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Distinguishing ventricular septal bulge versus hypertrophic cardiomyopathy in the elderly

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Abstract

The burgeoning evidence of patients diagnosed with sigmoidal hypertrophic cardiomyopathy (HCM) later in life has revived the quest for distinctive features that may help discriminate it from more benign forms of isolated septal hypertrophy often labelled ventricular septal bulge (VSB). HCM is diagnosed less frequently than VSB at older ages, with a reversed female predominance. Most patients diagnosed with HCM at older ages suffer from hypertension, similar to those with VSB. A positive family history of HCM and/or sudden cardiac death and the presence of exertional symptoms usually support HCM, though they are less likely in older patients with HCM, and poorly investigated in individuals with VSB. A more severe hypertrophy and the presence of left ventricular outflow obstruction are considered diagnostic of HCM, though stress echocardiography has not been consistently used in VSB. Mitral annulus calcification is very prevalent in both conditions, whereas a restrictive filling pattern is found in a minority of older patients with HCM. Genetic testing has low applicability in this differential diagnosis at the current time, given that a causative mutation is found in less than 10% of elderly patients with suspected HCM. Emerging imaging modalities that allow non-invasive detection of myocardial fibrosis and disarray may help, but have not been fully investigated. Nonetheless, there remains a considerable morphological overlap between the two conditions. Comprehensive studies, particularly imaging based, are warranted to offer a more evidence-based approach to elderly patients with focal septal thickening.

INTRODUCTION

An isolated hypertrophy of the basal segment of the interventricular septum protruding into the outflow tract of the left ventricle (LV), named ventricular septal bulge (VSB),[1–3] is fairly

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common in elderly individuals, and may be difficult to distinguish from genetic hypertrophic cardiomyopathy (HCM).[245] The matter has been recently reconsidered because of an increasing number of reports demonstrating that some HCM variants may have late onset in middle age and elderly individuals, and are compatible with normal longevity.[6–8] The widespread availability of non-invasive cardiac imaging modalities, particularly transthoracic echocardiography, has significantly contributed to this trend.[79] Coincident with these medical developments, patients are increasingly exposed to information from the media on sudden unexpected deaths due to HCM. Because of potential life-threatening complications associated with a diagnosis of HCM, the notion that isolated septal hypertrophy should be considered as 'normal for age' has been called into question.

As the number of older patients coming to cardiology services increases, and the use of cardiac imaging expands, distinguishing between HCM and VSB in elderly individuals will become more of an issue in the years to come. This review provides readers with a comprehensive and updated summary of the evidence available on differential diagnosis between HCM and VSB in the elderly. Empirically, we will start with the assumption that the two conditions are different, and will review and discuss data in support or against this hypothesis. Initial definitions, search strategy and selection criteria are summarised in box 1. Selected clinical and instrumental features in HCM versus VSB are discussed in the next paragraphs, and summarised in table 1. A practical differential diagnostic algorithm is proposed in the last paragraph.

DEMOGRAPHICS AND MEDICAL HISTORY

Elderly

Epidemiology of HCM is little known, and an unexplained increase in LV thickness is reported in a wide range (0.02%–0.23%) of the general adult population.[1011] No systematic data are available on the number of individuals diagnosed with HCM after the age of 60 years as compared with younger ages. They accounted for about 30% in a series of 277 patients with HCM,[6] though this is probably an underestimate of the true prevalence.[781819] On the contrary, it is widely recognised that the prevalence of VSB increases with age,[11415] ranging from 4% to 8% in individuals ≥60 years of age and reaching 10% in the eighth decade of life.[11415] Thus, VSB seems to be diagnosed more frequently than HCM at older ages.

Sex

Patients with VSB did not display a sex preference,[11415] in contrast to HCM, which has been generally characterised by a 3:2 male predominance,[6] at least at younger ages.[2021] A recent review of 969 consecutive American and Italian patients with HCM demonstrated a reversed 60% versus 30% female predominance only in patients older than 60 years of age.[22] This prevalence may however be driven by the well-known increased survival of females relative to males in older age groups. Thus, a clear gender difference in prevalence of HCM and VSB at older ages has yet to be established.

Family history

Family history is frequently disregarded during medical interview in elderly patients. A positive family history of HCM and/or sudden cardiac death (SCD), particularly in first-degree relatives, represents a very important piece of information to support a diagnosis of HCM.[1011] Nonetheless, several works have shown that a positive family history of HCM/SCD is significantly less common in older than in younger patients with HCM, with a prevalence of approximately 10%–20% in the former group.[7923] This decreased prevalence is likely due to the absence of a clear genetic background in HCM of the elderly (see genetics below).

Family history of HCM/SCD has been poorly investigated in VSB studies, and found in none of the 240 individuals diagnosed with VSB after a retrospective review of 4104 ambulatory echocardiograms.[14] Thus, available data weakly suggest that a positive family history of HCM/SCD can help confirming HCM and excluding VSB in elderly patients.

Hypertension

A history of hypertension has been frequently regarded as an exclusion criterion for HCM.[24] However, prevalence of hypertension dramatically increases with advancing age, to the point where more than half of people ≥60 years are affected. Thus, a history of hypertension can no longer be considered *tout court* as an exclusion criterion for HCM when dealing with elderly patients. Indeed, in contemporary adult HCM populations, prevalence of hypertension ranges from 20% to 60%.[20212325–29] The prevalence of hypertension in VSB observational studies ranges between 50% and 80%,[11415] thus slightly higher than that reported in HCM studies. However, considering that a conclusive independent association between hypertension and VSB has yet to be confirmed,[114–16] a history of hypertension is currently of little help in differentiating VSB from HCM.

SYMPTOMS AND PHYSICAL EXAMINATION

Symptoms

HCM in the elderly may be frequently misdiagnosed, because symptoms such as dyspnoea, chest pain, palpitations and syncope are more commonly attributed to other cardiac disorders such as coronary disease, valvular heart disease and atrial fibrillation. In general, elderly patients with HCM do present with exertional symptoms.[67930] On the contrary, the majority of VSB studies are retrospective in nature, where patients had been selected based on echocardiographic criteria and not because of their symptoms.[11415] Few case reports of symptomatic patients with VSB have been published in the literature.[412] Importantly, patients with HCM but not with VSB are routinely referred to exercise testing for prognostic stratification, where symptoms can be uncovered. The usefulness of stress testing in patients with VSB, although somehow suggested by the European guidelines,[10] has never been prospectively investigated.

Physical examination

Physical examination is often normal both in HCM and VSB, though an ejection systolic murmur due to dynamic left ventricular outflow tract (LVOT) obstruction may be

appreciated, and modified by manoeuvres that increase or reduce ventricular preload or afterload. This finding may help differentiate obstructive HCM from aortic stenosis,[10] but it has not been used for HCM versus VSB, and it has been described only in few contemporary HCM and VSB case reports.[8,12]

ELECTROCARDIOGRAPHY

Rest ECG

A 12-lead rest ECG is recommended in the initial evaluation of patients with HCM, and as a screening tool for first-degree relatives of patients with HCM.[10,11] ECG is a sensitive but nonspecific marker of left ventricular hypertrophy (LVH), because it is unable to distinguish among HCM, VSB, hypertension and aortic stenosis. LVH by ECG is found in about 60%–70% of patients with HCM,[29–31] whereas data are sparse in patients diagnosed with VSB.[4,5] The largest study to date found LVH at ECG in only 12% of patients with VSB. Thus, LVH by ECG appears more prevalent in elderly individuals with HCM than those with VSB, but provides little help with differential diagnosis.

Ambulatory ECG

ECG monitoring is not requested for HCM diagnosis, but recommended for risk stratification of SCD (ie, ventricular tachycardia) and stroke (ie, atrial fibrillation).[10,11] American HCM guidelines underline that the frequency of arrhythmias detected during ambulatory ECG monitoring is age related;[10] however, no specific data exist on the prevalence of atrial and ventricular arrhythmias in elderly patients with HCM. No published data on ambulatory ECG monitoring in patients with VSB are available.

ECHOCARDIOGRAPHY

LV shape and patterns of hypertrophy

LVH is the main echocardiographic feature of HCM. However, the distribution of hypertrophy within the LV walls and segments may significantly differ from one patient with HCM to another, and different patterns of LVH have been described [32] (figure 2). In general, HCM affects the interventricular septum more than other LV walls, and asymmetric septal hypertrophy (classically defined by a ratio between the septal and posterior wall diastolic thickness ≥1.3–1.5) has been considered as a key diagnostic feature to distinguish between HCM and LVH secondary to hypertension, which is generally symmetrical.[21] In addition, some patients with HCM exhibit asymmetric septal hypertrophy and a greater thickness of the basal as compared with the mid-distal portion of the septum, lending the characteristic sigmoidal septal shape (figure 2). Numerous studies confirmed a predominance of sigmoidal HCM among the elderly.[25,33,34] Experts recently estimated that almost half of the patients diagnosed with HCM have a sigmoidal pattern of LVH.[32]

Patients with VSB have also been usually characterised by an asymmetric septal hypertrophy particularly isolated to the upper segment (ie, with a proximal-to-mid/distal septal thickness ratio ≥1.3–1.5) (figures 1 and 3). Some Authors included subjects with sigmoid-shaped septum without hypertrophy,[15] but most VSB cohorts comprised only

individuals with a proximal septal wall thickness >12–13 mm,[12131416] applying the same entry criterion used in contemporary HCM cohorts.[2021] Thus, a considerable overlap exists between the two conditions. Nonetheless, patients with HCM generally display greater thickness of both the interventricular septum (frequently >15 mm) and the posterior wall (frequently >11 mm) than patients with VSB [216] (figure 3). Normal posterior wall thicknesses (ie, <11 mm) have been generally reported in VSB studies [11415] as compared with HCM studies in the elderlies, in which some degree of hypertrophy was also involving the posterior wall.[252930] Thus, a less severe degree of hypertrophy and a normal posterior wall thickness may potentially help differentiate between patients with VSB and elderly patients with HCM.

Aortoseptal angle

A sigmoid-shaped septum has been consistently associated with a sharper angulation between the long axes of the LV and the aorta (figure 3). Studies generally found an aortoseptal angle <110° in patients with VSB.[2312] It has been hypothesised that the age-related dilation and lengthening of the aorta might push the septum downward and kink its upper portion,[3] and that a sharper angle may favour a Venturi mechanism for the generation of LVOT obstruction.[2] However, no association was found between the aortoseptal angle and LVOT obstruction at rest in a recent study of 240 patients with VSB.[14] On the contrary, an aortoseptal angle ≤100° had a 27% sensitivity and 91% specificity for predicting provocable LVOT obstruction in a population of 160 patients with non-obstructive HCM.[35] Measurement of the aortoseptal angle by echocardiography is highly dependent on the position of the transducer and consequently poorly reproducible. Better and more standardised aortoseptal angle estimates may be obtained by cardiovascular MR (CMR), and one CMR study of 153 patients with HCM confirmed that a sharper aortoseptal angle was associated with dynamic LVOT obstruction.[27] Notably, the intraobserver and interobserver concordance was very high in this study (0.91 and 0.88, respectively), suggesting that CMR may be the optimal technique for measuring the aortoseptal angle in future HCM and VSB studies.

Mitral annulus calcification

Mitral annulus calcification (MAC) occurs with ageing. Unfortunately, no standard method of quantification of MAC exists, and both echocardiography (figure 3) and X-ray-based imaging modalities have been used to screen for the presence and severity of MAC. MAC has been demonstrated in about 30%–70% of elderly subjects with both HCM [9252931] and VSB.[1415] Some studies also suggested a higher prevalence of MAC when hypertension was associated.[1429] While MAC may simply represents an age-related phenomenon, conditions that elevate LV filling pressure such as HCM increase stress on the mitral apparatus, thus likely accelerating the development of MAC. However, the significance of MAC in HCM has been poorly investigated. Some authors suggested a contribution of MAC to LVOT obstruction in elderly patients with HCM,[30] which has also been acknowledged in recent European guidelines.[10]

LVOT obstruction

LVOT obstruction is a hallmark of HCM, and patients with HCM are currently classified based on the presence or absence of LVOT obstruction either at rest or under stress conditions. LVOT pressure gradients are routinely measured by echocardiography at rest and after physical exercise, Valsalva manoeuvre or amyl nitrite administration.[10,11] Systolic anterior movement of the mitral valve (SAM) and mitral-septal contact is believed to be responsible for LVOT obstruction in the majority of cases [3,6] (figure 3). Available evidence suggests a comparable 50%–70% prevalence of LVOT obstruction and SAM in younger and elderly patients with HCM.[7,23,25,29,31] LVOT obstruction is considered an important supportive diagnostic criterion for HCM, to the point that in one study patients initially classified as VSB were assigned a diagnosis of HCM after the demonstration of LVOT obstruction.[14] On the contrary, patients with VSB do not usually present with LVOT obstruction, at least at rest.[15,15] Although European guidelines state that stress echocardiography should be routinely considered in symptomatic patients with VSB in the same way as in patient with unequivocal HCM,[10] this recommendation does not reflect the common clinical practice, and the differential diagnostic role of stress echocardiography in patients with VSB has yet to be established in prospective studies.

LV diastolic and systolic function

With ageing, the human heart becomes thicker and stiffer and develops progressive LV diastolic dysfunction, characterised by progressive increase in LV filling pressure and, with time, an enlargement of the left atrium. In patients with HCM, these pathological changes progress in a more expedited fashion and usually in the contest of a preserved or increased global systolic function.[10] Current guidelines recommend a multiparametric evaluation of LV diastolic function, which includes the estimation of E/A ratio from mitral diastolic Doppler inflow, E/E′ ratio using tissue-Doppler derived early mitral annulus velocity (E′) and left atrial dimensions (figure 3). In patients with HCM, a restrictive LV filling pattern (characterised by a E/A ratio ≥2, a E/E′ ratio ≥14 and a left atrial volume ≥34 mL/m^2) is frequently encountered,[10] even at very old ages.[9] This is probably less evident in subjects diagnosed with a VSB, and one study comparing age-matched and gender-matched patients with VSB and HCM found significantly higher E/E′ ratio and left atrial dimension in the latter group.[16] These are to date the only few data available suggesting a worse diastolic function in HCM versus VSB.

Measurements of subtle LV systolic dysfunction by speckle tracking echocardiography may help differentiating between HCM and other forms of LVH,[37] including VSB. Patients with HCM have abnormalities in regional and global systolic longitudinal strain that are related to the site and degree of abnormal myocardial hypertrophy.[38] In particular, patients with sigmoidal HCM have more abnormal strain in the proximal septum than in other LV segments.[39] Further studies are needed to evaluate the diagnostic utility of these measurements in elderly patients with unspecified isolated proximal septal hypertrophy.

CARDIOVASCULAR MR

Developments in CMR technology and its increasing availability in many healthcare settings have led to a substantially greater role of this technique in the morphological characterisation and risk stratification of patients diagnosed with HCM.[10] However, its application has been limited in elderly patients with HCM, and none in patients with VSB. Therefore, only few concepts will be reported in the following paragraphs.

LV mass and LVH pattern

Quantification of LV mass with CMR is superior to echocardiography,[26] particularly in the setting of asymmetric LVH,[40] where conventional echocardiographic formulas assuming an ellipsoid geometry of the LV have clear limitations, and should probably be avoided (figure 2). LV mass in patients with hypertrophy confined only to a few segments in the LV wall, such as the elderly with sigmoidal HCM, may be within normal ranges even in the presence of clinically significant disease.[2641] Thus, increased LV mass is not a requirement for establishing a clinical diagnosis of HCM, and this parameter should not be used to distinguish between HCM and other asymmetric form of LVH associated with ageing, particularly a VSB.

Mitral valve abnormalities

CMR may be superior to echocardiography also in the evaluation of morphological and functional mitral valve abnormalities, which may lead to LVOT obstruction in patients with HCM.[42] In particular, CMR may allow superior evaluation of mitral valve leaflet length and number, and insertion sites of the papillary muscles. These findings are increasingly reported in patients with HCM, [43] and may support a diagnosis of HCM as opposed to VSB.

Late gadolinium enhancement

Late gadolinium enhancement allows visualisation and quantification of fibrotic areas within the myocardium. The pattern of mid-wall patchy fibrosis in hypertrophied segments of the myocardium, which is typical of HCM, is present in about 65% of patients with HCM, and may be of help in differentiating true HCM from other conditions,[44] including the VSB. However, no CMR study has yet explored this possibility. In addition, a much lower frequency of late gadolinium enhancement (37%) has been reported in patients with a late diagnosis of HCM,[7] thus questioning its utility in the differential diagnosis of HCM in elderly patients, and the effective existence of two separate clinical entities.

CORONARY ANGIOGRAPHY

Coronary angiography is recommended as a diagnostic tool in patients with suspected HCM and typical exertional chest pain.[1011] Prevalence of coronary artery disease (CAD) ranged from 0% to 40% in retrospective HCM studies of elderly patients, and very few data are available in VSB studies,[14] which in most cases enrolled asymptomatic patients who did not undergo coronary angiography.[115] Nonetheless, no independent association has been shown between CAD and either sigmoidal HCM or VSB. Intriguingly, however, a recent study of 5128 patients with CAD found that those who had asymmetric septal hypertrophy (5.8%) were significantly older and had a significantly higher frequency of obstructive CAD of the

right and the left circumflex coronary arteries.[45] This finding suggests that myocardial ischaemia due to CAD, particularly when involving arteries that supply the basal interventricular wall, may somehow contribute to the pathogenesis of VSB in the elderly, and perhaps to the sigmoidal pattern of LVH found in elderly HCM.

GENETICS

HCM is the most common autosomal dominant monogenic cardiac disease, but it has variable and age-related penetrance and may be due to de novo mutations absent in parents.[3246] Although several commercial genetic panels are available, the clinical use of genetic testing is limited, because of the vast genetic heterogeneity and the lack of association between prognosis and specific mutations. Among those tested, approximately 35% is found to be positive for a known gene.[2021] Yield of genetic testing is even lower in elderly patients with HCM, and approaches 10% in those with sigmoidal HCM (figure 2).[2334] Recently, two large HCM studies confirmed that a younger age at diagnosis and a reverse curve HCM were the principal predictors of mutation-positive HCM.[2021] Thus, genetic testing is currently not part of the routine assessment of patients with suspected HCM, particularly at older ages, as a final diagnosis of HCM primarily relies on the clinical phenotype.

Considering the very low probability of a patient with sigmoidal HCM being gene positive for a known HCM-related mutation, genetics has not been consistently studied in patients with VSB, and it seems of no help in the discrimination between the two conditions. European HCM guidelines states that ‘advice on family screening in this group is challenging, but should be guided by the implications for family members and the presence of suspicious symptoms in relatives’.[10] As the cost of genetic testing is expected to decrease in the coming years, widespread genotyping of elderly patients with HCM and VSB might be considered in the future and lead to the identification of pathological phenotypes and new HCM-causative mutations, which could potentially serve for the early diagnosis of HCM in younger family members.

HISTOLOGY

Histology remains the cornerstone for the diagnosis of HCM. Pathological hallmarks include myocyte hypertrophy and disarray. Myocyte disarray is found less frequently in bioptic specimens of older versus younger patients with HCM undergoing subaortic septal myectomy,[47] and it is absent or less relevant in other conditions, which macroscopically may simulate HCM, such as hypertensive heart disease and aortic stenosis.[48] There are no pathology data of VSB populations in the literature. Although myocyte disarray could potentially help differentiating true HCM from VSB in elderly patients, current guidelines do not recommend endomyocardial biopsy as part of the routine HCM diagnostic work-up.[10] Emerging imaging techniques that allow virtual histology may offer non-invasive alternatives for the assessment of myocardial disarray in the future.

PROPOSAL FOR A DIFFERENTIAL DIAGNOSTIC ALGORITHM

Our review of the available literature demonstrates a considerable overlap between VSB and HCM in elderly individuals, and the lack of distinctive diagnostic features. In an attempt to keep considering the two as separate phenotypes, a differential diagnostic flowchart based on evidence discussed in this review is proposed in figure 4. Family history, clinical presentation and echocardiographic measurements may be leveraged to adjudicate on a particular patient, with several cases falling into the ‘grey zone’ of uncertainty, and potentially candidates for more advanced and invasive diagnostics, including CMR, genetic testing and endomyocardial biopsy. However, distinguishing between HCM and VSB remains a clinical challenge and a topic of intense debate, and the question on whether or not VSB exists as a separate disease entity with different natural history and prognosis has to date no definite answer. Further research and clinical studies are warranted to develop superior diagnostic approaches capable of identifying elderly individuals who would deserve further clinical attention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Box 1 Definitions, search strategy and selection criteria

Definitions

- *Hypertrophic cardiomyopathy*: according to the most recent European and American guidelines, hypertrophic cardiomyopathy (HCM) is defined by the presence of a wall thickness ≥15 mm in one or more left ventricular myocardial segments that is not solely explained by abnormal loading conditions.[10,11]
- *Ventricular septal bulge*: a unique definition and specific diagnostic criteria are not established.[10] Studies generally include individuals with an isolated basal septal hypertrophy and a wall thickness >12–13 mm; sometimes a proximal-to-mid/distal septal wall thickness ratio ≥1.3–1.5 is used as an additional criterion, and the presence of left ventricular outflow tract obstruction as an exclusion criterion, because considered diagnostic for HCM. The phenotype has been variously labelled ventricular septal bulge (VSB),[1–3] sigmoid-shaped septum,[12] localised [4,5,13] or isolated [14] or discrete upper or basal septal hypertrophy.[15,16] Detailed definitions of VSB in each study are presented in online supplementary table S1. A case study is given in figure 1.

Search strategy

- PubMed and Embase were searched for articles in English and published before December 2014 by using the terms ‘hypertrophic cardiomyopathy’, ‘elderly’, ‘older adults’, ‘septal bulge’, ‘sigmoid septum’, ‘septal hypertrophy’ and ‘senile heart’, with filters.

Selection criteria

- This review is focused on elderly individuals, thus only case reports and studies of individuals ≥60 years of age were considered. A summary of main findings from each study is presented in online supplementary table S1.
- Studies of discrete subvalvar aortic stenosis, which instead is a fixed stenosis caused by a fibrous ridge in the left ventricular outflow tract just proximal to the aortic valve, were excluded, as well as studies of patients with aortic stenosis. Asymmetric pattern of wall thickening is found in about 20%–30% of patients with aortic stenosis;[17] however, they are routinely excluded from both HCM and VSB studies, and probably represent a different entity.

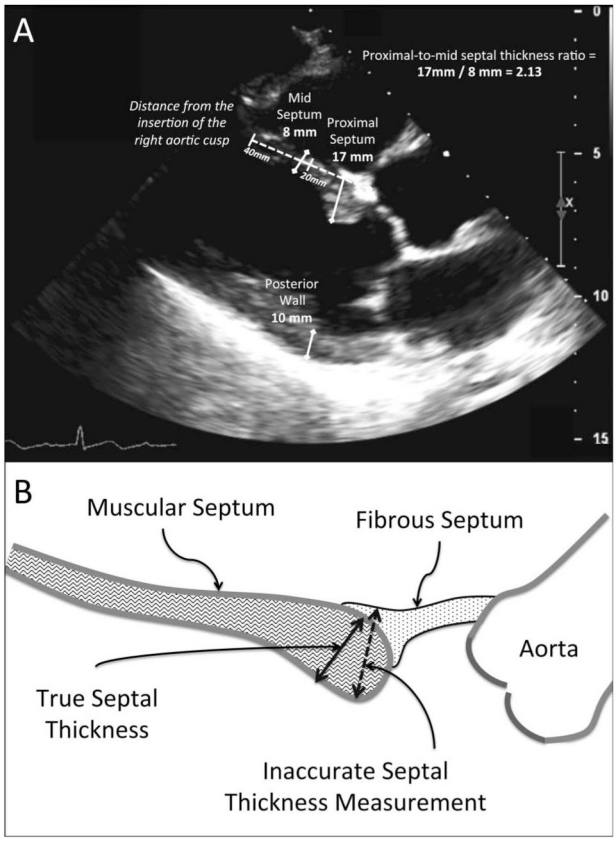

Figure 1.

Representative image illustrating measurement of isolated basal septal hypertrophy. Two-dimensional echocardiographic parasternal long-axis view from a 71-year-old male who met all the criteria for ventricular septal bulge (A). The maximal thickness of the proximal septum (measured within the first third of the septal length, usually within 20 mm from the insertion of the right aortic cusp) was 17 mm, which was approximately twice the thickness of the mid septum (usually measured at the second third of the septal length), measuring 8 mm. Note that the very proximal fibrous part of the septum should be discarded (B, dashed line). From the same parasternal view, the thickness of the posterior wall is usually measured, which could help in the differential diagnosis between ventricular septal bulge and hypertrophic cardiomyopathy (see the text and figure 3 for details, and the corresponding movie in the online supplementary data).

Nomenclature	Sigmoidal HCM	Reverse curve HCM	Apical HCM	Neutral HCM
Prevalence	40-50%	30-40%	10%	10%
Age group	> 50-60 years	< 50-60 years	< 50-60 years	< 50-60 years
Genetics +	10-20%	80-90%	30-40%	30-40%

Figure 2.

Patterns of left ventricular hypertrophy observed in patients with hypertrophic cardiomyopathy (HCM). The figure shows the most common septal morphologies in HCM. The table under the figure indicates estimates of the overall prevalence, the age at onset and the yield of genetic testing for each pattern. Modified from Bos *et al*,[32] Binder *et al*[34] and Lever *et al*.[25]

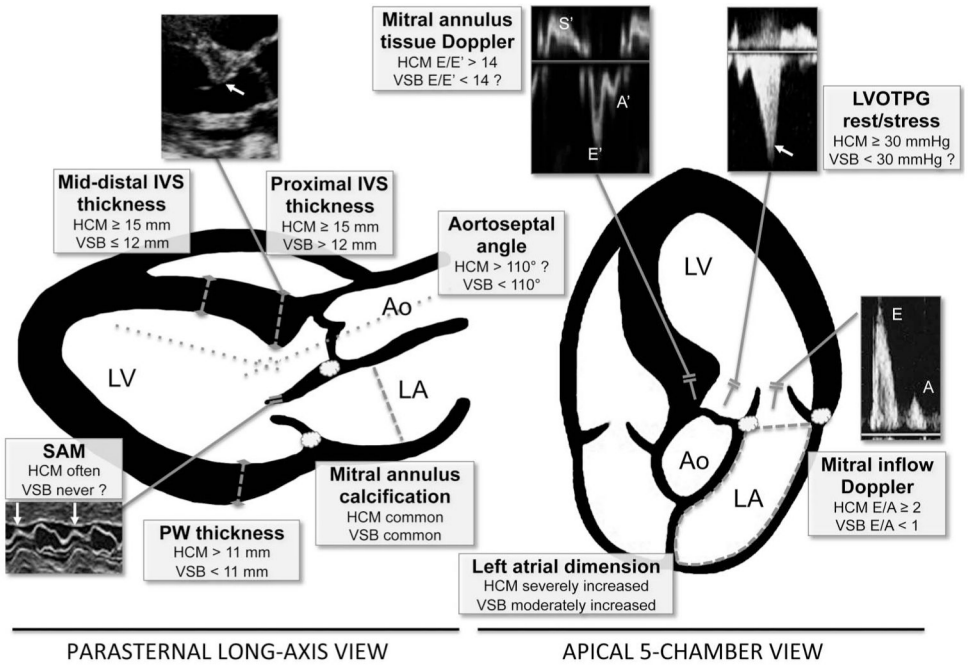

Figure 3.

Main echocardiographic features that could help in distinguishing between HCM and VSB in elderly patients. Ao, aorta; HCM, hypertrophic cardiomyopathy; IVS, interventricular septum; LA, left atrium; LV, left ventricle; LVOTPG, left ventricular outflow track pressure gradients; PW, posterior wall; SAM, systolic anterior movement of the mitral valve; VSB, ventricular septal bulge.

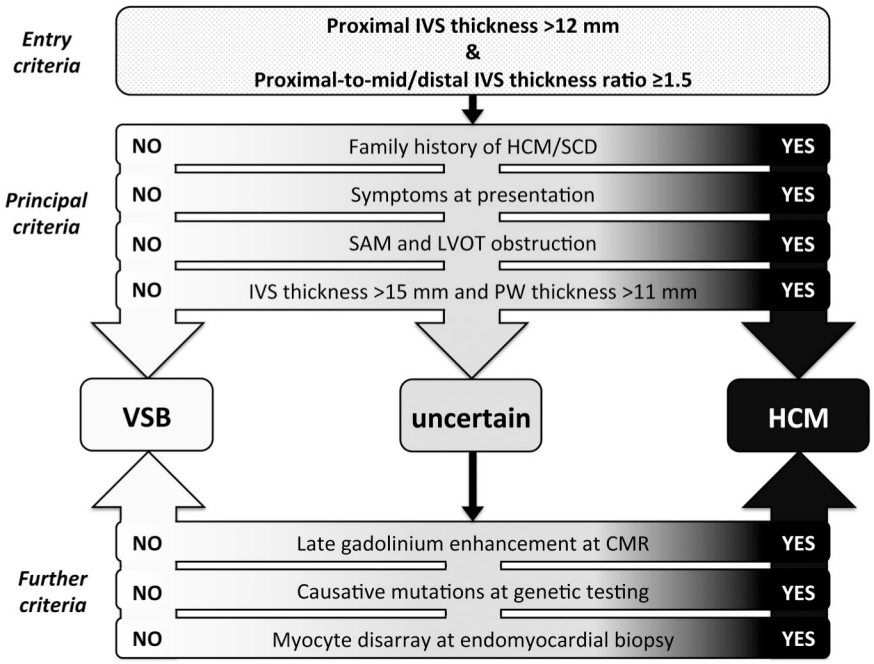

Figure 4.

Differential diagnostic algorithm of elderly individuals with an isolated proximal septal hypertrophy. An individual enters the differential diagnostic algorithm only if both the ‘entry criteria’ are met; subsequently, a diagnosis of HCM or VSB is established only if all (or most of) the ‘principal criteria’ are present or absent, respectively. In uncertain ‘grey’ cases, in which some principal criteria are present but other are absent, and a definitive diagnosis is sought, ‘further criteria’ involving CMR, genetic testing and endomyocardial biopsy may be considered. CMR, cardiovascular MR; HCM, hypertrophic cardiomyopathy; IVS, interventricular septum; LVOT, left ventricular outflow tract; PW, posterior wall; SAM, systolic anterior movement of the mitral valve; SCD, sudden cardiac death; VSB, ventricular septal bulge.

Table 1

Occurrence at diagnosis of selected clinical and instrumental features in elderly individuals with isolated basal septal hypertrophy

	HCM	VSB	Notes
1. Demographics and medical history			
Diagnosis at age ≥60 years	++	+++	Few data available on the prevalence of HCM in the elderly
Female predominance	+	–	Reversed female predominance only in patients with HCM ≥60 years
Family history of HCM/SCD	++	–	Few negative data available from VSB studies
History of hypertension	+	++	Different criteria for diagnosis in HCM and VSB studies
2. Symptoms and physical examination			
Chest pain, dyspnoea or syncope	+++	+	VSB diagnosed retrospectively, few case reports with symptoms
Dynamic systolic murmur	+	NA	Poorly investigated and reported in contemporary populations
3. Electrocardiography			
LVH (rest ECG)	++	+	Different criteria for diagnosis in HCM and VSB studies
Arrhythmias (ambulatory ECG)	++	NA	Recommended in patients with HCM to assess risk of SCD and stroke
4. Echocardiography			
Sigmoidal septum	+++	+++	This is the main imaging feature that equates the two conditions
IVS diastolic thickness ≥15 mm	+++	–	Thicker IVS in HCM than VSB studies
PW diastolic thickness >11 mm	+++	–	Thicker PW in HCM than VSB studies
Sharp aortoseptal angle	+	++	Little reproducible measurements by echo, only few CMR studies
Mitral annulus calcification	++	++	Different criteria for diagnosis in HCM and VSB studies
LVOT obstruction and SAM	+++	+	No prospective VSB study with stress echocardiography
LV diastolic dysfunction	++	+	Doppler data not available from older HCM and VSB studies
5. Cardiovascular MR			
LV mass and LVH patterns	+	NA	Few data in elderly patients with HCM and no data in patients with VSB
Mitral valve abnormalities	+	NA	Few data in elderly patients with HCM and no data in patients with VSB
Late gadolinium enhancement	+	NA	Few data in elderly patients with HCM and no data in patients with VSB
6. Coronary angiography			
Coronary artery disease	+	+	Potential link between RCA/LCX stenosis and sigmoidal LVH
7. Genetics			
Prevalence of known mutations	+	NA	Very low yield of genetic testing in elderly patients with HCM
8. Histology			
Myocyte disarray	++	NA	Biopsy not recommended in routine HCM diagnostic work-up

CMR, cardiovascular MR; HCM, hypertrophic cardiomyopathy; IVS, interventricular septum; LCX, left circumflex coronary artery; LV, left ventricular; LVH, left ventricular hypertrophy; LVOT, left ventricular outflow tract; NA, no evidences available; PW, posterior wall; RCA, right coronary artery; SAM, systolic anterior movement of the mitral valve; SCD, sudden cardiac death; VSB, ventricular septal bulge; −, negative evidences available; + to +++, from few to plenty of evidences available, arbitrary scale.