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Published in:
European Heart Journal - Quality of Care and Clinical Outcomes

DOI (link to publication from Publisher):
10.1093/ehjqcco/qcae031

Publication date:
2025

Document Version
Accepted author manuscript, peer reviewed version

Frequency of Misdiagnosis in Hypertrophic Cardiomyopathy

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Word count: 3116

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Abstract

Background

Hypertrophic Cardiomyopathy (HCM) is characterized by unexplained left ventricle hypertrophy (LVH) ≥15 mm. The condition is often hereditary and family screening is recommended to reduce the risk of adverse disease complications and premature death among relatives. Correct diagnosis of index patients is important to ensure that only relatives at risk of disease development are invited for family screening.

Purpose

To investigate if patients with ICD-10 codes for HCM (DI421) or hypertrophic obstructive cardiomyopathy (DI422) fulfilled recognised diagnostic criteria.

Methods

All patients with ICD-10 codes for HCM or HOCM at a Department of Cardiology were identified and had their diagnosis validated by a cardiac investigation or a review of their medical records and previous investigations.

Results

Two hundred and forty patients had ICD-10 codes for HCM/HOCM, of whom 202 (84%, 202/240) underwent re-examination, while 38 (16%, 38/240) had their hospital notes reviewed. Seventy-six patients (32%, n=76/240) did not fulfil diagnostic criteria, of whom 39, (51%, n=39/76) had normal (10 mm) or modest LV wall thickness (11-14 mm). The remaining 37 patients (49%, n=37/76) had LVH ≥15 mm, which was well-explained by uncontrolled hypertension, (32%, n=24/76), aortic valve stenosis (19%, n=7/76) or wild-type amyloidosis (16%, 6/76).

Conclusion

One-third of patients with ICD-10 codes for HCM or HOCM did not fulfil recognised diagnostic criteria. Incorrect diagnosis of HCM may cause unnecessary family investigations

which may be associated with anxiety, and a waste of health care resources. This highlights the need for specialised cardiomyopathy services to ensure correct diagnosis and management of HCM.

Keywords: Cardiomyopathy, Hypertrophic; diagnostic criteria; family screening; ICD-10 codes; healthcare organization

Key learning points

a. What is already known

- Hypertrophic cardiomyopathy is a common hereditary cardiac condition defined by unexplained left ventricle hypertrophy ≥15 mm.
- Due to the hereditary nature of HCM, a correct diagnosis of the condition is important to ensure that only relatives at risk of disease development are offered clinical investigations.
- It may be a challenge to distinguish HCM from other causes of myocardial hypertrophy.

b. What this study adds

- One-third of patients with an ICD-10 code for HCM or HOCM did not fulfil recognised diagnostic criteria of the conditions. This may result in unnecessary investigations of relatives who are not at risk of developing HCM.
- The results highlighted a need for more awareness about correct diagnosis of HCM

Introduction

Hypertrophic cardiomyopathy (HCM) is a common cardiac condition characterized by unexplained myocardial hypertrophy[1]. The condition is associated with a heterogeneous disease expression, ranging from mild symptoms to severe heart failure, arrhythmias, and sudden cardiac death[2].

Hypertrophic cardiomyopathy is defined by the presence of left ventricle wall (LVW) thickness ≥15 mm, which cannot solely be explained by increased loading conditions [1, 3, 4]. However, the diagnosis may be difficult, especially in elderly hypertensive patients who may present with the same pattern of LV hypertrophy as in HCM[5]. To differentiate HCM from other conditions associated with the development of LV hypertrophy, it is often helpful to obtain a thorough family history with information from hospital notes, death certificates and autopsy reports of relatives suspected of having cardiac disease including individuals who died suddenly[1, 4].

Since HCM may be hereditary, family screening is generally recommended to identify relatives at risk of disease development [1, 3, 4]. Therefore, correct use of ICD-10 codes for the conditions is important to ensure that only relatives with a true risk of developing HCM are offered cardiac investigations.

It was the aim of the study to investigate how often ICD-10 codes for HCM/hypertrophic obstructive cardiomyopathy (HOCM) were used in accordance with recommendations provided by current guidelines. Furthermore, we investigated if the presence of hypertension in affected individuals was likely to modify the disease expression of HCM.

Methods

The study was conducted in accordance with the Declaration of Helsinki and approved by the Danish Data Protection Agency (19/38530).

Study setting

This cross-sectional study was conducted at the Department of Cardiology, Odense University Hospital, (OUH), which serves as the main referral center for inherited cardiovascular conditions in the Region of Southern Denmark. OUH has a catchment area of 1.2 million inhabitants, (21% of the Danish population in 2021)[6].

Diagnostic criteria

A diagnosis of HCM or HOCM was considered to be fulfilled when patients met the diagnostic criteria suggested by ESC guidelines for the condition, which is defined by unexplained left ventricular hypertrophy ≥15 mm, not solely explained by abnormal loading conditions[1]. For adults ≥ 18 years with confirmed HCM in their family, LVH of ≥13 mm in the absence of abnormal loading conditions was also considered diagnostic[1].

Patient cohort

All patients who had an ICD-10 code of HCM or HOCM (DI422, DI421) at the Department of Cardiology, OUH, were identified by a search of the electronic patient archive in the period between 14.11.2015 - 02.10.2019.

All patients identified with an ICD-10 code for HCM/HOCM were referred to the University Hospital from Regional hospitals for re-examination. During the visitation procedure it was decided if patients should be (a) invited for a re-examination in the clinic for hereditary cardiovascular conditions which included a physical examination, 12-lead electrocardiography (ECG) and transthoracic echocardiogram (TTE) or (b) considered not to have HCM/HOCM based on a thorough review of their hospital records including the results of previous cardiac investigations, medical history and family history of cardiac disease.

Echocardiography

All patients underwent a standard 2-dimensional transthoracic echocardiographic evaluation, which included measurement of the maximal wall thickness, left atrial size, left ventricular (LV) ejection fraction, and LV outflow tract gradient. Maximal wall thickness was determined as the maximal thickness of the LV wall in any segment. Peak outflow tract gradient was determined from pulsed and continuous wave Doppler and derived from the modified Bernoulli equation. LV outflow tract obstruction was defined as a gradient ≥30 mmHg at rest or following provocation with Valsalva maneuver[1].

Cardiac magnetic resonance imaging

Cardiac magnetic resonance (CMR) imaging was performed utilizing ECG-gating and breath-hold techniques on a 1.5T scanner (Discovery MR450, GE Healthcare, Milwaukee, WI, USA). Steady-state free-presession cine images were acquired in standard short-axis and long-axis projections with a slice thickness and gap of 8/2 mm. The images were obtained with a flip angle of 60 degrees, an echo time of 1.5 ms, a repetition time of 3.3 ms, a matrix size of 224 × 224, a field of view of 360 × 360 mm, 24 views per segment, and 40 reconstructed phases. Native T1-mapping images were acquired in three short-axis slices using a modified Look-Locker inversion recovery sequence with a 5(3)3 scheme. Late gadolinium enhancement images in both short-axis and long-axis orientations were acquired utilizing a 2D inversion recovery fast gradient echo sequence, 10 minutes after intravenous administration of 0.2 mmol/kg gadoteridol (Prohance, Bracco Imaging, Gothenburg, Sweden), with inversion time of 240 ms to null the signal from normal myocardial tissue. The CMR images were analyzed using cvi42 post-processing software (Circle Cardiovascular Imaging Inc., Calgary, Alberta, Canada).

CMR was available for all patients.

Statistical analysis

Statistical analyses were performed using STATA/IC version 16.0. Descriptive statistics data are expressed as mean±SD for symmetrically distributed continuous data, median (interquartile range [IQR]) for skewed data and counts or percentages for categorical variables. Categorical variables were compared using the chi-square test or Fisher exact test as appropriate. Kruskal-Wallis was used in variables with more than two groups. A paired test and the Wilcoxon signed-rank test were used to compare symmetrically and skewed continuous data, respectively. A 2-sided p-value ≤ 0.05 was considered statistically significant.

Results

All patients (n=240) taking part of this investigation had primarily received and ICD-10 code of HCM/HOCM (DI421 or DI422), by cardiologists working at Regional Hospitals. Eighty-four percent (202/240) were referred from the Regional Departments of Cardiology to the clinic of hereditary cardiovascular conditions and re-examined. All available information about the remaining 16% (38/240) of patients was reviewed by expert cardiologists which included hospital notes, ECGs, and echocardiograms.

Overall, 23% (54/240) of the patients underwent CMR, conducted either during the initial assessment, (63%; 34/54), or upon re-examination at the clinic of hereditary cardiovascular conditions (37%; 20/54). CMR evaluation did not result in any changes of the diagnoses established by echocardiography.

Characteristics of patients who fulfilled diagnostic criteria of HCM or HOCM (Figure 1 & Table 1)

Sixty-eight percent, (164/240), of patients, had their diagnosis of HCM/HOCM confirmed. They had a median age of 63, (IQR:54;72), and 62%, (102/164), were males. The majority of patients were of Caucasian descent (93%, 152/164), while the remaining cohort originating from the Middle Eastern (4%, 7/164) or Asia (3%, 5/164).

Echocardiography revealed an average LVW thickness of 18 mm, (IQR:16;22), with septal hypertrophy being most frequent (84%, 138/164), followed by apical hypertrophy (15%, 25/164). One HCM patient had concentric hypertrophy and was shown to carry a disease-causing variant in the gene for *PRKAG2* (1%, 1/164). Thirty-four percent, (56/164), of HCM patients, had HOCM with a resting/Valsalva LV outflow gradient of more than 30 mmHg.

The majority of patients, (70%, 115/164), had no co-morbidities. However, 30% (49/164), did also have a diagnosis of uncontrolled hypertension. These patients had an average LVW thickness of 18 mm, (IQR:16;22). They were all normotensive at the time of diagnosis with a median age of 69 years (IQR:62;76). There were no differences in the disease expression between HCM patients with and without hypertension, except that HCM patients with hypertension were older at the time of diagnosis, (69 years (IQR:62;76) vs. 59 years (IQR:51;69), $p<0.01$). In addition, they carried a disease-causing variant in recognized HCM genes less frequently than normotensive patients (17% vs. 41%, $p=0.01$).

Eighty-seven percent of all patients (143/164) had ECG abnormalities, which included abnormal ST-segments (45%, 73/164), a pattern of LVH (24%, 39/164), bundle branch block (9%, 15/164), atrial fibrillation (7%, (11/164), or abnormal Q-waves (3%, 5/164).

Nine percent (14/164) had a family history of sudden cardiac death (SCD), while 18% (30/164) were shown to have a familial appearance of HCM following family screening studies. Genetic investigations were performed in 84% of the patients (137/164) and 34% (47/137) were shown to carry a disease-causing variant in a recognised HCM disease gene [7].

Characteristics of patients with LVW thickness ≥15 mm who did not fulfil HCM/HOCM diagnostic criteria (Figure 1 & Table 2)

Thirty-two percent, (76/240), of patients, did not meet the diagnostic criteria of HCM/HOCM of whom 49%, (37/76), had a median left ventricle wall thickness of 16 mm (IQR: 15;17). Sixty-five percent, (24/37), had uncontrolled hypertension and 58%, (14/24), of these patients had an echocardiogram with concentric hypertrophy in 58%, (Table 2). The remaining 42%, (10/24) had an isolated bulge of the basal septum of 15 mm (IQR:15;16), which protruded into the left ventricle outflow tract that caused an LV outflow gradient of more than 30 mmHg. The median age of patients was 74, (IQR:62;82), and 42%, (10/24), were males. Ninety-two percent, (22/24), of patients were Caucasian while 8%, (2/24), were of Middle Eastern origin. No one had a family history of sudden cardiac death (SCD) or a suspected familial appearance of HCM. The majority had an abnormal ECG, (75%, 18/24), LVH (67%, 16/24). Two were in atrial fibrillation.

Seven patients of Caucasian descent (9%, 7/76) with a median age of 82 years (IQR: 72;87) had a median concentric LVW thickness of 17 mm, (IQR: 15;18) which was explained by the presence of severe aortic stenosis with a median area of 0.7cm^2 (IQR: 0.6; 0.8), and a median gradient of 67 mmHg (IQR: 61;75)).

Six patients of Caucasian descent (8%, 6/76) with a median age of 71 years, (IQR: 66;75) had a concentric LVW thickness of 18 mm (IQR: 16;21) which was explained by wild-type ATTR amyloidosis. This was established following re-examination at the clinic of hereditary

cardiovascular conditions. One had received a pacemaker due to an atrioventricular block and one was in atrial fibrillation. The remaining four patients had either low-voltage, (33%, 2/6), or a normal ECG, (33%, 2/6). They all had a positive 3,3-diphosphono-1,2-propanodicarboxylic acid (DPD) scintigraphy (grade 3-4), which was consistent with ATTR amyloidosis with normal genetic and hematologic investigations.

Characteristics of patients with LVW thickness < 15 mm who did not fulfil HCM/HOCM diagnostic criteria (Figure 1 & Supplementary Table 1)

Fifty-one percent, (39/76), of patients did not fulfil recognised diagnostic criteria of HCM/HOCM. They had an LVW thickness < 15 mm of whom 38% (29/76) had an LVW thickness between 11-14 mm, which was explained by hypertension in 33% (25/76). These patients had a median age of 73, (IQR:63;81) and 48% were males. Among them, 80% (20/25) were of Caucasian descent while the remaining individuals originate from the Middle East, (2%, 3/25), or Asia, (8%, 2/25). No one had an apparent family history of HCM. Echocardiography showed that 60% (15/25) had concentric hypertrophy while 40% (10/25) had an isolated bulge of the basal septum which protruded into the left ventricle outflow tract with an average thickness of 14 mm, (IQR:13;14). The majority had a normal ECG, (64%, 16/25).

Four patients of Caucasian descent (5%, 4/76) with a median age of 88 years, (IQR:78;91) had severe aortic stenosis with an LVW thickness between 11-14 mm.

The remaining 10 patients (13%, 10/76) had a normal LVW thickness (10 mm). Their echocardiography was characterized by the presence of trabeculae localised in close proximity to the interventricular septum and had been included in the primary measurements. This led to a mis-interpretation of increased septal thickness and thereby a diagnosis of HCM, (Figure 2).

Management of patients with a misdiagnosis of HCM/HOCM

Patients who were re-investigated at the Clinic for hereditary cardiovascular conditions and shown not to fulfil HCM diagnostic criteria, (n=38) were informed about the misdiagnosis at the same visit. The referring physician of patients who did not fulfil diagnostic criteria following review of hospital notes, ECG's and echocardiography were informed in writing about the likely misdiagnosis and that family investigations were not indicated. They were encouraged to recall the patients to their clinic and inform them about the results of the review and the correct diagnosis.

In general, it was the impression that the majority of patients who had been misdiagnosed were relieved that they did not have a hereditary cardiac condition and that they were not at risk of passing the disease on to their offspring.

Discussion

In the current study, one-third of patients with an ICD-10 code for HCM or HOCM did not fulfil diagnostic criteria as suggested by ESC guidelines[1, 4]. The majority of non-diagnostic patients had LVH < 15 mm of whom 25% (10/39) had an entirely normal LV wall thickness (Figure 1, Supplementary Table 1).

Individuals with a normal LV wall thickness had most likely received the diagnosis due to misinterpretation of the findings by echocardiography since trabeculae in close proximity to the interventricular septum were included in the primary estimation of their wall thickness (Figure 2). Some of these patients even had CMR performed, which also reported a falsely increased thickness of the interventricular septum since the resolution of the CMR was unable to separate trabeculae from the interventricular septum (Figure 2). These findings underscored the importance of correct interpretation of findings by echocardiography, which

is still a fundamental investigation, in diagnosing HCM. As an example of misinterpretation of the results of imaging an asymptomatic 72-year-old patient with a history of hypertension and an abnormal ECG was initially diagnosed with HCM by echocardiography and subsequently referred for a CMR which was LGE positive, although the thickness of his interventricular septum was entirely normal (Figure 2). Unless these investigations had been reviewed by an expert cardiologist in hereditary cardiac conditions this would most likely have led to genetic investigations of HCM genes and family screening with the risk of incidental findings, overdiagnosis and unnecessary follow-up of his relatives.

Another significant proportion of the non-diagnostic patients, (26%, 20/76), had an isolated bulge localized at the basal part of the interventricular septum, which protruded into the LVOT and was associated with mild obstruction. These findings were predominantly identified in elderly patients (median age: 74) with hypertension and no history of familial disease and were not considered to be part of the disease expression in HCM/HOCM[8]. While patients with an isolated bulge may not need family screening, it remains important to investigate the degree of LVOT obstruction, which may require treatment to prevent symptoms and exercise-induced syncope.

The majority of the non-diagnostic patients with LVH ≥15 mm had clinical characteristics most likely explained either by hypertension or the presence of aortic stenosis. Similar findings have been reported previously in a smaller study in which almost one-third of patients, (n = 40/129), with an ICD-code for HCM or HOCM did not fulfil recognised diagnostic criteria. The majority had a true thickness of the interventricular septum of less than 15 mm following expert review of their echocardiography[9].

It is evident that a misdiagnosis of HCM may have a significant impact on patients and their relatives since it is not trivial to have or be at risk of developing a hereditary cardiac condition associated with a risk of adverse disease complications and SCD. This may well

have an impact on the quality of life and be associated with increased anxiety and emotional distress[10-12]. In addition, there is a considerable risk of overdiagnosis of relatives during follow-up who are not at risk of developing HCM[13]. Besides the negative impact on non-diagnostic patients and their relatives, a misdiagnosis of HCM may be associated with a considerable waste of the limited resources in the health care system.

Based on the findings in the current study it appeared to be important to increase the awareness about the diagnostic criteria of HCM/HOCM among cardiologists which is supported by the results of a recent survey among healthcare professionals[14]. This investigation showed that only half of the participants were aware that a diagnosis of HCM among index patients require the presence of unexplained LVH of at least 15 mm. In order to increase awareness continued educational programs may be required to ensure up-to-date knowledge about diagnosis and pitfalls by use of various imaging modalities including echocardiography and CMR. In the context of CMR, the distinction between hypertensive heart disease and HCM may be difficult even in the presence of mid-wall-fibrosis in LGE-positive individuals[15-18]. In addition, LV wall thickness measurement on CMR is highly variable even in an expert setting[19]. Recent reports have suggested that an individualised approach to estimate the threshold for LVH may be superior to make a correct diagnosis of HCM compared to the current standard definition[20]. However, larger validation studies of affected individuals with LVH are probably needed before promising new calculators may be used for individualised calculation of LVH[21].

In our current work-up to increase diagnostic accuracy of HCM, all available data of referred patients is reviewed ahead of the clinical visit. If the referral is dismissed, the referring colleague is informed about the reasons for the rejection. Furthermore, all referring cardiologist are invited to our monthly MDT-conferences with geneticists and pathologists for the purpose of education and to increase awareness of the diagnostic work-up in

hereditary cardiac conditions. It is our experience that the referring cardiologist often participate in these meetings and that they find them informative and useful.

Genetic investigations may be used to confirm the clinical diagnosis of HCM when a disease-associated variant has been identified in a recognised HCM gene. Although the majority of HCM patients appear to be gene-elusive this does not exclude the possibility of a familial appearance of HCM. However, a recent study showed that gene-elusive HCM patients have very few affected relatives who appeared to have a favourable prognosis[8]. So, if a diagnosis of HCM cannot be excluded by clinical investigations it may be considered to perform genetic investigations and provide a modified strategy for family screening in gene-elusive families as suggested previously, which is likely to increase the cost-benefit of family screening[8].

Limitations

This was a single-centre study at a referral hospital, which may have introduced selection bias with a potential impact on the results of the study.

Genetic investigations were not performed routinely in hypertensive patients with ≥15 mm which may have implicated missed diagnosis of HCM in hypertensive patients. In addition, patients who were not examined in the cardiomyopathy clinic but solely had their notes and clinical investigations reviewed may have introduced a bias since they did not have the same work-up as the majority of patients who were reviewed in the cardiomyopathy clinic.

Only 23% of the cohort underwent CMR, which may have left phenocopies undiagnosed.

Finally, it cannot be excluded that patients with HCM did not receive a correct ICD-10 code following examination by a cardiologist at a referring hospital, which may have introduced selection bias.

Conclusion

A substantial proportion of patients with an ICD-10 code for HCM/HOCM did not fulfil recognised diagnostic criteria which may cause unnecessary investigations of relatives who are not at risk of disease development. This may be harmful to otherwise healthy individuals and associated with a considerable waste of health care resources. The results of the study suggested that all patients suspected of having HCM should undergo expert evaluation in dedicated cardiomyopathy clinics to ensure correct diagnosis of HCM.

Acknowledgements

We would like to thank the families and physicians who made this study possible. We would also like to thank RN Helle Arnsted, for assistance in the clinical investigations

Funding

Dr. Nielsen received funding from the University of Southern Denmark and an unrestricted grant from Sanofi Aventis.

Conflict of interest: None declared

Data availability

Data supporting the results of the study will be made available upon reasonable request to reproduce the results or replicate the procedures.

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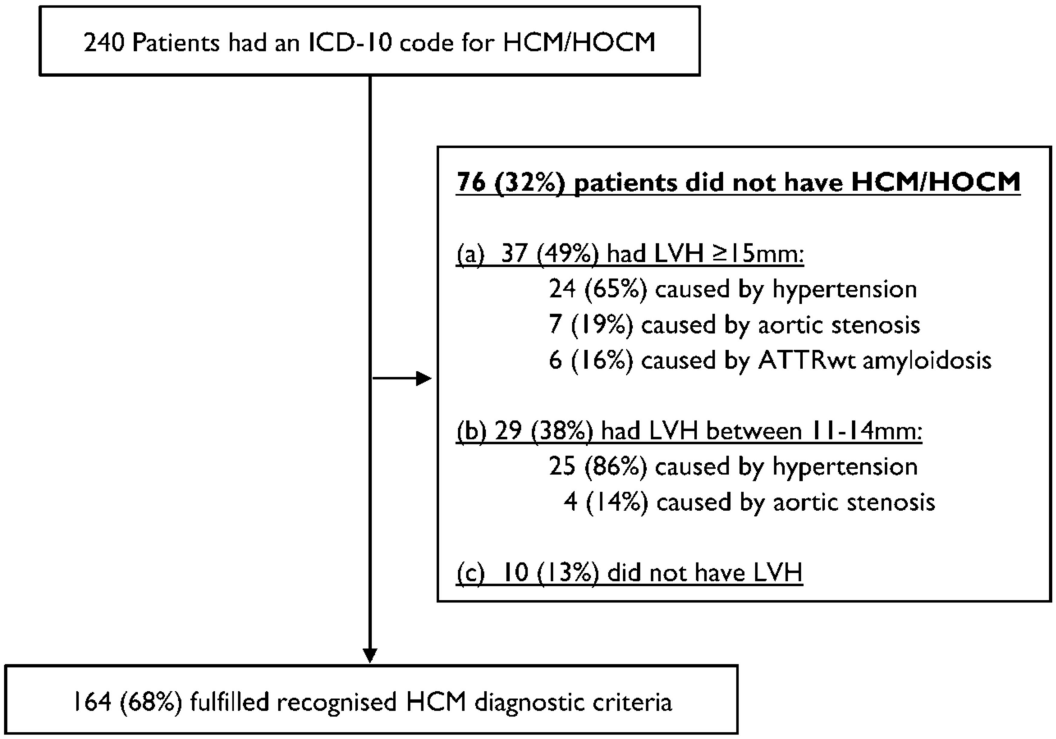

Figure 1 Characteristics of patients with an ICD-10 code for Hypertrophic Cardiomyopathy

Two hundred forty patients had an ICD-10 code for HCM (DI421 or DI422) of whom 68%, (164/240) fulfilled diagnostic criteria.

Abbreviations: ICD-10 The International Classification of Disease, Tenth Revision; HCM/HOCM, Hypertrophic cardiomyopathy/ Hypertrophic obstructive cardiomyopathy; LVH, Left ventricular hypertrophy

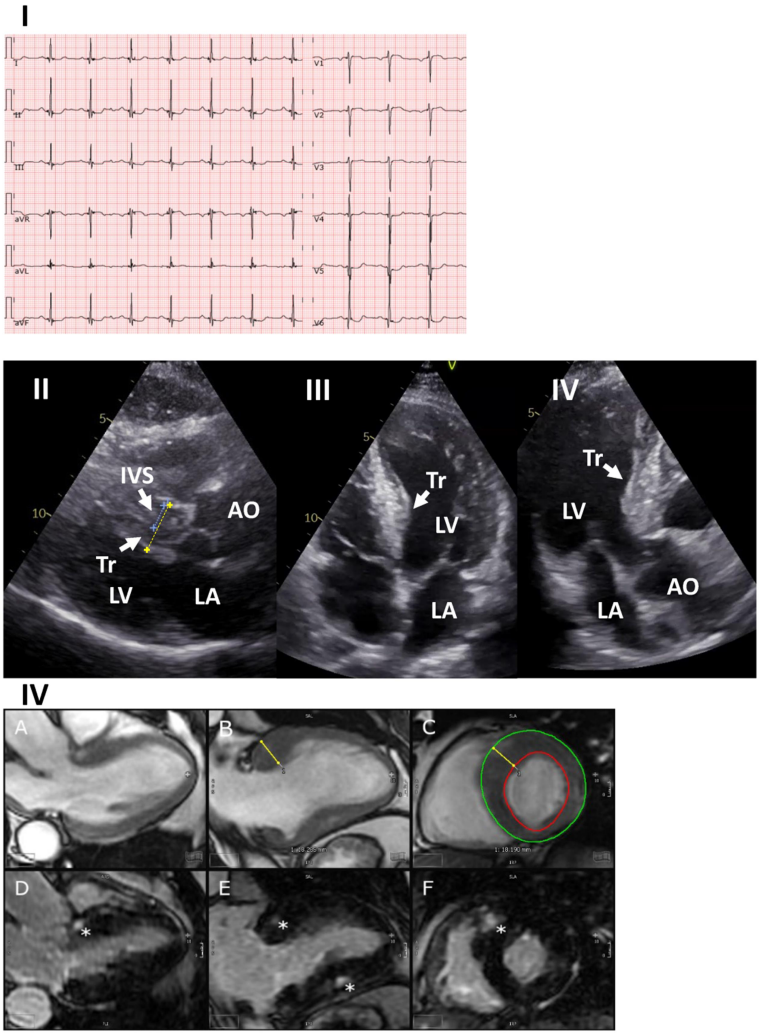

Figure 2 Echocardiography with trabeculae in close proximity to the interventricular septum interpreted as hypertrophic cardiomyopathy

A 72-year-old asymptomatic Caucasian male who had received triple antihypertensive therapy for the past 10 years, underwent a routine examination by his general practitioner. His ECG was abnormal with LVH, (I). A referral was made to the local cardiologist who performed an echocardiography. The measurements of the primary echocardiogram included the septum-marginal trabecula and a trabecula localised in the left ventricle in close proximity to the interventricular septum which was estimated to be 18 mm (II, parasternal long-axis, primary measurement in yellow) (III, four-chamber view; IV, apical 3

chamber/long axis views). The correct measurement of the septum was 11 mm (II, correct measurement in blue).

The local cardiologist referred the patient for CMR on the suspicion of HCM, (V). The results are shown in long-axis view (Va), two-chamber view (Vb), and basal short-axis view (Vc). The thickness of the interventricular septum was measured to 18 mm (Vb and Vc) and included the septum-marginal trabecula and a trabecula localised in the left ventricle (II, yellow measurement) although the correct thickness of the interventricular septum was 11 mm (II, blue measurement).

The myocardium showed late gadolinium enhancement (LGE) in a pattern suggestive of non-ischemic fibrosis (VD-F, areas with LGE are marked with white asterisk)

Abbreviations: AO, aorta; IVS; interventricular septum; LA, Left atrium; LV, Left ventricle; RA, Right atrium; Tr, Trabecula

	All HCM/HOCM patients (N = 164)	Normotensive HCM/HOCM patients (N=115)	HCM/HOCM patients with hypertension (N=49)	*P*-value
Age (*years*)	63 [54; 72]	59 [51; 69]	69 [62; 76]	<0.01
Gender (*male*)	102 (62%)	76 (66%)	26 (53%)	0.11
Ethnicity				
Caucasian	152 (93%)	107 (93%)	45 (92%)	
Middle Eastern	7 (4%)	6 (5%)	1 (2%)	-
Asian	5 (3%)	2 (2%)	3 (6%)	
Family history of SCD	14 (9%)	12 (10%)	2 (4%)	0.16
Familial appearance of HCM	30 (18%)	25 (22%)	5 (10%)	0.08
P/LP variant identified	47/137 (34%)	41/101 (41%)	6/36 (17%)	0.01
ECG pattern				
Normal	21 (13%)	12 (10%)	9 (18%)	0.16
Abnormal repolarization	73 (45%)	54 (47%)	19 (39%)	0.33
Abnormal Q-waves	5 (3%)	4 (3%)	1 (2%)	0.62
LVH patterns	39 (24%)	27 (23%)	12 (24%)	0.89
Bundle branch block/Pacemaker	15 (9%)	10 (9%)	5 (10%)	0.76
Atrial fibrillation	11 (7%)	8 (7%)	3 (6%)	0.85
Type of hypertrophy				
Concentric	1 (1%)	1 (1%)	-	-
Apical	25 (15%)	20 (17%)	5 (10%)	0.24
Septal	138 (84%)	94 (82%)	44 (89%)	0.20
MWT (*mm)*	18 [16; 22]	19 [17;21]	18 [16; 22]	0.43
LVOT obstruction	56 (34%)	37 (32%)	19 (39%)	0.41

Table 1 Clinical characteristics of patients with HCM/HOCM

Data are expressed as median and interquartile ranges or numbers (%).

Abbreviations: SCD, Sudden cardiac death; HCM, Hypertrophic cardiomyopathy; P/LP; Pathogenic/likely pathogenic, ECG, Electrocardiogram; LVH, Left ventricular hypertrophy; MWT, Maximum Wall Thickness; LVOT, Left Ventricular Outflow Tract

Table 2 Clinical characteristics of patients without HCM/HOCM and LVW thickness ≥15mm

	Patients with hypertension (N = 24)	Patients with aortic stenosis (N = 7)	Patients with wild-type ATTR amyloidosis (N = 6)
Age (*years*)	74 [62; 82]	82 [72; 87]	71 [66; 75]
Gender (*male*)	10 (42%)	2 (29%)	5 (83%)
Ethnicity			
Caucasian	22 (92%)	7 (100%)	6 (100%)
Middle Eastern	2 (8%)	-	-
Family history of SCD	-	-	-
Familial appearance of HCM	-	-	-
Comorbidity			
No additional comorbidity	15 (62%)	6 (86%)	6 (100%)
Diabetes (Type II)	4 (17%)	1 (14%)	-
Chronic renal failure	5 (21%)	-	-
ECG pattern			
Normal	6 (25%)	2 (29%)	2 (33%)
LVH pattern	16 (67%)	3 (43%)	-
Low-voltage	-	-	2 (33%)
Bundle branch block/Pacemaker	-	1 (14%)	1 (17%)
Atrial fibrillation	2 (8%)	1 (14%)	1 (17%)
Type of hypertrophy			
Concentric	14 (58%)	6 (86%)	6 (100%)
Isolated bulge of the basal septum	10 (42%)	1 (14%)	-
MWT (*mm*)	15 [15; 16]	17 [15; 18]	18 [16; 21]
LVOT obstruction	10 (42%)	-	-

Data are expressed as median and interquartile ranges or numbers (%).

Abbreviations: SCD, Sudden cardiac death; HCM, Hypertrophic cardiomyopathy; P/LP; Pathogenic/likely pathogenic, ECG, Electrocardiogram; LVH, Left ventricular hypertrophy; MWT, Maximum Wall Thickness; LVOT, Left Ventricular Outflow Tract