The diagnosis and treatment of hypertrophic cardiomyopathy (HCM) require special expertise. Physicians often encounter this disease in clinical practice, but there are few randomized clinical studies on the diagnosis and treatment of this disease, especially that on optimal treatment options. In 2002, The Japanese Circulation Society published the “Guidelines for Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy” (Chair: Junichi Yoshikawa). In 2007, the guidelines were revised to add new findings obtained during the five years after the launch of the first edition (Chair: Yoshinori Doi), and the second edition was used widely in clinical practice. During the five years after the release of the second edition, the American College of Cardiology Foundation (ACCF)/the American Heart Association (AHA) and the European Society of Cardiology (ESC) provided new guidelines on the diagnosis and treatment of cardiomyopathies. We decided to revise the guidelines to reconfirm the definition of HCM and add new findings.

Since few randomized clinical studies are available for the diagnosis and treatment of HCM, not only data in Japan but also those in Western countries were referred in this revision as in the previous ones. However, new clinical data have been accumulated consistently for 10 years since the release of the first edition of this guideline document. A number of new genetic mutations associated with HCM have been reported. Physicians are becoming increasingly aware of the importance of differentiating HCM from other conditions such as Fabry disease that may cause HCM-like cardiac hypertrophy but requiring different treatment. The clinical use of diagnostic imaging techniques especially cardiac magnetic resonance imaging (MRI) has become common, and physicians understand better the clinical significance of late gadolinium enhancement (LGE) on contrast-enhanced MRI. New findings have also been obtained for risk factors in high-risk patients. In the present revision, a section on device therapy is newly added to the chapter on non-pharmacotherapy to describe implantable cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy (CRT) in addition to the descriptions on pacemaker therapy in the previous versions. Data on the mid- and long-term outcome of percutaneous transluminal septal myocardial ablation (PTSMA) are added in this revision. In the present revision of the guidelines, members of the expert committee discussed in depth, and independent assessment committee members provided comments to make the
guidelines useful in clinical practice. We hope these guidelines will help clinicians treat patients with HCM.

In this document, recommendations for the diagnosis and treatment of HCM are described with their classification of recommendations and level of evidence grade. Classification of Recommendations and Level of Evidence are as follows:

Classification of Recommendations
Class I: There is evidence and/or general agreement that a given procedure or treatment is useful and effective.
Class II: There is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
Class IIa: Weight of evidence and data and opinion is in favor of usefulness and/or effectiveness.
Class IIb: Usefulness/efficacy is less well established by evidence/opinion.
Class III: There is evidence and/or general agreement that the procedure/treatment is not useful/effective, and in some cases may be harmful.

Level of Evidence
Level A: Data derived from multiple randomized clinical studies or meta-analyses.
Level B: Data derived from a single randomized study or large-scale non-randomized studies.
Level C: Only consensus opinion of experts and/or small-size clinical studies (including retrospective studies and registries).

1. Definition and Basic Pathophysiology

1. Definition and Classification
Clinically, cardiomyopathies are defined as a group of diseases of the myocardium associated with cardiac dysfunction where no other causes such as valvular disease and hypertension are present.1-4 Hypertrophic cardiomyopathy is defined by an increase in the thickness of the left or right ventricular wall or of both walls.5-7

In the report of the World Health Organization/International Society and Federation of Cardiology (WHO/ISFC) Task Force on the Definition and Classification of Cardiomyopathies published in 1980,8 cardiomyopathies are defined as “heart muscle diseases of unknown cause.” However, with advanced research and characterization of causative genes and abnormal sarcomere proteins, WHO/ISFC revised the definition by deleting the expression of “unknown cause” to “diseases of the myocardium associated with cardiac dysfunction.”1

It is expected that cardiomyopathies will be classified by cause when further studies clarify the causes of the disease in detail. As the classification based on clinical manifestations has been commonly used, the 1995 WHO/ISFC report kept the long-established categories of dilated, hypertrophic and restrictive cardiomyopathies, and add new categories of arrhythmogenic right ventricular cardiomyopathy, and unclassified cardiomyopathies (Table 1).1

The 1995 WHO/ISFC report uses specific cardiomyopathies to describe “heart muscle diseases that are associated with specific cardiac or systemic disorders,” and no longer uses the term “secondary cardiomyopathies.” Specific cardiomyopathies include ischemic, valvular, hypertensive, inflammatory (myocarditis) and metabolic cardiomyopathies, sensitivity and toxic reactions, peripartum cardiomyopathy, and general systemic disease including neuromuscular disorders, and connective tissue disorders.

In 2006, the AHA proposed a new definition and classification of cardiomyopathies.9 The AHA defined cardiomyopathies as a “heterogeneous group of diseases of the myocardium associated with mechanical and/or electrical dysfunction that usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilatation and are due to a variety of causes that frequently are genetic.” In 2008, the ESC revised the WHO/ISFC classification to define a cardiomyopathy as

<table>
<thead>
<tr>
<th>Abbreviations</th>
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<tbody>
<tr>
<td>ACCF: American College of Cardiology Foundation</td>
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<tr>
<td>ACE: angiotensin-converting enzyme</td>
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<tr>
<td>AHA: American Heart Association</td>
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<tr>
<td>AMP: adenosine monophosphate</td>
</tr>
<tr>
<td>ARB: angiotensin receptor blocker</td>
</tr>
<tr>
<td>CRT: cardiac resynchronization therapy</td>
</tr>
<tr>
<td>CT: computed tomography</td>
</tr>
<tr>
<td>DDD: dual-chamber, dual-pacing, dual-response</td>
</tr>
<tr>
<td>D-HCM: dilated phase of hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>ECG: electrocardiography</td>
</tr>
<tr>
<td>ESC: European Society of Cardiology</td>
</tr>
<tr>
<td>FDG-PET: fluorodeoxyglucose positron emission tomography</td>
</tr>
<tr>
<td>HCM: hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>HOCM: hypertrophic obstructive cardiomyopathy</td>
</tr>
<tr>
<td>ICD: implantable cardioverter-defibrillator</td>
</tr>
<tr>
<td>LGE: late gadolinium enhancement</td>
</tr>
<tr>
<td>LVOT: left ventricular outflow tract</td>
</tr>
<tr>
<td>MHLW: Ministry of Health, Labor and Welfare</td>
</tr>
<tr>
<td>MR: mitral regurgitation</td>
</tr>
<tr>
<td>MRI: magnetic resonance imaging</td>
</tr>
<tr>
<td>NYHA: New York Heart Association</td>
</tr>
<tr>
<td>PTSDA: percutaneous transluminal septal myocardial ablation</td>
</tr>
<tr>
<td>QOL: quality of life</td>
</tr>
<tr>
<td>RI: radioactive isotope</td>
</tr>
<tr>
<td>SAM: systolic anterior motion</td>
</tr>
<tr>
<td>WHO/ISFC: World Health Organization/International Society and Federation of Cardiology</td>
</tr>
</tbody>
</table>

Table 1. Definition and Classification of Cardiomyopathies by the 1995 WHO/ISFC Task Force

| Definition: |
| Cardiomyopathies are defined as diseases of the myocardium associated with cardiac dysfunction. |

| Classification: |
| 1. Dilated cardiomyopathy (DCM) |
| 2. Hypertrophic cardiomyopathy (HCM) |
| 3. Restrictive cardiomyopathy (RCM) |
| 4. Arrhythmogenic right ventricular cardiomyopathy |
| 5. Unclassified cardiomyopathy |

WHO/ISFC, World Health Organization/International Society and Federation of Cardiology.
“a myocardial disorder in which the heart muscle is structurally and functionally abnormal, in the absence of coronary artery disease, hypertension, valvular disease and congenital heart disease sufficient to cause the observed myocardial abnormality.”

With the advancement of molecular genetics in recent years, many genes associated with HCM have been identified, and research has revealed that diverse factors are responsible for the development of HCM. In the present guideline document, the definition of HCM as described in the 1995 WHO/ISFC report is used on the basis of the above-described proposals on cardiomyopathies by the AHA and ESC. Hypertrophic cardiomyopathy is defined as cardiomyopathies resulting from mutations in sarcomeric genes or other type of mutations, and those not associated with any other storage disease or systemic diseases affecting multiple organ systems on the basis of all available evaluations. Cardiac hypertrophy resulting from storage disease or systemic diseases affecting multiple organ systems is classified separately from HCM into “diseases causing HCM-like manifestations.” Physicians must be aware that patients with HCM-like manifestations due to specific causes may respond well to specific treatment. Table 2 lists several genes associated with HCM and diseases with HCM-like manifestations.

### Table 2. HCM and Diseases With HCM-Like Manifestations

<table>
<thead>
<tr>
<th>HCM:</th>
<th>Diseases with HCM-like manifestations:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myofilament protein mutations (See Table 4)</td>
<td>Familial diseases (See Tables 5 and 6)</td>
</tr>
<tr>
<td>β-Myosin heavy chain</td>
<td>Glycogen storage disease</td>
</tr>
<tr>
<td>Cardiac myosin-binding protein C</td>
<td>e.g., Pompe disease, PRKAG2 mutation, Forbes’ disease, and Danon disease</td>
</tr>
<tr>
<td>Cardiac troponin I</td>
<td>Lysosomal diseases</td>
</tr>
<tr>
<td>Cardiac troponin T</td>
<td>e.g., Anderson-Fabry disease, and Hurler disease</td>
</tr>
<tr>
<td>α-Tropomyosin</td>
<td>Mitochondrial disease</td>
</tr>
<tr>
<td>Essential myosin light chain</td>
<td>Syndromes</td>
</tr>
<tr>
<td>Regulatory myosin light chain</td>
<td>Noonan syndrome</td>
</tr>
<tr>
<td>α-Cardiac actin</td>
<td>LEOPARD syndrome</td>
</tr>
<tr>
<td>α-Myosin heavy chain</td>
<td>Friedreich’s ataxia</td>
</tr>
<tr>
<td>Titin</td>
<td>Beckwith-Wiedemann syndrome</td>
</tr>
<tr>
<td>Cardiac troponin C</td>
<td>Swyer syndrome</td>
</tr>
<tr>
<td>Muscle LIM protein</td>
<td>Others</td>
</tr>
<tr>
<td>Unknown causative genes</td>
<td>Familial amyloidosis</td>
</tr>
<tr>
<td></td>
<td>Obesity</td>
</tr>
<tr>
<td></td>
<td>Infant of diabetic mother</td>
</tr>
<tr>
<td></td>
<td>Athletes</td>
</tr>
<tr>
<td></td>
<td>Amyloidosis</td>
</tr>
</tbody>
</table>

HCM, hypertrophic cardiomyopathy.

### Table 3. Pathophysiology of HCM Described by the MHLW Idiopathic Cardiomyopathy Research Group in 2005

Hypertrophic cardiomyopathies are diseases of the myocardium associated with left and/or right ventricular hypertrophy where no other causes are present, and are characterized by asymmetric cardiac hypertrophy. Typically, the left ventricle is not dilated, and the left ventricular contractile function is normal or increased. The essential pathophysiology of HCM is left ventricular diastolic dysfunction due to cardiac hypertrophy.

1. HCM with left ventricular outflow tract obstruction is called hypertrophic obstructive cardiomyopathy (HOCM).
2. There are hypertrophic cardiomyopathies affecting specific regions of the heart, such as midventricular obstruction (obstruction is located in the middle of the left ventricle) and apical hypertrophic cardiomyopathy (hypertrophy is located in the apex of left ventricle).

3. During the course of HCM, the thickened ventricular wall becomes thinner, and left ventricular contractile dysfunction associated with ventricular cavity dilatation may develop and lead to manifestations similar to dilated cardiomyopathy. This is called dilated phase of hypertrophic cardiomyopathy (D-HCM). The diagnosis of D-HCM is confirmed by observation of clinical course. In patients without detailed observation, the diagnosis may be made based on the prior and definite diagnosis as HCM.

non-obstructive HCM be termed collectively as HCM, and HCM with LVOT obstruction be called hypertrophic obstructive cardiomyopathy (HOCM). There are HCM affecting specific regions of the heart, such as midventricular obstructive cardiomyopathy and apical hypertrophic cardiomyopathy. Hypertrophic cardiomyopathy presenting with features simulating dilated cardiomyopathy is described as dilated phase of hypertrophic cardiomyopathy (D-HCM).14,15

Table 4. Causative Gene Mutations of HCM

<table>
<thead>
<tr>
<th>Gene Locus</th>
<th>Protein</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myofilament/Sarcomeric HCM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Giant filament</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TTN 2q31</td>
<td>Titin</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Thick filament</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MYH7 14q11.2-q12</td>
<td>β-Myosin heavy chain</td>
<td>25–40</td>
</tr>
<tr>
<td>MYH6 14q11.2-q12</td>
<td>α-Myosin heavy chain</td>
<td>&lt;1</td>
</tr>
<tr>
<td>MYL2 12q23-q24.3</td>
<td>Regulatory myosin light chain</td>
<td>&lt;1</td>
</tr>
<tr>
<td>MYL3 3p21.2-p21.3</td>
<td>Essential myosin light chain</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Intermediate filament</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MYBPC3 11p11.2</td>
<td>Cardiac myosin-binding protein C</td>
<td>25–40</td>
</tr>
<tr>
<td>Thin filament</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNNT2 1q32</td>
<td>Cardiac troponin T</td>
<td>3–5</td>
</tr>
<tr>
<td>TNNI3 19p13.4</td>
<td>Cardiac troponin I</td>
<td>1–5</td>
</tr>
<tr>
<td>TPM1 15q22.1</td>
<td>α-Tropomyosin</td>
<td>1–5</td>
</tr>
<tr>
<td>ACTC 15q14</td>
<td>α-Cardiac actin</td>
<td>&lt;1</td>
</tr>
<tr>
<td>TNNC1 3p21.1</td>
<td>Cardiac troponin C</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Z-disc HCM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACTN2 1q42-q43</td>
<td>α-Actinin 2</td>
<td>&lt;1</td>
</tr>
<tr>
<td>ANKRD1 1q23.31</td>
<td>Cardiac ankyrin repeat protein</td>
<td>&lt;1</td>
</tr>
<tr>
<td>CSRSP3 11p15.1</td>
<td>Muscle LIM protein</td>
<td>&lt;1</td>
</tr>
<tr>
<td>LDB3 10q22.2-q23.3</td>
<td>LIM binding domain 3 (cypher)</td>
<td>1–5</td>
</tr>
<tr>
<td>MYOZ2 4q26-q27</td>
<td>Myozin 2</td>
<td>&lt;1</td>
</tr>
<tr>
<td>TCP1 17q12-q21.1</td>
<td>Telethonin</td>
<td>&lt;1</td>
</tr>
<tr>
<td>VCL 10q22.1-q23</td>
<td>Vinculin/Metavinculin</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Calcium-Handling HCM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>JPH2 20q13.12</td>
<td>Junctophilin 2</td>
<td>&lt;1</td>
</tr>
<tr>
<td>PLN 6q22.1</td>
<td>Phospholamban</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

Table 5. Disease-Causing Genes of HCM-Like Manifestation

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Gene</th>
<th>Locus</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular noncompaction</td>
<td>DTNA</td>
<td>18q12</td>
<td>α-Dystrobrevin</td>
</tr>
<tr>
<td>Barth syndrome/Left ventricular noncompaction</td>
<td>TAZ</td>
<td>Xq28</td>
<td>Tafazzin (G4.5)</td>
</tr>
<tr>
<td>Danon disease</td>
<td>LAMP2</td>
<td>Xq24</td>
<td>Lysosome-associated membrane protein 2</td>
</tr>
<tr>
<td>Fabry disease</td>
<td>GLA</td>
<td>Xq22</td>
<td>α-Galactosidase A</td>
</tr>
<tr>
<td>Forbes' disease</td>
<td>AGL</td>
<td>1p21</td>
<td>Amylo-1,6-glucosidase</td>
</tr>
<tr>
<td>Friedrich's ataxia</td>
<td>FXN</td>
<td>9q33</td>
<td>Frataxin</td>
</tr>
<tr>
<td>Noonan syndrome</td>
<td>KRAS</td>
<td>12p12.1</td>
<td>v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog</td>
</tr>
<tr>
<td>Noonan syndrome</td>
<td>SOS1</td>
<td>2p22-p21</td>
<td>Son of sevenless homolog 1</td>
</tr>
<tr>
<td>Noonan syndrome, LEOPARD syndrome</td>
<td>PTPN11</td>
<td>12q24.1</td>
<td>Protein tyrosine phosphatase, non-receptor type 11, SHP-2</td>
</tr>
<tr>
<td>Noonan syndrome, LEOPARD syndrome</td>
<td>RAF1</td>
<td>3p25</td>
<td>V-RAF-1 murine leukemia viral oncogene homolog 1</td>
</tr>
<tr>
<td>Pompe disease</td>
<td>GAA</td>
<td>17q25.2-q25.3</td>
<td>α-1,4-glucosidase deficiency</td>
</tr>
<tr>
<td>Cardiac hypertrophy associated with WPW syndrome</td>
<td>PRKAG2</td>
<td>7q35-q36.36</td>
<td>AMP-activated protein kinase</td>
</tr>
</tbody>
</table>

HCM, hypertrophic cardiomyopathy; WPW, Wolff-Parkinson-White; AMP, adenosine monophosphate.

2. Causes of Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy has long been known to run in families. In 1990, a study on the cause of familial HCM using molecular genetic techniques revealed families with myocardial β-myosin heavy chain gene mutations.16 In subsequent studies, more than 900 distinct mutations in at least 16 genes...
were reported as causes of HCM. The cause of familial HCM has been detected in about 50–60% of HCM families. Table 4 lists major causative genes of HCM, which shows autosomal dominant inheritance, and the frequency of mutations.\textsuperscript{17–19} Patients with mitochondrial diseases and Fabry disease, which are classified into specific cardiomyopathies, may present with HCM-like manifestations. Mutations in adenosine monophosphate (AMP)-activated protein kinase may cause glycogen storage disease presenting as HCM-like manifestations associated with WPW syndrome.\textsuperscript{20–24} Table 5 lists major diseases presenting as HCM-like hypertrophy and their disease-causing genes.\textsuperscript{18,25} Hypertrophic cardiomyopathy-like hypertrophy may also develop in patients with Pompe disease, Barth syndrome, Noonan syndrome, and LEOPARD syndrome.

### 3. Pathophysiology and Hemodynamics

Hypertrophic cardiomyopathy is characterized by an uneven myocardial hypertrophy associated with diastolic dysfunction which cannot be explained by pressure overload.\textsuperscript{26,27} Hypertrophic cardiomyopathy may cause a pressure gradient in regions with severe hypertrophy such as the LVOT and the mid ventricle.\textsuperscript{28,29} Abnormalities in coronary microcirculation may lead to myocardial ischemia and reduced coronary flow reserve, causing chest pain and other symptoms.\textsuperscript{30}

### 4. Prognosis

The most common causes of HCM-related death are sudden death, heart failure, and stroke which is usually embolic and associated with atrial fibrillation.\textsuperscript{31,32} In a large-scale epidemiological survey conducted in 2002 in Japan, the annual mortality rate among HCM patients was 2.8%.\textsuperscript{33} The cause of death was arrhythmia in 31.9%, and heart failure in 21.3%. In an analysis of 86 cases of HCM-related death in Western countries,\textsuperscript{34} the cause of death was sudden death in 44 patients (51%), heart failure-related death in 31 patients (36%), and stroke death in 11 patients (13%). Sudden death was most common in young patients (mean age: 45 years), while heart failure-related death was more common in midlife and beyond (56 years), and stroke developed in older patients (73 years).

### II Diagnosis

Figure 1 outlines the diagnostic pathway for HCM. Abnormal myocardial hypertrophy may be effectively demonstrated by echocardiography. For patients with limited echo windows and those with low quality of echocardiograms, cardiac computed tomography (CT) or cardiac MRI are used.\textsuperscript{35} Patients with abnormal electrocardiographic findings such as
abnormal Q waves and ST-T changes that are not otherwise explained should be examined in detail with a possibility of HCM in mind.  

1. Symptoms and Physical Findings

(1) Symptoms
Some patients with HCM are asymptomatic, but others have dyspnea, chest pain, palpitations, and syncope, among other symptoms.  

(2) Physical Findings
Double apical impulse and fourth heart sound are often present. When LVOT obstruction is present, the physician may hear an ejection systolic murmur caused by turbulent blood flow through an obstructed site, and, at times, an early systolic sound that occurs when the anterior mitral valve leaflet hits against the hypertrophied ventricular septum.

2. Evaluation Method

1. Electrocardiography (ECG), Holter ECG, Signal-Averaged ECG, Exercise ECG, Microvolt T-Wave Alternans, and Clinical Electrophysiological Testing
If 12-lead ECG shows abnormal Q waves, ST-T changes, negative T waves, and/or tall R waves in the left precordial leads which are not otherwise explained, HCM should be suspected. Hypertrophic cardiomyopathy is associated with diverse types of arrhythmias such as ventricular or supraventricular tachyarrhythmias and bradyarrhythmias, which may lead to syncope, sudden death, or cardiogenic thromboembolism. Since these arrhythmias are often asymptomatic, all patients suspected to have HCM should undergo Holter ECG. The validity of ventricular late potentials detected with signal-averaged ECG as a predictor of sudden death or lethal arrhythmias has not been demonstrated. Electrophysiological testing is indicated for the following:

Indications for Electrophysiological Testing in HCM Patients:
Class I
1. HCM patients resuscitated from cardiac arrest to determine the cause of cardiac arrest and assess the indication for ICDs.
2. Patients with symptomatic HCM in whom ventricular late potentials were observed in signal-averaged ECG.

Class II
1. Patients with nonobstructive HCM to investigate the cause of syncope.
2. HCM patients with nonsustained ventricular tachycardia which is multiplet or develops frequently.

Class III
1. HCM patients without ventricular tachycardia who show a significant pressure gradient which may explain syncope.

2. Echocardiogram and Doppler Echocardiogram
As the basic pathophysiological features of HCM are abnormal myocardial hypertrophy unassociated with ventricular cavity enlargement, two-dimensional echocardiography should be performed to assess the pattern of cardiac hypertrophy, and Doppler echocardiography should be performed to evaluate 1) the presence/absence of left or right ventricular obstruction such as LVOT gradient, 2) left ventricular diastolic function, and 3) presence/absence of complications such as mitral regurgitation (MR). When lesions are difficult to be visualized with echocardiogram, other imaging techniques such as cardiac CT and cardiac MRI should be used to make a diagnosis based on the comprehensive assessment of the patient.

Indications for Transthoracic Echocardiography in Patients Who Have or Are Suspected to Have HCM:
Class I
1. Morphological and hemodynamic evaluation in patients suspected to have HCM.
2. Reevaluation of HCM patients with obvious clinical changes or those who need echocardiographic information to determine pharmacotherapy.

Class II
1. Reevaluation of HCM patients without substantial clinical changes. (Excluding annual or semiannual follow-up echocardiography.)
2. Evaluation of left ventricular function to stratify prognostic risks.

Indications for Transesophageal Echocardiography in Patients Who Have or Are Suspected to Have HCM:
Class I
1. Patients with clinical and/or transthoracic echocardiographic features strongly suggestive of HCM in whom the quality of transthoracic echocardiogram is not sufficient to evaluate the status of the LVOT gradient and other hemodynamics.
2. Patients in whom chordal rupture is suspected as the cause of severe MR or acute deterioration of hemodynamics and who need detailed examination of the mitral apparatus.
3. Intraoperative monitoring during septal myotomy/myectomy.
4. Patients with atrial fibrillation in whom left atrial thrombi are suspected and/or electrical defibrillation is considered.

Class II
1. Routine reevaluation of patients with clinically stable HCM in whom no modification of treatment is considered.

3. Cardiac Catheterization (Including Endomyocardial Biopsy)
Noninvasive cardiac imaging modalities including echocardiography, Doppler echocardiography, cardiac CT, and cardiac MRI may be used in the assessment of HCM, but cardiac catheterization may also be required to evaluate morphological and functional assessment of the ventricles and to perform coronary angiography and endomyocardial biopsy to differentiate HCM from coronary artery disease and other specific cardiomyopathies.

Indications for Cardiac Catheterization for the Diagnosis and Assessment of HCM:
Class I
1. Coronary angiography to differentiate HCM from coro-
JCS Guidelines for Diagnosis and Treatment of Patients With HCM

Step 1: From symptom to suspicion of HCM

- Symptoms:
  - Shortness of breath
  - Dyspnea
  - Syncope
  - Dizziness
  - Thump sensation
  - Irregular pulse
  - Chest discomfort
  - Chest pain
  - Palpitations
  - Fatigue
  - Asymptomatic

- Detailed history taking:
  - Family history, Past history (including screening), Occupational history, Smoking/Drinking/Drug use

- Physical findings:
  - Large a wave of jugular pulse
  - Double apical impulse
  - Intense fourth sound
  - Systolic murmur (Crackles indicating alveolar fluid)
  - Pulse/Carotid pulse: bisferiens pulse
  - LVOT ejection murmur

- Points of differential diagnosis:
  - Findings suggestive of contractile dysfunction?
  - Findings suggestive of other causes of cardiac hypertrophy?

- Examination findings:
  - ECG:
    - Left atrial overload
    - Left ventricular hypertrophy
    - High R wave voltages
    - Abnormal Q wave
    - ST-T changes
    - Giant negative T waves
    - Rhythm disturbance
    - Conduction disturbance
  - Chest X-ray:
    - Normal or mild cardiomegaly
    - Increased venous distribution in the upper lung field

- Suspected conditions:
  - Cardiac hypertrophy
  - Diastolic dysfunction
  - LVOT obstruction
  - Arrhythmia

- Echocardiography

Step 2: Diagnosis of HCM by echocardiography

- Echocardiography/Doppler-echocardiography

- Normal LV wall motion:
  - Increased LV wall thickness
  - Assess the presence/absence and location of intraventricular obstruction
  - Blood flow acceleration in the ventricle
  - Mitral regurgitation
  - Patterns of abnormal relaxation
  - Pseudonormalized filling pattern
  - Restrictive filling pattern
  - Early diastolic inflow velocity at the mitral annulus obtained via tissue Doppler imaging
  - Estimate RV systolic pressure

- LV diastolic dysfunction:
  - LV inflow pattern
  - Patterns of abnormal relaxation
  - Pseudonormalized filling pattern
  - Restrictive filling pattern
  - Early diastolic inflow velocity at the mitral annulus obtained via tissue Doppler imaging

Hypertrophic cardiomyopathy (HCM)

Points for differential diagnosis during echocardiography:

- Abnormal valves
  - Cardiac hypertrophy due to vascular disease
  - Normal LV wall motion and thickness
  - LV enlargement/Reduced wall motion
  - Abnormal ECG
    - Restrictive cardiomyopathy (RCM)
    - Arrhythmogenic right ventricular cardiomyopathy (ARVC)
    - Dilated cardiomyopathy (DCM)
  - Dilated phase of hypertrophic cardiomyopathy (D-HCM)

(Figure 2 continued the next page.)
Circulation Journal Vol.80, March 2016

Coronary angiography
Detailed family prognosis.

1. Radioactive isotope (RI) angiography to assess left ven-

dial blood flow,
Cardiac radionuclide imaging techniques can assess myocar-

(1) Cardiac Radionuclide Imaging Techniques
Cardiac radionuclide imaging techniques can assess myocardial blood flow,68,69 myocardial metabolism,76,71 and myocardial sympathetic nerve function,72,73 which cannot be assessed with other techniques, and are useful in the prediction of prognosis.74,75

Indications for Cardiac Radionuclide Imaging to Diagnose or Assess HCM:

Class I
1. Radioactive isotope (RI) angiography to assess left ven-
tricular function76,77 in patients who cannot be assessed with echocardiography.

Class II
1. Myocardial perfusion imaging to assess abnormal left ventricular hypertrophy and predict the prognosis of patients with HCM.

2. Myocardial fatty acid metabolism imaging to assess myocardial damage and predict the prognosis of patients with HCM.

3. Myocardial sympathetic nerve imaging to assess myocardial damage and predict the prognosis of patients with HCM.

4. RI angiography to assess left ventricular morphology and function in patients who can be assessed with echo-
cardiography.

5. Pyrophosphate scintigraphy to rule out cardiac amyloido-
dosis and cardiac sarcoidosis.78,79

6. Gallium scintigraphy to rule out cardiac sarcoidosis.

7. Fluorodeoxyglucose positron emission tomography (FDG-PET) to assess myocardial metabolic damage.80,81

(2) Cardiac CT and Cardiac MRI
Cardiac CT and cardiac MRI are used in morphological as-
se ssment in patients with suspected HCM when echocardiog-
raphy does not provide a definitive answer.38 These techniques are especially useful in identifying thickening of the apex in patients with apical HCM in whom echocardiography does not provide sufficient information.32,83 Cine mode MRI may also be used in the assessment of left ventricular function, and provides similar information to contrast left ventriculography.

Late gadolinium enhancement on contrast-enhanced MRI is considered to represent myocardial fibrosis in HCM.84,85 In studies on the relationship between LGE and prognosis of HCM, LGE was significantly associated with cardiac death, sustained ventricular tachycardia or ventricular fibrillation, and appropriate ICD discharge, among other factors. These

Figure 2. Diagnostic flow charts for stepwise diagnosis. LVOT, left ventricular outflow tract; ECG, electrocardiography; EPS, electrophysiological studies; LV, left ventricular; SAM, systolic anterior motion; RV, right ventricular; LP, late potential; LGE, late gadolinium enhancement; MRI, magnetic resonance imaging.
findings suggest that LGE may be an independent predictor of adverse outcome.  

Indications for Cardiac CT and Cardiac MRI in Patients With HCM or Suspected HCM to Assess the Patient’s Condition:

Class I
1. Morphological and functional diagnosis in patients with suspected HCM when echocardiography is inadequate for evaluation.
2. Morphological and functional diagnosis in patients with suspected apical HCM.

Class II
1. Morphological and functional diagnosis in patients with HCM other than those with apical hypertrophy.
2. Differentiation from previous myocardial infarction and specific cardiomyopathies based on LGE.
3. Risk stratification of patients based on LGE.

Class III
1. Patients in whom respiratory or ECG-gated imaging is not feasible.

5. Genetic Diagnosis
Genetic diagnosis is difficult and not available in many institutions, but is effective in the diagnosis of specific types of HCM. The advancement of genetic analysis technology will make genetic diagnosis more common in the future. Ethical considerations are essential aspects in genetic diagnosis. Physicians must ensure that the patient decides whether he/she will undergo genetic testing by his/her own will, and the patient’s rights, privacy and information are protected.

3. Diagnostic Flow Charts

The diagnosis of HCM is made via several steps from simple initial examinations such as history taking and physical examination to invasive diagnostic examinations such as cardiac catheterization and endomyocardial biopsy. It is important to assess the patient for cardiac hypertrophy/diastolic dysfunction, LVOT obstruction, and various arrhythmias. Echocardiography should be used as the main diagnostic technique as it provides detailed information at the initial stage of diagnosis. There are several diagnostic steps from the point where HCM is first suspected, and then echocardiography, and finally cardiac catheterization to assess the pathophysiology and severity of HCM in detail. Figure 2 shows diagnostic flow charts in the following steps.

1. Step 1: Suspicion of HCM -- At general practice including non-cardiovascular physicians
2. Step 2: Diagnosis of HCM by echocardiography -- At outpatient cardiac clinic
3. Step 3: Examination of pathophysiology and severity of HCM -- Detailed assessment during hospitalization

It is important to differentiate HCM from other diseases associated with HCM-like hypertrophy as some HCM-like
Hypertrophic cardiomyopathy is often asymptomatic in children, and may be suspected during school physical examination or other routine health screening. Figure 3 shows a diagnostic flow chart for children, and Table 6 lists specific cardiomyopathies that should be differentiated from HCM.103–117

Hypertrophic cardiomyopathy is often asymptomatic in chil-
In HCM, sarcomere protein gene mutations are considered to cause increased contractile force leading to increased energy consumption, which induces myocardial hypertrophy. Abnormally high intracellular calcium concentration levels are also considered to be a cause of cardiac hypertrophy and left ventricular diastolic dysfunction in HCM, and research is being conducted to find treatment modalities to normalize intracellular calcium concentration.

Figure 4 shows treatment flow charts for HCM.

1. Management of Daily Life

1. Physical Activity
Competitive sports should not be allowed in principle. It is reasonable for patients with HCM to participate in some low-intensity sports. Extreme care should be taken particularly in high-risk patients. Careful management should be given during and immediately after exercise.

2. Sexual Activities
As heart rate and blood pressure increase during sexual intercourse, patients with HCM should receive sufficient pharmacotherapy and should be at the stable state before resuming sexual activity.

3. Pregnancy
As hemodynamics changes during pregnancy and childbirth, it is important to be aware that pregnancy and childbirth are associated with increased risk in women with HCM. During childbirth, the patient’s hemodynamics can be monitored with non-invasive techniques such as echocardiography and Doppler echocardiography. Preventive antibiotic treatment should be considered during childbirth and the puerperium in order to prevent infective endocarditis.

4. Alcohol and Tobacco Consumption
A small amount of ethanol (50 mL of a beverage containing 40% alcohol) induces a reduction in systolic blood pressure, an increase in systolic anterior motion (SAM) of the mitral valve, and an increase in LVOT gradient. Also, alcohol enhances sympathetic nerve activity and heart rate, drinking should therefore be discouraged in patients with HCM. Smoking may, at times, trigger coronary spasms in patients with HCM.

5. Infection Control
As the risk of infective endocarditis is high in patients with HCM, preventive oral antibiotic treatment is essential.

6. Prevention of Thromboembolism
Both elderly and younger patients with HCM may experience cardiogenic thromboembolism. Anticoagulation therapy with or without antiplatelets is essential for patients with HCM associated with atrial fibrillation.

7. Genetic Counseling
Genetic counseling by a clinical genetic specialist may be needed for the patient and his/her family members.

2. Pharmacotherapy
The purpose of pharmacotherapy in patients with HCM is to 1) improve prognosis, 2) alleviate symptoms, and 3) prevent...
complications.\textsuperscript{142–145}

Table 8 lists drugs used for pharmacotherapy of HCM.

(1) Asymptomatic Patients (Excluding Young Patients and High-Risk Patients)

There is no clear evidence on the efficacy of pharmacotherapy in asymptomatic patients.\textsuperscript{143,155}

Class I
None.

Class II
\(\beta\)-blockers, verapamil

(2) Symptomatic Patients (Mild or Moderate)

1) HOCM
\(\beta\)-blockers, negative inotropic calcium antagonists (e.g., verapamil and diltiazem), and Class Ia antiarrhythmic drugs (e.g., disopyramide and cibenzoline) are used.\textsuperscript{122,144,145,156,157} As calcium antagonists may increase the LVOT gradient by dilating peripheral blood vessels, these drugs should be used with caution.\textsuperscript{144,158}

Class I
\(\beta\)-blockers
verapamil, diltiazem

Class II (Note 1)
disopyramide
cibenzoline

Class III: Harm
The use of dihydropyridine calcium antagonists and drugs with positive inotropic effect in patients with severe LVOT obstruction.

Note 1: The use of disopyramide and cibenzoline is listed as Class II recommendations as these drugs have not been evaluated in large-scale clinical studies, but there is general agreement that these drugs are effective in reducing the LVOT gradient.

2) Non-Obstructive HCM
\(\beta\)-blockers and verapamil are effective in patients with exertional dyspnea and chest pain.\textsuperscript{144} It is unclear whether monotherapy of \(\beta\)-blockers or verapamil, or combined therapy with both drugs, is more effective.

Class I
\(\beta\)-blockers
verapamil, diltiazem

(3) Patients With Heart Failure

1) HOCM
Patients with a severe LVOT gradient should be treated with \(\beta\)-blockers and sodium channel blockers. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) are contraindicated for this patient population. Non-pharmacotherapy should be considered for patients not responding to pharmacotherapy.

Class I
Patients with LVOT obstruction: \(\beta\)-blockers, verapamil, and diltiazem

Patients with diastolic dysfunction: \(\beta\)-blockers, verapamil, and diltiazem

Patients with systolic dysfunction: diuretics, ACE inhibitors, and ARBs

Class II
Patients with LVOT obstruction: cibenzoline, and disopyramide

Class III: Harm
Drugs with negative inotropic effects for patients with severe systolic dysfunction (small doses of \(\beta\)-blockers may be used in tolerable cases).

ACE inhibitors and ARBs in patients with a severe LVOT gradient

2) Non-Obstructive HCM
Patients with heart failure associated with HCM and those with D-HCM should be treated similarly to those for patients with heart failure (See the Guidelines for Treatment of Chronic Heart Failure published by the Japanese Circulation Society [JCS 2010]\textsuperscript{154}). Patients with systolic dysfunction should be treated with diuretics, ACE inhibitors and ARBs.

Class I
Patients with diastolic dysfunction: \(\beta\)-blockers, verapamil, and diltiazem

Patients with systolic dysfunction: ACE inhibitors, ARBs and diuretics

Class II
None.

Class III: Harm
Drugs with negative inotropic effects for patients with severe systolic dysfunction (small doses of \(\beta\)-blockers may be used in tolerable cases).

(4) High-Risk Group
In order to prevent sudden death, high-risk patients should be treated aggressively regardless of the presence or absence of symptoms. Patients with nonsustained or sustained ventricular tachycardia are indicated for amiodarone and ICDs.\textsuperscript{44,159–162}

Table 7. Risk Factors for Sudden Death

<table>
<thead>
<tr>
<th>Major risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Cardiac arrest (ventricular fibrillation)</td>
</tr>
<tr>
<td>- Spontaneous sustained ventricular tachycardia</td>
</tr>
<tr>
<td>- Family history of premature sudden death (&lt;40 years)</td>
</tr>
<tr>
<td>- Unexplained syncope</td>
</tr>
<tr>
<td>- Extreme left ventricular hypertrophy (left ventricular wall thickness ≥30 mm)</td>
</tr>
<tr>
<td>- Nonsustained ventricular tachycardia on Holter ECG</td>
</tr>
<tr>
<td>- Abnormal blood pressure response during upright exercise</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Possible risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Dilated phase of hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>- Left ventricular apical aneurysm</td>
</tr>
<tr>
<td>- Left ventricular outflow tract obstruction</td>
</tr>
<tr>
<td>- Extensive late gadolinium enhancement by MRI</td>
</tr>
<tr>
<td>- Atrial fibrillation</td>
</tr>
<tr>
<td>- High-risk gene mutations</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Modifiable risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Intense exercise (competitive athletics)</td>
</tr>
<tr>
<td>- Coronary artery disease</td>
</tr>
</tbody>
</table>

ECG, electrocardiography; MRI, magnetic resonance imaging.
### Table 8. List of Drugs for the Treatment of HCM

<table>
<thead>
<tr>
<th><strong>β-blockers</strong></th>
<th>ISA</th>
<th>Overseas reports</th>
<th>Daily dose approved in Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>propranolol</td>
<td>Class I</td>
<td>Group 2</td>
<td>–</td>
</tr>
<tr>
<td>butoxolol</td>
<td></td>
<td></td>
<td>50 mg/day</td>
</tr>
<tr>
<td>bupronanolol</td>
<td></td>
<td></td>
<td>60–120 mg/day</td>
</tr>
<tr>
<td>bupranolol</td>
<td></td>
<td></td>
<td>15 mg/day</td>
</tr>
<tr>
<td>bucumolol</td>
<td></td>
<td></td>
<td>30–90 mg/day</td>
</tr>
<tr>
<td>befunolol</td>
<td></td>
<td></td>
<td>30–90 mg/day</td>
</tr>
<tr>
<td>nadolol</td>
<td>Group 4</td>
<td></td>
<td>40–80 mg/day</td>
</tr>
<tr>
<td>timolol</td>
<td></td>
<td></td>
<td>20 mg/day</td>
</tr>
<tr>
<td>lisinolol</td>
<td></td>
<td></td>
<td>10–20 mg/day</td>
</tr>
<tr>
<td>metoprolol</td>
<td>Class II</td>
<td>Group 4</td>
<td>–</td>
</tr>
<tr>
<td>atenolol</td>
<td></td>
<td></td>
<td>50–100 mg/day</td>
</tr>
<tr>
<td>bisoprolol</td>
<td></td>
<td></td>
<td>5–10 mg/day</td>
</tr>
<tr>
<td>betaxolol</td>
<td></td>
<td></td>
<td>5–80 mg/day</td>
</tr>
</tbody>
</table>

**Calcium antagonists**

| verapamil      | 240 mg/day | 360–480 mg/day | 120–240 mg/day |
| diltiazem      | None        |                | 90–180 mg/day |
| nifedipine*    | 10 mg (sublingually) | | 10–20 mg (sublingually) |

**Antiarrhythmic drugs**

| disopyramide   | 600–800 mg/day | 260–390 mg/day | 300 mg/day (*) |
| cibenzoline    |                |                | 300 mg/day (*) |

**ACE inhibitors**

| enalapril      | SOLVD | Initial dose: 5 mg/day | Target dose: 20 mg/day | Actual dose: 16.7 mg/day |
|               |       | Prevention trial | Treatment trial | CONSENSUS |
|               |       | Initial dose: 10 mg/day | Target dose: 20 mg/day | Maximum dose: 40 mg/day |
|               |       | Actual dose: 18.4 mg/day | Start at 2.5 mg/day | 5–10 mg/day |

| lisinopril     | ATLAS | Initial dose: 2.5–5 mg/day | Target dose: Low dose: 2.5–5 mg/day | High dose: 32.5–35 mg/day |
|               |       | Start at 2.5 mg/day in patients with renal disorder and elderly patients | 5–10 mg/day |

**Angiotensin receptor blockers**

| losartan       | ELITE II | Initial dose: 12.5 mg/day | Target dose: 50 mg/day | Actual dose: 42.6 mg/day |
|               |         | Start at 4 mg/day (2 mg/day for severe patients) | Maintenance dose: 8 mg/day | Hypertensive patients: 4–8 mg/day |
|               |         | Start at 2 mg/day in patients with renal disorder | 25–100 mg/day |

| candesartan    | CHARM | Initial dose: 4 or 8 mg/day | Target dose: 32 mg/day | Actual dose: 24 mg/day |
|               |       | Start at 4 mg/day (2 mg/day for severe patients) | Maintenance dose: 8 mg/day | Hypertensive patients: 4–8 mg/day |
|               |       | Start at 2 mg/day in patients with renal disorder | 40–80 mg/day (maximum dose: 160 mg/day) |

| valsartan      | Val-HeFT | Initial dose: 320 mg/day | Target dose: 50 mg/day | Actual dose: 254 mg/day |
|               |         | Start at 4 mg/day (2 mg/day for severe patients) | Maintenance dose: 8 mg/day | Hypertensive patients: 4–8 mg/day |
|               |         | Start at 2 mg/day in patients with renal disorder | 40–80 mg/day (maximum dose: 160 mg/day) |

Covered with the National Health Insurance; a: hypertension, angina pectoris, and tachyarrhythmia. b: verapamil -- ischemic heart diseases such as myocardial infarction and angina pectoris; diltiazem -- hypertension, angina pectoris. c: disopyramide -- tachyarrhythmia; cibenzoline -- tachyarrhythmia (cibenzoline has not been launched in the United States). d: hypertension and heart failure. e: hypertension. (*) Dose for patients with premature contraction and paroxysmal tachycardia. *Should not administered sublingually as acute hypotension and reflective tachycardia may develop.

Data on enalapril, lisinopril, losartan, candesartan, and valsartan were referred from the Guidelines for Treatment of Chronic Heart Failure (JCS 2010). HCM, hypertrophic cardiomyopathy; ISA, intrinsic sympathomimetic activity; ACE, angiotensin converting enzyme; SOLVD, Studies of Left Ventricular Dysfunction; CONSENSUS, Cooperative North Scandinavian Enalapril Survival Study; ATLAS, Assessment of Treatment with Lisinopril and Survival; ELITE II, Evaluation of Losartan in the Elderly Study II; CHARM, Candesartan in Heart failure Assessment of Reduction in Mortality and morbidity; ARCH-J, Assessment of Response to Candesartan in Heart failure in Japan; Val-HeFT, Valsartan Heart Failure Trial.
Positioning of Treatments for the Prevention of Sudden Death in Patients With HCM:

Class I
1. ICD therapy for patients with HCM who have a prior history of sustained ventricular tachycardia, ventricular fibrillation, or cardiac arrest.

Class II
1. ICD therapy or amiodarone for the primary prevention of sudden death.

(5) Arrhythmias

Class I
β-blockers, verapamil, diltiazem, Class Ia and Ic antiarrhythmic drugs and amiodarone.
Warfarin therapy for patients with atrial fibrillation.
(*) Catheter ablation may be indicated for patients with drug-resistant atrial fibrillation with a rapid ventricular response, type I atrial flutter, paroxysmal supraventricular tachycardia, or sustained ventricular tachycardia who have experienced syncope and significantly impaired quality of life (QOL). (See the Guidelines for Non-Pharmacotherapy of Cardiac Arrhythmias [JCS 2011]163 published by the Japanese Circulation Society.)

Indications for Pharmacotherapy of Arrhythmias Associated With HCM:

Class I
1. Patients with hemodynamically unstable atrial fibrillation or atrial flutter with a rapid heart rate.
2. Patients with paroxysmal supraventricular tachycardia.
3. Patients with symptomatic nonsustained ventricular tachycardia who have risk factors for sudden death.
4. Patients with sustained ventricular tachycardia.

Class II
1. Patients with symptomatic supraventricular or ventricular premature contractions.
2. Patients with asymptomatic or hemodynamically stable nonsustained ventricular tachycardia.

Class III: Harm
1. Patients with asymptomatic supraventricular or ventricular premature contractions.
2. Patients with asymptomatic bradycardia.

3. Non-Pharmacotherapy

1. Surgery (Septal Myotomy/Myectomy, Mitral Valve Surgery)
Surgery is the oldest known non-pharmacotherapy for HCM, and consistent results have been established. In Japan, only a small number of institutions have experience of a large number of surgical cases of HCM.

Indications for Surgical Treatment of HCM:

Class I
1. Patients with drug-resistant HOCM who have New York Heart Association (NYHA) functional class III or IV symptoms, and have a resting LVOT gradient of ≥50 mmHg.
2. Patients with drug-resistant HOCM who recovered from syncope, and have a resting or provokable LVOT gradient of ≥50 mmHg.

Class II
1. Patients with drug-resistant HOCM who have no or only mild symptoms with a resting LVOT gradient of ≥50 mmHg.

Class III: Harm
1. Asymptomatic patients with pharmacologically controllable HOCM.
2. Symptomatic patients with HCM without provokable LVOT gradient.

2. Device Therapy
(1) Dual-Chamber (DDD) Pacing for the Treatment of LVOT Gradient168–173

Class I
1. Patients who have a significant LVOT gradient causing symptoms that impair the patient’s QOL, and require permanent pacemakers for reasons other than HOCM (such as drug-induced bradycardia). (Note 1)

Class II
1. HOCM patients with symptoms that correlate with a significant pressure gradient and impair the patient’s QOL who have no other appropriate treatment options due to lack of efficacy or intolerance to drugs. (Note 1)

Class III: Harm
1. Patients who have no pressure gradient or bradycardia indicated for pacemaker implantation. (Note 1)

Note 1: Based on the Guidelines for Non-Pharmacotherapy of Cardiac Arrhythmias (JCS 2011)163 published by the Japanese Circulation Society.

(2) Implantable Cardioverter-Defibrillators (ICDs)162

Class I
1. Patients with a prior history of sustained ventricular tachycardia, ventricular fibrillation, or cardiac arrest.

Class IIa
1. Patients with nonsustained ventricular tachycardia; a family history of sudden death; syncope; a left ventricular wall thickness of ≥30 mm; or abnormal blood pressure response during exercise.

(3) Cardiac Resynchronization Therapy (CRT)174,175

Class I
1. Patients with NYHA functional class III or ambulatory class IV heart failure despite optimal pharmacotherapy, a left ventricular ejection fraction (LVEF) of ≤35%, a QRS interval of ≥120 msec, and sinus rhythm.

Class IIa
1. Patients with NYHA functional class III or ambulatory class IV heart failure despite optimal pharmacotherapy, a LVEF of ≤35%, a QRS interval of ≥120 msec, and atrial fibrillation.
2. Patients with NYHA functional class III or ambulatory class IV heart failure despite optimal pharmacotherapy, and a LVEF of ≤35% who have had or are planned to have a permanent pacemaker implanted, and require or are expected to require ventricular pacing frequently.

Class IIb
1. Patients with NYHA functional class II heart failure, a LVEF of ≤35% who are planned to have permanent pacemaker implanted and are expected to require ventricular pacing frequently.

Class III: Harm
1. Asymptomatic patients with low LVEF who are not indicated for pacemaker therapy.
2. Patients with limited physical activity due to chronic diseases other than heart failure or those suspected with a life expectancy of 12 months or less.
### Table 9. School Activity Management Table Published by the Japanese Society of School Health

**[Revised in 2011]**

<table>
<thead>
<tr>
<th>Name</th>
<th>M / F</th>
<th>Birth date</th>
<th>School</th>
<th>Grade</th>
<th>Class</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Diagnosis (findings)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Level of management Management needed: A, B, C, D, E</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No management needed</td>
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<tr>
<td>3. School sport club activity Name of club</td>
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<tr>
<td>Allowed (Note: Prohibited)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Next visit <em>years</em> <em>months later</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>or when symptoms develop</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**School Activity Management Table (for Junior and Senior High School Students)**

<table>
<thead>
<tr>
<th>Level of management</th>
<th>Requires treatment at home or in hospital</th>
<th>Goes to school but must avoid exercise</th>
<th>Can do mild exercise</th>
<th>Can do moderate exercise</th>
<th>Can do intense exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>B</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>C</strong></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td><strong>D</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>E</strong></td>
<td></td>
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</tbody>
</table>

**School Activity Management Table Published by the Japanese Society of School Health**

<table>
<thead>
<tr>
<th>Name</th>
<th>M / F</th>
<th>Birth date</th>
<th>School</th>
<th>Grade</th>
<th>Class</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of institution:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Name of physician: (seal)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Intensity of exercise**

- **Mild exercise (C, D, E - allowed)**
- **Moderate exercise (D, E - allowed)**
- **Intense exercise (E - allowed)**

**Type of sport**

<table>
<thead>
<tr>
<th>Sport activity</th>
<th>Intensity of exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild exercise (C, D, E - allowed)</td>
</tr>
</tbody>
</table>

**Sport activity**

- **Warming-up exercise**
- **Strength-training exercise**
- **Basic exercise**
- **Apparatus gymnastics**
- **Calisthenics**
- **Basic motion**
- **Light exercise**
- **Moderate exercise**
- **Intense exercise**

**Sport activity**

- **Basic**
- **Goal games**
- **Ball sports**
- **Net games**
- **Baseball-type games**
- **Golf**
- **Martial arts**
- **Dance**
- **Outdoor activity**
- **Cultural activities**
- **School events and other activities**

**Remarks**

- **Definitions**
  - Moderate exercise: Physical activities that increase respiratory rate in average students at the same age.
  - Intense exercise: Physical activities that increase respiratory rate and cause shortness of breath in average students at the same age.

- **Adapted from** The Japanese Society of School Health. Guide for the use of the School Activity Management Table for Children with Heart Disease, the 2011 revision. 2013: 3–11. [^1]
3. Percutaneous Transluminal Septal Myocardial Ablation (PTSMA)

Recently, PTSMA has been increasingly performed in clinical practice, and is being established as a treatment option for patients with HOCM. However, the long-term outcome of PTSMA is unclear at this time, and further accumulation of evidence is awaited.

Since April 2005, PTSMA is covered by the National Health Insurance.

Indications for PTSMA for the Treatment of HCM\textsuperscript{,176–185}

Class I
None.

Class II\textsuperscript{(Note 1)}

1. Patients with HOCM who have NYHA functional class III or IV symptoms, do not respond to pharmacotherapy, and have a resting or provokable LVOT gradient of $\geq 30$ mmHg.\textsuperscript{178,179,186}

2. Patients with HOCM who have experienced syncope.
due to LVOT gradient, and have a resting or provocable LVOT gradient of ≥30 mmHg.
3. Patients with drug-resistant atrial fibrillation associated with a significant LVOT gradient (≥30 mmHg).

Class III: Harm
1. Asymptomatic patients with medically controllable HOCM.
2. Symptomatic HCM patients without LVOT gradient.

Note 1: The use of PTSMA is not a Class I recommendation at present because of the lack of sufficient evidence.

4. Management and Treatment of Hypertrophic Cardiomyopathy in Children

1. Prevention and Management of Sudden Death
In the School Activity Management Table 2011 edition published by the Japanese Society of School Health (Table 9), high-risk children are prohibited from almost all types of sports and competitive athletics, and symptomatic children with HCM or those with HOCM are prohibited from moderate or intense physical activities (Figure 5).119,121

2. Indications for Pharmacotherapy
(See Table 10, RAPID ACCESS GUIDE)

3. Non-Pharmacotherapy
(1) Surgery
Septal myotomy/myectomy (Morrow procedure) have rarely been used in children, and the long-term outcome of these procedures is unclear.188-190

(2) Pacemaker Implantation
As data on the indications and efficacy of pacemaker implantation are limited in children, the use of pacemakers should be considered with caution.

(3) PTSMA
As PTSMA may induce myocardial scarring and thereby increase the risk of lethal arrhythmias and sudden death, this technique is not recommended for children.

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