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PULSE PRESSURE CLASSES AND HEMODYNAMIC PARAMETERS IN PATIENTS AT THE ANNUAL STAGE AFTER CARDIAC RESYNCHRONIZATION AND MEDICAL THERAPY

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The changes of functional blood circulation parameters in 19 patients (13 men and 6 women) at the annual stage after cardiac resynchronization (CRT) and drug therapy in pulse pressure classes (PP: I - very low PP - less than 20 mm Hg; II - low PP - from 20 to 40 mm Hg; III - normal PP - from 40 to 60 mm Hg; IV - high PP - from 60 to 80 mm Hg; V - very high - more than 80 mm Hg) were studied. The probability of differences between groups was determined with a Mann-Whitney U-test. Normalization of diastolic blood pressure (DBP), heart rate (HR) and left ventricular ejection fraction (LV EF) in all PP classes, systolic BP (SBP), end-systolic, end-diastolic volumes (ESV, EDV) in the III PP class patients at the annual stage after CRT and drug therapy were showed. The tendency of normalization of SBP in the IV class, posterior wall thickness of LV (PWLV), myocardial mass of LV (MMLV) and no change in interventricular septum thickness (IVS), left and right atrium (LA and RA), right ventricular (RV) sizes in all PP classes indicated the need for more active monitoring, careful selection of stimulation parameters and medical support correction of patients in IV PP class.

KEY WORDS: cardiac resynchronization therapy, medical therapy, pulse pressure, hemodynamic parameters

КЛАСИ ПУЛЬСОВОГО АРТЕРІАЛЬНОГО ТИСКУ ТА ГЕМОДИНАМІЧНІ ПОКАЗНИКИ У ПАЦІЄНТІВ НА РІЧНОМУ ЕТАПІ ПІСЛЯ КАРДІОРЕСИНХРОНІЗУЮЧОЇ ТА МЕДИКАМЕНТОЗНОЇ ТЕРАПІЇ

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Вивчено зміни функціональних показників кровообігу у 19 пацієнтів (13 чоловіків і 6 жінок) на річному етапі спостереження після кардіоресинхронізуючої (КРТ) і медикаментозної терапії в класах пульсового артеріального тиску (ПАТ: І – дуже низький – менше 20 мм. рт. ст., ІІ – низький – більше 20 – менше 40 мм. рт. ст., ІІІ – норма – 40–60 мм. рт. ст., ІV – високий – понад 60 – менше 80 мм. рт. ст., V – дуже високий – більше 80 мм. рт. ст.). Достовірність відмінностей між групами визначалася за допомогою U-критерію Манна-Уітні. Результати показали, у пацієнтів за весь період спостереження після КРТ і медикаментозної терапії відбувається нормалізація діастолічного АТ (ДАТ), частоти серцевих скорочень (ЧСС) і фракції викиду лівого шлуночка (ФВЛІІІ) у всіх класах ПАТ, систолічного АТ (САТ), кінцево-систолічного та кінцево-диастолічног об'єму (КСО та КДО) в ІІІ класі ПАТ. Тенденція нормалізації САТ в ІV класі, товщини задньої стінки ЛІІІ (ТЗСЛІІІ) і маси міокарда ЛІІІ (ММЛІІІ) і відсутність змін товщини міжшлуночкової перетинки (ТМІІІП), розмірів лівого та правого передсердя (ЛП та ПП), правого шлуночка (ПІІІ) у всіх класах ПАТ свідчать про необхідність більш активного моніторингу, ретельного підбору параметрів стимуляції і корекції медикаментозної підтримки пацієнтів у ІV класі ПАТ.

КЛЮЧОВІ СЛОВА: кардіоресинхронізуюча терапія, медикаментозна терапія, пульсовий артеріальний тиск, гемодинамічні показники

КЛАССЫ ПУЛЬСОВОГО АРТЕРИАЛЬНОГО ДАВЛЕНИЯ И ГЕМОДИНАМИЧЕСКИЕ ПОКАЗАТЕЛИ У ПАЦИЕНТОВ НА ГОДОВОМ ЭТАПЕ ПОСЛЕ КАРДИОРЕСИНХРОНИЗИРУЮЩЕЙ И МЕДИКАМЕНТОЗНОЙ ТЕРАПИИ

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Изучены изменения функциональных показателей кровообращения у 19 пациентов (13 мужчин и 6 женщин) на годовом этапе наблюдения после кардиоресинхронизирующей (КРТ) и медикаментозной терапии в классах пульсового артериального давления (ПАД: I – очень низкое – менее 20 мм. рт. ст., II – низкое – более 20 – менее 40 мм. рт. ст., III – норма – 40–60 мм. рт. ст., IV – высокое – более 60 – менее 80 мм. рт. ст., V – очень высокое ПАД - более 80 мм. рт. ст.). Достоверность отличий между группами определялась с помощью U-критерия Манна-Уитни. Результаты показали, у пациентов на всем периоде наблюдения после КРТ и медикаментозной терапии происходит нормализация диастолического АД (ДАД), частоты сердечных сокращений (ЧСС) и фракции выброса левого желудочка (ФВЛЖ) во всех классах ПАД, систолического АД (САД), конечно-систолического и конечно-диастолического объема (КСО и КДО) в III классе ПАД. Тенденция нормализации САД в IV классе, толщины задней стенки ЛЖ (ТЗСЛЖ) и массы миокарда ЛЖ (ММЛЖ) и отсутствие изменений толщины межжелудочковой перегородки (ТМЖП), размеров левого и правого предсердий (ЛП и ПП), правого желудочка (ПЖ) во всех классах ПАД свидетельствуют о необходимости более активного мониторинга, тщательного подбора параметров стимуляции и коррекции медикаментозной поддержки пациентов в IV классе ПАД.

КЛЮЧЕВЫЕ СЛОВА: кардиоресинхронизирующая терапия, медикаментозная терапия, пульсовое артериальное давление, гемодинамические показатели

INTRODUCTION

Cardiac resynchronization therapy (CRT) is widely used and has a positive clinical effect in patients with chronic heart failure (CHF), accompanied by cardiac dyssynchrony, however, medical support is not canceled [1].

Reflecting the elastic properties of the great vessels and left ventricular (LV) function [2], pulse pressure (PP) is one of the most important hemodynamic parameters and is an independent predictor of cardiovascular events [3]. Non-physiological PP promotes the dynamic load on the myocardium and the development of hypertrophy with subsequent development of cardiovascular events [4].

optimizing the heart function, synchronizing heart chambers contraction, CRT improves the pumping function of the heart [2, 5], which is accompanied by LV remodeling [1, 6]and changing hemodynamic parameters, including PP. However, the functional parameters of blood circulation changing in the PP classes in the long-term follow-up after CRT on background of medical therapy has not yet been studied.

MATERIALS AND METHODS

19 patients, including 13 men and 6 women were examined in the department of ultrasound and instrumental diagnostics with miniinvasive interventions of SI «V. T. Zaytsev Institute of General and Emergency Surgery NAMS of Ukraine». Mean age of the patients was 67 ± 9 years; all of them were implanted CRT in period from 2006 to 2015. Indications for pacemaker implantation were: atrioventricular (AV) block -21 % patients, bundle branch

block – 47 %, sick sinus syndrome (SSS) – 26 % patients, permanent bradysystolic form of atrial fibrillation (AF) – 26 %, dilated cardiomyopathy (DCM) – 21 % patients.

Exclusion criteria were: age less than 40 years, the presence of concomitant angina IV functional class (FC), chronic heart failure (CHF) IV FC, stimulation of the right ventricular (RV) and/or LV lesser than 50 % during the year of observation.

Systolic (SBP) and diastolic blood pressure (DBP), heart rate (HR), end-systolic (ESV), end-diastolic volumes (EDV), LV ejection fraction (LV EF), posterior wall thickness of LV (PWLV), interventricular septum thickness (IVS), myocardial mass of LV (MMLV), right atrium (RA), left atrium (LA) and RV sizes were evaluated before the implantation, in the early postoperative period (3–5 days), after 6 months and 1 year after CRT and medication depending on the PP classes.

SBP and DBP were measured by Korotkov's method according to the recommendations of the Association of Cardiologist of Ukraine for the prevention and treatment of hypertension by tonometer Microlife BP AGI-20 after 15 minutes rest. PP was calculated by the formula: PP=SBP-DBP (mm Hg).

Echocardiography study was performed with use of Siemens Cypress and Toshiba Applio 400 machines. LA, RA, RV, PWLV, IVS (measuring accuracy is 0.5 mm), end-systolic (ESS), end-diastolic (EDS) sizes were measured. LV EF was calculated using the formula: EF = (EDV–ESV)/EDV×100 %. The Simpson method was used for calculating EDV and ESV. MMLV was calculated using the Devereux formula:

 $MMLV=1.04 \times ((IVSd+PWLVd+EDS)^3-EDS^3)-13.6.$

Medication support of patients with CRT was provided with: rennin-angiotensin-aldosterone inhibitors (RAAI) (angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists (ARA II)), diuretics, antiarrhythmic drugs (beta-blockers and amiodarone), antithrombotic drugs (antiplatelet agents – acetylsalicylic acid (ASA), oral anticoagulants (AC) – warfarin/dabigatran), statins.

Patients were assigned into five classes according to levels of PP: I - very low - less than 20 mm Hg; II - low - from 20 to 40 mm Hg; III - normal - from 40 to 60 mm Hg; IV - high - from 60 to 80 mm Hg; V - very high PP - more than 80 mm Hg. In each groups of patients at the annual observation point SBP, DBP, HR, ESV, EDV, LVEF, PWLV, IVS, MMLV, RA, LA and RV sizes were determined. Functional parameters of blood circulation in the CRT (P/D) stimulation modes were assessed.

The data were brought into the Microsoft Excel base. For statistical evaluation of the

results were used the parametric criteria (M – mean, sd – standard deviation). Significant differences between groups were determined using the Mann-Whitney U-test. Probable results were determined at levels of reliability p < 0.05 and p < 0.01.

RESULTS AND DISCUSSION

In I, II and V PP classes there are no patients registered, in the III class -68 %, in the IV class -32 % of patients.

Table 1 shows SBP, DBP and HR values in patients within one year after CRT and medical support in different PP classes. Initially SBP in III class was in a range of the 1st degree of hypertension (AH) and IV – at the 2nd degree of AH, at the annual stage after CRT and drug therapy has reached physiological range in III and decreased till 1st degree of AH at the IV PP class. DBP was at the physiological level in all groups in the entire observation stage. Initially a low HR in the IV PP class normalized after implantation, in III class – was in the physiological range before and during the year after CRT and drug therapy.

Table 1 SBP, DBP and HR values (M \pm sd) in patients within one year after CRT and medical support in different PP classes

Functional values	PP										
	III class				IV class						
	Before CRT	After CRT			Before	After CRT					
		3–5 day	6 month	1 year	CRT	3–5 day	6 month	1 year			
SBP (mm Hg)	142 ± 8	145 ± 6	135 ± 8	133 ± 6^	162 ± 7*	156 ± 7*	149 ± 8	142 ± 3^			
DBP (mm Hg)	84 ± 6	85 ± 9	85 ± 4	84 ± 3	86 ± 8	85 ± 3	85 ± 4	86 ± 8			
HR (bpm)	73 ± 19	74 ± 20	68 ± 4	67 ± 5	50 ± 11	62 ± 7	68 ± 6^	67 ± 8^			

Note: * p < 0.05 – in current values between groups, ^ p < 0.05 – certain class of values before and after CRT.

Table 2 shows heart ultrasound values in patients within one year after CRT and medical support in different PP classes. Initially increased ESV and EDV, more pronounced in IV class, were normalized at III and tended to decrease in IV PP class without statistically significant differences between the groups at the annual stage after CRT and drug therapy. Initially reduced LV EF, more pronounced in IV class, came close to normal after 6 months and reached physiological range in a year in all

PP classes after CRT and drug therapy. Initially increased PWLV and MMLV, more pronounced in IV class tended to decrease in all PP classes without statistically significant differences between the groups at the annual stage after CRT and drug therapy. Equally increased IVS, LA, RA and RV sizes did not change in all PP classes in the entire period of observation after CRT on the background of medical therapy.

 $\begin{tabular}{ll} Table 2\\ Heart ultrasound values (M \pm sd) in patients within one year after CRT\\ and medical support in different PP classes\\ \end{tabular}$

Functi onal values	PP										
		III	class		IV class						
	Before CRT		After CRT		Before	After CRT					
		3–5 day	6 month	1 year	CRT	3–5 day	6 month	1 year			
ESV	98 ± 12	98 ± 15	70 ± 8	56 ± 11^	$134 \pm 21*$	134 ± 18*	$106 \pm 18*$	81 ± 12^			
EDV	174 ± 16	174 ± 9	142 ± 4	126 ± 11^	202 ± 10*	202 ± 11*	188 ± 24*	179 ± 6^			
LV EF (%)	43 ± 4	43 ± 6	50 ± 4	63 ± 5^	33 ± 4*	33 ± 7	43 ± 6	55 ± 8^			
PWLV (cm)	1.2 ± 0.1	1.2 ± 0.1	1.2 ± 0.1	1.1 ± 0.1	1.35 ± 0.2	1.35 ± 0.2	1.35 ± 0.1	1.3 ± 0.1			
IVS (cm)	1.2 ± 0.2	1.2 ± 0.2	1.2 ± 0.2	1.2 ± 0.1	1.3 ± 0.3	1.3 ± 0.3	1.3 ± 0.3	1.3 ± 0.2			
MMLV (cm)	354 ± 27	354 ± 31	328 ± 46	302 ± 23	426 ± 37*	426 ± 35*	406 ± 35*	381 ± 28*			
RA (cm)	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.1	3.9 ± 0.2	3.9 ± 0.2	3.9 ± 0.1	3.9 ± 0.1			
LA (cm)	4.3 ± 0.1	4.3 ± 0.1	4.3 ± 0.1	4.3 ± 0.1							
RV (cm)	5 ± 0.1	5 ± 0.1	5 ± 0.1	5 ± 0.2	5.1 ± 0.1	5.1 ± 0.1	5.1 ± 0.1	5.1 ± 0.2			

Note: * p < 0.05 – in current values between groups, ^ p < 0.05 – certain class of values before and after CRT.

Normalization of DBP, HR, LV EF in all PP classes; SBD, ESV and EDV in III class at the annual stage after CRT and drug therapy that were found is indirectly confirmed by data [6, 7].

Shown in our research decreasing of SBP in IV PP class to the level of the 1st degree of AH, and the downward trend PWLV and MMLV, no change in IVS, LA, RA and RV sizes in all PP classes after CRT and drug therapy is indirectly confirmed by data [8].

Our research has shown that PP is significant in the assessment of hemodynamic parameters in patients after CRT and drug therapy. More favorable changes of functional blood circulation parameters in III, and less – in IV PP classes at the annual observation stage after CRT indicate the need for further medical treatment in a high PP class. The given data are new.

CONCLUSIONS

1. Patients with indications don't have I, II and V PP classes, frequency of occurrence III

and IV classes represent 68 % and 32 %, respectively.

- 2. At the annual stage of CRT and drug therapy in both PP classes DBP, HR and LV EF are fully normalized, in III PP class SBP, ESV and EDV, and in IV PP class only partially normalization of SBP without achieving a physiological rate.
- 3. At the annual stage of CRT and drug therapy in both PP classes is a PWLV and MMLV tendency of normalization without statistically significant differences between the groups and no changes in the IVS, LA, RA, RV sizes.
- 4. More active monitoring, careful selection of stimulation parameters and correction of medical support for patients in IV PP class after CRT is need.

PROSPECTS FOR FUTURE STUDIES

Further investigation of the effect of drug therapy on the optimization of the PP in patients with implanted pacemaker depending on the mode of stimulation in the long pacing period seems to be a perspective direction of researches.

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