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

Summary. Most view Wolff-Parkinson-White (WPW) syndrome as a heart rhythm disorder. However, the actual syndrome still remains a problem in the choice of patient management tactics. Its significance is that young people of working age suffer from this pathology. Ventricular preexcitation syndromes are found 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, and much less frequently in the elderly. The prevalence of preexitation syndromes in the general population is approximately 0.15-0.25% and increases in combination with congenital heart defects - 0.5%. In 40-80% of patients, WPW syndrome is clinically manifested by various forms of cardiac arrhythmias (HRD).

Key words: Wolff-Parkinson-White, cardiac arrhythmias, atrial fibrillation, heart rate, effective refractory period, ventricular fibrillation, sudden cardiac death.

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СЫВОРОТОЧНЫЕ МАРКЕРЫ 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).

Ключевые слова: Вольфа-Паркинсона-Уайта, нарушений ритма сердца, мерцательной аритмии, частотой сердечных сокращений, эффективного рефрактерного периода, фибрилляции желудочков, внезапной сердечной смерти.

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 (ESR) of the additional conduction pathway (DPP) creates an opportunity for the development of flutter and ventricular fibrillation (VF). Conduction of impulses to the ventricles in a 1: 1 ratio with a frequency of up to 340 per minute during an episode of MA promotes the transformation of AF into VF, which is the main mechanism of sudden cardiac death (SCD) in patients with WPW syndrome [2,4].

To date, the key point in the diagnosis of ventricular preexitation syndromes and the prognosis of LRD remains non-invasive and endocardial electrophysiological examination (EPI) of the cardiac conduction system. The results obtained with EPI determine the further tactics of patient management [2, 9]. However, even non-invasive EPI has a number of contraindications and restrictions for use, in particular, the expediency of its use in asymptomatic patients and in early childhood is still being discussed [1,7].

The mechanisms of structural remodeling and progression of selective atrial fibrosis have not yet been studied in detail. Interstitial myocardial fibrosis is characterized by the predominant accumulation of type I collagen. Some of the many metabolic products of this protein are type I terminal propeptide procollagen (PICP), matrix metalloproteinase-9 (MMP-9), and tissue inhibitor of matrix metalloproteinases-1 (TIMP-1) [9,10]. Therefore, the level of PICP, MMP-9 and TIMP-1 can be used to judge the degree of synthesis and degradation of type I collagen in health and disease.

The above positions served as the basis for determining the goal and objectives of this study.

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

Materials and methods. In the cardiology departments of the clinic, 23 patients (main group) with syndromes of premature ventricular excitation were examined, the average age was 25.3 ± 9.15 years. The main group was divided into

two subgroups. The first consisted of patients with the Wolff-Parkinson-White (WPW) phenomenon (n = 11), the second - with WPW syndrome (n = 12). The comparison group consisted of 10 apparently healthy individuals. Electrophysiological examination of the cardiac conduction system (EPI) was carried out by the method of transesophageal electrical stimulation of the atria using an Astrocard-Polysystem EP/L electrostimulator (Meditek CJSC) and PEDSP-2 multipolar electrodes. As an assessment of the indicators of fibrosis factors, the quantitative determination of terminal propeptide daprocollagen type I (PICP), matrix metalloproteinase-9 (MMP-9), tissue inhibitor of metalloproteinases-1 (TIMP-1) was studied.

Results and its discussion. The highest indicators of MMP-9 were determined in patients with WPW syndrome - 96.1 ± 33.2 ng / ml, less in the group of the WPW phenomenon (54.3 ± 21.8 ng / ml; p = 0.0003). The maximum TIMP-1 level is determined in patients with 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 PICP level 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). In terms of PICP level, all examined patients significantly differed from practically healthy peers by 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 WPW syndrome (106.18 ± 16.5 ms) it was more significant compared to the phenomenon (115.25 ± 19.54 ms, p = 0.004). In the case of preexitation syndromes, the mean effective refractory period (ERP) of the additional conduction pathways (AP) was determined: in WPW syndrome - 240.0 ± 47.9 ms and 241.25 ± 30.84 ms in the phenomenon. At the same time, ERP in patients with WPW syndrome was significantly shorter (p = 0.049). In both groups, an inverse correlation was found with fibrosis biomarkers - MMP-9 and PICP.

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, clinically manifested by various LDCs, 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.

Also indicated are the quantitative values of fibrosis indicators for predicting an increased risk of developing LDCs, in particular AF, in patients with ventricular preexitation syndrome.

The greatest predictive value in relation to the progression of the WPW phenomenon into the syndrome, i.e. development of supraventricular tachyarrhythmias in patients with premature ventricular excitation syndromes was revealed for MMP-9, TIMP-1, PICP and a number of instrumental parameters.

In this work, additional criteria for the risk of arrhythmia in WPW syndrome are defined.

The value of MMP-9 above 80.3 ng / ml, TIMP-1 below 381.3 ng / ml and PICP above 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 AF in patients with ventricular preexitance syndrome.

The proposed criteria can be used in practical healthcare, which will provide timely diagnosis of the WPW syndrome and phenomenon, and will also allow determining the optimal tactics for managing these patients.

Conclusions. In patients with ventricular premature 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. 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 the parameters of MMP-9 and PICP. The data obtained represent the possible participation of fibrous

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

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