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EACVI DOCUMENT

EACVI survey on hypertrophic cardiomyopathy

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Aims The European Association of Cardiovascular Imaging (EACVI) Scientific Initiatives Committee performed a global survey to evaluate current practice for the assessment and management of patients with hypertrophic cardiomyopathy (HCM).

Methods and results A total of 213 centres from 38 different countries (87% European) responded to the survey. One hundred twenty-one (57%) centres followed HCM patients in a general cardiology outpatient clinic and 85 (40%) centres in a specialized HCM/cardiomyopathy clinic. While echocardiography was the primary imaging modality, cardiovascular magnetic resonance (CMR) has become an important complementary tool. Cardiac anatomy, left ventricular (LV) systolic, and diastolic function were assessed according to current European guidelines and recommendations. To evaluate LV obstruction, 49% of the centres performed bedside provocation manoeuvres in every patient and 55% of the centres used exercise stress echocardiography. The majority of centres used the 5-year risk assessment of sudden cardiac death (SCD) calculated with the HCM Risk-SCD score. However, 34% of the centres also used extensive non-infarct late gadolinium enhancement on CMR and 27% the presence of LV apical aneurysm to help select patients for primary prevention implantable cardioverter-defibrillator therapy. Ninety-nine percent of the responding centres performed regular imaging follow-up of HCM patients.

Conclusion Most centres followed European guidelines and recommendations for the diagnosis and management of patients with HCM. The importance of bedside provocation manoeuvres and exercise stress echocardiography to diagnose LV outflow obstruction requires emphasis. Additional risk markers for SCD are used in many centres and might indicate the need for an update of current European recommendations.

Keywords EACVI • survey • hypertrophic cardiomyopathy • multimodality imaging • sudden cardiac death

Introduction

In adults, hypertrophic cardiomyopathy (HCM) is defined by a left ventricular (LV) wall thickness ≥15 mm measured by any imaging technique in one or more LV myocardial segments that is not explained solely by loading conditions.[1] In first-degree relatives of patients with HCM, an unexplained increased LV wall thickness ≥13 mm is diagnostic for HCM. Sarcomeric protein gene mutations are the most common aetiology. The diagnosis and management of patients with HCM have been extensively elaborated in the 2014

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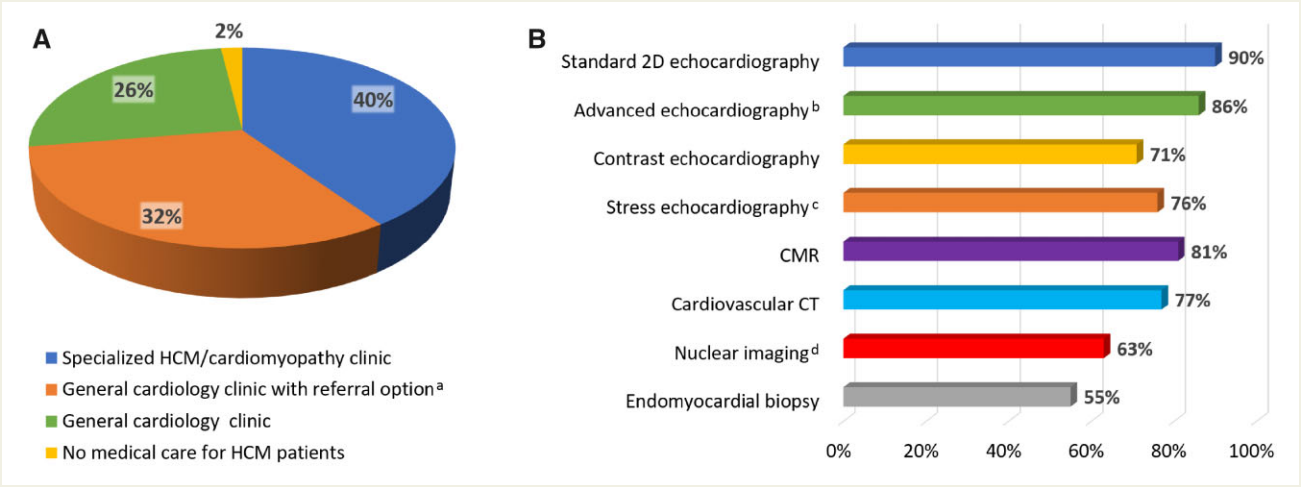

Figure 1 Organization of medical care for patients with HCM (*A*) and cardiac imaging availability (*B*) in the responding centres. The pie chart and the bar chart display the percentage of responding centres. [a]Option of referral to a specialized HCM/cardiomyopathy clinic; [b]including 3D and strain analysis; [c]exercise and/or vasodilator; and [d]including bone scintigraphy for transthyretin cardiac amyloidosis detection. CMR, cardiovascular magnetic resonance; CT, computed tomography; HCM, hypertrophic cardiomyopathy.

European Society of Cardiology (ESC) Guidelines.[1] Since then, new evidence on diagnosis, management and patient prognosis has accumulated.[2–4] Also, the role of multimodality imaging is further expanding in the assessment of HCM patients.[5,6]

The aim of the present survey from the European Association of Cardiovascular Imaging (EACVI) Scientific Initiatives Committee[7] was to investigate how HCM patients are imaged and managed in routine clinical practice across different centres in Europe and worldwide. In particular, this survey focused upon the organization of medical care, and the use of different imaging modalities in the detailed evaluation of cardiac anatomy, LV systolic and diastolic function, LV obstruction, myocardial ischaemia and myocardial fibrosis in patients with HCM. In addition, it explored the imaging-based strategies for sudden cardiac death (SCD) primary prevention and the long-term imaging follow-up of patients with confirmed disease as well as phenotype negative mutation carriers.

Methods

The present survey was conducted by the EACVI Scientific Initiatives Committee from 9 February to 6 April 2021 according to the published criteria (www.escardio.org/eacvi/surveys).[7–14] It consisted of 23 multiple-choice questions, available on an online platform that aimed at understanding how HCM patients are imaged and managed in routine clinical practice. Cardiology units in Europe and around the world, registered in the EACVI Scientific Initiatives Centers Network were invited to complete the online survey. In addition, the invitations to participate in the survey were disseminated via EACVI newsletter and social media.

Results

A total of 213 centres from 38 different countries responded to the survey, 186 (87%) were located in Europe [Armenia (1), Austria (1), Belarus (1), Belgium (5), Croatia (11), Cyprus (2), Czechia (1), Estonia (1), France (19), Georgia (1), Germany (5), Greece (27), Hungary (3), Italy (31), Latvia (3), Lithuania (1), The Netherlands (7), North Macedonia (4), Norway (7), Poland (2), Portugal (3), Romania (2), Serbia (1), Slovenia (11), Spain (10), Switzerland (5), Turkey (6), and UK (15)] and the rest worldwide [Brazil (2), Ecuador (2), Egypt (5), Lebanon (2), Mexico (10), Nigeria (1), Reunion (1), Syria (1), United Arab Emirates (1), and USA (1)].

The majority of centres were tertiary care hospitals or university centres (68%), followed by secondary care or district hospitals (17%), primary care centres (8%), and private hospitals (7%). Forty-one percent of the centres followed HCM patients in a specialized HCM or cardiomyopathy outpatient clinic. The majority of HCM patients were followed in a general cardiology outpatient clinic (57%), although more than half of these had the option of referring patients to a specialized HCM clinic when needed (*Figure 1A*). Overall, high availability of advanced modern cardiac imaging modalities was reported by the responding centres (*Figure 1B*) and exceeded the availability of myocardial biopsy assessments.

Assessment of cardiac anatomy, systolic, and diastolic function

To evaluate the degree of LV hypertrophy, most centres (57%) routinely reported the maximal thickness of the hypertrophied myocardium and described the distribution of LV wall thickening, 33% of the centres reported the thickness of all hypertrophied myocardial segments and 9% reported LV wall thickness according to the segmental model proposed by the American Society of Echocardiography (ASE) and the EACVI.[15] Among the 71% of the centres who had access to contrast echocardiography, the majority used it in cases where there was suspicion of apical hypertrophy, an apical aneurysm or a thrombus and when the extent of hypertrophy was difficult to visualize due to suboptimal image quality. Four percent of the centres

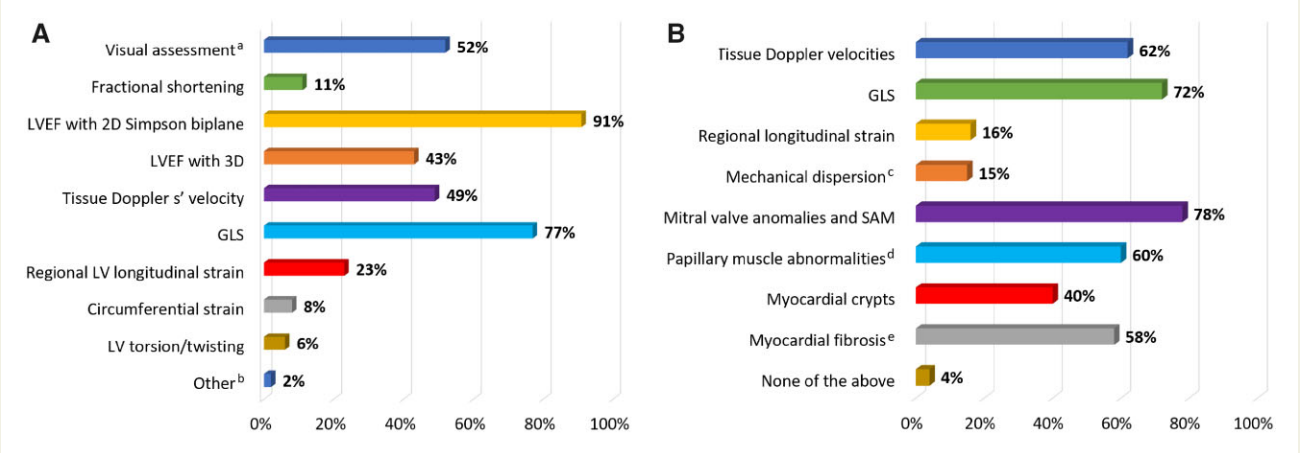

Figure 2 Assessment of LV systolic function and subtle markers of HCM. (*A*) The use of different echocardiographic parameters to assess LV systolic function in patients with hypertrophic cardiomyopathy. (*B*) The use of subtle markers of disease in genotype-positive phenotype-negative individuals. The bar charts display the percentage of responding centres. [a]Mild, moderate, severe LV systolic dysfunction; [b]mitral annular plane systolic excursion, CMR; [c]with speckle tracking echocardiography; [d]hypertrophy, apical insertion, anterior displacement, direct insertion into the anterior mitral valve leaflet; and [e]typical pattern of late gadolinium enhancement on CMR. CMR, cardiovascular magnetic resonance; GLS, global longitudinal strain; HCM, hypertrophic cardiomyopathy; LV, left ventricle; LVEF, left ventricular ejection fraction; SAM, systolic anterior movement.

used contrast echocardiography in every HCM patient to accurately measure LV wall thickness.

The use of different imaging parameters to assess LV systolic function in HCM patients is presented in *Figure 2A*. In addition, the assessment of subtle morphological and functional abnormalities to diagnose early mild expression of the disease among individuals carrying sarcomeric protein mutation but not fulfilling diagnostic criteria for HCM (LV wall thickness ≥13mm)[1] are presented in *Figure 2B*.

LV diastolic function was predominantly assessed according to the 2016 ASE and EACVI Recommendations,[16] either with the algorithm for patients with myocardial disease (63%) or with the algorithm for patients with normal left ventricular ejection fraction (LVEF; 32%). In indeterminate cases, additional echocardiographic parameters—pulmonary vein flow Doppler parameters (67%), mitral inflow pattern during standardized Valsalva manoeuvre (47%), isovolumetric relaxation time (41%), and left atrial (LA) strain (24%)—were most commonly employed, while diastolic stress test and cardiac catheterization for the purpose of LV diastolic function evaluation were used less frequently (in 16% and 9% of the responding centres, respectively).

Use of cardiovascular magnetic resonance and computed tomography

Among patients with unexplained LV wall thickening, cardiovascular magnetic resonance (CMR) was most commonly performed if there was a high clinical suspicion of HCM and normal/inconclusive echocardiogram, suboptimal echocardiographic windows, suspected apical HCM and to rule out other diagnoses (e.g. amyloidosis and Anderson–Fabry disease; *Figure 3A*). Among patients with confirmed HCM, 71% of the responding centres performed CMR in every patient at the initial evaluation. Other common indications were suboptimal acoustic windows on echocardiography, suspected apical aneurysm or thrombus and the evaluation of myocardial fibrosis in patients with intermediate risk for SCD to help guide primary prevention implantable cardioverter-defibrillator (ICD) therapy (*Figure 3B*). Myocardial fibrosis was assessed with late gadolinium enhancement (LGE; in 59% of the centres by visual assessment and in 49% by quantitative assessment), native T1 mapping (42%) and extracellular volume fraction (35%).

Cardiovascular computed tomography (CT) was most often used in HCM if there was another indication, e.g. the assessment of coronary artery disease (57% of the responding centres). Only 4% of the centres used cardiovascular CT as a second-line imaging method for the assessment of cardiac structure and function, but 33% used it as a third-line imaging modality when echocardiography was inconclusive and CMR was not available or contraindicated. Thirty-nine percent of the centres reported that they did not use cardiovascular CT routinely in HCM and in 2% of the centres CT was not available.

Assessment of left ventricular obstruction

To evaluate left ventricular outflow tract (LVOT) or mid-cavity obstruction with echocardiography, 49% of the responding centres reported using bedside provocation manoeuvres (Valsalva, sitting, and standing position) in every patient. Fifty-four percent of the centres reported the use of such measures only in cases of high clinical or imaging suspicion of obstruction. A total of 55% of centres performed exercise stress echocardiography and 9% pharmacological stress echocardiography when bedside manoeuvres failed to induce significant obstruction. Nine percent of the centres reported measuring LVOT area with CMR or 3D echocardiography to determine LVOT obstruction.

Two-dimensional transthoracic echocardiography and CMR were the most frequently used imaging techniques for the planning of septal reduction therapy (both used in 60% of the responding centres). 3D transthoracic echocardiography was employed in 29%,

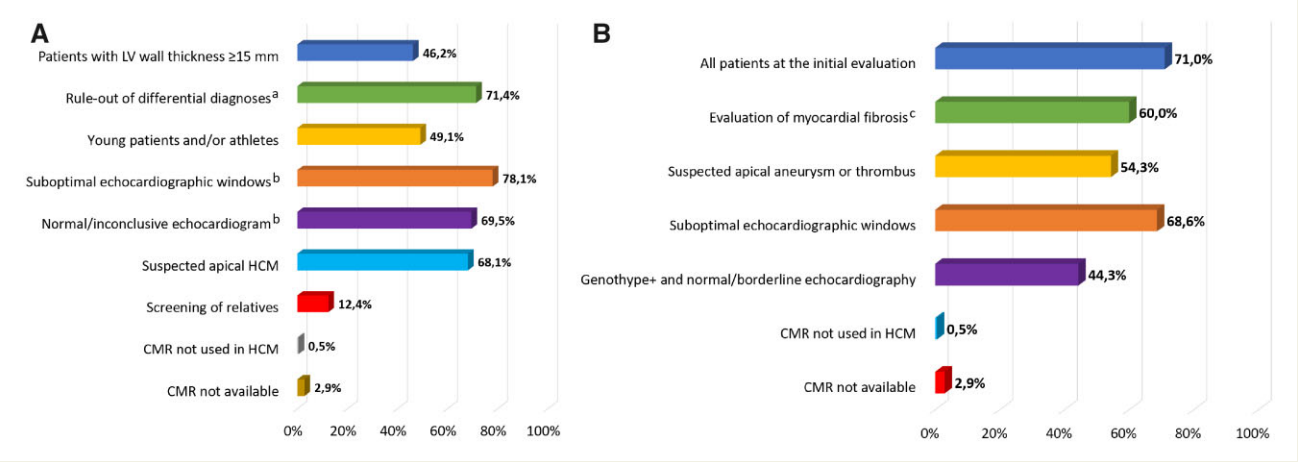

Figure 3 Indications for cardiovascular magnetic resonance in HCM. (*A*) The main indications for CMR in patients with suspected HCM. (*B*) The main indications for CMR in patients with confirmed HCM. The bar charts display the percentage of responding centres. [a]For example amyloidosis, Anderson–Fabry disease; [b]in high clinical suspicion of HCM (e.g. abnormal ECG findings); and [c]as a risk assessment for ICD implantation. CMR, cardiovascular magnetic resonance; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter-defibrillator.

transoesophageal echocardiography in 36%, and cardiac CT in 13% of the responding centres. Among 125 centres who performed percutaneous interventional septal ablation, 62% used LV contrast echocardiography with intracoronary contrast agent injection to guide the intervention.

Detection of coronary artery disease and myocardial ischaemia

Invasive coronary angiography was the preferred method to evaluate myocardial ischaemia in patients with HCM. It was used in 50% of the responding centres and it was supplemented by invasive functional testing in 28%. Coronary CT angiography was used in 44%, exercise stress echocardiography in 29%, stress perfusion CMR in 24%, stress perfusion with single photon emission CT in 20%, vasodilator stress echocardiography with coronary flow reserve measurement in 11%, and stress perfusion with positron emission tomography in 2% of the responding centres.

Sudden cardiac death risk assessment and prevention

Most of the responding centres (70%) followed the 2014 ESC Guidelines[1] recommendations for risk stratification and primary prevention of SCD in HCM. Seventeen percent of the centres followed the 2020 American Heart Association/American College of Cardiology (AHA/ACC) Guidelines[2] recommendations, 3% national guidelines, 9% local protocols/heart team decisions, and 1% expert opinions from the literature. Most centres selected patients for primary prevention ICD therapy based on the 5-year risk assessment of SCD calculated with the HCM Risk-SCD score (*Figure 4*). Maximum LV wall thickness ≥30 mm, extensive non-infarct LGE, LV apical aneurysm, and LV systolic dysfunction were the other important imaging parameters used to guide decisions for ICD therapy.

Imaging follow-up

Routine imaging follow-up of HCM patients with stable symptoms is presented in *Figure 5*. Transthoracic echocardiography was used by 95% of the centres and CMR by 36% of the responding centres, with eight centres (4%) depending solely on CMR. Patients were most commonly followed annually with echocardiography and every 2–5 years with CMR. Six centres (3%) reported the screening interval being dependent on the patient's age, whilst two centres (1%) performed repeat imaging only when clinically indicated.

Routine imaging screening of phenotype negative individuals carrying sarcomeric protein mutations and first-degree relatives of HCM patient with unknown genetic status was reported in 87%. The rest of the centres performed imaging when clinically indicated. In patients with no morphological or functional abnormalities and a normal ECG, patients, 12% of responding centres would repeat screening every year, 35% every 2 years, and 36% every 5 years. On the other hand, in patients with preclinical morphological or functional abnormalities or abnormal ECG findings, patients were screened every year by 32%, every 2 years by 18%, and every 5 years by 1% of the responding centres. Thirty-six percent of the centres reported the screening interval to be dependent on the patient's age.

Discussion

This global survey provides insight into the contemporary use of cardiac imaging in the assessment and management of patients with HCM.

Delivery of care and cardiac imaging availability

Diagnosis and management of patients with HCM requires special skills and competencies. The ESC guidelines do not specify the preferred healthcare model but emphasize that all patients and families should be managed in accordance with the same internationally

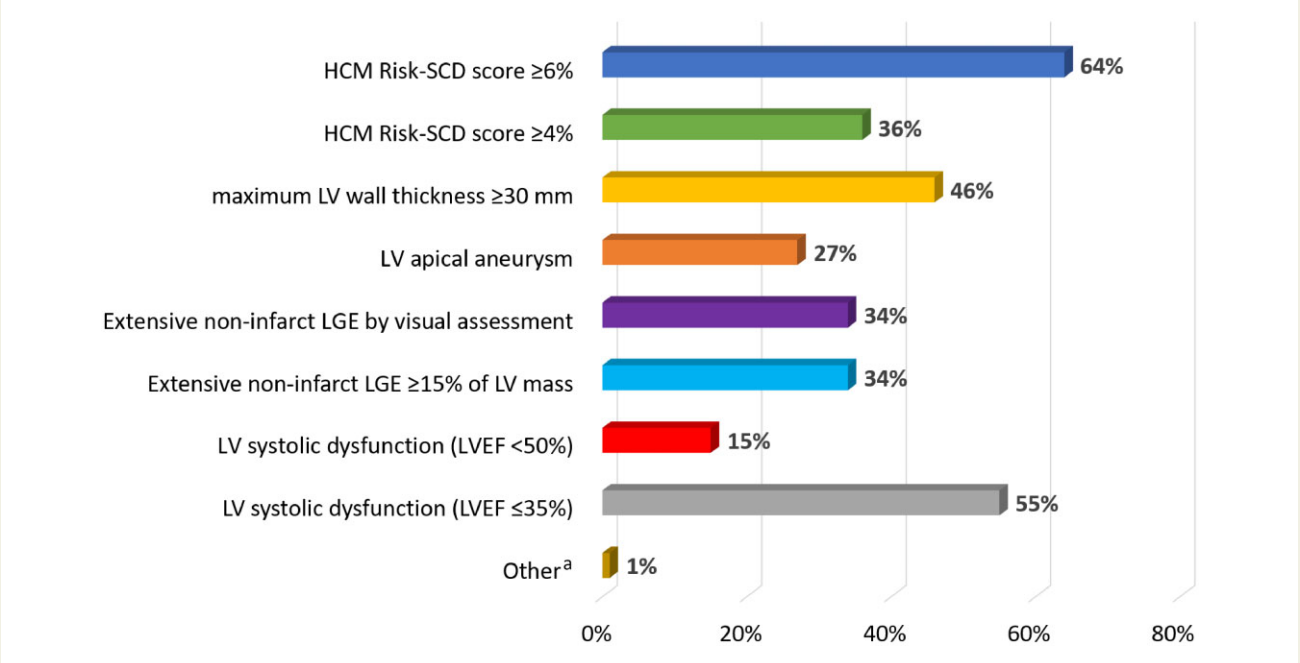

Figure 4 Sudden cardiac death risk assessment. The use of different imaging and clinical assessments to guide decision for primary prevention implantable cardioverter-defibrillator therapy in HCM is presented. The bar charts display the percentage of the responding centres. [a]Decisions based on the presence of complex ventricular arrhythmia, syncope, academic heart team opinion. HCM, hypertrophic cardiomyopathy; LGE, late gadolinium enhancement; SCD, sudden cardiac death.

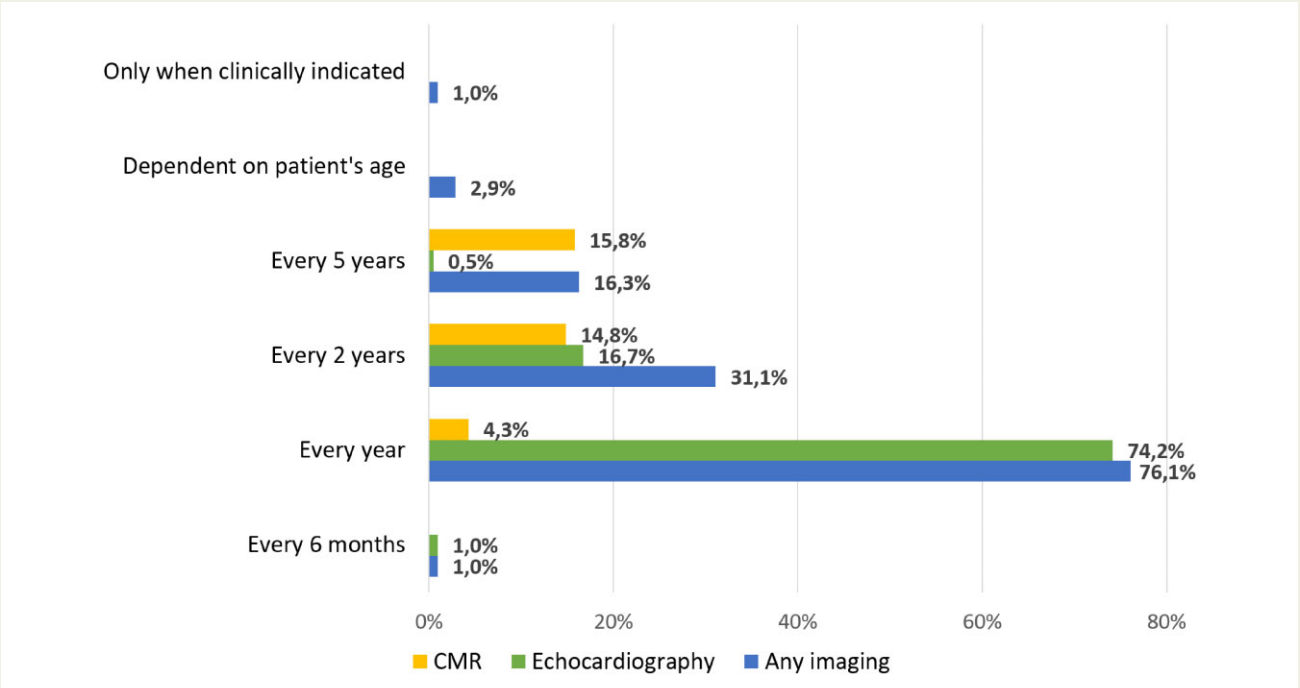

Figure 5 Imaging follow-up of HCM patients. The bar charts display the percentage of responding centres who followed their patients with cardiovascular magnetic resonance (CMR; yellow bars), echocardiography (green bars) and any imaging technique, i.e. CMR or echocardiography (blue bars), at different time intervals. CMR, cardiovascular magnetic resonance; HCM, hypertrophic cardiomyopathy.

agreed standards.[1] The recent AHA/ACC Guidelines promote a framework of HCM centres with three levels of competencies—the referral centres/physicians, primary HCM centres, and comprehensive HCM centres.[2] According to the results of the present survey, 72% of the responding centres were following or had an option to refer their patients to a specialized HCM/cardiomyopathy clinic (*Figure 1A*), revealing that a multilevel approach is gaining prominence in Europe as well.

Multimodality imaging is essential in diagnosis and clinical decision-making in patients with HCM.[1,2,5,6] Overall, high availability of modern cardiac imaging techniques was reported by the responding centres (*Figure 1B*), with presumably even higher availability when accounting for the referral options (i.e. <3% of the centres could not request a CMR or a CT). Importantly, access to advanced imaging was consistently higher than access to myocardial biopsy.

Assessment of cardiac anatomy, systolic, and diastolic function

The assessment of LV wall thickness is central to establishing the diagnosis and prognosis of patients with HCM. Maximal LV wall thickness and the distribution of wall thickening is currently the recommended standard of reporting[5,6] and it was the most common approach in the present survey. The use of contrast for LV cavity opacification is recommended when the extent of hypertrophy is difficult to visualize and when there is a suspicion of apical HCM, apical aneurysm or thrombus.[5,6] These were also the most common indications for performing contrast echocardiography in the present survey, although 29% of centres do not use this relatively simple technique in patients with HCM.

While LVEF is the most widely implemented imaging parameter to assess contractile heart function, global longitudinal strain (GLS) with speckle tracking echocardiography has been suggested to better reflect LV systolic function in hypertrophied hearts.[17] Moreover, GLS has shown incremental prognostic value for predicting heart failure symptoms and/or development of systolic dysfunction in patients with HCM.[18,19] The results of the present survey demonstrate wide adoption of GLS assessment (by 77% of the responding centres) in patients with HCM.

A comprehensive approach is necessary for the assessment of LV diastolic function and filling pressures in patients with HCM.[16] In addition to the parameters included in the ASE/EACVI Recommendations algorithm (mitral inflow *E*/*A*, average *E*/*e*′, tricuspid regurgitation velocity, and LA volume index), the evaluation of pulmonary vein atrial reversal velocity (Ar-A duration) is recommended in indeterminate cases. This recommendation is implemented in 66% of the surveyed centres. LA strain is also gaining prominence, being assessed by 24% of the responding centres.

Use of cardiovascular magnetic resonance

Echocardiography is the primary imaging modality in patients with HCM, with CMR offering complementary information.[1,2] CMR is of added value for accurate measurement of LV wall thickness, quantification of ventricular size and systolic function, detection of apical aneurysms, thrombi and subtle markers of disease. CMR is uniquely able to evaluate myocardial fibrosis, which can aid in diagnosis and patient risk stratification.[20] Therefore, the ESC Guidelines recommend performing CMR at the baseline assessment in every patient with HCM, providing there is no contraindication and the local resources and expertise permit.[1] This strategy has been adopted by 71% of the responding centres in the present survey, although even wider implementation would appear possible as only 3% of centres lack access to CMR.

Assessment of left ventricular obstruction

Obstructive HCM is the predominant form of HCM, accounting for 70% of the disease.[21] While 37% of patients are diagnosed at rest or with bedside provocative manoeuvres, such as sitting, standing and Valsalva strain, 33% are diagnosed additionally with stress echocardiography.[22] Therefore, the ESC and AHA/ACC Guidelines recommend performing bedside provocative manoeuvres in every patient, while exercise stress echocardiography is needed in symptomatic patients, in whom bedside manoeuvres fail to induce significant LVOT obstruction.[1,2] Moreover, LVOT obstruction is one of the key variables in the risk assessment for SCD in HCM. According to the results of the present survey, the adherence to the guidelines recommendations was not perfect—only half of the centres performed bedside provocation manoeuvres in every patient with the other half performing these only when there was clinical or imaging suspicion of LVOT obstruction. In addition, only 54% of centres performed exercise stress echocardiography when bedside manoeuvres failed to induce significant obstruction.

Sudden cardiac death risk assessment and prevention

Estimation of SCD risk is an integral part of clinical management allowing the appropriate selection of patients for primary prevention ICD therapy. The 2014 ESC Guidelines recommend the assessment of 5-year risk of SCD with the HCM Risk-SCD score calculator which includes the following imaging parameters—maximum LV wall thickness, LA diameter, and peak LVOT gradient.[1] On the other hand, recent 2020 AHA/ACC Guidelines advocate ICD selection based on the presence of different imaging risk factors—maximum LV wall thickness ≥30 mm in any segment, LV systolic dysfunction (LVEF <50%), the presence of LV apical aneurysm, and extensive LGE on CMR.[2] While some studies have promoted a threshold of LGE ≥15% of LV mass,[23,24] the guidelines define extensive LGE by either visual or quantitative assessment. The results of the present survey show that the majority of the centres followed the ESC Guidelines with 5-year HCM Risk-SCD score ≥6% being the most frequently used tool to guide ICD decision making (*Figure 4*). However, contemporary risk factors, particularly extensive LGE and LV apical aneurysms, have already been adopted by many centres and might indicate a need for an update of the European recommendations.

Imaging follow-up

Patients with HCM require lifelong follow-up to detect changes in symptoms and to evaluate the risk of adverse events. The ESC and AHA/ACC guidelines recommend transthoracic echocardiography every 1–2 years and whenever symptoms change.[1,2] Furthermore, CMR re-evaluation may be considered every 5 years (or even earlier

in patients with progressive disease) for the SCD risk assessment. The results of the present survey demonstrate wide adoption of the guidelines recommendations with 99% of the responding centres performing regular imaging follow-up (76% annually). First-line imaging modality was echocardiography; however, 36% of the responding centres also performed serial CMR (*Figure 5*). Eighty-seven percent of the responding centres performed serial follow-up imaging in first-degree relatives of patients with HCM to screen for phenotype development.

Implementation of the current European guidelines and recommendations

Most centres followed current European guidelines and recommendations[1,5] for the diagnosis and management of patients with HCM. A multimodality imaging approach has become standard. While echocardiography remains the primary imaging modality, wide adoption of CMR as a complementary tool for the initial evaluation, risk stratification and follow-up of patients with HCM was observed. Furthermore, advanced imaging parameters like GLS to detect subtle LV systolic dysfunction have been widely used. The utilization of contrast echocardiography to diagnose HCM patients with suboptimal echocardiographic image quality as well as bedside provocation manoeuvres and exercise stress echocardiography to diagnose patients with LVOT obstruction was imperfect and requires further emphasis. Additional risk factors for SCD are commonly used to guide decisions regarding primary prevention ICD therapy in many centres and might indicate a need for an update of the current European recommendations.

Limitations

The majority of responding centres were tertiary care centres or university hospitals in Europe. The survey findings may therefore not be generalizable to other clinical environments. The number of HCM patients treated in each centre was not known. In addition, despite an attempt to address clinically most relevant indications for cardiac imaging in HCM, certain topics, e.g. the septal reduction therapy strategies and subsequent patient management, were not covered due to the survey length constraints.

Conclusions

The results of the present survey provide several important insights into the contemporary use of cardiac imaging for the management of patients with HCM in Europe and worldwide. With a snapshot overview of the implementation of current guidelines and recommendations, the survey provides the basis for unifying imaging procedures across different countries, identified areas to target with education (e.g. optimal strategies to diagnose LVOT obstruction) and may help shape future guidelines and recommendations, particularly on the risk stratification and primary prevention of SCD.

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Conflict of interest: N.C. is a member of the international advisory board of Mavacamten-Myokardia-BMS. N.A.M. received speaker's fees from GE Healthcare and Abbott Vascular and participated to the Medical Advisory Board of Philips Ultrasound. B.A.P. received research support and lecture honoraria from General Electric Healthcare, Hitachi Aloka, and Bracco. M.R.D. has received speaker fees from Pfizer and Novartis and consultancy fees from Novartis, Jupiter Bioventures, and Silence therapeutics. The remaining authors have nothing to disclose.

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