УДК: 616.12-008.311

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FEATURES OF SERUM MARKERS OF MYOCARDIAL FIBROSIS IN THE DIAGNOSIS OF WOLF-PARKINSON-WHITE SYNDROME (WPW)

Summary. Most consider Wolff-Parkinson-White (WPW) syndrome to be an arrhythmia. However, the actual syndrome still remains a problem when choosing tactics for managing patients. Its significance is that this pathology affects people of young, working age. Ventricular preexcitation syndromes occur in all age groups and are verified in 1-30 patients per 10,000 people. However, in most cases, the clinical manifestation of the syndrome occurs between the ages of 10 and 20 years and is much less common in the elderly. The prevalence of preexcitation syndromes in the general population is approximately 0.15-0.25% and increases when combined with congenital heart defects - 0.5%. In 40-80% of patients, WPW syndrome is clinically manifested by various forms of cardiac arrhythmias (HRDs). Approximately half of these arrhythmias impair the quality of life and are often fatal [8]. The proportion of NRS with the participation of an additional path of atrioventricular conduction (AVS) reaches 54-75% of all supraventricular tachyarrhythmias (SVT), but without taking into account atrial fibrillation (AF).

Key words: high heart rate, accessory pathway, effective refractory period, ventricular fibrillation, accessory atrioventricular pathway.

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ОСОБЕННОСТИ СЫВОРОТОЧНЫХ МАРКЕРОВ ФИБРОЗА МИОКАРДА В ДИАГНОСТИКЕ СИНДРОМА ВОЛЬФА-ПАРКИНСОНА-УАЙТА (WPW)

Резюме. Большинство рассматривают синдром Wolff-Parkinson-White (WPW) как нарушение ритма сердца. Однако актуальный синдром, по-прежнему, остается проблемой, при выборе тактики ведения пациентов. Ее значимость в том, что данной патологией страдают лица молодого, трудоспособного возраста. Синдромы предвозбуждения желудочков встречаются во всех возрастных группах и верифицируются у 1-30 пациентов на 10 000 человек. Однако, в большинстве случаев клиническая манифестация синдрома происходит в возрасте от 10 до 20 лет и гораздо реже у лиц пожилого возраста. Распространенность синдромов предэкзитации в общей популяции составляет приблизительно 0,15-0,25% и возрастает при сочетании с врожденными пороками сердца – 0,5%. У 40-80% пациентов синдром WPW клинически проявляется разнообразными формами нарушений ритма сердца (НРС). Примерно половина данных аритмий ухудшают качество жизни и часто являются фатальными [8]. Доля НРС с участием дополнительного пути атриовентрикулярного проведения (ДАВС) достигает 54-75% всех наджелудочковыхтахиаритмий (НЖТ), однако без учета фибрилляции предсердий (ФП).

Ключевые слова: высокой частотой сердечных сокращений, дополнительного пути проведения, эффективного рефрактерного периода, фибрилляции желудочков, дополнительного пути атриовентрикулярного проведения.

Introduction. Approximately 1/3 of patients have paroxysms of atrial fibrillation (AF), which in many cases are the cause of dangerous cardiovascular events. The combination of AF with a high heart rate (HR) and a short effective refractory period (ERP) of the accessory conduction pathway (ATP) creates the opportunity for the development of flutter and ventricular fibrillation (VF). Conduction of impulses to the ventricles in a ratio of 1:1 with a frequency of up to 340 per minute during an episode of AF contributes to the transformation of AF into VF, which is the main mechanism of sudden cardiac death (SCD) in patients with WPW syndrome [2,4].

The probability of developing sudden death within 10 years among patients with ventricular preexcitation syndrome exceeds the general population risk and ranges from 0.15 to 0.39%. In some cases, SCD may be the first clinical manifestation of asymptomatic preexcitation [4, 6, 14].

To date, non-invasive and endocardial electrophysiological examination (EPS) of the cardiac conduction system remains the key point in the diagnosis of ventricular preexcitation syndromes and the prediction of HRS. The results obtained with EPS determine the further tactics of patient management [2, 9]. However, even non-invasive EPS has a number of contraindications and limitations for use, in particular, the expediency of its use in asymptomatic patients and in early childhood is still being discussed [1, 7]. Thus, in 20% of asymptomatic patients during endocardial EPS, AF was provoked with the further development of life-threatening ventricular HRS [4, 5]. V. Santinellietal. observed 293 patients with the phenomenon of WPW who underwent an EPS procedure, in which various HRS were induced and who were taking antiarrhythmic therapy for this reason. This prospective study showed that 17 patients had malignant arrhythmias during 67 months of follow-up after EPS, which casts doubt on aggressive management in asymptomatic individuals [8].

Purpose of the study. To study markers of collagen synthesis and degradation in blood serum in patients with ventricular preexcitation syndrome, to evaluate their predictive value in the development of tachyarrhythmias.

Materials and methods. In the conditions of the cardiology departments of the clinic, 23 patients (main group) with premature ventricular excitation syndromes were examined, the average age was 25.3±9.15 years. The main group was divided into two subgroups. The first group consisted of patients with the Wolff-Parkinson-White (WPW) phenomenon (n=11), the second - with the WPW syndrome (n=12). The comparison group consisted of 10 practically healthy individuals. An electrophysiological study of the conduction system of the heart (EPS) was carried out by transesophageal electrical atrial stimulation using an Astrocard-Polysystem EP/L electrostimulator (ZAO Meditech) and multipolar electrodes PEDSP-2. As an assessment of the parameters of fibrosis factors, the quantitative determination of type I terminal propeptide procollagen (PICP), matrix metalloproteinase-9 (MMP-9), and tissue inhibitor of metalloproteinases-1 (TIMP-1) was studied.

Results and its discussion. The highest levels of MMP-9 were determined in patients with WPW syndrome - 96.1±33.2 ng/ml, less in the WPW phenomenon group (54.3±21.8 ng/ml; p=0.0003). The maximum level of TIMP-1 is determined in patients with the WPW phenomenon and practically healthy peers (418.5±69.8 ng/ml and 461.7±72.2 ng/ml; p=0.27). In patients with WPW syndrome, TIMP-1 was significantly lower - 341.1±90.1 ng/ml (p=0.002; p=0.00012). The level of PICP in patients with WPW syndrome was 178.9±76.2 ng/ml, with the WPW phenomenon – 97.8±31.7 ng/ml (p=0.00014). All examined patients in terms of PICP levels significantly differed from practically healthy peers 69.4±23.9 ng/ml ($p<0.05$). Among the main group, a shortening of the PQ interval was revealed, and in patients with the WPW syndrome (106.18±16.5 ms) it was more significant compared to the phenomenon (115.25±19.54 ms, p=0.004). In preexcitation syndromes, the average effective refractory period (ERP) of accessory conduction pathways (ATP) was determined: 240.0±47.9 ms for WPW syndrome and

241.25±30.84 ms for the phenomenon. At the same time, in patients with WPW syndrome, ERP was significantly shorter (p=0.049). In both groups, an inverse correlation with fibrosis biomarkers, MMP-9 and PICP, was established.

Serum markers of synthesis and degradation (MMP-9, TIMP-1, PICP) were evaluated in patients with WPW syndrome and phenomenon. An increase in the concentration of MMP-9, PICP and a decrease in TIMP-1 were revealed in WPW syndrome, which is clinically manifested by various HRS, including AF. We have established correlations of the studied markers of collagen metabolism with the parameters of long-term ECG monitoring, echocardiographic and electrophysiological studies in the examined patients.

Quantitative values of fibrosis indicators are also indicated for predicting an increased risk of developing HRS, in particular AF, in patients with ventricular pre-excitation syndrome. The greatest prognostic value in relation to the progression of the WPW phenomenon into a syndrome, i.e. development of supraventricular tachyarrhythmias in patients with premature ventricular excitation syndromes was detected for MMP-9, TIMP-1, PICP and a number of instrumental parameters.This paper defines additional risk criteria for arrhythmia in WPW syndrome. The value of MMP-9 above 80.3 ng/ml, TIMP-1 less than 381.3 ng/ml and PICP more than 140.8 ng/ml may be criteria for an increased risk of transformation of the WPW phenomenon into a syndrome with subsequent development of supraventricular tachyarrhythmias. The concentration of MMP-9 in the blood serum, exceeding 92 ng/ml, is a criterion for an increased risk of developing AF in ventricular pre-excitation syndrome.

Conclusions. In patients with premature ventricular excitation syndromes, a change in the fibrous matrix was revealed: an increase in the concentration of MMP-9, PICP and a decrease in TIMP-1. The WPW syndrome is characterized by a pronounced imbalance of serological markers of collagen synthesis and degradation than the phenomenon. ERP DPP was inversely correlated with MMP-9 and PICP scores. The data obtained represent the possible involvement of fibrous

myocardial disorganization in the formation of cardiac arrhythmias in premature ventricular excitation syndromes.

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