DOI: 10.20514/2226-6704-2023-13-3-181-195
УДК 616.127-007.61-036-07
EDN: GGLHPG

**Е.В. Резник*[1,2], Т.Л. Нгуен[1], М.С. Дикаева[1], И.О. Сиренова[3], А.В. Саликов[3], О.В. Гаврилова[2], Е.Н. Платонова[2], Г.Н. Голухов[2]**

[1]— ФГАОУ ВО РНИМУ им. Н.И. Пирогова МЗ РФ, Москва, Россия
[2]— ГБУЗ ГКБ № 31 ДЗМ, Москва, Россия
[3]— ГБУЗ ГКБ им. В.М. Буянова ДЗМ, Москва, Россия

# ОСОБЕННОСТИ ДИАГНОСТИКИ И ТЕЧЕНИЯ ГИПЕРТРОФИЧЕСКОЙ КАРДИОМИОПАТИИ В РЕАЛЬНОЙ КЛИНИЧЕСКОЙ ПРАКТИКЕ

**E.V. Reznik*[1,2], T.L. Nguyen[1], M.S. Dikaeva[1], I.O. Sirenova[3], A.V. Salikov[3], O.V. Gavrylova[2], E.N. Platonova[2], G.N. Golukhov[2]**

[1]— Pirogov Russian national research medical University of the Ministry of healthcare of the Russian Federation, Moscow, Russia
[2]— City Clinical Hospital № 31 of Healthcare Department of Moscow, Moscow, Russia
[3]— City Clinical Hospital n.a. V.M. Buyanova of Healthcare Department of Moscow, Moscow, Russia

# Features of Diagnostics and Course of Hypertrophic Cardiomyopathy in Real Clinical Practice

**Резюме**

**Введение и цель.** Гипертрофическая кардиомиопатия (ГКМП) характеризуется наличием утолщения стенки левого желудочка (ЛЖ), не связанного с увеличением постнагрузки (артериальной гипертензией и стенозом устья аорты). В большинстве случаев ГКМП обусловлена мутациями в генах саркомерных белков и наследуется по аутосомно-доминантному механизму. В ряде случаев ГКМП может быть обусловлена накоплением в миокарде таких веществ, как амилоид, гликоген и др. Целью нашей работы стало проанализировать особенности диагностики и течения ГКМП в реальной клинической практике. **Материал и методы.** Проведен ретроспективный анализ медицинской документации 80 пациентов (56,3 % мужчин) с ГКМП, диагностированной в многопрофильном стационаре г. Москвы в период с 2007 по 2021 год. Диагноз ГКМП у всех пациентов был установлен на основании данных эхокардиографии. Медиана (здесь и далее в скобках указаны 25- и 75-процентили) возраста составила 57 (48,5; 63) лет. Продолжительность госпитализации составила 8 (6; 12,5) дней. **Результаты.** Причиной госпитализации являлись синдром стенокардии у 35 %, подозрение на острый коронарный синдром у 16,3 %, пароксизм фибрилляции предсердий (ФП) у 11,3 %, другие нарушения ритма у 2,5 %, декомпенсация хронической сердечной недостаточности у 11,3 %, обмороки у 7,5 %, гипертонический криз у 3,8 %, необходимость проведения коронароангиографии у 3,8 %, постановки электрокардиостимулятора у 2,5 %, имплантации кардиовертера-дефибриллятора у 1,2 %, медицинского освидетельствования для решения вопроса о годности к воинской службе у 1,2 %, острое нарушение мозгового кровообращения у 1,2 %, гипотония у 1,2 %, лекарственная брадикардия у 1,2 % пациентов. До анализируемой госпитализации инфаркт миокарда в анамнезе был диагностирован у 15 %, артериальная гипертензия — у 53,8 %, хроническая сердечная недостаточность — у 77,6 %, хроническая болезнь почек — у 21,3 % пациентов. Толщина стенки ЛЖ ≥1,5 см выявлена у 91,2 %. Симметричная форма гипертрофии ЛЖ имела место у 22,1 %, апикальная — у 5,2 %, гипертрофия папиллярной мышцы — у 1,3 %, ассиметричная гипертрофия межжелудочковой перегородки — у 71,4 % пациентов. Постоянная обструкция выносящего тракта ЛЖ (ОВТ ЛЖ) выявлена у 62,8 % (9,0 % пациентов была выполнена септальная редукция в анамнезе), преходящая ОВТ ЛЖ — у 1,3 %, необструктивная ГКМП — у 35,9 %. Фракция выброса (ФВ) ЛЖ (по Симпсону) составила 63 (55-70)%, ХСН со сниженной ФВ ЛЖ <40 % выявлена у 3,8 %, с умеренно сниженной ФВ ЛЖ (40-49 %) — у 5 %, с сохраненной ФВ ЛЖ — у 68,8 % пациентов. У 47,5 % имело место переднесистолическое

*Контакты: Елена Владимировна Резник, e-mail: elenaresnik@gmail.com
*Contacts: Elena V. Reznik, e-mail: elenaresnik@gmail.com
ORCID ID: http://orcid.org/0000-0001-7479-418X

движение передней створки митрального клапана, у 7,14 % описано пролабирование передней створки митрального клапана. Митральная регургитация зарегистрирована у 75 % пациентов. Фибрилляцией предсердий (ФП) страдали 45 % пациентов с ГКМП: постоянной формой 15 %, пароксизмальной 23,8 %, персистирующей 6,2 % пациентов. За время госпитализации желудочковая тахикардия зарегистрирована у 7,5 %, наджелудочковая тахикардия — у 3,8 %. Нарушения проводимости отмечены у 36,3 % пациентов, из них атриовентрикулярная блокада у 6,3 %, блокада правой ножки пучка Гиса у 21,3 %, левой ножки — у 15 %, синдром Вольффа–Паркинсона–Уайта — у 1,3 %. Имплантация электрокардиостимулятора в анамнезе была у 5 %, в том числе в связи с приступами Морганьи-Эдамса-Стокса — у 3,8 % пациентов. За время наблюдения, медиана которого составила 87 (интерквартильный размах 45-131,5) месяцев, умерло 13,8 % пациентов с ГКМП. У умерших пациентов достоверно чаще встречалась ОВТ ЛЖ (у умерших 100 %, у живых 58,2 %, p = 0,006) и ФП (у умерших 72,7 %, у живых 40,6 %, p=0,047). Генетическое тестирование и исключение фенокопий ГКМП не было проведено во время госпитализации и не было рекомендовано ни одному больному. **Заключение.** В реальной клинической практике в большинстве случаев проводится лишь фенотипическая диагностика ГКМП по данным эхокардиографии, не проводится скрининг на генетические мутации и инфильтративные заболевания сердца, фенотипически неотличимые от ГКМП. Необходимо широкое внедрение генетического тестирования и скрининга на инфильтративные заболевания сердца для своевременной диагностики патологии, требующей назначения специфической патогенетической терапии для улучшения прогноза пациентов.

***Ключевые слова:*** *инфильтративные заболевания сердца, гипертрофическая кардиомиопатия, хроническая сердечная недостаточность, фенокопии, генетика, вторичная ГКМП, амилоидоз, болезнь Фабри*

## Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

## Источники финансирования

Авторы заявляют об отсутствии финансирования при проведении исследования

Статья получена 10.07.2022 г.
Принята к публикации 15.02.2023 г.

**Для цитирования:** Резник Е.В., Нгуен Т.Л., Дикаева М.С. и др. ОСОБЕННОСТИ ДИАГНОСТИКИ И ТЕЧЕНИЯ ГИПЕРТРОФИЧЕСКОЙ КАРДИОМИОПАТИИ В РЕАЛЬНОЙ КЛИНИЧЕСКОЙ ПРАКТИКЕ. Архивъ внутренней медицины. 2023; 13(3): 181-195. DOI: 10.20514/2226-6704-2023-13-3-181-195. EDN: GGLHPG

## Abstract

**Introduction and purpose.** Hypertrophic cardiomyopathy (HCM) is characterized by left ventricular (LV) wall thickening not associated with increased afterload (hypertension and aortic stenosis), is usually caused by mutations in sarcomeric protein genes, and is inherited in an autosomal dominant manner. Unlike HCM, myocardial hypertrophy in its phenocopies is associated with the accumulation of substances such as amyloid, glycogen, etc. in the myocardium. The aim of our work was to analyze the features of the diagnosis and course of HCM in real clinical practice. **Material and methods.** A retrospective analysis of medical records of 80 patients (56.3 % of men) discharged with a diagnosis of HCM from a multidisciplinary hospital in Moscow in the period from 2007 to 2021 was carried out. The diagnosis of HCM in all patients was established on the basis of echocardiography data. The median age (25th and 75th percentiles are indicated in brackets) was 57 (48.5; 63) years. The duration of hospitalization was 8 (6; 12.5) days. **Results.** The reason for hospitalization was angina syndrome in 35 %, suspicion of acute coronary syndrome in 16.3 %, paroxysmal atrial fibrillation (AF) in 11.3 %, decompensation of chronic heart failure in 11.3 %, syncope in 7.5 % %, hypertensive crisis in 3.8 %, coronary angiography in 3.8 %, pacemaker implantation in 2.5 %, consultation with an arrhythmologist in 2.5 %, implantation of a cardioverter-defibrillator in 1.2 %, medical examination to resolve the issue of fitness for military service in 1.2 %, acute cerebrovascular accident in 1.2 %, hypotension in 1.2 %, drug bradycardia in 1.2 % of patients. Before hospitalization, a history of myocardial infarction was diagnosed in 15 %, arterial hypertension — in 53.8 %, chronic heart failure — in 77.6 %, chronic kidney disease — in 21.3 % of patients. Prior to the analyzed hospitalization, a history of myocardial infarction was diagnosed in 15 %, arterial hypertension in 53.8 %, chronic heart failure in 77.6 %, chronic kidney disease in 21.3 % of patients. LV wall thickness ≥1.5 cm was detected in 91.2 %, symmetrical form of hypertrophy — 22.1 %, apical — 5.2 %, papillary muscle hypertrophy — 1.3 %, interventricular septum — 71.4 % of patients. Permanent obstruction of the LV outflow tract (LVOTO) was detected in 62.8 % (9.0 % of patients had a history of septal reduction), transient LVOTO — in 1.3 %, non-obstructive HCM — in 35.9 %. The ejection fraction (EF) of the LV (according to Simpson) was 63 (55-70) %, CHF with reduced LV EF <40 % was detected in 3.8 %, with a moderately reduced LV EF (40-49 %) — in 5 %, with preserved LV EF — in 68.8 % of patients. Anterior systolic movement of the anterior leaflet of the mitral valve occurred in 47.5 %, prolapse of the anterior leaflet of the mitral valve was described in 7.14 %. Mitral regurgitation was registered in 75 % of patients. 45 % of patients with HCM suffered from AF: permanent 15 %, paroxysmal 23.8 %, persistent 6.2 % of patients. During hospitalization, ventricular tachycardia was registered in 7.5 %, supraventricular tachycardia — 3.8 %, conduction disturbances were noted in 36.3 % of patients, of which atrioventricular block in 6.3 %, blockade of the right bundle branch block in 21.3 %, left bundle branch block in 15 %, and Wolff-Parkinson-White syndrome in 1.3 % . Implantation of a pacemaker in history was in 5 %, including in connection with Morgagni-Adams-Stokes attacks — in 3.8 % of patients. During a median follow-up of 87 (interquartile range 45–131.5) months, 13.8 % of patients with HCM died. In deceased patients, LVOTO was significantly more common (in the dead 100 %, in the living 58.2 %, p = 0.006) and AF (in the dead 72.7 %, in the living 40.6 %, p = 0.047). Genetic testing and exclusion of HCM phenocopies was not performed during hospitalization and was not recommended for any patient. **Conclusion.** In real clinical practice, in most cases, only phenotypic diagnosis of HCM is carried out according to echocardiography, and screening for genetic mutations and HCM phenocopies is not performed. It is necessary to widely introduce genetic testing and screening for HCM phenocopies for the timely diagnosis of pathology that requires the appointment of specific pathogenetic therapy to improve the prognosis of patients.

***Key words:*** *infiltrative heart disease, hypertrophic cardiomyopathy, chronic heart failure, phenocopies, genetics, secondary HCM, amyloidosis, Fabry disease*

## Conflict of interests

The authors declare no conflict of interests

## Sources of funding

The authors declare no funding for this study

Article received on 10.07.2022
Accepted for publication on 15.02.2023

**For citation:** Reznik E.V., Nguyen T.L., Dikaeva M.S. et al. Features of Diagnostics and Course of Hypertrophic Cardiomyopathy in Real Clinical Practice. The Russian Archives of Internal Medicine. 2023; 13(3): 181-195. DOI: 10.20514/2226-6704-2023-13-3-181-195. EDN: GGLHPG

HCM — hypertrophic cardiomyopathy, LV –left ventricle, EF — ejection fraction, CHF — chronic heart failure, CHFpEF — chronic heart failure with preserved ejection fraction, ECG — electrocardiogram, EchoCG — echocardiography, NT-proBNP — N-terminal pro brain natriuretic peptide, hsTn — high sensitive troponin, LVH — left ventricular hypertrophy, AF — atrial fibrillation, CAG — coronary angiography, AH — arterial hypertension, GFR — glomerular filtration rate, LVOTO — left ventricular outflow tract obstruction

## Introduction

Hypertrophic cardiomyopathy (HCM) is the most common genetic cardiovascular disease worldwide. Its prevalence in the general population is 1 per 500 people [1]. This heart disorder is characterized by unexplained left ventricular hypertrophy (LVH) in the absence of other cardiac and noncardiac conditions that could lead to its development [1]. Hypertrophic cardiomyopathy caused by mutations of genes encoding the sarcomere proteins or associated to it account for more than half of all disease case [1]. There have been 1,500 mutations identified in at least 15 genes encoding the sarcomere proteins [1].

One of the criteria for HCM diagnosis in adults is increased wall thickness ≥15 mm in one or more LV segments (determined by any visualization methods: EchoCG, MRI/CT), which cannot be explained by an increase in pressure load alone [1]. In some patients, atypical HCM is reported, which is manifested as less pronounced LVH, concentric LVH, apical hypertrophy, left ventricular outflow tract obstruction with systolic anterior motion of the anterior mitral leaflet, provided that a high risk of sudden death persists [1]. In some cases, it is difficult to differentiate HCM from hypertensive or athlete's heart.

Moreover, a pronounced increased LV wall thickness can be observed in some infiltrative heart diseases, which are called HCM phenocopies. They include several disorders such as glycogen storage disorders, mucopolysaccharidosis, amyloidosis, Fabry disease, etc. [1–3] Hypertrophic cardiomyopathy and its phenocopies differ both in hypertrophy pathogenesis and clinical features, course, and prognosis, due to which both clinical and molecular genetic diagnosis is required to establish HCM in clinical practice.

**The study is aimed at** analyzing the specificity of HCM diagnosis and course in real-life clinical practice.

## Materials and methods

A prospective, cross-sectional study was performed. The analysis included all cases of HCM diagnosis following the results of electronic database of the multi-speciality hospital for the period 2007 through 2021 and medical records of the specified 80 patients (43.7 % women, 56.3 % men) with HCM. The HCM diagnosis was established based on echocardiographic (EchCG) data. Maximum LV wall thickness at diastole ≥15 mm, unexplained by abnormal pre- and postload [4], or LV wall thickness at diastole ≥13 mm in relatives of persons with HCM or in persons with a positive genotype[5] were used as diagnostic criteria for HCM.

The median age in patients with HCM was 57 years (hereinafter, an interquartile range 48.5; 63 is given in the brackets). Among patients with HCM, men slightly prevailed: 56.3 % (n = 45). Causes of hospitalization in patients with HCM were diverse, including angina pectoris in 28 (35 %), acute coronary syndrome in 13 (16.3 %), paroxysmal atrial fibrillation (AF) in 9 (11.3 %), decompensated chronic heart failure (CHF) in 9 (11.3 %), syncope and presyncope in 6 (7.5 %) patients (Figure 1).

A post hoc analysis of EchoCG findings obtained by highly qualified specialists using ultrasonic diagnostic apparatuses of expert class. All LV measurements were performed in accordance with the guidelines of the American Society of Echocardiography. LV ejection fraction (EF) was measured using the biplane method of disks (modified Simpson method). The left ventricular outflow tract obstruction (LVOTO) was diagnosed using the Doppler echocardiography at maximum (peak) pressure gradient in the left ventricular outflow tract ≥30 mm Hg at rest or during provocative testing. Asymmetrical septal HCM was diagnosed at interventricular septum (IVS) thickness ≥15 mm and the ratio of IVS/LV posterior wall thickness ≥1.3 [1]. Apical HCM was diagnosed in patients with LV hypertrophy limited to left ventricular apex [1]. Images for papillary muscle measurements were obtained from the parasternal short axis projection. The maximum diameters of the anterolateral and posteromedial papillary muscles were measured at the midline in the parasternal short axis view at the end of diastole. The horizontal diameter was measured in parallel with a line drawn between the center of the LV cavity and the papillary muscle at the point of its attachment to the LV wall. The vertical diameter was measured perpendicular to the above-described line.

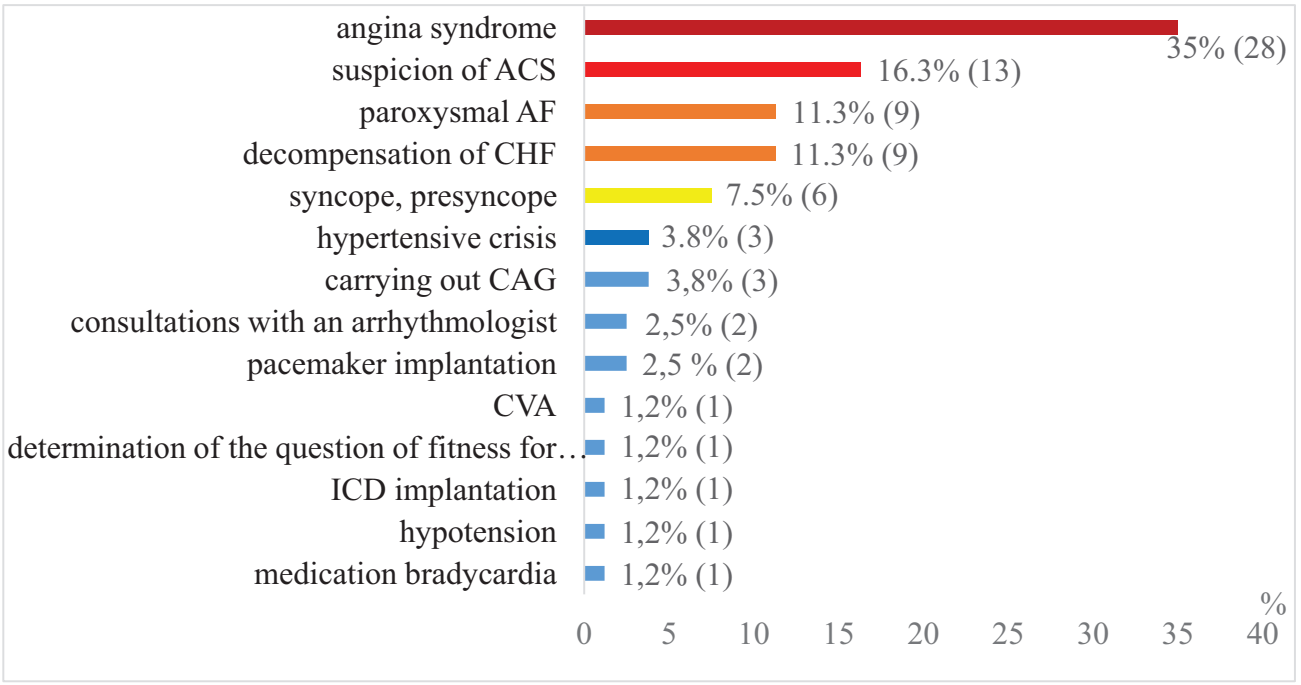


***Figure 1.*** *Reasons for hospitalization in patients with HCM*
**Note:** ACS — acute coronary syndrome, AF — atrial fibrillation, CHF — chronic heart failure, CAG — coronary angiography, CVA — acute cerebrovascular accident, ICD — implantable cardioverter-defibrillator

According to the Kobayashi criteria, papillary muscle hypertrophy was defined by a diameter ≥11 mm of at least one papillary muscle in the horizontal or vertical direction or in both directions [5]. The pulmonary artery systolic pressure (PASP) was estimated noninvasively using transthoracic echocardiographic data on peak tricuspid regurgitation rate, taking into account the diameter of inferior vena cava and its collapse during inspiration. Pulmonary hypertension was diagnosed at values >30 mm Hg.

The analysis included all available electrocardiograms (ECG); Cornell criteria, Sokolow-Lyon index, and electrocardiographic QRS voltage were assessed. The voltage in extremity leads <5 mm or precordial leads <10 mm was considered low [2]. QRS complex that are ventricular in origin and artifacts were disregarded.

The glomerular filtration rate (GFR) was calculated using the CKD-EPI formula to assess the functional state of the kidneys. The presence and severity of proteinuria were evaluated based on the urinalysis findings. The data obtained in the laboratory investigations conducted during and before the index hospitalization were regarded. A clinical and instrumental criterion for chronic kidney disease (CKD) was a persistent decrease in GFR <60 mL/min/1.73 $m^2$ and/or urine markers of kidney injury for 3 months or more. The levels of N-terminal pro brain natriuretic peptide (NT-proBNP), serum troponin, and urinary albumin excretion were not assessed for technical reasons.

In real-life clinical practice, no genetic testing or exclusion of HCM phenocopies was performed in any patient. In 2020-2022, to exclude HCM phenocopies in 55 patients with LVH (including 5 (9.1 %) of the patients analyzed above), genetic testing was performed as part of the research work at the Department of Propaedeutics of Internal Medicine, Faculty of Medicine, N.I. Pirogov Russian National Research Medical University, Ministry of Health of the Russian Federation.

Patients' prognosis was assessed via telephone calls and analysis of available medical records 87 (45–131.5) months later. The endpoint was all-cause mortality.

Statistical analysis was performed using SPSS 26 software. Since some of the obtained data did not follow the normal distribution law, non-parametric methods were used. The central tendency and attribute variance are presented as the median and the interquartile range. Intergroup differences in two independent groups were assessed using the Mann–Whitney test. In the qualitative data analysis, the absolute and relative frequencies were determined for each attribute value. When comparing the relative frequencies of the attribute in two groups and the correlation coefficients, hypotheses of their equality were tested using a two-tailed statistical significance test. The chi-square test (maximum likelihood method) was used to compare groups by qualitative characteristics. The patients' survival rate was assessed using the Kaplan–Meier survival curves. The level $p<0.05$ was considered statistically significant.

## Results

Over the period 2007 to 2021, in one of the multispeciality hospitals in Moscow, HCM was diagnosed in 80/560,901 hospitalized patients (0.0143 %; 14.3/100,000 patients/year, 1:6,993 of hospitalized patients a year). All patients with HCM were discharged from the Cardiology Department (Table 1).

On admission to hospital, complaints of angina pain/heaviness in the chest in 44 (55 %) patients with HCM; dyspnea in 41 (51.3 %); weakness and/or fatigue in 30 (37.5 %); palpitation, impaired cardiac function in 25 (31.3 %), fainting/presyncope in 10 (12.5 %), lower extremity edema in 7 (8.8 %) patients.

According to the patients' medical history, 12 (15 %) patients had previously diagnosed miocardial infarction (MI), without significant coronary artery stenosis on coronary angiography in 6 (50 %), with evidence-based coronary artery stenosis in 3 (3.8 %) of them; stenting of the infarct-related artery was performed in 2 (2.5 %) of them.

43 (53.8 %) of patients had a history of arterial hypertension (AH): grade 1 in 6 (7.5 %), grade 2 in 9 (11.3 %), and grade 3 in 28 (35 %) patients. On admission, arterial hypertension was detected in 1 (1.3 %) patient.

14 (17.5 %) of patients with HCM had a history of type 2 diabetes mellitus (DM); impaired glucose tolerance was detected on admission in 10 (12.5 %) patients.

The diagnosis of CHF was recorded in 62 (77.6 %) of patients with HCM: 71.1 % had New-York Heart Association (NYHA) functional class II/III; 61.8 % had stage IIA CHF according to the Vasilenko-Strazhesko classification. Among the signs of CHF, hydrothorax was detected in 5 (8.1 %) patients, of whom 3 (4.8 %) had right-sided hydrothorax; 2 (3.2 %) had bilateral hydrothorax; 7 (11.3 %) had hepatomegaly; 1 (1.6 %) had ascites.

On EchoCG, IVS thickness was 1.8 (1.4–2.3) cm; basal IVS segment thickness was 2.06 (1.8–2.3) cm; LV posterior wall thickness was 1.4 (1.2–1.6) cm. IVS and/or LV posterior wall thickness >1.5 cm was detected in 91.2 % patients with HCM. Symmetric form of HCM in 22.1 %, apical form in 5.2 %, papillary muscle hypertrophy in 1.3 %, IVS hypertrophy in 71.4 % of patients. Obstructive HCM was diagnosed in 64.1 % (latent LV ventricular outflow tract obstruction (LVOTO) was detected in 1.3 %); nonobstructive form was diagnosed in 35.9 % of patients with HCM. A history of septal reduction surgery was recorded in 9.0 % of patients. The median maximum pressure gradient in the left ventricular outflow tract (LVOT) in patients with LVOTO was 53 (28–105) mm Hg; the mean pressure gradient in (LVOT) was 30 (15–49) mm Hg. The left atrium anteroposterior diameter was 4.5 (4.0–5.2) cm; its volume was 102.5 (63–140) mL; the right atrium area was 16 (14.5–22.5) $cm^2$. The left ventricular end-diastolic diameter was 4.3 (4.0–4.8) cm; its end-diastolic volume was 80 (70–100) mL. LV EF was 63 (55–70)%. Chronic heart failure with reduced LV ejection fraction <40 % was diagnosed in 3 (3.8 %), with moderately reduced LV EF in 4 (5 %), with preserved LV EF(CHFpEF) in 55 (68.8 %) patients (Figure 2).

***Table 1.*** *Frequency of diagnosing HCM in a multidisciplinary hospital for the period from 2007 to 2021*

| Year | Number of patients treated in hospital | Number of patients diagnosed with HCM | % of patients diagnosed with HCM among those treated in a hospital | HCM diagnostic frequency/ 100 thousand people/year |
|---|---|---|---|---|
| 2007 | 20212 | 6 | 0,0297 | 29,70 |
| 2008 | 26134 | 5 | 0,0191 | 19,10 |
| 2009 | 30268 | 6 | 0,0198 | 19,82 |
| 2010 | 28855 | 8 | 0,0277 | 27,72 |
| 2011 | 30569 | 4 | 0,0131 | 13,09 |
| 2012 | 29720 | 5 | 0,0168 | 16,82 |
| 2013 | 30078 | 6 | 0,0199 | 19,95 |
| 2014 | 39735 | 3 | 0,0076 | 7,55 |
| 2015 | 42024 | 9 | 0,0214 | 21,42 |
| 2016 | 46047 | 4 | 0,0087 | 8,69 |
| 2017 | 45909 | 4 | 0,0087 | 8,71 |
| 2018 | 49604 | 10 | 0,0202 | 20,16 |
| 2019 | 47027 | 5 | 0,0106 | 10,63 |
| 2020 | 45206 | 3 | 0,0066 | 6,64 |
| 2021 | 49513 | 2 | 0,0040 | 4,04 |
| **2007-2021** | **560901** | **80** | **0,0143** | **14,26** |

**Note:** HCM — hypertrophic cardiomyopathy

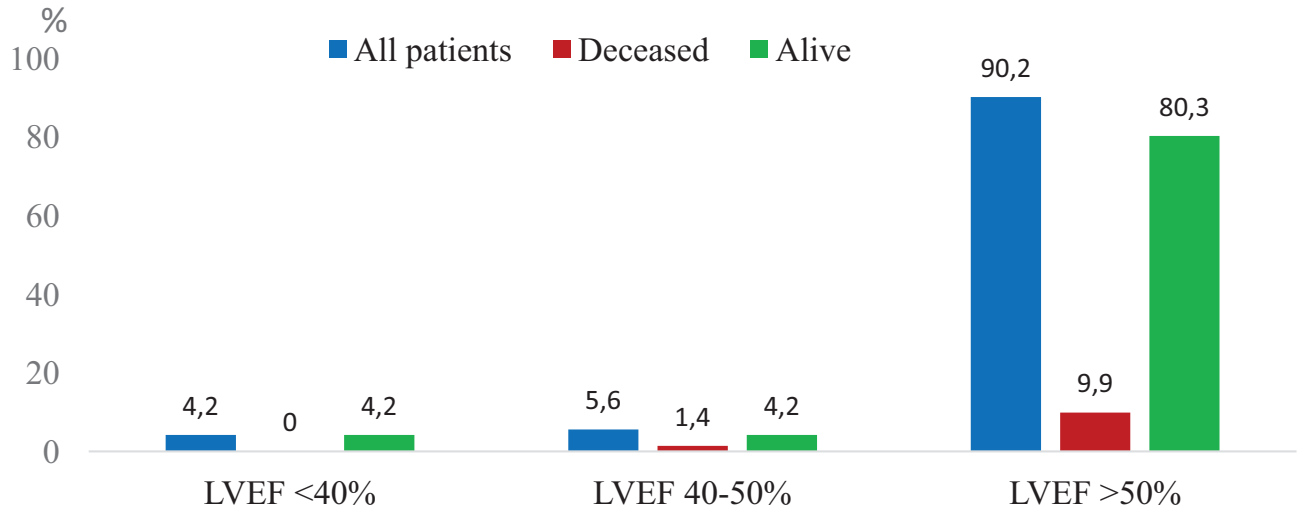


***Figure 2.*** *Systolic function of the left ventricle in patients with HCM*
**Note:** LVEF — left ventricular ejection fraction

Systolic anterior motion of the mitral leaflet was recorded in 38 (47.5 %) patients. Mitral valve prolapse was recorded in 7.14 % patients. Secondary mitral regurgitation was registered in 60 (75 %) patients.

EchoCG findings revealed calcinosis of cardiac structures in 13 (16.3 %) patients: only calcinosis of mitral valve leaflets in 3 (3.8 %); only calcinosis of aortic valve in 2 (2.5 %); calcinosis of both mitral and aortic valves in 8 (10 %).

Diffuse left ventricular (LV) hypokinesis was detected in 5 (7.2 %) patients, local hypokinesis in 5 (7.2 %); akinesis was detected in 1 (1.4 %) patient (all these patients had a history of myocardial infarction); 2 (2.9 %) patients had LV apical dissynergy against a background of complete left bundle branch block.

Signs of pulmonary hypertension were detected in 21 (35 %) patients, for whom mean pulmonary arterial pressure (MPAP) was calculated; in 20 (33.3 %) patients, MPAP was not recorded in the EchoCG protocol. In patients with HCM, 14 (23.3 %) had grade 1 pulmonary hypertension (MPAP <50 mm Hg), 5 (8.3 %) had grade 2 PH (MPAP 50–80 mm Hg), and 2 (3.4 %) had grade 3 PH (MPAP >80 mm Hg).

Diastolic LV dysfunction was detected in 37 (51.4 %) patients with HCM: 24 (33.3 %) had relaxation disorder, 12 (16.7 %) had pseudonormalization, 1 (1.4 %) had restriction; 5 (6.9 %) had normal diastolic function in their medical records. In 30 (41.7 %) patients, diastolic LV function was not assessed (Figure 3).

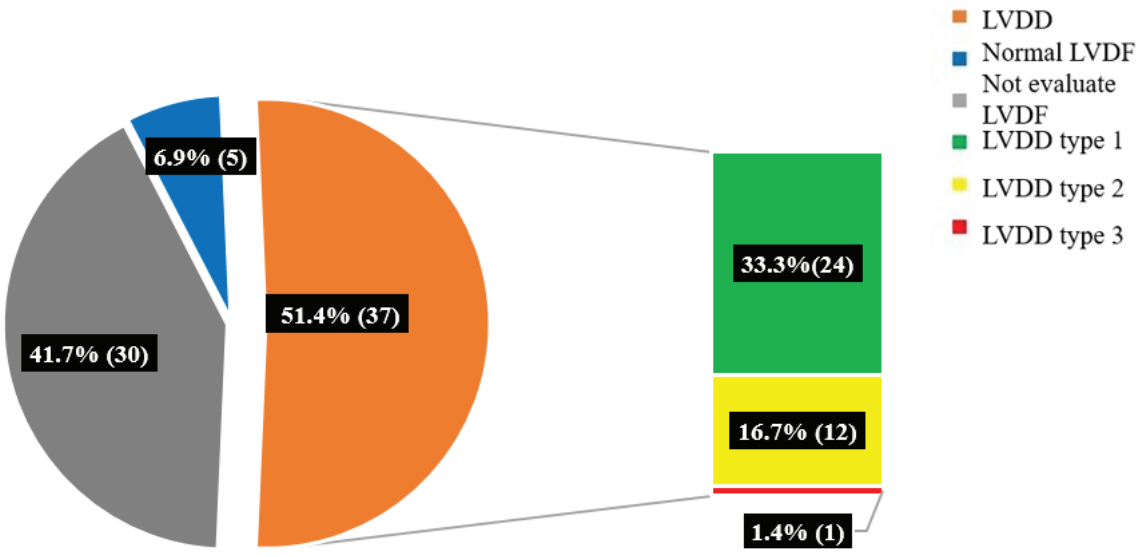


***Figure 3.*** *Diastolic function of the left ventricle in patients with HCM*
**Note:** LVDD — left ventricular diastolic dysfunction, LVDF — left ventricular diastolic function

Pericardial effusion was detected in 9 (12.5 %) patients.

The analysis of available ECG data recorded during the last hospitalization revealed voltage signs of LVH in 36 (48 %), low-voltage on ECG in 1 (1.3 %) patient (Figure 4). A negative T wave in precordial leads (often in V2–V6) was recorded in 36 (48 %) patients. An abnormal Q wave on ECG was recorded in 8 (10 %) patients (all of them had a history of MI/postinfarction cardiosclerosis (PICS)): 4 (5 %) in inferior leads, 1 (1.3 %) in lateral leads, 2 (2.5 %) in anteroseptal leads and LV apex, 1 (1.3 %) in inferior and lateral leads.

Atrial fibrillation was detected in 36 (45 %) patients with HCM: permanent AF in 12 (15 %), persistent AF in 5 (6.2 %), and paroxysmal AF in 19 (23.8 %).

During hospitalization, ventricular tachycardia was reported in 6 (7.5 %) patients: of whom, unstable ventricular tachycardia was recorded during 24-hour Holter ECG monitoring in 4 (5 %) patients and on 12-lead ECG in 2 patients. Supraventricular tachycardia was detected in 3 (3.8 %) patients with HCM: in 2 (2.5 %) during 24-hour Holter ECG monitoring, in 1 (1.3 %) on 12-lead ECG (Figure 5).

Cardiac conduction disorders were revealed in 29 (36.3 %) patients: atrioventricular (AV) blockage in 6 (6.3 %) patients, including degree 1 AV blockade in 2 (2.5 %), degree 3 AV blockade in 3 (3.8 %); right bundle branch block in 17 (21.3 %), left bundle branch block in 12 (15 %) patients. Wolff–Parkinson–White syndrome was detected in (1) 1.3 % patient (Figure 6). Morgagni–Adams–Stokes attack was reported in 3 (3.8 %) patients with HCM. 4 (5 %) patients had a history of cardiac pacemaker implantation. Implantation was caused by degree 3 atrioventricular blockade in 3 (3.8 %) patients after ventricular septal resection, bradycardiac permanent AF in 1 (1.3 %) patient.

In patients with HCM, the glomerular filtration rate (GFR) was 65 (56–78.8) mL/min/1.73 m2 (n=71). Chronic kidney disease was reported in 22 (31 %) patients, provided that most of them had stages 3a and 3b (Figure 7). Proteinuria was detected in 17 (25 % of patients, n=68), proteinuria >1 g/L was detected in 3 (4.4 %), and nephrotic syndrome was detected in 1 (1.5 %) patient with HCM (Figure 8).

The hospitalization duration in patients with HCM was 8 (6; 12.5) days. 87 (45–131.5; min 1, max 180) months after discharge, 11 (13.8 %) patients died. In the dead patients, the time from HCM diagnosis to death was 10 (3–12, min 0, max 17) years.

dead patients were more likely to have a history of LVOTO and AF compared to alive patients ($X^2$=10.09; p=0.006 and $X^2$=3.96; p=0.047, respectively) (Figure 9, 10).

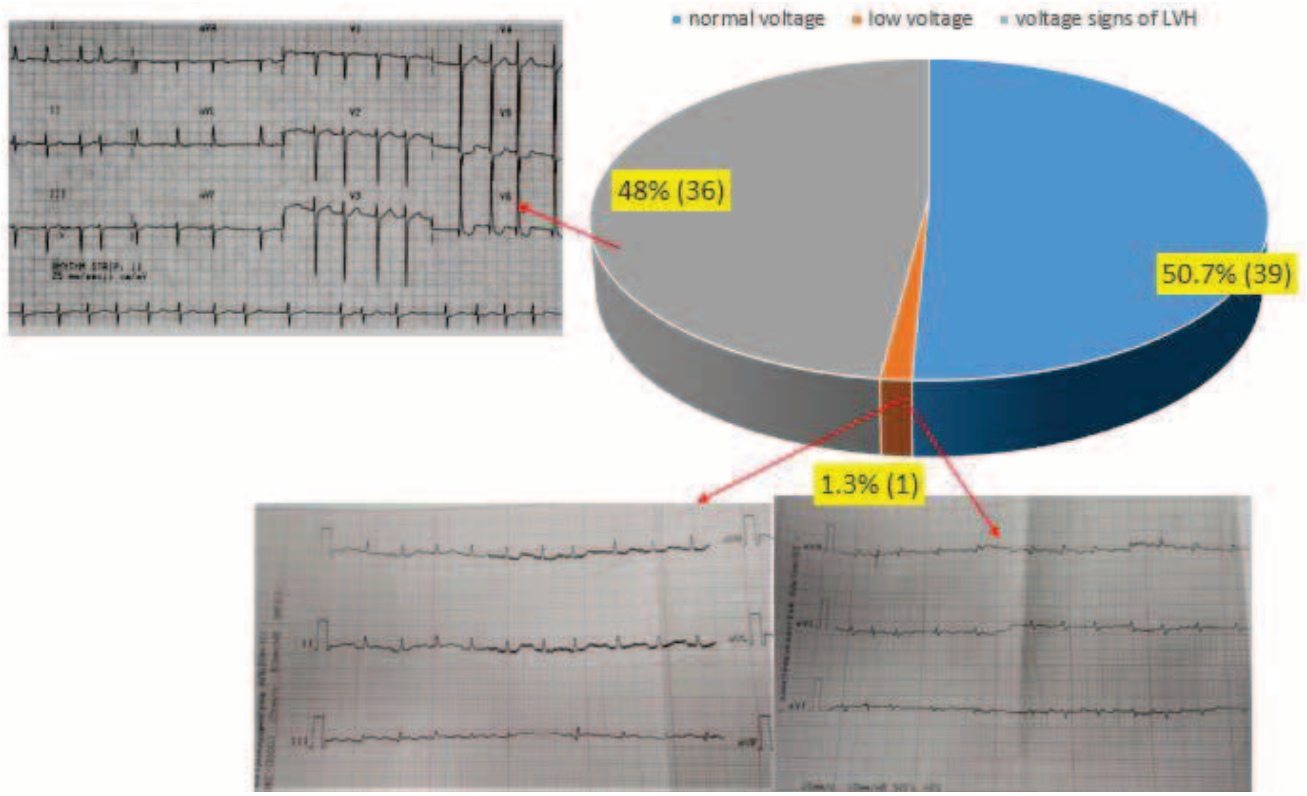


***Figure 4.*** *ECG in patients with HCM*
**Note:** LVH — left ventricular hypertrophy

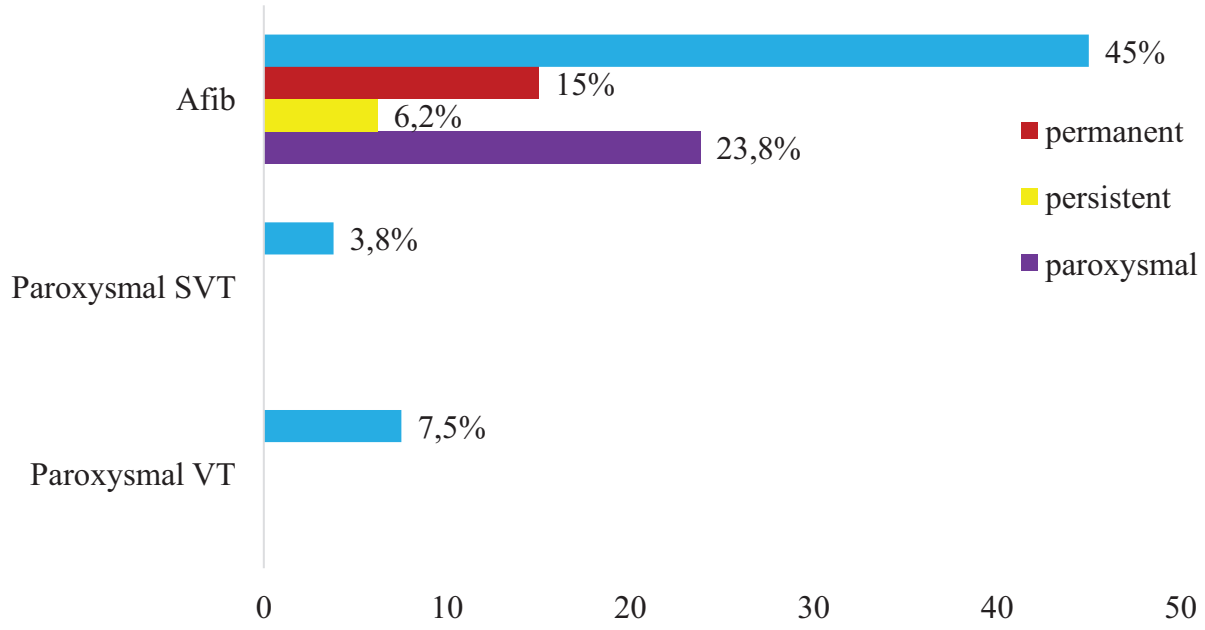


***Figure 5.*** *Arrhythmias in patients with HCM*
**Note:** Afib — atrial fibrillation, SVT — supraventricular tachycardia, VT — ventricular tachycardia

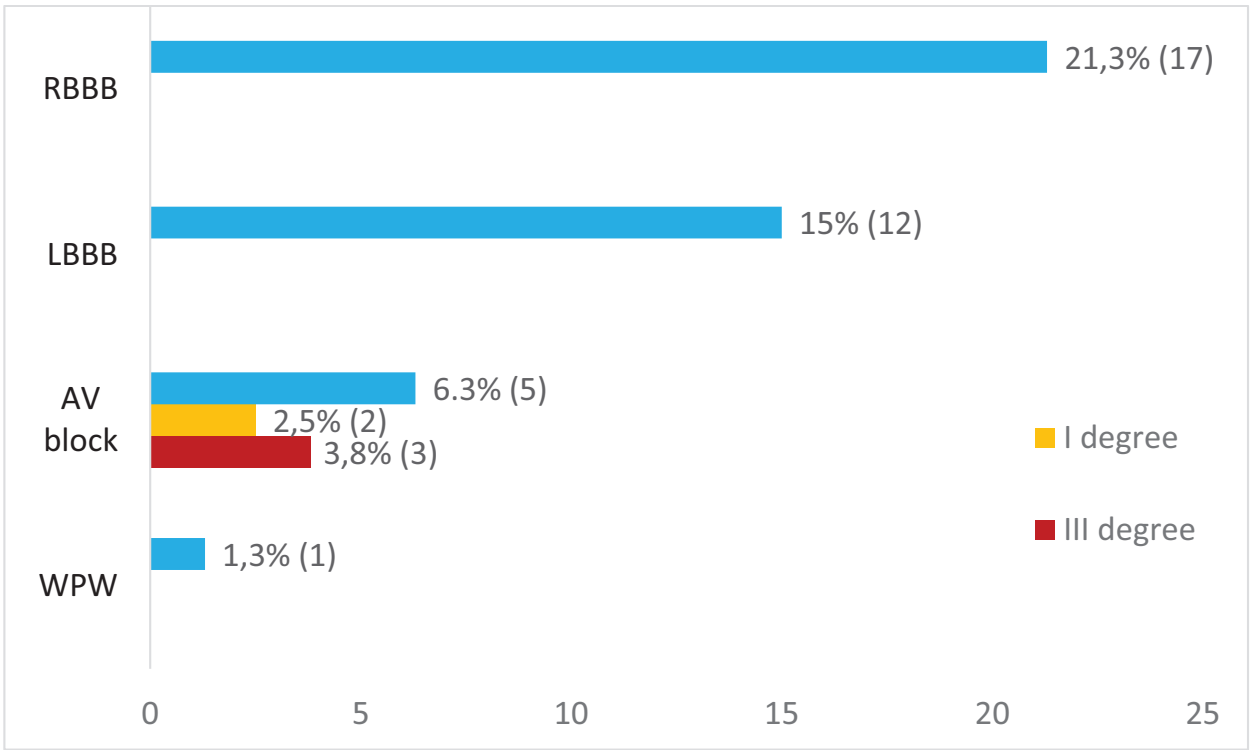


***Figure 6.*** *Conduction disorders in patients with HCM*
**Note:** RBBB — right bundle branch block, LBBB — left bundle branch block, AV — atrioventricular, WPW — Wolff-Parkinson-White Syndrome

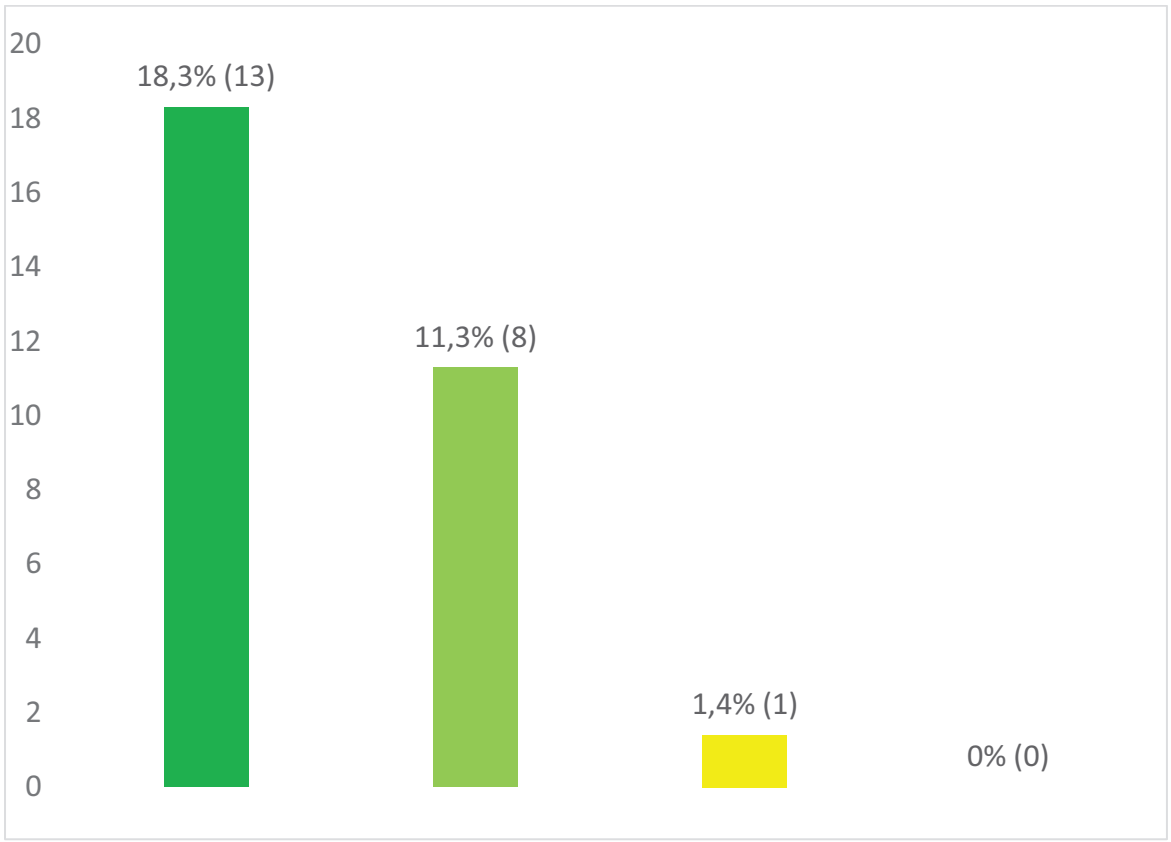


***Figure 7.*** *CKD in patients with HCM*

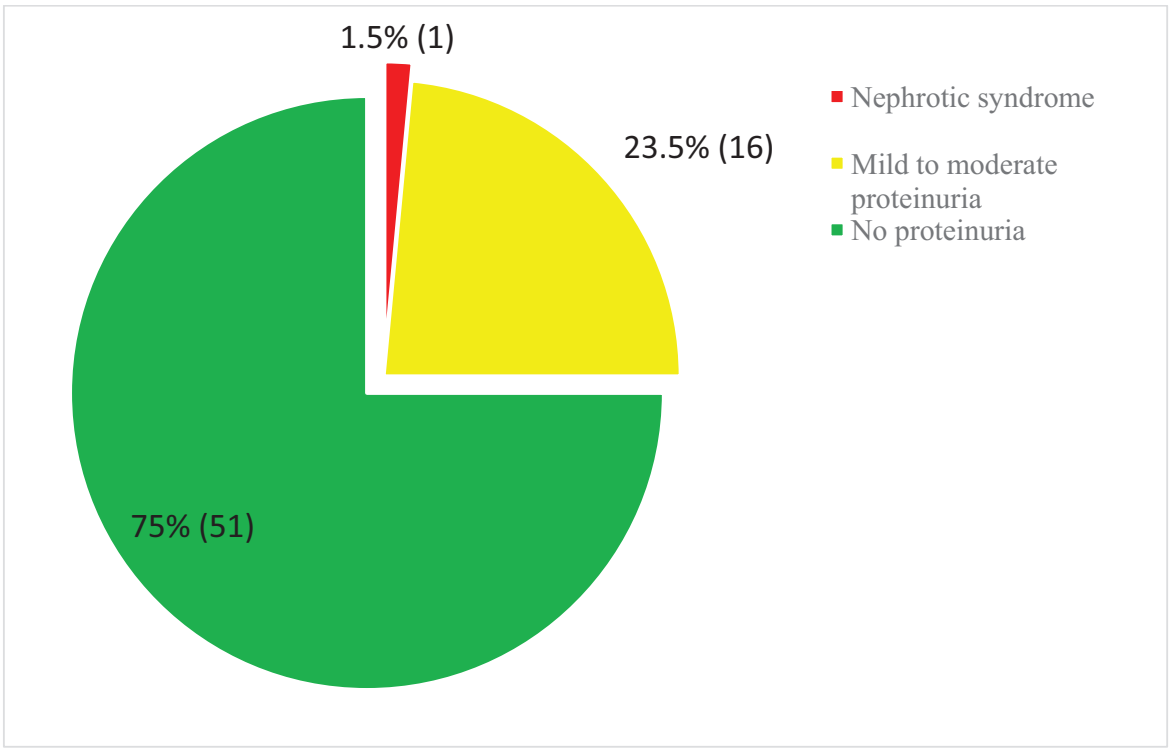


***Figure 8.*** *Proteinuria in patients with HCM*

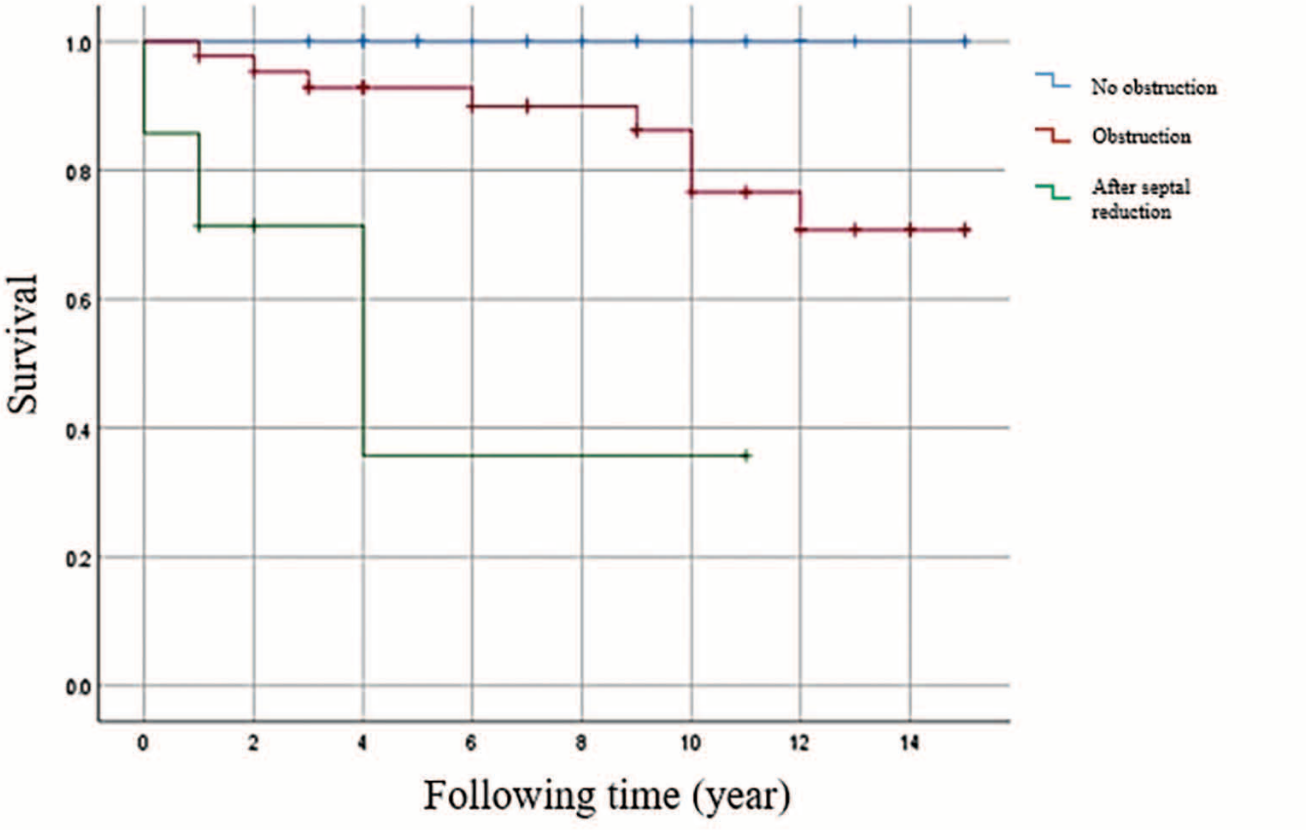


***Figure 9.*** *Kaplan-Meier curve of the proportion of patients after septal reduction therapy, with or without left ventricular obstruction among 80 patients with hypertrophic cardiomyopathy (HCM).*

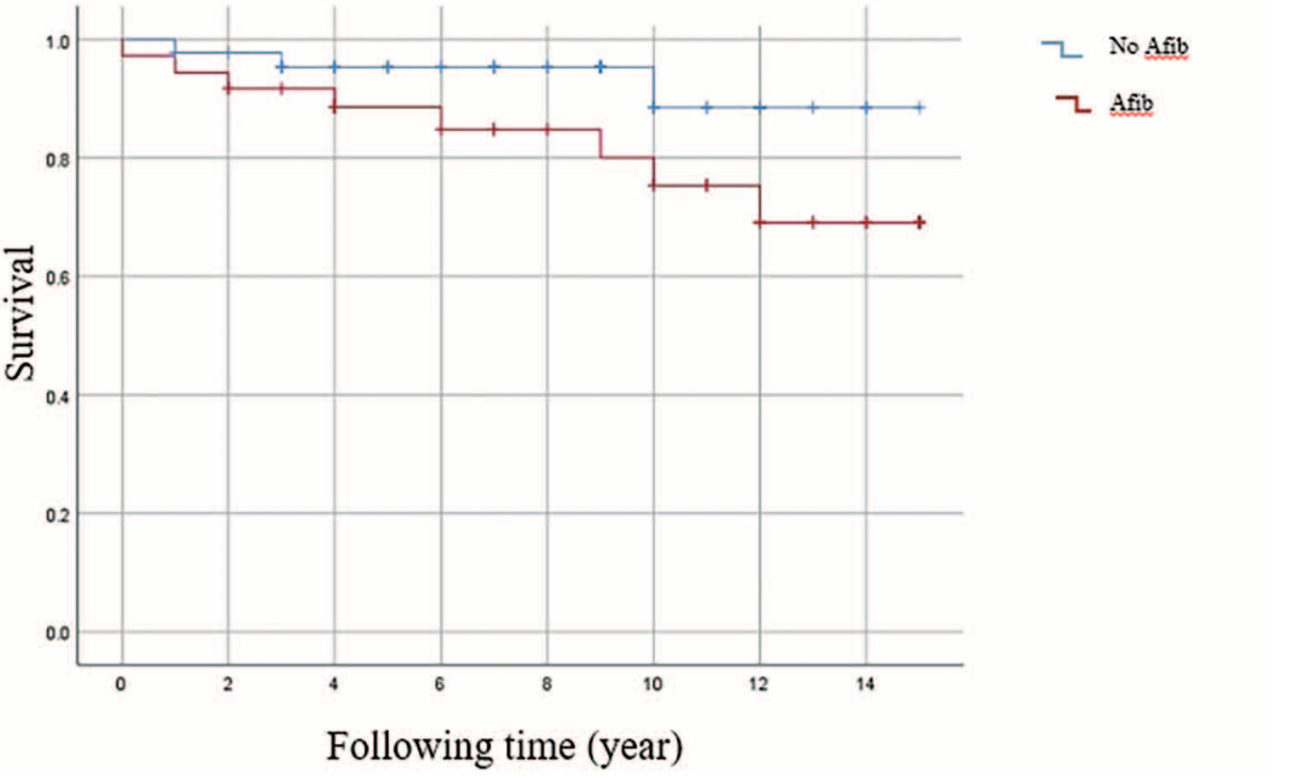


***Figure 10.*** *Kaplan-Meier curve of the proportion of patients with or without Afib among 80 patients with hypertrophic cardiomyopathy (HCM).*

**Note:** Afib — atrial fibrillation

*Table 2. Comparison of characteristics in deceased and surviving patients with HCM*

| Parameter | Deceased (n=11) | Alive (n=69) | p |
|---|---|---|---|
| Proteinuria, g/l | 0.26 (0.00-2.00) | 0.09 (0.00-3.0) | 0.29 |
| **Presence of LVOT obstruction, %** | **100** | **58.2** | **0.006** |
| LV wall thickness, mm | 19.5 (17.8-24.3) | 20.9 (18-23.7) | 0.37 |
| **Presence of Afib, %** | **72.7** | **40.6** | **0.047** |
| Presence of conduction disturbance, % | 45.5 | 34.8 | 0.5 |
| Arterial hypertension, % | 36.4 | 56.5 | 0.22 |
| GFR ml/min/1.73 m2 | 96(60-104) | 64.5 (56-76) | 0.087 |
| Diabetes | 36.4 | 58 | 0.39 |
| LA diameter (mm) | 49.4 (45-52) | 45 (40-51.4) | 0.23 |
| LA volume (ml) | 99 (81.5-202) | 105 (60-140) | 0.83 |
| LV EDD (mm) | 41 (39-51) | 43.3 (40-47.6) | 0.9 |
| LV EDV (ml) | 94.5 (80-126) | 80 (68-97) | 0.27 |

**Note:** LVOT — left ventricular outflow tract, LV — left ventricle, Afib — atrial fibrillation, GFR — glomerular filtration rate, LA — left atrium, EDD — end-diastolic diameter, EDV — end-diastolic volume

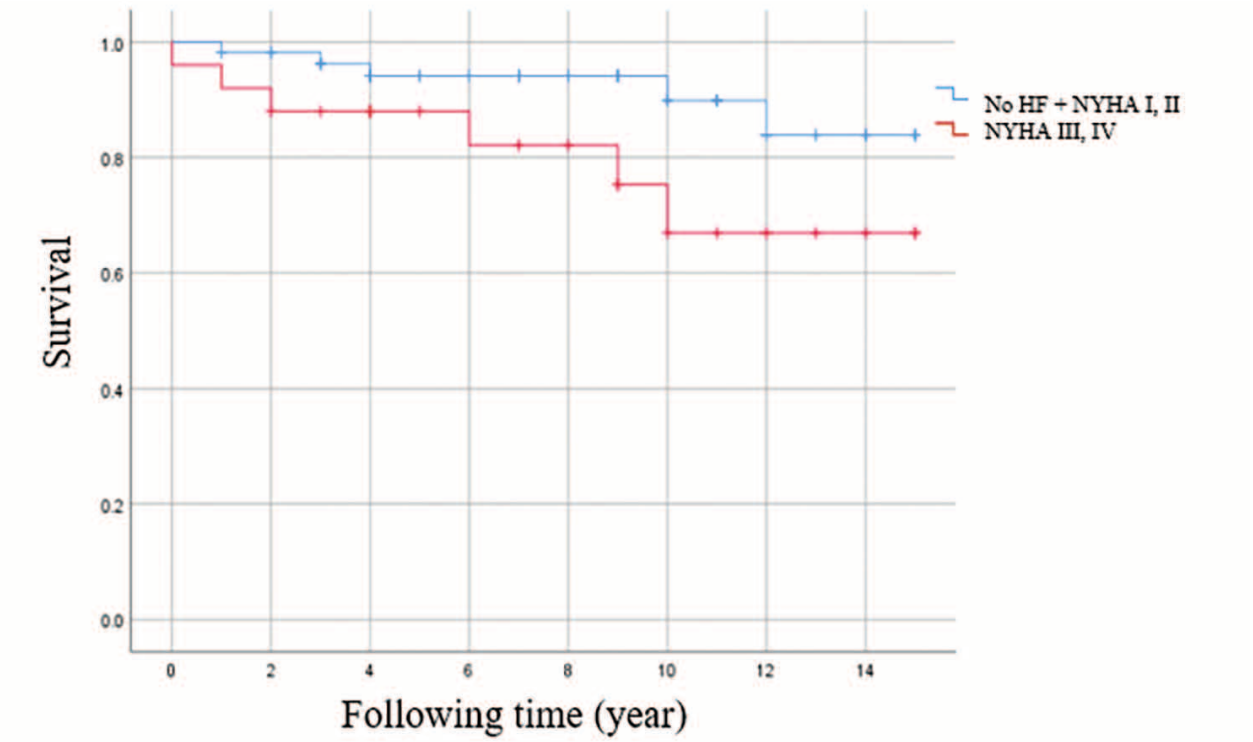


***Figure 11.*** *Kaplan-Meier curve of the proportion of patients with different classes of CHF or without it among 80 patients with hypertrophic cardiomyopathy (HCM) (p=0.073)*

**Note:** HF — heart failure

Age, sex, severity, and form of LVH, LVEF, LV end-diastolic diameter and volume, LV diastolic function, left atrial dimension and volume, degree of proteinuria, GFR, NYHA functional class of CHF, CHF stage (according to the Vasilenko-Strazhesko classification), history of arterial hypertension, myocardial infarction, and diabetes mellitus in dead and alive patients were not significantly different (Table 2, Figure 11).

Fifty-five patients with LVH (5 (9.1 %) of the above-analyzed patients) underwent genetic testing to rule out HCM phenocopies. Of them, sarcomere protein gene mutations (true HCM) were found in 12 (21.8 %) patients, a transthyretin gene mutation (ATTR amyloidosis) was revealed in 1(1.8 %) patient.

## Discussion

According to the published data, cases of HCM were diagnosed in 122 countries. Approximately 20 million people worldwide have this disorder, which is much greater than the previously estimated number of patients. HCM is not diagnosed in about 90 % of cases [1].

Over the period 2007 to 2021, in the multi-speciality hospital, the HCM detection rate was 14.26 per 100,000 patient-years. There is no similar statistical information on the website of the Federal State Statistics Service of the Russian Federation or in the available literature. In the period 1984 to 2016, the detection rate of HCM in the Rochester Epidemiology Project (Minnesota, USA) was 8.0/100,000person-years [6]. The differences may be due to the small sample size of the study and the inclusion of only hospitalized patients. Taking into account the HCM prevalence in the general population, which is 1 per 500 people, a lot of HCM cases are not diagnosed in real-life clinical practice [1].

A distinctive feature of HCM is heterogeneity of clinical manifestations, ranging from asymptomatic course to severe CHF and sudden cardiac death. Typical morphological signs of HCM include hypertrophy, cardiomyocyte damage, and cardiac fibrosis [1]. This disorder is characterized by disturbed myocardial calcium metabolism, inefficient energy use, and microvascular dysfunction. According to the data obtained in this study and published in literature, it is accompanied by impaired local and reduced global contractility, LV diastolic dysfunction, cardiac valve insufficiency, rhythm and contractility disorders, CHF (in 77.6 %, including CHFpEF in 68.8 % patients) [1,5].

In the guidelines of the European Society of Cardiology, the NT-proBNP, BNP assay is recommended as a mandatory criterion for the CHFpEF diagnosis (until 2021 and CHFpEF). This recommendation is not always followed in general clinical practice, and therefore this index was not evaluated in the patients with HCM in this study. According to the results of some authors, NT-proBNP, BNP level, high-sensitivity troponin can help differentiate HCM from its phenocopies and even distinguish phenocopies from each other. Liu H. et al. demonstrated that a significantly greater level of NT-proBNP [5,803.5 (2,533–13,969) vs. 1,513 (656–3,516), p=0.001)] and troponin T [91.9 (53.85–223.45) vs. 17.3 (11.9–45.3), p=0.001] in patients with cardiac amyloidosis compared to the patients with HCM. By contrast with HCM, the diagnosis of cardiac amyloidosis can be ruled out at normal values of NT-proBNP. None of the patients with cardiac AL amyloidosis had NT-proBNP <55 pmol/L. Hu K. et al. found that the levels of high sensitive troponin (hsTn) and NT-proBNP were much greater in the cardiac amyloidosis group [median: hsTn 98 pg/mL, NT-proBNP 4,110 pg/mL] than in the group of Friedrich's ataxia [hsTn 14 pg/mL, NT- proBNP 40 pg/mL] and in the Fabry disease group [hsTn 18 pg/mL, NT-proBNP 131 pg/mL, P<0.001 in both groups]. hsTn >60 pg/mL (sensitivity 0.79, specificity 0.93) and NT-proBNP >1,000 pg/mL (sensitivity 0.91, specificity 0.93) allowed differentiating cardiac amyloidosis from Friedrich's ataxia and Fabry disease [7,8]. For this reason, a large-scale implementation of the test for these biomarkers in patients with left ventricular hypertrophy and especially with HCM.

In HCM, AF is the most frequent persistent arrhythmia. Its prevalence depends on the disease severity and makes up from 22 % in patients with HCM to 32 % in patients with HCM waiting for implantation of cardioverter defibrillator and electric cardiac pacemaker [9]. In this study, a greater incidence of AF was found in patients with HCM: in 45 % of cases. Cardiac conduction disorders were detected in every third patient; in 9 % of patients, cardiac conduction disorders occurred after IVS resection. Such frequency is comparable with the frequency of AF and cardiac conduction disorders in patients with amyloidosis found in one of the studies [2]. It is likely that the group of patients with HCM was heterogeneous, the diagnosis was generally established based on EchoCG data, and its phenocopies (e.g., cardiac amyloidosis) were not ruled out. According to the results of previous studies, the frequency of hereditary ATTR amyloidosis in patients with diagnosed HCM is 5 % and reach 7.6 % at the age of 55 years and older [3]. In the recent study in the cohort of Afro-Caribbean patients with unexplained LV hypertrophy, cardiac amyloidosis was found in 33.9 % of patients [10].

A meta-analysis by Liu Q. et al. demonstrated that in patients with HCM, NYHA functional class, AF, and LVOT obstruction were significant prognostic factors of cardiovascular death [11]. Moreover, NYHA class III/IV was the most important risk factor for cardiovascular mortality and the strongest prognostic factor for overall

mortality. In this study, dead patients with HCM were significantly more likely to have LVOTO (p=0.006) and AF (p=0.047); there were differences in NYHA functional class between dead and alive patients; however, they were not statistically significant (p=0.073). This may be due to a small sample size and heterogeneity of the patient cohort in the study, possible presence of hypertensive patients in patients with established HCM diagnosis, as well as specificity of CHFpEF diagnosis in the absence of biomarker detection (BNP, NT-proBNP).

The survival rate of patients after the surgery aimed at reducing the pressure gradient in LVOT (myectomy, alcohol septal ablation) is lower than in patients without surgery and without obstruction. This may be explained by the greater severity of clinical symptoms and presence of higher CHF FC in patients requiring myectomy [11] This is consistent with the results of this study.

The frequency of patients with a history of myocardial infarction in the study was much greater than in the Taiwan study (15 % and 3 %), [12]and the frequency of patients with myocardial infarction without significant coronary stenoses was similar to the results of Puwanant S. et al. study (7.5 % and 9 %, respectively) [13]. In addition to coronary atherosclerosis, microvascular dysfunction, intramural coronary stenosis and endothelial dysfunction may contribute to the development of ischemia and/or myocardial infarction in HCM. In HCM phenocopies, especially in cardiac amyloidosis, ECG changes or local contractility abnormalities on echoCG may mimic the clinical presentation of MI and be due to amyloid deposition in the LV wall or coronary arteries [2,3].

In the study, half of the patients with HCM had a history of arterial hypertension (AH), 35 % had a history of grade 3 AH. The result obtained in the study does not differ from those in the previous studies [14]. Although these two disease areas can be comorbid, genetic testing is required in patients with AH to confirm HCM in order to rule out hypertensive heart disease as the cause of LVH.

Low (even normal) voltage of QRS complexes observed in some patients with HCM are a manifestation of mass-voltage dissociation. This may be one of signs of HCM phenocopies and require screening to reveal the causes of HCM (genetic test, biopsy, etc.).

In this study, 30 % of patients with HCM had a carbohydrate metabolism disorder (17.5 % had DM). This is twice as high as in the general population and similar to the DM frequency in the cohort of patients with HCM in Taiwan [12]. DM may be a cause of microvascular dysfunction and MI without significant coronary stenosis in the patients with HCM. Patients with HCM and DM have a higher cardiovascular risk. They have higher FC and more pronounced heart failure due to LV diastolic dysfunction. It is interesting that the clinical presentation of diabetic cardiomyopathy can develop in the patients with DM, manifesting as LVH, diastolic dysfunction, left atrial dilation [15]. LVH caused by DM is aggravated by AH and renal dysfunction [15]. In patients with LVH and DM, especially in the presence of AH, renal dysfunction, genetic testing is required to confirm HCM and perform differential diagnosis with diabetic cardiomyopathy.

In this study, kidney disease was found in every third patient with HCM; however, it was not pronounced in most patients. Proteinuria detected in the urinalysis was mainly mild; no tests for albuminuria or daily proteinuria/albuminuria were conducted. It is generally acknowledged that in patients with such cardiovascular diseases (CVD) as coronary heart disease (CHD) and chronic heart failure (CHF) CKD is a significant risk factor associated with adverse outcomes. However, the significance of CKD in HCM is still unclear [16]. On the one hand, CKD is closely related to the progression of LVH and cardiac fibrosis. On the other hand, LV hypertrophy and diastolic dysfunction may promote a decrease in GFR and development of renal dysfunction in patients with HCM [16]. Screening of urinary albumin excretion, including daily albuminuria, is required for timely diagnosis of renal disorders in patients with HCM. It is notable that pronounced LVH in combination with renal disorders can be considered as “a red flag” of systemic amyloidosis and other infiltrative heart diseases [2,3], requiring screening for HCM phenocopies.

According to the genetic testing in patients with HCM, sarcomere protein gene mutations were detected in 21.8 % of patients, while a transthyretin gene mutation (hereditary ATTR amyloidosis was diagnosed) was revealed in 1.8 %. Clinicians should be suspicious of this disease and perform screening to rule it out in patients with HCM who have the mentioned “red flag” symptoms [16].

## Study restrictions

Due to the retrospective design of the study, different causes and timing of hospitalization, different clinical manifestations and applied medical and economic standards of patient management, not all of the tests required for patients with HCM according to the current guidelines were conducted; genetic testing and exclusion of HCM phenocopies were not performed either.

## Conclusion

In real-life clinical practice, HCM is probably diagnosed less frequently than it occurs. Moreover, overdiagnosis of HCM in patients with arterial hypertension

and diabetes mellitus, as well as underdiagnosis of HCM phenocopies cannot be excluded. All patients with HCM require EchoCG according to up-to-date protocols, including the assessment of diastolic function, mass index, cardiac strain, pulmonary hypertension, etc., evaluation of troponin and NTproBNP levels, genetic testing, as well as other tests to exclude phenocopies. Considerable achievements and wide availability of genetic testing facilitate the detection of sarcomere mutations that cause HCM, as well as the diagnosis of other genetic diseases that can mimic HCM. Visualization techniques are not always reliable when it comes to differentiation of these conditions. Although HCM phenocopies are relatively rare, it is extremely important to distinguish these conditions at an early stage, since their natural course, treatment and prognosis are significantly different from those in HCM with sarcomere mutations. In this study, sarcomere protein gene mutations were found in each fifth patient, while a transthyretin gene mutation (ATTR amyloidosis) was revealed in 2% of patients with pronounced LVH. This confirms the need for wide implementation of genetic testing, screening for HCM phenocopies and their inclusion in the Program on State Guarantees in the Russian Federation for timely use of specific pathogenetic therapy and improvement of patients' prognosis.


### Вклад авторов:

Все авторы внесли существенный вклад в подготовку работы, прочли и одобрили финальную версию статьи перед публикацией

**Резник Е.В. (ORCID ID: https://orcid.org/0000-0001-7479-418X):** разработка дизайна исследования; организация набора материала, редактирование текста рукописи

**Нгуен Т.Л. (ORCID ID: https://orcid.org/0000-0002-8856-4542):** создание базы пациентов, статистическая обработка и представление результатов, обзор публикаций по теме статьи, написание текста рукописи

**Дикаева М.С. (ORCID ID: https://orcid.org/0000-0002-5071-5771):** создание базы пациентов

**Сиренова И.О. (ORCID ID: https://orcid.org/0000-0002-5449-331X):** организация набора материала, редактирование текста рукописи

**Саликов А.В (ORCID ID: https://orcid.org/0000-0003-0442-7725):** организация набора материала, редактирование текста рукописи

**Платонова Е.Н. (ORCID ID: https://orcid.org/0000-0001-5198-9531):** научная консультация, редактирование рукописи

**Гаврилова О.В. (ORCID ID: https://orcid.org/0000-0002-9864-1222):** научная консультация, редактирование рукописи

**Голухов Г.Н. (ORCID ID: https://orcid.org/0000-0002-0161-005X):** научная консультация, редактирование рукописи

### Author Contribution:

All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication

**Reznik E.V. (ORCID ID: https://orcid.org/0000-0001-7479-418X):** study design development; organizing the recruitment of material, manuscript editing

**Nguyen T.L. (ORCID ID: https://orcid.org/0000-0002-8856-4542):** creating a patients' database, statistical processing and presentation of results, review of publications on the article topic, writing the manuscript text

**Dikaeva M.S. (ORCID ID: https://orcid.org/0000-0002-5071-5771):** creating a patients' database

**Sirenova I.O. (ORCID ID: https://orcid.org/0000-0002-5449-331X):** organization of material recruitment, manuscript editing

**Salikov A.V. (ORCID ID: https://orcid.org/0000-0003-0442-7725):** organizing the recruitment of material, manuscript editing

**Platonova E.N. (ORCID ID: https://orcid.org/0000-0001-5198-9531):** scientific consultation, manuscript editing

**Gavrilova O.V. (ORCID ID: https://orcid.org/0000-0002-9864-1222):** scientific consultation, manuscript editing

**Golukhov G.N. (ORCID ID: https://orcid.org/0000-0002-0161-005X):** scientific consultation, manuscript editing


### Список литературы / References:


1 Maron B.J. Clinical Course and Management of Hypertrophic Cardiomyopathy. N Engl J Med. 2018; 379: 655–68. doi:10.1056/NEJMra1710575

2 Резник Е.В., Степанова Е.А., Нгуен Т.Л., и др. Ретроспективный анализ поражения сердечно-сосудистой системы у больных системным амилоидозом. Кардиоваскулярная терапия и профилактика. 2021; 20(1): 2496. doi:10.15829/1728-8800-2021-2496 Reznik E.V., Stepanova E.A., Nguyen T.L., et al. Retrospective analysis of cardiovascular involvement in patients with systemic amyloidosis. Cardiovascular Therapy and Prevention. 2021; 20(1): 2496. doi:10.15829/1728-8800-2021-2496 [In Russian].

3 Резник Е.В., Нгуен Т.Л., Степанова Е.А., et al. Амилоидоз сердца: взгляд терапевта и кардиолога. Архивъ внутренней медицины. 2020; 10: 430–57. doi:10.20514/2226-6704-2020-10-6-430-457 Reznik E.V., Nguyen T.L., Stepanova E.A., et al. Cardiac Amyloidosis: Internist and Cardiologist Insight. The Russian Archives of Internal Medicine. 2020; 10(6): 430-457. doi:10.20514/2226-6704-2020-10-6-430-457 [In Russian].

4 Maron B.J., McKenna W.J., Danielson G.K., et al. American College of Cardiology/European Society of Cardiology clinical expert consensus document on hypertrophic cardiomyopathy. A report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents and the European Society of Cardiology Committee for Practice Guidelines. J Am Coll Cardiol. 2003; 42: 1687–713. doi:10.1016/s0735-1097(03)00941-0

5 Authors/Task Force members, Elliott P.M., Anastasakis A., et al. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: The Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). European Heart Journal. 2014; 35: 2733–79. doi:10.1093/eurheartj/ehu284

6 Masood M., Sherif A.A., Jaliparthy K., et al. Abstract 17019: Secular Trends in Dilated and Hypertrophic Cardiomyopathy in an Epidemiological Cohort in Olmsted County, Minnesota. Circulation. 2018; 138: A17019–A17019. doi:10.1161/circ.138.suppl_1.17019

7 Liu H., Bai P., Xu H-Y., et al. Distinguishing Cardiac Amyloidosis and Hypertrophic Cardiomyopathy by Thickness and Myocardial Deformation of the Right Ventricle. Cardiology Research and Practice. 2022; 2022:e4364279. doi:10.1155/2022/4364279

8 Hu K., Liu D., Salinger T., et al. Value of cardiac biomarker measurement in the differential diagnosis of infiltrative

cardiomyopathy patients with preserved left ventricular systolic function. J Thorac Dis. 2018;10:4966–75. doi:10.21037/jtd.2018.07.56

9 Patten M., Pecha S., Aydin A. Atrial Fibrillation in Hypertrophic Cardiomyopathy: Diagnosis and Considerations for Management. J Atr Fibrillation. 2018; 10:1556. doi:10.4022/jafib.1556

10 Inamo J., Ozier-Lafontaine N., Atallah A., et al. Frequency of cardiac amyloidosis inpatients with unexplained left ventricular hypertrophy: The Caribbean Amyloidosis Study. Archives of Cardiovascular Diseases Supplements. 2018; 10:29. doi:10.1016/j.acvdsp.2017.11.055

11 Liu Q., Li D., Berger A.E., et al. Survival and prognostic factors in hypertrophic cardiomyopathy: a meta-analysis. Sci Rep 2017; 7:11957. doi:10.1038/s41598-017-12289-4

12 Lee C., Liu P., Lin L., et al. Clinical characteristics and outcomes of hypertrophic cardiomyopathy in Taiwan—a tertiary center experience. Clin Cardiol. 2007; 30:177–82. doi:10.1002/clc.20057

13 Puwanant S., Trongtorsak A., Wanlapakorn C., et al. Acute coronary syndrome with non-obstructive coronary arteries (ACS-NOCA) in patients with hypertrophic cardiomyopathy. BMC Cardiovascular Disorders. 2021; 21:556. doi:10.1186/s12872-021-02373-z

14 Wang A. Hypertension and Hypertrophic Cardiomyopathy. Hypertrophic Cardiomyopathy, ed. Naidu S.S. Springer, Cham. 2019; 221–30. doi:10.1007/978-3-319-92423-6_16

15 Резник Е.В., Нгуен Т.Л., Голухов Г.Н. Особенности ведения больных с хронической сердечной недостаточностью и сахарным диабетом. Рациональная Фармакотерапия в Кардиологии. 2021;17(2):341-350. doi:10.20996/1819-6446-2021-04-05. Reznik E.V., Nguyen T.L., Golukhov G.N. Management of Patients with Chronic Heart Failure and Diabetes Mellitus. Rational Pharmacotherapy in Cardiology. 2021; 17:341–50. doi:10.20996/1819-6446-2021-04-05 [In Russian].

16 Huang F-Y., Zhang J-L., Huang B-T., et al. Renal function as a predictor of outcomes in patients with hypertrophic cardiomyopathy: A cohort study of a hospitalized population. Clinica Chimica Acta. 2021; 512:92–9. doi:10.1016/j.cca.2020.11.022