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Echocardiography in the assessment of intraventricular flows and pressure gradients in obstructive hypertrophic cardiomyopathy

Aim	To evaluate results of myomectomy by intraventricular pressure gradients (IVPG) and blood flows in patients with obstructive hypertrophic cardiomyopathy (OHCMP).
Material and methods	The study included a total of 76 subjects, 42 patients with OHCMP (mean age, 39±7 years) and 34 healthy volunteers (mean age, 41±3 years). Prior to and after myomectomy, transthoracic echocardiography was performed and followed by digital image processing and calculation of IVPG and left ventricular (LV) vortex flows. Vector analysis was used to estimate the myocardial displacement rate (V), vortex flows, and LV apex-to-base pressure gradients.
Results	The study showed a dynamic decrease in the LV apex-to-outflow IVPG by more than 50% and recovery of myocardial contraction velocity in the septal area ($p<0.001$). The decrease in LV cavity pressure gradient serves as an index for evaluating the effectiveness of OHCMP correction. Myomectomy reduces the load on the myocardium and abolishes mitral valve regurgitation with improvement of LV blood flows as also evidenced by the dynamics of long axis velocity change during the cardiac cycle (dL/dt) and the myocardial contraction velocity (V).
Conclusion	Effectiveness of the surgical correction of OHCMP is based on the dynamics of myocardial contraction velocities, vortex blood flows, and a decrease in LV apex-to-base IVPG.

Keywords	Hypertrophic cardiomyopathy; intraventricular pressure gradient; intracardiac blood flows
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Introduction

Hypertrophic cardiomyopathy is one of the most common hereditary cardiomyopathies with a rate of about 1:500 in the general adult population [1, 2]. The matter of diagnosis and treatment in obstructive hypertrophic cardiomyopathy (OHCMP) is now widely discussed in relation to clinical practice. Obstruction is caused by myocardial hypertrophy and systolic contact between the anterior mitral valve (MV) leaflet and the interventricular septum (IVS) [3–6]. Over the past decade, the rate of OHCMP diagnosis has increased progressively in the general population. This trend is due to an increased incidence of this disease and the wider practical application of high-quality instrumental techniques for examination of the heart, especially echocardiography. There is currently no ultimate answer to whether drug and surgical treatments are effective. It is generally accepted that treatment is effective, if the pressure gradient between the left ventricular (LV) cavity and its outflow tract decreases by a magnitude of 2–3 after surgery [7–9]. The use of surgical techniques, i.e., myoseptectomy, correction of MV, chordae, and papillary muscles, continues to be under discussion worldwide [9, 10], although questions still remain about the efficacy of surgeries [11]. Moreover, residual LV gradients and the distribution of turbulent flows are unclear with regard to the volume of surgery. Modern methods of examination, such as vector analysis, evaluation of turbulent intracardiac blood flows, can be introduced into clinical practice to help understand the course of compensation processes, and assess the adequacy of surgical correction in cardiac pathologies [12, 13]. The literature currently discusses the assessment of turbulent blood flows in valve pathologies, coronary heart disease, and the possibility of using this new way of evaluating myocardial function.

Aim

To evaluate myectomy results by intraventricular pressure gradients (IVPG) and blood flow in patients with OHCMP.

Material and methods

A prospective examination was performed in 42 patients admitted for surgical treatment of OHCMP. All

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patients underwent transaortic myoseptectomy and resection of papillary muscles. The mean age of patients was 39±7 years of age. 28 patients were male, and 14 were female. The control group included 34 healthy volunteers whose mean age was 41±3 years. Patients with unsatisfactory ultrasound location, heart rate and conduction disorders were excluded from the analysis.

The local ethics committee approved the study. All subjects signed informed consent to participate in the study.

Echocardiography

All subjects underwent transthoracic echocardiography at rest on a VIVID 7 Dimension device with a VIVID E93.5–5.5 MHz multi-frequency array transducer using standard electrocardiogram (ECG) techniques. Patients with OHCMP were examined before surgery and on day 7–10 after surgery.

Transthoracic echocardiography included grayscale M-modal and 2D registration (not less than 50 fps), color, pulsed wave, and continuous-wave Doppler in the area of LV outflow tract (LVOT) and the mitral, aortic, and tricuspid valves. All static and moving-image examinations (3–5 cardiac cycle cine loops) were stored in the EchoPAC 7 and Multivox workstation memory for subsequent assay and processing.

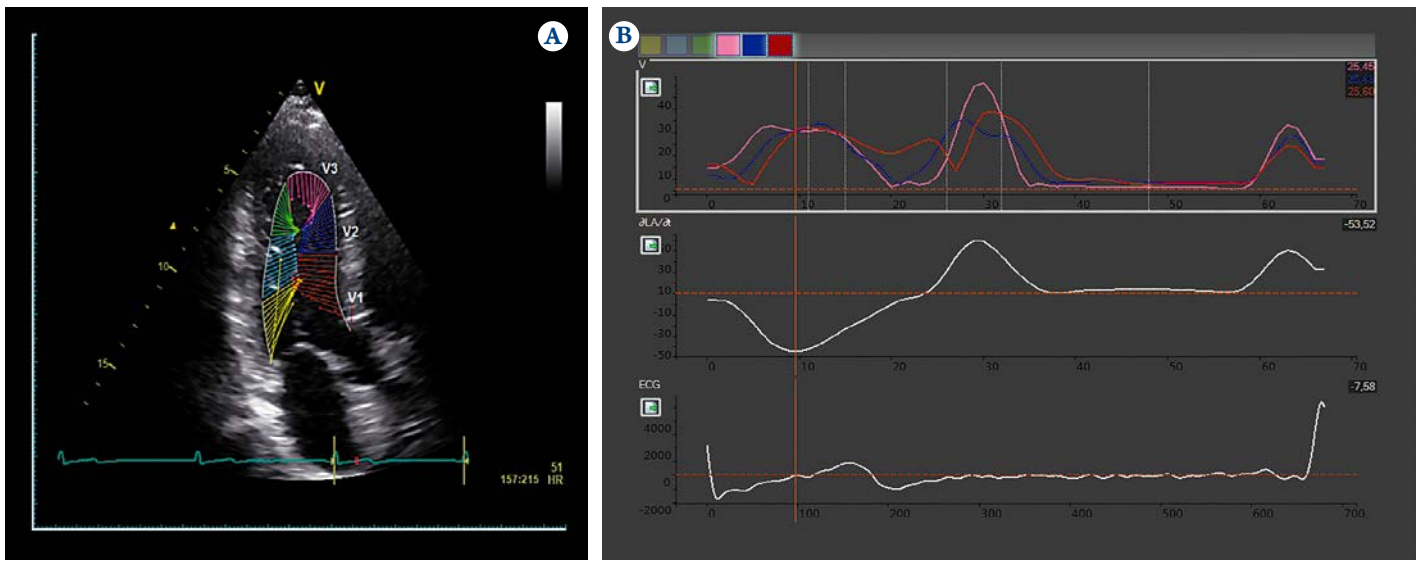
M-modal measurements of the diastolic and systolic thickness of the IVS and the LV posterior wall were made in the standard parasternal long-axis view. Left ventricular end-systolic volume (LVESV) and end-diastolic volume (LVEDV), and left ventricular ejection fraction (LVEF) were determined in the apical four- and two-chamber views using the method of disks (modified Simpson's rule).

The systolic spectrum of linear blood flow velocity in the LVOT was registered in the pulsed wave Doppler mode. The reference volume was set at the center of LVOT, 10 mm proximal from the closed aortic valve leaflets, thus determining the maximum pressure gradient.

Off-line analysis of echocardiograms. Myocardial contraction rate

In order to obtain quantitative vector analysis data, one cardiac cycle was selected from the stored cine loops in each of the three apical views of the LV of satisfactory image quality (50–80 frames per cycle). The LV endocardial contour was then manually traced in the best quality frame. It was then refined frame by frame, and, if necessary, corrected so that the tracing line coincided with the endocardial border throughout the selected cardiac cycle. Next, the image processing software algorithm built a vector profile of myocardial motion. An 18-segment model was used for the LV, with 6 segments in each of the three sections at three levels: basal, middle, and apical. The vector analysis provided quantitative information about the movement of each segment, i.e., myocardial contraction rate (V) (Figure 1). This in turn was used to evaluate the LV myocardial contraction in the basal, middle, and apical IVS at R-waves, the start and end of the T-wave in the ECG. Next, a comparative analysis of the normal and pathological

Figure 1. Vectors of myocardial contraction velocities in a healthy person during the maximum ejection phase in the apical three-chamber view (A) and curves (top-to-bottom) of myocardial contraction velocities in the interventricular septum. Rates of changes in the long axis, ECG (B)



Markers: the red vertical line represents maximum ejection. The graphs correspond to the vector colors: yellow – posterior basal segment; blue – posterior middle segment; green – posterior apical segment; pink – anteroseptal apical segment (V_3); blue – anteroseptal middle segment (V_2); dark-red – anteroseptal basal segment (V_1).

pattern was carried out considering the rate of change in the LV long axis (dL/dt).

Intraventricular pressure gradient and blood flows

Measurable parameters (velocity, pressure gradients) of intraventricular blood flows were estimated using an iterative phase retrieval technique for color Doppler images according to the methods [12, 13]. The algorithm involves extracting digital characteristics of the flows and tracking the cavity contour. This can be corrected manually because cardiac motion may significantly change the contour, thus requiring additional adjustment and estimation of the flow profiles, shear stress, and elasticity. Blood viscosity was taken as equal to 3.88 MPa, corresponding to normal blood viscosity. LV vortex flows were estimated by the velocity gradients of the main vector fields. Data obtained for all three cardiac cycles was estimated to avoid the effects of computation errors that occur at the beginning of the calculation. The resulting images contained quantitative characteristics of blood flows and apical-to-basal LV IVPG. Figure 2 displays images at different moments of normal systole.

The use of the phase structure of the cardiac cycle is fundamental in estimating these parameters. The phases of isovolumic stress, maximum ejection, and end-systole were selected as the reference points.

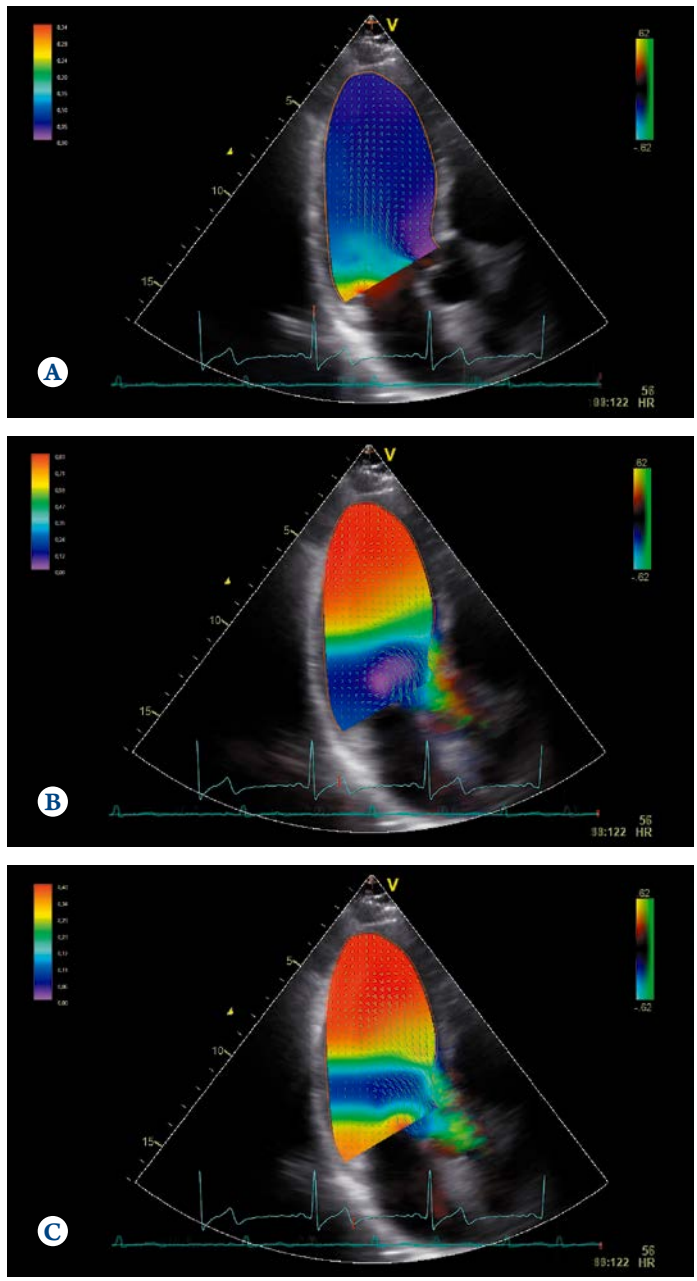
Statistical analysis of the data obtained was carried out using Statistica 12.0 and JMP 7. The results are presented as the mean and the standard deviation (M±SD) in graphs and tables. The obtained data was compared. The significance of differences was evaluated using the Student t-test and the Mann-Whitney U-test, depending on the distribution of variables and the chi-squared test. A correlation analysis was performed, and the bivariate Pearson correlation coefficients (r) were calculated to identify the correlations between the characteristics being analyzed and the observations. The critical level of statistical significance $p \leq 0.05$ was used in all statistical analysis procedures.

Results

Correlations between the rate of myocardial contraction and intraventricular pressure gradient

Before the surgery, the peak LVOT pressure gradient in patients with OHCMP was more than 50 mmHg (Table 1). On patients with OHCMP Systolic ejection (SE) was complicated by higher than normal contraction velocities in the IVS area. Statistically significant differences between patients of the compared groups were observed in LVEDV and LVESV, and IVS thickness. LVEF was normal. Myocardial hypertrophy develops into the LV cavity and reduces its volume. Some patients with OHCMP had a significant reduction of the LV cavity in systole, especially if the LV wall thickness was more than 2 cm accompanied by hypertrophy of the papillary muscles. In these cases, a pressure gradient of more than 50 mmHg can be registered in systole. The rate of change in the long LV axis was not directly dependent on the rate of change in the LV volume, and low values of dL/dt within 20–30 mm/s observed in the entire sample of patients with OHCMP. Figure 3 shows the myocardial velocity vectors and graphs of the IVS velocities in a patient with OHCMP before and after myectomy.

Figure 2. Color mapping of intraventricular pressure gradients superimposed by intracardiac blood flow vectors (green arrows) in a healthy person during systole: R wave (A), the beginning of T wave (B), the end of T wave (C)



To the left is the pressure gradient scale in mmHg, to the right is the blood flow velocity scale.

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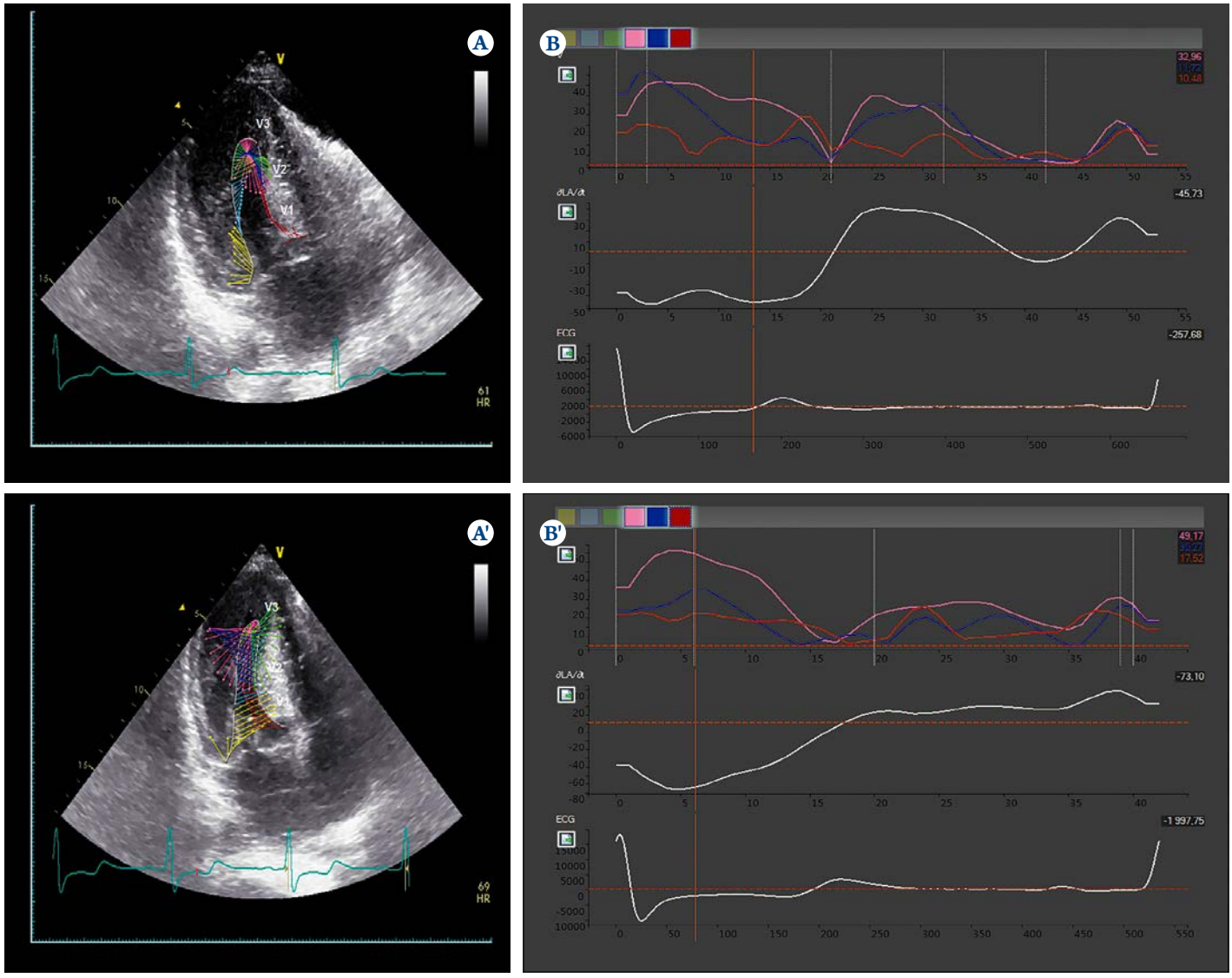
Figure 3. Myocardial contraction velocity vectors in a patient with OHCMP during maximum ejection before surgery (A) and on day 7 after surgery (A'); apical three-chamber view and curves (top-to-bottom) of the rate of myocardial contraction. Rate of change in the long axis, ECG before surgery (B) and on day 7 after surgery (B')



Markers: the red vertical line represents maximum ejection. The graphs correspond to the vector colors:
yellow – posterior basal segment; blue – posterior middle segment; green – posterior apical segment;
pink – anteroseptal apical segment (V_3); blue – anteroseptal middle segment (V_2); dark-red – anteroseptal basal segment (V_1).
On the left of the graphs is the rate of myocardial contraction. OHCMP, obstructive hypertrophic cardiomyopathy.

The analysis of basal contraction velocity (V1) in healthy persons and patients with OHCMP showed that this indicator was significantly twice as reduced before and after surgery, in comparison with the normal values during the entire phase of SE (Figure 4, A). There was no correlation between systolic phases of the cycle, both normal and after surgery. This is evidenced by the coefficient of determination (r^2=0.27).

The contraction velocities in the middle IVS, both before and after surgery, were higher than normal during the maximum ejection (S-wave) but did not correlate. The trend is the same for the apical (see Figure 4, B, C). It is typical of increased IVPG and additional vortex flows in LV overload against resistance.

Turbulent flows and relationship with pressure gradient

During the phase of the maximum ejection, a healthy person has uniform and clockwise blood flow with one basal turbulent vortex (Figure 2). During maximum ejection, in patients with OHCMP before surgery, the main ejection flow and the turbulence zone are shifted to the middle LV with the formation of additional swirl zones along the posterior and inferior LV walls of the main flow (Figure 5, B). This is due to the high flow velocity in LVOT associated with IVS hypertrophy. The surgical removal of an additional barrier in the septum changes the flow pattern, resulting in the normalization of its direction and velocities at the end of the systolic blood ejection (Figure 5, B').

Table 1. Hemodynamics in patients with obstructive hypertrophic cardiomyopathy

Parameter	Normal (1)	Before surgery (2)	After surgery (3)	p		
				p_{1-2}	p_{1-3}	p_{2-3}
Heart rate, beats/min	67±6	62±10	64±7	0.01	0.3	0.22
Systolic arterial pressure, mmHg	124±11	121±18	132±10	0.48	0.05	0.06
Diastolic arterial pressure, mmHg	73±6	73±10	80±2	0.36	0.07	0.08
LV CDR, ml	97±16	76±26	108±7	<0.001	0.07	<0.001
LV CSR, ml	38±8	20±7	40±3	<0.001	0.13	<0.001
Shock ejection, ml	53±13	55±21	67±5	0.28	0.09	0.11
LV LV, %	63±5	74±6	62±1	<0.001	0.22	<0.001
Ventricular septum thickness, cm	0,9±0,1	2,2±0,4	1,9± 0,3	<0.001	<0.001	0.07
ΔP BTR VTLJ, mmHg	2±0,3	69±19	13±3,1	<0.001	<0.001	<0.001
dL/dt (s), mm/s	73±12	43±20	41±16	<0.001	<0.01	0.94
dL/dt (d), mm/s	77±20	23±15	42±14	<0.001	<0.001	0.01

LV CDR – the final diastolic volume of the left ventricle; LV CSR – the final systolic volume of the left ventricle;
LV LV – the ejection fraction of the left ventricle; BTR VTLJ – peak pressure gradient in the outflow tract of the left ventricle;
dL / dt – the rate of change of the long axis in the systole (s) and diastole (d).

Surgical correction of the LVOT obstruction decreases the mean pressure gradient (see Table 1) and increases LVEDV and LVESV. LVEF decreased by a mean of 16% and remained normal. The rate of change of the long LV axis (dL/dt) in diastole became significantly higher after surgery.

The decrease gradient in the LVOT is accompanied by the recovery and normalization of the systolic ejection pattern. Blood flow after surgery is almost the same as in a healthy person (Figure 5, A'–B'). Surgical treatment did not immediately result in the complete recovery of intraventricular hemodynamics in some cases. Thus, normalization of myocardial contraction velocities (V) indirectly characterizes the positive energy process in the myocardium, while taking into account decreased pressure gradient and normalization of blood flows.

The estimation of intracardiac pressure gradients in patients with OHCMP is of particular interest. Altered spatial geometry, smaller LV cavity, papillary muscle hypertrophy, severe disorders of segmental contraction and relaxation result in changes in the formation and distribution of intraventricular blood flows and pressure gradients within the LV cavity. The elimination of pressure gradient in LVOT improves the conditions for SE.

It is interesting to note that patients with OHCMP have several apex-to-base IVPG levels during isovolumic stress. The normal pressure gradient is not more than 0.2 mmHg, and 2.5–4 mmHg in patients with OHCMP. After myectomy, the peak gradient between LV and aorta decreased significantly, and IVPG decreased simultaneously by a magnitude of 3 when compared to the baseline. During maximum ejection, IVPG normally is less than 0.5 mmHg and more than 2.5 mmHg in patients with OHCMP. The elimination of LVOT hypertrophy is accompanied by reduced IVPG and the elimination of additional turbulent

Figure 4. Myocardial contraction velocities (mm/s) in the basal (V_1), middle (V_2), and apical (V_3) segments of the interventricular septum in healthy persons and patients with obstructive hypertrophic cardiomyopathy before and after surgery

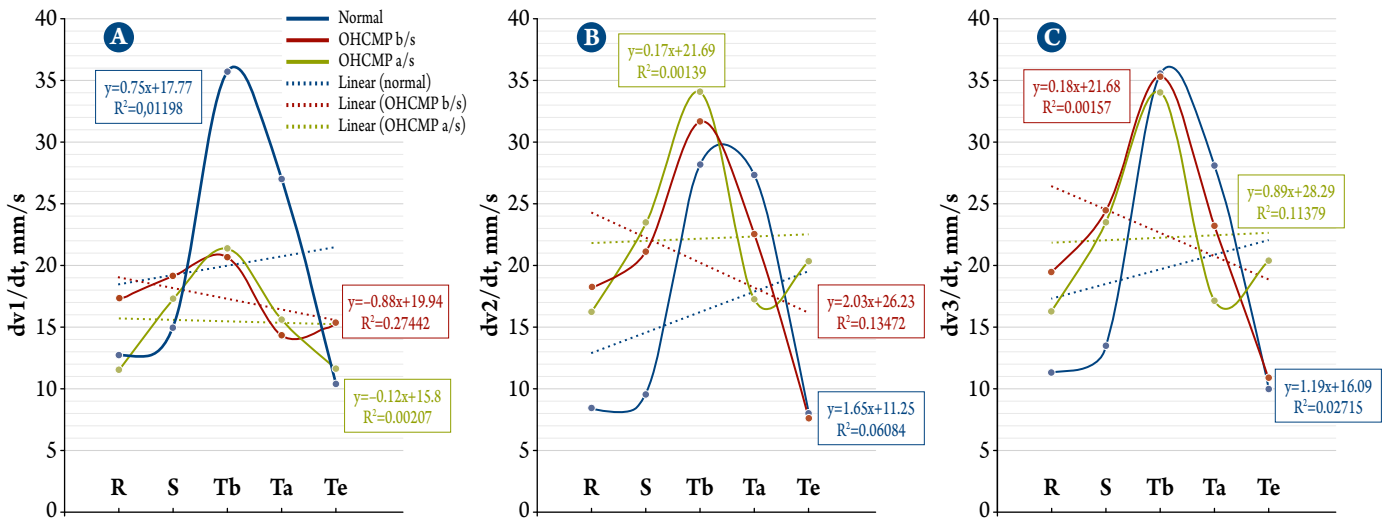


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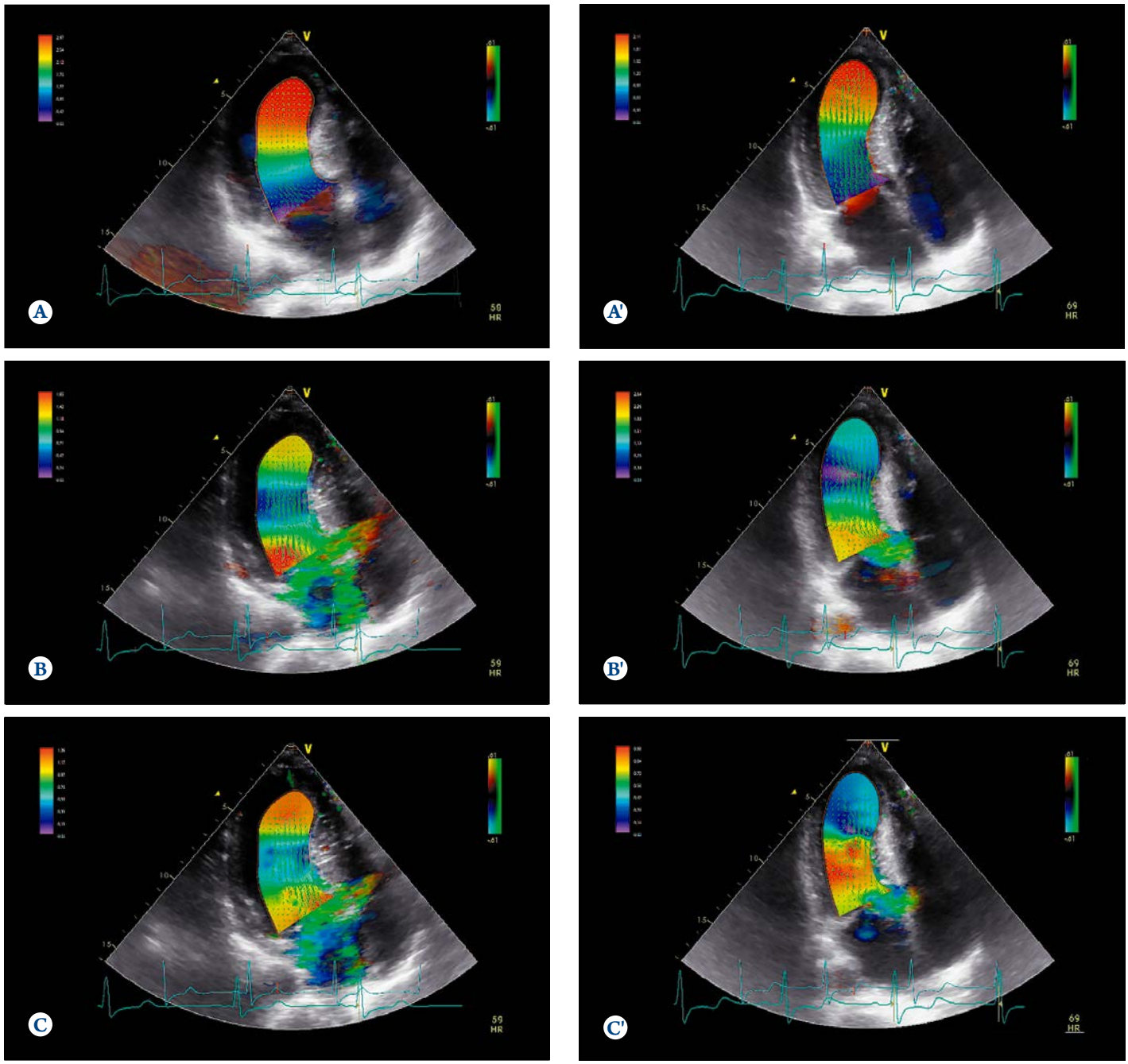
Figure 5. Color mapping of intraventricular pressure gradients superimposed by intracardiac blood flow vectors (green arrows) in patients with OHCMP during systole before surgery: R wave (A), the beginning of T wave (B), the end of T wave (C); on day 7 after surgery: R wave (A'), the beginning of T wave (B'), the end of T wave (C')



To the left is the pressure gradient scale in mmHg, to the right is the blood flow velocity scale.
OHCMP, obstructive hypertrophic cardiomyopathy.

blood flows. Thus, during maximum ejection, IVPG was not more than 0.6–0.9 mmHg, which can be considered as a criterion for the adequacy of the surgery.

Severe IVPG occurs during blood ejection between the narrowed outflow tract and the rest of the LV. Measurements of apex-to-base intraventricular pressure gradient revealed an increase during the maximum ejection and in diastole (Figure 6).

Greatest IVPG is observed during maximum ejection, mainly in the mid-LV. After adequate correction, the apex-to-base pressure gradient is almost normal at all levels during the cardiac cycle.

Discussion

OHCMP is characterized by IVS thickening and restricted motility, reduction of the LV cavity, and enlargement of the left atrium [14, 15]. Movement of the mitral valve (MV) anterior leaflet results in a significant acceleration of blood flow in the LVOT. This is accompanied by an increased pressure gradient and mitral regurgitation grade 1–2. The

pathological motion of the MV anterior leaflet toward the IVS is aggravated by the abnormal arrangement of papillary muscles which is unable to keep the MV leaflets closed. A relatively long closure of the anterior leaflet with the IVS results in IVPG, and its magnitude characterizes the degree of LVOT obstruction. In severe cases, IVPG can reach 80–100 mmHg. The three main factors influencing the magnitude of pressure gradient and the degree of LVOT obstruction are LV myocardial contractility, pre- and post-load dimension. Thus, the anterior systolic motion of the anterior MV leaflet in OHCMP is caused by an imbalance between the anatomy, blood flow velocity and pressure gradient in the LV cavity. The imbalance between blood flow and pressure gradient is certainly associated with structural changes in MV and papillary muscles, which were observed in almost 95–100% of patients with OHCMP. When the pathology was corrected, LVOT obstruction was eliminated, and mitral regurgitation was corrected, and IVPG approached normal values (see Figure 6). The normalization of the systolic and diastolic myocardial velocity can be considered a favorable prognostic sign of the recovery of myocardial function and the adequacy of the correction.

The higher the LV contractility, the greater the linear velocity of the blood flow in the narrowed part of the LVOT. These observations show that myocardial hypertrophy and LV remodeling in OHCMP differ from other pathologies accompanied by myocardial hypertrophy (hypertonic heart disease, aortic stenosis).

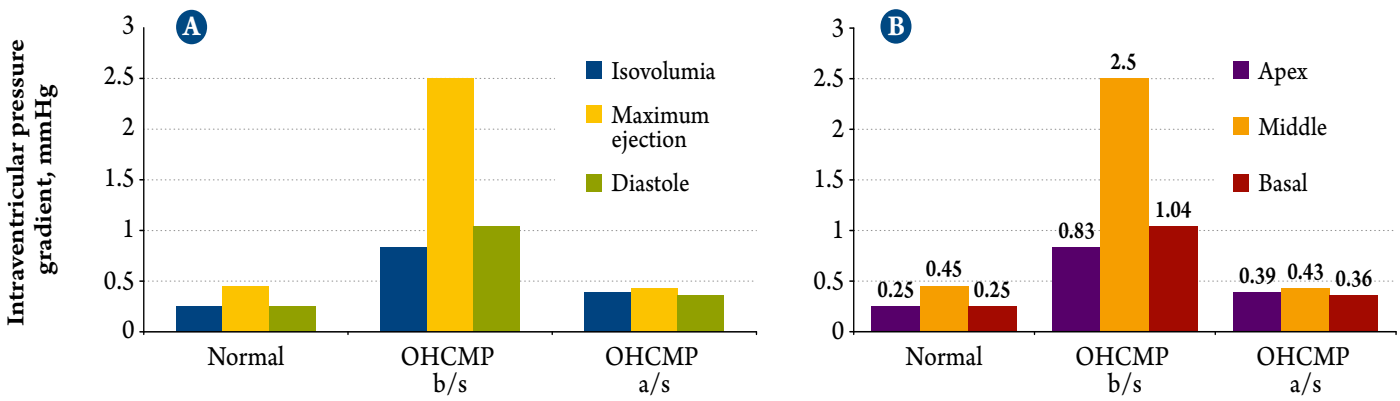
Turbulent blood flows in the heart cavities are essential motion elements to ensure dynamic balance between myocardial stress and arterial pressure during the cardiac cycle [5, 16]. The vector characteristics of the blood flow distribution in the cavities of the heart allow blood flow velocity directly in different parts of the LV to be estimated and calculated. Velocity vectors have several directions: transverse, longitudinal, and oblique relative to the blood flow. There are two forms of motion in the LV: a high-velocity internal flow and a lower-velocity external flow, which helically envelope the internal flow toward and from the apex. These flows determine the contraction and filling forces of the LV. In healthy people the flow is clockwise. This is accompanied by a change in the ventricular geometry with an even distribution of myocardial deformations. The LV remodeling involves altered geometry and disrupted ejection dynamics and diastole.

The LVOT muscle block, which increases as the myocardium contracts, causes a change in direction in blood flow. The main part is directed from the mid-LV along the anterior mitral leaflet. Before the surgery, there is a high-velocity turbulent flow in the LVOT area.

When studying changes in the LV pressure gradient during the cardiac cycle, we observed a mosaic pattern of pressure gradient over virtually the entire cycle. However, this is more likely during the ventricular filling phase. For example, 2D echocardiography showed that the cross-sectional LVOT area at the beginning of systole was less than 3–4 cm^2 in 95% of patients with OHCMP and the mean pressure gradient was 69 mm Hg. Imaging of the intraventricular blood flows and apex-to-base pressure gradients showed that myocardial contraction velocities, attributable to its deformation, are associated with changes in the heart's anatomical structures and influence the formation and direction of the flow.

The use of imaging information relating to myocardial motion over time provides new quantitative characteristics which reflect the heart's condition in a particular patient. Changes in turbulent blood flow in the cardiac cavities can be characteristic of various pathophysiological processes, especially, systolic and diastolic changes in the deformation [16–18]. This effect is essential for the reproduction and understanding of the processes which occur in both normal and abnormal conditions. From a scientific and practical point of view, it was necessary to understand and determine whether the turbulent flow actually occurs in the LV in patients with OHCMP, in what period of the heart cycle, and if so, whether it is possible to diagnose the probable level of occurrence of an additional pressure gradient in the cavity.

Figure 6. Intraventricular pressure gradient in healthy persons and patients with hypertrophic cardiomyopathy before and after surgery during isovolumic stress, maximum ejection, and diastole (A), apical, middle, and basal pressure gradients (B)



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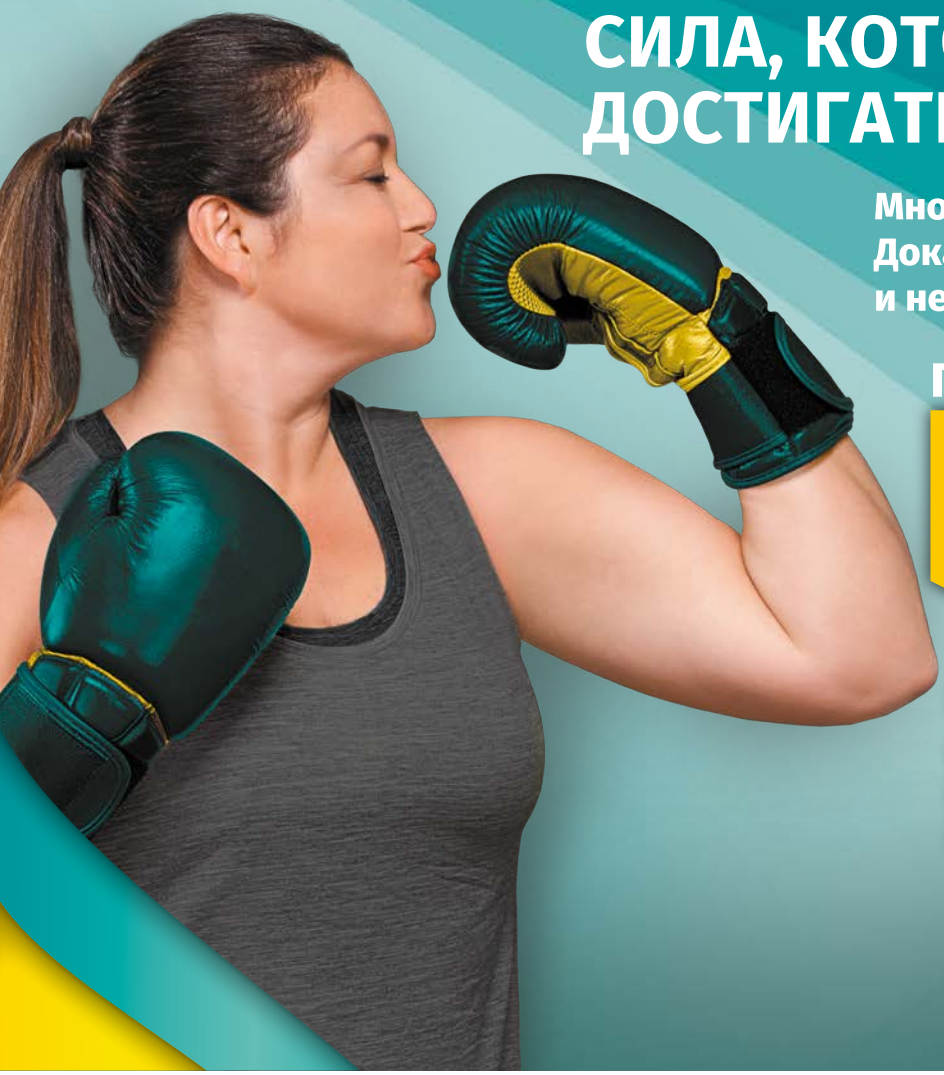

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КРАТКАЯ ИНСТРУКЦИЯ ПО МЕДИЦИНСКОМУ ПРИМЕНЕНИЮ ЛЕКАРСТВЕННОГО ПРЕПАРАТА ДЖАРДИНС®[6]

Регистрационное удостоверение: ЛП-002735. **Торговое наименование:** ДЖАРДИНС. **Международное непатентованное наименование:** эмпаглифлозин. **Лекарственная форма:** таблетки, покрытые пленочной оболочкой. **Состав.** 1 таблетка, покрытая пленочной оболочкой, содержит: *действующее вещество:* эмпаглифлозин – 10,000 мг/25,000 мг. **Фармакотерапевтическая группа.** Гипогликемическое средство для перорального применения – ингибитор натрийзависимого переносчика глюкозы 2 типа. **Код АТХ:** A10BK03. **Показания к применению.** Для терапии сахарного диабета 2 типа у взрослых пациентов с неадекватным гликемическим контролем в дополнение к диетотерапии и физическим упражнениям: в качестве монотерапии; в качестве комбинированной терапии с другими гипогликемическими препаратами, включая инсулин. Препарат показан пациентам с сахарным диабетом 2 типа и высоким сердечно-сосудистым риском* в комбинации со стандартной терапией сердечно-сосудистых заболеваний с целью снижения: общей смертности за счет снижения сердечно-сосудистой смертности; сердечно-сосудистой смертности или госпитализации по поводу сердечной недостаточности. **Высокий сердечно-сосудистый риск определен как наличие хотя бы одного из следующих заболеваний и/или состояний: ИБС (инфаркт миокарда в анамнезе, шунтирование коронарных артерий, ИБС с поражением одного коронарного сосуда, ИБС с поражением нескольких коронарных сосудов); ишемический или геморрагический инсульт в анамнезе; заболевания периферических артерий (с симптоматикой или без).* **Противопоказания.** Гиперчувствительность к эмпаглифлозину и/или любому вспомогательному веществу в составе препарата. Сахарный диабет 1 типа. Диабетический кетоацидоз. Непереносимость лактозы, дефицит лактазы, синдром глюкозо-галактозной мальабсорбции (в состав препарата входит лактозы моногидрат). Почечная недостаточность при СКФ <45 мл/мин/1,73 м². Беременность и период грудного вскармливания. Возраст старше 85 лет. Возраст до 18 лет (в связи с недостаточностью данных по эффективности и безопасности). **С осторожностью.** Пациенты с риском развития гиповолемии (применение гипотензивных препаратов со случаями артериальной гипотензии в анамнезе). При заболеваниях желудочно-кишечного тракта, приводящих к потере жидкости. Возраст старше 75 лет. Применение в комбинации с производным сульфонилмочевины или инсулином. Инфекции мочеполовой системы. Диета с низким содержанием углеводов. Диабетический кетоацидоз в анамнезе. Низкая секреторная активность бета-клеток поджелудочной железы. **Применение при беременности и в период грудного вскармливания.** Применение эмпаглифлозина во время беременности противопоказано ввиду недостаточности данных по эффективности и безопасности. Данные, полученные в доклинических исследованиях у животных, свидетельствуют о проникновении эмпаглифлозина в грудное молоко. Не исключается риск воздействия на новорожденных и детей при грудном вскармливании. Применение эмпаглифлозина в период грудного вскармливания противопоказано. При необходимости применения эмпаглифлозина в период грудного вскармливания кормление грудью следует прекратить. **Способ применения и дозы.** *Монотерапия или комбинированная терапия.* Рекомендуемая начальная доза составляет 10 мг (1 таблетка дозировкой 10 мг) 1 раз в сутки. Препарат следует принимать внутрь, запивая водой. В случае если суточная доза 10 мг не обеспечивает адекватного гликемического контроля, доза может быть увеличена до 25 мг (1 таблетка дозировкой 25 мг) 1 раз в сутки. Максимальная суточная доза составляет 25 мг. Препарат ДЖАРДИНС может приниматься независимо от приема пищи в любое время дня. При совместном применении препарата ДЖАРДИНС с производным сульфонилмочевины или с инсулином может потребоваться снижение дозы производного сульфонилмочевины/инсулина из-за риска развития гипогликемии. *Действия при пропуске приема одной или нескольких доз лекарственного препарата.* При пропуске дозы пациенту следует принять препарат, как только он об этом вспомнит. Не следует принимать двойную дозу в течение одних суток. *Применение препарата в особых группах пациентов.* Применение препарата у пациентов с почечной недостаточностью при СКФ менее 45 мл/мин/1,73 м² противопоказано. Пациентам с СКФ ≥45 мл/мин/1,73 м² коррекции дозы не требуется. Эмпаглифлозин не должен применяться у пациентов с терминальной стадией почечной недостаточности или у находящихся на гемодиализе. Пациентам с нарушениями функции печени коррекции дозы не требуется. **Побочное действие.** Общая частота нежелательных реакций у пациентов, получавших эмпаглифлозин или плацебо, в клинических исследованиях была сходной. Наиболее частой нежелательной реакцией была гипогликемия, отмечавшаяся при применении эмпаглифлозина в комбинации с производным сульфонилмочевины или инсулина. Нежелательные реакции, наблюдавшиеся у пациентов, получавших эмпаглифлозин в плацебоконтролируемых исследованиях, распределены по системно-органным классам с указанием частоты их возникновения согласно рекомендациям ВОЗ: очень часто (≥1/10), часто (от ≥1/100 до <1/10), нечасто (от ≥1/1000 до <1/100). **Очень часто.** *Нарушения со стороны обмена веществ и питания* – гипогликемия (при совместном применении с производным сульфонилмочевины или инсулином). **Часто.** *Инфекционные и паразитарные заболевания* – вагинальный кандидоз, вульвовагинит, баланит и другие генитальные инфекции, инфекции мочевыводящих путей (в том числе пиелонефрит и уросепсис). *Нарушения со стороны кожи и подкожных тканей* – зуд (генерализованный), сыпь на коже. *Нарушения со стороны почек и мочевыводящих путей* – увеличение мочевыделения. *Общие расстройства и нарушения в месте введения* – жажда. *Лабораторные и инструментальные данные* – повышение концентрации липидов в плазме крови. **Нечасто.** *Нарушения со стороны кожи и подкожных тканей* – крапивница. *Нарушения со стороны сосудов* – гиповолемия. *Нарушения со стороны почек и мочевыводящих путей* – дизурия. *Лабораторные и инструментальные данные* – снижение скорости клубочковой фильтрации, повышение концентрации креатинина в плазме крови, повышение гематокрита. *Полный перечень нежелательных реакций с указанием их абсолютной частоты представлен в инструкции по медицинскому применению.* **Условия хранения.** При температуре не выше 25 °С. Хранить в недоступном для детей месте. **Срок годности.** 3 года. Не следует принимать препарат по истечении срока годности. **Условия отпуска.** По рецепту. ***Полная информация представлена в инструкции по медицинскому применению.***

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The maximum intensity is observed during the ejection phase. After the stage of the lower blood flow velocity the stage of rapid increase in the diastolic velocity occurs, with the maximum reached at the base. It is not clear yet what causes this effect, and perhaps myocardial fibrosis plays a particular role. The issues of myocardial deformation in hypertrophy in patients with valvular heart disease, hypertensive heart disease, and hypertrophic cardiomyopathy are currently a matter of extensive discussion in the literature [11]. The relationship between myocardial fibrosis and deformation is addressed in the literature, and is based on the results of echocardiography and magnetic resonance imaging.

Reduced myocardial deformation was shown to be characteristic of the pathological myocardium [11]. Indeed, some patients had no improvements in the early posto-perative period. This may be due to the fact that the longitudinal deformation in these patients is associated with pressure gradient and also depends on some factors, such as damaged cardiomyocytes. Myocardial deformation undoubtedly largely determines the function of the myocardium and, particularly, affects the velocities and turbulence of blood flow in the cardiac cavities.

Surgical correction of the pathology normalized the systolic and diastolic functions of the myocardium by improving perfusion and normalizing coronary circulation due to lower LV pressure [4, 18].

Studies to assess the efficacy of surgical correction of obstructive hypertrophy must continue, first of all, to determine pressure gradients and blood flows and their correlations, since they are the main factors of maintaining SE and relieving LV from overload. This, in turn, will contribute to the development of new surgical treatments in OHCMP.

The presence of turbulence determines the potential activity, which allows it to be evaluated qualitatively. Based on the findings of blood flow and IVPG in the LV, it should be noted that, in patients with OHCMP, these two processes are inextricably linked and are virtually predictors of surgical treatment efficacy. Other authors obtained the same results after the elimination of LVOT obstruction [14, 17]. Decreasing the apex-to-base gradient in the LV results in the normalization of blood flow and the improvement of intracardiac hemodynamics. The LVOT pressure gradient after surgery does not exceed 15–20 mmHg. The myocardial function can be assessed by systolic and end-systolic myocardial tension, changes in the contraction velocity and stress, ventricular blood flows, and apex-to-base pressure gradient.

However, patients with OHCMP need dynamic observation and the assessment of blood flow and IVPG after surgery. The quantitative assessment of pressure gradients and vortex blood flows shown in this way, allowed for surgical correction of the pathology in patients with OHCMP in the clinical setting to be evaluated.

Conclusion

Intraventricular pressure gradient directly affects the systolic and diastolic function of the myocardium. The reduction of the pressure gradient in the left ventricle outflow tract and the minimization of the apex-to-base pressure gradient in the left ventricular cavity is one of the indicators to measure the efficacy of surgical correction of obstructive hypertrophic cardiomyopathy. The elimination of hypertrophy and the normalization of mitral valve function contribute to the normalization of intraventricular blood flows. Also, the values of myocardial contraction velocity during the cardiac cycle reflect early changes in the left ventricular function in a reasonably objective fashion. The clinical use of the evaluation of the outcomes of the surgical treatment of obstructive hypertrophic cardiomyopathy is based on a new diagnostic algorithm of simultaneous recording of myocardial contraction velocities, intraventricular pressure gradient, and blood flows according to echocardiography.

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