### **ORIGINAL ARTICLE**

# FREQUENCY AND NATURE OF DISORDERS IN PSYCHO-EMOTIONAL AND AUTONOMIC SYSTEMS IN PATIENTS WITH MIDDLE FACIAL INJURY

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Maksym Nazarevych, Roman Ohonovskyi, Khrystyna Pohranychna, Oleh Mokryk, Yuriy Melnychuk, Andriy Stasyshyn DANYLO HALYTSKYI LVIV NATIONAL MEDICAL UNIVERSITY, LVIV, UKRAINE

#### ABSTRACT

The aim: Scientific work aims at determining the frequency and nature of disorders in psycho-emotional and autonomic systems in patients with combined trauma of the middle face.

**Materials and methods:** Examination included 112 patients with combined trauma of the middle face. Their psycho-emotional state was assessed using the Impact of Event Scale (IES) and the Hospital Anxiety and Depression Scale (HADS). All patients were tested using questionnaires developed by Wayne A.M.. The Kerdo index was used to assess autonomic tone, while autonomic reactivity was determined using a Czermak-Gering carotid sinus test. Biochemical markers of stress - adrenocorticotropic hormone (ACTH), cortisol and anti-stress system -  $\beta$ -endorphins, and Garkavi L.Kh. adaptation index.

**Results:** Patients with severe traumatic brain injury – 26.78%, and severe fractures of the facial bones – 48.21%. The consequence of traumatic events is the appearance of post-traumatic stress disorders in their mental function. Post-traumatic stress is also manifested at the hematological level in the characteristic stress reactions: the growth in the blood of stress markers – ACTH and cortisol and anti-stress factors, including β-endorphins

**Conclusions:** Middle facial injuries cause disorders of the psycho-emotional sphere, which are manifested in anxiety and depressive disorders. The post-traumatic period is accompanied by stress disorders, which are confirmed by hematological studies with a significant increase in stress markers (ACTH and cortisol) and an insignificant increase in anti-stress factors in the blood. Insufficient stress-limiting function of the hypothalamic-pituitary system slows down the healing process and requires appropriate correction.

KEY WORDS: middle facial bone injury, stress reactions, hypothalamic-pituitary system, β-endorphins, adrenocorticotropic hormone, cortisol

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# **INTRODUCTION**

Data from the studied literature sources indicate that all injuries of the middle area of the face have a number of common features. Statistical indicators reveal a fairly high percentage of their frequency, which ranges from 33% to 55% of all facial injuries. They are mainly caused by serious traffic accidents (up to 89.5%) and domestic injuries. [1, 2].

In all cases, such injuries are accompanied by multiple, often multi-fragmentary fractures of the zygomatic-orbital complex, upper jaw, nasal bone base. However, they have in common not only one anatomical area of injury, but also the fact that in 86-100% of cases, they are combined with a closed traumatic brain injury [3-5].

Common features of such cases are violation of vascular trophism of the brain with the occurrence of reflex spasm and vasodilation of blood vessels, slow blood flow and increased capillary penetration [6]. Against this background, there is a change in the secretion of hormones of the hypothalamic-pituitary system, adrenocorticotropic and somatotropic hormones [7]. There is also a violation of the regulatory function of the central nervous system, in particular, insufficient production of calcitonin, which leads to a slowdown in reparative osteogenesis and prolongation of the post-traumatic rehabilitation period [8]. In addition, since the middle area of the face is the most clinically significant area of the face with a number of cranial nerves and vessels and where is close contact with the dura mater. Such conditions, according to many scientists, create many risks to the lives of patients, including a long period after the injury and require timely and effective correction [9].

#### THE AIM

Given the above and significant practical interest in the treatment of patients with combined trauma of the maxillofacial area, this scientific work aims at determining the frequency and nature of disorders in psycho-emotional and autonomic systems in patients with combined trauma of the middle face.

#### MATERIALS AND METHODS

The examination included 112 patients, diagnosed with a combined trauma of the middle part of the face, who were hospitalized in the Department of Maxillofacial Surgery or the Department of Neurosurgery of the Lviv City Municipal Hospital. All patients, depending on the type of combined

Types of combined middle facial injury	Number of cases (%)		Total	
(according to the classification of Fraerman A.P., Terman T.E., 1974)	Males	Females		
1 type:	15 patients	4 patients	19 patients	
severe traumatic brain injury and severe damage to the facial skeleton	(79%)	(21%)	(100%)	
2 type:	6 patients	5 patients	11 patients	
severe traumatic brain injury and minor damage to the facial skeleton	(54,5 %)	(45,5 %)	(100%)	
Type 3:	38 patients	9 patients	47 patients	
mild traumatic brain injury and severe damage to the facial skeleton	(80,8 %)	(19,2 %)	(100%)	
4 type:	29 patients	6 patients	35 patients	
mild traumatic brain injury and minor damage to the facial skeleton	(82,8 %)	(17,2 %)	(100 %)	
Total	88 patients	24 patients	112 patients	
	(81%)	(19%)	(100%)	

#### Table I. Distribution of patients depending on the type of combined middle facial injury

**Table II.** Distribution of patients with traumatic injuries of the middle face by age and sex

Ano of motion to	Sex		
Age of patients	Males	Females	
From 18 to 24	15	3	
From 25 to 44	46	11	
From 45 to 60	21	8	
From 61 to 75	6	2	
Total – 112	88	24	

mid-facial trauma, were divided into four clinical groups according to the classification of A.P. Fraerman and Y.E. Telman [10,11].

The distribution of patients depending on the detected injury was as follows (tables I, II):

The psycho-emotional state of patients who experienced traumatic stress was assessed using the Impact of Event Scale (IES) and the Hospital Anxiety and Depression Scale (HADS) [12].

To assess the presence or absence of disorders of autonomic tone before injury, all patients were tested using questionnaires developed by Wayne A.M. with co-authors (2003) (Table I, VI) [13].

To assess autonomic tone, we used the Kerdo index, which allows judging the state of autonomic reactions under stress in total [14]. Vegetative Kerdo index was determined as follows: VI = 1 - (blood pressure diast / pulse). When the effects of the sympathetic and parasympathetic divisions of the autonomic nervous system on the cardiovascular system are balanced, the autonomic index approaches zero. A positive value of the index indicates sympathicotonia, while a negative value indicates parasympathicotonia.

Autonomic reactivity was determined using the Czermak-Gering carotid sinus test, which evaluates the rate and duration of changes in autonomic parameters in response to pressure on reflexogenic zones. It is used to assess the reactivity of the parasympathetic division of the ANS.

The Czermak-Gering test is performed as follows: after

15 minutes of adaptation (resting), the upper third of the sternoclavicular-mammary muscle below the angle of the mandible is lightly pressed on one side for 20 seconds to feel the pulsation of the carotid artery. Starting from the 15th second from the start of pressure, repeated measurement of average heart rate is carried out.

According to these tests, there are three types of reactions: normal type - slowing of the pulse by  $4.9 \pm 2.69$  beats / min (M  $\pm$  o) for the sinocarotid reflex; sympathetic type – reflex is absent or inverted; parasympathetic type - slowing of the pulse by more than 12 beats / min.

An orthostatic test was also performed to assess the compensatory responses of the cardiovascular system. The patient was placed in a supine position for 3-5 minutes and heart rate was measured. After that, the patient stood up in a vertical position and three minutes later he had his heart rate re-measured. Normally, heart rate increases by 10-16 beats per minute. An increase of more than 16 beats per minute indicates autonomic dysfunction.

The type of general nonspecific adaptive response of the organism under traumatic stress was determined by the percentage of lymphocytes in the leukocyte formula, their ratio to the percentage of segmented neutrophils - Garkavi L.Kh. adaptation index [15].

Criteria for adaptive reactions:

a) stress response: lymphocytes less than 20%, adaptation index less than 0.3;

b) training reaction: lymphocytes - 21-27%, adaptation index - 0.31-0.50;

c) reaction of quiet activation: lymphocytes - 28-33%, adaptation index - 0,51-0,7;

d) reaction of increased activation: lymphocytes - 34–42%, adaptation index - 0.71-0.90;

e) reactivation reaction: lymphocytes higher than 43%, adaptation index higher than 0.90;

e) defective adaptation reaction: peripheral blood leukocytes - 4.0 ′ 109 / l and less.

The level of reactivity was determined by the degree of deviation from the norm of the elements of the blood formula: high, medium, low and very low.

Biochemical markers of stress - adrenocorticotropic hormone (ACTH), cortisol and anti-stress system -  $\beta$ -en-

The severity degree of combined mid-facial injury	Assessment of anxiety level on the hospital anxiety and depression scale (HADS)	Assessment of depression disorders on the hospital anxiety and depression scale (HADS)
1 type	17,1±2,1 points * <b>p=0.004191</b>	15,4±1,9 points * <b>p=0.000617</b>
2 type	13,9±1,5 points * <b>p=0.040726</b>	12,8±1,4 points * <b>p=0.004243</b>
3 type	15,4±1,8 points * <b>p=0.012927</b>	11,3±1,6 points * <b>p=0.044969</b>
4 type	9,6±1,4 points	7,1±1,3 points

Table III. Level of anxiety and depression disorders in patients with traumatic mid-facial bone injuries (at the start of postoperative rehabilitation)

\* Note: statistical significance of indicators in the group was compared with the results obtained in patients with severity degree 4 of combined mid-facial trauma.

Table IV. Assessment of the autonomic nervous system in patients with combined mid-facial trauma depending on its severity

Research criterion of autonomic nervous	The severity degree of the combined mid-facial injury (according to the classification of Fraerman A.P., Telman Yu.E., 1974)				
system	l type	ll type	lll type	IV type	
Wayne's questionnaire (points)	18,2±1,7 * <b>p=0.097894</b>	17,9±1,6 * <b>p=0.115500</b> p < 0,05	16,1±1,3 * <b>p=0.40485</b>	14,5±1,4	
Kerdo index	0,71±0,07 * <b>p=0.005297</b>	0,64±0,05 * <b>p=0.012827</b>	0,52±0,04 * <b>p=0.55022</b>	0,49±0,03	
Carotid sinus reflex (Gering)	Slowing the pulse rate by 4,1±0,7 * <b>p=0.001373</b> beats / min.	Slowing the pulse rate by 4,5±0,9 * <b>p=0.023204</b> beats / min.	Slowing the pulse rate by 5,9±0,5 * <b>p=0.16377</b> beats / min.	Slowing the pulse rate by 6,8±0,4 beats / min.	
Orthostatic test (beats / min.)	by 36,9±2,5 * <b>p=0.000276</b>	by 35,1±2,7 * <b>p=0.002881</b>	by 27,6±2,1 * <b>p=0.32582</b>	by 24,8±1,9	

\* Note: statistical significance of indicators in the group was compared with the results obtained in patients with severity degree 4 of combined mid-facial trauma.

Table V. The state of pain perception and functional activity of the autonomic nervous system during the tourniquet test in patients with combined middle facial trauma

The severity degree of combined mid-facial	Indicators of the autonomic nervous system reactivity during the tourniquet test		Indicators of pain perception in patients during the tourniquet test		
the classification of A.P. Fraerman and Yu.E. Telman)	Pulse rate (beats / min)	Perfusion index (conventional units)	Visual-analog scale of pain (points)	Tensoalgometry data (pain sensitivity threshold) (g / cm2)	
1 degree	93,7±3,6	2,9±0,6	6,1±0,5	169,4±2,7	
	<b>p=0.000297</b>	p=0.012853	<b>p=0.000027</b>	p=0.002059	
2 degree	86,3±2,7	3,5±0,4	5,7±0,8	171,9±2,4	
	<b>p=0.008536</b>	<b>p=0.033057</b>	<b>p=0.007131</b>	p=0.007668	
3 degree	81,5±2,1	4,2±0,7	4,9±0,6	174,3±2,5	
	<b>p=0.088066</b>	<b>p=0.418244</b>	<b>p=0.020875</b>	<b>p=0.038090</b>	
4 degree	74,9 ± 3,2	4,9 ± 0,5	3,2 ± 0,4	182,7 ± 3,1	

\* Note: statistical significance of indicators in the group was compared with the results obtained in patients with severity degree 4 of combined mid-facial trauma.

dorphins were studied in peripheral venous blood. Blood for the study was taken in the morning (08: 00-9: 00). Determination of cortisol was performed by immunochemical method using electrochemiluminescent detection on the analyzer with a test system Cobas 6000, Roche Diagnostics (Switzerland). Reference values - 6.2-19.4 mcg / dl. The conversion factor  $\mu$ g / dl x 27,586 = nmol / l. Determination of ACTH (pg / ml) was performed by immunochemical method with chemiluminescent detection (CLIA). Immulite analyzer and test system (Siemens AG), Germany were used.

Quantitative determination of the marker of the anti-stress system of  $\beta$ -endorphin in blood plasma (pg / ml) was performed by enzyme-linked immunosorbent assay using the kit "Uscn Life Science Inc." (USA).

Mathematical and statistical processing of all obtained digital research results was performed using a personal computer with the appropriate software package "StatSoft

The severity degree of	Stress-limiting system	Stress-releasing system			
the combined craniofacial	β-endorphins	ACTH	Cortisol	Garkavi stress index	
trauma	(pg/ml)	(pg/ml)	(nmol/l)		
1 degree	4,89±1,12 pg/ml	60,25 ± 6,17 pg/ml	449,15±20,11 nmol/l	0,99 ± 0,13	
	**p=0,028364	**p=0,002811	**p=0,000184	**p=0,052270	
2 degree	5,12±1,17 pg/ml	52,13±4,25 pg/ml	431,82±19,35 nmol/l	0,97±0,12	
	**p=0.044804	**p=0,013229	**p=0.00136	**p=0,05695	
3 degree	11.38 ± 1,19 pg/ml	53,44 ± 5,36 pg/ml	402.78± 16.51 nmol/l	0,90 ± 0,11	
	**p=0.07902	**p=0.021810	**p=0.01814	**p=0,11422	
4 degree	8.46±1.13 pg/ml	39,90 ± 2,18 pg/ml	347,94 ±15,62 nmol/l	0,64 ± 0,12	
	*p=0.070542	*p=0.04752	*p=0.013613	*p=0.077448	
Norm of healthy person	5.31±1,28 pg/ml	34,18 ± 1,79 pg/ml	299.83 ±10,57 nmol/l	0,35 ± 0,09	

<b>Table VI.</b> Manifestations of stress reactions in the blood of patients with combined	mid-facia	l trauma of	varying	severity
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Note: \* We compared the results obtained in this group with the data found in healthy individuals.

\*\* The results obtained in this group were compared with the data found in patients with grade 4 combined craniofacial trauma.

Statistica 8" and "Microsoft Excel", which is recommended for this type of processing methods. Given that all the studied data had the nature of variation series with a statistical set of normal (symmetrical) distribution, indicators of descriptive statistics with the definition of values as: mean (M)  $\pm$  standard error (m) were used to analyze statistical characteristics of individual groups.

Mean values in different groups were compared using the Student's method, while relative values - using the Pearson parametric criterion  $\chi 2$ . The differences were considered significant at p <0,05.

#### RESULTS

Psychological testing was performed on all patients before surgery. Its results are presented in table III.

Screening diagnosis of anxiety and depression on the HADS scale revealed clinical manifestations of anxiety of varying degrees in all patients. It was characteristic that the severity of anxiety signs coincided in direct proportion with the severity of traumatic brain injury, which coincides with the data of literature sources [16-18]. Thus, the highest number of points (up to  $17.1 \pm 2.1$ ) was found in patients with severe traumatic brain injury and severe damage to the facial skeleton. As the severity of the injury decreased, the quantitative indicators that characterized the changes in the psycho-emotional state decreased: the patients with type 3 severity, according to the classification of A.P. Fraerman and Yu.E. Telman, experienced a drop in scores to  $15.4 \pm 1.9$ , the group with type 2 severity - to  $13.9 \pm 1.5$  points. The lowest number of points (9.6  $\pm 1.4$  points), and accordingly the manifestations of anxiety were found in the patients with mild traumatic brain injury.

A similar pattern was found for signs of depression. It was absent only in male patients with mild traumatic brain injury and mild facial skeletal injury (up to 7.1  $\pm$  1.3 points on the HADS scale). As the severity of the injury increased, the quantitative indicators increased to 11.3  $\pm$  1.6 points and 12.8  $\pm$  1.4 points in patients with type 3 and 2 severity, respectively, and 15.4  $\pm$ 1.9 points in the most severe diagnosed injuries. These data also completely coincide with the studied data of literature sources [19, 20, 21]. All this indicates that traumatic brain injury is almost always accompanied by depression of mental function and therefore requires correction.

Against the background of post-traumatic disorders in the psycho-emotional state of such patients, we found other dysfunctions of central regulatory mechanisms, in particular, disorders of the autonomic nervous system, the severity of which depended directly on the severity of trauma, as confirmed by Wayne's questionnaire (Table IV). There was an increase in the number of points from  $14.5 \pm 1.4$  in patients with mild damage to  $18.2 \pm 1.7$  points in the most severe cases.

The orthostatic test, which characterizes the increase in heart rate, revealed the dominance of the tone of the sympathetic nervous system in all examined patients. These data were also observed when comparing the carotid sinus reflex and studying the Kerdo index. It was also found that in persons with mild traumatic brain injury, the clinical manifestations of autonomic dysregulation were less pronounced and closer to normotony.

Studies using a provocative tourniquet test also indicated that psycho-emotional stress affects pain perception (Table V). Indicators of pain sensitivity thresholds and subjective assessment of pain were statistically significantly different between the groups of injury severity: in patients with the most severe variants of injury, the pain sensitivity threshold was the lowest (169.4 ± 2.7 g / cm<sup>2</sup>), while in patients with relatively the lightest damage it reached 182.7 ± 3.1 g / cm<sup>2</sup> (at p≤0.05).

Laboratory studies have also confirmed that disorders of the regulatory function of the CNS are also accompanied by activation of the hypothalamic-pituitary system, which is manifested by an increase in blood biochemical parameters of the stress-releasing system (ACTH and cortisol hormones). The obtained research data are presented in table VI.

It was found that the nature of stress reactions depended on the severity of brain damage. Statistically significant increases in ACTH and cortisol were observed in all examined patients with middle facial trauma. However, the increase in these hormones was directly related to the severity of the traumatic brain injury. In the most severe cases (1 degree of severity of combined craniofacial trauma according to the classification of A.P. Fraerman and Yu.E. Telman), ACTH made up  $60.25 \pm 6.17$  pg / ml at p $\leq$ 0.01, while cortisol - 449.15 ± 20.11 nmol / l with p $\leq$ 0.01. There was also a fairly large and statistically significant increase in patients with grade 2 and 3 severity of injury.

There were also changes in the stress-limiting system - the growth of  $\beta$ -endorphins was insignificant and not statistically proven: at 1 degree of severity, their level was only at 4.89 ± 1.12 pg / ml (p≥0.05), and at Grade 2 - 5.12 ± 1.17 pg / ml (p≥0.05). Thus, this system inadequately and ineffectively responded to the growth of an antagonistic system, and the balance shifted sharply towards stress-activating mechanisms. Many authors attribute this to a traumatic violation of the regulatory mechanisms of the CNS at the level of the hypothalamic-pituitary system [22].

This fact of development of post-traumatic stress was also confirmed by the revealed changes as regards leukocyte-lymphocyte structure of blood. Increased activation of the stress index according to Garkavi was found in patients with 1 to 3 degrees of severity of craniofacial trauma. Thus, in patients with 1 degree of severity, this figure was the highest, at  $0.99 \pm 0.13$  (p $\leq 0.05$ ). In group 2, it was almost the same ( $0.97 \pm 0.12$ , p $\leq 0.05$ ), in 3 -  $0.90 \pm 0.11$ , p $\leq 0.05$ . In the 4th group it was the smallest -  $0.64 \pm 0.12$  with p $\geq 0.05$ .

#### DISCUSSION

After analyzing the data of the studied literature sources, it can be stated that all injuries of the midfacial area have a number of common features. According to statistics, the frequency of these injuries is fairly high, from 33% to 55% of all facial injuries. In all cases, such traumas are accompanied by multiple, often multi-fragment fractures of the zygomatic-orbital complex [1, 2]. However, they have in common not only one anatomical area of injury, but also the fact that in 86-100% of cases, they are combined with a closed traumatic brain injury [3-5]. We have not found any research on the state of the psycho-emotional sphere and the autonomic nervous system, though.

Psychological testing was performed on all patients before surgery. Screening diagnosis of anxiety and depression on the HADS scale revealed clinical manifestations of anxiety of varying degrees in all patients. It was characteristic that the severity of the signs of anxiety coincided in direct proportion with the severity of the traumatic brain injury. A similar pattern was found for signs of depression. It was absent only in male patients with mild traumatic brain injury and mild facial skeletal injury (up to 7.1  $\pm$  1.3 HADS scale). As the severity of the injury increased, the quantitative indicators increased to 11.3  $\pm$  1.6 points and 12.8  $\pm$ 1.4 points in patients with type 3 and 2 severity, respectively, and 15.4  $\pm$  1.9 points in case of the most severe diagnosed injuries.

Against the background of post-traumatic disorders in the psycho-emotional state of such patients, we found other dysfunctions of central regulatory mechanisms, in particular, disorders of the autonomic nervous system, the severity of which depended directly on the severity of trauma, as confirmed by Wayne's questionnaire. There was an increase in the number of points from 14.5  $\pm$  1.4 in patients with mild damage to 18.2  $\pm$  1.7 points in the most severe cases.

Studies using a provocative tourniquet test have also shown that psycho-emotional stress affects pain perception. Indicators of pain sensitivity thresholds and subjective assessment of pain varied significantly among the groups of injury severity: in patients with the most severe variants of injury, the pain sensitivity threshold was the lowest (169.4  $\pm$  2.7 g / cm2), while in patients with relatively the lightest damage, it reached 182.7  $\pm$  3.1 g / cm2 (with p≤0.05).

Laboratory studies have also confirmed that disorders of the regulatory function of the CNS are also accompanied by activation of the hypothalamic-pituitary system, which is manifested by an increase in biochemical parameters of the stress-releasing system (ACTH and cortisol hormones) in blood. A statistically significant increase in ACTH and cortisol was observed in all examined patients with middle facial trauma. However, the increase in these hormones was directly related to the severity of the traumatic brain injury. In the most severe cases, the ACTH index made up  $60.25 \pm 6.17$  pg / ml at p≤0.01, while that of cortisol - 449.15 ± 20.11 nmol / l with p≤0.01. There was also a fairly large and statistically significant increase of this indicator in patients with 2 and 3 grade of injury severity.

This fact of development of post-traumatic stress was also confirmed by the revealed changes from leukocyte-lymphocyte structure of blood. Increased activation of the stress index according to Harkavi was found in patients with 1 to 3 degrees of severity of craniofacial trauma. Thus, in patients with 1 degree of severity, this figure was the highest, reaching  $0.99 \pm 0.13$  (p $\leq 0.05$ ). In group 2, it was almost the same ( $0.97 \pm 0.12$  with p $\leq 0.05$ ), in group 3 -  $0.90 \pm 0.11$  with p $\leq 0.05$ . In the 4th group, it was the smallest -  $0.64 \pm 0.12$  with p $\geq 0.05$ .

The data we received confirm the opinion of many scientists that even with a minor injury of the middle part of the face, in 80% of cases there are signs of brain damage, headache, general weakness of sleep rhythm, and nausea [8, 9]. This causes psycho-emotional manifestations in the form of personal anxiety, cognitive impairment, asthenia and depression, which are accompanied by autonomic disorders such as diffuse hyperhidrosis, acrohypothermia, blood pressure lability, palpitations, heat and paraesthesia of the extremities.

Also a frequent complication of such traumas is a violation and insufficient stress-limiting function of the hypothalamic-pituitary system, which not only complicates the course of the disease, but also slows down the healing process and in all cases requires appropriate correction [22].

#### CONCLUSIONS

The middle facial injury in more than 80% of cases is accompanied by traumatic brain injury of varying severity. These injuries cause disorders of the psycho-emotional sphere, which are manifested in anxiety and depressive disorders, the severity of which is directly proportional to the severity of the injury. Along with this, there are always signs of shifts in the regulatory sphere of the CNS with a shift of balance towards the dominance of the sympathetic autonomic system over the parasympathetic one. The post-traumatic period is accompanied by stress disorders, which are confirmed by hematological studies with a significant increase in stress markers (ACTH and cortisol) and an insignificant increase in blood stressors. Insufficient stress-limiting function of the hypothalamic-pituitary system slows down the healing process and requires appropriate correction.

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# ORCID and contributionship:

Maksym Nazarevych: 0000-0002-5064-1776<sup>B</sup> Roman Ohonovskyi: 0000-0003-0959-0863<sup>A,D</sup> Khrystyna Pohranychna: 0000-0002-3366-0799<sup>D,F</sup> Oleh Mokryk: 0000-0002-4237-3812<sup>A</sup> Yuriy Melnychuk: 0000-0002-8434-3419<sup>B</sup> Andriy Stasyshyn: 0000-0002-6168-494X <sup>E, F</sup>

# **Conflict of interest:**

The Authors declare no conflict of interest.

#### CORRESPONDING AUTHOR Khrystyna Pohranychna

Danylo Halytskyi Lviv National Medical University 69 st. Pekarska, 79010 Lviv, Ukraine tel: +380987762355 e-mail: pohranychna@ukr.net

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