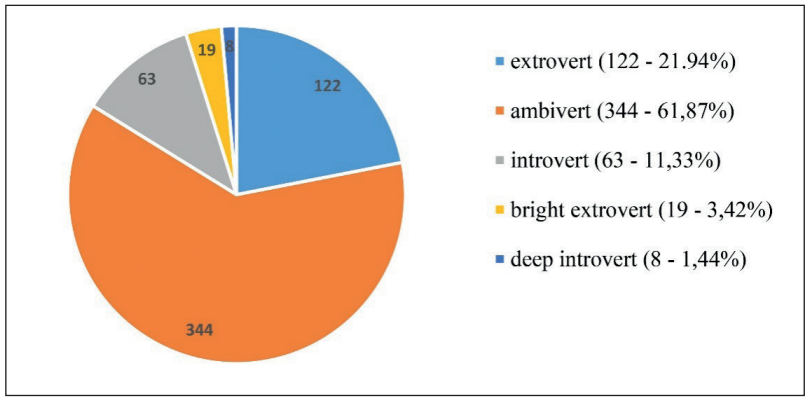

Fig. 1. Extraversion/introversion (quantity)

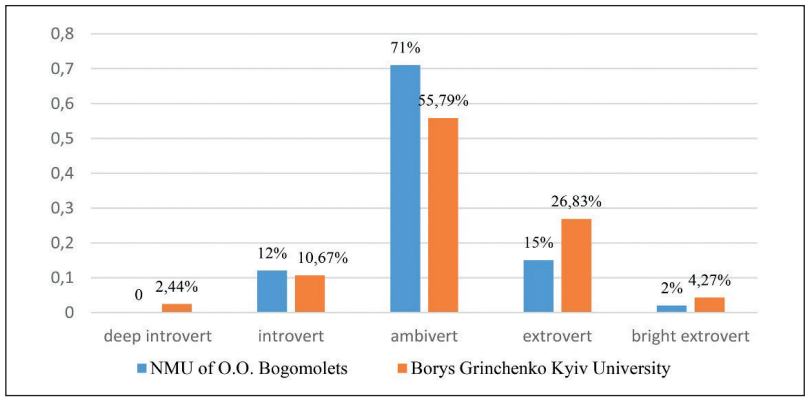

Fig. 2. Expression of extraversion/introversion (comparison)

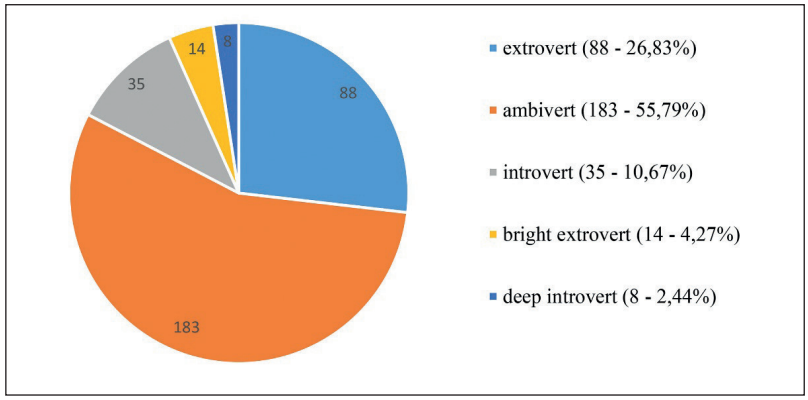

Fig. 3. Expression of extroversion and introversion among students of Borys Grinchenko Kyiv University

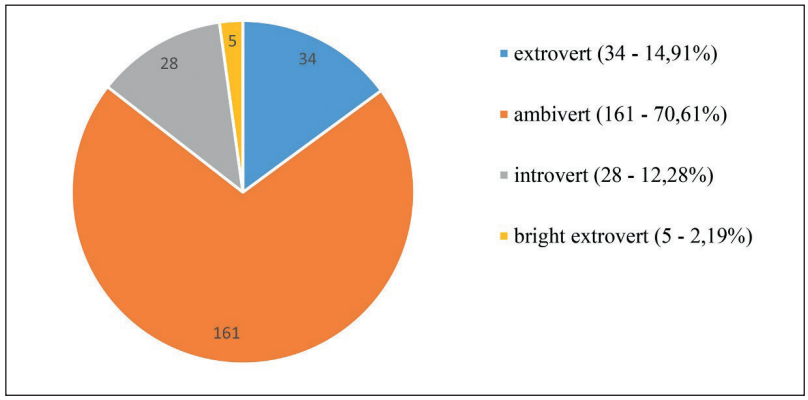

Fig. 4. Expression of extroversion and introversion among students of Bogomolets National Medical University

students with a high and very high level of neuroticism are 11.93% more than at Borys Grinchenko Kyiv University, and with a low level of neuroticism, it is 1.92% less (Fig. 6-8).

An intensive index was calculated to characterize the frequency, level, and distribution of negative internal factors (extraversion, neuroticism) among students.

An extensive indicator of personal characteristics was calculated to study the specific weight, structure, distribution, and composition of negative internal factors and analysis of the distribution into components (Table IV).

According to the calculation data, among the students of Bogomolets National Medical University, extroversion

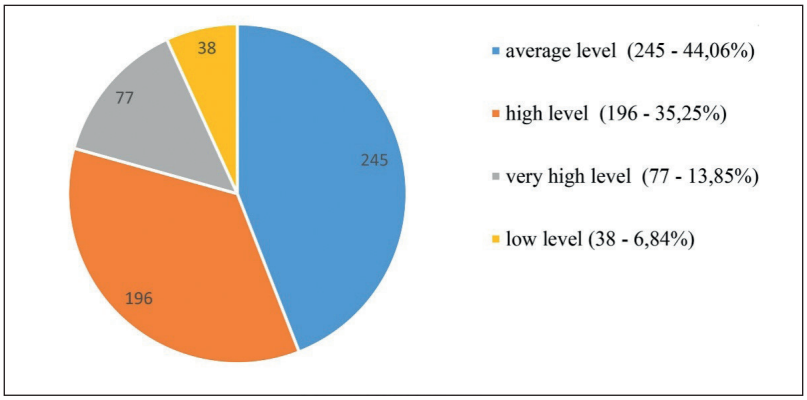

Fig. 5. Level of neuroticism

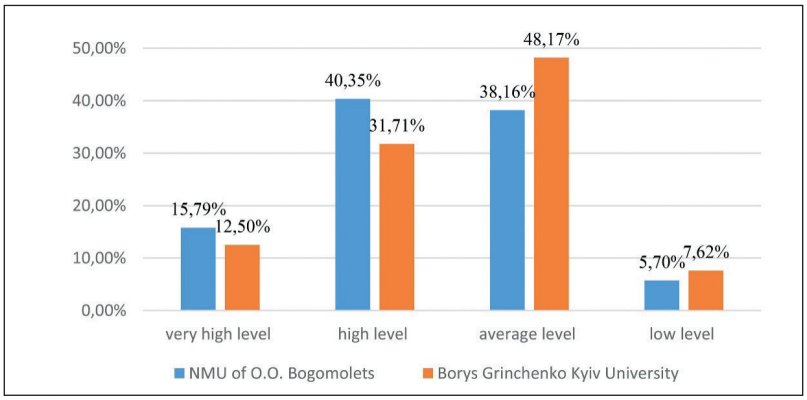

Fig. 6. Level of neuroticism (comparison)

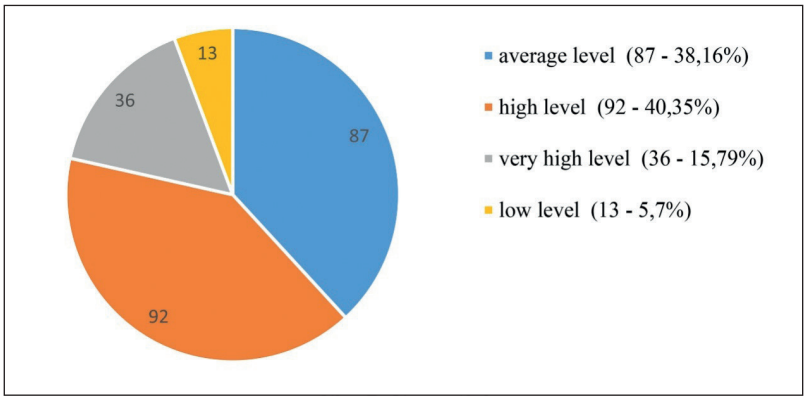

Fig. 7. The level of the neuroticism of students of Bogomolets National Medical University

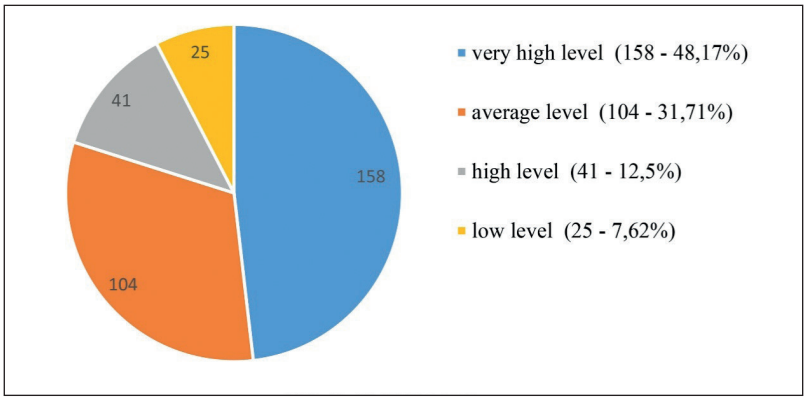

Fig. 8. The level of neuroticism among students of Borys Grinchenko Kyiv University

and neuroticism are more common than among students of Borys Grinchenko Kyiv University, respectively, by 17.105; 6,402 and 24.1 cases. The prevalence of negative internal factors is quite high among students. The specific gravity, structure, and distribution of internal factors in students are correlated with the frequency, level, and distribution of internal factors.

When analyzing the received data of the empirical study, it was found that the number of high indicators of personal characteristics exceeds the number of surveyed students.

This indicates that the interviewed respondents are negatively affected by several internal factors, which require further research.

DISCUSSION

The goal of the study was achieved, and internal factors were identified that can be predictors of EBS. It was established that the influence of internal factors on the student can be from one group or several.

When comparing indicators of the influence of negative internal factors on students of two universities, it was found that Borys Grinchenko Kyiv University has 12.71% more students who do not belong to risk groups than Bogomolets National Medical University. Also, Borys Grinchenko Kyiv University has 2.13% more students belonging to one of the groups. Students negatively affected by two risk groups are 17.28% more among medical students.

Manifestations of emotional burnout syndrome in students include decreased motivation to study, dissatisfaction with the learning process, conflicts with colleagues and teachers, chronic fatigue, exhaustion, nervousness, unreasonable excitement, boredom, longing, irritability, and distancing from colleagues and relatives. The specified symptoms in patients are not detected simultaneously and do not appear with the same force. There are always individual manifestations and variations because EBS is a reaction of an individual personality. EBS is a complex of experiences and responses to them in the form of behavior, which is caused by a decrease in work capacity and physical and mental well-being in interpersonal relationships [11].

CONCLUSIONS

The paper analyzes theoretical approaches to studying the peculiarities of psychological factors of emotional burnout of students. The presence and influence of internal factors on the development of EBS have been theoretically proven. The methods used to study the internal psychological factors of students have been selected. The peculiarity of the influence of internal factors (personal characteristics) on the possibility of the development of EBS among students has been determined.

Empirical research has established a significant prevalence of personal characteristics, which may have signs of negative internal factors, among students. It was found that medical students studying at the Bogomolets National Medical University feel the influence of negative internal factors more than students studying at the Borys Grinchenko Kyiv University.

It has been established that several negative internal factors influence students. Features of the possible manifestation and prevalence of internal risk factors of EBS are the basis of unhealthy behavior among student youth and indicate the need for a comprehensive approach to its prevention and the need for the development and application of modern adequate methods, forms, and methods of prevention.

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ORCID and contributionship:
Svitlana P. Palamar: 0000-0001-6123-241X [A-F]
Tetiana S. Gruzieva: 0000-0001-9254-7561 [E, F]
Liudmyla L. Nezhyva: 0000-0001-9520-0694 [A-C]
Viktor Y. Yelenskyi: 0000-0002-7605-8001 [A, B, C]
Nina M. Rudenko: 0000-0002-6274-9311 [E, F]
Mykola M. Khomik: 0000-0002-1201-7702 [F]
Yuriy Y. Savchenko: 0000-0003-3662-2787 [A, E, F]

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CORRESPONDING AUTHOR
Svitlana P. Palamar
Borys Grinchenko Kyiv University
18/2 Shamo Blvd, 01601 Kyiv, Ukraine
tel: +380507444635
e-mail: svetlana_03@ukr.net

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ORIGINAL ARTICLE

SAFETY OF PROPOFOL ANESTHESIA DURING NEUROSURGICAL OPERATIONS

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Hennadiy P. Pasichnyk[1,4], Jan Bilawicz[2,5], Yaroslav M. Pidhirnyj[3], Romana O. Merza[3]

[1]STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

[2]MEDICAL UNIVERSITY OF WARSAW, WARSAW, POLAND

[3]DANYLO HALYTSKYI NATIONAL MEDICAL UNIVERSITY, LVIV, UKRAINE

[4]SHUPYK NATIONAL HEALTHCARE UNIVERSITY OF UKRAINE, KYIV, UKRAINE

[5]INSTITUTE OF PSYCHIATRY AND NEUROLOGY OF WARSAW, WARSAW, POLAND

ABSTRACT

The aim: The purpose of this study was to assess the safety of propofol use during neurosurgical operations of different durations.

Materials and methods: 72 patients were divided into three groups depending on the type of operations; it were group 1 (ventriculostomy), group 2 (hematoma removal), and group 3 (tumor removal), the anesthesia durations in these groups were 65±5 min, 145±7 min and 225±10 min, respectively. Total propofol doses in patients of groups 1, 2, and 3 were 452±22 mg, 710±42 mg, and 966±51 mg, respectively. Before intervention and 1 h post operation, blood gas composition, serum levels of transaminase, triglycerides, creatine phosphokinase, and potassium, rate of urine output, level of mean arterial pressure, and heart rhythm rate were determined.

Results: No significant deviations concerning hemodynamic indicators, blood gas composition, changes of creatine kinase activity were found for any group patients during the perioperative period. The rate of urine output in all patients reached above 0.5 ml/kg/h without saluretics use. The deviated transaminase values returned to their normal ones during 24 h post intervention. The triglycerides levels were in normal range proving the absence of propofol doses used on the lipid metabolism.

Conclusions: Anesthetic protection of neurosurgical interventions using propofol in doses 2.5-3 mg/kg and 3.60.3 mg/kg/h for induction anesthesia and for anesthesia support, respectively, is safe and does not lead to dangerous undesired consequences. However, the propofol use for prolonged patient sedation and his/her adaptation for prolonged lung ventilation needs further studies.

KEY WORDS: propofol, propofol infusion syndrome (PRIS), anesthesia, dose

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INTRODUCTION

After propofol implementation to clinical practice, it became pretty fast an alternative of other intravenous hypnotics due to its gentle introduction to anesthesia, minimal hemodynamic effect, and fairly quick and predictable anesthesia completion. Due to quick onset of action, distribution phase, and short half-period, propofol is used successfully both for anesthesia induction and support and for continuous patient sedation in intensive therapy clinics [1].

However, in 1991 a case of propofol "withdrawal syndrome" was described after two-week propofol sedation of a one-and-half year girl with severe burns [2]. In 1992, a report was published concerning limb convulsions in two children (2½ and 4 years old) after cessation of continuous high dose propofol infusions, the children having been intubated because the croup as a result of acute respiratory virus infections (ARVIs). Both children made a full recovery [3]. However, in the same time a communication appeared in the "British Medical Journal" about five dead children (aged from four weeks up to 6 years); they all were intubated because of severe ARVIs and were sedated by high propofol doses; all of them had lipidemic blood sera and metabolic acidosis and died from myocardial insufficiency accompanied by bradyarrhythmia. The autopsies of patients having been demonstrated no convincing data, the authors proposed the proposal-carrier emulsion to be a damaging factor in children organisms [4]. Since then, a more meticulous study of propofol pharmacokinetics and pharmacodynamics has begun.

Besides, the propofol infusion syndrome (PRIS) attracted attention due to a publication indicating the propofol to be a single factor of complications development in neurosurgical patients [5].

The PRIS may also develop soon after the introduction of low propofol doses (83 μg/kg/min) during a short period of time. The frequency of PRIS development reaches approximately 1% [6, 7]. It proves the clinicians are to follow closely the PRIS signs appearance at once following the propofol introduction and during all the treatment period regardless of this drug dose.

Table I. Indicators in patients before and after propofol-using anesthesia

INDICATOR	NORM	Group 1		Group 2		Group 3	
		2st stage	2nd stage	1st stage	2nd stage	1st stage	2nd stage
MAP, mm Hg	>65	70±6	77±8	67±7	68±5	66±6	70±10
Heart rate per minute	70-80	78±4	80±4	72±5	82±4	78±6	78±2
pH	7.35-7.45	7.37±0.12	7.27±0.13	7.43±0.12	7.40±0.18	7.37±0.10	7.29±0.12
pO_2, mm Hg	83-108	89±10	90±10	87±8	89±10	89±10	92±4
pCO_2, mm Hg	36-44	42±6	40±6	48±6	40±6	48±6	42±2
AST, U/l	<35	32±6	34±6	32±5	35±4	34±4	40±6
ALT, U/l	<45	42±6	44±6	34±2	38±8	32±6	48±2
K^+, mM/l	4.5-5.4	4.5±0.6	4.0±0.6	4.9±0.2	4.6±0.9	4.4±0.4	4.5±0.6
Rate of urine output, ml/min	>0.5	0.6±0.5	0.8±0.3	0.6±0.5	0.9±0.7	0.5±0.1	0.6±0.5
Creatine phosphokinase (MM-isomer), U/l	24-170	98±12	99±11	98±6	108±12	128±23	139±9
Triglycerides, mM/l	0-1.7	0.6±0.2	0.6±0.1	0.4±0.3	0.5±0.1	0.8±0.1	0.7±0.2

THE AIM

The aim of this investigation was the evaluation of propofol use safety during neurosurgical interventions of different durations.

MATERIALS AND METHODS

We have investigated 72 patients having undergone neurosurgical interventions – ventriculostomies, removal of intracranial hematomas, and intracerebral tumors. According to the ASA, the anesthesia risks were assessed as a risk of II-III degrees.

The study was conducted according to the principles of the Council of Europe Convention on Human Rights and Biomedicine, World Medical Association Declaration of Helsinki on the ethical principles for medical research involving human subjects, and current Ukrainian regulations. The local ethics committee approved the study protocol. All the patients signed an informed consent.

All the patients were divided into three groups according to the anesthesia duration, these indicators having been 65±5 min, 145±7 min and 225±10 min for patients of groups 1, 2, and 3, respectively. The patients of the group 1 underwent endoscopic ventriculostomy; decompressive craniotomy accompanied by subdural hematoma removal and intracranial tumor removal were realized for patients of groups 2 and 3, respectively. In all cases, propofol (2.5-3 mg/kg) was taken for induction anesthesia. After fentanyl (100 μg) and myorelaxants introduction, tracheal intubation was made followed by the establishment of mechanical lung ventilation. The respiratory support was carried out using an anesthesia and respiratory station «Drager Primus Anesthesia Machine + Sevofluran» and an oxygen-air mixture containing FiO2 (40 %). To support the state of anesthesia, propofol was taken at a dose 3.6±0.3 mg/kg/h. The total propofol doses were 452±22 mg, 710±42 mg, and 966±51 mg for patients of groups 1, 2, and 3, respectively.

In all cases, diazepine tranquilizers (diazepam) were used for premedication 40 min before the start of intervention.

The rate of infusion therapy (balanced crystalloids) during surgery was 2-3 ml/kg/h.

Blood gases as well as the levels of transaminases, triglycerides, creatine phosphatase (its MM-isomer), and potassium ions levels were determined in all cases before surgery (1st stage) and in 1 h following the surgery completion (2nd stage); rate of urine output, level of mean arterial pressure (MAP), and heart rate were also checked.

Our data are presented as an arithmetic mean ± standard deviation (M ± δ). Examination of the correspondence of the indicator distribution to normal ones was carried out according to the Kolmogorov-Smirnov consistency criterion, comparison of indicators in progressive dynamics was realized using the Wilcoxon criterion [8].

RESULTS

According to the data available [9,10], the PRIS includes in most cases the following clinical symptoms: incomprehensive metabolic acidosis, lactic acidosis, progressing and refractory bradycardia, refractory heart insufficiency and/or cardiovascular collapse, hepatomegaly, hyperglyceridemia, signs of muscle damage (increased levels of creatine phosphokinase, myoglobulinemia and/or myoglobinuria), acute kidney failure, fever. We decided to investigate some signs able to testify the development of different symptoms demonstrating the negative propofol effect in neurosurgical patients. Our results are presented in the Table I.

According to results of our investigations, we had no statistically significant deviations in hemodynamics data in all three patient groups during all the period of anesthesia and postoperative period. We did not observe any cardiac arrhythmias having being seen on the cardio monitor and detected in ECG data having being written on paper media with an interval of 15 min. All the further ECG results were analyzed together with specialists in functional diagnostics and cardiology.

The indicators of blood gases in our patients had no significant deviations both before interventions and during postoperative period.

The rate of urine output in all propofol-anesthetized patients was above 0.5 ml/kg/h without saluretics use.

We have not found any changes of the creatine phosphokinase (its MM-isomer) activity. In patients of the group 3, the transaminase deviations from the upper normal limit returned to their normal activity in 24 h after surgeries.

The triglyceride levels in our patients did not overstep the bounds of normal physiological ranges; we evaluate these data as the absence of propofol effect in these doses on the lipid metabolism.

DISCUSSION

While carrying out our investigation we have found out the propofol use in doses taken for neurosurgical interventions of varying complexity and duration is rather safe. We have not seen any significant changes concerning different organs activity and any PRIS signs.

The propofol infusion syndrome is interpreted as mitochondrial lipid metabolism damage being a consequence of continuous use of this drug. It is accompanied by the development of hypertriglyceridemia, metabolic acidosis, arrhythmias leading to refractory bradycardia, hyperlipidemia, rhabdomyolysis, and myoglobinemia [11].

The PRIS is thought to develop as a result of fatty acids utilization damage in mitochondria leading to some changes in the chain of tissue respiration. The role of mitochondrial defects in this process is not proved; however, there are some suspicions concerning individual peculiarities of some persons prone to PRIS development. There are also hypotheses taking into consideration some metabolite-mediated damages and neuro-muscular defects [12].

In some literary sources describing the PRIS pathophysiology there are opinions propofol to increase the activity of malonyl-coenzyme A leading to the inhibition of carnitine palmitoyl transferase 1. As a result, long-chain fatty acids become unable to enter the mitochondria [13]. Beta-spiral oxidation and respiratory chain disengage, so neither middle-chained nor short-chain free fatty acids cannot be utilized; this circumstance leads to myocytolysis process. The energy supply is lower than the need for it; the energy deficiency leads to necrosis in cardiomyocytes and peripheral muscles. Besides, free fatty acid accumulation becomes a cause of arrhythmias development.

At the same time, some researchers underline the propofol to possess negative inotropic effect due to the decrease of sympathetic tone and antagonism to beta-blockers and calcium channels. It leads to increased body need for catecholamine supporting the hemodynamics stability. Because of the increase of "catecholamine wave" it is necessary to speed up the pace of propofol infusion aiming to assure the sufficient sedation [14]. In such a way, "the enchanted circle" closes.

To avoid the PRIS development, it is necessary to adhere strictly to the algorithm including additional examination of patients for whom propofol should be used for anesthesia during interventions of different duration as well as for medical sedation in intensive care units; it is also necessary to determine the levels of triglycerides, lactate dehydrogenase, creatine phosphokinase, transaminases etc. For the same purpose, propofol dosing and duration of application should be optimized. To reduce the lipid load and to prevent any possible bacterial contamination, it would be better to apply 2% propofol-EDTA solution and its combination with other hypnotics, pain killer drugs, benzodiazepines [15].

In the Discussion the authors demonstrate their results achieved for their scientific purposes; they consider the originality of these results and of their methodological approaches as well as some limitations of data obtained.

CONCLUSIONS

Regardless the anesthesia duration, the propofol use for anesthesia of neurosurgical interventions in doses of 2.5-3.0 mg and 3.60.3 mg/kg/h for induction anesthesia and for the support of anesthesia is a safe approach; it does not lead to undesired effects in the perioperative period.

The safety problem of propofol use for patient prolonged sedation and his/her adaptation for long mechanical lung ventilation needs further studies.

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ORCID and contributionship:
Hennadiy P. Pasichnyk:0000-0002-4481-5696 [A,B,D,F]
Jan Biławicz: 0000-0003-4129-9275 [A,B,E]
Yaroslav M. Pidhirnyj: 0000-0002-6926-9257 [B-E]
Romana O. Merza:0000-0002-4746-9004 [B,C]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Hennadiy P. Pasichnyk
State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department
5 Verhnia St., 01014 Kyiv, Ukraine
tel: +380631357688
e-mail: docpasichnyk@gmail.com

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ORIGINAL ARTICLE

CLINICAL OUTCOMES AND COMPLICATIONS OF ENDOVASCULAR SURGERY IN PATIENTS WITH CHRONIC LIMB-THREATENING ISCHEMIA

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Vasyl V. Shaprynskyi[1], Yevhen V. Shaprynskyi[2]

[1]STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

[2]NATIONAL PIROGOV MEMORIAL MEDICAL UNIVERSITY, VINNYTSIA, UKRAINE

ABSTRACT

The aim: To review the results of endovascular treatment in patients with chronic threatening ischemia of lower extremities as well as to assess the level of complications developed after the use of modern endovascular technologies.

Materials and methods: 243 patients with occlusive-stenotic lesions of major arteries of infrarenal aorta, operated on by various endovascular techniques, were studied. 51 of them (20.98%) had multi-level lesions. All experimental group patients (83) were thoroughly evaluated preoperatively including assessment of probable development of arterial thrombosis of affected extremity after the surgery. Besides, endovascular treatment algorithm developed and introduced by the authors on the basis of individual anatomical and hemodynamic parameters was used.

Results: Thrombosis was the major early postoperative complication in both study groups, being registered in 21 patients (10.6%). The incidence of thrombosis was statistically higher in the control group as compared to experimental group – 11.53% and 7.14%, respectively ($p<0.05$). 15 patients of both groups underwent amputations – 12 patients (7.5%) in the control group, and 3 patients (3.6%) in experimental group. Early postoperative mortality rate was 2.56% in the control group, while there were no deaths in experimental group in early postoperative period.

Conclusions: Continuous ultrasound monitoring, avoidance of subintimal positioning of endovascular devices, use of rotary-mechanical thromboaspiration, drug-coated balloons and stents, regional thrombolytic therapy, as well as the concept of angiosome-directed therapy used in the study for restoration of artery patency, made it possible to improve treatment outcomes and decrease complications.

KEY WORDS: atherosclerosis, critical ischemia, endovascular treatment

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INTRODUCTION

Nowadays, endovascular techniques proved to be an effective alternative to traditional surgeries due to a number of advantages: lower incidence of surgical injury, precise imaging of occlusive-stenotic artery lesions, accurate positioning of delivery devices, lower operative risk, shorter hospital stay, fewer perioperative complications and lower mortality rate [1, 2].

Thrombosis secondary to arterial dissection or residual stenosis is known to be the major early postoperative complication after lower extremity revascularization via endovascular approach. The incidence of early postoperative thrombosis ranges from 1–3% to 10–25% [3]. It occurs mostly in the femoral-popliteal region. Poor outflow pathways and their inadequate preoperative and intraoperative assessment can cause thrombosis as well [4, 5].

Zimmermann A, Ludwig U, Eckstein HH (2016) emphasize the importance of determining true indications for endovascular treatment of critical limb ischemia. They define three groups of most common probable complications after endovascular interventions: those related to endovascular access, complications depending on the method of percutaneous transluminal angioplasty (PTA), and the third group is represented by general complications [6]. Whatever the complications, they significantly worsen short-term results of treatment and indirectly affect long-term outcomes.

THE AIM

The aim of the study was to review the results of endovascular treatment in patients with chronic threatening ischemia of lower extremities as well as to assess the level of complications developed after the use of modern endovascular technologies.

MATERIALS AND METHODS

The study was conducted in compliance with the major principles of GCP guidelines (1996), Council of Europe Convention on Human Rights and Biomedicine (1997), World Medical Association Declaration of Helsinki on

ethical principles for medical research involving human subjects (1964-2000) and Order of Ministry of Health of Ukraine № 281 of November 1, 2000, being approved by the ethics committee at State Research Institution «Scientific and Practical Center for Preventive and Clinical Medicine» of State Administrative Department (Order № 112 of April1, 2010).

In the center of minimally invasive surgery at State Research Institution "Scientific and practical center of preventive and clinical medicine" (Kyiv), 243 in-patients with occlusive-stenotic lesions of major arteries of infrarenal aorta operated on by various endovascular techniques from 2014 to 2022, were studied. 51 patients (20.98%) had multi-layer lesions. There were 175 males (72.0%) and 68 females (28.0%), their age ranging from 46 to 86 years. The right lower extremity was affected more frequently than the left one – 148 patients (60.9%) and 95 patients (39.1%), respectively.

Rutherford classification of chronic lower extremity ischemia (1997) was used in the study. According to this classification, 43 patients (17.69%) had stage 3, 74 patients (30.45%) – stage 4, 69 patients (28.38%) – stage 5, 55 patients (22.63%) – stage 6.

All the patients were divided into two groups. The control group consisted of 160 patients (65.8%) operated on in the period of 2014-2018; they underwent routine examinations and standard treatment. 83 patients (34.2%) who underwent endovascular surgery in 2019-2022 were included in experimental group. All experimental group patients were thoroughly evaluated preoperatively including assessment of probable development of arterial thrombosis of affected extremity after the surgery. Besides, endovascular treatment algorithm developed and introduced by the authors on the basis of individual anatomical and hemodynamic parameters, was used in this group. Among 243 patients, 25 (10.3%) had previously undergone surgery at other hospitals.

Treatment of patients in experimental group included restoration of blood flow in peripheral arteries on the basis of angiosome concept using drug-coated balloons and stents, and some patients received regional thrombolytic therapy. It should be noted that all puncture techniques in experimental group were performed under ultrasound guidance. Besides, ultrasound intraoperative monitoring of arterial blood flow was performed as well.

Balloons and stents coated with special drugs (paclitaxel), which are known to decrease the risk of restenosis after angioplasty of atherosclerotic segments, were used in 52 cases (67.5%). In 46 of them (88.5%), angioplasty was performed using drug-coated balloons, while 6 patients underwent angioplasty with uncoated balloons but with drug-eluting stents.

Regional fibrinolytic therapy was the first stage of treatment in 18 (21.7%) patients with arterial thrombosis because of stenotic lesions. The patency of affected segments was thus partially restored followed by standard endovascular techniques. Thrombosis of tibial segments developed after angioplasty in 4 patients after successful intraoperative regional fibrinolytic therapy.

Either streptokinase or alteplase solution was used for regional fibrinolytic therapy. Alteplase administration regimen suggested and introduced in clinical practice by the authors was similar to acute ischemic stroke therapy principle. Intraarterial bolus dose of alteplase was 10 mg over 1-2 minutes, and the remainder 90 mg was infused over two hours, followed by regional administration of heparin solution infused at a dose of 1000 units/hour for 10-14 hours.

According to anatomic region affected, all 243 patients with occlusive-stenotic lesions of infrarenal aortic branches underwent endovascular reconstructions on the following segments: aortoiliac – 4, iliofemoral – 14, femoropopliteal – 92, popliteal-tibial – 84 and tibial-pedal – 49. Indications for endovascular surgery were based on recommendations of TASK II classification.

Endovascular operations were performed under local infiltration anesthesia using 2% lidocaine solution with intravenous sedation. Needle puncture of the artery with subsequent introducer placement was performed by Seldinger technique. In experimental group, introducer placement was performed under ultrasound guidance minimizing the number of artery punctures, thus decreasing the damage to its walls, as well as dissection and post-puncture hematomas. Heparin solution (5.000 units) was administered through introducer. Arteriography was performed to determine the severity and the length of stenotic occlusive lesions, as well as anatomic bases for revascularization. Recanalization of stenotic-occlusive segment was performed with 0.035 or 0.014-inch diameter guidewire. In experimental group, intraluminal antegrade insertion of the guidewire was attempted if possible, otherwise retrograde tibial or pedal approaches were used. Distal end of the guidewire was positioned in relatively patent artery. After the guidewire had advanced across the lesion, control arteriography was performed to determine the diameter and the length of balloon catheter for angioplasty. Predilatation of affected segment was performed in 22% of cases using smaller diameter balloon to prevent dissection. Finally, angioplasty was performed with balloons corresponding to the size of affected artery, the procedure lasting for 2-3 minutes. In 12% of patients this was followed by placing the stents because of the signs of arterial wall dissection due to severe calcification. After surgery completion, the introducer was removed and manual compression technique was used for 15 minutes in 90% of patients, followed by application of compression roller. The remainder 10% (especially obese patients) required Angio-Seal closure device to seal arterial puncture site. Postoperatively, the patients received 75 mg of clopidogrel and 75-100 mg of aspirin daily for 6 months, followed by lifelong monotherapy.

Endovascular surgery was considered technically successful in case of restoration of blood circulation in the affected arterial segments, and if no postoperative complications developed (dissections, thromboses, hematomas).

Table I. Endovascular surgery techniques and their distribution by affected arterial segments

Affected segments		Type of endovascular surgery	Number	Total
I	Aortoiliac	Balloon angioplasty and stenting	4	4
II	Iliofemoral	Balloon angioplasty and stenting	8	14
		Balloon angioplasty	3	
		Rotational mechanical thrombus aspiration (Rotarex) with balloon angioplasty of iliac segment	3	
III	Femoropopliteal	Balloon angioplasty	66	92
		Balloon angioplasty and stenting	12	
		Rotational mechanical thrombus aspiration (Rotarex) with balloon angioplasty	7	
		Rotational mechanical thrombus aspiration (Rotarex) with balloon angioplasty and stenting	3	
		Regional thrombolytic therapy with balloon angioplasty	4	
IV	Popliteal-tibial	Balloon angioplasty	64	84
		Balloon angioplasty and stenting	6	
		Rotational mechanical thrombus aspiration (Rotarex) with balloon angioplasty	2	
		Regional thrombolytic therapy with balloon angioplasty	12	
V	Tibial-pedal	Balloon angioplasty	47	49
		Regional thrombolytic therapy with balloon angioplasty	2	

RESULTS

Endovascular surgery techniques and their distribution by affected arterial segments are presented in Table I.

According to table I, balloon angioplasty was the most common procedure being performed in 180 patients (74.08%); 29 patients (11.94%) underwent balloon angioplasty with stenting, 18 patients (7.4%) – regional thrombolytic therapy with balloon angioplasty, 13 patients (5.35%) – rotational mechanical thrombus aspiration (Rotarex) with balloon angioplasty and 3 patients (1.23%) – rotational mechanical thrombus aspiration (Rotarex) with balloon angioplasty and stenting.

In occlusive-stenotic lesions of aortoiliac segment (AIS), balloon angioplasty with stenting was used in 4 patients, bilateral access being used in 3 of them.

In case of combined AIS and infrainguinal lesions, crossover femoral artery access was commonly used, thus simultaneous endovascular repair was performed in those segments.

Balloon angioplasty with stenting (8 patients) and balloon angioplasty (3 patients) were performed in occlusive-stenotic lesions of arteries in iliofemoral segment (IFS).

Self-expanding stents were used, with their most accurate positioning, being of great significance in ostial lesions. If external iliac artery was affected, only stenting was performed. Besides, 3 patients underwent rotational mechanical thrombus aspiration (Rotarex system) with balloon angioplasty. Thus, stenting was the main endovascular procedure in occlusive-stenotic arterial lesions of AIS and IFS.

In occlusive-stenotic lesions of femoropopliteal segment (FPS), both balloon angioplasty (66 patients) and balloon angioplasty with stenting (12 patients) were performed. Antegrade access was chosen in cases of combined lesions of tibial and pedal arteries. To cross occluded FPS, 0.035-inch diameter hydrophilic guidewires with balloon diagnostic catheters were used. Balloon catheters, 4–6 mm in diameter and 6–20 cm in length were guided through the artery to the blockage to dilate short lesions in FPS.

If more extended occlusive lesions were detected, subintimal angioplasty was used after the failure of intraluminal crossing.

In cases when antegrade recanalization of femorotibial arterial segment was impossible, retrograde pedal puncture access under ultrasound guidance was used. Such approaches proved to be effective in recanalization of arteries in more complicated anatomic pathology.

Regional thrombolytic therapy with balloon angioplasty was instituted in 4 patients of experimental group with FPS lesions. 7 patients underwent rotational mechanical thrombus aspiration (Rotarex system) with balloon angioplasty and rotation mechanical thrombus aspiration (Rotarex system) with balloon angioplasty and stenting 3.

Antegrade access with 0.014 or 0.018-inch diameter guidewire was predominantly used in patients with occlusive-stenotic lesions of popliteal-tibial arterial segments (PTS). Low-profile balloon catheters, 2–3 mm in diameter and about 220 mm in length, were inserted for artery dilatation. 64 patients underwent balloon angioplasty, and 6 patients – balloon angioplasty with stenting. Thus, stenting in this segment was not as common as in the proximal segments. In 2 patients, the technique of rotation mechanical thrombus aspiration by Rotarex device with balloon angioplasty of the popliteal segment was used. Regional thrombolytic therapy with balloon angioplasty was instituted in 12 experimental group patients with PTS thrombocclusion.

In occluded arteries of tibial-pedal segment (TPS), antegrade access was mostly chosen as well. In 74% of patients

with TPS lesions, angiosome concept was used implying restoration of circulation in the targeted artery, which is responsible for supplying the region of tissue damage. Similar low-profile balloon catheters were used for dilatation. Balloon angioplasty was performed in 47 patients. Regional thrombolytic therapy with balloon angioplasty was performed in 2 patients of experimental group.

DISCUSSION

Thrombosis was the major early postoperative complication developed in15 patients (6.2%) of both study groups. The incidence of thrombosis in early postoperative period was found to be statistically higher in the control group as compared to experimental group – 12 patients (7.5%) versus 3 patients (3.6%) ($p < 0.05$) – due to preoperative fibrinolytic therapy provided in case of thrombo-occlusion, avoidance of subintimal recanalization and ultrasound guidance. In 2 of 3 patients of experimental group, blood flow was restored, thus saving the limb, while one patient underwent amputation at the level of the upper third of the leg. In 6 of 12 control group patients, endovascular revascularization was successful after early arterial thrombosis. However, 6 patients underwent amputations after the failure to restore patency of the arteries – one of them at the level of the upper third of the thigh and 5 – at the level of the upper third of the leg, such results being consistent with published data [7].

Mathematical model for logistic regression with heterogeneity of variance was used to analyze factors contributing to the development of re-occlusion in early postoperative period. The following criteria were found to be of great significance: the presence of complex anatomical conditions (beta = 3.5080, p = 0.034), the presence of two or more multi-layer occlusions (beta = 9.0073, p = 0.002), technical errors in the course of surgeries (beta = 8.0802, p = 0.004). Besides, the risk of re-occlusion was found to increase significantly with increasing length of the lesion (beta = 0.5214, p = 0.005). Increase of the length of artery lesion by every extra centimeter proved to increase the risk of re-occlusion in 1.68 times. Prognostic mathematical model of re-occlusion risk developed by the authors proved to be highly informative, highly sensitive and highly specific.

No statistical differences between two groups were found in the incidence of such local complications as hematomas, wound bleeding, lymphorrhea, tissue edema. They developed in 12 patients of the control group (7.5%) and 6 patients of experimental group (7. 22%).

An important success criterion in surgical treatment of patients with critical limb ischemia is considered to be saving and maintaining functional limbs.

Of 243 patients, 14 patients (5.76%) underwent primary lower extremity amputations. Low percentage of primary amputations was due to the adequate preoperative preparation: the choice of treatment tactics, endovascular surgery technique, the use of fibrinolytic therapy. At the same time, limb amputations were performed at different levels in 12 of 160 patients (7.5%) in the control group, and in 2 of 83 patients (2.4%) in experimental group. Of 14 amputees, 4 underwent above-knee amputations and 10 – below-knee amputations because of re-thrombosis in early postoperative period.

In early postoperative period, mortality rate was 2.56% in the control group (4 deaths), while there were no lethal outcomes in experimental group. Acute myocardial infarction was the most common cause of death.

The results obtained in the study, concerning the number of saved extremities and the level of intra- and postoperative complications correlate with those achieved by other authors after endovascular revascularization of extremities [8].

Thus, the concept of angiosome-directed therapy used in the study, continuous ultrasound monitoring, avoidance of subintimal positioning of endovascular devices, use of rotor-mechanical thromboaspiration, drug-coated balloons and stents, as well as regional thrombolytic therapy, made it possible to decrease the number of postoperative complications from 7.5% to 3.61%, repeated operations – from 6.25% to 1.2%, amputations – from 3.75% to 1.2%, postoperative mortality rate – from 2.5% to 1.2%.

CONCLUSIONS

1. Introduction of well-structured algorithm in treatment of patients with occlusive-stenotic diseases of lower extremities made it possible to choose optimal extent of endovascular reconstructive surgery for every patient and achieve good therapy outcomes.
2. Puncture of arteries under ultrasonic guidance proved to be associated with decreased number of complications. Adequate hemostasis during the operation and adequate vacuum drainage of wounds resulted in significant decrease of postoperative wound complications and early restoration of patients' activity.
3. The study of risk factors for re-occlusion after endovascular revascularization, as well as the development of prognostic mathematical model to assess the risk of possible re-occlusion in early postoperative period are considered the key factors in its prevention.

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ORCID and contributionship:
Vasyl V. Shaprynskyi: 0000-0002-1437-7410 [A-D]
Yevhen V. Shaprynskyi: 0000-0002-4949-3163 [D-F]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Vasyl V. Shaprynskyi
State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department
5 Verkhnia St., 01014 Kyiv, Ukraine
tel: +380633702104
e-mail: vasyl.shaprynskyy@gmail.com

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ORIGINAL ARTICLE

IMPACT OF THE NASAL VALVE SHAPE ON THE OLFACTORY FUNCTION AND SUBJECTIVE PERCEPTION OF THE NASAL BREATHING

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Volodymyr O. Shkorbotun[1,2], Maksym O. Ovsiienko[2,3]

[1]STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

[2]SHUPYK NATIONAL HEALTHCARE UNIVERSITY OF UKRAINE, KYIV, UKRAINE

[3]MUNICIPAL NON-PROFIT ENTERPRISE «KYIV CITY CLINICAL HOSPITAL No.9», KYIV, UKRAINE

ABSTRACT

The aim: To study the impact of the internal nasal valve shape on respiratory and olfactory nose function as well as on quality of life.

Materials and methods: The study involved 17 volunteers who noted satisfaction of nasal breathing in the absence of changes during endorhinoscopy. The study was conducted in two stages: stage 1 involved assessing initial indicators of quality of life by the SNOT-22 questionnaire, performing active anterior rhinomanometry, and estimating the olfactory function (Sniffin' Sticks); stage 2 consisted in re-assessing the mentioned indicators after changing the shape and lumen of the internal nasal valve. The sodium alginate self-hardening gel was used for simulating the narrowing of the nasal valve. It was applied to the mucous in the upper part of the nasal valve area, obturating the diffuser above the level of attachment of the middle nasal turbinate to a depth of 3-4 mm from nasal vestibule.

Results: Air resistance did not change significantly after partial blockage of the internal nasal valve, although, 16 out of 17 patients showed signs of hyposmia with an average Sniffin' Sticks test score 8.68 ± 0.15.

Conclusions: The simulated partial blockage of the internal nasal valve lumen in its upper part in the area of the diffuser does not significantly affect the resistance of the air passing through the nasal passages, but the olfactory function is impaired, which is reflected the quality of life.

KEY WORDS: nasal aerodynamics, rhinomanometry, olfactometry, quality of nasal breathing, quality of life

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INTRODUCTION

The nasal valve is located in the anterior part of the nasal cavity at the edge of lateral cartilages incorporating the anterior ends of the inferior turbinates, the inner surface of the wing of the nose and nasal septum [1]. Cross-sectional area of the nasal vestibule and the internal nasal valve is the region of the greatest nasal airflow resistance [2-4], while due to enlarged nasal turbinates (diffuser) the airflow in this area slows down to a significant degree and turbulences occur [3,5,6].

Most of the inhaled flow distributes in the inferior and middle passage while only 5-15% of flow passes through the upper passage where the olfactory region is located due to the anatomical structures forming the nasal valve [7,8].

The deformities of the nasal valve may impair the dynamics of nasal airflow, affecting the level of transition from laminar to turbulent flow and reducing the volume of air that passes through the upper nasal passage.

Modern functional reconstructive surgery to restore or improve nasal breathing is mainly aimed at eliminating bony-cartilaginous deformations in the lower and middle parts of the nasal cavity [9,10]. However, there is a proportion of patients who have certain complaints about the quality of life, in particular, a subjective perception of dissatisfaction with nasal breathing even after surgical restoration of the lumen of nasal passages and restoration of nasal breathing. It can be explained by olfactory dysfunction.

There are a number of experimental studies on simulating conductive olfactory dysfunction by an obstruction of the upper nasal passage along its entire length with blocking of the olfactory recess with various materials [11,12]. According to olfactometry results, all patients noted disordered smell perception, in particular dysosmia, and in some cases even anosmia.

To determine the impact of nasal valve deformity on the olfactory function, there was conducted a study assessing the state of olfactory function in patients in modeling the changes in the shape of nasal valve while maintaining the upper nasal passage unobstructed. Such a study would allow for determining the impact of the nasal valve on the odor perception acuity.

The results of the study may be extrapolated to pathological conditions in the area of the external and internal nasal valve in the clinic, which will help explain the cause of patients' dissatisfaction with nasal breathing and increase

the effectiveness of functional reconstructive surgery of the nose.

THE AIM

The aim was to study the impact of the shape of the internal nasal valve on respiratory and olfactory function of the nose as well as on subjective perception of the quality of life according to the SNOT-22 questionnaire.

MATERIALS AND METHODS

The study involved 17 patients who consented to an additional examination.

The Research Protocol was approved by the local ethics committee of the Municipal Non-Profit Enterprise "Kyiv City Clinical Hospital No.9" in accordance with the WMA Declaration "Ethical Principles For Medical Research Involving Human Subjects". All the patients signed an informed consent.

Examinations were conducted on the basis of the Department of Otorhinolaryngology of the Municipal Non-Profit Enterprise "Kyiv City Clinical Hospital No.9", which is a clinical site of the Department of Otorhinolaryngology of Shupyk National Healthcare University of Ukraine.

The age of the patients ranged from 22 to 45 years (33.7±1.7). There were 7 (41%) women (34.2±2.4 years) and 10 (59%) men (33.3±2.4 years).

Criteria for inclusion of patients in the study were the absence of complaints of nasal breathing disorders, as well as the absence of visual pathological changes during anterior rhinoscopy and endorhinoscopy.

Exclusion criteria included patient's complaints about impaired respiratory and olfactory functions, internal nasal deformities, asymmetric nasal lumen and pathological narrowing in the area of external and internal nasal valve.

The neurological and allergy statuses were assessed in all patients to avoid possible sinonasal allergic manifestations and olfactory dysfunction.

The study was conducted in two stages: stage 1 involved assessing initial indicators of subjective perception of quality of life, performing rhinomanometry, and estimating the state of olfactory function; stage 2 consisted in re-assessing the mentioned indicators after changing the shape and lumen of the internal nasal valve. The sodium alginate self-hardening gel was used for simulating the narrowing of the upper part of the nasal valve and its diffuser. It was applied to the mucous membrane in the area of the upper part of the nasal valve, obturating the diffuser in the direction above the level of attachment of the middle nasal turbinate to a depth of 3-4 mm from nasal vestibule.

Sodium alginate is odorless, does not irritate the mucous membrane, can be easily removed with vacuum aspirator without leaving any marks. Sodium alginate is an additive and ingredient in the food industry and is widely used in medicine and cosmetology [13,14].

The impact of the function of the nose on patients' quality of life was determined using SNOT-22 (Sinonasal outcomes test – 22) questionnaire in the validated Ukrainian version [15, 16].

The study of nasal breathing was carried out according to the standard method of active anterior rhinomanometry using OPTIMUS rhinomanometr (Ukraine, state registration number No.14777/2015). Airway resistance was measured at a pressure of 150 Pa/cm3/second with a quiet inhale and exhale. Total airway resistance (Rtotal) was calculated automatically by the formula Rtotal = RR*RL*(RR + RL)-1 [17]. Rtotal ≤0.25 was taken as the norm of total resistance [18].

Olfactometry was carried out using Sniffin' Sticks psychophysical test (Burghardt®, Wedel, Germany) [19], which involved pen-like dispensing devices. Each side of the nose was studied separately as well as both sides together. Odor identification was performed using alternative visual signals of forced choice with an assessment in scores: 12-11 scores - normosmy, 10-7 - hyposmia, < 7 - anosmia.

Statistical analysis was carried out in the Statistica program using non-parametric statistics based on the normal distribution. The confidence interval (CI) was 95%, the margin of error was less than 5% ($P < 0.05$). The Mann-Whitney test was used to compare the results in groups .

RESULTS

The results of the examination obtained at stage 1 of the study are presented in Table I.

As can be seen from Table I, at stage 1 of the examination all patients were satisfied with the quality of life and noted satisfaction with nasal breathing. In assessing the quality of life during the survey using SNOT-22, the average score was 3.47±0.63, which corresponded to the indicators of apparently healthy people.

According to the results of rhinomanometry, the average total airway resistance at a pressure of 150 Pa/cm3/second (Rtotal) was within the normal range, namely 0.16±0.01 Pa/cm3/second, while the average resistance during unilateral examination of each side of the nose separately was 0.33 ±0.02 Pa/cm3/second on the left and 0.34±0.02 Pa/cm3/second on the right.

The results of Sniffin' Sticks olfactometric test in quiet inhaling through both sides of the nose were 11.47±0.12 scores. When examining the left and right sides of the nose separately, the average score was 11.76±0.01 and 11.35±0.11.

The findings suggest that all patients were satisfied with the quality of nasal breathing and the quality of life, and according to the data of rhinomanometry and olfactometry, the obtained indicators were within the normal range. Some differences in indicators during unilateral study of airway resistance in each side of the nose separately have not impacted the overall respiratory assessment through both sides of the nose at the same time.

Table I. Indicators of patients' quality of life according to SNOT-22, rhinomanometry and olfactometry at stage 1 of the study

No. of patient	SNOT-22 scores	Airway resistance at a pressure of 150 Pa/cm3/second			Sniffin`Sticks olfactometry		
		R_L	R_R	R_{total}	Left	Right	Total
1	1	0.52	0.41	0.23	11	11	11
2	3	0.25	0.16	0.11	12	12	12
3	3	0.25	0.53	0.17	12	11	11
4	0	0.44	0.48	0.23	12	12	12
5	6	0.24	0.2	0.11	11	11	11
6	1	0.22	0.42	0.14	12	12	12
7	0	0.31	0.37	0.17	12	11	12
8	7	0.47	0.4	0.22	12	12	11
9	4	0.46	0.48	0.23	12	11	12
10	6	0.35	0.47	0.2	12	11	11
11	6	0.33	0.16	0.11	12	12	12
12	4	0.42	0.32	0.18	12	11	11
13	2	0.22	0.27	0.12	12	11	12
14	7	0.4	0.32	0.18	11	11	11
15	7	0.31	0.31	0.15	11	11	11
16	2	0.31	0.3	0.15	12	11	12
17	0	0.21	0.23	0.11	12	12	11
M ± m	3.47±0.63	0.33±0.02	*0.34±0.02*	*0.16±0.01*	*11.76±0.1*	*11.35±0.11*	*11.47±0.12*

The results of the study of patients after changing the shape and lumen of the internal nasal valve are presented in Table II.

After applying sodium alginate gel and partially blocking the upper part of the nasal valve, resulting in its shape change, no patient noted a local reaction or worsening of the general condition.

To the question "Has your subjective perception of the quality of nasal breathing changed?" after changing the shape of the nasal valve, 13 patients answered "Yes" and noted functional discomfort when breathing through the nose; 3 patients did not feel any changes.

The data presented in Table II show that the total airflow resistance after partial blocking of the nasal valve during the study in the calm nasal breathing did not change significantly, both in the unilateral examination and in the overall indicator. The results of the total resistance (Rtotal) after rhinomanometry were 0.19±0.01 Pa/cm3/second, during unilateral examination: on the left – RL – 0.37±0.02 Pa/cm3/second, on the right – RR – 0.41±0.03 Pa/cm3/second.

At the same time, during the olfactometric study with calm breathing through both sides of the nose simultaneously, the study of the olfactory function using the Sniffin' Sticks test showed signs of hyposmia in the vast majority of patients although they did not indicate olfactory dysfunction. When examining the left and right sides of the nose separately, the average score was 8.23±0.29 and 8.7±0.23, respectively, when examining breathing through both sides of the nose, it was 8.82±0.19.

The data on the differences in indicators of patients' quality of life and rhinomanometric and olfactometric examination obtained at the first and second stages of the study are presented in Table III.

Thus, after partial blocking of the internal nasal valve, 82% of patients noted some nasal breathing discomfort, although the resistance of air passing through the nasal passages did not change significantly (Table III). The results of olfactometric examination showed that 16 out of 17 patients had signs of hyposmia with an average score of 8.68±0.15 according to the Sniffin' Sticks tests. Only one patient (No.17) had no changes in the olfactory function, i.e. normosmia. According to rhinomanometry data, the initial airflow resistance after partial valve blocking did not change significantly in this patient, although he also noted some nasal breathing discomfort.

Therefore, the simulated partial blocking of the upper part of the internal nasal valve has no significant impact on the resistance of air passing through the nasal passages, but the olfactory function is impaired, and it is most likely to have the major impact on patients' assessment of the quality of nasal breathing and, accordingly, the quality of life.

DISCUSSION

The discussion of the research results necessitates turning to the fundamentals of nasal aerodynamics [3,20-23], in particular the aerodynamics of the upper nasal passage, which plays an important role in full implementation of the function of olfactory analyzer.

Table II. Indicators of patients' quality of life according to SNOT-22, rhinomanometry and olfactometry after blocking upper part of the internal nasal valve

No. of patient	SNOT-22 scores	Airway resistance at a pressure of 150 Pa/cm3/second			Sniffin`Sticks olfactometry		
		R_L	R_R	R_{total}	Left	Right	Total
1	9	0.53	0.47	0.25	9	9	9
2	6	0.19	0.29	0.12	9	10	9
3	11	0.36	0.61	0.22	9	8	8
4	6	0.6	0.52	0.28	9	8	8
5	9	0.24	0.34	0.2	9	8	8
6	8	0.29	0.33	0.15	9	10	10
7	4	0.48	0.44	0.23	10	10	9
8	10	0.41	0.5	0.22	8	8	9
9	6	0.34	0.62	0.22	7	7	9
10	11	0.32	0.59	0.21	8	9	8
11	8	0.35	0.2	0.13	9	9	9
12	5	0.53	0.4	0.23	8	9	8
13	5	0.31	0.23	0.13	7	8	8
14	10	0.42	0.4	0.22	9	7	9
15	9	0.42	0.46	0.22	5	10	9
16	5	0.31	0.33	0.16	7	9	9
17	1	0.24	0.24	0.12	8	9	11
M ± m	7.23±0.67	0.37±0.02	0.41±0.03	0.19±0.01	8.23±0.29	8.7±0.23	8.82±0.19

Table III. Indicators of patients' quality of life, rhinomanometric and olfactometric examination and their differences

Research stages	Number of cases	SNOT-22 scores	Airway resistance at a pressure of 150 Pa/cm3/second			Sniffin`Sticks olfactometry		
			R_L	R_R	R total	Left	Right	Total
Stage 1 (M±m)	17	3.47±0.63	0.33±0.02	0.34±0.02	0.16±0.01	11.76±0.43	11.35±0.49	11.47±0.51
Stage 2 (M±m)	17	7.23±0.67	0.37±0.02	0.41±0.03	0.19±0.01	8.23±0.29	8.7±0.23	8.82±0.19
Difference	-	*P<0.05*	*P>0.05*	*P>0.05*	*P>0.05*	P<0.05	P<0.05	P<0.05

It is known that in the initial phase of inspiration, the air current has laminar flow, it passes through the entrance to the nasal cavity and is distributed to the nasal passages at the level of the internal nasal valve [24]. In cases of wide lower and middle nasal passages and the internal nasal valve pathology, the majority of air passes through them to posterior naris in laminar flow [25], reducing the volume of air that passes through the upper nasal passage, where the olfactory recess is located. In their research, Mlynski et al. [3,23] concluded that when the air passes through the narrowest place at the nasal cavity entrance, due to enlarged nasal turbinates (diffuser), the airflow in this area slows down to a significant degree which is accompanied by an increase in dynamic pressure with the formation of turbulences contributing to the flow of air to the upper nasal passage. These data suggest that a decrease in the volume of air rising to the upper nasal passage and possible change in the level of transition from laminar to turbulent flow lead to impaired aerodynamics of the nose and can cause olfactory dysfunction.

Thus, even a partial change in the shape of the internal nasal valve, which does not significantly affect the respiratory function of the nose, due to impared ventilation of the upper nasal passage causes olfactory dysfunction, which takes part in the development of the subjective perception of satisfaction with nasal breathing and, accordingly, the quality of life.

The results of the research increase understanding of the root causes of complaints of nasal breathing and quality of life in patients with nasal valve deformities and after functionally reconstructive interventions in the nasal cavity, in particular septoplasty, with satisfactory rhinomanometry indicators.

CONCLUSIONS

1. Changing the shape of the internal nasal valve with its partial blocking in the area of the diffuser has no significant effect on airflow resistance during rhinomanometry.

2. Partial blocking of the upper part of the internal nasal valve, even with an unobstructed upper nasal passage along the entire length, causes impairment of odor perception acuity.
3. When performing surgical interventions on the septum and upper parts of the nose, it is important to pay attention to the functional state of the upper part of the nasal valve, in particular in the area of the diffuser, which plays a significant role in ventilation of the upper parts of nasal cavity.

The prospects for further research may include studying local changes in aerodynamics in the area of the external and internal nasal valve, the impact of airflow disruption on the olfactory function, as well as elucidating the mechanisms of developing subjective perception of satisfaction with nasal breathing and quality of life.

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ORCID and contributionship:
Volodymyr O. Shkorbotun: 0000-0003-0769-6242 [A,E,F]
Maksym O. Ovsiienko: 0000-0002-1597-5607 [B-E]

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CORRESPONDING AUTHOR
Maksym O. Ovsiienko
Kyiv City Clinical Hospital No. 9
1 Ryzka str., 04060 Kyiv, Ukraine
tel: +380977367228
e-mail: ovsienko1988@gmail.com

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ORIGINAL ARTICLE

MODERN APPROACHES TO CHOOSING SHAVER BLADE FOR ENDOSCOPIC SURGERY OF THE NASOPHARYNX AND PARANASAL SINUSES USING 3D MODELING

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Yaroslav V. Shkorbotun[1,2], Kateryna V. Liakh[1,2]

[1]STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

[2]SHUPYK NATIONAL HEALTHCARE UNIVERSITY OF UKRAINE, KYIV, UKRAINE

ABSTRACT

The aim: To determine the effectiveness of the use of 3D printed templates of shaver blades for choosing the optimal blade shape for endoscopic surgery of the nasopharynx and paranasal sinuses.

Materials and methods: The shaver blade templates with bending angles of 40°, 60°, 90° and 120° for powered endoscopic sinus surgery were made according to the manufacturer catalog using the Asiga 3D printer and Dental TOOTH material. There were examined 100 patients who underwent endoscopic powered sinus interventions (50 – adenoidectomy, and 50 – removal of the maxillary sinus cysts). The patients with each type of intervention were divided into subgroups of 25 people. The subgroups differed by the approach to choosing shaver blades: using 3D templates – in the main subgroup, and traditional –in the control.

Results: The average number of shaver blades used for adenotomy in patients of the main group was 1.04±0.04, and in the control group – 1.36±0.09 ($p<0.05$). In patients of both subgroups, the 40° shaver blade, which is standard for adenotomy and recommended by most manufacturers, was most often used. In the control subgroup, it was used significantly more often. The frequency of the use of other shaver blades – 60° and 90° in both subgroups did not differ significantly and amounted to 40.0% (CI 95% 21.8; 61.1) and 36.0% (CI 95% 18.7; 57.4).

Conclusions: The use of 3D templates for choosing a shaver blade reduces the number of blades used in adenoidectomy by 23.5%, for maxillary sinus cysts operation – by 18.2%.

KEY WORDS: sinusotomy, adenectomy, shaver, rhinosurgery, 3D-templates

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INTRODUCTION

Modern approach to surgical treatment of patients with upper respiratory tract disease is based on ensuring high efficiency of the intervention with minimal traumatic impact on the surrounding tissue. It is of particular relevance in sinus surgery, since the anatomy of the nasal cavities, paranasal sinuses and nasopharynx has a complex spatial structure (a large number of individual cavities limited by bone walls), which often makes it difficult to access the intervention site [1]. That is why in recent decades, endoscopic sinus surgery with the use of angled scopes and shavers with blades of different bending angles has become the gold standard. The benefits of the powered method of tissue removal include the targeting of the impact with minimal damage to the surrounding structures [2-5].

When performing interventions with shavers, it is important to choose the optimal type of blade, because each of them has restrictions on the impact zone specified by geometrical configuration, in particular, the bending angle, which varies from 0 to 120 degrees. To address this issue in sinus surgery, preoperative planning is advisable, which includes the choice of appropriate optics and tools [6, 7]. However, this approach is not always effective, since it is not always possible to preestimate the soft tissue boundary displacement, especially during interventions on the nasopharynx.

Due to the relatively high cost of shaver blades and their regulated single use, the choice of the optimal blade angle in each case is an important clinical issue with an economic component (power-assisted adenoidectomy and sinus surgery).

Since 3D models have recently become more widely used in medical technology [8, 9], including medical instruments [10-12], it is possible to create the best replica of the tool, even with a complex surface and configuration, and use it as a template.

We believe that choosing the optimal shaver blade for sinus surgery based on intraoperative fitting of the blade templates holds promise and needs to be studied in the clinic.

THE AIM

The aim was to determine the effectiveness of the use of 3D printed templates of shaver blades for choosing the optimal blade shape for endoscopic surgery of the nasopharynx and paranasal sinuses.

Table I. Lymphoid tissue location in the nasopharynx during endoscopy.

Lymphoid tissue location in the nasopharynx	Subgroup n (%)		P-value
	Main n=25	Control n=25	
Vault	25 (100.0%) CI 95% 83.4;100	25 (100.0%) CI 95% 83.4;100	P≥0.05
Peritubal sections	14 (56.0%) CI 95% 35.3;74.9	15 (60.0%) CI 95% 38.9;78.2	P≥0.05
Perichoanal sections	12 (48.0%) CI 95% 28.3;68.3	12 (48.0%) CI 95% 28.3;68.3	P≥0.05

Note: CI 95% – confidence interval 95%; P – p-value (statistical significance).

Table II. Data on the use of shaver blades for adenotomy in children.

Number of shaver blades used	Subgroup n (%)		P
	Main n=25	Control n=25	
1 shaver blade used	24 (96.0%) CI 95% 77.7;99.8	16 (64.0%) CI 95% 42.6;81.3	P<0.05
More than 1 shaver blade used	1 (4,0%) CI 95% 0.2;22.3	9 (36.0%) CI 95% 18.7;57.4	P<0.05
Total	25 (100%)	25 (100%)	

Note: CI 95% – confidence interval 95%; P – p-value (statistical significance).

Table III. Data on the use of shaver blades for sinus surgery.

Number of shaver blades used	Subgroup n (%)		P-value
	Main n=25	Control n=25	
1 shaver blade used	23 (92.0%) CI 95% 72.5;98.6	17 (68.0%) CI 95% 46.5;84.3	P<0.05
More than 1 shaver blade used	2 (8.0%) CI 95% 1.4;27.5	8 (32.0%) CI 95% 15.7;53.6	P<0.05
Total	25 (100%)	25 (100%)	

Note: CI 95% – confidence interval 95%; P – p-value (statistical significance).

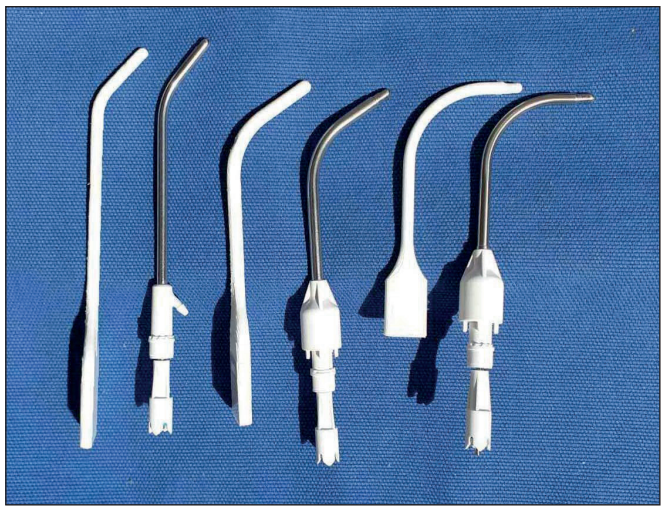

Fig. 1. Shaver blades with bending angles of 40º, 60º, and 90º and their 3D templates

MATERIALS AND METHODS

There were made 40°, 60°, 90° and 120° shaver blade templates for endoscopic surgery for the study. The templates were made as tools, one end of which matched the configuration of blades (thickness, length, bending point and angle) for powered interventions according to the catalog [13], and the other end was a flat handle, which made it comfortable to hold the template in hand.

They were printed on the Asiga 3D printer using DentalTOOTH material that can be sterilized and is certified for medical use.

Figure 1 presents original blades and their 3D replicas which were used as templates during the intervention.

The study involved 100 patients, including 50 children with nasopharyngeal adenoid hypertrophy who underwent endoscopic powered adenotomy, and 50 adults with maxillary sinus cyst who underwent endoscopic sinus surgery with access through the middle nasal passage.

In both groups, patients were divided into subgroups of 25 people depending on the method of choosing a shaver blade. The main subgroup includes 25 children and 25 adults who underwent intervention with shaver blade templates.

The age of patients in the group of children ranged from 2 to 14 years. The average age of children was 5.98±0.38. There were 31 boys (62.0%) and 19 girls (38.0%).

The age and gender distribution of patients is presented in Figure 2.

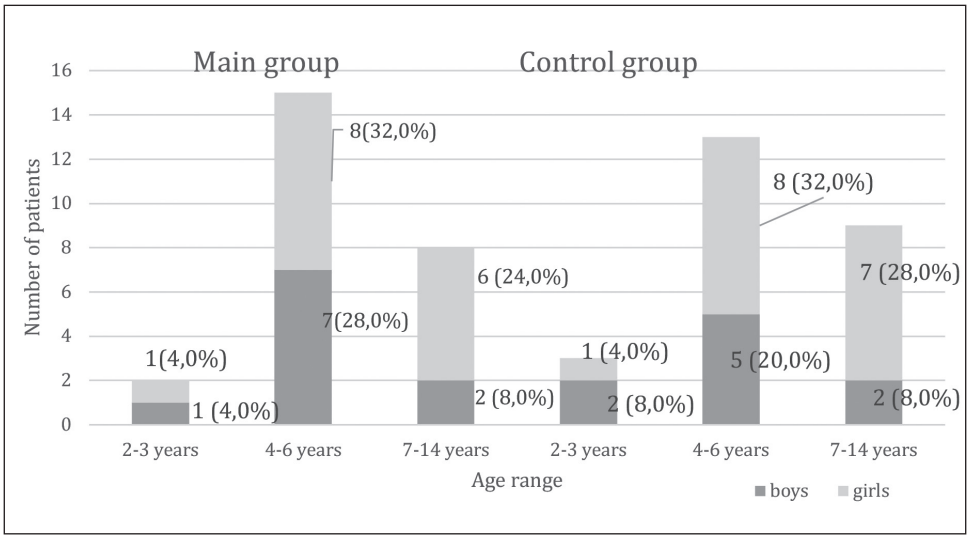

Fig. 2. The age and gender distribution of patients who underwent adenotomy. Note: *– p<0.05.

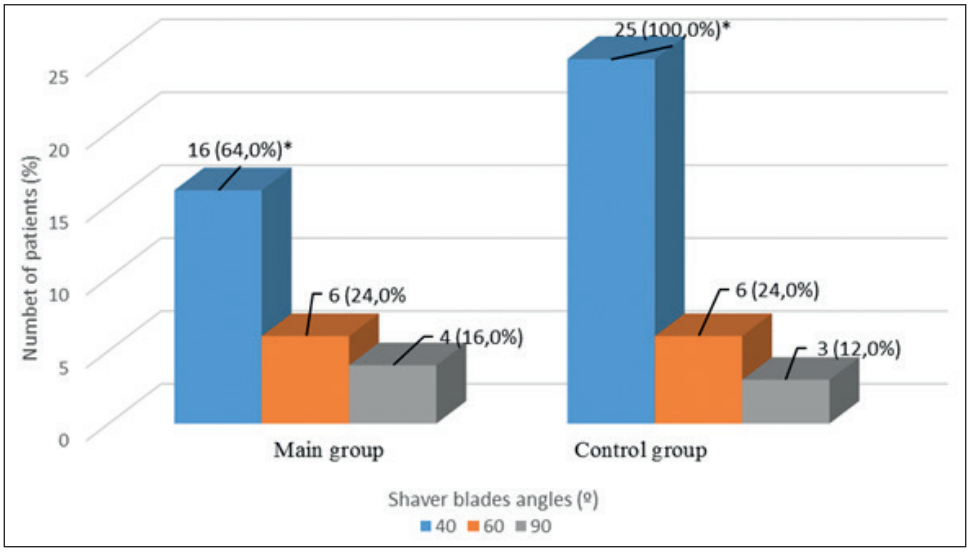

Fig. 3. Data on the use of different types of shaver blades for adenotomy in children. Note: *– p<0.05.

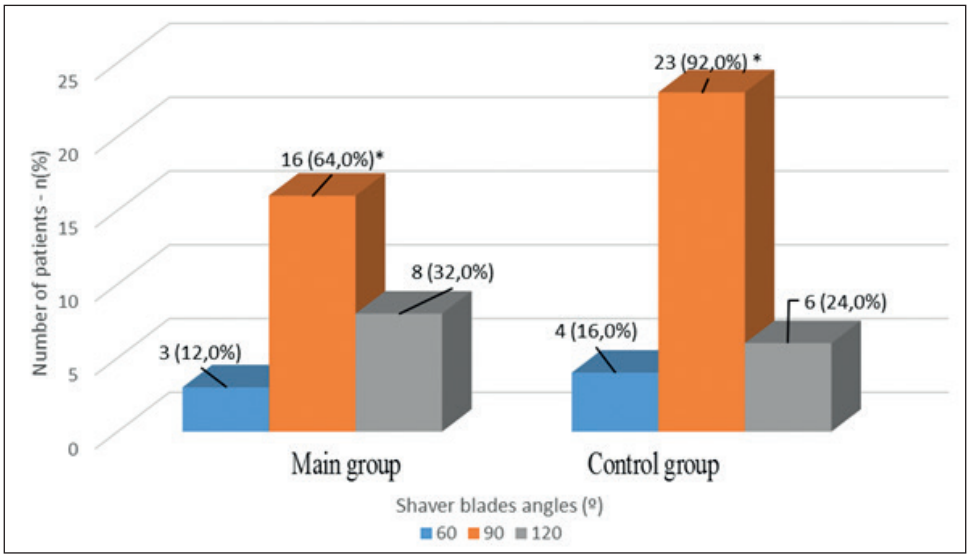

Fig. 4. Data on the use of shaver blades for endoscopic sinus surgery. Note: *– p<0.05.

As can be seen from the data presented in Figure 2, the subgroups were compared in terms of both gender and age.

The age of adult patients ranged from 19 to 46 years, with an average age of 34.4±1.09. There were 21 men (42.0%) and 29 women (68.0%). The distribution by age and gender subgroups was compared.

The study was conducted in accordance with the principles of the Council of Europe Convention on Human

Rights and Biomedicine, World Medical Association Declaration of Helsinki on the ethical principles for medical research involving human subjects, and current regulations of the Ministry of Health of Ukraine. The study protocol was approved by the local ethics committee. All patients signed an informed consent to participate in the study.

The spatial properties of the site of surgical intervention, which might influence the choice of the shaver blade, were studied. Thus, the location of lymphoid tissue in different parts of the nasopharynx (vault, peritubal and perichoanal sections) was analyzed, and in patients with the maxillary sinus cysts, the location of the cyst relative to the anterior border of the maxillary sinus ostium was studied based on the results of intraoperative endoscopy.

During the research, there was kept data on the shaver blades that were used for the intervention: the bending angle and the need to replace the initially chosen blade with a template with different bending angle were taken into account to ensure complete removal of lymphoid tissue during adenotomy or cyst walls during endoscopic sinus surgery. The data were compared in the subgroups depending on the method of choosing shaver blade.

The approach to choosing the blades in subgroups of children who underwent adenotomy differed. The optimal bending angle of the shaver blade for each patient of the main subgroup was determined by template contacting with the boundaries of adenoid vegetations under visual control. The blade was considered optimal if it covered the whole area of lymphoid tissue in the nasopharynx that was planned for removal. In the control subgroup, after visual control of the nasopharynx, the lymphoid tissue was initially removed with a standard blade for adenotomy (40° angle), and then, depending on the location of the hard-to-reach tissues that needed to be removed, the blade with an angle of 60° or 90° was chosen.

In the main subgroup of patients with cysts of the maxillary sinus, after the formation of access to the sinus, there was performed fitting of the shaver blade template under endoscopic control of the planned intervention site, focusing on the reachability of the entire area of cyst attachment to the sinus walls. This was the basis for choosing a blade. In the control subgroup, the choice of a blade for removing cysts was carried out on the basis of a visual assessment of the cyst location relative to the enlarged maxillary sinus ostium, with further use of the alternative blade with a larger or smaller angle in case it was impossible to completely remove the cyst with the initially chosen blade.

Statistical processing of the results obtained during the study was carried out using the EZR statistical software package. The obtained data were processed by methods of variation statistics with the calculation of statistical significance of differences between the control and the study groups. For this purpose, the methods of parametric (Student's t-test) and nonparametric statistical analysis ($\chi 2$ test) were used. A 95% confidence interval (CI) was calculated by the Wilson method with correction for continuity, the margin of error was less than 5% ($p<0.05$) [14].

RESULTS

Data on the location of the lymphoid tissue of adenoid vegetations in different parts of the nasopharynx found during endoscopic removal of adenoid vegetations in comparison subgroups are presented in Table I.

As can be seen from Table 1, the lymphoid tissue location in the nasopharynx in the subgroups did not differ significantly and was characterized by a predominance of location in the vault, and less often in the peritubal and perichoanal sections.

The research results on the use of shaver blades in patients with adenoid vegetations are presented in Table II.

As shown by the data presented in Table 2, the use of 3D templates for the choice of shaver blades for adenotomy significantly increased the proportion of patients who underwent intervention with a single blade. The average number of shaver blades used for adenotomy in patients of the main group was 1.04±0.04, which is 23.5% less than in the control group – 1.36±0.09 ($p<0.05$).

Data on the type of shaver blade for adenotomy are presented in Figure 3.

As can be seen from Figure 3, in patients of both subgroups, the 40° shaver blade, which is standard for adenotomy and recommended by most manufacturers, was most often used. The difference in the frequency of the use of such blades in subgroups is significant ($p<0.05$). Its 100.0% frequency of the use in the control subgroup can be explained by the methodology of the study. In the control subgroup, a standard shaver blade was used to remove adenoid vegetations, and then, if necessary, alternative blades were chosen, depending on the location of adenoid remnants. At the same time, the frequency of successful removal of lymphoid tissue from the vault using a 40° shaver blade at the level of 64.0% (CI 95% 42.6; 81.3) confirms its choice as a standard one, as its use provides a high percentage of efficiency.

The findings on the proportion of patients who required the use of 60° and 90° blades during adenotomy in the subgroups did not differ significantly and amounted to 40.0% (CI 95% 21.8; 61.1) and 36.0% (CI 95% 18.7; 57.4).

The analysis of the use of blades in patients with endoscopic removal of maxillary sinus cysts showed the same patterns.

The results of the analysis on the location of cysts relative to the anterior border of the maxillary sinus ostium showed that in most patients of both subgroups, namely in 14 (56.0% CI95% 35.3; 74.9) people from the main subgroup and 15 (60% CI95% 38.9; 78.2) people from the control, the anterior border of the cyst attachment was located posteriorly from the area of the maxillary sinus ostium, and did not differ significantly. This may indicate that in these patients, the anterior border of the cyst attachment could be reached with shaver blades with a bend angle of less than 90° or less.

Data on the use of shaver blades for endoscopic sinus surgery are presented in Table III.

Summarizing the results on the use of the shaver blades presented in Table III, it should be noted that the propor-

tion of interventions using 2 blades to remove cysts in the main subgroup was significantly lower, which was obviously due to the use of 3D blade templates during the surgery.

The average number of shaver blades that were used during sinus surgery in the main subgroup was 1.08±0.05, which was significantly less than in the control subgroup – 1.32±0.09 ($p<0.05$), with a difference of 18.2%.

The results of the analysis of the proportion of patients who underwent sinus surgery with a separate type of shaver blade in proportion to the total number of patients in the subgroup is presented in Figure 4.

As can be seen from the data presented in Figure 4, shaver blades with an angle of 90° are most often used in both subgroups. There is a significant difference in the proportion of operations during which this type of blade was used in the subgroups, with a reduction in its size when using the templates. The total proportion of patients who underwent surgery with 60° and 120° blades in the subgroups did nor differ and was 44.0% (CI 95% 25.0; 64.7) in the main subgroup, and 40.0% (CI 95% 21.8; 61.1) in the control.

DISCUSSION

The lymphoid tissue location in the nasopharynx in the peritubal and perichoanal sections, according to the literature, are most often referred to as hard-to-reach areas [3, 6]. It is obvious that in order to remove lymphoid tissue in these areas of the nasopharynx, it is necessary to use alternative shaver blades [3]. The proportion of patients who required the use of 60° and 90° blades during adenotomy is also confirmed by the results of the analysis of the lymphoid tissue location in the nasopharynx during endoscopic examination before the intervention (Table I). Thus, the use of the templates for choosing the optimal shaver blade has reduced the proportion of interventions using several shaver blades, which can decrease the amount of consumables for power-assisted adenotomy and make the intervention duration shorter without the need to change the shaver blade.

In order to cure patients with cyst of maxillary sinuses in is need to througly remove it in place of fixation [5]. The location of the maxillary sinus cyst out of reach of the 90° shaver blade when accessed through the dilated maxillary sinus ostium in both groups is observed with the same frequency. Moreover, the change of the blade from 90° to one with a larger bending angle – 120°, is more often noted than to a smaller one – 60°, which is consistent with data on the frequency of cyst location in front of the level of the osteomeatal complex. The changing of the blades in the endoscopical rhinosurgery couse the growing of economic costs and that is actual aspect in nowertime [2].

One of the benefits of the proposed method for choosing a shaver blade is that its use leads to a decrease in the injury rate and cost of the intervention. After all, if it is impossible to achieve complete removal of the cyst membrane with the initially chosen blade, the surgeon faces the need to use another shaver blade with a different bending angle or expand the existing access, which increases the surgical injury.

Thus, the proposed method for choosing the optimal shaver blade for endoscopic sinus surgery is effective and can be recommended for use in clinical practice.

CONCLUSIONS

The use of 3D templates for choosing the shaver blade for endoscopic interventions in the nasopharynx and paranasal sinuses increases the efficiency of choosing the optimal blade.

The proportion of patients who required the use of an alternative shaver blade to the standard one with a bending angle of 40° during endoscopic powered adenotomy was 38.0%. The proportion of patients who required a blade with a bending angle other than 90° during sinus surgery was 42.0%.

The use of 3D templates when choosing a shaver blade reduces the number of blades used in nasopharyngeal interventions by 23.5%, and when removing the maxillary sinus cysts – by 18.2%.

PROSPECTS OF FURTHER STUDIES

A prospective direction of further research is the study of predictability of the optimal shaver blade at the stage of intervention planning, based on the data on preoperative tomography, taking into account the chosen sinus access option. It is advisable to study the limiting factors in the use of the blade for adenotomy, such as failure to remove lymphoid tissue and the risk of injury to the soft palate.

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ORCID and contributionship:
Yaroslav V. Shkorbotun: 0000-0002-3103-7194 [A-F]
Kateryna V. Liakh: 0000-0003-4863-948X [B,D,F]

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CORRESPONDING AUTHOR
Yaroslav V. Shkorbotun
State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department
5 Verkhnia St., 01014 Kyiv, Ukraine
tel: +38 (044) 254-64-54
e-mail: lorkiev@ukr.net

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ORIGINAL ARTICLE

ASSOCIATION OF LEFT ATRIAL SPONTANEOUS ECHO CONTRAST WITH CLINICAL AND HEMODYNAMIC CHARACTERISTICS OF PATIENTS WITH LONG-TERM EPISODES OF PERSISTENT ATRIAL FIBRILLATION

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Yaroslav V. Skybchyk[1, 2], Kyrylo O. Mikhaliev[3], Oleg J. Zharinov[1,2]

[1]SHUPYK NATIONAL HEALTHCARE UNIVERSITY OF UKRAINE STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

[2]HEART INSTITUTE OF THE MINISTRY OF HEALTH OF UKRAINE, KYIV, UKRAINE

[3]STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE», KYIV, UKRAINE

ABSTRACT

The aim: To identify clinical and hemodynamic factors, associated with left atrial spontaneous echo contrast (LASEC) (LASEC in general, and the dense LASEC), in non-valvular persistent atrial fibrillation (AF) patients with the duration of AF episode ≥90 days.

Materials and methods: The cross-sectional study consecutively enrolled 115 persistent AF patients with the duration of its episode ≥90 days (82 (71,3 %) males; mean age 59 ± 11 years). Transthoracic (TEE) and transesophageal echocardiography (TEE) were performed. LASEC (by TEE) was observed in 79 (68,7 %) patients. The dense (moderate-to-severe) LASEC was detected in 23 (20,0 %) cases.

Results: Heart failure (HF) stage C (OR 2,09 (95 % CI 1,24-3,53); p=0,006), lower TEE-derived left atrial appendage (LAA) flow velocity (FV) (OR 0,94 (95 % CI 0,91-0,98); p=0,003), and the presence of TTE-derived pulmonary hypertension (PH), appeared to be strongly associated with LASEC (AUC for logistic regression model: 0,83 [95 % CI 0,75-0,89]). The presence of diabetes mellitus type 2 (DM) (OR 2,34 (95 % CI 1,13-4,86); p=0,027), along with lower LAA FV (OR 0,83 (95 % CI 0,76-0,91); p<0,001), were strongly associated with dense LASEC (AUC: 0,89 [95 % CI 0,82-0,94]).

Conclusions: The TEE-derived LASEC in patients with long term episodes (≥90 days) of persistent AF was strongly associated with HF stage C and TTE-derived PH, and with lower TEE-derived LAA FV. The presence of DM, in addition to lower LAA FV, was related to dense LASEC.

KEY WORDS: left atrial spontaneous echo contrast, persistent atrial fibrillation

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INTRODUCTION

The prognostic value of atrial fibrillation (AF) is mostly determined by the significantly increased risk of major cardiac and cerebrovascular complications, including thromboembolic events [1]. The progression of AF is closely related to the ongoing myocardial remodeling, with gradual loss of chances for sinus rhythm (SR) restoration and maintenance. Cardiomyopathy caused by long-term episodes of AF includes the changes of left atrial (LA) structure and function, recently denoted as atrial cardiomyopathy [2].

The protocol of cardioversion (CV) in the management of persistent AF patients includes transesophageal echocardiography (TEE) [3]. LA spontaneous echo contrast (LASEC) (also known as (echogenic) «smoke») is a common TEE-detected finding in patients with non-valvular AF [4, 5]. LASEC intensity is classified into four degrees (mild, mild-to-moderate, moderate and severe) [6], with moderate and severe degrees merged into «dense LASEC» pattern [7].

LASEC is a phenomenon, related to two essential aspects in the management of persistent AF patients. First, it might be considered a result of LA remodeling (including LA appendage [LAA]), fibrosis, dilation and decreased LA/LAA hemodynamic function, thus being a risk factor of AF recurrence after SR restoration, and, consequently, its progression [2, 4, 5, 8]. At the same time, LASEC is a result of interaction between multiple hematologic and hemorheological factors, that, combined with impaired blood flow and endocardial damage, form the thrombogenic milieu in the atria, especially LA/LAA. Therefore, LASEC received a special attention as a marker of thromboembolic risk in non-valvular AF [9, 10]. The role of LASEC as a possible marker of thromboembolic risk and predictor of clinical course of arrhythmia may even be more in patients with long-term episodes of AF lasting ≥3 months (≥90 days), with presumably established atrial cardiomyopathy and, consequently, less chances for effective SR control.

THE AIM

The aim of the study was to identify the clinical and hemodynamic factors, associated with LASEC (the presence of LASEC in general, and the dense LASEC), in

non-valvular persistent AF patients with the duration of AF episode ≥90 days.

MATERIALS AND METHODS

The cross-sectional study consecutively enrolled and analyzed clinical, laboratory and instrumental data from 115 persistent AF patients with the duration of its episode ≥90 days (82 (71,3 %) males, 33 (28,7 %) females; mean age (mean ± standard deviation) 59 ± 11 years), who were hospitalized during the period 2017-2021 with the intention to perform a direct current (DC) CV.

The study was conducted in accordance with the principles of the Council of Europe Convention on Human Rights and Biomedicine, World Medical Association Declaration of Helsinki on the ethical principles for medical research involving human subjects, and current national regulations. The study protocol was approved by the local ethics committee. All the patients signed an informed consent.

The study did not include patients with valvular AF, long-standing persistent AF, acute cardiovascular and cerebrovascular events, implanted antiarrhythmic devices, severe comorbidities (including malignancies with life expectancy less than 1 year), the detection of intracardiac thrombus on TEE, and a lack of informed consent.

Among the enrolled patients, AF was first diagnosed at the age of (median (Me) with interquartile range [IQR]) 54 (48-60) years, with the duration of its anamnesis and the last episode, respectively, 5 (3-6) years and 100 (97-120) days. Body mass index (BMI) was (Me [IQR]) 30,7 (26,3-34,3) kg/m^2; 67 (58,3 %) patients were obese.

The essential hypertension (HTN) was registered in 98 (85,2 %) patients, stable coronary artery disease (SCAD) – in 53 (46,1 %), previous myocardial infarction (MI) – in 12 (10,4 %). Percutaneous and surgical myocardial revascularization have already been performed in 15 (13,0 %) and 4 (3,5 %) cases, respectively.

The chronic heart failure (HF) was diagnosed in all the enrolled patients: stage B – in 31 (27,0 %) cases, and stage C – 84 (73,0 %) [11]. The NYHA functional classes of HF [11] were distributed as follows: I – 1 (0,8 %) case, II – 70 (60,9 %), III – 30 (26,1 %), and IV – 14 (12,2 %) patients.

The median risk of thromboembolic complications, assessed by the CHA_2DS_2-VASc scale [3], was (Me [IQR]) 3 (2-4) points. The AF-related symptoms classes, according to the EHRA classification system [3], were distributed as follows: 2b – 61,7 % patients (n=71), 3 – 26,1 % (n=30), and 4 – 12,2 % (n=14) cases.

Diabetes mellitus type 2 (DM) was diagnosed in 17 (14,8 %) patients, being medically compensated in 10 cases. The history of chronic obstructive pulmonary disease had 3 (2,6 %) patients.

The median (Me [IQR]) fasting glucose, total serum cholesterol and serum creatinine levels were 5,8 (5,4-6,2) mmol/l, 4,8 (3,9-5,8) mmol/l and 95 (87-109) μmol/l, respectively. The median (Me [IQR]) estimated glomerular filtration rate (eGFR) (by CKD-EPI equation) was 69,9 (58,6-80,3) ml/min/1,73 m^2.

The ECG-synchronized transthoracic echocardiography (TTE) was performed in all patients by use of the harmonic imaging ultrasound system (Philips iE33, Philips Medical Systems, the Netherlands; P4-2 phased array transducer 2-4 MHz). The median left ventricular (LV) ejection fraction (EF) (Me [IQR]) was 53 % (40-62 %). Pulmonary hypertension (PH) was present in 101 (87,8 %) patients: mild – 86 (85,2 %), moderate – 14 (13,9 %), and severe – in 1 (0,9 %) case. Mitral regurgitation (MR), being detected in 96 (83,5 %) patients, was distributed as follows: mild – in 73 (76,0 %) cases, and moderate – in 23 (24,0 %) patients. Tricuspidal regurgitation (TR) was revealed in 94 (81,7 %) patients, i.e. mild – in 79 (84,0 %), moderate – 11 (11,7 %), and severe – in 4 (4,3 %) cases.

The ECG-synchronized transesophageal echocardiography (TEE) was performed in all the patients using multiplane TEE transducer 4-7 MHz, with assessment of LAA functional state (by the value of LAA blood flow velocity [FV]), and the LASEC presence and severity. The median LAA FV (Me [IQR]) was 36 (29-45) cm/s (the min-max range 13-78 cm/s). The LASEC presence and intensity [6] was distributed as follows: 0 (absence of echogenicity); 1+ (mild); 2+ (mild-to-moderate); 3+ (moderate); and 4+ (severe).

All the patients received guideline-directed pharmacotherapy at baseline and in the pre-DC CV period [3, 11].

The total sample of patients was subdivided into three groups: without LASEC (grade «0») – 46 (40,0 %), $LASEC_{1-2}$ (pooled group with grades «1+» and «2+») – 46 (40,0 %), and $LASEC_{3-4}$ (pooled group with grades «3+» and «4+» [dense LASEC]) – 23 (20,0 %) cases. To study the factors, associated with presence of LASEC in general, the enrolled sample of patients was dichotomized into «LASEC» (n=79 [68,7 %]) and «no LASEC» (n=46 [31,3 %]) groups. Correspondingly, we dichotomized the enrolled sample of patients into «$LASEC_{3-4}$» (n=23 [20,0 %]) and «no $LASEC_{3-4}$» (n=92 [80,0 %]) groups, aiming at the determining the factors, associated with dense LASEC.

The data analysis was performed by the use of the statistical software programs (Statistica v. 13.3 (TIBCO Software Inc., USA); IBM SPSS Statistics v. 26.0 (Armonk, NY: IBM Corp., USA); MedCalc v. 20.113 [MedCalc Software Ltd, Belgium]). Continuous variables were presented as Me (IQR). Categorical variables were presented as absolute and relative (%) frequency. To compare characteristics between the studied groups, we used Kruskal-Wallis H test (for continuous variables) and χ^2 test (for categorical variables), with the following Mann-Whitney U-test and Fisher`s exact test, respectively, for *post hoc* comparisons. To determine the factors, associated with LASEC and $LASEC_{3-4}$, we used stepwise logistic regression analysis. The strength of the association between the studied factors and LASEC/$LASEC_{3-4}$ was measured by an odds ratio (OR) with 95 % confidence interval (CI). The discriminative power of the logistic regression models was assessed by the value of area under curve (AUC). The strong association of the studied factors with LASEC/dense LASEC was considered in case of AUC ≥0,8. A 2-tailed $p<0,05$ was considered statistically significant (considering the Bonferroni correction).

Table I. Baseline clinical characteristics of patients in groups without and with LASEC of different grades

Parameters		No LASEC N=46	$LASEC_{1-2}$ N=46	$LASEC_{3-4}$ N=23	p
Age, years		56 (52-64)	63 (54-69)	59 (51-65)	0,114
Males, n (%)		32 (69,6)	33 (71,7)	17 (73,9)	0,928
Females, n (%)		14 (30,4)	13 (28,3)	6 (26,1)	
Age AF onset, years		51 (48-57)	59 (50-63)	55 (46-61)	p_{1-2} = 0,040
BMI, kg/m^2		30,2 (25,7-33,0)	30,6 (26,0-34,3)	33,8 (30,5-36,7)	p_{1-3} = 0,018
BSA, m^2		2,02 (1,91-2,29)	2,09 (1,97-2,22)	2,13 (2,03-2,35)	0,229
HTN, n (%)		39 (84,8)	40 (87,0)	4 (82,6)	0,886
SCAD, n (%)		14 (30,4)	27 (58,7)	12 (21,7)	p_{1-2} = 0,039
History of MI, n (%)		2 (4,3)	5 (10,9)	5 (21,7)	0,083*
History of PCI, n (%)		2 (4,3)	11 (23,9)	2 (8,7)	p_{1-2} = 0,042
HF stage, n (%)	B	22 (47,8)	6 (13,0)	3 (13,0)	p_{1-2} = 0,002
	C	24 (52,2)	40 (87,0)	20 (87,0)	p_{1-3} = 0,022
CHA_2DS_2-VASc score, points		2 (2-3)	3 (2-4)	3 (2-4)	0,068**/***
DM, n (%)		3 (6,5)	6 (13,0)	8 (34,8)	p_{1-3} = 0,037

Notes: BSA – body surface area; PCI – percutaneous coronary intervention; p_{1-2} – statistical significance of difference between no LASEC and $LASEC_{1-2}$; p_{1-3} – statistical significance of difference between no LASEC and $LASEC_{3-4}$; * – p_{1-3}=0,090; ** – p_{1-2}=0,090; *** – CHA_2DS_2-VASc score in the pooled LASEC group: 3 (2-4) points (vs. 2 (2-3) points in no LASEC group; p=0,026)

Table II. Baseline echo parameters (TTE and TEE) of patients in groups without and with LASEC of different grades

Parameters	No LASEC N=46	$LASEC_{1-2}$ N=46	$LASEC_{3-4}$ N=23	p
LAV_i, cm^3/m^2	45,7 (38,5-54,9)*	48,8 (40,8-56,4)	52,3 (48,2-63,7)**	p_{1-3}=0,033
RAV_i, cm^3/m^2	35,0 (30,6-41,2)***	34,8 (29,0-47,2)	37,1 (32,1-52,9)**	0,472
LV EDV_i, cm^3/m^2	56,9 (48,8-60,4)	57,8 (51,3-65,7)	66,5 (48,7-85,3)	0,273
LV ESV_i, cm^3/m^2	23,3 (19,5-32,8)	26,1 (20,3-35,3)	35,4 (23,0-56,0)	0,053
LV EF, %	59 (40-63)	54 (48-61)	46 (35-53)	p_{1-3}=0,025 p_{2-3}=0,022
PH, n (%)	32 (69,6)	46 (100)	23 (100)	p_{1-2}<0,001 p_{1-3}=0,004
MR, n (%)	33 (71,7)	42 (91,3)	21 (91,3)	p_{1-2}=0,087#
TR, n (%)	37 (80,4)	36 (78,3)	21 (91,3)	0,399
LAA FV, cm/s	41 (35-54)	36 (32-45)	27 (19-29)	p_{1-2}=0,096 p_{1-3}<0,001 p_{2-3}<0,001

Notes: RAV_i, EDV_i and ESV_i – respectively, right atrial volume, LV end-diastolic volume and end-systolic volume, indexed by BSA; p_{1-2} – significance of difference between no LASEC and $LASEC_{1-2}$; p_{1-3} – significance of difference between no LASEC and $LASEC_{3-4}$; p_{2-3} – significance of difference between $LASEC_{1-2}$ and $LASEC_{3-4}$; * – n=41; ** – n=22; *** – n=36; # – frequency of MR in the pooled LASEC group: 63/69 (91,3 %) (vs. 33/46 (71,7 %) in no LASEC group; p=0,009)

RESULTS

The studied groups of patients were comparable by several baseline clinical characteristics, including age, gender and HTN frequency (Table I). At the same time, $LASEC_{3-4}$, as compared to no LASEC group, was characterized by the higher BMI and more frequent DM. Additionally, the fre-

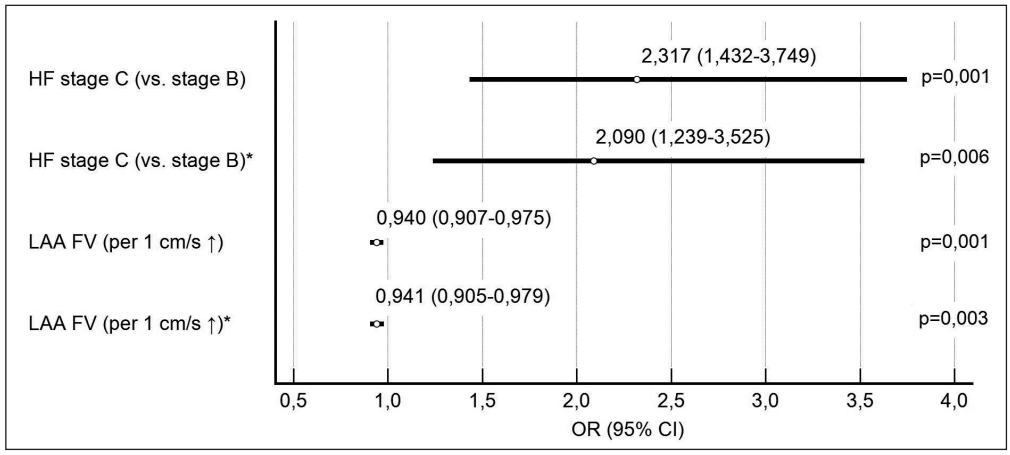

Fig. 1. Factors, strongly associated with LASEC in persistent AF patients. * – adjusted for the presence of PH; ↑ – increase

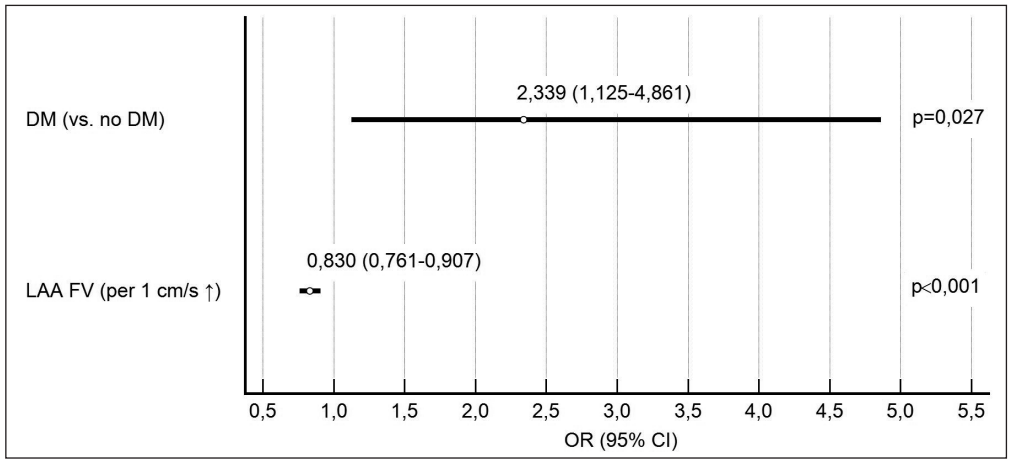

Fig. 2. Factors, strongly associated with dense LASEC in persistent AF patients. ↑ – increase

quency of MI history tended to be higher in patients with $LASEC_{3-4}$ (vs. no LASEC group). Such parameters, as age of AF onset, the frequency of SCAD and history of PCI, were higher in $LASEC_{1-2}$, in comparison with no LASEC (statistically significant) and $LASEC_{3-4}$ group (numerically, but insignificant). The CHA_2DS_2-VASc score was higher in patients with LASEC in general, as opposed to no LASEC group. Finally, the frequency of HF stage C was significantly higher in both $LASEC_{1-2}$ and $LASEC_{3-4}$, as opposed to no LASEC group (Table I).

The compared groups did not differ significantly by the duration of AF anamnesis, distribution of NYHA and EHRA classes, and the studied laboratory parameters.

$LASEC_{3-4}$ group, in comparison with no LASEC one, was characterized by the higher value of LA volume, indexed by BSA (LAV_i) and more depressed LV EF (Table II). Besides, $LASEC_{1-2}$ and $LASEC_{3-4}$ groups were represented totally by patients with PH. The frequency of MR was higher in patients with LASEC in general, as compared to no LASEC group. Lastly, LAA FV had a tendency to decrease with more LASEC degree (Table II).

The stepwise logistic regression analysis revealed the certain factors, strongly associated with LASEC in persistent AF patients with the duration of AF episode ≥90 days, namely the HF stage C status and lower TEE-derived LAA FV, as well as the presence of TTE-derived PH (AUC 0,829; 95 % CI 0,748-0,893) (Fig. 1; data presented as unadjusted and adjusted for the presence of PH). At the same time, the presence of DM, along with lower LAA FV, appeared to be strongly associated with dense LASEC in such patients (AUC 0,887; 95 % CI 0,815-0,939) (Fig. 2).

DISCUSSION

LASEC is a relatively common phenomenon in patients with AF [5]. We observed LASEC in 68,7 % of the enrolled patients, which is consistent with the data, suggesting that the prevalence of LASEC may exceed 50 % in patients with non-valvular AF, being more frequent in non-paroxysmal than paroxysmal AF [4, 5].

The presence of HF stage C and DM turned out to be strongly associated with LASEC and dense LASEC, respectively. It has been widely accepted, that these factors increase the risk of thromboembolic complications in patients with AF, and are tightly related to AF progression, electrical and structural remodeling of the myocardium [1, 3, 12].

Despite being significantly higher in the LASEC group (as compared to no LASEC one), the CHA_2DS_2-VASc score did not appear to be an independent marker of LASEC in the enrolled patients. The existing data suggest that the predictive value of the CHA_2DS_2-VASc scoring system for LASEC in non-valvular AF is limited. This score doesn't include a whole spectrum of factors prob-

ably associated with LASEC formation, such as AF type, biochemical (renal dysfunction, hyperuricemia, etc.) and echocardiographic parameters, such as LV hypertrophy and function, LA size, fibrosis and dysfunction, and LAA dysfunction [2, 5, 8, 13, 14].

We also revealed the presence of PH to be strongly associated with LASEC. In turn, PH is related to the increased LV filling pressure and, consequently, LA pressure [10, 15]. From a therapeutic perspective, treatment aimed at decreasing LV filling pressure should be considered to reduce a risk of embolic events and AF progression [15].

From the pathophysiological viewpoint, LASEC is closely related to the condition of the atrial tissue [13]. AF and atrial fibrosis are interrelated in a vicious circle manner, and the increased atrial fibrosis can cause LASEC and LA thrombus formation [5]. We revealed a strong association between lower LAA FV and LASEC, including its dense pattern. In general, this association reflects the extensive LA remodeling with formation of atrial cardiomyopathy [2, 8, 14]. Moreover, the significance of LA fibrosis as a factor related to LASEC, increases substantially in persistent AF, in contrast to its paroxysmal pattern, where this relationship is determined, to a greater extent, by LA size and function [14].

LASEC occurs under various pathological conditions, including structural, hemodynamic and biological changes. The presence of LASEC is not only the echo sign of the thrombogenic milieu in the atria, but also reflects the complex process of LA remodeling. Thus, considering the LASEC`s pathophysiology, its prediction may contribute to both thromboembolic and AF recurrence risk stratification in patients with non-valvular AF [1, 5, 7, 9]. Consequently, the therapeutic strategies, aiming to modify the factors, associated with LASEC, bring the potential to reduce the risk of thromboembolic complications, and to increase the effectiveness of SR maintenance after CV [1-3, 8, 9]. In case of primary persistent AF patients, the early rhythm control may confer additional benefits by modulating electrical and structural atrial remodeling, and, finally, by improving clinical outcomes in such patients [1, 15].

The present study is subjected to some limitations, inherent to its retrospective, single-center design. The obtained results reflect the real-world practice of enrollment of patients with long-term episodes of persistent AF for CV. Another minor limitation is the lack of data on LV diastolic dysfunction. Further research is needed to visualize myocardial fibrosis in atria and study electrophysiological properties of atrial tissue.

CONCLUSIONS

The TEE-derived LASEC in patients with long term episodes (≥90 days) of persistent AF was strongly associated with the presence of HF stage C and TTE-derived PH, and with lower TEE-derived LAA FV. The presence of DM, in addition to lower LAA FV, was related to dense LASEC. Apart from LASEC *per se*, these clinical and hemodynamic factors should be considered at management of such patients, aiming at further reduction of the thromboembolic risk and prevention of AF progression.

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ORCID and contributionship:
Yaroslav V. Skybchyk: 0000-0002-4443-3137 [A-D]
Oleg J. Zharinov: 0000-0002-4089-9757 [A, E, F]
Kyrylo O. Mikhaliev: 0000-0003-3759-6699 [B-D]

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CORRESPONDING AUTHOR
Yaroslav V. Skybchyk
Shupyk National Healthcare University of Ukraine
5A Bratyslavska st., 02660 Kyiv, Ukraine
tel: +380503700397
e-mail: slavik292@gmail.com

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ORIGINAL ARTICLE

MORPHOLOGICAL JUSTIFICATION OF THE SIGNIFICANCE OF LUMBAR ARTERIES IN THE PREVENTION OF SPINAL CORD ISCHEMIA IN ATHEROSCLEROTIC LESIONS OF ABDOMINAL AORTA

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Valentyn Y. Smorzhevskiy[1], Olena O. Dyadyk[1], Igor V. Boiko[2], Yevhenii S. Sikalenko[1]

[1]SHUPYK NATIONAL HEALTHCARE UNIVERSITY OF UKRAINE, KYIV, UKRAINE

[2]STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

The aim: To investigate atherosclerosis of the abdominal part of the aorta and atherosclerosis of the lumbar arteries, aimed at improving surgical tactics during reconstructive interventions on the abdominal part of the aorta in patients with multifocal atherosclerosis.

Materials and methods: 20 autopsies were performed. The macro preparation consisted of the part of the abdominal aorta 1x1 sm taken along with a separated lumbar artery for 1-1,5 sm. Histological cuts were coloured with hematoxylin and eosin. The histochemical research was conducted in order to establish changes in all layers of blood vessels. The immunohistochemical research was carried out along with generally accepted histological methods in 10 cases to determine the morphological vessel wall functional state, connective tissue and smooth muscle components.

Results: In all cases there were morphological signs of aortic atherosclerosis with different degrees of damage to the lumen. In none of the analyzed cases did we establish pathomorphological signs of atherosclerosis of the lumbar artery distal to the mouth. In the walls of the lumbar arteries, we noted the preservation of the layered structure, the integrity of the endothelial cells, the normal arrangement of smooth muscle cells.

Conclusions: It was established that there cannot be the atherosclerotic occlusion of the lumbar artery, since there are no signs of atheromatous lesions in its walls, the structure of all layers is preserved, the endothelial damage is absent, the location and structure of the lining cells is normal.

KEY WORDS: atherosclerosis, abdominal aorta, the morphology of the aorta and lumbar arteries.

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INTRODUCTION

At the time of the study, there is insufficient data on the link between ischemic spinal cord strokes and the correlation of spinal cord blood supply. Therefore, we sought to investigate atherosclerosis of the abdominal aorta and atherosclerosis of the lumbar arteries, and study the nature of their atherosclerotic lesions, because when surgical interventions are performed on the abdominal part of the aorta after endarterectomy from the aorta or removing of the "aneurysmal cup", we always observe the free passage of the mouths of the lumbar arteries with varying degrees of retrograde blood flow. And we never observed occlusion of the lumbar artery itself, but only the overlap of the ear of the latter with plaques or thrombus from the aorta.

Although diseases of the peripheral arteries for atherosclerosis have been well studied, there is insufficient data on the ischemic pathology of the spinal cord in connection with atherosclerosis, despite the fact that areas of the spinal cord that are «softened» due to atherosclerosis were first described in the late 19th century [1]. Like atherosclerosis, myelopathies from focal necrosis, valerian degeneration and neuronal atrophy are referred to as «old age diseases». These nerve degradations may manifest as incomprehensible local and generalized paresthesia, paresis, muscle atrophy, pain, urinary incontinence, decreased proprioceptive sensitivity and balance, hyper reflection or decreased tendon reflexes [2].

From an anatomical and pathophysiological point of view, current knowledge and understanding of atherosclerosis confirm the hypothesis of the tendency to form atheromatous plaques more often near arterial bifurcations [3].

Due to a violation of normal laminar blood flow, the tension acting on the inner shell of the vessel causes endothelial damage and inflammatory reaction [3]. The numerous divisions of the arteries through which blood must pass to penetrate the spinal cord, and the «flat and curved» nature of these vessels, support the theory that degenerative changes in neurons may be associated with atherosclerotic changes in the vascular system that perforate the spinal cord [4, 5]. Despite this association, few studies have been conducted to assess the existence of such a correlation between these two variables. In the majority of available literature, studies and descriptions of spinal cord blood supply dating back to the mid-20th century,

only speculative conclusions and untested hypotheses have been made [1]. In the limited number of studies that exist, most of them seem to support the availability of correlations. However, most of these data are more than three decades old. Furthermore, in the existing literature, studies were conducted on a sample population from different European countries such as Germany, France, England, Italy, the Netherlands, and Japan [1, 4, 6-13]. The paucity of current literature requires further research using more modern specific histological methods to establish or disprove a pathological link between systemic atherosclerosis and myelopathy.

Tubbs R and co-authors found no atherosclerotic lesions of arteries supplying blood to the spinal cord in any pathohistological material from patients with atherosclerosis of the aorta in histological studies of spinal cord arteries [14].

They explain this by the fact that due to the large number of arterial divisions in the spinal arterial network, turbulent blood flow and pressure on the vascular wall are limited, which does not contribute to the development and deposition of plaques.

THE AIM

The aim of the research was to investigate abdominal aortic and lumbar atherosclerosis, study the nature of their atherosclerotic lesions to improve surgical tactics in reconstructive interventions on the abdominal part of the aorta in patients with multifocal atherosclerosis.

MATERIALS AND METHODS

Of the total number of autopsies that were selected for our study (n = 20), 14 were male, 6 were female. The average age at the time of death was 65.5±4.5 years. The cause of death of the patients was an acute cardiovascular failure, acute renal failure, and multiple organ failure. Our study did not include autopsy cases that had spinal cord pathology or underwent spinal cord surgery. After the corpse was randomly selected (from a total of 35 bodies) for incision, samples of the macro preparation were collected and placed in a 10% neutral formaline. These samples consisted of a part of the abdominal aorta of 1 x 1 cm taken together with the separated lumbar artery for 1-1,5 cm.

After the autopsy, the resulting fragments of macro preparations of the arteries were placed in a 10% neutral formalin. The samples are represented by a part of the abdominal aorta of 1 x 1 cm taken together with the separated lumbar artery for 1-1,5 cm.

Vascular preparations have been comprehensively studied at the Department of Pathological and Topographic Anatomy of Shupyk National Healthcare University of Ukraine (Head of the Department, professor Dyadik O.O.). This clinical research, before being planned, passed bioetical examination by the commission on ethics of the Shupyk National Healthcare University of Ukraine, Ministry of Health of Ukraine. The research was performed in compliance with the principles of bioethics and legislative norms and requirements for conducting clinical/biomedical research, namely: the Declaration of Helsinki (1964-2013), Constitution of Ukraine and the Civil Code of Ukraine (2006), Fundamentals of Ukrainian legislation on health care (1992), Guidelines for clinical studies of the Ministry of Health of Ukraine № 42-7.0:2005 "Medicines. Good clinical practice" (2005), Standard regulations on ethics commissions at medical institutions conducting clinical trials (Order of the Ministry of Health of Ukraine № 690 from 23.-9.2009).

In the pathomorphological study, the resulting vascular fragments of the arterial type – fragments of the abdominal part of the aorta and lumbar artery – were recorded in a 10% solution of neutral buffered formalin (pH 7.4) for at least 24-36 hours. After fixing the material, the necessary sections were cut for the evaluation of parts, which were then processed in the Excelsior AS (Thermo Fisher Scientific, UK), and then poured into paraffin blocks on the HistoStar (Thermo Fisher Scientific, UK). Serial histological cuts with a thickness of 2-3mkm were produced from the obtained paraffin blocks on the rotating microtome NM 325 (ThermoShandon, UK).

The obtained histological sections were stained with hematoxylin and eosin, and a histochemical study was performed to establish changes in all layers of vessels, the presence of collagen, smooth muscle fibres, signs of fibrogenesis processes, and van Gyson's picrofuxin staining was performed [15-17].

Along with the generally accepted histological methods, we did immunohistochemical research in 10 cases to determine the morphological and functional state of the vessel wall, connective tissue and smooth tissue components. For the immunohistochemical analysis the cuts were placed on adhesive rocks Super Frost Plus (Menzel, Germany). For the high-temperature treatment of epitopes of antigens we used a citrate buffer with pH6, EDTA buffer pH8, the detection system Vitro Master Polymer Plus Detection System (Peroxidase) including chromogen DAB Quanto (Master Diagnostica, Spain). The monoclonal antibodies (MAT) of the mouse to the smooth ligament actin (α-SMA, Clone 1A4 (asm-1)) were used, and rabbit MAT - to the vimentin (Vimentin, Clone SP20).

The presence and severity of expression of α-SMA and vimentin were evaluated according to the visual analog scale of the prevalence of expression: 0 - not visualized/no color, 1- less than 1/3 of the area of the drug, 2 - from 1/3 to 2/3 of the area of the drug, 3 - more than 2/3 of the area of the drug; and intensity scale: 0-color is not visualized (not available), 1-weak color intensity, 2-moderate color intensity, 3-expressed color intensity. The evaluation of expression was carried out according to the recommendations of D.J. Dabbs and other authors [17-19].

Pathomorphological research, photo archiving was carried out using ZEISS optical microscopes (Germany) with the data processing system "AxioImager. A2" with enlarged lenses 5x, 10x, 20x, 40x, binocular pin 1.5 and glasses 10 with ERC 5s and "Carl Zeiss" Primo Star with camera Axiocam105 colour.

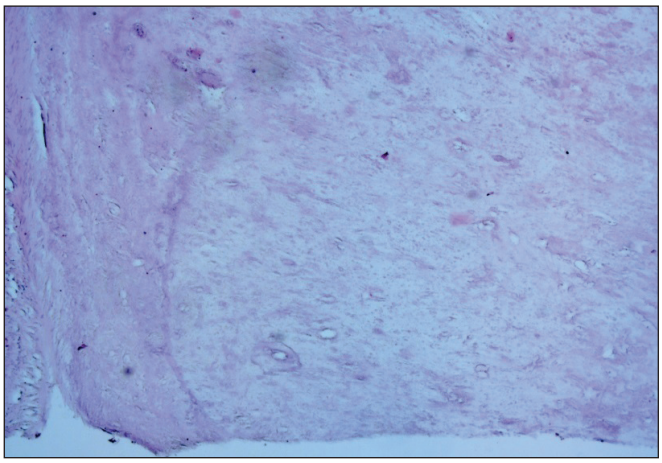

Fig. 1. Fragment of the aortic wall with a large atheromatous plaque. Coloured by hematoxylin and eosin. Zoom to 50 times.

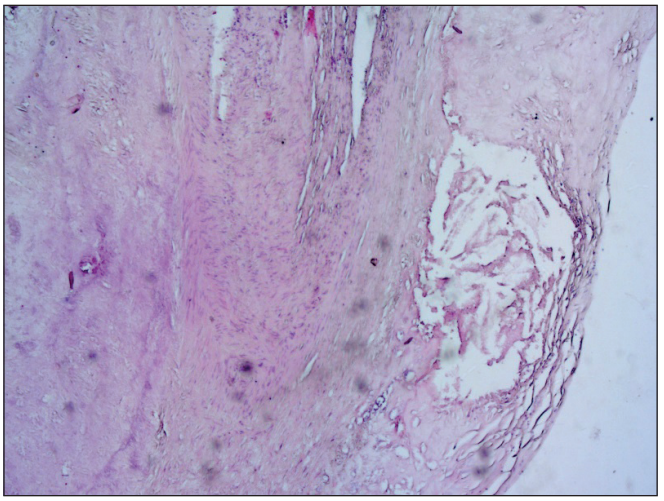

Fig. 2. A new atheromatous plaque is subadventitally located next to a large atheromatous plaque. Coloured by hematoxylin and eosin. Zoom to 50 times.

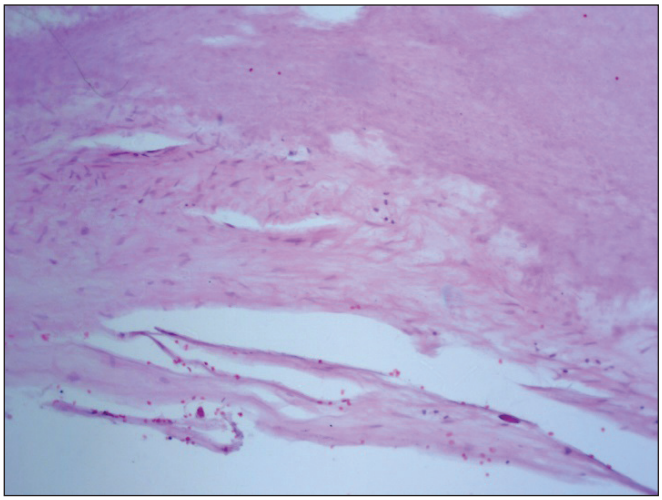

Fig. 3. Fragment of the wall of the aorta, the atheromatous-changes area, and the formation of splinter-like vessels. Zoom to 100 times.

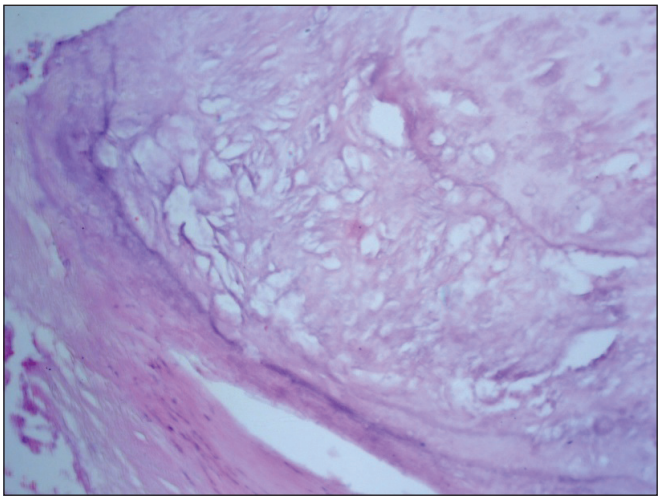

Fig. 4. Fragment of the wall of the aorta, the atheromatic-changed area, the layering area under the plaque. Coloured by hematoxylin and eosin. Zoom to 100 times.

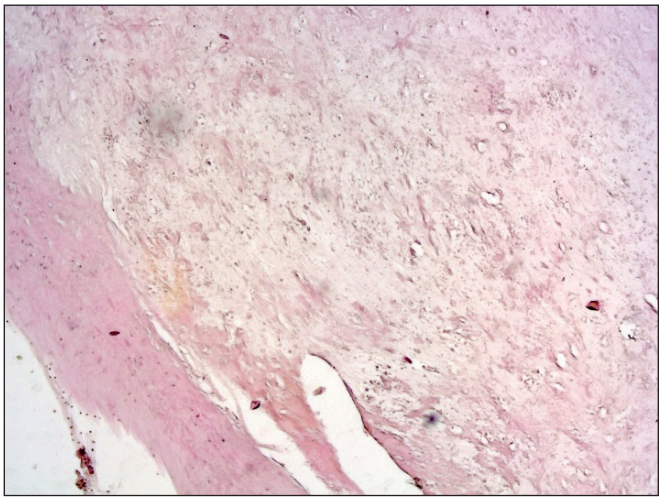

Fig. 5. Fragment of the aortic wall, atheromatic-changed area, layering area under the plaque, the segmental proliferation of young connective tissue in the area around the atheromatic plaque. Coloured according to van Gyson. Zoom to 50 times.

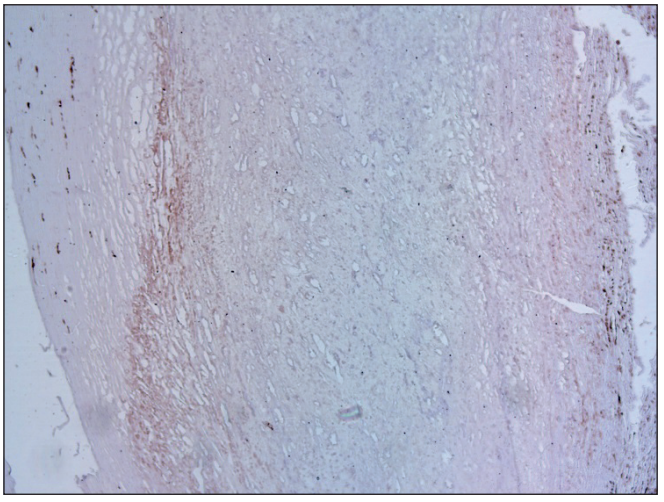

Fig. 6. Fragment of the aortic wall, achromatically altered area, insignificant segmental expression of connective tissue components. The immunohistochemical research from MAD to Vimentin. Zoom to 100 times.

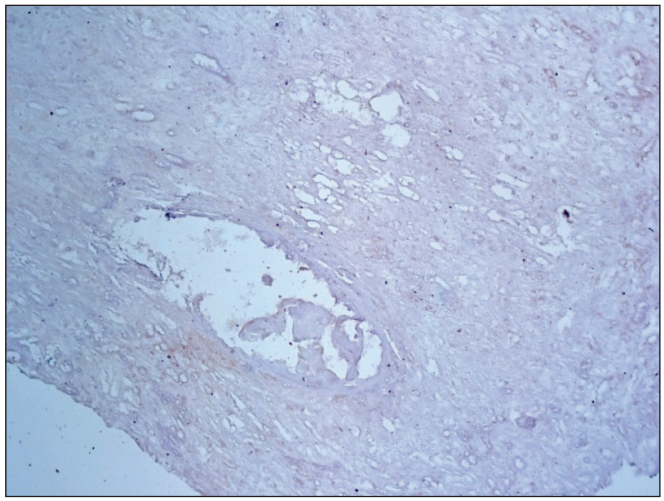

Fig. 7. Fragment of the aortic wall, an atheromatic plaque near the advent layer, and absence of vimentin expression. The immunohistochemical research from MAD to Vimentin. Zoom to 100 times.

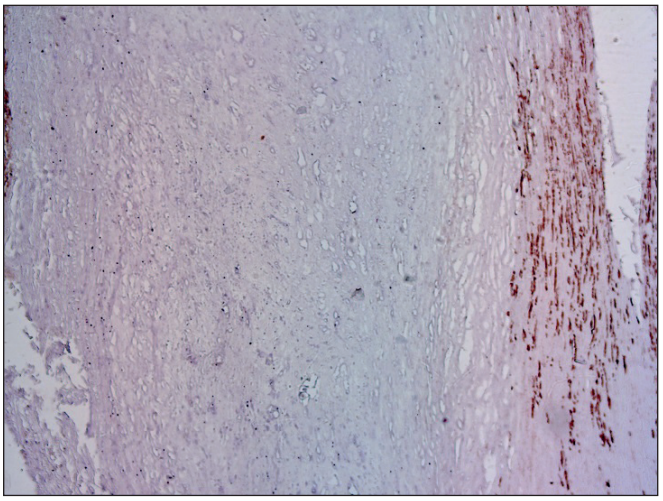

Fig. 8. Fragment of the wall of the aorta, atheromatic plaque, in the zone of adventication positive smooth membrane cells. The immunohistochemical research from MAD to α-SMA. Zoom to 100 times.

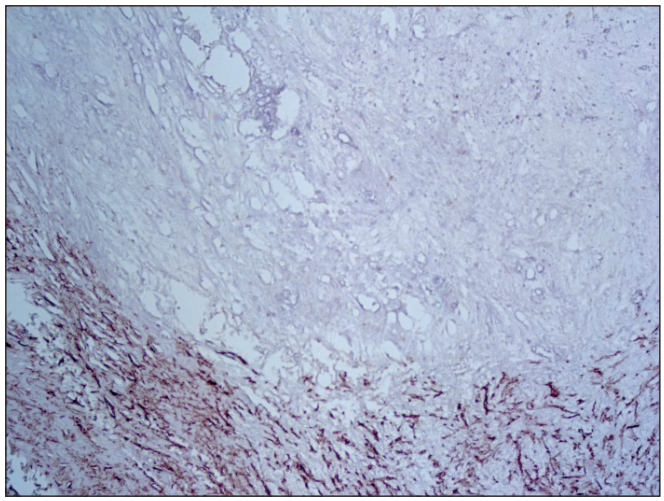

Fig. 9. Fragment of the wall of the aorta, atheromatous plaque, positive unordered smooth ligaments in the zone of adventitia, fragments of positive cells. The immunohistochemical research from MAD to α-SMA. Zoom to 100 times.

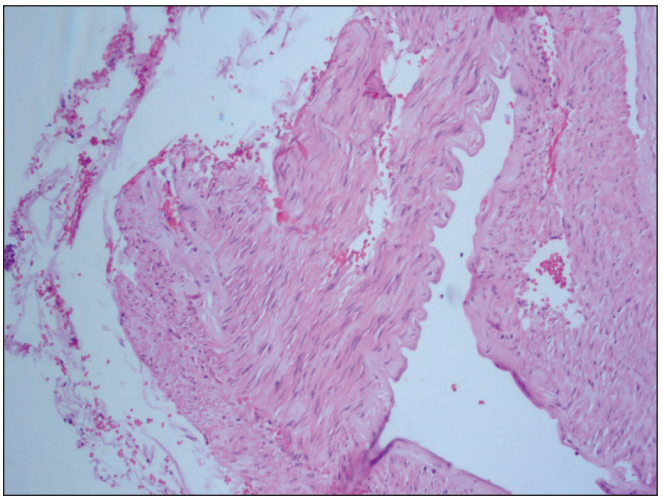

Fig. 10. Lumbar artery. The layered structure is preserved, the proliferation of smooth ligament cells is segmentally pronounced, and there are signs of spasm. Coloured by hematoxylin and eosin. Zoom to 50 times.

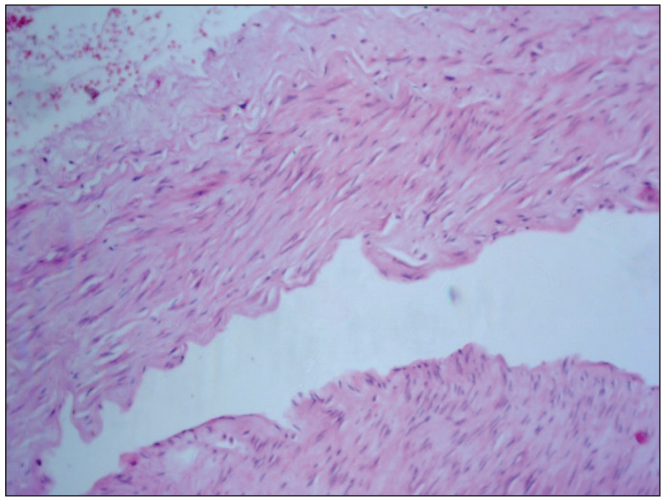

Fig. 11. Lumbar artery. The layer structure of the wall, the integrity of endothelial cells, the normal location of smooth ligaments, and signs of spasm are preserved. Coloured by hematoxylin and eosin. Zoom to 100 times.

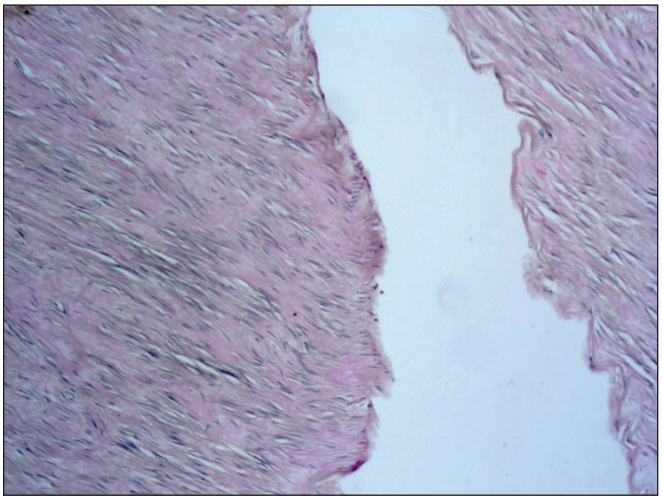

Fig. 12. Lumbar artery. The layer structure of the wall, the integrity of endothelial cells, the positive coloration of collagen structures are preserved. Colouring by van Gyson. Zoom to 100 times.

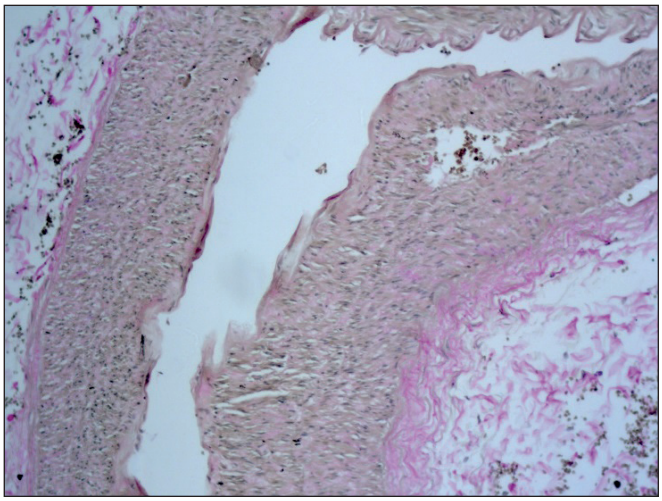

Fig. 13. Lumbar artery. The layer structure of the wall, the integrity of endothelial cells, the positive colouration of collagen structures, and the perivascular segmental growth of young connective tissue are preserved. Colouring by van Gyson. Zoom to 100 times.

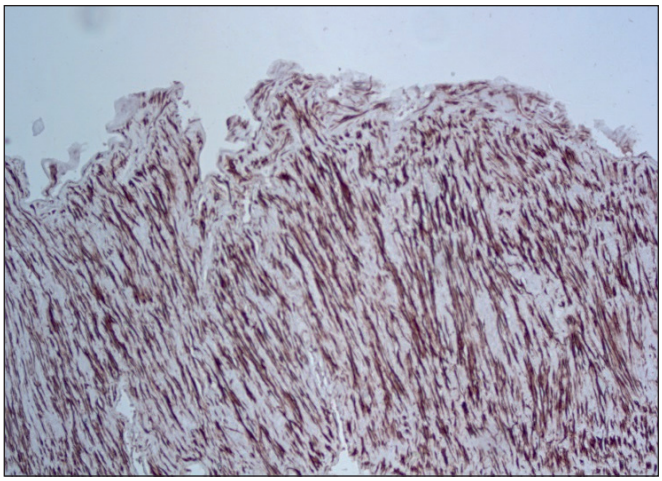

Fig. 15. Lumbar artery. The normal course of elements of the vessel wall. The positive expression of connective cells and collagen fibres. The immunohistochemical research from MAD to Vimentin. Zoom to 100 times.

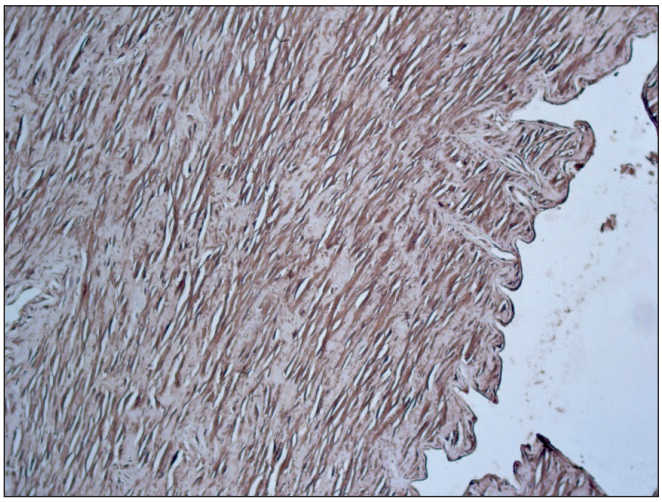

Fig. 17. Lumbar artery. Positive expression of normally built and located lining cells in the wall of the lumbar artery, part of the cells with signs of hypertrophy, undamaged endothelium. The immunohistochemical research from MAD to α-SMA. Zoom to 100 times.

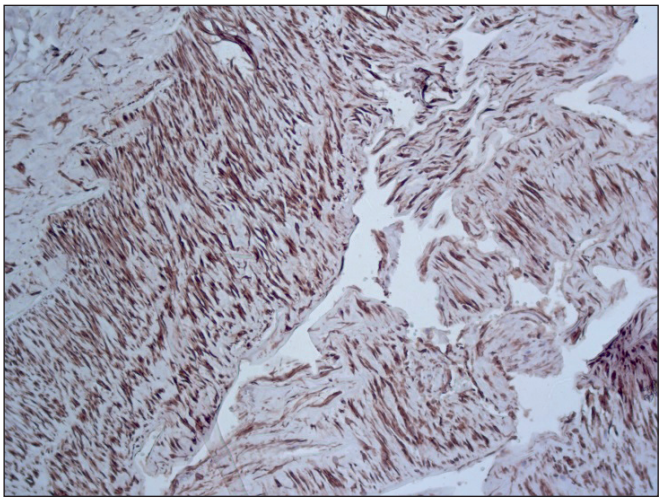

Fig. 14. Lumbar artery. Positive expression of connective cells and collagen fibers. The immunohistochemical research from MAD to Vimentin. Zoom to 100 times.

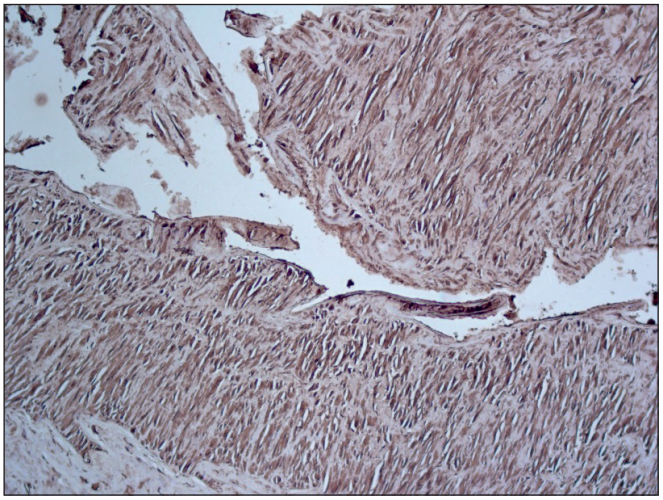

Fig. 16. Lumbar artery. The positive expression of normally located smooth ligament cells in the wall of the lumbar artery. The immunohistochemical research from MAD to α-SMA. Zoom to 100 times.

RESULTS

In 20 cases of the autopsy of patients who had manifestations of abdominal aortic atherosclerosis, we collected fragments of the aorta with lumbar arteries and conducted a comprehensive pathomorphological study of the lesions of these arteries.

We established morphological signs of aortic atherosclerosis with varying degrees of lumen occlusion in all cases. We have not established any pathomorphological signs of atherosclerosis of the lumbar artery more distant than the throat in the analyzed cases.

A comprehensive pathomorphological examination of the affected areas of the aorta and lumbar artery was carried out. It should be noted that the informed voluntary consent of the patient was not taken for this study, because in the event of death this consent would be unethical. Information about patients who entered the study is not disclosed.

After a pathomorphological study of fragments of the affected area of the abdominal aorta with manifestations

of atherosclerosis, we found that while carrying out macroscopic examination the atheromatous plaques and atheromatous ulcers of various sizes were available. In the microscopic study of these areas, there were observed ulcers of the endothelium, a sharp thickening of the wall of the aorta due to atheromatous masses, destruction of layers, and the appearance of atheromatous areas closer to adventism (Fig. 1).

In some cases of the manifestation of the progression of atherosclerosis, we found out that in the appearance of new areas of atheromatous lesions closer to adventism near large atheromatous plaques or ulcers (Fig. 2). In some cases of manifestation of progression of atherosclerosis we found the appearance of new areas of atheromatous lesions closer to adventism near large atheromatous plaques or ulcers (Fig. 2).

We realized that in certain areas the manifestations of initial neoangiogenesis were observed in the form of the formation in the wall of the aorta near the atheroma-changed areas of thick vessels (Fig. 3).

In the areas of atheromatous plaques and ulcers, we also observed the layering of subordinate tissues, which is a prerequisite for the formation of aneurysm changes and aneurysms (Fig. 4).

It should be noted that in the areas of layering, fibro and fibrillogenesis processes are weakly expressed. There is a weak growth of immature connective tissue, which may not contribute to the stabilization of the atheromatous process in this area of lesion (Figure 5).

There was an unequal positive expression of smooth ligament cells around atheromatous areas, in the zone of adventism during the immunohistochemical research (Fig. 8).

The immunohistochemical research was made from MAT to the connective tissue marker vimentin and MAT to the smooth ligament actin α-SMA.

During the immunohistochemical research from MAT to vimentin we found a poorly defined segmental expression (Fig. 6), and a complete absence of expression in some parts of the areas including zones with signs of progression of atheromatous lesions and the formation of new atheromatous plaques near the advent layer (Fig.7).

It should be noted that positive smooth ligament cells were located without a certain order. There were fragmented cells of varying degrees of severity of expression (Fig. 9).

When studying fragments of the separated lumbar artery, in no case did we find any morphological signs of the atheromatous lesion (Fig. 10).

We noted the preserved layer structure, the integrity of endothelial cells, the normal location of smooth ligaments, and segmental hypertrophy of a part of the cells in the walls of the lumbar arteries (Fig. 11).

When doing histochemical research - staining by van Guyson - we found that in the areas of thickening of the middle layer in the lumbar arteries there was a positive reaction with collagen fibres (rose-red colour). The intensity of the colour was not pronounced, indicating the normal structure of the vessel wall, and the absence of manifestations of sclerosis (Fig. 12).

In the part of the investigated lumbar arteries in the advent zone, the segmental growth of young connective tissue was observed perivascularly (Fig. 13).

We carried out the immunohistochemical research from MAD to the binding tissue marker vimentin and MAD to the smooth ligament actin α-SMA.

During the immunohistochemical research from MAD to vimentin we clearly showed the normal structure of the preserved layers of lumbar arteries, the normal location of connective-cellular structures in the layers of the vessel, the absence of manifestations of wall disorders, the absence of signs of atheromatic lesions (Fig.14, Fig.15).

There was a pronounced positive expression of normally parallelly located smooth ligament cells observed in the wall of the lumbar arteries during the immunohistochemical research (Fig. 16). There was no damage to the vascular endothelium.

Part of the smooth ligament cells with signs of hypertrophy, absence of atheromatous vascular lesion (Fig. 17).

DISCUSSION

Ischemia and infarction of the spinal cord (the so-called "senile paraplegia" mentioned in the older literature) have received little attention compared to other areas of the body, such as the heart and brain. Spinal cord infarctions are thought to account for only 1% of all strokes. Hughes and Brownell postulated that the spinal cord is much less susceptible to atherosclerosis than the brain due to its complex blood supply and a tendency toward developing collateral flow. However, the morbidity and mortality related to spinal cord ischemia may be overlooked due to the difficulty of diagnosis. Also, a condition such as atherosclerosis may not be acutely fatal but is capable of leading to a myriad of other conditions that are more likely to be diagnosed at post-mortem autopsies, such as thrombosis, embolus, aneurysm, or anterior spinal artery syndrome (Spiller syndrome) [14].

According to the research of R. Shane Tubbs was identified proximal atherosclerosis in the majority of cadavers but with varying degrees of luminal occlusion. The greatest degree of luminal occlusion was found in the descending abdominal aorta. No specimen was found to have atherosclerosis of the anterior or posterior spinal or radicular arteries. No spinal cord histology showed signs of ischemia, even in specimens with a significant large parent vessel (vertebral artery and aorta) occlusion due to atherosclerosis. Neuropathology of these adjacent cord segments revealed no signs of ischemia or demyelination [14].

The comprehensive pathomorphological research of the aorta and lumbar arteries gives us grounds to believe that insufficient blood supply to the spinal cord does not occur due to atherosclerosis of the arteries that supply blood to the spinal cord, but rather the overlap of the lumen of the lumbar artery with atherosclerotic plaques from the aorta in the mouths of these arteries [14]. This in turn proves the importance of preserving the lumbar arteries as a source of blood supply to the spinal cord during reconstructive

surgical interventions on the abdominal aorta [10]. The problem in the absence of antegrade blood flow through the lumbar arteries is connected with atherosclerosis of the aorta.

CONCLUSIONS

During the research, thanks to comprehensive pathomorphological studies involving histochemical and immunohistochemical methods, the difference in the type of structure of the aorta and lumbar arteries was proved. The aorta is an elastic type of structure of the arteries. The lumbar arteries are muscular ones. It was established that there cannot be the atherosclerotic occlusion of the lumbar artery, since there are no signs of atheromatous lesions in its walls, the structure of all layers is preserved, the endothelial damage is absent, the location and structure of the lining cells is normal.

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ORCID and contributionship:
Valentyn Y. Smorzhevskiy: 0000-0001-8410-3944 [A, F, E]
Olena O. Dyadyk: 0000-0002-9912-4286 [A, C, E, F]
Igor V. Boiko: 0000-0002-2929-5549 [B, E]
Yevhenii S. Sikalenko: 0000-0001-7652-8918 [B-E]

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The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Yevhenii S. Sikalenko
Shupyk National Healthcare University of Ukraine
9 Dorogozhytska St., 04112 Kyiv, Ukraine
tel: +380970004340
e-mail: esikalenko@gmail.com

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ORIGINAL ARTICLE

ASSOCIATION OF FRACTIONAL FLOW RESERVE WITH CLINICAL AND ANGIOGRAPHIC CHARACTERISTICS OF PATIENTS WITH STABLE CORONARY ARTERY DISEASE

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Mykola V. Stan[1, 2], Kyrylo O. Mikhaliev[3], Oleg J. Zharinov[1, 2], Andriy V. Khokhlov[2], Anatolii M. Kravchenko[3], Borys M. Todurov[1, 2]

[1]SHUPYK NATIONAL HEALTHCARE UNIVERSITY OF UKRAINE, KYIV, UKRAINE
[2]HEART INSTITUTE OF THE MINISTRY OF HEALTH OF UKRAINE, KYIV, UKRAINE
[3]STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

The aim: To identify clinical and angiographic factors, associated with fractional flow reserve (FFR), in stable coronary artery disease (CAD) patients.

Materials and methods: The study consecutively enrolled 68 patients with stable CAD (mean age (63±8,0) ys) and angiographically intermediate coronary lesions (diameter stenosis 50-90 %), with FFR assessment. Stable angina of CCS classes II and III was diagnosed in 42 (62 %) and 15 (22 %) patients, respectively; left ventricular hypertrophy (LVH) – 27 (40 %); severe coronary stenosis (SCS) (70-90 %) – 46 (68 %). The overall CAD complexity was assessed by SYNTAX score. FFR «negative» group (FFR_{NEG}) included the patients with non-significant FFRs (>0,80) (n=28 [41 %]). In case of at least one significant FFR (≤0,80), a patient was assigned to FFR «positive» group (FFR_{POS}) (n=40 [59 %]).

Results: FFR_{POS} (vs. FFR_{NEG}, respectively) was characterized by the higher frequency of angina class III (32 % vs. 7 %; p<0,001), LVH (53 % vs. 21 %; p=0,010) and SCS (98 % vs. 25 %; p<0,001). The SYNTAX score was strongly associated with FFR ≤0,70 and ≤0,65, and moderately – with FFR ≤0,65.

Conclusions: In patients with stable CAD and intermediate coronary artery stenosis, the presence of at least one functionally significant lesion (FFR ≤0,80) was associated with the higher prevalence of angina class III, LVH and more advanced coronary stenosis (≥70 %). The greater overall CAD complexity increased the probability for the angiographically significant coronary lesions to be more functionally compromised.

KEY WORDS: fractional flow reserve, stable coronary artery disease

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INTRODUCTION

The invasive coronary angiography (ICA) has been traditionally recognized as a standard reference test for the assessment of obstructive epicardial coronary artery disease (CAD) [1-3]. However, there is a frequent mismatch between the angiographic and haemodynamic findings, especially in patients with intermediate coronary stenoses or multivessel disease [2]. Thus, numerous coronary physiology tests are recommended to be integrated into the management of stable CAD (SCAD) patients, with the aim to detect ischemia and guide the strategy of revascularization [4, 5].

The assessment of fractional flow reserve (FFR) is recommended in the current guidelines as one of the criteria, which may influence the decision regarding myocardial revascularization [1-3, 6, 7]. This might be especially valuable to define hemodynamic significance of angiographically intermediate coronary lesions [2, 3, 8]. At the same time, there is an obvious need to understand relation of FFR to the clinical data, lesion-specific traits and overall CAD complexity [9, 10].

THE AIM

The aim of the study was to identify the clinical and angiographic factors, associated with FFR, in SCAD patients.

MATERIALS AND METHODS

The cross-sectional study consecutively enrolled and analyzed the data from 68 patients with SCAD and intermediate coronary lesions (luminal narrowing with a diameter stenosis 50-90 % [2]), with concomitant FFR assessment, during the period 2019-2021.

The study was conducted in compliance with the basic principles of the Council of Europe Convention on Human Rights and Biomedicine, World Medical Association Declaration of Helsinki on the ethical principles for medical research involving human subjects, and current national regulations. The study protocol was approved by the local ethics committee. All the patients provided written informed consent.

The study did not include patients with acute coronary syndrome within the last month, acute heart failure,

contraindications to adenosine administration, severe comorbidities, severe valvular heart disease, previous cardiac surgery, left main disease, coronary lesions with stenosis <50 % and >90 %, and the lack of informed consent.

We enrolled 45 (66 %) males and 23 (34 %) females aged 39 to 82 ys; mean age 63 ± 8,0 ys. Body mass index (BMI) was (median (Me); interquartile range [IQR]) 29,1 (26,1-32,4) kg/m^2; 27 (40 %) patients were obese.

The essential hypertension (HTN) was diagnosed in 64 (94 %) patients; stable angina pectoris – 57 (84 %) (including 42 (74 %) and 15 (26 %) patients with Canadian Cardiovascular Society (CCS) classes II and III [1], respectively); previous myocardial infarction (MI) – 30 (44 %); previous stroke or transient ischemic attack (TIA) – 10 (15 %); atrial fibrillation (AF) 15 (22 %); and chronic heart failure (HF) stage B – in 25 (37 %), and stage C – in 43 (63 %) cases [11]. Percutaneous coronary intervention (PCI) has been already performed in 24 (35 %) cases.

Diabetes mellitus type 2 (DM) was present in 19 (28 %) patients, peripheral arterial disease (PAD) – 12 (18 %), chronic kidney disease (CKD) – 18 (27 %). Two (3 %) patients had either chronic obstructive pulmonary disease or bronchial asthma, respectively.

All the patients received guideline-directed pharmacotherapy [1, 11].

The mean (Me [IQR]) fasting glucose, total serum cholesterol and serum creatinine levels were 5,9 (5,3-6,7) mmol/l, 4,5 (3,6-5,7) mmol/l and 89 (78-95) μmol/l, respectively. The mean (Me [IQR]) estimated glomerular filtration rate (by CKD-EPI equation) was 74,0 (63,8-84,1) ml/min/1,73 m^2.

The transthoracic echocardiography was performed according to the standard protocol. Left ventricular (LV) myocardial mass was calculated by the ASE-modified cube formula, and indexed by height^{2,7} [12], considering the widespread obesity among the enrolled patients. LV hypertrophy (LVH) was identified in 27 (40 %) patients. The mean LV ejection fraction was (Me [IQR]) was 58 % (52-61 %).

ICA was performed by the use of the Optima IGS 330 angiography system (GE Hualun Medical Systems Co., Ltd., China) according to the standard practice. The stenosis of the epicardial coronary artery was considered in case of a lesion with a visually assessed diameter stenosis of at least 50 % in a vessel larger than 2 mm in diameter [2]. We analyzed the stenotic lesions in three main epicardial coronary arteries, namely left anterior descendent (LAD), circumflex (Cx) and right coronary artery (RCA), as well as their branches. In case of the trunk of main coronary artery to be unaffected, the lesion(s) of its branch(es) was (were) assigned to the territory of the corresponding main artery. The stenotic lesions, related to the territory of LAD, were observed in 48 (71 %) patients, Cx – 26 (38 %), and RCA – 21 (31 %). Proximal lesion of LAD was detected in 15 (22 %) patients. Regarding the number of the affected territories, 46 (68 %) patients presented with single vessel disease, 17 (25 %) – 2-vessel, and 5 (7 %) – 3-vessel CAD.

In case of ≥2 stenotic lesions in the territory of main coronary artery, the maximal value among these lesions was analyzed. The stenotic range 50-69 % was referred as «moderate» (n=22 [32 %]), and 70-90 % – as «severe» coronary stenosis (SCS) (n=46 [68 %]) [13].

The overall CAD complexity was assessed by the SYNTAX score [2]. The average SYNTAX score was (Me [IQR]) 7 (5-11) points, varying from 1 to 20 points.

The FFR measurement was performed according to the standard practice [4, 5]. Hyperemia was achieved through the peripheral intravenous infusion of adenosine (Sodium adenosine triphosphate) at a weight-adjusted rate (equivalent to a standard dose of 140 μg/kg/min). FFR was calculated as the ratio of the mean intracoronary pressure, measured distally to the target lesion, in relation to the mean aortic pressure at the time of maximal hyperemia.

Totally, we analyzed 108 coronary lesions (moderate – 46 (42,6 %), and severe – 62 [57,4 %]) with corresponding FFR values. FFR ≤0,80 conventional units (c.u.) was considered as hemodynamically significant [4, 5]. According to this cut-off value, there were 55 (50,9 %) non-significant and 53 (49,1 %) significant lesions.

For the purpose of group assignment, we used the single patient`s available FFR value, or the minimal one among the several (≥2) available values per patient. In case of all the available FFRs to be hemodynamically non-significant (>0,80 c.u.), a patient was assigned to FFR «negative» group (FFR_{NEG}). On the contrary, in case of at least one available FFR ≤0,8 c.u., a patient was assigned to FFR «positive» group (FFR_{POS}). Accordingly, we subdivided the enrolled sample of patients into two groups: FFR_{NEG} (n=28 [41 %]) and FFR_{POS} (n=40 [59 %]).

The data analysis was performed by the use of the statistical software programs (Statistica v. 13.3 (TIBCO Software Inc., USA); IBM SPSS Statistics v. 26.0 (Armonk, NY: IBM Corp., USA) and MedCalc v. 20.113 [MedCalc Software Ltd, Belgium]). Quantitative variables were presented as Me (IQR), and qualitative ones – as absolute and relative (%) frequency. To compare the studied groups, we used Mann-Whitney U-test (for quantitative variables) and χ^2 test with the following z-test, as required (for qualitative variables). The relationship between the quantitative variables was determined by the use of *Spearman`s rank coefficient* of correlation (ρ). To determine the factors, associated with binary groups, based on the presence of at least one available FFR value equal or less than the certain cut-off (from ≤0,80 to ≤0,60, with 0,05 decrement), we used stepwise logistic regression analysis. The discriminative power of the logistic regression models was assessed by the value of area under curve (AUC). A 2-tailed p<0,05 was considered statistically significant.

RESULTS

The FFR_{POS} group tended to be older as compared to FFR_{NEG} one, and was characterized by the higher frequency of CCS class III angina cases (Table I).

We did not observe any significant differences between the compared groups by the studied laboratory and the majority of echocardiographic parameters. At the same time,

Table I. Baseline clinical characteristics of patients in FFR_{NEG} and FFR_{POS} groups

Parameters		FFR_{NEG} N=28	FFR_{POS} N=40	p
Age, years		62 (57-68)	66 (61-71)	0,099
Males, n (%)		20 (71)	25 (63)	0,444
Females, n (%)		8 (29)	15 (37)	
BMI, kg/m^2		29,1 (25,6-30,9)	29,1 (26,3-32,9)	0,582
HTN, n (%)		26 (93)	38 (95)	0,712
Angina CCS class, n (%)	No angina^z	11 (39)	0	<0,001
	II	15 (54)	27 (68)	
	III^z	2 (7)	13 (32)	
History of MI, n (%)		14 (50)	16 (40)	0,414
History of PCI, n (%)		12 (43)	12 (30)	0,275
HF stage, n (%)	B	12 (43)	13 (32)	0,383
	C	16 (57)	27 (68)	
AF, n (%)		8 (29)	7 (17)	0,279
History of stroke/TIA, n (%)		5 (18)	5 (12)	0,539
DM, n (%)		7 (25)	12 (30)	0,651
CKD, n (%)		8 (29)	10 (25)	0,743

Note: ^{z} – statistically significant difference by z-test

Table II. Baseline ICA characteristics of patients in FFR_{NEG} and FFR_{POS} groups

Parameters		FFR_{NEG} N=28	FFR_{POS} N=40	p
LAD territory lesion, n (%)		18 (64)	30 (75)	0,340
LAD territory max stenosis, %		60 (50-60)*	75 (65-80)**	<0,001
Cx territory lesion, n (%)		9 (32)	17 (42)	0,387
Cx territory max stenosis, %		65 (60-70)$^{\#}$	75 (70-80)$^{\#\#}$	0,005
RCA territory lesion, n (%)		10 (36)	11 (27)	0,471
RCA territory max stenosis, %		55 (50-70)$^{\$}$	80 (70-80)$^{\$\$}$	<0,001
SCS, n (%)		7 (25)	39 (98)	<0,001
CAD complexity (vessels), n (%)	1-vessel	20 (71)	26 (65)	0,599
	2-vessel	7 (25)	10 (25)	
	3-vessel	1 (4)	4 (10)	
SYNTAX score, points		6 (4-9)	7 (5-12)	0,096

Notes: * – n=18; ** – n=30; $^{\#}$ – n=9; $^{\#\#}$ – n=17; $^{\$}$ – n=10; $^{\$\$}$ – n=11

LVH was more prevalent in FFR_{POS} group (vs. FFR_{NEG}: 53 % vs. 21 %, respectively; p=0,010), without a significantly different distribution of its degrees in the compared groups.

The ICA data suggested a more pronounced maximal stenosis and the prevailed SCS cases in FFR_{POS} group, as opposed to FFR_{NEG} one. The studied groups were comparable by the number of diseased vessel territories, with the SYNTAX score tended to be higher in FFR_{POS} (Table II).

At lesion-level, the majority of severely affected lesions (70-90 %) were functionally significant (49 of 62 [79,0 %]), as opposed to the sample of moderately narrowed ones (50-69 %), where only 4 of 46 lesions (8,7 %) had FFR ≤0,80 c.u. (p<0,001). Moreover, we revealed a strong negative correlation between the luminal stenosis and FFR in the whole sample of the studied lesions (ρ= –0,827; p<0,001 [n=108]), with weak correlation among functionally non-significant lesions (ρ= –0,421; p=0,001 [n=55]), and moderate – among the significant ones (ρ= –0,618; p<0,001 [n=53]). Furthermore, such a correlation was strong in the sample of severely affected lesions (ρ= –0,702; p<0,001 [n=62]), and non-significant – among the moderate ones (ρ= –0,268; p=0,072 [n=46]).

At the patient-level, SYNTAX score negatively, but weakly correlated with FFR in the whole sample of the enrolled patients (ρ= –0,411; p<0,001 [n=68]), with the absence of significant correlation in FFR_{NEG}, and moderate correlation in FFR_{POS} group (Fig. 1).

The stepwise logistic regression analysis revealed the SCS and SYNTAX score to be strongly (or moderately)

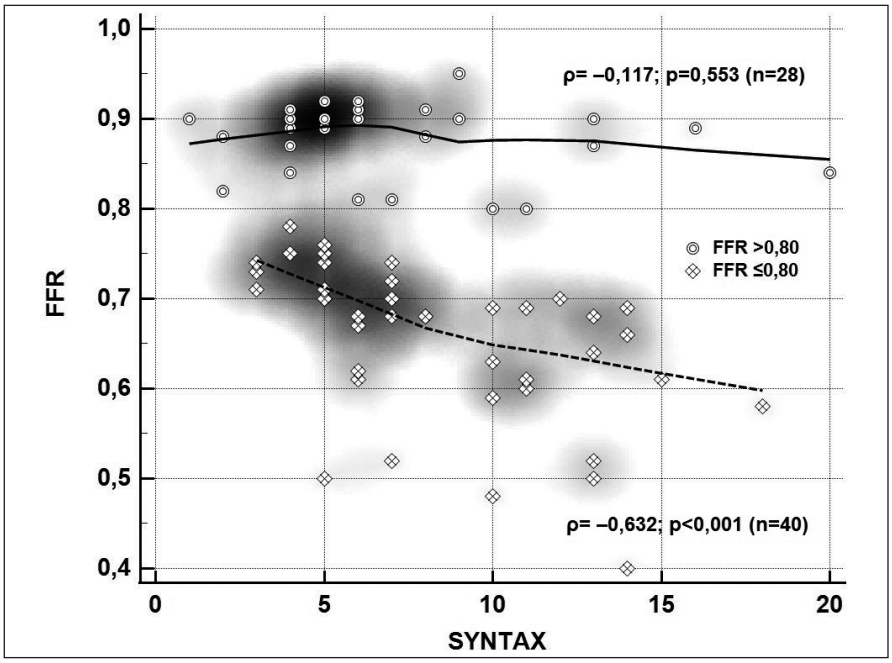

Fig. 1. Correlation of SYNTAX score with FFR in FFRNEG and FFRPOS groups. LOESS smoothing span – 80 %. Heat map applied.

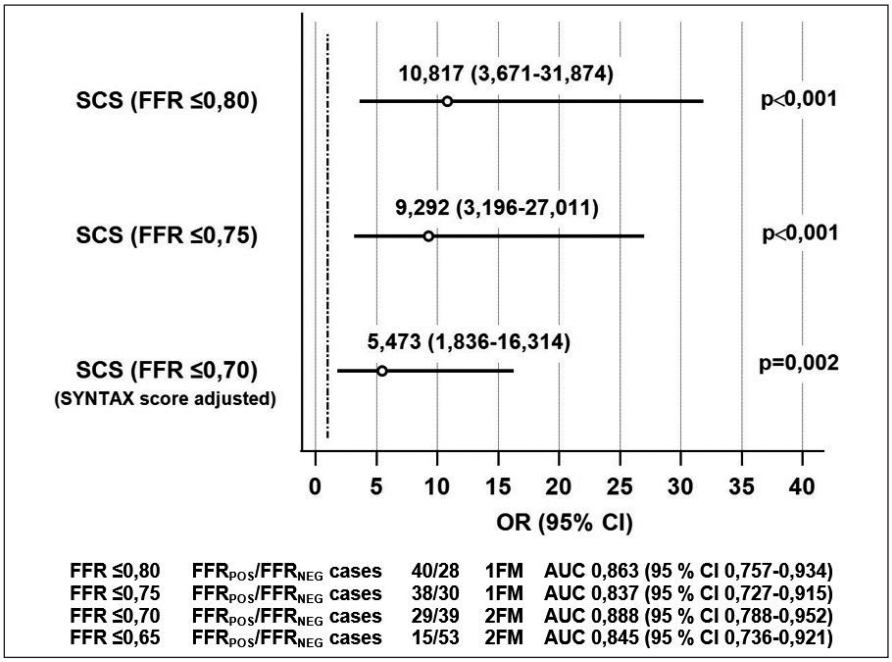

Fig. 2. Logistic regression analysis: SCS as a factor, strongly (AUC ≥0,8) associated with the presence of at least one available FFR ≤ corresponding cut-off value (≤0,80; ≤0,75; ≤0,70; and ≤0,65) (forest plot). OR – odds ratio. CI – confidence interval. 1FM – 1-factor model (SCS as a predictor). 2FM – 2-factor model (SCS and SYNTAX score as predictors). Data on SCS as a predictor of FFR ≤0,65 not shown on the forest plot.

associated with the presence of at least one FFR, being equal or less than the corresponding cut-off value (Fig. 2 and 3). In particular, the SCS was strongly associated with all but one (the lowest) of the selected cut-offs (Fig. 2). Furthermore, the SYNTAX score appeared to be strongly associated with the FFR ≤0,70 and FFR ≤0,65. In contrast to SCS, the SYNTAX score was the only factor, (moderately) associated with FFR ≤0,60 (Fig. 3).

DISCUSSION

The present real-world study revealed clinical and angiographic characteristics of SCAD patients, associated with the presence of functionally significant, angiographically intermediate coronary lesions, namely the higher prevalence of CCS III class angina, LVH and the more advanced coronary stenosis (≥70 %). These results reflect certain relationship between FFR and traditional indications for revascularization, such as angina functional class and CAD severity [1-3]. At the same time, the FFR-guided revascularization might be prioritized for the cases of less severe angina, considering the potential existence of, at least, two distinct clusters of such patients with different hemodynamic consequences of angiographically intermediate lesions.

The present study revealed a significant relationship between the degree of coronary stenosis by ICA and the FFR value, both at lesion- and patient-related levels. It is worth

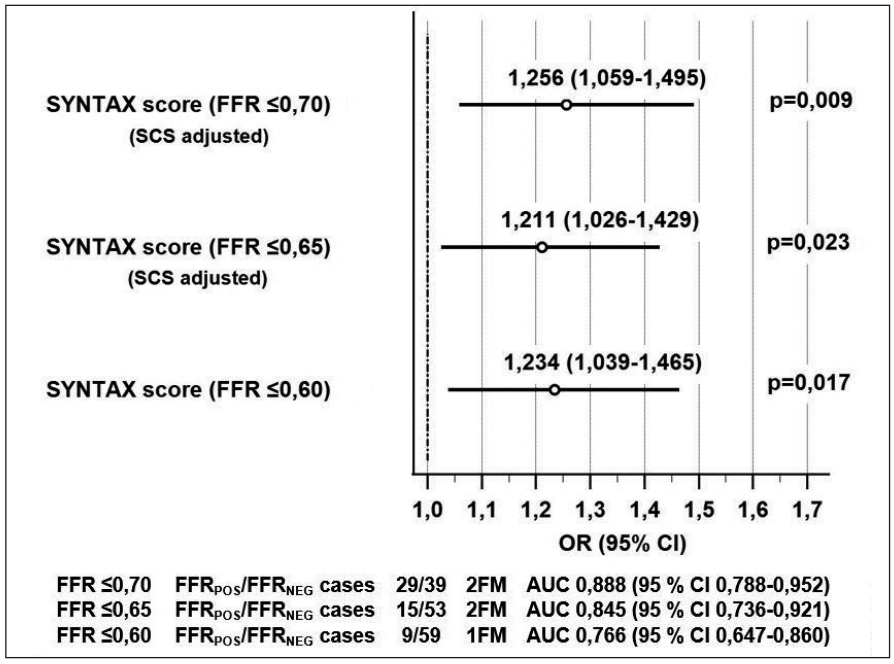

Fig. 3. Logistic regression analysis: SYNTAX score as a factor, associated with the presence of at least one available FFR ≤ corresponding cut-off value (strongly (AUC ≥0,8) associated with FFR ≤0,70 and ≤0,65; and moderately (0,7≤AUC<0,8) associated with FFR ≤0,60) (forest plot). OR – odds ratio. CI – confidence interval. 1FM – 1-factor model (SYNTAX score as a predictor). 2FM – 2-factor model (SCS and SYNTAX score as predictors).

mentioning, that we included a wide range of lesions, with a diameter stenosis 50-90 %, which, according to current ECS/EACTS guidelines, are considered as «intermediate» ones [2]. At the same time, the recently published ACC/AHA/SCAI guidelines [3] recommended the use of FFR in a restricted range of «intermediate» coronary lesions, namely (40) 50-70 %, to guide the decision to proceed with PCI in SCAD patients. Regarding the majority of severely affected lesions to be functionally significant, our results are closer to the ACC/AHA/SCAI approach, reasoning to modify the indications for FFR-guided revascularization, in particular to apply a stricter limitation of appropriate lesions to be functionally assessed (namely 50-70 % in stenosis) [3, 8]. However, it has been shown, that a certain proportion of severely stenotic lesions may not result in detectable ischemia [14, 15]. Considering the widely accepted imperfect relationship between luminal stenosis and FFR [4], the latter can be useful in guiding revascularization decisions even in severely affected lesions (70-90 %) [7]. In this case, the relationship of plaque morphology and FFR may also help to explain better outcomes, associated with FFR-guided therapy [16].

The results regarding the relations of the extent and severity of CAD with the functional significance of coronary lesions, might be especially important for patients with multivessel CAD, constituting approximately a third of the enrolled sample. It is generally accepted, that in patients with multivessel CAD, an assessment of overall CAD complexity, such as the SYNTAX score, may be useful to guide revascularization, with the completeness of revascularization to be prioritized [2, 3]. Therefore, the FFR measurement is a reasonable addition to the SYNTAX score, favoring the achievement of functionally complete revascularization, being a preferred strategy for PCI in SCAD patients [2]. At the same time, an increase in CAD complexity in SCAD patients with SCS is associated with the higher probability of the lesions to be more functionally affected, and associated with the higher risk of major adverse cardiovascular events, if not revascularized. Thus, besides providing a binary index for decision-making, baseline FFR values can independently predict future clinical events in the deferred lesions, and might be used to provide a risk stratification [6, 7, 17].

The present study is subjected to some limitations, inherent to its retrospective, single-center design and modest sample size. The obtained results reflect the real-world practice of enrollment of SCAD patients, referred to the catheterization laboratory to perform an ICA with concomitant assessment of physiological significance of intermediate coronary lesions. However, all enrolled patients presented with mild CAD complexity (SYNTAX score ≤22 [2]), with a predomination of single vessel disease, thus the obtained results cannot be entirely generalized to the population of SCAD patients with more complicated CAD. Other limitations could be related to the lack of data on the LV MM, assessed by truncated ellipsoid formula [12], and the data on the extent of the myocardial ischemia.

CONCLUSIONS

In patients with SCAD and angiographically intermediate coronary artery stenosis (50-90 %), the presence of at least one functionally significant coronary lesion (FFR ≤0,80 c.u.) was associated with the higher prevalence of angina CCS III class, LVH and more advanced coronary stenosis (≥70 %). The greater overall CAD complexity, as assessed by the SYNTAX score, in addition to the higher degree of coronary stenosis, increased the probability that the anatomically significant coronary lesions would be more functionally compromised.

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ORCID and contributionship:
Mykola V. Stan: 0000-0001-9741-9075 [A-D]
Kyrylo O. Mikhaliev: 0000-0003-3759-6699 [B-D]
Oleg J. Zharinov: 0000-0002-4089-9757 [A, E, F]
Andriy V. Khokhlov: 0000-0003-1688-0500 [A, B, E]
Anatolii M. Kravchenko: 0000-0001-6863-0197 [E, F]
Borys M. Todurov: 0000-0002-9618-032X [A, E, F]

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CORRESPONDING AUTHOR
Mykola V. Stan
Shupyk National Healthcare University of Ukraine
5A Bratyslavska st., 02660 Kyiv, Ukraine
tel: +380967426038
e-mail: stankolja1989@gmail.com

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ORIGINAL ARTICLE

SELENIUM-ASSOCIATED MECHANISMS OF PROGRESSION OF NONALCOHOLIC FATTY LIVER DISEASE IN HYPERTENSIVE PATIENTS

DOI: 10.36740/WLek202211121

Iryna I. Tverezovska, Natalia M. Zhelezniakova
KHARKIV NATIONAL MEDICAL UNIVERSITY, KHARKIV, UKRAINE

ABSTRACT

The aim: To determine the role of selenium and Selenoprotein P in the intensification of inflammation processes, deviations of the functional state of the liver and the progression of changes in its parenchyma in patients with NAFLD and hypertension.

Material and methods: Study included 100 gender and age matched NAFLD patients: 49 (67.3 % women) hypertensive (main group) and 51 (58.8 % women) non-hypertensive NAFLD patients. 20 individuals (55.0 % women) formed control group. Diagnosis of NAFLD and hypertension was made according to respective guidelines. All patients underwent measurement of liver transferases, selenium, Selenoprotein P, IL-8 and IL-10.

Results: In both study groups, ALT and AST levels were significantly predominant in patients with steatohepatitis than steatosis. Increase in IL-8 and IL-10 was found in main study groups but not in subgroup analysis. In hypertensive NAFLD patients with steatosis, ALT correlated with selenium and Selenoprotein P. A direct correlation was between the de Ritis index and IL-8. Selenium correlated with IL-8 but not IL-10. Selenoprotein P correlated inversely with IL-8 and directly with IL-10.

Conclusions: Intensification of inflammation and depletion of antioxidant protection under presence of hypertension deepen redox violations in NAFLD patients. Such changes can be only partially compensated by anti-inflammatory and antioxidative activity. Selenium and Selenoprotein **P** are important substances in progression of NAFLD and should be assessed regarding diagnosis and treatment of NAFLD patients.

KEY WORDS: NAFLD, hypertension, selenium, Selenoprotein P

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INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is one of the most common metabolic diseases of the liver, and is associated with lipid accumulation in hepatocytes under absence of alcohol abuse [1-3]. Cardiovascular comorbidities comprise to the increased levels of morbidity and mortality [4]. Currently, data on the impact of selenium on the development and course of NAFLD vary greatly. However, it is common that selenium and selenium-containing proteins (i. e. Selenoprotein P), play a direct role in the regulation of antioxidant protection and fibrosis intensity.

Selenium is an essential trace element that regulates antioxidant defense, hormone metabolism and immune response via the metabolism of selenoproteins [2, 5]. Main source of selenium is diet, however its concentration in foods significantly depends on its environmental levels, being the lowest in Europe [6–12]. Selenium has very narrow boundaries beyond which it can cause toxicity [7, 13]. Thus, high level of selenium may cause hepatotoxicity [14] and is a direct risk factor for NAFLD [5], dyslipidemia, type 2 diabetes mellitus and HTN [5–7, 12, 15].

Assessment of the state of the redox system in patients with NAFLD may have a positive clinical effect [5, 12], as NAFLD and cardiovascular pathology have several common pathogenetic mechanisms, such as increased lipid peroxidation, endothelial dysfunction, and inflammation, while fatty infiltration promotes the accumulation of adipose tissue and stimulates the expression of inflammatory cytokines, which triggers hypertension development [13, 16].

THE AIM

The aim was to determine the role of selenium and Selenoprotein P in the intensification of inflammation processes, deviations of the functional state of the liver and the progression of changes in its parenchyma in patients with NAFLD and hypertension.

MATERIALS AND METHODS

Study included 100 NAFLD patients. 49 hypertensive NAFLD patients (67.3 % women and 32.7 % men) were included in main group. Comparison group involved 51 non-hypertensive NAFLD patients (58.8 % women and 41.2 % males). 20 relatively healthy individuals (55.0 % women and 45.0 % men) formed control group. Groups were gender-matched (χ^2=1,219, p=0,544).

Table I. Baseline values of BMI and blood pressure in study groups

Indices	Control (n = 20)	NAFLD+HTN (n = 49)	NAFLD (n = 51)	p_{1-2}	p_{1-3}	p_{2-3}
BMI, kg/m²	24,3 [21,9; 26,0]	27,8 [26,6; 28,5]	27,3 [24,2; 28,3]	< 0,001	0,004	0,031
SBP, mm Hg	120,0 [110,0; 120,0]	150,0 [145,0; 158,0]	125,0 [115,0; 130,0]	< 0,001	0,012	< 0,001
DBP, mm Hg	80,0 [70,0; 80,0]	90,0 [85,0; 90,0]	80,0 [70,0; 80,0]	< 0,001	0,918	< 0,001

Note:
p_{1-2} – significance of differences between control and main group;
p_{1-3} – significance of differences between control and comparison group;
p_{2-3} – significance of differences between main and comparison groups.

Table II. Biochemical parameters of patients by subgroup analysis depending on the liver damage grade Me [LQ; UQ]

Index	NAFLD+HTN (n = 49)		p_{1-2}	NAFLD (n = 51)		p_{3-4}
	Steatosis (n = 27)	Steatohepatitis (n = 22)		Steatosis (n = 30)	Steatohepatitis (n = 21)	
ALT, U/L	44.0 [43.0; 46.0]	47.0 [44.5; 49.0]	0.002	35.0 [33.0; 37.3]	39.0 [35.0;42.0]	0.011
AST, U/L	51.0 [49.0; 53.0]	56.5 [54.0; 57.0]	<0.001	40.0 [39.0; 41.0]	45.0 [43.0; 48.0]	<0.001
De Ritis index	1.15 [1.10; 1.21]	1.17 [1.15; 1.25]	0.129	1.14 [1.01; 1.18]	1.13 [1.08; 1.30]	0.455
AP, U/L	286.0 [220.0; 326.7]	283.0 [211.2; 317.4]	0.469	196.8 [166.9; 237.6]	228.3 [195.7; 258.8]	0.062
GGTP, U/L	93.0 [77.2; 105.6]	99.9 [72.3; 112.1]	0.410	65.3 [42.6; 73.0]	65.5 [53.6; 78.1]	0.368

Note:
p_{1-2} – significance of differences between steatosis and steatohepatitis in main group;
p_{3-4} – significance of differences between steatosis and steatohepatitis in comparison group.

Table III. IL-8, IL-10, selenium and Selenoprotein P in studied patients depending on presence of steatosis and steatohepatitis, Me [LQ; UQ]

Indices	NAFLD+HTN (n = 49)		p_{1-2}	NAFLD (n = 51)		p_{3-4}
	Steatosis (n = 27)	Steatohepatitis (n = 22)		Steatosis (n = 30)	Steatohepatitis (n = 21)	
IL-8, pg/ml	29.1 [24.9; 31.1]	32.5 [27.6; 40.7]	0,077	23,1 [18,9; 26,4]	21,9 [19,2; 24,4]	0,444
IL-10, pg/ml	20.3 [17.9; 23.1]	20.7 [16.1; 26.0]	0,928	11,8 [10,4; 13,6]	12,1 [10,8; 14,0]	0,394
Sel P, ng/mL	19,9 [7,3; 26,7]	19,5 [8,0; 26,8]	0,817	42,7 [40,8; 45,5]	43,2 [42,3; 45,8]	0,599
Sel, µg/L	42,4 [34,5; 49,5]	46,0 [42,3; 49,5]	0,169	69,9 [62,4; 77,5]	66,4 [57,0; 78,1]	0,394

Note:
p_{1-2} – significance of differences between steatosis and steatohepatitis in main group;
p_{3-4} – significance of differences between steatosis and steatohepatitis in comparison group.

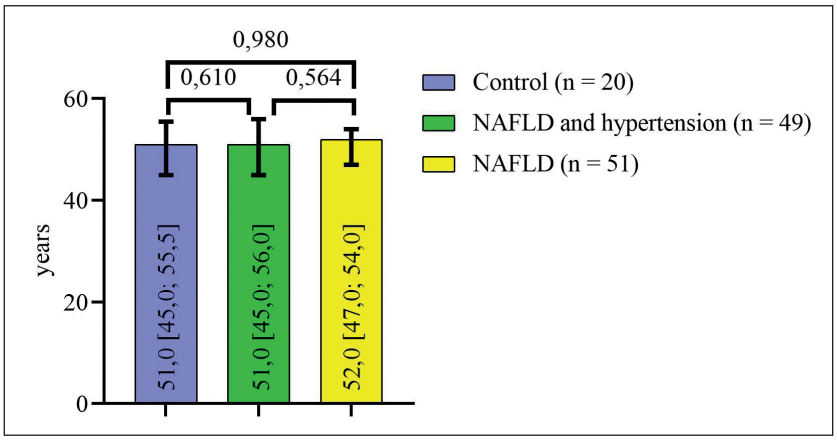

Fig 1. Age distribution of studied patients, Me [LQ; UQ]

Study groups were age-matched (figure 1). Median age in main group was 51.0 [45.0; 56.0] years (p_{1-2}=0,610, p_{2-3}=0,564); comparison and control group: respectively 52.0 [47.0; 54.0] years (p_{1-3}=0,980) and 51.0 [45.0; 55.5] years.

Analysis showed that 28,6 % and 71,4 % of patients in main group had 1st and 2nd stage of hypertension; 32.7 % and 67.3 % had hypertension of 1 and 2 grade (figure 2).

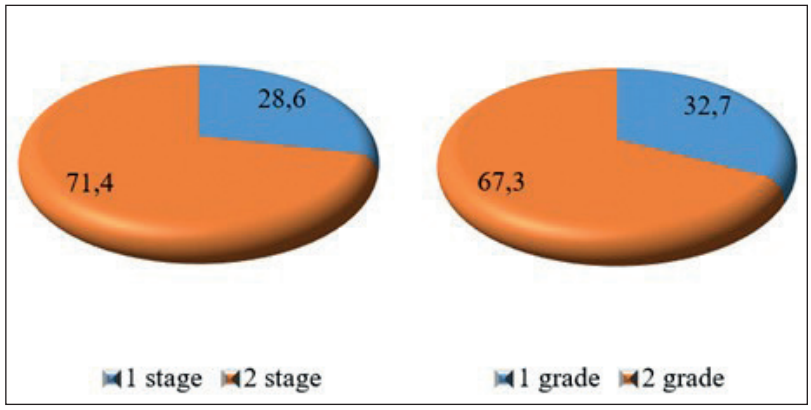

Fig 2. Stages and grade of hypertension in patients of main group, %

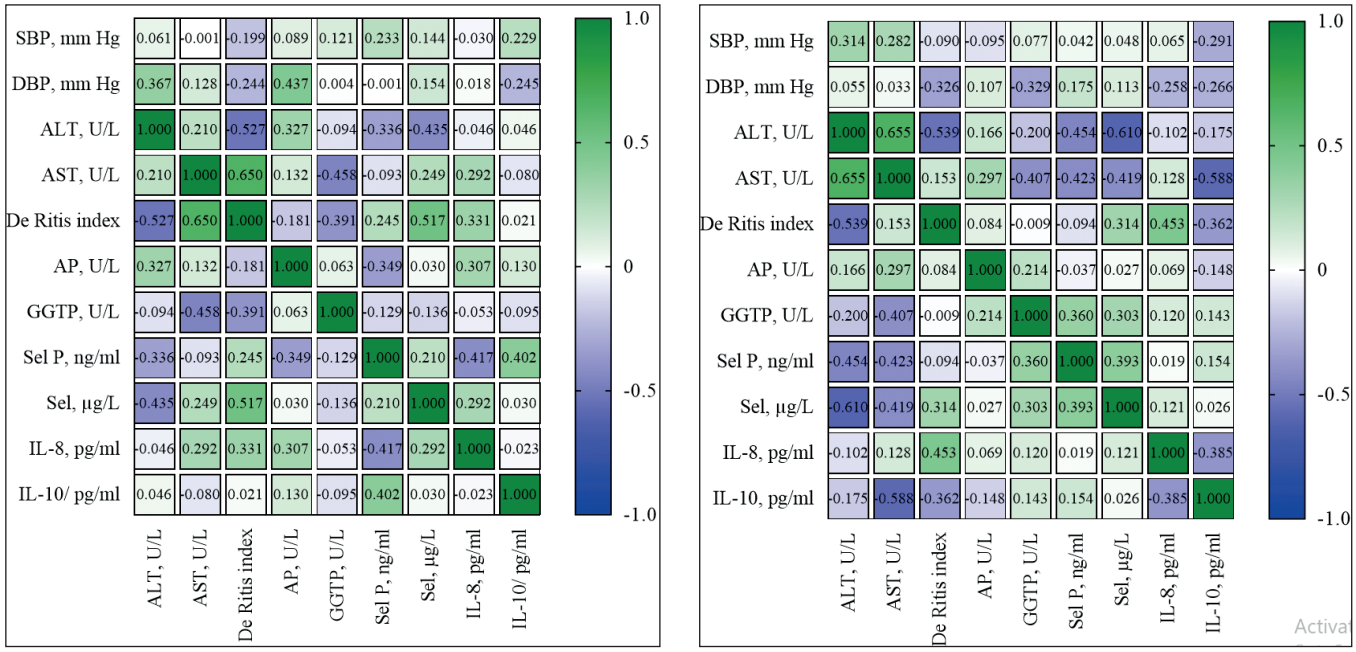

Fig. 3. Correlations of studied parameters in hypertensive NAFLD patients with steatosis (fig. 3a) and steatohepatitis (fig. 3b)

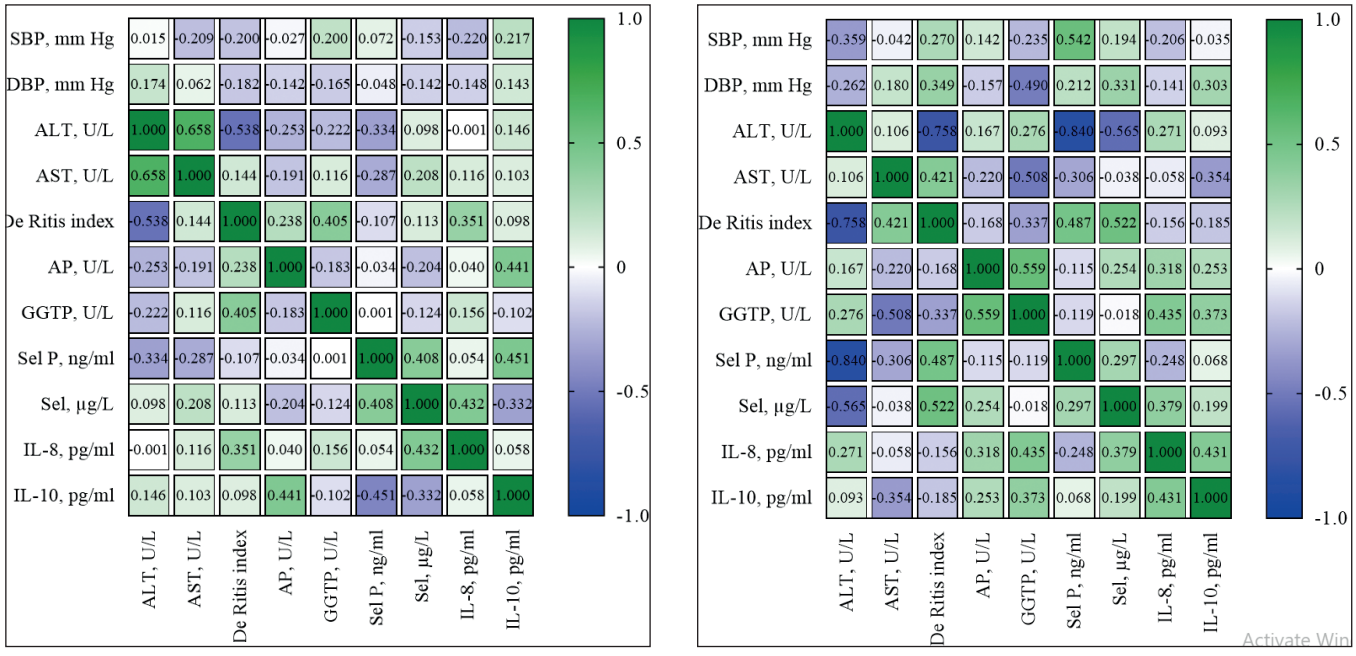

Fig. 4. Correlations of studied parameters in non-hypertensive NAFLD patients with steatosis (fig. 4a) and steatohepatitis (fig. 4b)

In main group 55.1 % and 44.9 % of patients had steatosis and steatohepatitis respectively. In comparison group steatosis was found in 58.8 % and steatohepatitis – in 41.2 % patients (χ^2=0,141, p=0,707).

The diagnosis of nonalcoholic fatty liver disease was made according to the practical guidelines of the European Association for the Study of Liver Diseases and the European Association for the Study of Obesity (2016) [17]. The diagnosis of hypertension was made according to the criteria of the European Society of Cardiology and the European Society of Hypertension (2018) [18]. All patients underwent testing of alcohol abuse for differential diagnosis of NAFLD and alcoholic fatty liver disease according to AUDIT (Alcohol Use Disorders Identification Test) [19].

All patients were assessed for levels of alanine-aminotransferase (ALT), aspartate-aminotransferase (AST), total bilirubin and its fractions according to standard kinetic method. Gamma-glutamiltranspeptidase (GGTP) and alkaline phosphatase (AP) were measured using respectively enzyme-colorimetric and colorimetric methods.

De Ritis index was calculated as ratio of AST to ALT. Body mass index (BMI) was calculated as ratio of body mass (kg) to squared body height (cm).

Levels of interleukin (IL) -8, IL-10, selenium and Sel P were measured using ELISA method (USA). Ultrasound examination of the liver was carried out according to the standard method on an empty stomach on the device Samsung (Medison) SonoAce X8.

All patients provided written consent to participate in research in accordance with the recommendations of the Ethics Committees for Biomedical Research, Ukrainian Health Legislation and the Declaration of Helsinki of 2000, European Community Directive 86/609 On Human Participation in Biomedical Research.

IBM SPSS 25.0 (trial version) for Windows were used for statistical analysis. Kolmogorov-Smirnov & Lilliefors test showed non-normal distribution so nonparametric statistics was used. For qualitative variables median (Me) and interquartile range was calculated. Significance of differences was assessed using Mann-Whitney U-test. Categorical variables were presented as percentage (%). Significance of differences was assessed using Pearson's chi-squared test. Correlations were calculated using Spearman Rank-Order Correlation Coefficient. Significance threshold in calculations was considered as p=0.05.

RESULTS

Median BMI (table I) in all study groups corresponded to normal or increased. The lowest BMI was in the control group (24,3 [21,9; 26,0] kg/m^2), the highest – in main group (27,8 [26,6; 28,5] kg/m^2, p_{1-2} < 0,001), in comparison group BMI was 27,3 [24,2; 28,3] kg/m^2 (p_{1-3}= 0,004). Non-hypertensive NAFLD patients had significantly lower BMI compared to hypertensive (p_{2-3}=0,031).

Patients of main group had significantly higher systolic (SBP) and diastolic blood pressure (DBP) than in control group. SBP in comparison group was significantly higher than in control (p=0.012), but DBP did not differ significantly (p=0.918) (table I).

In steatohepatitis patients, median levels of ALT and AST were significantly (p < 0.001) higher than in steatosis patients both in hypertensive and non-hypertensive NAFLD patients. Noteworthy that GGTP levels did not differ between subgroups, and AP had trend to significant increase in steatohepatitis non-hypertensive patients. De Ritis index also showed tendency to significant increase in steatohepatitis hypertensive NAFLD patients (table II).

Moreover, median IL-8 and IL-10 in hypertensive and non-hypertensive NAFLD patients were found in patients with steatohepatitis. Noteworthy, that IL-8 levels were higher in steatosis NAFLD-only patients, but the difference was not significant. Nonsignificant increase in IL-8 was found in steatohepatitis NAFLD+HTN patients (table III)

Median of Sel P was non-significantly higher in patients with steatohepatitis than in steatosis, but median selenium levels were higher in steatosis than in steatohepatitis subgroup (table III).

Correlation analysis revealed that steatosis patients with comorbid NAFLD and HTN (figure 3a) have reverse correlation between Sel P and Sel with ALT: respectively ρ=-0,336 (p=0,087) and ρ=-0,435 (p=0,023). Levels of AP reversely correlated with levels of Sel P (ρ=-0,349, p=0,074) and directly with ALT (ρ=0,327, p=0,096). Selenoprotein P showed reverse correlation with IL-8 (ρ=-0,417, p=0,030) and direct with IL-10 (ρ=0,402, p=0,038). Direct relationship was also found between DBP and ALT and AP: respectively ρ=0,367 (p=0,060) and ρ=0,437 (p=0,023).

In patients with NAFLD+HTN and steatohepatitis (fig. 3b) levels of Sel P and selenium showed significant reverse correlation with ALT: respectively ρ=-0,454 (p=0,034) та ρ=-0,610 (p=0,003). Similar picture was found regarding Sel P, Sel and AST: respectively ρ=-0,423 (p=0,050) and ρ=-0,419 (p=0,052). Reverse correlation was revealed between AST and IL-10 (ρ=-0,588, p=0,004).

In steatosis patients with NAFLD (fig. 4a) reverse correlations were found between Sel P, ALT (ρ=-0,334, p=0,071). Index of de Ritis correlated directly with levels of proinflammatory IL-8(ρ=0,351, p=0,057). Levels of AP correlated directly with IL-10 (ρ=0,441, p=0,015). Noteworthy, Sel P correlated directly with selenium (ρ=0,408, p=0,025) and proinflammatory Il-10 (ρ=0,451, p=0,012), but selenium levels — directly with Il-8 (ρ=0,432, p=0,017) and reversely with IL-10 (ρ=-0,332, p=0,073).

In NAFLD-only patients with steatohepatitis (fig. 4b) there was found strong reverse correlation between Sel P and ALT (ρ=-0,840, p < 0,001) and AST (ρ=-0,306, p=0,177). Noteworthy, AST levels significantly reversely correlated with GGTP (ρ=-0,508, p=0,019) and selenium correlated with IL-8 (ρ=0,379, p=0,090). De Ritis index directly correlated with Sel P and selenium: respectively ρ=0,487 (p=0,025) and ρ=0,522 (p=0,015). Direct relationship was found between AP and GGTP (ρ=0,559, p=0,008)

DISCUSSION

In present study, patients with NAFLD had a significantly higher body weight. Obesity cannot be considered a risk factor for NAFLD, as almost 40% of patients with NAFLD

had normal BMI [17, 20]. Our study determined that patients with NAFLD had significantly higher median of SBP, confirmed by Ye et al. [20].

Steatohepatitis, as advanced liver damage, is accompanied by more potent release of liver enzymes because of hepatocyte damage followed by fibrosis [16]. In both study groups, ALT and AST levels were significantly predominant in patients with steatohepatitis than steatosis. Ma et al. [16] showed that normal ALT levels are associated with steatosis, but 19.0 [95.0 % CI 13.0–27.0] % of patients with steatohepatitis also had normal ALT levels. Zhang et al. [21] showed that higher levels of transferases were recorded precisely at a low concentration of selenium.

The highest IL-8 and IL-10 were obtained in hypertensive NAFLD patients, which may be due to the presence of more intense liver damage secondary to chronically elevated systemic pressure. Trend to a significantly higher IL-8 in patients with steatohepatitis was determined only in the main group, while in the comparison group the medians were the same. IL-10 levels slightly but not significantly prevailed in patients with steatohepatitis in both groups.

Currently, studies do not have a unanimous conclusion on the exact effect of selenium and Selenoprotein P levels on the pathogenesis of NAFLD and its comorbidities. The results suggest a negative effect of selenium at both low and high serum levels. This is due to the deficiency of antioxidant substances (Selenoprotein P), as well as to the formation of hepatotoxicity and acceleration of fibrosis [8, 9, 22].

In hypertensive NAFLD patients and steatosis, ALT was inversely correlated with levels of selenium and Selenoprotein P, while selenium correlated directly with the de Ritis index, which is confirmed in other studies where a negative association of selenium and the morphological state of the liver is shown. A direct correlation was obtained between the de Ritis index and IL-8, which may indicate a possible relationship between the intensity of inflammation of the liver parenchyma and damage grade. Selenium levels showed a weak correlation with IL-8 levels and no correlation with IL-10. At the same time, Sel P correlated inversely with IL-8 and directly with IL-10.

Patients with NAFLD and steatosis revealed an inverse correlation between ALT and Sel P, a direct correlation between the de Ritis index and IL-8, and direct between Sel P, selenium, and IL-10. The existing correlation of IL-10 and Sel P in this subgroup may indicate a link between the anti-inflammatory reaction and the protective effect of Sel P in patients at the initial stage of liver damage according to NAFLD.

In patients with NAFLD and steatohepatitis, a direct correlation between SBP and selenium was determined. This can be explained by the possible involvement of selenium during initial stages of liver damage in the formation of hypertension. ALT correlated inversely with both selenium and Sel P, which may indicate initial activation followed by decompensation of antioxidant protection secondary to hepatocyte damage. A weak correlation was determined between the levels of selenium and IL-8, which may also indicate the intensity of antioxidative protection against the background of a nonspecific inflammatory reaction. Wang et al. [23] showed the presence of a direct relationship between high levels of selenium and an increase in ALT levels, especially in selenium concentrations> 130 μg/L. Other authors [6] emphasize that the interdependence between selenium and ALT is not linear, but U-shaped, which is especially marked in the concentration of selenium> 120 μg/L and is associated with a higher risk of diabetes and cardiovascular diseases [2, 12, 15, 25].

Lin et al. [5] showed that in patients with advanced liver damage but not NAFLD mean selenium levels were significantly lower than in control group. Selenium deficiency is directly related to the degree of liver damage and at normal baseline serum levels, supplementation may trigger NAFLD development.

CONCLUSIONS

The presence of concomitant hypertension causes deeper violations in redox balance due to depletion of the antioxidant system and intensification of inflammation, which is only partially compensated by the expression of anti-inflammatory cytokines. The results of the study indicate the important role of selenium and Selenoprotein P in the progression of NAFLD and the need to consider their levels in the diagnosis and dynamics of treatment of such patients.

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ORCID and contributionship:
Iryna I. Tverezovska: 0000-0001-6661-8725[A-D]
Natalia M. Zhelezniakova: 0000-0002-5786-9378[A, E, F]

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CORRESPONDING AUTHOR
Iryna I. Tverezovska
Kharkiv National Medical University
27 Byblyka st., 61091 Kharkiv, Ukraine
tel: +380990909570
e-mail: irenadler21@gmail.com

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ORIGINAL ARTICLE

PROGNOSTIC POTENTIAL OF LYMPHOCYTE-TO-MONOCYTE RATIO AND CASPASE-8 IN PREDICTION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE DEVELOPMENT

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Volodymyr M. Tverezovskyi, Valeriy A. Kapustnyk, Borys O. Shelest, Olga L. Sadovenko
KHARKIV NATIONAL MEDICAL UNIVERSITY, KHARKIV, UKRAINE

ABSTRACT

The aim: To investigate the prognostic potential of lymphocyte-to-monocyte ratio and caspase-8 levels in prognosis of COPD development in healthy individuals.

Materials and methods: 77 individuals were involved into the study: 47 with COPD and 30 healthy volunteers. Patients underwent examination according to GOLD 2022 Guidelines. Caspase-8 serum levels were measured by ELISA. Lymphocyte-to-monocyte ratio was calculated.

Results: In crude and adjusted models lymphocyte-to-monocyte ratio and caspase-8 were associated with COPD development (respectively OR = 0.371 [95.0 % CI 0.217–0.634], p<0.006 and OR = 12.823 [95.0 % CI 2.104–78.134], p = 0.006). Additionally, systolic blood pressure had direct association with COPD (OR = 1.196 [95.0 % CI 1.028–1.391], p = 0.021). Noteworthy, diastolic blood pressure showed significant reverse association in univariate but not in multivariate analysis: OR = 0.850 [95.0 % CI 0.743–0.974] (p = 0.019) and OR = 0.820 [95.0 % CI 0.665–1.012] (p =0.064).

Conclusions: Decreased lymphocyte-to-monocyte ratio and increased caspase-8 levels are important predictors of COPD development and can serve as an additional tool for early diagnosis of COPD in healthy individuals.

KEY WORDS: COPD, immunity, apoptosis

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) presents significant medical burden with continuously increasing incidence and prevalence, and is third most common cause of death worldwide. It is characterized by chronic violations in respiratory function, such as airflow limitation and alveolar space impairment [1]. Noxious gases inhalation, as well as smoking, are considered as major risk factors for COPD development [2, 3].

Monocyte-macrophage interplay is important mechanism in COPD development. Induced by noxious gasses inhalation, macrophages trigger production of various cytokines. However, systemic inflammation in COPD also determines changes in inflammatory state of peripheral blood [1]. Authors state that increased amount of macrophages was found in bronchial wall samples of current and ex-smokers suggesting persistent inflammatory reaction even in case of smoking cessation.

Extrinsic apoptotic pathway initiator caspase-8 — cysteine-aspartate specific protease [4] — regulates not only apoptotic activity but also triggering of other forms of cellular death [5]. It was found that Cas-8 is involved in development of respiratory violations in COPD via activation of emphysematous changes and remodeling of bronchial wall [6].

Lymphocyte to monocyte ratio is one of inflammatory indices, such as neutrophil-to-lymphocyte or platelets-to-lymphocyte ratio, which are related to immunological violations observed in different pathologies such as cardiovascular diseases or cancers [7]. Thus, higher LMR was shown to be associated with better outcomes, such as increased survival in melanoma patients [8].

THE AIM

The aim was to investigate the prognostic potential of lymphocyte-to-monocyte ratio and caspase-8 levels in prognosis of COPD development in healthy individuals.

MATERIALS AND METHODS

The main group included 47 patients with COPD and 30 healthy individuals were included in the control group. Study groups were matched by age and gender.

Diagnosis of COPD was made according to GOLD guidelines (2022) and all patients underwent respective examinations [9]. The examination was performed in remission, which was characterized by stable clinical symptoms and external respiration function parameters.

Inclusion criteria were: signed informed consent to participate in study, age > 18 years, absence of COPD (for control group) and presence of stable COPD (for COPD group).

Exclusion criteria: absence of signed informed consent, acute exacerbation of COPD, other pulmonary diseases (bronchial asthma, interstitial and autoimmune diseases),

Table I. Baseline characteristics of enrolled patients, Me [IQR]

		Control (n=30)	COPD (n=47)	p
Age, years		63.0 [55.5; 65.0]	62.0 [59.0; 66.0]	0.477
Gender (no., %)	*Males*	18 (60.0)	33 (70.2)	0.854
	Females	12 (40.0)	14 (29.8)	
BMI, kg/m²		28.9 [26.1; 31.3]	27.1 [25.9; 32.3]	0.541
SBP, mm. Hg		120.0 [115.0; 130.0]	130.0 [120.0; 130.0]	0.027
DBP, mm. Hg		80.0 [80.0; 85.0]	80.0 [75.0; 80.0]	0.001
Hemoglobin, g/L		145.0 [136.5; 154.0]	150.0 [138.0; 160.0]	0.062
SR, cm/h		5.0 [4.0; 10.0]	6.0 [4.0; 10.0]	0.768
RBC, 10^{12}/L		4.7 [4.3; 4.9]	4.8 [4.3; 5.2]	0.149
WBC, 10^9/L		5.0 [5.0; 6.0]	5.9 [4.8; 6.9]	0.612
Rods neutrophils, %		2.5 [2.0; 4.0]	3.0 [2.0; 4.0]	0.851
Segmented neutrophils, %		55.0 [50.8; 61.0]	59.0 [54.0; 63.0]	0.028
Eosinophils, %		2.0 [2.0; 2.0]	2.0 [1.0; 3.0]	0.193
Lymph, %		36.0 [30.0; 40.0]	28.0 [26.0; 31.0]	< 0.001
Monocytes, %		4.0 [4.0; 6.0]	8.0 [6.0; 9.0]	< 0.001
LMR		7.75 [5.92; 10.0]	3.75 [2.89; 4.67]	< 0.001
Cas-8, ng/ml		2.83 [2.58; 3.01]	3.48 [2.99; 3.72]	< 0.001

Note: BMI — body mass index; SBP — systolic blood pressure; DPB — diastolic blood pressure; SR — sedimentation rate; RBC — red blood cells; WBC — white blood cells; LMR — lymphocyte-to-monocyte ratio; Cas-8 — caspase-8

Table II. Associations of studied parameters with presence of COPD

	Univariate			Multivariate *		
	OR	95.0 % CI	p	OR	95.0 % CI	p
Age, years	1.060	0.982–1.144	0.136	1.173	0.983–1.399	0.076
Gender	1.571	0.601–4.110	0.357		—	
BMI, kg/m²	0.993	0.905–1.089	0.879		—	
SBP, mm. Hg	1.094	1.018–1.176	0.015	1.196	1.028–1.391	0.021
DBP, mm. Hg	0.850	0.743–0.974	0.019	0.820	0.665–1.012	0.064
Hemoglobin, g/L	1.042	0.999–1.086	0.056		—	
SR, cm/h	1.034	0.916–1.167	0.587		—	
RBC, 10^{12}/L	2.436	0.778–7.624	0.126		—	
WBC, 10^9/L	1.287	0.901–1.838	0.165		—	
Rod neutrophils, %	1.078	0.753–1.545	0.681		—	
Segmented neutrophils, %	1.069	0.996–1.148	0.066		—	
Eosinophils, %	0.816	0.525–1.268	0.366		—	
Lymph, %	0.855	0.785–0.932	< 0.001		—	
Monocytes, %	1,916	1,419–2.588	< 0.001		—	
LMR	0.455	0.321–0.643	< 0.001	0.371	0.217–0.634	< 0.001
Cas-8, ng/ml	11.273	3.100–40.995	< 0.001	12.823	2.104–78.134	0.006

Note: * — Backward Wald method; BMI — body mass index; SBP — systolic blood pressure; DPB — diastolic blood pressure; SR — sedimentation rate; RBC — red blood cells; WBC — white blood cells; LMR — lymphocyte-to-monocyte ratio; Cas-8 — caspase-8.

diabetes mellitus and endocrine pathology, hypertension and major cardiovascular events.

Lymphocyte-to-monocyte ratio (LMR) was calculated as lymphocyte count divided by monocyte count and presented as absolute value.

Body mass index (BMI) was calculated as ratio of body mass in kilograms and body height in meters squared and presented as value in kg/m^2.

Caspase-8 (Cas-8) serum levels were assessed by ELISA using Human Caspase-8 ELISA kit (ElabScience, USA).

Table III. Comparison of prognostic potential of LMR in Cas-8 different combinations

	Model 1			Model 2			Model 3		
	OR	95.0 % CI	p	OR	95.0 % CI	p	OR	95.0 % CI	p
Age, years	1.067	0.959–1.188	0.235	1.157	1.001–1.336	0.049	1.173	0.983–1.399	0.076
SBP, mm. Hg	1.135	1.033–1.248	0.009	1.134	1.006–1.279	0.040	1.196	1.028–1.391	0.021
DBP, mm. Hg	0.903	0.792–1.030	0.129	0.890	0.754–1.050	0.168	0.820	0.656–1.012	0.064
LMR		—		0.393	0.252–0.611	< 0.001	0.371	0.217–0.634	< 0.001
Cas-8, ng/ml	12.819	3.224–50.974	< 0.001		—		12.823	2.104–78.134	0.006

Note: SBP — systolic blood pressure; DPB — diastolic blood pressure; LMR — lymphocyte-to-monocyte ratio; Cas-8 — caspase-8.
* — Cas-8 only (Nagelkerke $R^2 = 0.436$; HL-GoF: $\chi^2 = 11.454$, $p = 0.177$);
‡ — LMR only (Nagelkerke $R^2 = 0.661$; HL-GoF: $\chi^2 = 6.483$, $p = 0.593$);
‡ — both Cas-8 and LMR (Nagelkerke $R^2 = 0.750$; HL-GoF: $\chi^2 = 2.955$, $p = 0.937$).

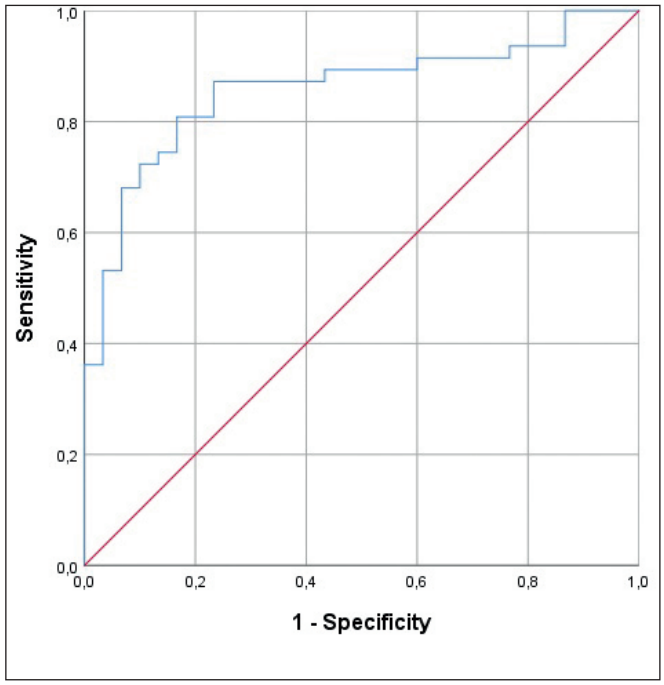

Fig. 1. ROC-analysis of model 1 with Cas-8 as a predictor of COPD development

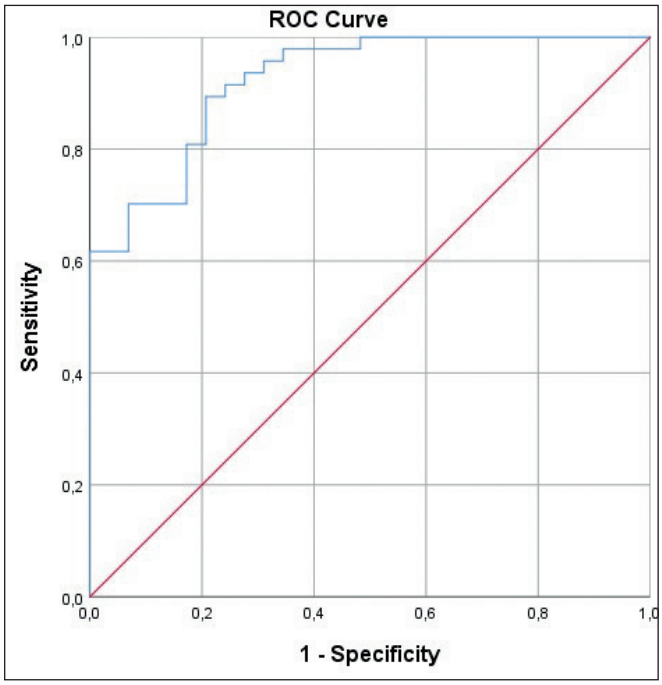

Fig. 2. ROC-analysis of model 1 with LMR as a predictor of COPD development

All patients provided written consent to participate in research in accordance with the recommendations of the Ethics Committees for Biomedical Research, Ukrainian Health Legislation and the Declaration of Helsinki of 2000, European Community Directive 86/609 On Human Participation in Biomedical Research.

STATISTIC METHODS

We calculated median (Me) and interquartile range (IQR) for continuous variables. Differences between unrelated samples were calculated using Mann-Whitney U-test. Categorical variables were presented in absolute and percent values. Pearson's Chi-squared test was used to assess differences between groups.

Logistic regression with enter and backward Wald methods was used to calculate association with binary outcome. Nagelkerke R^2 and Hosmer-Lemeshow goodness-of-fit (HL-GoF) were used to estimate development models' quality.

Coding of groups in regression models was as follows: control — reference group; COPD — comparison group. Gender reference group included female patients.

Significance level (p) in the study was taken as lower than 0.05. Statistical calculations were performed in IBM SPSS 25.0 (trial version) for Windows.

RESULTS

Table I presents baseline characteristics of patients included in the study. There was no significant difference in age and gender (p-values respectively 0.477 and 0.854). Median SBP was higher in COPD patients than in controls (p = 0.027); DBP also differed between groups significantly (p = 0.001).

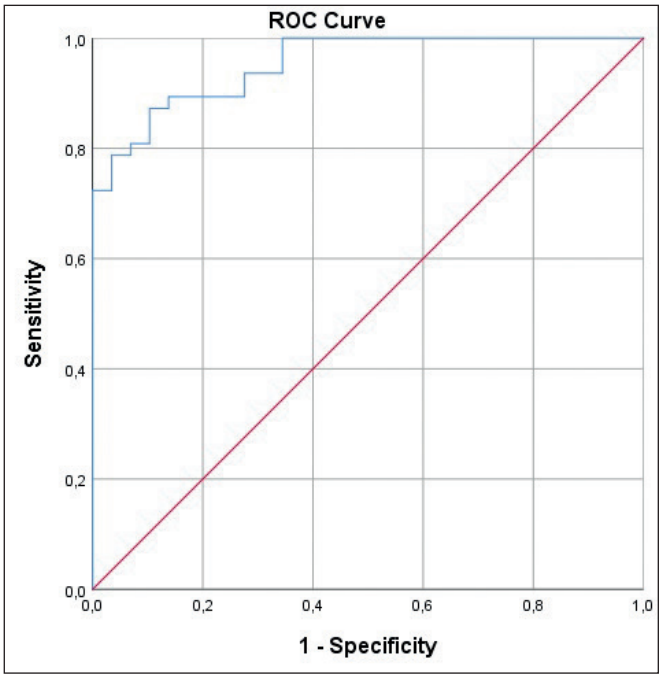

Fig. 3. ROC-analysis of model 1 with Cas-8 and LMR as a predictors of COPD development

In hemogram analysis revealed higher levels of hemoglobin in COPD patients (p = 0.062), segmented neutrophils (p = 0.028) and monocytes count (p < 0.001). Noteworthy, median lymphocytes count was lower in COPD patients than in controls (p < 0.001). Other common blood count parameters did not differ between study groups.

Results showed that healthy individuals had significantly higher median LMR than COPD patients (respectively 7.75 [5.92; 10.0] vs. 3.75 [2.89; 4.67], p < 0.001) but lower median Cas-8 levels (respectively 2.83 [2.58; 3.01] ng/ml vs. 3.48 [2.99; 3.72] ng/ml, p < 0.001).

In both univariate and multivariate analysis, increased SBP had direct association with COPD: respectively OR = 1.094 [95.0 % CI 1.018–1.176] (p = 0.015) and OR = 1.196 [95.0 % CI 1.028–1.391] (p = 0.021). Noteworthy, DBP showed significant reverse association in univariate analysis but not in multivariate: OR = 0.850 [95.0 % CI 0.743–0.974] (p = 0.019) and OR = 0.820 [95.0 % CI 0.665–1.012] (p =0.064) (table II).

Lymphocytes and monocytes count was also significantly (p<0.001) associated with COPD development in univariate analysis (respectively OR = 0.855 [95.0 % CI 0.785–0.932] and OR = 1.916 [95.0 % CI 1.419–2.588]). Those parameters were not included in multivariate analysis in order to avoid multicollinearity.

In both analyses, increased LMR was significantly (p<0.001) inversely associated with COPD: OR = 0.455 [95.0 % 0.321–0.643] and OR = 0.371 [95.0 % CI 0.217–0.634] for univariate and multivariate respectively. Similar trend was also found regarding Cas-8 levels but the association was direct: OR = 11.273 [95.0 % CI 3.100–40.995] (p<0.001) and OR = 12.823 [95.0 % CI 2.104–78.134] (p = 0.006) (table II).

Further three models of prognosis of COPD development in healthy individuals are introduced. All models included age, SBP and DBP, and model 1 included Cas-8 levels only, model 2 included LMR value only and model 3 included both Cas-8 levels and LMR value (table III).

Thus, model 1 demonstrates that increased Cas-8 is directly associated with COPD development (OR = 12.819 [95.0 % CI 3.224–50.974], p<0.001. In Model 2 lymphocyte-to-monocyte ratio revealed reverse association with COPD development: OR = 0.393 [95.0 % CI 0.252–0.611], p<0.001. In addition, in Model 3 it can be seen that both Cas-8 and LRM are significantly associated with COPD development: respectively OR = 12.823 [95.0 % CI 2.104–78.134] (p = 0.006) and OR = 0.371 [95.0 % CI 0.217–0.634] (p<0.001).

Analysis also found that model 1 with Cas-8 only had the lowest parameters of Nagelkerke R^2 and Hosmer-Lemeshow test, while model 2 with LMR included had much higher indices of overall goodness of fit and variance explained. Finally, including both Cas-8 and LRM gave the highest results of both Nagelkerke R^2 and goodness-of-fit, suggesting greater prognostic ability in prediction of COPD in healthy individuals.

Quality of developed models was checked by computing of ROC-analysis. Figure 1 shows that model 1 had AUC = 0.858 [95.0 % CI 0.773–0.943], p < 0.001. Model 2 (figure 2) had AUC = 0.923 [95.0 % CI 0.866–0.980], p < 0.001, and Model 3 — AUC = 0.953 [95.0 % CI 0.913–0.994], p < 0.001 (figure 3).

DISCUSSION

Estimation of hemogram parameters is rapid and relatively costless diagnostic method as common blood count analysis is performed routinely. Various studies report possible prognostic role of hemogram indices in prediction of wide spectrum of diseases from cardiovascular pathology to neoplasms.

Lymphocytes are known to play a vital role in induction of cellular apoptosis via cytotoxicity and inhibition of proliferation, e. g. in tumors [10]. Studies in cancer patients showed that monocytes trigger tumor cell growth and vascularization thus promoting its survival and development.

Goto et al. [11] report that systemic inflammation determines worse course and poorer outcomes of disease, especially in cancer patients, where lower lymphocyte count is connected with decrease in immunological defensive reaction. Research states that lower LMR was associated with shorter disease-free survival (p = 0.006).

In research of [8] patients, who died during 28 day after acute exacerbation of COPD had higher neutrophil and lower lymphocytes counts than in survived patients: 10.60±3.97 vs. 6.81±5.68 (p<0.001) and 1.22±0.75 vs. 0.86±0.67 (p<0.001). In addition, LMR in survived patients was higher than in died subgroup: 2.26±1.79 vs. 1.62±1.19 (p=0.061).

Lang et al. [12] reported that LMR higher than 2.5 was significant prognostic factor for overall survival of lung cancer patients both in non-adjusted and multivariate

models. Further analysis showed that higher LMR was significantly (p = 0.037) linked to disease-free survival. In the present research, it was found that patients with COPD have lower lymphocyte count but higher monocyte count compared to control group. Lymphocyte-to-monocyte ratio in COPD patients was also lower than in controls. Noteworthy, lower LMR was significantly associated with COPD in univariate and multivariate models.

Regarding additional prognostic factors, blood pressure and levels of Cas-8 were independently linked with COPD development. It should be stated that increased systolic blood pressure was significantly associated with COPD in both non-adjusted and adjusted models. Despite being normotensive, COPD patients showed significantly higher systolic blood pressure than in control group.

Arslan et al. [13] reported a direct correlation of SBP with CRP levels in COPD patients suggesting the interplay of increased systemic blood pressure and systemic inflammation. Compared to controls, patients with COPD also had significantly (p = 0.001) higher mean SBP but only during nighttime. Byrd et al. [14] found that compared to normotensive COPD patients hypertensive ones had increased mortality and cardio-vascular events rate (HR = 1.27 [95.0 % CI 1.12–1.45] and HR = 1.18 [95.0 % CI 1.01–1.39]. On the other hand, the study showed that COPD patients with low SBP and DBP are also at the risk group. Thus, HR for all-cause mortality in low SBP patients was 1.36 [95.0 % CI 1.13–1.63]. Lower DBP revealed direct association with both all-cause mortality and cardio-vascular events rate: respectively HR = 1.15 [95.0 % CI 1.00–1.32] and HR = 1.34 [95.0 % CI 1.13–1.59]. In the present research, it was found that higher systolic blood pressure is significantly associated with COPD while higher diastolic blood pressure showed indirect association. Such findings may suggest the need for continuous monitoring of systolic and diastolic blood pressure even in normotensive healthy individuals in order to provide timely correction of those parameters.

LIMITATIONS OF STUDY

Present study has several limitations. Primarily, it is relatively small sample size. Additionally, we did not perform continuous supervision of patients in order to evaluate association of LMR and caspase-8 levels with incidence of COPD. Moreover, involved patients with COPD had stable course of the disease and further study on relationship of LMR and caspase-8 levels with development of exacerbations are needed.

CONCLUSIONS

Present findings suggest that the lymphocyte-to-monocyte ratio could act as a significant predictor of COPD development. Decreased ratio shows significant association with COPD indicating on strong effect of immunological violations in its pathogenesis. Additionally, increased apoptotic activity, depicted in increased caspase-8 levels, provides a valuable association with COPD. Both study groups were normotensive, however, results show direct association of increased SBP and DBP with COPD, which should be taken into account for providing prophylactic measures. Despite LMR and Cas-8 levels are reliable predictors, the highest accuracy of is achieved in case of inclusion of both LMR and caspase-8 levels. Further studies of LMM and caspase-8 with larger samples of COPD patients are necessary, which allow finding a new data on their association with additional COPD parameters.

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ORCID and contributionship:
Volodymyr M. Tverezovskyi: 0000-0002-9953-9553 [A-D]
Valerii A. Kapustnyk: 0000-0002-4543-8343 [E, F]
Borys O. Shelest: 0000-0001-5528-8302 [B, E]
Olga L. Sadovenko: 0000-0001-7160-8070 [B, E]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Volodymyr M. Tverezovskyi
Kharkiv National Medical University
4 Nauki ave, 61000 Kharkiv, Ukraine,
tel: +380950078076
e-mail: vtverezovskyi@gmail.com

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A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article
Responsibility for statistic*al analysis, D – Writing the article, E – Critical review, F – Final approval of the article*

ORIGINAL ARTICLE

5-HT$_3$ SEROTONIN RECEPTOR BLOCKERS FOR INTENSIVE THERAPY OF TRAUMATIC DISEASE IN PATIENTS WITH MULTIPLE TRAUMA

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Yuliya V. Volkova[1], Kostiantyn G. Mykhnevych[1], Volodymyr I. Ponomaryov[2], Dmytro V. Dmytriiev[3], Kostiantyn D. Dmytriiev[3], Kseniia I. Lyzohub[4], Serhii M. Potapov[1]

[1]KHARKIV NATIONAL MEDICAL UNIVERSITY, KHARKIV, UKRAINE

[2]EDUCATIONAL AND SCIENTIFIC MEDICAL INSTITUTE OF THE NATIONAL TECHNICAL UNIVERSITY «KHARKIV POLYTECHNIC INSTITUTE», KHARKIV, UKRAINE

[3]NATIONAL PIROGOV MEMORIAL MEDICAL UNIVERSITY, VINNYTSIA, UKRAINE

[4]KHARKIV MEDICAL ACADEMY OF POSTGRADUATE EDUCATION, KHARKIV, UKRAINE

ABSTRACT

The aim: To find the most rational choice of drugs that have anti-emetic effect in patients with polytrauma in acute and early periods.

Materials and methods: We examined 82 patients with polytrauma, 62 men and 20 women. The age of patients ranged from 19 to 50 years. Patients were divided into the main and control group with 36 and 46 people respectively, who did not differ significantly by sex, age, anthropometric data, the nature and severity of injuries, and the time from injury to admission to hospital.

Results: Full antiemetic effect was achieved in 72.4% of patients, where metoclopramide was used. Complete antiemetic effect was achieved in 96.3% of patients, where sturgeon was used. Decrease of peristaltic activity does not increase postoperative intestinal paresis, and also prevents irritable bowel syndrome and diarrhea caused by dysbacteriosis on the background of antibiotic therapy. Anxiolytic effect without sedative effect and impairment of motor coordination, decrease of the somatic and psychopathological symptoms intensity in alcohol-toxic withdrawal syndrome contributes to the correct interpretation of the traumatic disease.

Conclusions: Use of drugs with antiemetic effect is an important part of the complex of traumatic disease treatment in patients with polytrauma. The use of osetron is rational in patients with polytrauma with cranio-abdominal injuries.

KEY WORDS: multiple trauma, serotonin receptors, intensive therapy

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INTRODUCTION

Scientific interest in the problem of polytrauma arose in the last 20-30 years due to a significant increase in disability [1, 2] and mortality [35].

On the basis of modern ideas, traumatic disease is considered depending on the severity, extent, nature and localization of injuries [6]. Its dynamics is evaluated in the treatment conditions, which are based on the principles of the pathogenetic approach, taking into account the specific understanding of the mechanisms of action of drugs. Taking into account the conditions for the occurrence of a traumatic disease, it is quite clearly possible to characterize the phenomena that occur both at the time of mechanical damage to any organ, and after correction of a violation of its integrity, due to functional changes [7].

It has been proven that the course of a traumatic disease determines the reactivity of the organism, which is manifested by the characteristics and types of both nervous and humoral regulation of functions [8, 9]. One of the important pathogenetic mechanisms of the development of complications in patients with polytrauma are the effects caused by stimulation of nerve fibers located directly in the tissues, and receptor formations. At the same time, there is an intense afferent impulsation through the conductors of various kinds, which, outside the application of therapeutic measures, persists for a long time during and after injury [10, 11]. In turn, the damage of specific cells leads to the release of various kinds of active substances and the violation of the corresponding functions. For example, the violation of the integrity of the connective tissue is accompanied by the destruction of mast cells, which leads to massive resorption of amines [12], some of which are peptide synaptic mediators.

It is known that 5-hydroxytryptamine (5-NT) - serotonin is essential in the formation of pain syndrome [13, 14]. It belongs to the group of indoleamines and is derived from the tryptophan, via its hydroxilation. Serotonin is found in various organs and tissues, including platelets, pheochromocytes of the intestine and adrenal medulla. It realizes its action through a system of serotonin receptors located on different types of enteric plexus neurons, on smooth muscle and epithelial cells of the gastrointestinal

tract and brain cells [15].

Currently, 7 types of serotonin receptors have been identified. Drugs that have affinity for 5-HT receptors can affect the transmission of nerve impulses at the receptor and interneuron levels, and regulate the impaired motility of the gastrointestinal tract. A large number of serotonergic receptors are found in the structures of the brain, and serotonergic fibers are part of descending antinociceptive structures. A decrease in serotonin levels leads to a decrease in the pain threshold and increased pain [4, 16].

Taking into account the peculiarities of the course of a traumatic disease, it is interesting from a pathogenetic point of view to use antagonists of type 3 serotonin receptors (5 – HT3) during the period of acute reaction to the injury and its early period.

THE AIM

Considering the above data, we conducted a study, the purpose of which was to find the most rational choice of drugs that have anti-emetic effect in patients with polytrauma in acute and early periods of traumatic illness.

MATERIALS AND METHODS

We examined 82 patients with polytrauma, 62 men and 20 women. The age of patients ranged from 19 to 50 years. For a comparative analysis, 2 groups of patients were selected, the control and main, 36 and 46 people respectively, who did not differ significantly by sex, age, anthropometric data, the nature and severity of injuries, and the time from injury to admission to hospital. The severity of polytrauma was 24.50 ± 4.32 in the main group and 25.12 ± 5.08 in the control group, and 10-13 according to TS scale. Combination of injuries was considered during the inclusion of patients into the study, as they can influence the course of the traumatic disease. Injuries were classified as following: TBI – traumatic brain injury, A – abdominal, T – thoracic, S – skeletal.

In this case, preference was given to victims with the presence of combined cranio-abdominal injuries, one of the clinical manifestations of a traumatic disease in which is vomiting of various etiologies.

The level of consciousness of patients on admission on a scale of Glasgow com was 13.24 ± 1.76 points with no significant difference between the groups ($p > 0.05$).

All patients underwent laparotomy with the full scope of surgical correction in the conditions of programmed intravenous anaesthesia with mechanical ventilation with the introduction of muscle relaxants. Step by step, a surgical intervention was performed in the presence of intracranial pathology, the primary surgical treatment of wounds; in patients with injuries of the musculoskeletal system – trauma correction for severe injuries in a reduced volume in a minimally invasive manner, in other cases – metal osteosynthesis, application of the Ilizarov apparatus. In the presence of a thoracic injury – puncture or drainage of the pleural cavity according to Bulau.

The duration of stay of patients in the operating room averaged 161.2 ± 25.7 minutes. After being transferred to the intensive care unit, all patients were extubated during the first day of hospital stay.

Patients with impaired hemodynamics who required adrenaline correction were excluded from the study. At the same time, in the postoperative period 61.1% In the main group needed additional administration of dosages of dopamine, and 13.9% dosages of the injured control group. In the main group of patients, these figures were 58.7% and 15.2%, respectively.

Taking into account the peculiarities of managing patients with polytrauma, such as urgency, the inability to fully collect anamnestic data and often forced polypharmacy caused by the selection of drugs based on an individual approach, metoclopramide 0.14 ± 0.02 mg / kg body weight was also administered in premedication to prevent a possible dyspeptic syndrome. After being transferred to the department, its daily dosage was 0.41 ± 0.05 mg / kg body weight in a single ampoule mode (10 mg) intravenously every 8 hours for 5 days. In turn, patients of the main group received sturgeon (ondansetron hydrochloride dihydrate) 0.06 ± 0.01 mg / kg body weight during premedication. In the postoperative period, its daily dosage was 0.11 ± 0.01 mg / kg body weight in the mode of one ampoule (4 mg) intravenously every 12 hours for 5 days.

The clinical manifestations of dyspeptic syndrome, the intensity of peristalsis in points on the Orel VV scale were investigated in all patients during the first 5 days of hospitalization, the intensity of pain according to VAS on the background of the introduction of non-steroidal anti-inflammatory drugs (narcotic analgesics in the postoperative period were not used).

In order to achieve representativeness between the groups, the degree of blood loss was determined on the basis of the amount of blood in the abdominal and pleural cavities, using a calculation method according to the formula F.D. Moore and based on data from the table G.A. Barashkova, P. Casal. Hemodynamic parameters: stroke volume (SV), the minute cardiac volume (MCV) was determined by the method of integral rheography by M.I. Tishchenko, blood pressure - using the resuscitation-surgical monitor "UTAS-300M".

To assess the reliability of differences the t-student criterion was used. When $p < 0.05$ differences were considered as statistically significant.

RESULTS

The results of the study have shown that the use of osetron in victims with polytrauma during sedation and in the postoperative period is the most optimal.

From the first hours of the postoperative period, a score of peristalsis intensity was performed in both groups.

When conducting a comparative analysis of the data, it is clear that, on the background of complex therapy, all peristalsis tended to increase and by the end of the acute period of the traumatic disease reached 2 points with no

Table I. Dynamics of hemodynamic parameters in both study groups

Indicator	group	1 day	2 day	3 day	5 day
BPs, mmHg.	Control	101.3±7.4	106.6±11.5	100.1±9.6	93.5±5.8
	Main	98.8±5.9	108.2±9.4	99.7±10.2	96.1±10.3
SV, ml	Control	48.7±7.2	58.4±6.2	58.5±2.7	66.1±7.1
	Main	55.4±5.6	58.1±3.1	62.7±3.2	68.4±8.5
CO, l/min.	Control	5.4±0.2	5.4±0.9	5.5±0.2	6.2±0.6
	Main	5.5±0.7	5.7±0.3	6.0±0.4	6.3±0.2

* $p > 0.05$

statistically significant difference between the groups ($p > 0.05$).

The study of the intensity of pain using the VAS scale revealed a strong tendency for it to decrease in all patients, more pronounced in patients of the main group in the absence of a statistically significant difference between the groups ($p > 0,05$).

In a comparative analysis of hemodynamic parameters, we found no significant difference between their indices in both groups (Table I).

However, it was interesting to identify the fact of a persistent increase in the dosage and time required for exogenous administration of dopamine in patients in the control group. In our opinion, this may be due to the blocking of dopamine D2 receptors by metoclopramide and requires a special study.

When used in the prevention and treatment of vomiting in the victims of the control group of metoclopramide, the full antiemetic effect was achieved in 72.4% of patients. At the same time, such possible side effects of this drug as extrapyramidal disorders and impaired concentration of attention made it difficult for the differential diagnosis of the clinical condition of the patients.

When used in the prevention and treatment of vomiting in patients of the main group of sturgeon, a complete antiemetic effect was achieved in 96.3% of patients. It was determined that the clinical effect of this drug, such as a decrease in peristaltic activity, does not aggravate postoperative intestinal paresis, but, on the contrary, is an element for the prevention of irritable bowel syndrome and diarrhea on the background of dysbacteriosis caused by massive antibiotic therapy. In turn, the effects of the sturgeon, such as anxiolytic action without a sedative effect and impaired motor coordination, the relief of somatic and psychopathological symptoms in alcohol-toxic withdrawal syndrome contributes to the correct interpretation of the clinical manifestations of traumatic disease, which makes it the drug of choice in the clinic of polytrauma.

DISCUSSION

Our results regarding the effectiveness of osetron (ondansetron) for the prevention of intra- and postoperative nausea/vomiting were also proven by other studies. Thus, Parra-Güiza R. et al [17] stated the prophylactic effectiveness of ondansetron compared to placebo in the prevention of nausea and vomiting during subarachnoid anesthesia during cesarean section. The frequency of vomiting was higher in the placebo group (37%) compared to ondansetron (16%). In addition, the incidence of nausea was higher in the placebo group (75%) compared to ondasetron (56%; $p = 0.005$).

Also, other researchers [18] stated a probable ($p < 0.001$) good effectiveness of ondansetron (both in a dosage of 8 mg and when used in a dose of 4 mg) in the postoperative period (after 24 hours) compared to placebo in the prevention of postoperative nausea and vomiting during cesarean section in pregnant women. Thus, they reliably ($p < 0.001$) determined the frequency of nausea 24 hours after cesarean section when using ondansetron only at a dosage of 4 mg (3.1%) compared to using a placebo (9.4%) and nausea and vomiting only when using a placebo (12.5%)). However, the probable difference of postoperative nausea and vomiting was not significant among the study groups at 48 hours ($p = 0.086$) and 4 days ($p = 0.409$) after surgery: respectively, after 48 hours of using ondansetron – 1.6% and using placebo – 3.1% and after 4 days after surgery – only when using placebo – 1.6%. The incidence of postoperative nausea and vomiting was similar between the ondansetron groups at different dosages (8 mg and 4 mg); however, the incidence of nausea was higher in the placebo group than in the ondansetron-treated groups, whereas nausea and/or vomiting did not occur in the ondansetron 8 mg group during all postoperative periods studied. Most cases of nausea and vomiting were observed in the placebo group after 24 hours (12.5%), 2 (3.1%), and 4 (1.6%) days, as well as nausea alone (9.4%, 4.7%, and 0 respectively).

CONCLUSIONS

1. An important component of the complex treatment of traumatic disease in victims with polytrauma is the use of drugs with antiemetic effect.
2. An interesting from the pathogenetic point of view is the use of type 3 serotonin receptor antagonists (5-HT3) in the treatment of traumatic disease.
3. In patients with polytrauma with cranio-abdominal injuries, the use of osetron is the most rational from the pathogenetic point of view.

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The ethical approval was obtained from Bioethics Committee of the Kharkiv National Medical University. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008, as well as the national law. Informed consent was obtained from all the patients included in the study.

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ORCID and contributionship:

Volkova Yuliya Viktorivna: 0000-0001-8000-5802 [A, B, D-F]
Mykhnevych Kostiantyn Georgiyovich: 0000-0002-6135-7121 [D]
Vladimir Ivanovich Ponomaryov: 0000-0003-2513-3187 [D, E]
Dmytriiev Dmytro Valeriyovich: 0000-0001-6067-681X [D, E]
Dmytriiev Konstyantun Dmytrivich: 0000-0003-22696291 [D, E]
Lyzohub Kseniia Ihorivna: 0000-0001-9149-7208 [D]
Potapov Serhii Mykolayovich: 0000-0002-5718-3341 [D]

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Volodymyr I. Ponomaryov
Educational and Scientific Medical Institute of the National Technical University «Kharkiv Polytechnic Institute»
79 Pushkinska st., 61022 Kharkiv, Ukraine
tel: +38(063)7486769
e-mail: Ponomaryov_VI@ukr.net@ukr.net

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ORIGINAL ARTICLE

ASSESSMENT OF THE EFFICIENCY OF ANALGETIC ACTION OF ULTRASOUND-GUIDED FICB AS A COMPONENT OF PERIOPERATIVE MULTIMODAL ANALGESIA IN ERAS- STRUCTURE IN OBESE PATIENTS UNDERGOING TOTAL HIP REPLACEMENT

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Viktoriia V. Yevsieieva[1, 2], Radoslaw Maslon[3], Yevgeniy O. Skobenko[1], Maksym O. Malimonenko[1], Daniil D. Kravchenko[1], Valentyn O. Kuprii[1], Vasyl L. Shmahoi[1]

[1]STATE SCIENTIFIC INSTITUTION «CENTER FOR INNOVATIVE MEDICAL TECHNOLOGIES OF THE NATIONAL ACADEMY OF SCIENCES OF UKRAINE», KYIV, UKRAINE
[2]STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE
[3]INDEPENDENT PUBLIC HEALTHCARE COMPLEX, KEDZIERZYN-KOZLE, POLAND

ABSTRACT

The aim: To compare the efficiency of analgetic action of Ultrasound-guided FICB and prolonged EA as the components of perioperative multimodal analgesia in ERAS-structure in obese patients undergoing THR.

Materials and methods: The retrospective study included 80 patients with obesity, who underwent elective anterolateral THR under conditions of low-flow inhalation anesthesia with sevoflurane in combination with PEA (n1=38) or with FICB (n2=42). Primary endpoints: VAS pain level during the first postoperative day.

Results: Static and dynamic VAS pain scores were similar in both groups during the first 6 hours. Since the 8th postoperative hour, there was a statistically significant increase in both static and dynamic VAS pain scores in the FICB group. A significant difference in static and dynamic VAS pain scores was obtained with a trend toward an increase in the PEA group within 48 hours ($p < 0.05$).

Conclusions: USG- FICB is an effective, practically feasible, minimally invasive and safe regional method for eleclive anterior-lateral THR and can be an alternative to PEA in obese patients.

KEY WORDS: ERAS, obesity, ultrasound- guided FICB, multimodal analgesia, Total hip replacement

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INTRODUCTION

Total hip arthroplasty (THA) is recognized as the most effective method of treating the terminal stage of coxarthrosis and femoral neck fracture from the point of view of pain relief and restoration of functional capacity [1]. The constant increase in the number of THA procedures in the world over the past 20 years is caused by both social awareness and longer professional activity among the population [2].

A special group constitute obese patients. Despite the fact that obesity is directly related to osteoarthritis of the hip joint at a younger age, these patients have a high level of perioperative complications, which is due to the technical difficulties of performing surgical intervention, and such concomitant pathology as type 2 diabetes, hypertension (HTN), coronary heart disease (CHD) and others [3].

One of the fundamental elements of modern reconstructive surgery of the hip joint and the best method of preventing postoperative complications is early rehabilitation and mobilization of the patient, which forms the basis of the modern ERAS protocol for orthopedic interventions [4]. But the implementation of this concept is impossible without high-quality multimodal perioperative analgesia with minimization of the need for opioids and side effects associated with their systemic use, which is especially important in obese patients [5]. The problem of perioperative analgesia and opioid load in patients with normal weight is completely solved by neuraxial types of anesthesia and local infiltration anesthesia of the surgical intervention site [6, 7]. In obese patients, the use of neuraxial methods of anesthesia is often limited by technical difficulties, negative effects on systemic hemodynamics, and inflammatory processes associated with existing type 2 DM [8].

Since today there are no single guidelines or strong recommendations for choosing the type of analgesia, including the type of regional blockade in elective hip arthroplasty in obese patients, the search for the optimal combination of anesthetic techniques in this group of patients is still ongoing [9].

Recently, Ultrasound Guided Fascia Iliaca Compartment Block (USG-FICB) has become widely used as a fast, proven safety and efficacy method of analgesia for hip fracture [10-12].

Table I. Baseline characteristics.

Variables	PEA group (n=38)	FICB group (n=42)	P
Female gender	16 (42 %)	19 (45 %)	0.007
Age (years)	53.32 (±11.05)*	51.46 (± 11.73)*	0.518
BMI	42 (35-48)**	41 (36-45)**	0.006
ASA grade			0.332
ASA I	0 (0.0%)	0 (0.0%)	
ASA II	20 (58 %)	22 (68 %)	
ASA III	18 (47 %)	20 (47 %)	
ASA IV	0 (0.0%)	0 (0.0%)	
Hypertension	30 (78 %)	32 (76 %)	0.223
Coronary artery disease	18 (47%)	23 (54%)	0.218
Diabetes mellitus type2	10 (26 %)	13 (30 %)	0.205
OSA	5 (13 %)	4 (9 %)	0.162
Duration of surgery (minutes)	92.8±23.6	86.5±21.8	0.241
Duration of general anesthesia (minutes)	95.2±22.7	98.3±24.2	0.326

*-Values are mean (± standard deviation)
**-Values are median (interquartile range)

Table II. The values characterizing early patient recovery after general anaestesia.

Variables	PEA group (n=38)	FICB **group (n=42)**	P
Opening eyes, min	4 [3-6]	6 [6-8]	0.1
Effective spontaneous breathing, min	3 [2-4]	4 [4-6]	0.07
Extubation, min	4 [3-6]	6 [7-8]	0.07
The level of postoperative pain for VAS	0 [0-0]	1 [0-2]	0.1

Values were presented as median (Q1-Q3)
*Statistically significant value

THE AIM

Therefore, the aim of this retrospective study was to compare the effectiveness of a single ultrasound-guided FICB injection with continuous lumbar EA as components of perioperative multimodal analgesia in the ERAS in obese patients undergoing total hip arthroplasty.

MATERIALS AND METHODS

Our study was performed in line with the principles of the Declaration of Helsinki. Also, the Local Ethics Committee of State Scientific Institution Center For Innovative Medical Technologies of the National Academy of Sciences of Ukraine approved this study. All participants signed an informed consent. The study included 80 patients with obesity of various degrees, who in the period from April 2021 to July 2022 underwent planned anterolateral hip arthroplasty under conditions of multi-component low-flow inhalation anesthesia with sevoflurane in combination with prolonged EA (PEA) (n1=38) or in combination with USG-FICB (n2=42). USG-FICB was the choice for patients who failed to have an epidural catheter due to technical difficulties, use of anticoagulants, or patient refusal of epidural analgesia. All operative interventions were performed by one orthopedic and anaesthesiology team.

Anaesthesia protocol. Patients in both groups received multimodal preemptive analgesia (MPA) in the form of intravenous administration of acetaminophen 1000 mg, dexketoprofen 50 mg, and nefopam 20 mg intramuscularly 30 minutes before induction anesthesia. Ondansetron 8 mg and dexamethasone 4 mg were administered intravenously to prevent postoperative nausea and vomiting (PONV). Patients in the PEA group (n1=38) underwent catheterization of the epidural space at the lumbar level in the operating room before induction anaesthesia.

In both research groups, induction of anaesthesia was performed by IV administration of propofol - 1.5-2 mg/kg ideal body weight (IBW) in fractions until the clinical symptoms of narcosis were reached, fentanyl 0.005% - 0.1-0.2 mg. Tracheal intubation was performed using a video laryngoscope after relaxation against the background of atracurium besylate at a dose of 500-600 mg/kg (IBW) or rocuronium bromide at a dose of 0.6-1.0 mg/kg (IBW).

Maintenance of anesthesia: oxygen-sevoflurane mixture FiO2 - 45-50%, sevoflurane - MAC 0.7-1.0 at a flow of no more than 1 L/min. BIS indicators were maintained at the level of 45-55. Relaxation was maintained by fractional administration of atracurium besylate in a dose of 10-20 mg or rocuronium bromide in the same dose every 30-40 minutes. Intraoperative monitoring in both groups was carried out according to the Harvard standard.

Table III. Comparison of static VAS scores between the two groups.

Postoperative hours	PEA group (n=38)		FICB group (n=42)		p
	Min-max	Med [Q1-Q3]	Min-max	Med [Q1-Q3]	
2 hours	0-3	1 [0-2]	0-3	1 [0-2]	>0,05
4 hours	2-4	2 [0-3]	0-3	1 [0-2]	>0,05
6 hours	0-2	0[0-2]	0-4	1 [0-2]	>0,05
8 hours	0-2	0 [0-3]	2-5	2 [0-3]	< 0,05*
12 hours	0-2	0 [0-2]	2-5	3 [0-3]	>0,05
24 hours	0-4	1 [0-3]	0-3	1 [0-2]	> 0,05
48 hours	2-5	2 [0-3]	0-2	0 [0-0]	< 0,05*

Values were presented as median (Q1-Q3)
*Statistically significant value

Table IV. Comparison of Dynamic VAS scores between the two groups.

Postoperative hours	PEA group (n=38)		FICB group (n=42)		p
	Min-max	Med [Q1-Q3]	Min-max	Med [Q1-Q3]	
2 hours	0-3	1 [0-2]	0-3	1 [0-2]	>0,05
4 hours	0-4	2 [0-3]	0-3	1 [0-2]	>0,05
6 hours	0-3	0[0-2]	0-4	1 [0-2]	>0,05
8 hours	0-3	0 [0-3]	2-5	2 [0-3]	< 0,05*
12 hours	0-3	0 [0-2]	2-5	2 [0-3]	< 0,05*
24 hours	0-4	1 [0-3]	0-3	1 [0-2]	> 0,05
48 hours	2-5	2 [0-3]	0-3	1 [0-2]	< 0,05*

Values were presented as median (Q1-Q3)
*Statistically significant value

Table V. Perioperative complications associated with the method of analgesia

Variables	PEA group (n=38)	FICB group (n=42)	P
Intraoperative hypotension, %	31 (81%)	3(5%)	< 0,01*
Postoperative hypotension, %	20 (52%)	0	< 0,01*
Post FICB hematoma	N/A	0	_
Back pain after PEA	8 (21%)	N/A	_
PONV	5 (13%)	7 (16%)	0,28
No. of patients with postoperative opioid administered	0	0	_
Urinary retention	4 (10%)	0	< 0,01*
Muscle weakness	15 (39%)	3 (7%)	< 0,01*

*Statistically significant value

For the purpose of intraoperative analgesia in the PEA group (n1=38) in 10 min. before the surgical incision, bupivacaine solution 0.25%-10.0 was injected bolus into the epidural space at the lumbar level, followed by prolonged administration of bupivacaine solution 0.25%- 7-10 ml/h using a perfusor. In patients of the FICB group (n=42), the pleural fascia block was performed after intubation of the trachea in the "in plane» technique under ultrasound control with the help of a linear sensor by injection through a 22-gauge Stimuplex needle, at an angle of 30 degrees to the skin. After identification of vessels and nerve, aspiration sample, bupivacaine solution 0.25%-40.0 was injected through Stimuplex 22 gauge needle. After 10 minutes, a surgical incision was made.

Postoperative analgesia in the PEA group (n1=38) was carried out by continuous infusion of bupivacaine solution 0.125% - 5.0 ml/h using a pump at pain intensity according to the visual analog scale (VAS) up to 5 points; with pain intensity according to VAS above 5 points, the rate of infusion of bupivacaine solution 0.125% was increased until the pain-relieving effect was achieved. After removal of the epidural catheter, pain relief was provided by prescribing multimodal analgesia in the form of IV acetaminophen 1000 mg every 6 hours in combination with IV dexketoprofen 50 mg and IM nefopam 20 mg.

Patients of the FICB group (n=42) received postoperative analgesia taking into account the intensity of pain accord-

ing to the VAS: up to 5 points - multimodal analgesia in the form of intravenous administration of acetaminophen 1000 mg every 6 hours in combination with intravenous dexketoprofen 50 mg and intramuscular administration nefopam 20 mg; with pain intensity above 5 points - FICB was performed according to the above-mentioned method.

The assessment of pain according to VAS was carried out for the first time on the operating table, immediately after extubation of the trachea, then - 1, 4, 6, 8, 12 and 24 hours after the operation twice (before analgesia and 30 minutes after analgesia).

Interpretation of data according to the VAS scale:

0 – no pain;

1-3 points – weak pain;

4-5 points – moderate pain;

6-9 points – severe pain;

10 points is the strongest pain (unbearable).

Interpretation of analgesia results:

1) no pain – 0 points;

2) adequate analgesia – 1-4 points;

3) additional analgesia is necessary (moderate pain) - 5 points;

4) pain relief by means of narcotic analgesics is necessary (severe pain) - 6-10 points.

Primary endpoints: VAS pain level during the first postoperative day.

Secondary endpoints were total opioid consumption and perioperative complications related to the chosen method of analgesia.

Statistical data processing was performed using methods of variation and descriptive statistics using the statistical analysis package SPSS Statistics, version 23. Before starting the data analysis, all indicators were checked for normal distribution using the Shapiro-Wilcoxon test. Statistical indicators of mean values (M) and standard deviation (SD) were used in the study. To assess statistically significant differences of the mean values of quantitative traits subject to the law of normal distribution, parametric assessment methods were used in the dependent groups (Student's t-test). Pearson's test ($\chi 2$) was used in the comparative analysis of qualitative parameters (frequency distributions) between groups of patients. Differences in the results obtained were deemed statistically significant at $p < 0.05$, which provides a 95% probability level.

RESULTS

The patients'demographic and comorbidy characteristics are summarized in Table I. There was no statistically significant difference in gender, age, body mass index, ASA classification and comorbidities.

The values characterizing early patient recovery after general anatsthesia are given in Table II. The values have been estimated from zero sevoflurane end-expiratory concentration and the last relaxant introduction after 30 minutes at the earliest. As can be seen from the data in Table II, there was no statistically significant difference between the indicators of early post-anaesthesia rehabilitation in both groups, which we associate with the low intraoperative dose of fentanyl, namely 0.93 ± 0.12 μg / kg /h in the PEA group vs 1.04 ± 0.18 μg / kg /h in the FICB group, (p=0.08).

According to the data presented in Tables III and IV, static and dynamic VAS pain scores were similar during the first 6 hours. Since the 8th postoperative hour, there was a statistically significant increase in both static and dynamic VAS pain scores in the FICB group, which we attribute to the gradual cessation of local anaesthetic action. Dynamic pain scores had a statistically significant tendency to increase by the 12th postoperative hour in the FICB group, which we attribute to the period of patient activation. In 31 (73%) patients, this situation required a repeat USG-FICB procedure. There was also a significant difference in static and dynamic pain scores according to the VAS in the PEA group after 48 hours ($p < 0.05$), which was due to the termination of the introduction of local anaesthetic into the epidural space and activation of the patient.

Perioperative complications associated with the chosen method of analgesia are presented in Table V. As can be seen from the given data (Tab. V), hypotensive episodes occurred significantly more often in the PEA group (n=38) compared to the FICB group (n=42), both intraoperatively and in the postoperative period. In the intraoperative period, the lowest MBP (Meane blood pressure) levels were recorded in the PEA group after bolus injection of local anesthetic into the epidural space, namely at the level of 60±7.5 mmHg. . In 4 cases, administration of low doses of epinephrine was necessary to correct MBP. In the early postoperative period, hypotensive episodes were also significantly more frequent in the PEA group than in the FICB group: 17 (44%) and 2 (4%), respectively, $p < 0.05$. Also, in the postoperative period, in the PEA group, 8 (21%) patients experienced discomfort in the back, in the area of the epidural catheter placement, and 4 (10%) patients had urinary retention after removal of the urinary catheter.

In the FICB group, intraoperative MBP fluctuations were within the stress norm with a tendency to hypertension during traction of the operated lower limb - 87 ± 5.8 mmHg in combination with an increase in heart rate, which required an additional dose of fentanyl, which statistically did not influence the indicators of early post-anaesthesia rehabilitation. There was no case of post-procedural hematoma formation in the FICB group. In addition, FICB was successfully performed without any complications in 9 (21%) patients who were taking antiplatelet drugs or oral anticoagulants preoperatively at the fact of coronary artery stenting.

PONV (postoperative nausea and vomiting) episodes were equal in both groups. A statistically significant difference was achieved in terms of muscle weakness frequency in the PEA group compared to the FICB group: 15 (39%) and 3 (7%) respectively, $p < 0.01$, which in turn significantly affected the time of early patient mobilization. Patients in the FICB group were activated within an average of 16 ± 3.5 hours, which fitted into the framework of the first postoperative day, while in the PEA group, patients were activated within an average of 32 ± 4.6 hours after surgery.

DISCUSSION

Nowadays obesity is one of the principal problems in the whole world. Patients with obesity have hugely variable co-morbid conditions that complicate their perioperative period considerably. Therefore, the decrease of general dose of opioids, pain control, and early mobilization are the most important factors in the treatment patients undergoing total hip replacement.

The use of neuraxial anaesthetic techniques in patients with the normal-weight can reduce the perioperative risks associated with the use of general anesthesia and systemic opioids and provides safe and effective postoperative analgesia for most orthopedic operations. In obese patients, the use of neuraxial methods of anaesthesia is often limited, first of all, by technical difficulties of implementation. Palpation of bony landmarks and identification of the midline are more difficult, and the presence of fat packs may cause a false-positive loss of resistance during needle advancement [13]. Identification of intervertebral structures by ultrasound is even more difficult in such patients. There are data on failure and complications when using ultrasound during epidural anesthesia [14]. Therefore, the search for alternative methods of regional anesthesia in this group of patients is still ongoing.

Since there are positive data on the effectiveness of FICB in the prehospital stage for femoral fracture, the aim of our study was to find out whether USG- FICB can be an alternative to PEA in the perioperative analgesia scheme during total hip arthroplasty in morbidly obese patients.

In our study, we observed that USG-FICB provided a level of analgesia similar to PEA in hip arthroplasty in the perioperative period and had a pronounced opioid-sparing effect- opioid consumption was statistically the same in both study groups. In the FICB group combined with general inhalation low-flow anaesthesia with sevoflurane, patients had more stable hemodynamic parameters. Perioperative hypotension was observed more often in PEA group patients.

Regarding postoperative analgesia, PEA provided statistically better analgesia within 18 hours, which we attributed to the gradual withdrawal of local anaesthetic action in the FICB group. And, although patients in this group needed to repeat the FICB after 8 hours, their activation occurred significantly earlier. In addition, there were practically no such phenomena as muscle weakness, back pain and urinary retention, which improved the comfort of recovery. USG-FICB has been successfully performed without complications in patients receiving antiplatelet or anticoagulant therapy, which can be considered as an alternative type of regional anaesthesia in hypocoagulable patients.

CONCLUSIONS

USG-FICB is an effective, practically feasible, minimally invasive and safe regional method as a component of perioperative multimodal analgesia in the structure of ERAS for planned anterior-lateral total hip arthroplasty and can be an alternative to PEA in obese patients.

A limitation of this study would be the relatively small sample size.

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patients with damage to the capsular-ligamentous apparatus of large joints (code: 726)», at the place of study - the State Scientific Institution «Center of innovative medical technologies of the National Academy of Sciences of Ukraine, Kyiv.

ORCID and contributionship:
Viktoriia V. Yevsieieva: 0000-0002-5812-487X [A, B, D]
Radoslaw Maslon: 0000-0002-5606-1289 [A, E, F]
Yevgeniy O. Skobenko: 0000-0001-81744033 [B, E]
Maksym O. Malimonenko: 0000-0001-5013-4857 [B]
Daniil D. Kravchenko: 0000-0001-7489-5140 [B, D]
Valentyn O. Kuprii: 0000-0003-3026-5053 [B, C]
Vasiliy L. Shmagoi: 0000-0003-2635-4125 [B]

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CORRESPONDING AUTHOR
Viktoriia V. Yevsieieva
State Scientific Institution «Center for Innovative Medical Technologies of the National Academy of Sciences of Ukraine», Kyiv, Ukraine
22 Voznesens'kyy uzviz St., 04053 Kyiv, Ukraine
tel: +380504408286
e-mail: doc-evv@outlook.com

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ORIGINAL ARTICLE

MINIMALLY INVASIVE PERCUTANEOUS NEPHROLITHOTRYPSY IN THE TREATMENT OF PATIENTS WITH KIDNEY STONES

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Roman A. Zhuravchak, Myhajlo D. Dyachuk, Andriy Z. Zhuravchak
STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

The aim: To evaluate the outcomes and complications rate of minipercutaneous nephrolithotripsy (MPCNL) for renal stones treatment.

Materials and methods: MPCNL was performed to 123 patients with kidney stones from January 2020 till November 2021. All operations were performed under endotracheal inhalation anesthesia. After the ureteral catheter was introduced ultrasound controlled punction of kidney collecting system and work channel dilation were performed. Stones were fragmented by holmium laser. The fragments extracted passively with fluid flow through the outer sheath. Operation ended by introduction of nephrostomy tube 14Ch.

Results: In total 135 MPCNLs were performed in 123 patients. The average duration of operations was 55±5,4 minutes and stone size was 1,6±0,2 sm. 12 patients were performed simultaneous MPCNL on both sides. The simultaneous MPCNL duration amounted 105±8,1 min. In 3 (2,2%) cases residual stones were observed. The average hospital stay was 1,31±0,2 days. The renal drainage was removed in 24 ± 3,2 hours after operation. Acute pyelonephritis was presented in 4 (3,3%) and postoperative bleeding in 2 (1,6%) patients, which were stopped by antibacterial and hemostatic drugs with drainage occlusion respectively.

Conclusions: To advantages of MPCNL belong short hospital stay, high safety level, insignificant intraoperative and postoperative bleeding, good operation field visualization, opportunity of quick removal of renal drainage, ureteral and urethral catheters. Benefit in patients with severe comorbidities, opportunity of simultaneous bilateral MPCNL and almost complete postoperative pain absence allow to consider MPCNL the operation of choice in kidney stone management.

KEY WORDS: minipercutaneous nephrolithotripsy, renal stone, bilateral

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INTRODUCTION

Percutaneous nephrolithotripsy (PCNL) has been widely used in everyday urological practice for a long time. In 1955 W.E. Goodwin et al. first described the technique of percutaneous nephrostomy access, and 20 years later I. Femstrom and V. Johansson (1976) first reported on percutaneous nephrolithotomy for removal of large and staghorn kidney stones [1,2]. Technical improvement of the method in combination with the acquisition of experience led to the achievement of its high efficiency and safety. At the same time, the risk of developing complications, primarily bleeding, despite innovative access technologies remains at a fairly significant level. According to the data of large studies summarizing the experience of more than 5000 interventions, the need for hemotransfusion is about 10%, and selective embolization of branches of the renal artery – 3%.

One of the options for minimization of traumatic effect on intrarenal vascular structures is to reduce the size of percutaneous access due to the miniaturization of the tool. The use of nephroscopes with an outer tube diameter of less than 18F is classified as minimally invasive percutaneous nephrolithotripsy (MPCNL).

The history of usage minimally invasive percutaneous interventions for treatment urolithiasis originates in pediatric endourology. In 1997, Healal M. and co-authors reported successful MPCNL in 2year old child using a 10F pediatric cystoscope to remove kidney stones with no residual fragments and complications [3]. Jackman and co-authors in 1998 published the results of eleven procedures in patients aged from 2 to 6 years with the 11F sheath with 85% stone free rate (SFR) with minimal morbidity [4]. Same authors presented 89% SFR of 13F "mini-perc" technique using a ureteroscopy sheath for PCNL in nine patients aged 40-73 years with stone burdens of <2 cm2 [5].

However, the size of the mininephroscope working channel was not exceed 5 Ch. The efficiency of disintegration of large stones was limited due to these technical limitations. One of the main reasons was the use of pneumatic, ultrasonic, and electrokinetic energy sources in contact lithotripters. They did not provide high performance with the corresponding diameter of the probe. In addition, there was no effect of lapaxy, which led to the spread of small fragments throughout the renal collecting system and increased the frequency of residual stones. The combination of such circumstances became the reason for the decreased enthusiasm of urologists for MPCNL. It even led to the appearance in the 2000s of critical articles that questioned the feasibility of the method. Thus, Giusti and co-authors, comparing the results of MPCNL, standard PCNL and tubeless PCNL in the treatment of kidney stones up to 2 cm in diameter, concluded that the only advantage of minimally invasive surgery was a

lower need for blood transfusions and less hematocrit drop (4.49% vs 6.31%) [6]. At the same time MPCNL was characterized by longer duration of intervention, pronounced pain syndrome and duration of inpatient treatment. The frequency of complete liberation from stones with MPCNL was 77.5%, 100% in the tubeless PCNL group and 94% in the standard PCNL group. Finally authors concluded: we no longer perform miniperc.

Next wave of interest to MPCNL, which has been observed in recent decade, is due to the widespread use in everyday urological practice of holmium lasers as a highly effective tool of stone disintegration. Changes in the design of the mininephroscope outer tube, made it possible to create a "vacuum cleaner" effect due to the formation of a low-pressure zone. It allows under visual control effectively washout stone fragments that correspond to the diameter of the outer tube. According to the data of Lahme S. and Zimmermanns V. based on the experience of more than 500 operations the results of MPCNL and standard PCNL are comparable in the frequency of freeing from stones [7]. At the same time, the MPCNL has similar complications rate as extracorporeal shock-wave lithotripsy (ESWL). The authors emphasize that the results of the minimally invasive surgery did not depend on the size, location of the calculus and the age of the patients. They recommend minimally invasive surgery as the surgery of choice in the treatment of patients with kidney stones larger than 1 cm.

THE AIM

The aim of the study was to evaluate the outcomes and complications rate of MPCNL for renal stones treatment.

MATERIALS AND METHODS

We retrospectively analyzed the results of treatment of 123 patients with nephrolithiasis who underwent MPCNL in the Department of Minimally Invasive Surgery of the State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department from 2020 to 2021. The primary outcomes include SFR and postoperative morbidities.

Our study was carried out according to the requirements of the Council of Europe Convention on Human Rights and Biomedicine, World Medical Association Declaration of Helsinki on the ethical principles for medical research involving human subjects. It also complies with regulations of the Ministry of Health of Ukraine. The study design was confirmed by the local ethics committee and all patients were informed and agreed to participate in it in written.

Before surgery all patients underwent general laboratory tests of blood and urine, biochemical blood analysis for creatinine and urea and urine culture as well. The presence of a stone was confirmed by clinical data and visualization methods: kidney ultrasound examination, kidneys ureter and bladder (KUB) X-ray, intravenous urography and/or kidney computed tomography (CT). Stone size was measured on the KUB X-ray or CT scan either by ultrasound examination. If multiple stones were present, the total stone size was estimated as the sum of the length of each stone. All patients were admitted at the day of surgery.

Cephalosporines were routinely prescribed 30 min pre-surgery for prophylactic and for 3 days after. Other groups of antibiotics were used if results of preoperative urine culture indicated cephalosporines resistance. All surgical interventions were performed under general anesthesia, which made it possible to get better patient myorelaxation.

At the first stage of the intervention, the patient was in a lithotomy position. Using the cystoscope, a 5F ureteral catheter was installed into the renal pelvis on the affected side followed by 18F Folley's catheter installation. A ureteral catheter is needed for dilatation of the renal collecting system. This improves the visualization during creating access to the kidney. Next the patient was rotated to the prone position. Access was performed under ultrasound control, taking into account the anatomical features of the renal collecting system and the location of calculi in it. To improve visualization, a syringe with 0.9% pH NaCl is attached to the ureteral catheter and pumped into the collecting system. Guidewire was introduced through the needle sheath into the collecting system after successful puncture. We used an Amplatz fascial dilator for dilatation the access tract. The 16 Fr metal sheath was then passed over the dilator and a 12F mininephroscope (Richard Wolf GmbH, Knittlingen, Germany) introduced into the renal collecting system. Its visual inspection was carried out, the number, size and localization of stones determined. Holmium laser lithotripter (Lumenis Versapulse Powersuite, 100W, Israel) were used for stone fragmentation. The stone fragments were mainly washed out using the suction hydrodynamic effect. Sometimes we used forceps to remove fragments, especially when they were fixed on clots.

At the end of the operation visual inspection of renal collecting system and ultrasound control were carried out for the presence of residual fragments. The operation was completed by passing the 14F nephrostomy drain through the outer sheath into the renal pelvis which was fixed to the skin with 1 suture.

Surgical duration was measured from the moment of puncture to the putting nephrostomy tube. Operative findings, complications and outcomes were documented. Nephrostomy tube routinely was removed on the next postoperative day followed by urethral and ureteral catheters removal. All patients were prescribed diclofenac (75 mg daily) and Paracetamol (500 mg two times daily). Intravenous 100mg Infulgan was used for additional pain control when needed. Renal ultrasonography and KUB were performed before discharge to confirm the stone-free status and detect the perirenal urinoma or hematoma if occurred.

RESULTS

A total of 135 MPCNL were performed in 123 patients. 63 (51%) women and 60 (49%) men were treated. The average age of the patients was 49.6±2.7 years, the youngest - 21

Table I. Patient and stone characteristics

Age ±SD (year)	49.6±2.7
Men (%)	60 (48,8%)
Women (%)	63 (51,2%)
Right side (%)	51 (41,5%)
Left side (%)	60 (48,8%)
Bilateral (%)	12 (9,7%)
Stone size ±SD (cm)	1.6±0.2

Table II. Intra and postoperative parameters

Procedure duration one side ±SD (min)	55±5.4
Procedure duration bilateral ±SD (min)	105±8.1
Hospital stay ±SD (day)	1.31±0.2
Stone free rate	97,8%
Complications	
Infection	4 (3.3%)
Heamoragic	2 (1.6%)

years, the oldest - 78 years. Stone size varied from 1,1 cm to 3 cm and the average was 1.6±0.2 cm (Table I).

The average duration of the operation was 55±5.4 minutes (Table II). The time of surgical intervention depended on the size of the stones, their location, density and number, the anatomical structure of the kidney, and the patient's weight.12 patients underwent a simultaneous MPCNL on both sides. The operation was started from the side where the clinical symptoms were more prominent. In the absence of intraoperative complications, the intervention continued from the other side. There was no case when planned bilateral simultaneous MPCNL was performed on only one side. The duration of the simultaneous bilateral MPCNL was 105±8.1 min.

Presence of residual calculi was detected in 3 (2,2%) cases during the control ultrasonography. Two of three residual stones were initially located in the parallel calyx to nephrostomy channel and in one - fragments migrated there during disintegration. However, the size of residual stones did not exceed 0.5 cm, and none of these patients underwent an additional procedure.

All patients were admitted to the hospital on the day of surgery and stayed there for an average of 1.31±0.2 days (Table II).

The nephrostomy was removed 24±3,2 hours after the operation, and the ureteral and urethral catheters were usually removed in another 2-4 hours. In 4 (3.3%) patients hyperthermia, chills and other signs of acute pyelonephritis were observed. In these patients nephrostomy drainage and catheters were not removed on the first postoperative day and until normalisation their condition. The nephrostomy drainage was also removed later than on the first day in cases of bleeding, which manifested itself in the form of wetting of the bandage and/or the release of intensely blood-stained urine, or blood clots along the drain (2 (1.6%) patients) (Table II).

DISCUSSION

Minimally invasive percutaneous lithotripsy has firmly taken its place among the methods of treatment of kidney stones. There are many reports about benefits of the minimal invasiveness of MPCNL as compared with standard PCNL. Ghazala, S.G. and co-authors reported about 90% SFR in MPCNL group compared with 70% in retrograde intrarenal surgery (RIRS) group (P = 0.053) [8]. Comparing this indicator in patients after MPCNL and PCNL T. Knoll et al. notify 96% and 92% SFR at day 1 respectively [9]. Complete stone clearance was achieved in 91.4% in series of 70 patients currently reported by Aarthy P. et al. [10]. Our results of 97,8% SFR are consistent with the data of these authors. A slightly higher efficiency of freeing the kidneys from stones in our series may be due to the smaller size and complexity of the stones. Recent data of Lin C.-H. with 83.9% SFR for stones above 2 cm (mean 36.69 ± 19.76 mm) also prove this suggestion [11].

Data available in the literature indicate a steady reduction in the duration of MPCNL from the beginning of 2000 to today. Lahme, S., et al reported 99.2 min average operating time in 2001 [12]. Meanwhile Ghazala, S.G. et.al reduce this time to 36.6 min in 2021 [8]. Our operating time data (55±5.4 min) also follows this trend. In our opinion, the difference in the duration of the operation in different studies is mainly determined by the stage of creating access to the kidney. In turn, it is dependent on navigation method and the surgeon's experience is also important. There are different studies of tubeless and total tubeless MPCNL. Some of them report less pain and better patients quality of life in postoperative period [9,11]. But patients in our cohort when discussing surgical options of treatment did not choose tubeless procedure mainly because of need to remove JJ catheter as additional procedure. They prefer to get the nephrostomy drainage and ureteral catheter staying in bed until next postoperative morning, but leave the hospital without any "tubes". And it did not required the use of additional analgesics only in 4 (3,3%) cases. Zhang Y. et al also presented such drainage tactic with similar results [13].

Recent studies evaluating laboratory parameters of glomerular filtration rate and serum creatinine report minor damage to the kidney function when carrying out MPCNL [14, 15, 16]. This fact and low complication rate allow safely use MPCNL for simultaneous bilateral procedure. We performed 12 such operations and did not note serious complications in any case. Respective results also presented by Aarthy P. et al [10].

As reported by numerous researchers, MPCNL is accompanied by a low level of blood loss and does not require blood transfusion [11, 12, 13, 17]. Taking this into account, we performed the MPCNL in 3 patients who were taking indirect anticoagulants (Warfarin) due to concomitant pathology. All these patients switched to direct anticoagulants (Clexan) 5 days before the operation and hematuria was not presented in their postoperative period.

CONCLUSIONS

The MPCNL technique has a number of advantages: short hospital stay, safety of the intervention, low intraoperative and postoperative blood loss, good visualization of the operative field, the possibility of quick removal of the nephrostomy, ureteral and urethral catheter. The possibility of intervention in patients with severe concomitant pathology and bilateral, as well as almost complete absence of pain syndrome opens up new, broader indications for the use of MCPNL in the treatment of kidney stones.

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ORCID and contributionship:
Roman A. Zhuravchak: 0000-0003-2764-2188 [B-D]
Myhajlo D. Dyachuk: 0000-0003-0390-4489 [B]
Andriy Z. Zhuravchak: 0000-0002-4255-0428 [A,D-F]

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CORRESPONDING AUTHOR

Andriy Z. Zhuravchak
State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department
5 Verhnya st., 01014 Kyiv, Ukraine
tel: +380676708951
e-meil: zhuravchak67@gmail.com

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ABSTRACT BOOK

SCIENTIFIC AND PRACTICAL CONFERENCE INVOLVING YOUNG SCIENTISTS «CURRENT ISSUES OF CLINICAL AND PREVENTIVE MEDICINE: INTERDISCIPLINARY ASPECTS AND INNOVATIVE TECHNOLOGIES» NOVEMBER 03, 2022, KYIV, UKRAINE

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WELCOME SPEECH OF THE DIRECTOR OF THE STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT

Dear participants of the conference!

On behalf of the State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department ((SIS «RPC PCM» SAD)), I sincerely congratulate you on the start of the scientific and practical conference involving young scientists «Current Issues of Clinical and Preventive Medicine: Interdisciplinary Aspects and Innovative Technologies»!

(SIS «RPC PCM» SAD) is unique and one of the best medical institutions of Ukraine, which has been successfully operating for over 90 years, the main areas of activity of which are as follows: implementation of applied scientific research in the fields of preventive and clinical medicine; provision of medical care (primary, specialized and highly specialized, urgent and emergent); undergraduate and postgraduate training of doctors, including internships and postgraduate studies, continuous professional development of doctors and junior specialists with medical education, advanced training of specialists with non-medical education in the provision of emergency medical care.

Scientific and research work carried out in the scientific departments of (SIS «RPC PCM» SAD) (internal medicine, minimally invasive surgery, organization of medical care) is carried out by creative groups of researchers led by scientists known in Ukraine. The powerful material and technical base of the (SIS «RPC PCM» SAD) makes it possible to carry out diagnosis, treatment and prevention of diseases using the most advanced technologies and compliance with international treatment standards, to conduct scientific research at the level of world achievements in preventive and clinical medicine. Over the course of its existence, the (SIS «RPC PCM» SAD) has formed a powerful scientific potential for planning and carrying out scientific research in accordance with priority tasks in the field of preserving and strengthening the health of the population. Our leading scientists closely cooperate with leading scientific institutions and institutions not only of our country, but also of other countries. It is noteworthy that one of the focuses is the training of scientific personnel, because young scientists are a reserve for the future development of science.

In the work of the current conference, scientists representing various scientific, medical and preventive institutions and higher educational institutions – both domestic and foreign – will take part in the work of the current conference, along with researchers and graduate students of the (SIS «RPC PCM» SAD). According to the program of the scientific event, in the format of oral and poster presentations, consideration of a wide range of problematic issues in the fields of preventive and clinical medicine is provided, in particular in the following directions: improvement of medical care (diagnosis, treatment) for patients of a therapeutic and surgical profile; continuous improvement of the quality of providing medical care to the population; organization and management of healthcare facilities; experience in implementing programs for monitoring the health of patients in accordance with the strategy of risk management of non-communicable diseases; peculiarities of the organization of providing medical assistance to the population during the period of martial law.

I am deeply convinced that expert reports, lively discussions, exchange of experience, new ideas, views and concepts of the speakers and participants of the conference will contribute to the generalization of the results of fundamental and clinical research, with the prospect of their implementation in the work of treatment and prevention measures in Ukraine and, accordingly, to increase the quality medical assistance to the population.

I wish all participants of the scientific-practical conference success, constructive work and new achievements! I am sure that the determination of priority areas of clinical and fundamental research, taking into account the challenges of today, will potentially contribute to the optimization of the health care system in order to achieve the level of social expectations of the population!

Sincerely,
Dmytro DIACHUK
Director of SIS «RPC PCM» SAD,
Academician of the National Academy
of Medical Sciences of Ukraine,
Doctor of Medical Sciences,
Senior Researcher
(Kyiv)

ORGANIZATION OF THE PROVISION OF MEDICAL ASSISTANCE TO PATIENTS WITH SECONDARY AND TERTIARY HYPERPARATHYROISIS

Dmytro D. Diachuk, Rimma P. Tkachenko
STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

Introduction: Unlike primary hyperparathyroidism, where the hyperfunction of the parathyroid glands is due to the initial mainly tumoral enlargement of one or more parathyroid glands, secondary hyperparathyroidism develops as a result of chronic stimulation of parathyroid cells by external factors. The main components of the pathogenesis – hypocalcemia, hyperphosphatemia, and a decrease in the synthesis of active 1,25-dihydroxyvitamin D3 – are the consequences of several pathophysiological events associated with chronic renal failure, mainly in its terminal stage.

With the progression of chronic renal failure, especially with the start of hemodialysis treatment, the mechanisms of compensation for disturbing homeostasis become ineffective and deepen pathological changes, and disturbances in phosphorus-calcium metabolism lead to the development of systemic complications, in particular, osteodystrophy and secondary hyperparathyroidism, sclerosis of vessels, valvular apparatus of the heart and muscles what fabrics

Adequate correction of these violations is a guarantee of preserving the quality of life and reducing the mortality of patients.

The aim: To increase the effectiveness of surgical treatment of secondary and tertiary hyperparathyroidism in patients with chronic renal failure.

Materials and methods: Bibliosemantic and analytical methods and the method of conceptual modeling.

Results: The long-term existence of secondary hyperparathyroidism with insufficient effectiveness of its conservative treatment leads to severe, sometimes disabling complications in the form of severe osteodystrophy, disorders of the musculoskeletal system, systemic calcification of vessels and soft tissues, psycho-neurological disorders and others, which can be stopped or prevented the timely operation.

The analysis of modern domestic and international literature proved that the majority of researchers paid priority attention to the study of clinical and diagnostic aspects of secondary hyperparathyroidism and the search for the most effective methods of treatment of such patients. However, systemic issues of improving the organization of medical care for patients with secondary and tertiary hyperparathyroidism remain insufficiently studied.

All organizational aspects of medical care for patients with secondary and tertiary hyperparathyroidism need scientific justification for clear regulation, including improvement of regulatory and medical-technological support, and integrated management of patients, with compliance with the requirements of continuity at all stages of medical care. One of these stages is the development and implementation at the level of a multidisciplinary healthcare institution of a local protocol for secondary (specialized) and tertiary (highly specialized) medical care for patients with secondary and tertiary hyperparathyroidism.

Conclusions: The organization of medical care for patients with secondary and tertiary hyperparathyroidism against the background of chronic renal failure requires close cooperation of a multidisciplinary team consisting of a nephrologist, a surgeon, and an anesthesiologist, ensuring the development and implementation of medical and technological documents. To evaluate the results (both short-term and long-term) of surgical treatment of this category of patients, it is necessary to conduct a longer follow-up in the postoperative period.

KEY WORDS: secondary and tertiary hyperparathyroidism, chronic renal failure, local medical care protocol

CERTAIN ASPECTS OF THE ORGANIZATION OF OPHTHALMIC CARE FOR PATIENTS WITH DIABETES

Dmytro D. Diachuk, Anna S. Zdelova
STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

Introduction: According to the WHO, 285 million people suffer from visual impairment in the world, of which 39 million are blind and 246 million have reduced vision.
The prevalence of ophthalmic diseases is significantly influenced by the intense rhythm of life of a modern person, constant overloads, stress, long-term use of computer equipment, deteriorating environmental conditions, exposure to aggressive solar radiation, problems with the light environment, and other factors. Over the last decade in Ukraine, the incidence rate of diseases of the eyes and their accessory apparatus has increased by 18.3% (from 93.1 to 110.1 per 1000 people). The share of this type of pathology in the structure of the total morbidity also increased - from 7.1 to 7.2%. The high prevalence of ophthalmic pathology among the population was also revealed by studies conducted in the regions.
The aim: To improve the quality of ophthalmic care for patients with diabetes by improving the medical care system based on integrated management.
Materials and methods: We used the method of systematic approach and analysis for the formation of research tasks and their solution.
Results: In the structure of diseases of the endocrine system, nutritional disorders, and metabolic disorders among the adult population, diabetes is the most common pathology.
The analysis of the dynamics of the general and primary incidence of diabetes over the past five years shows a clear decrease in the primary and general incidence of diabetes among the population of Kyiv (the approximation probability indicators are quite high - 0.97 and 0.8, respectively), which can testify to a decrease in appeals from the population and/or a low rate of diagnosis of this pathology.
Among the patients of the State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department, the dynamics above the indicated indicators are relatively stable, the trend of changes during the years 2017-2021 is unreliable, which may indicate a sufficient level and effectiveness of preventive interventions to prevent the development of the disease, as well as the development of complications.
Conclusions: Despite the well-established system for the prevention of endocrine pathology, in particular diabetes, the problem of prevention and treatment of early and late complications of diabetes on the part of the organ of vision, which significantly impair the quality of life and cause irreversible vision loss, and in some cases blindness, remains an urgent problem. According to statistics, half of patients remain undiagnosed.
The most frequent complications of diabetes on the part of the organ of vision are diabetic retinopathy, which is manifested by the occlusion of small vessels and their pathological permeability. Among adult patients, vision loss due to DR occurs in 8-15% of cases. In patients with insulin-dependent diabetes mellitus, 5-7 years after the onset of the disease, clinically significant symptoms appear in 15-20% of cases, after 10 years - in 50-60%, and after 30 years in almost all patients. With non-insulin-dependent diabetes, due to late diagnosis, DR is detected in 15-30% of cases, after 10 years - in 50-70%, and after 30 years in almost 90% of patients.
In order to improve the detection of retinal pathology in the early stages, the clinical route of a patient with ophthalmic pathology in a multidisciplinary health care center in the part of clinical support of a patient with diabetes requires improvement.

KEY WORDS: morbidity of the population, chronic non-infectious diseases, endocrine pathology, retinal pathology

SIMULATION OF HEATING OF TISSUES OF THE MENISCUS OF THE KNEE JOINT DURING RADIOFREQUENCY RESECTION

Bogdan Ya. Gryshchuk[1], Igor V. Boiko[1], Vladyslav V. Shlykov[2]

[1]STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

[2]NATIONAL TECHNICAL UNIVERSITY OF UKRAINE «IGOR SIKORSKY KYIV POLYTECHNIC INSTITUTE», KYIV, UKRAINE

ABSTRACT

Introduction: A study of the heating temperature of knee joint meniscus tissues and high-frequency (HF) plasma that occurs around the active electrode of the arthroscopic bipolar radiofrequency (RF) resector was conducted.

The aim: Experimentally determine the temperature parameters of RF meniscus resection using a bipolar radiofrequency arthroscopic meniscus resector, and compare the results with the mathematical model of RF meniscus resection built in the Comsol environment.

Materials and methods: The study was conducted on 30 macropreparations of the meniscus of the human knee joint. The results of the study were compared with a model for the process of RF resection of the meniscus. To find the optimal conditions for RF tissue resection, it is important to know the optimal exposure parameters, such as: the temperature of the RF plasma and meniscus, mechanical load on the meniscus, and the duration of the resection process. To determine these parameters, the process of heating the meniscus and adjacent tissues was simulated in Comsol Multiphysics 5.1 software.

Results: For the implementation of the 3D model, the initial conditions were adopted: the temperature of the conductive liquid in which the meniscus is located is 15°C, the current is 10 A, the frequency is 100 kHz, the output power is 400 W, and the resection process time is 3 s. Simulation of the RF resection process shows simultaneous and uniform heating to 36°C - 37°C of the meniscus and tissues of the knee joint and conductive liquid NaCl 0.9%. In the model, the maximum temperature on the surface of the meniscus of 31.0°C is reached in 0.9 s, in the experiments - in 0.6 s. In the experiments, the temperature of 32.5°C is reached in 0.9 s, the confidence interval is 1°C, $p<0.001$ for the data.

Conclusions: Therefore, the use of a bipolar RF resector containing an electrode in the form of a loop, due to the relatively low temperature of the RF plasma of 37°C, which does not lead to damage (denaturation) of non-target tissue, is an opportunity to achieve better results in the treatment of the meniscus of the knee joint.

KEY WORDS: arthroscopy, radiofrequency resection, meniscus, knee joint, mathematical modeling

ANALYSIS OF THE INFORMATIVENESS OF PERIOPERATIVE VISUAL DIAGNOSTICS OF UTERINE FIBROIDS

Anton B. Khabrat, Olena O. Lytvak
STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

Introduction: Due to modern reproductive technologies which made expansion of the age limits of the fertile period and fact that uterine fibroids (UF) are becoming more common in younger women, there is a need for a more detailed study of the problem of organ-preserving treatment of UF. Individualized selection of access and scope of surgical treatment will make possible to reduce the high frequency of disease recurrence and increase the probability of desired pregnancy.

The aim: To analyze the methods of visual diagnosis used in reproductive age women with uterine fibroids.

Materials and methods: We reviewed and retrospectively analyzed the inpatient health records of 200 patients with UF. Depending on the types of visual diagnostics used in the preoperative examination were formed groups: I group (n=120) – patients were examined only by the sonographic method; II group (n=80) – patients were examined by MRI and ultrasound. The diagnosis was confirmed by the results of histopathological examination. The average age of the examined was 33 ± 3 years.

Results: In patients of both study groups among all detected myomatous nodes were determined sonographically: solitary nodes – in 141 (71%), with an average diameter of 1.5±0.5 sm; multiple - in 59 (29%) people, with an average diameterof 3.5±0.5 sm. The structure of solitary nodes according to the FIGO classification was characterized as follows: type SM0 - 35 (25%), SMI -21 (15%), SMII - 20 (14%), O3-6 type - 65 (46%). Multiple nodes in various combinations were found: SM0/O3-4 type - 33 (56%), SM1/O3-4 type -20 (34%), SM2/O3-4 type - 16 (10%).

Comparative analysis of the MRI and sonographic studies results determined the number of myomatous nodes inpatients of the II group (n=80 (100%): by ultrasound - solitary nodes in 52 (65%), multiple in 28 (35%), and by MRI - a solitary nodule in 37 women (according to FIGO classification - type SM0 – 16 women, SMI in 8 patients, SMII in 8 patients, O3-6 typein 5 women), two nodules in 27 people and three myomatous nodules in 16 women (among multiple myomas n=43 (100%) according to the FIGO classification, , were diagnosed: SM0/O3-4 type- 20 (47%), SM1/O3-4 type -13 (30%), SM2/ O3-4 type -10 (23%), and according to MP type: MP1 - 16 (37%), MP2 -11 (26%), MP3 -16 (37%), and among solitary nodes n=37 (100%): MP1 - 27 (71%), MP2 -10 (29%). The frequency of cases of inconsistency the clinical situation with ultrasound data interms of the number and localization of myomatous nodes in multinodular UF, especially in SM0-2/O3-4 type combinations, was 39, 0%, and when was using MRI - 8.0% ($p<0.05$). Retrospective data of the scope of surgical intervention have showed probable differences between patients depending on the type of applied visual diagnostics and on the type of nodes, their diameter, localization, number and combination of different nodes by type in the patient. The structure of organ-preserving surgical intervention in the scope of myomectomy is presented as follows: hysteroscopy - 118 (59%), a combination of laparoscopy and hysteroscopy - 50 (25%), in 28 (14%) a combination of laparoscopy and hysteroscopy was converted to laparoscopic-vaginal access and 2.0% were converted to laparoscopic laparotomy. In the 1st group (n=120(100%)) where only preoperative ultrasound was used, a higher specific weight of conversions from hysteroscopy to laparoscopy - 36 cases (30%), from a combination of laparoscopy and hysteroscopy to laparoscopic-vaginalaccess - 24 (20%) and from laparoscopy laparotomy - 12 (10%).

Conclusions: Ultrasound in the perioperative period is unable to fully determine clear navigation for the operation, especially for multinodular UF and hard-to-reach UF localization for hysteroscopic myomectomy. This clinical problem can be solved by using MRI in the perioperative diagnostic and intraoperative sonography.

KEY WORDS: uterine fibroids, hysteroscopy, sonography, magnetic resonance imaging, perioperative period

TESTING OF THE COMPATIBILITY OF THE ORTHOPEDIC IMPLANTS MATERIAL BY USING ATOMIC FORCE MICROSCOPY (AFM)

Hlib O. Lazarenko, Igor V. Boiko
STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

Introduction: Rejection reaction or manifestation of hypersensitivity to the implant material is observed in 6 – 30% of cases of surgical intervention. The rejection reaction to the body on exogenous materials (implants) is manifested as a local aseptic inflammation with the formation of a fibrous capsule around them, that leading to loss of their functional properties. The recipient organism reaction to foreign body depends on both branches of immune system, and particular importance to them has the absorption of protein and reaction of the body cells to surface of the implants.

Certain electron in homogeneity of the surface of materials plays the role of the binding centers of Ig and cells. Adhesion of IgG on surface of the implants provokes to the activation of the immune system, that leading to the development of persistent non-infectious (aseptic) inflammation. Material of implants that contact with the recipient organism determined by allocation of the last anti-inflammatory mediators, which cause the process that can lead to selective dissolution of the components of implants and, in the future, it can cause the destruction of implant. Selective dissolution of implants products can lead to toxic effects on cells, or stimulate synthesis of some proteins. Absorption or accumulation proteins of various toxic substances and formation around the material dense layer of the extracellular matrix, is important for the biological behavior of the material (attachment cells or bacteria to surface of materials).

The aim: To determine the possibility of using Atomic Force Microscope (AFM) to predict the reaction of the organism on the implant (foreign body).

Materials and methods: The most effective tools for the study of internal and intermolecular forces are AFM. AFM studies of the bioadhesive separation force were performed on a scanning probe microscope Dimension 3000 NanoScopeIIIa (Veecocorp.) Both in air and in liquid. Before surgery, 5 ml of blood were taken from patients, from the serum of which by standard methods total IgG was isolated. After purification and dilution to the appropriate concentration of 2 μg/ml, IgG was applied to the AFM probe, the technology is described in the guideline. Functionalized probes with applied IgG of the patient were tested for compatibility of the implant material with the patient's body. The value of the force of separation of the probe from the IgG of the recipient by the surface of the implant was considered to assess the compatibility of the material with the patient's body. The higher the value of the force of separation, the more likely the development of a reaction of rejection of the implant by the body. The basis for the hip implant was the titanium alloy Ti6Al4V.

Results: According to the results of testing with AFM, it was found that the forces of interaction of IgG on the surface of the prosthesis significantly exceed the force of interaction with the surface without IgG (34-56 nN against 5-8 nN, respectively). According to hematological studies, it is seen that the tension of the body's immune system is determined after implant placement. According to long-term clinical observations, 8 of 11 (73%) patients complained of implant pain three months later.

Conclusions: Therefore, the medical-biological research of artificial biomaterials remains relevant and significant. The method of testing the compatibility of the implant material with the recipient's body using AFM can allow: a. At the preoperative stage, determine the possibility of occurrence of processes of rejection of the implant. b. Provide compatibility with body implants and choose the most appropriate and / or to provide drugs to prevent rejection. c. Data received through research, allow the doctor to choose the necessary tactics of patients in the postoperative period.

KEY WORDS: rejection reaction, metal allergic reaction, aseptic loosing, testing of biocompatibility

PECULIARITIES OF MENSTRUAL FUNCTION IN FEMALES WHO HAVE SUFFERED COVID-19

Alla O. Petruk, Olena O. Lytvak
STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

Introduction: The neuromodulatory cascade that controls the regulation of gonadotropin-releasing hormone (GnRH) can be changed due to activation the hypothalamic-pituitary-gonadal axis (HPG), which negatively affects the functional state of the reproductive females system. Considering the context of the COVID-19 epidemic, in particular, stress, vaccination, COVID-19 therapy, and COVID-19 disease may play a role for such changes.

The aim: To evaluate menstrual changes and peculiarities of the functional state of the reproductive system in females who have suffered Covid-19.

Materials and methods: We reviewed and retrospective analyzed inpatient and outpatient medical records of 378 women during 2020-2021. In particular, the clinical characteristics of the menstrual cycle were studied, the factors affecting menstrual function disorders (MFD) in women before and after the suffering of Covid-19, or after vaccination against the SARS-coronavirus. The level of stress was also determined using an online survey. All women were divided into groups: Group I – 177 patients with MFD after suffering from Covid-19; II group (comparison) – 121 women with MFD after vaccination against the SARS-CoV-2 infection; group K (control) – 80 women without MFD after suffering from Covid-19 or vaccination. The average age of women was 34.7±2.6 years.

Results: Comparing the data and results of a retrospective clinical study, it was found that 152 (40%) women reported about MFD and more often had symptoms of anxiety and loneliness than complained about bad mood (45% vs. 25%, $p < 0.01$). 24 (16%) those women had MFD before Covid-19. Menstrual cycle changes in females of the 1st group: 30 (17%) had delayed menstruation during the disease, 16 (9%) reported the absence of expected menses 1 month after the first disease, 13 (7%) after 3 months, and 4 (2%) - after 6 months. The average number of missed menstrual cycles was 3.7±1.6. Menstrual cycle changes were manifested by worsening premenstrual symptoms (PMS) – 13 (7%). The average cycle length was 28 days, the same as before the pandemic, but with a significantly wider range (25–30 days) ($p = 0.01$). The median number of bleeding days was 5 (4–6) and did not changed ($p = 0.3$). Menstrual cycle changes in 121 females of the II group: 26 (21%) «sometimes» had the expected periods - 1-2 episodes within 6 months, where the first episode appeared 1 month after the first vaccination; in 24 (20%), the beginning of «missing» the expected menses wa snoted 1 month after the second vaccination; 38 (31%) - noted polymenorrhea 1 month after the first vaccination, and 55 (45%) - 1 month after the second vaccination; 57 (47%) of women noted algodysmenorrhea 1 month after the first vaccination and 15 (12%) - 1 month after the second vaccination. Amenorrhea was diagnosed in 5% of patients after the first vaccination and 3% after the second ($p < 0.01$). The frequency of dyshormonal disorders of the thyroid gland in women of the 1st group was 63.0%, in patients of the 2nd group - 47.7%, hyperprolactinemia was observed in 31.0% and 39.4%, respectively; hyperestrogenia – 50% and 21%; hyperandrogenism – 39% and 20%. The concentration of LH inpatients of the 1st group is almost twice as high as the indicators of the patients of the 2nd group. The index of free T is almost 1.5 times higher in patients of the II group compared to I group and by 2.5 times compared to control group, which may indicate the role of hyperandrogenism against the background of hyperprolactinemia in the development of MFD and anovulation syndrome, especially against the background of stressors.

Conclusions: MFD are associated with worsening of mental health and disruption of central regulatory and feed back mechanisms in the pituitary-thyroid-ovarian system under the influence of stressors. The development of MFD in female after suffiring COVID-19 is characterized by changes in hormonal homeostasis. Identified changes in the production of gonadotropins against the background of normal and elevated estrogen concentrations indicate a violation of the central mechanisms of regulation and feedback in the pituitary-thyroid-ovarian system. After assessing for psychological stress levels, COVID-19 vaccination status and therapy, comorbidities, and other factors we should investigate how deep they are.

KEY WORDS: menstrual cycle disorder, COVID-19 pandemic, psychological distress, oligomenorrhea/amenorrhea, dysmenorrhea

STOMATOLOGICAL DISEASES IN CHILDREN AND BAD ENVIRONMENT

Zoryana B. Popovych, Mykola M. Rozhko, Nataliia I. Kukurudz
IVANO-FRANKIVSK NATIONAL MEDICAL UNIVERSITY, IVANO-FRANKIVSK, UKRAINE

ABSTRACT

Introduction: Chemical and biological pollution of air, water and soil as well as climate change are among the factors that directly affect human health according to the World Health Organization. Children in particular are very susceptible to bad environmental conditions due to the functional immaturity of their adaptive and protective mechanisms. Adverse environmental factors prove to have a negative impact on all organs and systems of the human body by causing various disorders. We have studied the reasons for such high prevalence of stomatological diseases and their dependence on harmful ecological factors. The researches were carried out at the Dentistry Department of the Educational and Scientific Institute of Postgraduate Education of the IFNMU. Our study was conducted in Kalush and the Kalush region as this district was assigned with the status of "emergency ecological situation" in 2010, which arose as a result of the closure of potash and magnesium production followed by subsequent flooding of the Dombrovskyy quarry.

The aim: The aim of our investigation was the study of the relationship between stomatological diseases in children and the influence of environmental factors.

Materials and methods: In order to establish the prevalence of stomatological diseases we have examined more than 820 schoolchildren aged 6-17 years from Kalush and the Kalush district. The examination was permitted by parents with the support and assistance of the Department of Education at Ivano-Frankivsk Regional State Administration, for which we express our sincere gratitude. An oral examination in children was performed to establish the prevalence of stomatological disorders. Some time after, we also analyzed medical documentation, observation logs.

Results: The results gained from conducted examination suggest that the prevalence of stomatological disorders in general is 82,2–94,3%. In particular, the periodontal disorders were diagnosed in 35,3–78, 3% of all examined; 31,4–43,7% of children were affected by orthodontic pathology. Moreover, the rapid course of multiple dental caries prevailed. Pulpitis and apical periodontitis were diagnosed in 34,7%. Cheilitis (angular and exfoliative) and glossitis (most often desquamative) were revealed in 24,3% of children. There was also a combination of several types of pathology. For example: periodontal disease and caries, cheilitis, periodontal disease and orthodontic pathology. Many children were affected by somatic problems as well (identified on the basis of medical records).

Conclusions: The conducted research has revealed a high prevalence of stomatological diseases among the children's population (according to WHO criteria), which can be caused by ecological factors of the environment.

KEY WORDS: examination of children, ecological situation

THE STUDY OF 24-HOUR AMBULATORY BLOOD PRESSURE PROFILE AS AN IMPORTANT COMPONENT OF PATIENT-CENTERED APPROACH IN THE TREATMENT OF HYPERTENSION

Nataliia M. Pryplavko, Anatolii M. Kravchenko
STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

Introduction: Chronotherapy is a complex of diagnostic and therapeutic measures, which are based on the search for optimal regimens for the treatment of arterial hypertension (AH), taking into account the daily rhythms of the body and him sensitivity to treatment. This approach in AH is aimed not only at normalizing day and night blood pressure (BP), but also at transforming pathological diurnal rhythms into normal ones.

The aim: To evaluate the chronobiological profile of BP in men of working age and to investigate the effectiveness of AH treatment when taking antihypertensive drugs in the evening.

Materials and methods: 24-Hour ambulatory BP monitoring (ABPM) was performed in 53 men of working age, the average age of patients was 49±0.28 years. All the patients had AH of II and III stages according to ESC classification. The BP profile and the effectiveness of antihypertensive therapy when prescribing drugs in the evening after a month of outpatient treatment were investigated.

Results: Taking into account the 24-hour BP profile, patients with AH were classified into: 1. Dipper – normal (optimal) degree of night BP reduction (circadian index (CI) 10-20%) – 21 (39.62%) 2. Non-dipper insufficient degree of night BP reduction (CI 0-10%) – 22 (41.5%). 3. Over-dipper – excessive reduction of BP at night (CI >20%) – 7 (13.2%). 4. Night-peaker – the inverted nature of the daily curve was noted as a night peak (CI <0%), the level of night BP is higher than the day – 3 (5.67%). Antihypertensive drugs (combination of angiotensin-converting enzyme inhibitor and calcium channels blockers) were prescribed in the evening. In the control ABPM, after one month of outpatient treatment, the target levels of BP and normalization of the 24-hour profile were achieved in 56% among patients with AH.

Conclusions: The obtained preliminary results indicate that the using of chronotherapeutic approach is a potentially promising method to improve the effectiveness of AH treatment. However, the scientific data available today require further research to evaluate the effectiveness of therapy prescribed taking into account the chronobiological profile of AH.

KEY WORDS: arterial hypertension, 24-hour ambulatory blood pressure monitoring, chronotherapy

METHOD FOR PREVENTION OF HYPOCALCEMIA IN PATIENTS WITH THYROTOXICOSIS UNDERGOING ELECTIVE THYROID SURGERY

Sergii A. Sheptukha, Maryna O. Kylymnuchenko
STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

Introduction: A significant increase in the number of cases of diffuse toxic goiter (DTG) in Ukraine leads to an increase in the number of surgical interventions on the thyroid gland. One of the probable complications when performing thyroid surgery is postoperative hypocalcemia. At present, there are no strong recommendations for preventing the postoperative hypocalcemia in patients undergoing surgery with DTG. In this regard, the issue of conducting research and studying the methods of its prevention remains relevant.

The aim: To develop and implement clinical interventions for the prevention of postoperative hypocalcemia among patients operated on DTG.

Materials and methods: The paper presents the results of a study of 77 patients with DTG that were operated in the State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department. At the time of operative intervention, all patients were in euthyroid condition with doses of 5 mg/day to 30 mg/day tiazolone administration.

Results: According to the study desing and the results of determining the level of antibodies to the thyrotropin receptors, the patients were divided into 2 groups: group I – patients with Graves` disease (57 people), group II – patients with Plummer's disease (20 people). In the first group, surgical intervention was performed in the volume of thyroidectomy. In the second group, 12 thyroidectomies and 8 hemithyroidectomies were performed. Due to the technique used, the visualization of the pterygoid glands has been greatly simplified and the probability of their accidental removal has decreased significantly. For both groups of patients at the preoperative stage, 10-14 days before surgery, calcium preparations were administered at a dose of 1 gram per day. At 7 days before surgery, the dose was increased to 2 grams per day. After the surgical intervention, 60 ml (600 mg) of calcium glucanate was injected intravenously with 400 ml of saline solution, and 40 ml (400 mg) with 400 ml of saline for the next day. The day after the operation, patients were prescribed calcium supplements at a dose of 3 grams per day with a gradual reduction of the dose. The rate of dose reduction was adjusted on the basis of patient complaints, the presence or absence of clinical symptoms of hypocalcemia and the level of calcium ionized in the blood (if necessary). The obligatory stage of the survey was the determination of the level of ionized calcium in the blood at the preoperative stage and 2 days after the operation. According to the results of laboratory studies, the level of calcium ionized at the preoperative stage was at the level of the upper limit of norm and in some cases and above it. In the postoperative period, there was a clear tendency to decrease the level of calcium ionized in the blood despite the preventive measures. Laboratory confirmation of a decrease in calcium levels below the reference values in 5 cases. Clinical manifestations of hypocalcemia are found in 2 patients. Sustained hypoparathyroidism was not detected in the studied groups.

Conclusions: Prophylactic administration of calcium preparations to patients with an established diagnosis of DTG in the preoperative and postoperative periods significantly reduces the likelihood of postoperative hypocalcemia. Routine monitoring of ionized calcium blood level after surgery contributes to the early detection and timely correction of the clinical symptoms of hypocalcemia.

KEY WORDS: thyroid gland, diffuse toxic goiter, calcium ionized, postoperative hypocalcemia, euthyroidism

RELATIONSHIPS OF PRO-, ANTI-INFLAMMATORY MARKERS AND LEVELS OF SELENOPROTEIN P AND SELENIUM WITH LIVER DAMAGE GRADE IN PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE

Iryna I. Tverezovska, Natalia M. Zhelezniakova
KHARKIV NATIONAL MEDICAL UNIVERSITY, KHARKIV, UKRAINE

ABSTRACT

Introduction: The prevalence of nonalcoholic fatty liver disease (NAFLD) is estimated at 25.2% worldwide. Selenoprotein P (Sel P) is synthesized and secreted by hepatocytes and is the main source and transporter of Selenium (Sel) in the body. Selenium is an important trace element for the functioning of antioxidant protection, closely related to the development of steatosis and fibrosis. Data suggest a decrease in Sel P expression during the active phase of the disease. At the same time, an increase in its levels may have a protective effect on the processes of steatosis and fibrosis.

The aim: To assess the levels and relationships of interleukin 8 and 10 (IL-8, IL-10), Sel and Sel P levels in patients with NAFLD depending on the degree of liver damage.

Materials and methods: The study included: 49 patients of the main group (G1) with NAFLD and hypertension (67.3% of women); 51 patients of comparison (G2) group with NAFLD (58.8% women) and 20 relatively healthy individuals (G3) (55.0% women). Mean age: 51.0 [45.0; 56.0] years in the G1, 52.0 [47.0; 54.0] years in the G2 and 51.0 [45.0; 55.5] years in G3 (p=0.564). The groups were gender and age matched ($\chi^2 = 1,219$, $p = 0,544$). Steatosis (a) was identified in 55.1% of G1 and 58.8% of G2; and steatohepatitis (b) — in 44.9% of G1 and 41.2% of G2 respectively ($\chi^2 = 0,141$, $p = 0,707$). Sel P, Sel, IL-8, IL-10 levels evaluated with standard methods by ELISA Kit (ElabScience, USA). Statistical analysis of the obtained data was carried out using the MS Excel 2013 (trial version) and IBM SPSS 25.0 (trial version) for Windows. For quantitative variables, the median (Me) and interquartile range [LQ; UQ] was calculated. For comparing of age, Sel, Sel P, IL8 and 10 levels Mann-Whitney coefficient was used, for qualitive indicators Pearson's coefficient (χ^2). Spearman's rank correlation coefficient was used to calculate the correlation,

Results: In patients of the main group with steatosis (G1a) levels of Sel P were 19,9 [7,3; 26,7] ng/ml and 19,5 [8,0; 26,8] ng/ml with steatohepatitis (G1b) ($p_{G1a-b} = 0,817$). Levels of Sel were 42,4 [34,5; 49,5] µg/L and 46,0 [42,3; 49,5] µg/L, ($p_{G1a-b} = 0,169$) respectively. Levels of IL-8 in patients with steatosis were 29.1 [24.9; 31.1] pg/ml, steatohepatitis — 32.5 [27.6; 40.7] pg/ml, $p_{G1a-b} = 0,773$). Levels of IL-10 were respectively 20.3 [17.9; 23.1] pg/ml and 20.7 [16.1; 26.0] pg/ml ($p_{G1a-b} = 0,928$).

In patients of the comparison group with steatosis (G2a) levels of Sel P were 42,7 [40,8; 45,5] ng/ml and 43,2 [42,3; 45,8] ng/ml with steatohepatitis (G2b) ($p_{G2a-b} = 0,599$). Levels of Sel were 69,9 [62,4; 77,5] µg/L and 66,4 [57,0; 78,1] µg/L, ($p_{G2a-b} = 0,394$) respectively. Levels of IL-8 in patients with steatosis were 23,1 [18,9; 26,4] pg/ml, steatohepatitis — 21,9 [19,2; 24,4] pg/ml ($p_{G2a-b} = 0,444$). Levels of IL-10 were respectively 11,8 [10,4; 13,6] pg/ml and 12,1 [10,8; 14,0] pg/ml ($p_{G2a-b} = 0,455$).

In the main group with steatosis reverse correlation was between Sel P and IL-8 ($\rho = -0,417$, $p = 0,030$) and direct with IL-10 ($\rho = 0,402$, $p = 0,038$), with steatohepatitis direct correlation was between Sel P and Sel ($\rho = 0,393$, $p = 0,070$)

In the comparison group with steatosis direct correlation registered between Sel P and IL-10 (ρ=0,451, $p = 0,012$), between Sel and IL-8 ($\rho = 0,432$, $p = 0,017$) and reverse between Sel and IL-10 ($\rho = -0,332$, $p = 0,073$). In patients with steatohepatitis stronger correlation was between Sel P and IL-10 (ρ=0,511, $p = 0,011$), and between Sel and IL-8 ($\rho = 0,379$, $p = 0,090$).

Conclusions: Sel R, IL-8, and IL-10 levels did not differ significantly depending on the presence of steatohepatitis or steatosis in patients with NAFLD. Direct correlation between Sel and IL-8 can be result of increasing levels of Sel as response on inflammation activity, Instead, the presence of direct correlations between Sel P and IL-10 suggests more intense anti-inflammatory and antioxidant activation in patients with steatohepatitis, compared with patients with steatosis.

KEY WORDS: nonalcoholic fatty liver disease, Selenoprotein P, steatosis, steatohepatitis

DYNAMIC PATTERN OF THE RESPIRATORY DISEASES MORBIDITY IN CHILDREN TREATED IN 2011-2021 IN THE STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT

Yevheniia I. Vezhnovets, Yurii B. Yashchenko
STATE INSTITUTION OF SCIENCE «RESEARCH AND PRACTICAL CENTER OF PREVENTIVE AND CLINICAL MEDICINE» STATE ADMINISTRATIVE DEPARTMENT, KYIV, UKRAINE

ABSTRACT

Introduction: The most common diseases among children are respiratory diseases. The actual question is the study of the dynamics of morbidity in children of different age groups for the effective organization of the prevention of these diseases.

The aim: To study the dynamics of respiratory diseases incidence in children aged 0-17years old, who were treated in the State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department in 2021-2021.

Materials and methods: The author analyzed children's morbidity according to the standard 12 Report on diseases, registered in patients residing in the medical-preventive institution service region, for 20 by the State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department in 2011-2021. The study estimated respiratory diseases morbidity in children, calculated per 1000 children aged 0-17 years and defined dynamic trends in 2011-2021.

Results: Respiratory diseases incidence in children aged 0-17 years has increased by 4 times (from 229.78 to 919.42 per 1000) in 2021 compared to 2011. The respiratory diseases in children in 2021 made 71% of all children diseases, which is almost twice as much as in 2012 (33%). The age structure of the firstly registered respiratory diseases cases was as follows: 57% in children aged 0-6 years, 34% in children aged 7-14 years, 9% in teenagers aged 15-17 years. During 2011-2019 the age structure of children respiratory diseases did not differ significantly. From 2011 till 2021 positive trend in the diseases dynamics was observed (R^2= 0.83, $p<0.05$). The pneumonia incidence in children in 2021 decreased by 3.8 times compared to 2011 (from 11.43 to 3.03 per 1000). As for the age structure, the pneumonia occurrence in 2019 prevailed in children aged 7-14 years (52%), then in the group of 0-6 years (39%) and the third place was taken by the teenagers aged 15-17 years (9%). During 2011-2021 a trend towards decreased pneumonia incidence in children was noted (R^2=0.6, $p>0.05$).

Conclusions: During 2011-2021 a reliable dynamics of an increase in the respiratory diseases incidence was registered, which requires improved preventive measures on the level of primary medical; service rendered by the State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department.

KEY WORDS: pneumonia, pediatrics, morbidity rate