CASE STUDY

VENTRICULAR ECTOPIC ACTIVITY - A PREDICTOR OF SUDDEN CARDIAC DEATH IN PATIENTS WITH ATRIAL FIBRILLATION AND POST-INFARCTION LEFT VENTRICULAR ANEURISMS

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ABSTRACT

The article presents a clinical case of a patient who died suddenly from a rapid transformation of ventricular extrasystole into high-grade ectopy during persistent atrial fibrillation. All electrical events preceding death were recorded by the Holter monitor, which the patient was wearing at the time.

It was revealed that post-infarction left ventricular aneurysm can be specified as the main predictor of sudden cardiac death, given that the myocardial scar tissue is an arrhythmogenic substrate of pathological re-entry circuits to initiate high-rate ventricular arrhythmias. Heart rate variability and heart rate turbulence, as well as frequent ventricular ectopy plays significant role in the pathological mechanisms of fatal arrhythmias.

Complex cardiac arrhythmias combined with changes in the autonomic regulation of the cardiovascular system are early predictors of sudden cardiac death.

KEY WORDS: Sudden cardiac death, left ventricular aneurysm, arrhythmia

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INTRODUCTION

Sudden cardiac death (SCD) is a death from heart disease that occurred within an hour from the onset of symptoms. Estimation of the true prevalence of this phenomenon is difficult, but it is estimated that in the United States alone, about 250-400 thousand people die annually from the SCD [1]. It is also known that the risk of SCD increases with age, and it is two to three times higher among men. The causes of sudden death are extremely diverse, but structural pathology of the heart is usually in the first place [2]. However, mainly functional impairments cause abnormal impulse formation with dangerous ectopy generation, or its myocardial conduction with the development of asystole or lethal bradyarrhythmia. [1]. The most common cause of SCD is ventricular tachycardia (VT) [3]. For one study involving 157 outpatient patients who lost consciousness while wearing ECG Holter devices, 62% of the deaths were due to VT leading to ventricular fibrillation (VF). Only 8% of the subjects first developed VF, and 13% - torsades de pointes. Bradyarrhythmias and ventricular asystole were detected in 17% of the subjects [4]. Distinguishing SCD from a number of other clinical conditions such as aortic dissection, pulmonary artery thromboembolism, pericardial tamponade, etc., is often quite difficult [2]. In this case, data of an anamnesis and interviews with witnesses have high priority. An important role in the differentiation of SCD is also the examining predictors of its occurrence, which are covered in the following clinical case.

CASE REPORT

The article presents a clinical case of a patient who died suddenly from a rapid transformation of ventricular extrasystole into high-grade ectopy secondary to persistent atrial fibrillation (AFib). All electrical events preceding death were recorded by a Holter monitor, which the patient was wearing at the time. Along with the measurement of heart rate variability (HRV) at that moment, one of the methods for predicting SCD was the evaluation of cardiac heart rate turbulence (HRT) indicators.

A 56-year-old patient A. was admitted to the Ivano-Frankivsk Central City Hospital (Ukraine) with signs of heart failure on August 18, 2015 for treatment management and extension of therapeutic regimen. The patient was hospitalized in a Cardiology Department. Upon admission to the hospital, the patient without any specific life history complained of shortness of breath, palpitations, edema of the lower extremities, dry cough, general weakness, and dizziness. Life anamnesis – without any features. *Anamnesis of the disease*: persistent AFib, ischemic heart disease, anterior wall left ventricular (LV) myocardial infarction (MI) with postinfarction LV aneurysm (PILVA) in 2013, when he was diagnosed with third degree arterial hypertension, and stage III chronic kidney disease. The patient periodically underwent an in-patient treatment in the Cardiology Department because of decompensation of heart failure. During the last three months, he received the

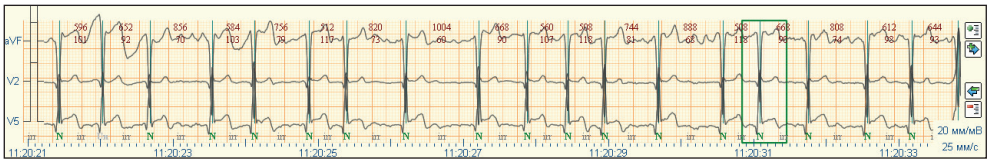

Fig. 1. ECG-phenomenon of the patient A. at the beginning of the monitoring.

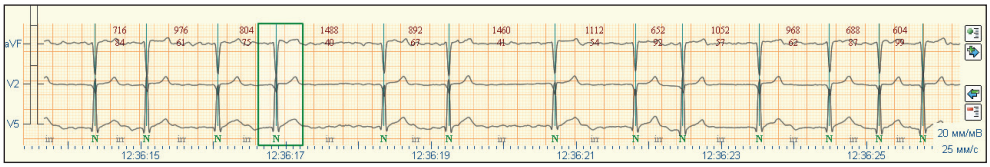

Fig. 2. ECG-phenomenon of the patient A.: bradycardia.

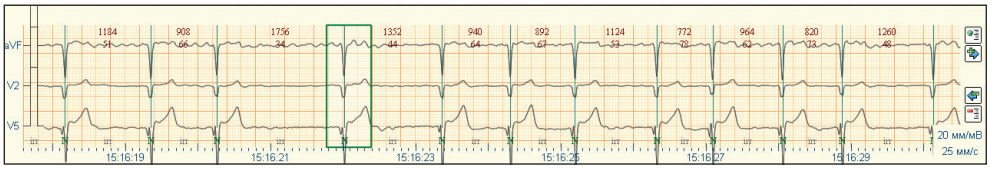

Fig. 3. ECG-phenomenon of the patient A.: an acute decrease in the amplitude of the QRS complexes.

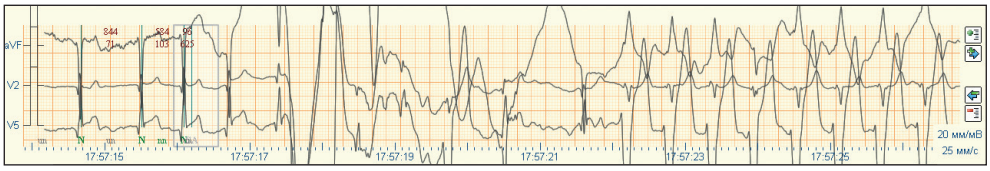

Fig. 4. ECG-phenomenon patient A.: First occurrence of ventricular tachycardia.

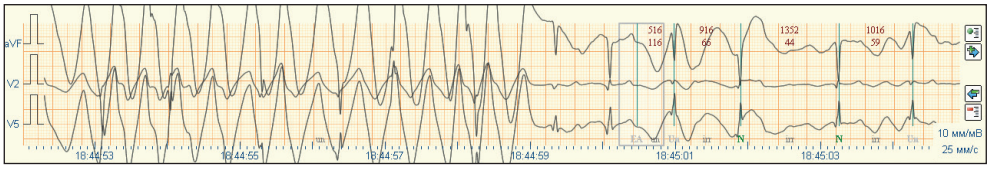

Fig. 5. ECG-phenomenon of patient A: the appearance of second ventricular tachycardia.

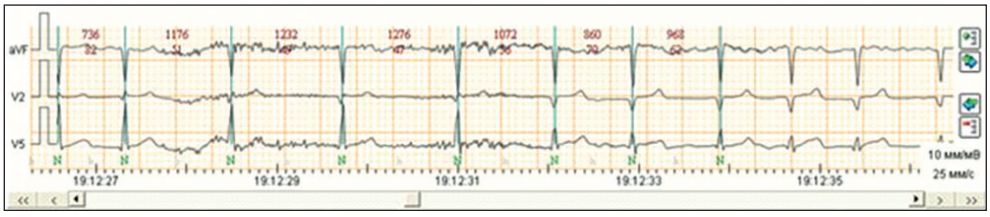

Fig. 6. ECG-phenomenon of the patient A: oscillation of the QRS complexes amplitude.

following drugs: warfarin - 2.5 mg once -daily, carvedilol - 3,125 mg – twice-daily, ramipril - 1.25 mg once-daily, veroshpyrone - 25 mg 1 once-daily, torasemide 5 mg twice a week**.** Also, from time to time, used Zelenin drops 20-30 / day in case of slow heartbeat. At the time of admission, the patient's condition was medium severe. The skin was pale, acrocyanosis, edema of the lower extremities. During patient examination: breathe rate - 25-26 breaths/min., inspiratory dyspnea. During heart auscultation – weakened and arrhythmic cardiac tones, 2nd tone accent on the aorta. Heart rate - 50 beats/min, blood pressure - 90/60 mmHg (left arm), 100/70 mmHg (right arm). Enlarged liver by 2 cm. ECG at the time of admission: AFib with ventricular rate of 30-40 beats/min, frequent ventricular extrasystoles, QRS width 100 msec, QT - 360 msec. Changes in V1-V4 leads with a typical "frozen" elevation of segment ST. Negative T wave in V5-V6 leads. The echocardiographic examination revealed calcification of the aortic valve with regurgitation ("2+", gradient - 15.1 mmHg). The diameter of the left atrium was 4.7 cm, the LV ejection fraction (LVEF) - 38%. Akinesis of the anterior, septal, and apical segments and LV aneurysm were diagnosed. Right ventricle (RV) - 3.6 cm with blood regurgitation on tricuspid valve (TV) ("3+"). The pulmonary hypertension was 47 mm Hg.

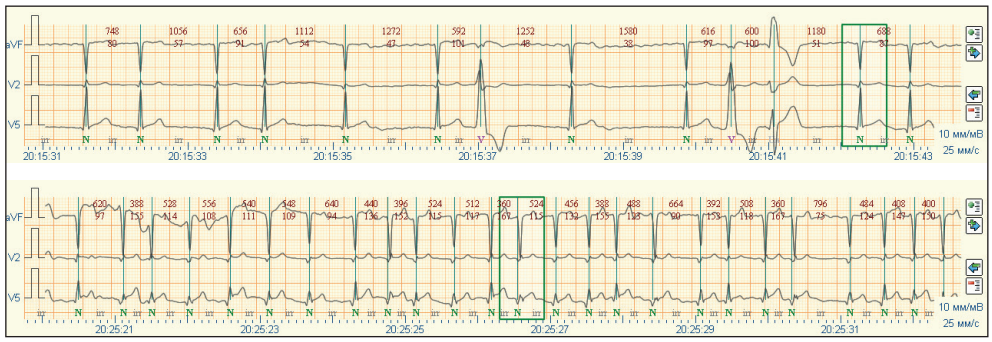

Fig. 7. ECG-phenomenon of patient A.: "heating" AFib.

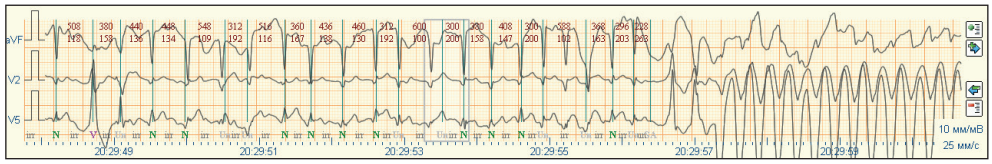

Fig. 8. ECG-phenomenon of patient A: initiation of the third ventricular tachycardia.

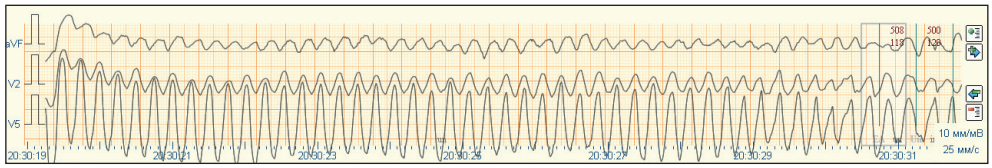

Fig. 9. ECG-phenomenon of the patient A: fluctuations in the width and amplitude of the ventricular tachycardia.

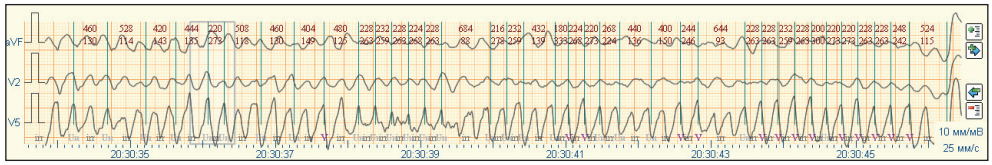

Fig. 10. ECG-phenomenon of patient A: progressing disorganization of ventricular tachycardia morphology.

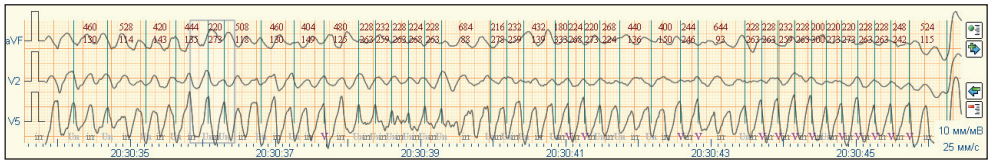

Fig. 11. ECG-phenomenon of patient A: large-wave ventricular fibrillation.

During the week, the patient's condition slightly improved under the influence of treatment. Dyspnea and signs of fluid retention on the lower extremities have decreased. Only mild general weakness was noted. The heart rate and arterial pressure were 60-70 beats/min., and 115/80 mm Hg correspondingly. An ECG showed an increase of ventricular beats frequency to 70-75/min, alongside the appearance of ventricular bigeminy episodes. 02/09/2015 the patient received a 24-hour ECG monitor. In the morning, the patient was found dead by the medical staff, after 15 days in the hospital. Monitoring showed the electrical phenomena preceding the ventricular extrasystole (VE), that are displayed in Fig. 1-13.

At the beginning of the monitoring (Fig. 1), around10-11 am on 02/09/2015, AFib was determined (baseline rhythm of the patient) with frequent VE. LV aneurism was also noted by the deviation of ST segment. It should be noted, that during the monitoring, there were also fluctuations of the ST segment, which may indicate on coronary blood flow disorders. VE were monotonically monomorphic in nature. It is also worth noting, that the patient was tendent to bradycardia with the occurrence of periodic pauses (Fig. 2). At around 3:00 p.m., a sharp change in the electrical properties of the ventricle myocardium was noted (decrease in voltage and moderate expansion of QRS complexes) (Fig. 3). Subsequently, unsystematic fluctuations in the amplitude and width of the QRS complexes were observed during the day. Interestingly, according to information, provided by medical personnel, patient at that moment did not file any complaints. At about 6:00 p.

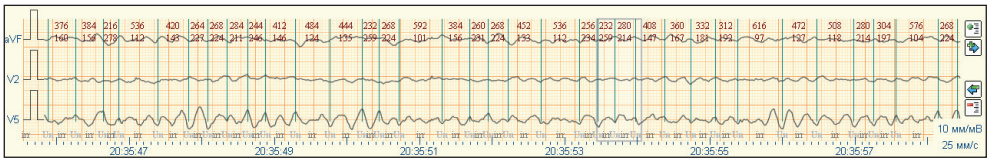

Fig. 12. ECG-phenomenon of patient A: small-wave ventricular fibrillation.

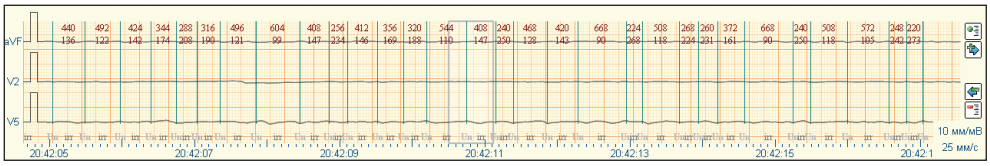

Fig. 13. ECG-phenomenon of the patient A.: asystole of the ventricles.

m, the paroxysm of tachycardia with wide QRS complexes developed, with ventricular rate around 200 beats/min (Fig. 4). Tachycardia can be categorized by the high probability of ventricular involvement. The dominant negative deviation of the QRS complexes in V5 should be emphasized, their predominantly positive deviation in the allocation of VF. These signs suggest that the source of tachycardia is located in the LV, namely - in its anterior-septal zone. The echocardiography diagnosed the presence of the aneurysmal dilation of LV. The emergence of tachycardia was preceded by VE. QRS complexes of extrasystoles and tachycardia were identical. Interestingly, the adhesion intervals of the VE and tachycardia were different, what suggests a different mechanism of their formation despite their monomorphic nature. VE can be classified as early; they occur immediately after the ending of the T wave (Fig. 1). Tachycardia, on the contrary, arose after a delay in the ventricular tissue, what characterizes its possible mechanism as a "re-entry". Nevertheless, their monomorphic character allows us to assume that the structures of the LV, where the VE were formed, as well as the path that depolarized the myocardium, was identical. The tachycardia lasted for several seconds and terminated solely, then the AFib with the previous ventricular pattern was restored . An hour later, a new paroxysm of tachycardia with wide complexes launched (Fig. 5). This tachycardia arose from a similar mechanism, as the first one, but it had signs of electrical activity significant disruption. QRS complexes were already considerably wider this time, and their width was constantly changing. It is difficult to determine the source of tachycardia from the recording, but the morphology of both paroxysms was remotely similar, so we can assume that they have the same origin. However, the frequency of the second tachycardia was significantly higher (around 300 beats/min.), as the variability of individual complexes. After a short paroxysm, the second tachycardia also spontaneously terminated with the restoration of AFib. After the termination of the second ventricular tachycardia, some interesting ECG phenomena were observed. First of all, the amplitude of the QRS complexes (Fig. 6) varied without a clear regularity, which reflected, probably, the change of the main electrophysiological properties of the heart tissue and the violation of the conductivity in the myocardium. The significant increase in the frequency of the AFib outgoing waves to the ventricle is also worth noting ("heating of the AFib ") and increase in total heart rate, which was accompanied by the ST segment elevation (Fig. 7). On the background of such "warming", the paroxysm of the third tachycardia with wide complexes occurred in a few minutes (Fig. 8). Its appearance also had some certain features. QRS complexes with clear "wide / narrow" cycles and "short / long" R-R intervals (from 228 to 408 msec) began to appear on the background of the high frequency AFib. This, obviously, created the prerequisites for "scanning" premature impulses of the whole substrate of tachycardia. After the "short / long" R-R intervals, a pair of extrasystoles from the right ventricle appeared, which became a trigger factor for tachycardia with wide complexes and very high frequencies (around 300 beats/min). Morphology of tachycardia suggests that its origin was in the same area as the first two. It is worth noting the role of AFib in the initiation of the tachycardia. The VT was characterized by fluctuations within the broad limits of its electrophysiological properties and very quickly, within one minute, began to degrade into VF (Fig. 9-10). At first, the amplitude of the QRS complexes sharply decreased, reflecting the fact that the destruction of the general depolarization wave of the ventricles and the formation of several smaller, competing fronts with a higher rate of transmission. Further, the disorganization of tachycardia morphology continued to increase, and it quickly became a large wave VF (Fig. 11). The variety of complexes amplitudes and their different morphology, with gradual loss of characteristic features, is drawn on itself. The individual elements of the complexes have ceased to transform into the small-wave fibrillation, and became irreversible (Fig. 12). A few minutes later, the ventricles asystole was confirmed and the electrical activity of the heart had stopped (Fig. 13). After analyzing the dynamics of all electrical phenomena and the clinical and anamnestic data of the patient, several key elements can be distinguished. First, there are many predictors of the SCD emergence. Thus, it has long been known that there are several crucial factors in the pathogenesis of VF at once: passing myocardial ischemia and the phenomenon of reperfusion, changes in vegetative effects, electrolyte balance and pH. Hypokalemia and hypomagnesaemia

may be the cause of late ventricular potential, which, along with prolongation of the QT interval, may lead to fatal arrhythmias [1]. And, as already mentioned, early VE is one of the most common direct causes of the SCD, which goes into irreversible VT [5]. And the most common mechanism of its occurrence in patients with coronary artery disease is the "re-entry" mechanism . This is especially true for people with acute coronary artery disease, where VE may occur even without prolongation of the QT interval. VT without a basis of ischemic heart disease occurs more rarily, and is usually associated with an abnormal anatomy of the coronary vessels or their embolism, inflammation or dissection [6]. Considering the features of the VT initiation in patient A., it is possible to state with a high possibility, that the "re-entry" mechanism has become a leading factor in VT occurrence. Cerebral changes and presence of aneurysmatic dilation of the LV (ADLV) in patient A. became the pathological substrate for "re-entry" loop.

It should also be noted and the localization of most ventricular ectopies, in our opinion, coincided with the location of scar tissue. The important SCD predictors include also reduced LV systolic function. It is also believed that with a decrease of LVEF, the number of sudden cardiac deaths increases proportionally [5]. The LVEF of 38% could also be an important predictor for the VF occurrence in patient A. Often, ECG changes are not informative in terms of fatal electrical events prediction in a patient, but in many cases ECG shows structural changes in the myocardium [6], QT prolongation [7], RV dysplasia, hypertrophic cardiomyopathy [5], Brugada syndrome [8], or preexcitation [9], Also, the detection of specific "frozen" ST segment curve (as in a patient A.) may indicate on a LV aneurysm and the presence of an appropriate arrhythmogenic substrate with delayed impulse conduction trough the myocardial tissue, that triggers the "re-entry" loop. Pulmonary repolarization markers include: QT interval variation, T-wave alteration [8], and the HRV violations [7]. HRV is determined by Fourier frequency analysis of RR intervals and reflects the sympathetic and parasympathetic effects on the heart [8]. The predictive value of this indicator, however, remains controversial. Streinbinger and co-authors showed that HRV allows to predict fatal arrhythmias in patients with MI. The risk of their occurrence during the 2 years of follow-up was 32 times higher (!) in individuals after MI with HRV index less than 20 ms in compared to the control group [8]. The data, mentioned above, echoes with the results of the patient's HRV analysis. During the last hours of patient's life, there was a gradual decrease in the regulatory systems voltage index up to 15 times lower than the physiological norm, and in the last minute, on the contrary, a sharp increase (10 times), which lasted 5- 7 minutes and can be interpreted as an agony state.

Alongside the HRV study, one of the methods for SCD predicting is the evaluation of cardiac HRT indicators. It was noted, that short-wave oscillations of the heart cycle (RR-intervals) occur after VE. This phenomenon was first described by a research group led by Schmidt in 1999, and later it became the basis for the definition of the HRT. As a rule, sinus rhythm becomes accelerated immediately after VE, and then again slows down, returning to the original state. The Schmidt group proposed two indicators of the HRT: the beginning of turbulence (turbulence onset) (To) and turbulence slope (Ts). To is the magnitude of the sinus rhythm acceleration immediately after the VE, and Ts is the intensity of the sinus rhythm slowdown, which occurs after acceleration. To is calculated as the ratio of the differences between the sums of the values of the first two sinus RR intervals that appear after the VE, and the following two sinus RR intervals before the VE to the sum of the two sinus RR intervals before the VE, expressed as a percentage. The values of To <0% and Ts> 2.5% ms / RR are considered normal and To> 0% and Ts <2.5% ms / RR are pathological [7]. The To phenomenon is related to the fact, that the cardiomyocyte ion channels at the time of ectopic excitation have not yet fully recovered, which leads to the potential the action (PA) shortening. Premature contraction is associated with incomplete diastolic filling of the heart chambers, resulting in reduced stroke volume (SV) and reduced contractility (Franck-Starling mechanism). This, in turn, reduces the level of blood pressure, leading to the activation of aortic and carotid baroreceptors, and heart rate increase through the baroreflex arc. Desynchronization of ventricular contractions during VE also has a certain value [5]. The phenomenon of Ts can be explained as following: after compensatory pause, the slow ionic channels of cardiomyocytes are completely restored, what leads to prolonged PA, increase of the blood pressure, and elevated blood pressure, in turn, reduces heart rate through the baroreflex arc. Thus, the formation of HRT can be schematically presented as following: VE causes a compensatory pause, resulting in decrease of blood pressure, which causes an increase of the heart rate and elevated blood pressure, and later leads to a decrease in heart rate through a baroreflex [5]. The evaluation of HRT values in patient A. revealed the following patterns. The To ratio was> 1.47%, while the Ts was 1.36% ms / RR. The value of the sinus rhythm acceleration immediately after the VE (To) was higher than normally, and Ts - lower, indicating a rapid increase in heart rate and insufficient reduction after VE, increased bathmotropic and dromotropic functions of the myocardium, as well as the activation secondary pacemakers with the emergence of life - threatening arrhythmias [7].

Incident AFib is associated with an increased risk of SCD in the general population. AFib, the most common heart arrhythmia affecting up to 5 million Americans, is now linked to an increased risk of SCD, according to a recent study published in the Journal of the American Medical Association [2]. The association was studied in two population cohorts, finding that the risk triples for those with incident AFib and doubles after the onset of AFib. Researchers believe this study confirms AFib should no longer be viewed as "a benign condition." More than 15,000 adults, aged from 45 to 64, participated in the Atherosclerosis Risk in Communities (ARIC) and Cardiovascular Health Study (CHS). Studies were aimed to identify

the SCD predictors in persons with AFib. It included all participants who attended 1st visit (1987-89) and had no prior AFib (n = 14,836). Incident AFib was identified from ECG studies and hospitalization discharge codes. SCD was physician-adjudicated. Trial used cause-specific Cox proportional hazards models, followed by stepwise selection (backwards elimination, removing all variables with p>0.10) to identify SCD predictors in participants with AFib. AFib occurred in 2321 (15.6%) participants (age 45-64, 58% male, 18% black). Over a median of 3.3 years, SCD occurred in 110 of those with AFib (4.7%). Predictors of SCD included elder age, body mass index (BMI), coronary heart disease, hypertension, diabetes, current smoking, left ventricular hypertrophy, increased heart rate, and decreased albumin. Predictors were associated only with SCD, and included increased BMI (HR per 5-unit increase, 1.15, 95% CI, 0.97-1.36, p = 0.10), increased heart rate (HR per SD increase, 1.18, 95% CI 0.99-1.41, p = 0.07), and low albumin (HR per SD decrease 1.23, 95% CI 1.02-1.48, p = 0.03). In the ARIC study, SCD predictors in AFib that were not associated with non-sudden CV death, included increased BMI, increased heart rate, and low albumin [10].

Oklahoma Heart Institute cardiac electrophysiologist, Dr. David Sandler, agrees with the researchers' comments, "Not only does AFib predispose to stroke, heart failure, and death, but the arrhythmia per se may increase the risk of death from ventricular tachyarrhythmias. The latter is potentially preventable; to this end, additional research to identify predictors of sudden cardiac death in patients with AFib is much needed." [3].

We can conclude that the SCD predictors cover several factors [1, 3, 5, 7]. One of the important links in the cascade of fatal arrhythmias, is the presence of LV aneurysms, which creates the necessary pathological basis for the formation of re-entry loops [6]. Wee-timed detection of electrical violations and their correction will prolong the duration and improve the quality of life of Ukrainians. One way to prevent fatal arrhythmias in people with many adverse factors may be implantation of the cardioverter - defibrillator [1]. And the aim of primary care physicians is to identify such patients in time and redirect them to the appropriate facilities.

CONCLUSIONS

Complex cardiac arrhythmias combined with changes in the autonomic regulation of the cardiovascular system are early predictors of sudden cardiac death. These facts and the presented clinical case point to difficulties in diagnosing cardiovascular pathology. Although, early use of a number of clinically available non-invasive electrophysiological examinations will allow early diagnosis of risk factors and prevention of sudden cardiac death. Prospects for further research. Knowledge about the pathological mechanisms of fatal arrhythmias among patients with chronic ischemic heart disease and concomitant AFib will allow practitioners to use up-to-date diagnostic and treatment methods in a timely manner for the prevention of fatal complications among this category of patients. Further research is needed to confirm these findings in larger community-based cohorts and to elucidate the underlying mechanisms to facilitate prevention. The processes involved in reperfusion injury might provide targets for improved outcomes after myocardial infarction but that aim has thus far not been met in the clinic. By studying new molecules in different experimental settings and protocols, insight has been gained about important factors for possible future clinical applications of drugs with cardioprotective, antiarrhysmic properties. Taking into account the analysis of the literature, the given data indicate the prospect of using cardiometabolic agents (phosphocreatine) in the treatment regimen of patients with existing heart failure on the background of myocardial ischemia due to myocardial remodeling and the consequences of conditioning myocardium.

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Conflict of interest:

The Authors declare no conflict of interest.

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