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Phenotypic, Epidemiologic, and Imaging Features of Hypertrophic Cardiomyopathy: A Single-Center Experience

ORIGINAL INVESTIGATION

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ABSTRACT

Background: Hypertrophic cardiomyopathy (HCM) is a complex myocardial disorder with heterogeneous clinical presentations and structural manifestations. This study aimed to assess the distribution, clinical characteristics, and diagnostic approaches in a regional cohort of patients with HCM.

Methods: Patients diagnosed with HCM at a tertiary cardiomyopathy clinic between October 2021 and November 2024 were retrospectively analyzed. Patients were classified into obstructive, latent obstructive, non-obstructive, or apical phenotypes based on clinical and imaging findings. Comprehensive demographic, clinical, and imaging data were collected for detailed analysis, providing valuable insights into the phenotypic diversity of HCM.

Results: The cohort included 701 patients with a median age of 53 years of whom 68% were male. The phenotypic distribution comprised 9.3% apical, 38.1% non-obstructive, 32.5% resting obstructive, and 20.1% latent obstructive HCM. Implantable cardioverter-defibrillator implantation was more common in obstructive phenotypes, particularly in the latent obstructive group. Although late gadolinium enhancement (LGE) was more frequently observed in apical HCM, post-hoc analysis showed no significant difference in prevalence across subgroups. In contrast, LGE extent was significantly greater in the apical group. Genetic testing, performed in 32% of patients, revealed a 44% positivity rate, with MYBPC3 and MYH7 being the most commonly detected mutations. The overall mortality rate was 2.8%, with heart failure identified as the leading cause of death.

Conclusion: In this large regional cohort of HCM patients, obstructive and non-obstructive phenotypes were predominant, with a notable burden of genetic mutations and a low overall mortality rate primarily driven by heart failure. These findings emphasize the clinical heterogeneity of HCM and highlight the importance of comprehensive diagnostic evaluation.

Keywords: Cardiac magnetic resonance imaging, echocardiography, epidemiology, genetic testing, hypertrophic cardiomyopathy

INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is an inherited myocardial disorder characterized by left ventricular hypertrophy (LVH) that cannot be fully explained by loading conditions. Over the past 3 decades, numerous studies have assessed the prevalence of HCM in the general population using echocardiography and cardiac magnetic resonance imaging (CMR), as well as clinical diagnoses derived from electronic health records and billing databases.[1]

Echocardiographic studies estimate its prevalence in the general population to range between 0.2% and 0.5%.[2] Recognized as one of the most common cardiomyopathies, HCM exhibits a broad spectrum of clinical presentations, ranging from asymptomatic individuals to those at significantly elevated risk of sudden cardiac death (SCD). The condition is primarily attributed to autosomal dominant mutations in genes encoding sarcomeric proteins, which account for the pronounced phenotypic and clinical heterogeneity observed in affected individuals.[3]

Hypertrophic cardiomyopathy demonstrates substantial phenotypic diversity, including obstructive, non-obstructive, and apical subtypes, with varying prevalence across different populations. This phenotypic variability arises from the interplay of genetic predispositions and environmental factors, influencing disease presentation, progression, and prognosis.[4,5] Although each phenotype has been associated with distinct patient-specific clinical and prognostic characteristics, the literature in this field continues to evolve, with new insights emerging regularly.[6]

Advances in cardiac imaging, particularly in echocardiography with the development of new techniques and the increased accessibility of CMR, have significantly facilitated the diagnostic process in HCM patients and enabled detailed phenotypic differentiation.[7] The multimodality approach has also improved the early detection of asymptomatic individuals, providing valuable insights into prognostic processes. Additionally, the widespread use of genetic analyses through family screening programs has further enhanced the identification of asymptomatic patients.[5] This progress has also allowed for the close monitoring of individuals described as genotype-positive but phenotype-negative, facilitating the identification of factors contributing to disease development in this population.[8] Despite these advancements, the underdiagnosis of HCM persists, emphasizing the need for broader application and accessibility of these technologies to improve patient outcomes.[9]

Considering the significant role of genetic factors in this patient population, the influence of environmental and geographical factors further underscores the importance of regional and population-specific data. Phenotypic characteristics, along with their clinical, imaging, and prognostic features, may vary across different regions. Given the limited data available in the country, the primary aim of this study is to investigate the epidemiological features, phenotypic profiles, and prognostic outcomes of the HCM population followed at the center.

METHODS

This retrospective observational study included patients aged 18 years and older who had been evaluated at the cardiomyopathy outpatient clinic of a tertiary referral center between October 2021 and November 2024. Patients with a confirmed diagnosis of HCM during this period were identified from institutional databases and electronic medical records, and their clinical, imaging, and laboratory data were subsequently analyzed. The inclusion criteria required a confirmed diagnosis of HCM based on clinical and imaging findings, in accordance with the 2023 European Society of Cardiology (ESC) guidelines. Although patient enrollment began in 2021, all diagnoses were retrospectively verified using the 2023 ESC criteria, which are consistent with the diagnostic definitions outlined in the 2014 version; therefore, no reclassification or classification bias was introduced.[2,10] The HCM was defined as a LV wall thickness of ≥15 mm in any myocardial segment, not attributable solely to loading conditions. Additionally, wall thickening of 13-14 mm was considered diagnostic when accompanied by features such as a family history of HCM, pathogenic genetic mutations, or abnormal electrocardiographic (ECG) findings.[2] Exclusion criteria included patients with other causes of;

1. LVH such as hypertensive heart disease and aortic stenosis,
2. Infiltrative/storage cardiomyopathies (e.g., amyloidosis, Anderson-Fabry disease, glycogen storage diseases),
3. Patients with incomplete clinical or imaging data were also excluded.

The 24-hour ambulatory blood pressure monitoring was performed on all hypertensive patients. The distinction between hypertensive LVH and HCM with concomitant hypertension was made using a comprehensive multimodality approach, including echocardiographic morphology, CMR characteristics, and, when available, genetic findings. In cases of clinical or laboratory suspicion of infiltrative or storage diseases, or when genetic mutations were identified, patients were referred to a metabolism specialist for further evaluation. Based on disease-specific red flags, α-GalA enzyme activity was evaluated, and lyso-Gb3 levels were measured in males for the diagnosis of Anderson-Fabry disease, while genetic testing was conducted in females to confirm the diagnosis.[11] For suspected amyloidosis, 99m-technetium-pyrophosphate (99mTc-PYP) cardiac scintigraphy was conducted. Furthermore, the exclusion of clonal dyscrasia was ensured through a comprehensive diagnostic assessment, including a serum-free light-chain assay, along with serum and urine protein electrophoresis with immunofixation.[2]

Cardiac Imaging Characteristics

Cardiac imaging was performed using transthoracic echocardiography (TTE) and CMR imaging to assess structural and functional parameters. The TTE was conducted for all participants using a Philips Epiq 7 echocardiography device (Philips Medical Systems, Andover, MA, USA).

Interventricular septal (IVS) and posterior wall (PW) thickness were measured in the parasternal long-axis view using TTE as recommended.[12] In accordance with current guidelines for the assessment of HCM, all LV wall segments were systematically evaluated from base to apex at end-diastole, preferably using the 2D parasternal short-axis view. Wall thickness measurements were obtained at the levels of the mitral valve, mid-ventricle, and apex. In cases with a sigmoid septum, IVS thickness was measured distal to the area of septal bulging. The highest

HIGHLIGHTS

- Obstructive and non-obstructive phenotypes were predominant in this large regional cohort of hypertrophic cardiomyopathy (HCM) patients.
- A notable burden of genetic mutations, particularly in MYBPC3 and MYH7, was observed.
- Overall mortality was relatively low and mainly driven by heart failure.
- Findings emphasize the clinical heterogeneity of HCM.
- The importance of comprehensive diagnostic evaluation in HCM is underscored.

wall thickness measured in any segment was recorded as the maximal wall thickness (MWT). These methodological principles were followed to ensure a comprehensive evaluation and accurate identification of hypertrophic segments.[12]

LV ejection fraction (LVEF) calculated using the biplane Simpson's method while left atrial diameter was evaluated in the parasternal long-axis view. The presence and severity of systolic anterior motion of the mitral valve were assessed in the parasternal long-axis and apical 3- and 5-chamber views using 2-dimensional and color Doppler imaging. Resting and provoked LV outflow tract (LVOT) gradients were assessed via continuous-wave Doppler under basal conditions and after maneuvers such as the Valsalva maneuver or exercise. Pulmonary artery systolic pressure was estimated based on the tricuspid regurgitation jet velocity, with the addition of right atrial pressure derived from inferior vena cava (IVC) assessment. Tricuspid annular plane systolic excursion (TAPSE) was measured from the apical four-chamber view using M-mode at the lateral tricuspid annulus. Right ventricular hypertrophy (RVH) was assessed by measuring RV free wall thickness in the subcostal view at end-diastole. A thickness ≥5 mm was considered indicative of RVH. The IVC diameter and its respiratory variation were evaluated in the subcostal long-axis view to estimate right atrial pressure, in line with guideline recommendations. Diastolic function was assessed in accordance with current guidelines.[12]

The CMR was performed using a 1.5 T scanner (Magnetom Aera; Siemens Medical Solutions, Erlangen, Germany) with phased-array body coils and prospective cardiac gating. The LVEF was calculated from short-axis cine images using the modified Simpson's method, and MWT was measured perpendicularly during end diastole. Apical aneurysms were assessed by carefully examining the apical segments in multiple long-axis and short-axis cine views for dyskinetic motion, thinning, and saccular outpouching of the myocardial wall. Myocardial fibrosis was identified through late gadolinium enhancement (LGE) imaging, performed 10-15 minutes after intravenous gadolinium administration. The presence of LGE was assessed by visual evaluation.[13] An experienced radiologist, blinded to clinical data, visually assessed and scored each segment for LGE distribution. Extensive LGE was defined as an LGE volume accounting for at least 15% of the LV mass.[14]

Phenotype Classification

Three distinct phenotypes of HCM were identified and analyzed in this study. Representative echocardiographic, ECG, and CMR findings across different HCM phenotypes are shown in Figure 1.

1. Obstructive HCM

This phenotype includes patients with a LVOT gradient ≥30 mmHg. The obstructive phenotype was evaluated in 2 distinct subgroups. Resting obstructive HCM is characterized by a persistent LVOT gradient of ≥30 mmHg at rest. In contrast, latent obstructive HCM refers to cases where the LVOT gradient is <30 mmHg at rest but increases to ≥30 mmHg during provocation, such as the Valsalva maneuver or exercise.[2,15] Provocation testing was routinely performed in all patients. The Valsalva maneuver was conducted by instructing patients to forcefully exhale against a closed airway (typically into a manometer) to maintain an intrathoracic pressure of approximately 40 mmHg for 10-15 seconds while in the supine position. This maneuver reduces preload and may enhance dynamic LVOT gradients in patients with obstructive physiology.[16] A standardized squat-to-stand maneuver was used as a physiologic provocation method. Patients were asked to perform rapid squatting followed by immediate standing, which transiently alters preload and afterload, thereby amplifying dynamic gradients in susceptible individuals.[16] In selected patients, a semi-supine bicycle exercise echocardiography was performed. The protocol involved progressive workload increments (usually 25 W every 2-3 minutes) while imaging was conducted in the left lateral decubitus position using continuous-wave Doppler to assess dynamic LVOT gradients during peak exertion. This method allows simultaneous assessment of exercise-induced gradients and symptoms.[17]

2. Non-Obstructive HCM

Patients classified as having non-obstructive HCM demonstrated no evidence of LVOT obstruction, either at rest or during physiologic provocation (e.g., Valsalva maneuver or exercise). To ensure a more homogeneous subgroup for analysis, only patients without apical involvement were included in the non-obstructive category. Specifically, individuals with isolated apical hypertrophy or mixed patterns involving the apex were excluded, thereby focusing this group on patients with asymmetric septal or concentric hypertrophy patterns that did not generate dynamic obstruction.

3. Apical HCM

This phenotype is characterized by predominant hypertrophy localized to the apex of the left ventricle. Apical HCM is identified by the presence of asymmetric LVH mainly localized to the LV apex, with an apical wall thickness of at least 15 mm and an apical-to-posterior wall thickness ratio greater than or equal to 1.5.[2]

Data Collection

Demographic and clinical data were recorded during patients' initial evaluations at the cardiomyopathy outpatient clinic. These included basic patient characteristics, comorbidities, family history of cardiomyopathy or SCD, and key clinical symptoms such as syncope, dyspnea, and palpitations. Functional capacity was assessed using the New York Heart Association (NYHA) classification to evaluate symptom severity and activity limitations.

Medication data were also collected, encompassing both treatments initiated prior to the first visit and those prescribed during follow-up. Baseline laboratory parameters were obtained at the time of the initial evaluation, including estimated glomerular filtration rate, creatine kinase-MB, troponin, and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels. These biomarkers were recorded to establish a biochemical and cardiac profile for each patient.

Electrocardiographic findings at the initial visit were also documented, including heart rhythm (e.g., sinus rhythm or

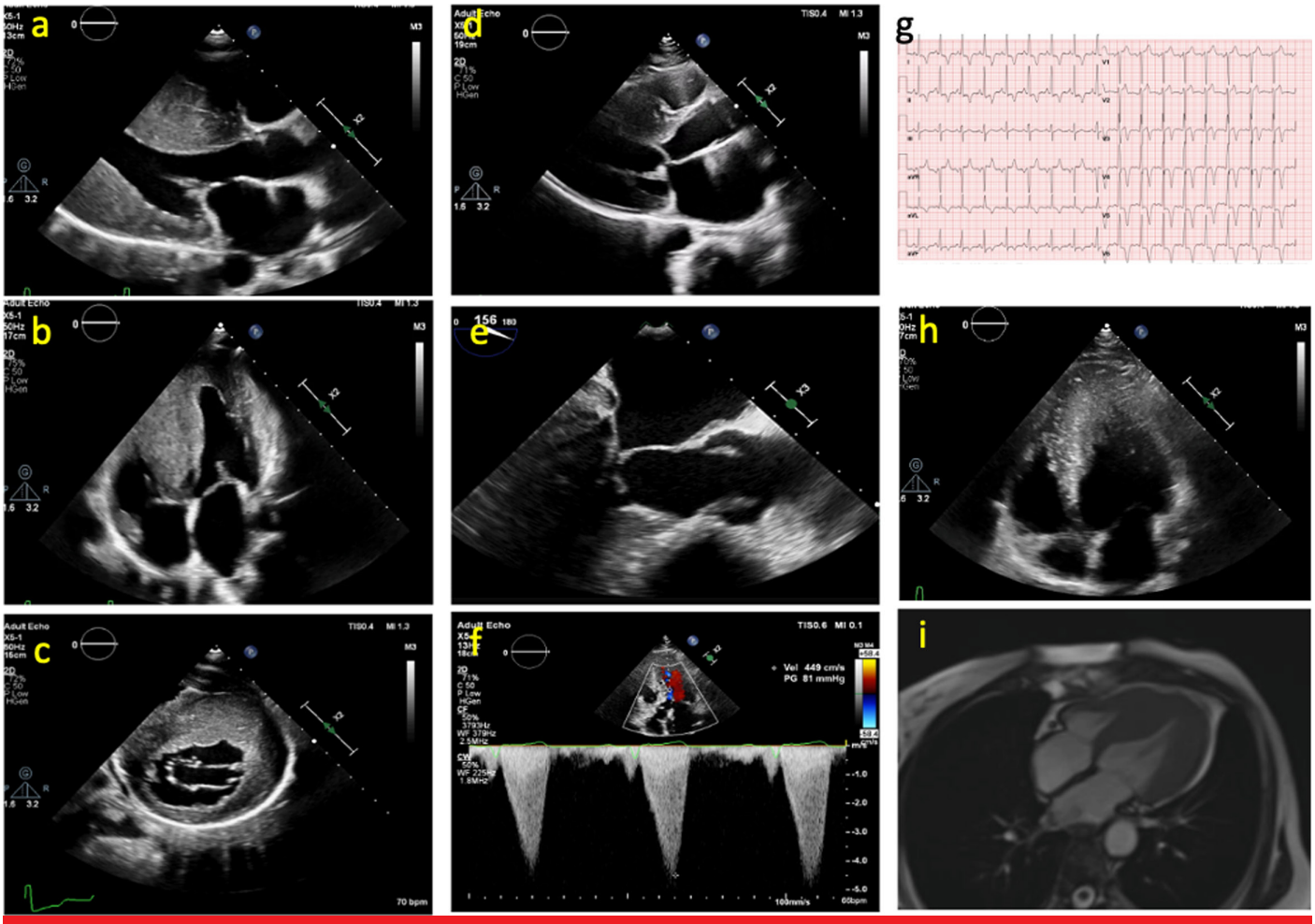

Figure 1. Multimodality imaging examples illustrating different hypertrophic cardiomyopathy (HCM) phenotypes. Parasternal long-axis view (a), apical 4-chamber view (b), and parasternal short-axis view (c) showing asymmetric septal hypertrophy without left ventricular outflow tract obstruction in a patient with non-obstructive HCM. Parasternal long-axis view showing systolic anterior motion (SAM) of the mitral valve and septal contact (d), transesophageal echocardiographic view of SAM at systole (e), and continuous-wave Doppler revealing a high LVOT gradient of 81 mmHg (f). Electrocardiogram showing giant negative T-waves, suggestive of apical involvement (g). Apical four-chamber view displaying marked apical hypertrophy with preserved basal dimensions (i). Cardiac magnetic resonance imaging confirming isolated apical hypertrophy.

atrial fibrillation), heart rate, PR interval, extreme hypertrophy, QRS duration, and corrected QT (QTc) interval.

The estimated 5-year risk of SCD was calculated using the ESC HCM Risk-SCD model, which includes clinical and echocardiographic parameters such as age, MWT, left atrial diameter, LVOT gradient, family history of SCD, unexplained syncope, and the presence of non-sustained ventricular tachycardia (NSVT).[18]

Data regarding the presence of implantable cardioverter-defibrillators (ICDs) and documented appropriate ICD shocks were retrospectively obtained from electronic medical records and device follow-up reports from the arrhythmia clinic. Information on previous septal reduction procedures, including alcohol septal ablation and surgical myectomy, was retrospectively obtained from hospital electronic records, catheterization laboratory reports, and surgical databases.

Clinical outcome data, including all-cause mortality, appropriate ICD shocks, NYHA functional class at last follow-up, and occurrence of septal reduction therapies, were retrospectively collected from electronic medical records and outpatient follow-up data.

Genetic Testing

Genetic testing was offered to all patients and performed in those who provided consent, using next-generation sequencing panels that included key sarcomeric and related genes known to be associated with HCM, such as MYH7, MYBPC3, and TNNT2. Variant classification followed the 2015 ACMG/AMP guidelines, and results were categorized as pathogenic, likely pathogenic, variants of uncertain significance (VUS), or benign/likely benign.[19] A result was considered positive if a pathogenic or likely pathogenic variant was identified. In cases where a VUS was detected—particularly in one of the core HCM-related genes and if supported by family history—segregation analysis was performed in

first-degree relatives. Genetic counseling was provided to all index cases before and after testing, and cascade screening was offered to families when clinically indicated. Variant interpretation was supported by multiple databases including ClinVar, gnomAD, HGMD, and in silico prediction tools (e.g., CADD, SIFT, MutationTaster). Pedigree analysis was also performed to assess inheritance patterns in families with multiple affected individuals.

Statistical Analysis

All statistical analyses were performed using R software (version 4.1.0 or later; R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed data are presented as mean ± standard deviation (SD), whereas non-normally distributed variables are expressed as median with interquartile range (IQR). Categorical variables are reported as counts and percentages.

Comparisons between more than 2 groups were conducted using the Kruskal–Wallis test for continuous variables and the chi-square or Fisher's exact test for categorical variables, as appropriate. When overall group differences were significant, post hoc pairwise comparisons were performed using the Dunn–Bonferroni method.

A 2-tailed *P* value <.05 was considered statistically significant. Descriptive and comparative analyses were designed to characterize differences in clinical, imaging, and genetic features across HCM phenotypes.

RESULTS

Study Population

Among the 701 patients with HCM, 228 (32.5%) had resting obstruction, 141 (20.1%) had latent obstruction, 267 (38.1%) were classified as non-obstructive, and 65 (9.3%) had an apical phenotype. The median follow-up time was 13.0 months (IQR: 4.0-26.0 months). The mean follow-up duration was 16.5 months with a standard deviation of 12.8 months. The median age was similar across subgroups (53.0 years), and the majority of patients were male (68%), with a significantly higher male proportion in the non-obstructive group (75%, *P*=.028). Hypertension was present in 51% of the overall cohort. A statistically significant difference in hypertension prevalence was observed across subgroups, primarily driven by a higher prevalence in the non-obstructive group compared to the apical group (*P*=.003).

Regarding functional capacity, NYHA class II was the most common across all groups (51% overall). Symptoms such as dyspnea, syncope, angina, and palpitations were frequently reported, particularly dyspnea (43% overall), without statistically significant differences between subgroups.

The median SCD risk score differed significantly among groups (*P* < .001), being highest in the resting-obstructive

Table 1. Baseline Demographic and Clinical Characteristics of the Study Cohort According to Hypertrophic Cardiomyopathy Phenotypes

	Overall	Resting-Obstructive	Latent-Obstructive	Non-Obstructive	Apical	
Variables	**n=701**	**n=228**	**n=141**	**n=267**	**n=65**	***P*²**
Sex (female), n (%)	224 (32)	86 (38)	47 (33)	68 (25)	23 (35)	.028
Age, years	53.0 (45.0, 62.0)	55.0 (46.0, 63.0)	52.0 (44.0, 60.0)	53.0 (44.0, 62.0)	53.0 (44.0, 61.0)	.178
BMI	28.4 (25.7, 31.6)	28.5 (25.8, 31.6)	27.8 (26.2, 31.5)	28.5 (25.7, 31.2)	28.0 (25.6, 31.2)	.975
Family history of CM, n (%)	115 (17)	39 (17)	32 (23)	33 (13)	11 (17)	.055
Family history of SCD, n (%)	84 (12)	30 (13)	19 (14)	29 (11)	6 (9.4)	.688
Atrial fibrillation, n (%)	130 (19)	52 (23)	24 (17)	45 (17)	9 (14)	.220
HT, n (%)	355 (51)	101 (45)	79 (56)	151 (57)	24 (37)	.003
DM, n (%)	101 (15)	31 (14)	25 (18)	38 (14)	7 (11)	.547
CAD, n (%)	190 (27)	52 (23)	37 (27)	82 (31)	19 (29)	.248
Stroke, n (%)	19 (2.7)	4 (1.8)	4 (2.9)	11 (4.1)	0 (0)	.225
Smoking, n (%)	168 (25)	47 (21)	36 (27)	70 (27)	15 (23)	.427
NYHA, n (%)						.066
1	195 (29)	52 (24)	47 (35)	72 (29)	24 (39)	
2	337 (51)	110 (50)	63 (47)	139 (56)	25 (41)	
3	117 (18)	49 (22)	22 (16)	35 (14)	11 (18)	
4	13 (2.0)	7 (3.2)	2 (1.5)	3 (1.2)	1 (1.6)	
Syncope, n (%)	85 (12)	31 (14)	22 (16)	24 (9.1)	8 (13)	.196
Presyncope, n (%)	101 (15)	40 (18)	25 (18)	31 (12)	5 (7.8)	.059
Dyspnea, n (%)	298 (43)	107 (47)	65 (46)	102 (38)	24 (38)	.167
Angina, n (%)	139 (20)	42 (19)	27 (20)	62 (24)	8 (13)	.215
Palpitation, n (%)	143 (21)	51 (23)	28 (20)	54 (21)	10 (16)	.701
SCD score	2.2 (1.5, 3.4)	2.7 (2.0, 4.4)	2.2 (1.7, 3.7)	1.8 (1.3, 2.8)	1.9 (1.3, 3.0)	<.001

Values are expressed as median with interquartile range (IQR, 25th, 75th percentile).
BMI, body mass index; CAD, chronic artery disease; CM, cardiomyopathy; DM, diabetes mellitus; HT, hypertension; NYHA, New York Heart Association; SCD, sudden cardiac death.

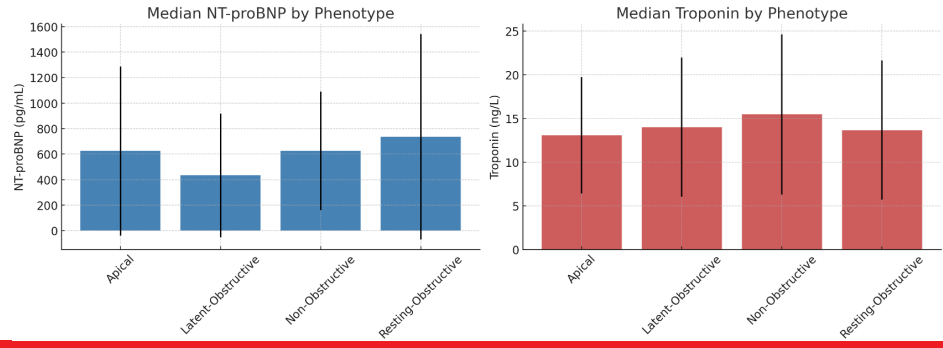

Figure 2. Median NT-proBNP and troponin levels across different hypertrophic cardiomyopathy (HCM) phenotypes. Error bars represent the interquartile range (IQR).

group (median 2.7, IQR 2.0-4.4) and lowest in the non-obstructive group (median 1.8, IQR 1.3-2.8). Table 1 summarizes the baseline demographic and clinical characteristics of the study group.

Implantable cardioverter-defibrillators were present in 11.8% of patients, with the highest prevalence observed in the latent-obstructive HCM subgroup. A statistically significant difference in ICD implantation rates was identified only between the latent-obstructive and non-obstructive subtypes (18% vs. 8.3%, $P=.022$); no significant differences were observed in other pairwise comparisons among the subgroups.

Beta-blockers were prescribed in 80.7% of the total cohort, with the highest usage in obstructive (83.8%) and latent-obstructive (82.3%) groups. Diuretics were prescribed in nearly one-third of patients (31.8%), with the highest use in the non-obstructive phenotype (37%). Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers were administered to 42% of patients overall, with significantly different usage across subgroups ($P=.004$), highest in the non-obstructive group (46%) and lowest in the apical group (31%). Oral anticoagulants were used in 15% of the cohort, with no statistically significant difference among subtypes ($P=.097$).

Regarding laboratory findings, NT-proBNP levels showed significant variation across HCM subtypes ($P=.006$). The highest median NT-proBNP level was observed in the resting-obstructive group (737.0 pg/mL [212.2-1820.0]), while the lowest was found in the latent-obstructive group (433.0 pg/mL [121.0-1091.0]). The NT-proBNP values in non-obstructive and apical groups were similar to the overall median level of

Table 2. Therapeutic Interventions, Medication Use, and Laboratory Findings According to Hypertrophic Cardiomyopathy Phenotypes

Characteristic	Overall n = 701	Resting-obstructive n = 228	Latent-obstructive n = 141	Non-obstructive n = 267	Apical n = 65	P[2]
Presence of ICD, n (%)	83 (11.8)	31 (14)	25 (18)	22 (8.3)	5 (7.7)	.022
Alcohol septal ablation, n (%)	37 (5.3)	28 (12)	9 (6.4)	0 (0)	0 (0)	<.001
Surgical myectomy, n (%)	17 (2.4)	9 (3.9)	5 (3.5)	3 (1.1)	0 (0)	.095
Disopyramide, n (%)	68 (9.9)	51 (22.3)	17 (12)	0 (0)	0 (0)	<.001
Beta blocker, n (%)	566 (80.7)	191 (83.8)	116 (82.3)	213 (79.8)	46 (70.8)	.030
Metoprolol	367 (54)	134 (58.7)	80 (56.7)	121 (45.3)	37 (56.9)	
Bisoprolol	114 (17)	41 (17.9)	22 (15.6)	44 (17)	6 (9.2)	
Calcium channel blockers, n (%)	139 (19.8)	41 (17.9)	30 (21.2)	59 (22)	9 (13.8)	.380
Diuretics, n (%)	223 (31.8)	64 (28)	46 (32.6)	99 (37)	14 (21.5)	.030
ACEi or ARBs, n (%)	284 (42)	76 (34)	68 (49)	120 (46)	20 (31)	.004
OACs, n (%)	103 (15)	44 (20)	20 (14)	31 (12)	8 (13)	.097
eGFR, mL/min/1.73 m^2	93.0 (74.3, 105.0)	92.0 (74.2, 105.0)	95.6 (78.0, 108.0)	92.0 (70.4, 103.5)	95.3 (83.1, 107.6)	.093
CKMB, ng/mL	2.9 (2.0, 4.2)	3.0 (2.0, 4.5)	2.8 (1.8, 4.5)	2.9 (2.0, 4.1)	2.4 (1.8, 3.2)	.285
Troponin, ng/L	14 (8, 24)	13 (9, 25)	15 (8, 26)	14 (9, 24)	14 (7, 23)	.553
NT-ProBNP, pg/mL	626.2 (206.9, 1,466.0)	737.0 (212.2, 1,820.0)	433.0 (121.0, 1,091.0)	625.0 (221.0, 1,162.0)	623.8 (302.4, 1,644.5)	.006

Values are expressed as median with interquartile range (IQR, 25th, 75th percentile).
ACE, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; CKMB, creatine kinase-MB isoenzyme; eGFR, estimated glomerular filtration rate; ICD, implantable cardioverter-defibrillator; NT-ProBNP, N-terminal pro B-type natriuretic peptide; OAC, oral anticoagulant.

626.2 pg/mL (206.9-1466.0). Differences in biomarker profiles among HCM phenotypes are depicted in Figure 2. Table 2 shows the medication use, therapeutic history, and the laboratory findings of the patients.

Imaging Characteristics and Genetics

Electrocardiographic parameters were largely similar among HCM subtypes. The QRS duration showed a statistically significant difference across groups ($P = .043$). The shortest median QRS duration was observed in the apical group (87 ms [80-97]), while the longest was in the resting- and latent-obstructive groups (94 ms in both) (Table 3).

Echocardiographic assessment revealed significant differences among HCM subtypes in multiple structural and functional parameters. Left ventricular ejection fraction was preserved in all groups but was significantly lower in the apical group compared to others ($P < .001$). Interventricular septal thickness, PW thickness, and MWT were all significantly lower in the apical group, while the highest values were observed in the resting- and latent-obstructive groups ($P < .001$ for all). Significant mitral regurgitation, which is defined as more than moderate, was present in 18.4% of the overall cohort, with a significantly higher prevalence in the resting-obstructive group (30.2%, $P < .001$). This was notably more frequent compared to latent-obstructive (12.7%), non-obstructive (12.3%), and apical (13.8%) groups. Left atrial diameter also varied significantly across subtypes, with larger dimensions in the obstructive phenotypes ($P < .001$). Pulmonary artery systolic pressure, TAPSE, and IVC diameter did not differ significantly among groups ($P = .208$, .064, and .406, respectively), suggesting similar RV function and filling pressures across phenotypes. Table 3 shows ECG and echocardiographic findings of the study group.

Cardiac magnetic resonance imaging was available in 84% of the overall cohort, with the highest utilization in the apical group (100%) and the lowest in the resting-obstructive group (79%) ($P = .001$). Although the overall median CMR-LVEF was 60.0% across subgroups, statistically significant differences were observed ($P < .001$). Specifically, LVEF values were significantly lower in the non-obstructive group compared to the obstructive, latent-obstructive, and apical subtypes. No significant differences were noted among the other groups.

Table 3. Electrocardiographic, Echocardiographic, and Cardiac Magnetic Resonance Imaging Findings Across Hypertrophic Cardiomyopathy Phenotypes

	Overall	Resting-obstructive	Latent-obstructive	Non-obstructive	Apical	
Characteristic	**n = 701**	**n = 228**	**n = 141**	**n = 267**	**n = 65**	***P*²**
Electrocardiography						
Heart rate, bpm	73.0 (65.0, 83.0)	73.0 (65.0, 82.5)	74.0 (65.0, 85.0)	72.0 (65.0, 82.0)	73.0 (65.5, 83.5)	.981
QRS duration, ms	92.0 (84.0, 102.0)	94.0 (85.0, 104.0)	94.0 (84.0, 102.0)	92.0 (84.0, 102.0)	87.0 (80.0, 97.0)	.043
QTc duration, ms	445 (426, 464)	448 (428, 466)	445 (429, 464)	442 (422, 463)	447 (433, 464)	.123
Echocardiography						
LVEF, %	60 (60, 65)	60 (60, 65)	60 (60, 65)	60 (55, 65)	60 (57, 60)	<.001
IVS, mm	17.0 (15.0, 20.0)	18.0 (16.0, 21.0)	17.0 (15.7, 20.8)	17.0 (15.0, 20.0)	13.0 (11.7, 15.0)	<.001
PW, mm	12.0 (11.0, 14.0)	12.5 (11.0, 14.0)	12.0 (10.5, 13.0)	13.0 (11.0, 14.0)	11.0 (10.0, 12.0)	<.001
MWT, mm	18.0 (16.0, 21.0)	18.0 (16.0, 21.9)	17.2 (16.0, 21.0)	17.0 (15.3, 20.5)	16.0 (14.0, 18.0)	<.001
E/e'	12.6 (10.0, 16.0)	12.5 (9.0, 15.7)	11.0 (9.2, 16.0)	12.6 (10.0, 16.5)	13.0 (10.5, 16.0)	.612
LA diameter, mm	41.0 (37.0, 46.0)	43.0 (38.5, 48.0)	41.0 (37.0, 45.0)	40.0 (37.0, 46.0)	39.0 (34.6, 42.0)	<.001
Rest gradient, mm Hg	31 (20, 48)	45 (35, 62)	17 (14, 22)	NA (NA, NA)	NA (NA, NA)	<.001
Provoked gradient, mmHg	60 (41, 86)	79 (62, 100)	40 (34, 51)	NA (NA, NA)	NA (NA, NA)	<.001
Mitral regurgitation, n (%)	129 (18.4)	69 (30.2)	18 (12.7)	33 (12.3)	9 (13.8)	<.001
PAPs , mm Hg	27.0 (23.0, 35.0)	29.0 (24.0, 35.0)	26.0 (21.0, 30.0)	26.0 (23.0, 37.0)	28.5 (23.5, 39.0)	.208
TAPSE, mm	21.1 (20.0, 23.2)	22.0 (20.0, 25.0)	21.0 (19.3, 23.0)	21.0 (20.0, 23.0)	20.0 (18.0, 22.0)	.064
IVC diameter, mm	15.3 (13.0, 19.0)	16.0 (13.0, 20.0)	15.0 (12.0, 18.0)	15.0 (12.8, 19.0)	14.5 (12.4, 18.0)	.406
Cardiac magnetic resonance imaging						
Presence of CMR, n (%)	587 (84)	179 (79)	120 (85)	223 (84)	65 (100)	.001
CMR-LVEF, %	60.0 (56.0, 62.0)	60.0 (57.0, 62.0)	60.0 (56.0, 62.0)	60.0 (55.0, 61.0)	60.0 (55.0, 63.0)	<.001
CMR-MWT, mm	18.5 (16.0, 22.0)	19.0 (16.7, 23.0)	18.7 (16.5, 22.0)	18.0 (15.3, 21.2)	18.0 (15.5, 21.7)	.039
CMR-RVEF, %	60.0 (56.0, 62.0)	60.0 (57.0, 62.0)	60.0 (56.0, 62.0)	60.0 (55.0, 61.0)	60.0 (55.0, 63.0)	.278
Presence of LGE, n (%)	502 (86)	146 (82)	100 (83)	194 (87)	62 (95)	.045
Extensive LGE, n (%)	146 (25)	32 (18)	24 (20)	66 (30)	24 (37)	.003
Apical aneurysm, n (%)	17 (3.0)	7 (4.1)	3 (2.7)	1 (0.5)	6 (9.7)	.001

Values are expressed as median with interquartile range (IQR, 25th, 75th percentile).
CMR, cardiac magnetic resonance; CMR-LVEF, cardiac magnetic resonance left ventricular ejection fraction; CMR-MWT, cardiac magnetic resonance-mean wall thickness; IVC, inferior vena cava; IVS, interventricular septum; LA, left atrium; LGE- late gadolinium enhancement; LVEF, left ventricular ejection fraction; MWT, mean wall thickness; PAPs, systolic pulmonary artery pressure; PW, posterior wall; TAPSE, Tricuspid annular plane systolic excursion.

Maximal wall thickness on CMR (CMR-MWT) differed significantly among subgroups ($P=.039$), with the highest values in the resting- and latent-obstructive groups and the lowest in the apical group. Late gadolinium enhancement was present in 86% of patients who underwent CMR. Although the prevalence appeared numerically higher in the apical group (95%, $P=.045$), post-hoc analysis revealed no statistically significant difference between subgroups. Extensive LGE was identified in 25% of the total cohort, again with the highest proportion in the apical group (37%) and lowest in the resting-obstructive group (18%) ($P=.003$). Apical aneurysms were detected in 3% of all patients, but were significantly more frequent in the apical group (9.7%) compared to other subtypes ($P=.001$). Table 3 reflects the imaging characteristics of the study group.

Genetic testing was performed in 221 patients (32% of the overall cohort), with similar proportions across HCM subtypes (range: 29%-38%, $P=.534$). Among those tested, 41% had a positive result, 37% were negative, and 22% carried a variant of uncertain significance (VUS), with no significant difference in distribution between subgroups ($P=.473$). The most frequently identified pathogenic or likely pathogenic mutations were in MYBPC3 (39% of positive cases) and MYH7 (26%), followed by MYL3 and TNNI3. Compound mutations were identified in 2.2% of genetically tested patients. No significant differences in gene distribution were observed among phenotypic subgroups ($P=.252$), although MYBPC3 mutations were numerically more common in obstructive and apical HCM, and compound mutations were only observed in the latent-obstructive group. Figure 3 shows the genetic results, distribution to the different phenotypes, and the specific gene results of the study population.

Clinical Outcomes

Implantable cardioverter-defibrillator shock was documented in 15% of patients with a device, with the highest rate observed in the apical group (40%), though this difference was not statistically significant ($P=.219$). Non-sustained ventricular tachycardia was identified in 17% of the overall cohort, with comparable rates across subgroups ($P=.906$).

Overall mortality was 2.9%, ranging from 1.4% in the latent-obstructive group to 4.8% in the resting-obstructive group ($P=.168$). Causes of death included heart failure (35%), SCD (25%), acute coronary syndrome (10%), surgical myectomy (10%), aortic dissection (5%), lung cancer (5%), respiratory failure (5%), and traffic accident (5%). No statistically significant difference in cause-specific mortality was observed among the subgroups ($P=.960$). Table 4 summarizes the clinical outcomes of the patients. Given the limited number of clinical events, performing a robust statistical comparison was not feasible. Nevertheless, for descriptive purposes, a comparison between patients with and without clinical outcomes is provided in the Supplementary Table 1. Pairwise

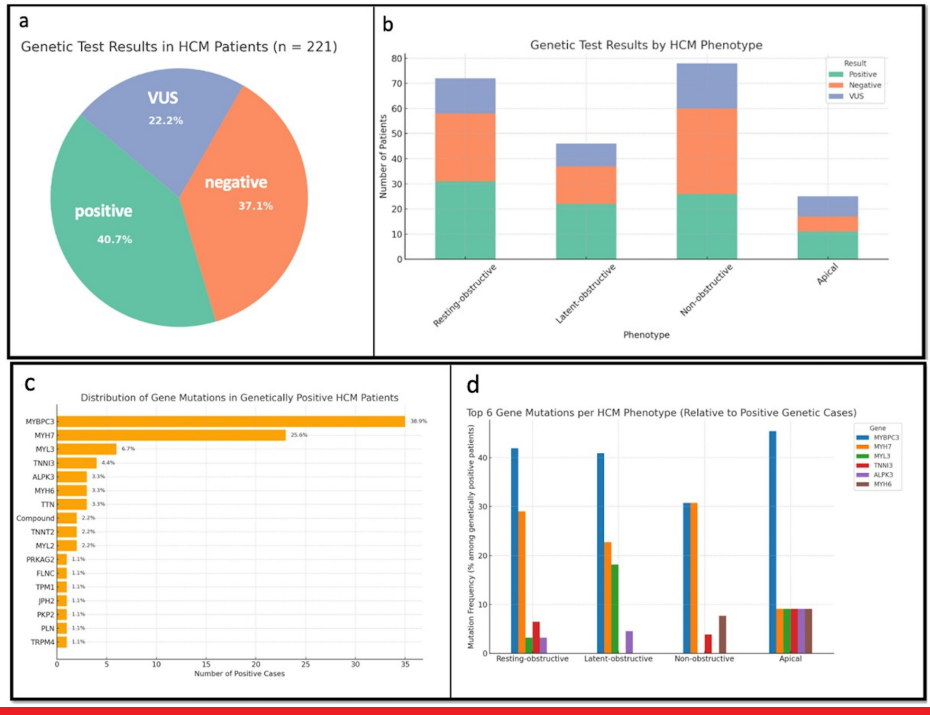

Figure 3. Genetic testing results in patients with HCM. (a) Distribution of genetic test results among 221 patients who underwent genetic testing. Results were categorized as positive (pathogenic or likely pathogenic variants), negative, or variant of uncertain significance (VUS). (b) Genetic test outcomes stratified by HCM phenotype, including resting-obstructive, latent-obstructive, non-obstructive, and apical subtypes. Distribution of gene mutations in genetically positive hypertrophic cardiomyopathy (HCM) patients. (c) Frequency of individual gene mutations among genetically positive cases. MYBPC3 and MYH7 were the most commonly detected mutations, followed by MYL3, TNNI3, ALPK3, and MYH6. (d) Distribution of the top 6 gene mutations stratified by HCM phenotype (resting-obstructive, latent-obstructive, non-obstructive, and apical), relative to genetically positive cases.

Table 4. Clinical Outcomes of the HCM Patients

	Overall	Resting-obstructive	Latent-obstructive	Non-obstructive	Apical	
Characteristic	**n = 701**	**n = 228**	**n = 141**	**n = 267**	**n = 65**	***P*²**
Follow-up, months	13.0 (4.0, 26.0)	13.0 (4.0, 28.3)	13.0 (3.0, 27.0)	13.0 (4.0, 24.0)	13.5 (3.7, 26.5)	.496
ICD shock, n (%)	12 (14.4)	4 (12.9)	2 (8)	4 (18.1)	2 (40)	.219
NSVT, n (%)	117 (17)	37 (16)	23 (16)	44 (16)	13 (20)	.906
Mortality, n (%)	20 (2.9)	11 (4.8)	2 (1.4)	5 (1.9)	2 (3.1)	.168
Mortality reasons, n (%)						.960
Heart failure, n (%)	7 (35)	3 (27)	0 (0)	3 (60)	1 (50)	
Sudden death, n (%)	5 (25)	2 (18)	1 (50)	1 (20)	1 (50)	
ACS, n (%)	2 (10)	0 (0)	1 (50)	1 (20)	0 (0)	
Aortic dissection, n (%)	1 (5.0)	1 (9.1)	0 (0)	0 (0)	0 (0)	
Surgical myectomy, n (%)	2 (10)	2 (18)	0 (0)	0 (0)	0 (0)	
Lung cancer, n (%)	1 (5.0)	1 (9.1)	0 (0)	0 (0)	0 (0)	
Respiratory failure, n (%)	1 (5.0)	1 (9.1)	0 (0)	0 (0)	0 (0)	
Traffic accident, n (%)	1 (5.0)	1 (9.1)	0 (0)	0 (0)	0 (0)	

Values are expressed as median with interquartile range (IQR, 25th, 75th percentile).
ACS, acute coronary syndrome; ICD, implantable cardioverter-defibrillator; NSVT, nonsustained ventricular tachycardia.

post-hoc comparisons using Dunn's test with Bonferroni correction were performed for variables showing significant overall differences in the tables, and the results are presented in Supplementary Table 2.

DISCUSSION

This study provides a comprehensive analysis of a large cohort of HCM patients, highlighting phenotypic variability and its clinical implications. The findings emphasize the importance of cardiac imaging, genetic testing, and clinical risk stratification in understanding the heterogeneity of HCM and guiding individualized patient management. Notably, data on HCM in Türkiye remains scarce, making this study a valuable contribution to understanding the disease within the region.

Although no gender differences in the prevalence of HCM are expected, a male predominance is evident in the study population, as observed in nearly all reports.[20,21] This disparity may be partly attributed to sex-related differences in symptom perception, pain threshold, and comorbid conditions such as obesity, which can influence the clinical presentation and timing of diagnosis in women.[22,23] However, evidence suggests that female HCM patients may have worse clinical outcomes, underscoring the critical importance of thorough diagnostic evaluations in this patient group.[24,25]

The study population includes 3 distinct phenotypes, with obstructive patients further categorized into rest and latent types to emphasize the importance of evaluating the latent subgroup. According to the literature, one-third of cases are obstructive at rest, one-third with provocation, and one-third non-obstructive.[26] The prevalence of apical HCM varies across studies, with rates reaching up to 25% in Asian populations and reported between 5% and 15% in Western societies.[27,28] In this cohort, the prevalence was 9.3%, which aligns with European data. However, with the increasing use of CMR, the diagnosis of apical HCM has become more frequent, and it is reasonable to predict that its prevalence will rise in the near future.[29,30] Latent-obstructive HCM prevalence in the cohort was 20.8%, slightly lower than reported, likely due to the possibility of limited use of provocation maneuvers. Accurate performance of the Valsalva maneuver, exercise echocardiography, or simple exercises during routine evaluations is essential for proper diagnosis.[31] To ensure optimal assessment, particularly in resource-limited settings, evaluations should be conducted in specialized centers with experienced clinicians.

Phenotypic comparisons in the study have yielded significant findings, particularly regarding patients with obstructive phenotype. Despite advances in treatment strategies, the resting-obstructive subtype remains the most common and clinically apparent form of HCM. In the study findings, although the comparison of functional capacity—which reflects heart failure symptoms—did not reach statistical significance, NYHA class III and IV patients were numerically more frequent in the resting-obstructive group. Consistent with this, and in a statistically significant manner, NT-proBNP levels were notably higher in the resting-obstructive subtype. Additionally, the presence of significant mitral regurgitation, which plays a role in both the pathophysiology and clinical presentation of these patients, was more prevalent in this group. It is also important to note that none of the patients in the cohort were treated with myosin inhibitors, which are increasingly used worldwide. Given the demonstrated benefits of these agents—such as improving clinical symptoms, enhancing functional capacity, and reducing NT-proBNP levels in obstructive HCM—it can be suggested that their wider adoption might help reverse these adverse findings in this specific patient population.

The use of CMR at a rate of approximately 84% in the study highlights its critical role in identifying phenotypic differences. The CMR is universally recommended by all guidelines as an indispensable tool for both the initial evaluation and

follow-up of cardiomyopathy patients.[2,15] Notably, CMR data revealed significant differences between groups, particularly in the assessment and frequency of LGE. The presence of LGE was observed in 95% of patients with apical HCM, a rate markedly higher compared to other phenotypes, but no statistical difference. Additionally, the extensive LGE observed in apical HCM patients, now recognized as a risk criterion for primary prevention ICD implantation, was significantly more prevalent in this phenotype. These findings not only underscore the potential inadequacy of current approaches in guiding primary prevention strategies for apical HCM but also highlight the need to reassess the clinical perspective and management algorithms. They emphasize the importance of developing dedicated risk stratification tools and ensuring closer follow-up and tailored care for this specific subgroup of patients. Furthermore, the presence of apical aneurysm, another well-known SCD risk factor, was also found to be more common in apical HCM patients. This observation aligns with previously reported data in the literature.[32,33]

The rate of genetic testing in the study was relatively low, reflecting the challenges of accessing genetic analysis in the country. However, recent regulatory changes aimed at improving access have enabled genetic testing to be performed in 221 patients, representing 32% of the study population. It is anticipated that these rates will increase over time, providing a more comprehensive understanding of the genetic basis of HCM in the population. Genetic analysis is particularly critical for population-specific characterizations, as environmental and geographic influences contribute to significant heterogeneity across different populations.[34,35] In the cohort, genetic positivity was identified in 41% of tested patients, a rate comparable to global reports.[3,5] Consistent with the literature, the MYBPC3 and MYH7 genes accounted for 70% of all positive results. While genotype-phenotype correlations were not statistically significant, the rate of genetic positivity was numerically lower in the non-obstructive subtype compared to the obstructive and apical phenotypes, which showed similar proportions of positive findings. This contrasts with the widely held view that genetic transmission in apical HCM is low, with positivity rates around 10%-30% reported in the literature.[36-38] The findings suggest the need for further investigation, as this discrepancy may be attributable to population-specific factors. A more definitive conclusion will require larger patient cohorts and increased rates of genetic testing to clarify these observations.

In the population, the proportion of patients with an implanted ICD was 11.8%, with 15% of these patients experiencing ICD shocks during follow-up. While ICD implantation rates were higher among patients with obstructive HCM, no clinical significance is claimed for this observation. Regarding ICD shocks, no significant differences were observed between groups, likely due to the limited number of events, which restricted meaningful statistical analysis. The overall mortality rate in the study cohort was 2.8%, with heart failure identified as the most common cause of death. Advances in treatment strategies and the use of ICDs have brought life expectancy in HCM patients closer to that of the general population. Notably, the prevention of SCD through ICD therapy has allowed for a more detailed observation of the natural progression of the disease.[39] Looking ahead, it can be hypothesized that the "burn-out" pattern in HCM will become increasingly prevalent, with disease outcomes progressively influenced by heart failure rather than SCD.[40,41] Consequently, identifying patients at risk of developing burn-out and implementing preventive measures will likely represent one of the major challenges in HCM management. Developing novel therapeutic strategies aimed at this subgroup will be essential for improving long-term outcomes in these patients. Although the current study provides valuable early insights into the demographic and clinical characteristics of patients with HCM, the median follow-up duration of approximately 13 months is relatively short for a chronic, slowly progressive condition such as HCM. Consequently, the mortality and ICD data reported here should be interpreted as preliminary and descriptive rather than prognostic. Longer-term follow-up from the institutional registry is ongoing and is expected to offer a more comprehensive evaluation of disease progression, arrhythmic risk, and survival outcomes in this population.

Study Limitations

The retrospective and single-center nature of the study may introduce selection bias, potentially overrepresenting more symptomatic or severe cases, and thus limiting the generalizability of the findings to broader HCM populations. Second, genetic testing was performed in 32% of the cohort, which restricts the exploration of genotype-phenotype correlations and limits insights into the genetic underpinnings of HCM in this population. This may also result in underestimating the role of specific genetic mutations in shaping phenotypic diversity. Also, the potential impact of specific genetic variants on clinical outcomes could not be assessed due to incomplete genetic data and the cross-sectional design of the study. Future longitudinal studies combining comprehensive genotyping with systematic follow-up are warranted to clarify genotype-driven differences in prognosis and adverse event risk. Third, while the study includes a relatively large and diverse cohort, it was conducted at a single tertiary center, which may limit the generalizability of the findings to other populations or healthcare systems. Additionally, the region-specific nature of the study provides valuable localized data but may not capture the full spectrum of HCM phenotypes observed globally. Furthermore, because this analysis was cross-sectional, longitudinal clinical outcomes such as mortality, arrhythmias, or other adverse cardiac events could not be systematically evaluated, and survival analyses were not feasible. Although CMR data were available for most patients, the study design and lack of uniform long-term follow-up precluded reliable assessment of the prognostic implications of LGE and other CMR-derived parameters. Lastly, the follow-up period, while reasonable, may not be sufficient to fully evaluate long-term outcomes, particularly regarding disease progression and mortality. The reliance on advanced imaging techniques like CMR, although beneficial, may not be feasible in all clinical settings,

potentially affecting the reproducibility of findings. Despite these limitations, this study provides significant insights into the phenotypic diversity and clinical management of HCM and lays the groundwork for future multicenter, prospective research.

CONCLUSION

This study provides valuable insight into the phenotypic spectrum and clinical characteristics of HCM within a regional cohort, representing the first epidemiological data from this population. Obstructive HCM—particularly the resting-obstructive subtype—emerged as the most prevalent and clinically dominant form, associated with more advanced heart failure symptoms, elevated NT-proBNP levels, and a higher prevalence of significant mitral regurgitation. The widespread use of cardiac MRI enhanced the detection of apical variants and LGE, both essential elements in contemporary risk stratification. Genetic testing was performed in approximately one-third of patients, with MYBPC3 and MYH7 mutations most commonly identified across phenotypes. These findings, grounded in a population-specific context, highlight the value of regional data in shaping individualized management strategies and enriching the global understanding of HCM phenotypes.

Ethics Committee Approval: This study was approved by the Ethics Committee of University of Health Sciences, İstanbul MehmetAkif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital (Approval no: 2025.02-13; Date: 04.03.2025).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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Supplementary Table 1. Comparison of baseline characteristics and imaging features according to clinical outcomes

Characteristic	Overall n = 701	Clinical outcome - n = 681	Clinical outcome + n = 20	*P*
Sex, n (%)	224 (32%)	215 (32%)	9 (45%)	0.204
Age, years	53.0 (45.0, 62.0)	53.0 (44.0, 62.0)	55.0 (48.0, 64.0)	0.211
Presence of ICD, n (%)	83 (12%)	81 (12%)	2 (10%)	1.000
Troponin, ng/L	14.0 (8.0, 24.3)	14.0 (8.0, 24.0)	25.7 (15.8, 80.0)	0.003
NT-ProBNP, pg/mL	626.2 (206.9, 1,466.0)	617.1 (194.0, 1,393.0)	1,759.0 (1,002.0, 4,888.0)	0.001
QRS duration, ms	92.0 (84.0, 102.0)	92.0 (84.0, 102.0)	95.0 (94.0, 116.0)	0.034
QTc duration, ms	445.0 (426.0, 464.0)	445.0 (426.0, 464.0)	468.0 (438.0, 485.0)	0.012
LVEF, %	60.0 (60.0, 65.0)	60.0 (60.0, 65.0)	50.0 (43.5, 65.0)	0.007
MWT, mm	18.0 (16.0, 21.0)	17.8 (16.0, 21.0)	19.1 (16.5, 22.1)	0.157
Type of HCM, n (%)				0.168
1	228 (33%)	217 (32%)	11 (55%)	
2	141 (20%)	139 (20%)	2 (10%)	
3	267 (38%)	262 (38%)	5 (25%)	
4	65 (9.3%)	63 (9.3%)	2 (10%)	
LA diameter, mm	41.0 (37.0, 46.0)	41.0 (37.0, 46.0)	43.0 (39.6, 50.4)	0.088
Rest gradient, mm Hg	13.0 (2.0, 35.0)	12.0 (2.0, 34.0)	36.0 (2.0, 56.5)	0.014
Provoked gradient, mm Hg	60.0 (41.0, 88.0)	60.0 (41.0, 86.0)	78.0 (56.0, 107.0)	0.180
Significant MR, n (%)	129 (20%)	118 (19%)	11 (58%)	0.001
TAPSE, mm	21.1 (20.0, 23.2)	21.9 (20.0, 23.3)	19.0 (17.0, 21.0)	0.047
RVH, n (%)	32 (6.3%)	29 (5.8%)	3 (25%)	0.033
PAPs, mm Hg	27.0 (23.0, 35.0)	27.0 (23.0, 34.0)	33.0 (26.0, 42.0)	0.075
IVC diameter, mm	15.3 (13.0, 19.0)	15.0 (13.0, 18.3)	19.2 (15.5, 20.8)	0.047
CMR LVEF, %	66.0 (63.0, 71.0)	66.0 (63.0, 71.0)	70.0 (53.0, 74.0)	0.620
CMR MWT, mm	18.5 (16.0, 22.0)	18.4 (16.0, 22.0)	22.3 (20.0, 26.0)	0.035
CMR RVEF, %	60.0 (56.0, 62.0)	60.0 (56.0, 62.0)	57.5 (52.0, 63.0)	0.413
LGE, n (%)	502 (86%)	490 (86%)	12 (86%)	1.000
Extensive LGE, n (%)	146 (25%)	143 (25%)	3 (21%)	1.000
NSVT, n (%)	117 (17%)	114 (17%)	3 (15%)	1.000

CMR- Cardiac magnetic resonance imaging, HCM- Hypertrophic cardiomyopathy, ICD - Implantable cardiac defibrillator, IVC- inferior vena cava, LA- Left atrium, LGE- late gadolinium enhancement, LVEF- Left ventricular ejection fraction, MR- mitral regurgitation, MWT- Mean wall thickness, NSVT- Nonsustanined ventricular tachycardia, NT-ProBNP- N-terminal pro B-type natriuretic peptide, PAPs- systolic pulmonary artery pressure, PW- posterior wall, RVEF – right ventricular ejection fraction, RVH: right ventricular hypertrophy, TAPSE- Tricuspid annular plane systolic excursion

Supplementary Table 2. Pairwise post-hoc comparisons of clinical, echocardiographic, and CMR characteristics across hypertrophic cardiomyopathy phenotypes

Variables	Comparison
LA diameter	Resting-obstructive vs Non-obstructive (p=0.038)
	Resting-obstructive vs Apical (p<0.001)
	Latent-obstructive vs Apical (p=0.007)
	Non-obstructive vs Apical (p=0.002)
Sex	Resting-obstructive vs Non-obstructive (p=0.011)
Hypertension	Resting-obstructive vs Non-obstructive (p=0.023)
	Latent-obstructive vs Apical (p=0.028)
	Non-obstructive vs Apical (p=0.012)
Diuretics	There were no statistically significant pairwise comparisons.
Beta-blockers	Non-obstructive vs Apical (p=0.009)
ICD	Latent-obstructive vs Non-obstructive (p=0.015)
Alcohol septal ablation	Resting-obstructive vs Non-obstructive (p<0.001)
	Latent-obstructive vs Non-obstructive (p=0.018)

	Resting-obstructive vs Apical (p<0.001)
Disopyramide	Resting-obstructive vs Latent-obstructive (p=0.004)
	Resting-obstructive vs Non-obstructive (p<0.001)
	Latent-obstructive vs Non-obstructive (p<0.001)
	Resting-obstructive vs Apical (p<0.001)
ACE/ARB use	Resting-obstructive vs Latent-obstructive (p=0.018)
	Resting-obstructive vs Non-obstructive (p=0.022)
NT-proBNP	Latent-obstructive vs Resting-obstructive (p=0.003)
QRS duration	Resting-obstructive vs Apical (p=0.019)
LVEF (Echocardiography)	Resting-obstructive vs Non-obstructive (p<0.001)
	Latent-obstructive vs Non-obstructive (p<0.001)
	Resting-obstructive vs Apical (p=0.001)
	Latent-obstructive vs Apical (p=0.019)
IVS thickness	Resting-obstructive vs Non-obstructive (p=0.001)
	Resting-obstructive vs Apical (p<0.001)
	Latent-obstructive vs Apical (p<0.001)
	Non-obstructive vs Apical (p<0.001)
Posterior wall thickness	Resting-obstructive vs Latent-obstructive (p=0.007)
	Latent-obstructive vs Non-obstructive (p=0.015)
	Resting-obstructive vs Apical (p<0.001)
	Non-obstructive vs Apical (p<0.001)
MWT (Echocardiography)	Resting-obstructive vs Non-obstructive (p=0.009)
	Resting-obstructive vs Apical (p<0.001)
	Latent-obstructive vs Apical (p<0.001)
	Non-obstructive vs Apical (p=0.004)
Rest gradient	All intergroup differences were statistically significant ($p < 0.001$), except for the comparison between the apical and non-obstructive groups ($p = 0.999$).
Provoked gradient	Resting-obstructive vs Latent-obstructive (p<0.001)
Mitral regurgitation	Resting-obstructive vs Non-obstructive (p<0.001)
Presence of CMR	Resting-obstructive vs Apical (p<0.001)
	Latent-obstructive vs Apical (p=0.021)
	Non-obstructive vs Apical (p=0.004)
CMR-LVEF	Resting-obstructive vs Non-obstructive (p<0.001)
	Latent-obstructive vs Non-obstructive (p<0.001)
CMR-MWT	Resting-obstructive vs Non-obstructive (p=0.039)
LGE presence	Resting-obstructive vs Apical (p=0.025)
Extensive LGE	Resting-obstructive vs Non-obstructive (p=0.019)
	Resting-obstructive vs Apical (p=0.008)
	Latent-obstructive vs Apical (p=0.034)
Apical aneurysm	Non-obstructive vs Apical (p<0.001)

ACE- Angiotensin-converting enzyme inhibitors, ARBs - Angiotensin receptor blockers, CMR- cardiac magnetic resonance imaging, ICD- Implantable cardioverter-defibrillator, IVS- interventricular septum, LA- left atrium, LGE- late gadolinium enhancement, LVEF- left ventciular ejection fraction, MWT- maximal wall thickness, NT-ProBNP- N-terminal pro B-type natriuretic peptide
Overall group differences were assessed using the Kruskal–Wallis test, followed by Dunn's post-hoc test with Bonferroni correction. Only statistically significant pairwise comparisons are reported.