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Znaczenie elektrokardiografii oraz rejestracji holterowskiej z uwzględnieniem zmienności rytmu serca w ocenie ciężkości i rokowania u pacjentów z ostrą zatorowością płucną niewysokiego ryzyka

Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu w dyscyplinie nauki medyczne

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3. SUMMARY (STRESZCZENIE W JĘZYKU ANGIELSKIM)

Title: The role of short- and long-term electrocardiography, extended by the heart rate variability analysis, in the assessment of severity and prognosis in patients with non-high risk acute pulmonary embolism.

Background: Acute pulmonary embolism (APE) is one of the main manifestations of venous thromboembolism (VTE) and is the third most common cardiovascular disease in the world. The annual incidence of APE ranges from 39 to 115 cases per 100,000 inhabitants. Despite advances in early recognition of APE, early diagnosis and optimal management in the acute phase still remain major clinical challenge. The ECG is a cheap, widely available and frequently used diagnostic device, remaining, in the form of long-term monitoring or serially repeated recordings, the standard of care in intensive cardiac care units. The occurrence of various electrocardiographic abnormalities in the course of APE has been described in the literature, but their relationship with the clinical course and the risk of early death has not yet been fully established. Moreover, data from the literature indicate a more frequent occurrence of specific cardiac arrhythmias, along with some indicators of dysfunction of the cardiac autonomic system (cANS), including fainting and syncope, in the course of APE. The current state of knowledge on electrocardiographic abnormalities, cardiac arrhythmias and dysfunction of the cardiac autonomic nervous system in diseases with dominant involvement of the right ventricle (including APE) is discussed in the review part of the work, which are publications No. 1 and No. 2 of the series.

Aim: The aim of the study was to determine the importance of electrocardiographic recording, both short-term (standard ECG) and prolonged (performed using the Holter method, taking into account heart rate variability), as an additional tool in the diagnosis and assessment of the prognosis of patients with APE, in relation to routinely used methods.

Methods: Consecutive patients with radiologically confirmed non-high risk APE were qualified for this prospective study and immediately after admission, subjected to standard diagnostic and therapeutic procedures as a part of intensive cardiac care. All patients underwent the 12-lead ECG, routine laboratory tests (including assessment of NT-proBNP and cardiac troponins), along with transthoracic echocardiography with a detailed assessment of right ventricular function. During the first 48 hours of hospitalization, 24-hour Holter electrocardiographic recording was performed, extended by the analysis of time-domain parameters of heart rate variability (HRV), which were included due to their importance in describing the functions of cANS. Based on the results obtained, the risk of early death in the course of APE was determined according to the current guidelines of

the European Society of Cardiology (ESC). Then, a detailed statistical analysis of the relationship between the obtained electrocardiographic results and echocardiographic indicators of right ventricular dysfunction and NT-proBNP concentration was performed. In addition, the incidence of specific electrocardiographic abnormalities associated with APE was assessed, including the division into subgroups of the risk of early death in the course of APE. The detailed scope of the research methods used is described in the original works of the presented series, which constitute Publications No. 3 and No. 4.

Results: The presented results concern two groups of patients with different sizes. The first study group (presented in Publication No. 3) consisted of 166 patients with an average age of 56.3 years, while the second group (presented in Publication No. 4) consisted of 197 patients with an average age of 59.0 years. In both groups women constituted 54%. According to the current ESC guidelines, low risk APE was detected in 20% and 30% of patients in the first and second groups, respectively. Intermediate-low risk APE was diagnosed in 40% and 34% of participants, respectively, while intermediate-high risk APE was classified in 40% and 36% of the study cohorts, respectively.

In the group of patients presented in Publication No. 3, increasing cANS dysfunction was demonstrated along with increasing overload of the right ventricle demonstrated by echocardiography or NT-proBNP concentration. Lower values of HRV parameters such as RMSSD ($p=0.02$) and pNN50 ($p=0.03$) as well as lower, bordering on statistical significance values of SDNN ($p=0.05$) were found in the group of patients with intermediate risk APE compared to the group with low risk of death. The univariate regression analysis showed significant relationships between SDNN and all echocardiographically assessed indicators of right ventricular overload and NT-proBNP concentration. The multivariate analysis confirmed the relationship between the SDNN value and the size of the inferior vena cava (OR 0.91, 95% CI 0.21-0.92; $p=0.014$) and between the SDNN value and the NT-proBNP concentration (OR 0.83, 95% CI 0.04-0.91; $p=0.041$).

In the group of patients presented in Publication No. 4, it was shown, that with the increasing risk of death in the course of APE, specific and typical electrocardiographic abnormalities such as S1Q3T3 complexes ($p=0.02$), inverted T waves in the V1-V4 ($p=0.0002$) and others occurred more frequently. The finding of the ECG without any abnormalities was associated with a good prognosis, because such recordings were present in as many as 24% of patients in the low risk group, and only in 1% of patients in the intermediate-high risk group ($p=0.0005$). It was also shown that with a worse risk category, a significant deterioration of SDNN ($p=0.001$), SDANN ($p=0.01$) and triangular index ($p=0.02$) was observed. Moreover, significant correlations were found between the above HRV parameters and echocardiographic parameters indicating right ventricular overload and NT-proBNP concentration (for instance, correlation coefficient r value between SDNN and NT-proBNP stood at -0.38, $p<0.000001$).

Conclusions:

1. In patients with intermediate-high risk APE, compared to patients with low risk of death, there was a significantly more frequent occurrence of typical abnormalities in the standard ECG indicating acute overload and/or ischemia of the right ventricle, such as: the presence of S1Q3T3 complexes, decreased QRS voltage in the limb leads <5 mm, inverted T waves in leads V1-V4 and ST segment depressions in leads V4-V6.
2. In patients with low risk APE compared to patients with intermediate-low and intermediate-high risk of death, a significantly higher incidence of the standard ECG without any significant abnormalities was found.
3. In patients with APE, regardless of the risk of death, a significant relationship was found between the degree of right ventricular overload and the severity of cardiac autonomic dysfunction. It was also showed that patients with intermediate-low risk and intermediate-high risk APE had more severe dysfunction of the cardiac autonomic system than those with low risk of death, and one of the manifestations of which were significantly lower SDNN values in those groups of patients.
4. The importance of short- and long-term electrocardiographic recording in the diagnosis and assessment of the risk of early death in patients with non-high risk APE requires further researches.