The Cardiomyopathies

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13.1 Introduction

Cardiomyopathies comprise a heterogeneous group of disease of the myocardium. Historically in the WHO/International Society and Federation of Cardiology classification of 1996, cardiomyopathies were defined as primary disorders of unknown cause. Heart muscle diseases of known cause or associated with systemic disorders were classified as secondary. However, this distinction between primary and secondary heart muscle disease has become redundant, as the cause of previously idiopathic disorders has been discovered.

Recently the American Heart Association proposed that cardiomyopathies are "myocardial diseases 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 are frequently genetic." The American Heart Association panel also suggested that ion channelopathies and disorders of conduction should be considered cardiomyopathies as well because channel mutations alter biophysical properties and protein structure, thereby creating structurally abnormal ion channel interfaces and architecture.

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The European Society of Cardiology (ESC) has assumed that the clinically most useful method for diagnosing and managing the cardiomyopathies is a classification in which heart muscle diseases are grouped according to ventricular morphology and function. The ESC has defined cardiomyopathies as "myocardial disorders 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." The ESC classification consists of the following categories:

- Hypertrophic cardiomyopathy (HCM)
- Dilated cardiomyopathy (DCM)
- Restrictive cardiomyopathy (RCM)
- Arrhythmogenic right ventricular (RV) cardiomyopathy (ARVC)
- Unclassified, e.g., left ventricular (LV) noncompaction

The cause of each cardiomyopathy is taken into account by replacing the traditional division of primary and secondary by a new division into *familial* (or genetic) and *nonfamilial* (nongenetic). The nonfamilial category is subdivided into idiopathic cause and acquired cardiomyopathies in which LV dysfunction is a complication of another disorder (e.g., myocarditis, drugs, pregnancy, endocrine disorders, tachycardiomyopathy).

There is no ideal classification; however, from an echocardiographic point of view, the classification based on structure and function is the most useful. This chapter will describe

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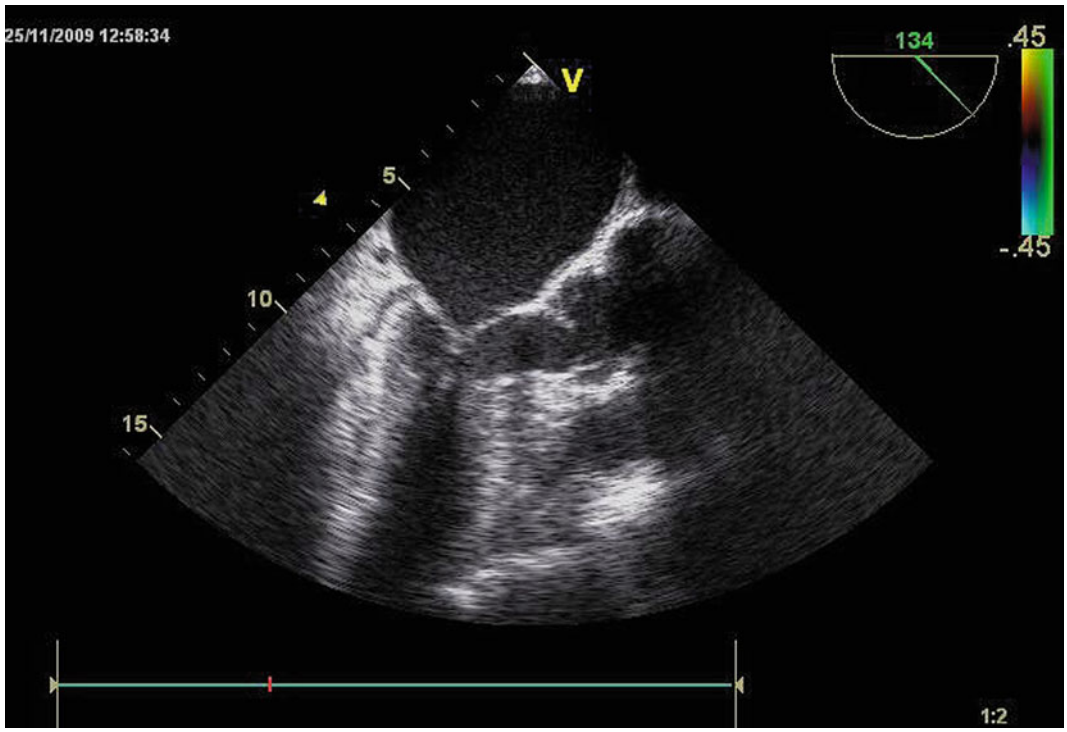

Fig. 13.1 Asymmetrical hypertrophy in hypertrophic cardiomyopathy

HCM, DCM, RCM, ARVC, and LV non-compaction according to the ESC classification.

13.2 Hypertrophic Cardiomyopathy

HCM is clinically defined in the presence of LV hypertrophy and in the absence of hypertension and valve disease. LV hypertrophy occurs in one in 500 of the general population and this incidence includes all kinds of hypertrophy. HCM is a familial disease with an autosomal pattern of inheritance, caused by mutations in genes encoding for sarcomeric proteins, usually resulting in an asymmetrical pattern of LV hypertrophy.

The echocardiographic diagnostic criteria in HCM include:

1. *Asymmetrical septal hypertrophy*. LV thickness, evaluated at the septum and free wall level, is considered abnormal when it is greater than 15 mm (Fig. 13.1) and is defined as asymmetrical when there is a septal to free wall thickness ratio between 1.3 and 1.5. A value greater than 30 mm is a risk factor for sudden cardiac death.
   The distribution of hypertrophy may be anterior septal, anterior and posterior septal, posterior basal wall, or apical (e.g., in Japanese people).
2. *Systolic anterior motion (SAM) of the mitral valve*. SAM is characterized by an abrupt anterior movement of the mitral valve in systole (Fig. 13.2), reaching its peak before maximum movement of the posterior wall (this characteristic allows one to differentiate true SAM from "pseudo SAM," which is produced by an exaggerated anterior motion of the mitral valve and reaches its peak after the full contraction of the posterior wall). A Venturi effect is thought to be responsible for dragging the anterior mitral leaflet into the LV outflow tract (LVOT). The severity of SAM is correlated with the severity of LVOT obstruction.
3. *Pressure gradient across the LVOT*. This gradient may be variable, because obstruction is dynamic. A value of 30 mmHg or greater has physiological consequences, and is associated

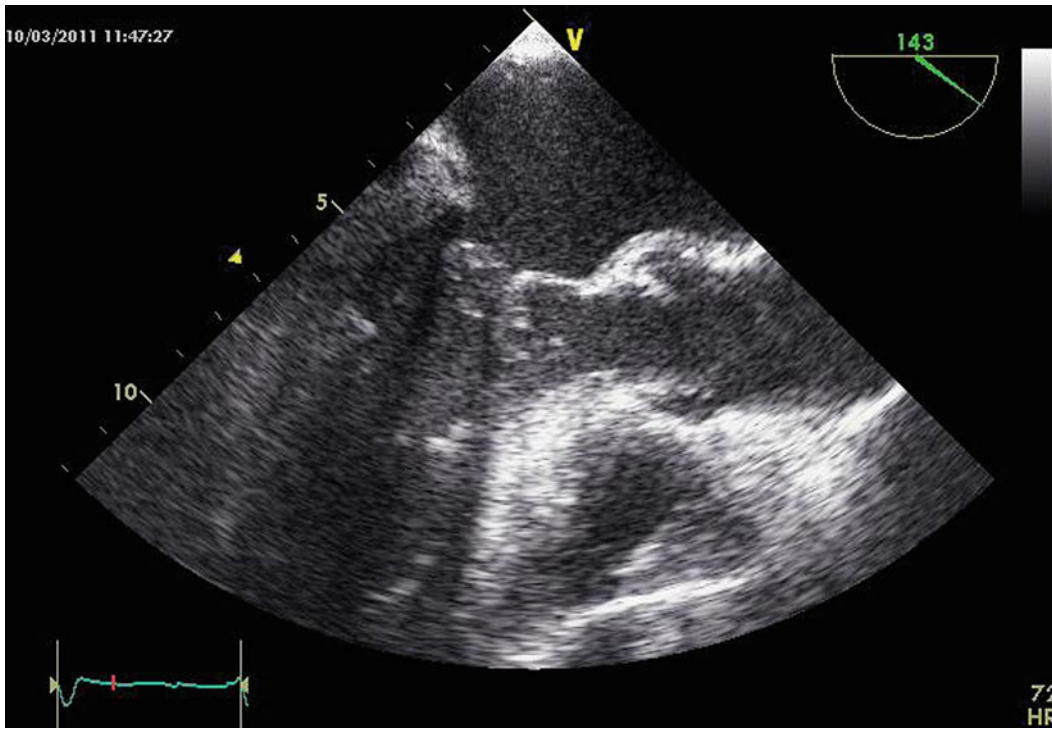

Fig. 13.2 Systolic anterior motion in hypertrophic cardiomyopathy

with progression to New York Heart Association class III–IV and death from heart failure or stroke, especially in patients aged over 40 years.

4. *Dynamic mitral regurgitation*. Mitral regurgitation is a consequence of SAM which induces abnormal mitral leaflet coaptation. The evaluation of the presence and degree of mitral regurgitation is performed by color Doppler echocardiography. The regurgitant jet is usually posteriorly directed, and an anterior or central jet may occur in the presence of an intrinsic mitral valve disease due to annular, papillary, or leaflet disease (Fig. 13.3).
5. *Small LV cavity*. Mid-cavity obstruction may occur owing to muscular apposition in a small LV cavity, with excessive hypertrophy of the mid-ventricle and papillary muscles.
6. *Diastolic dysfunction*. Almost all patients with HCM have some degree of LV diastolic dysfunction. The mechanisms linked to diastolic dysfunction are complex and include altered contraction and relaxation of sarcomeric protein, altered sensitivity to calcium, disarray of and increased amount of extracellular matrix, increased wall thickness, and ischemia.

Diastolic dysfunction is assessed by analysis of both transmitral spectral Doppler flow velocity (E) and mitral annular velocity (E').

Transmitral blood flow is represented by an early E wave and a late A wave on pulsed wave Doppler echocardiography, isovolumic relaxation is slowed, the rate of rapid filling is diminished, the atrial contribution to filling is increased, as well is LV stiffness. Unfortunately in HCM, the E wave varies with preload and does not correlate well with LV hypertrophy.

Tissue Doppler imaging (TDI) provides more accurate evaluation of diastolic dysfunction. Early diastolic mitral annular velocities are significantly reduced, and the ratio of transmitral velocity E/E' is higher and appears to correlate with New York Heart Association functional class. The ratio of early transmitral (E) to tissue Doppler early diastolic (e') velocities of the lateral mitral annulus accurately quantifies LV pressures, in particular before atrial contraction; $E/e' > 10$ showed the best sensitivity

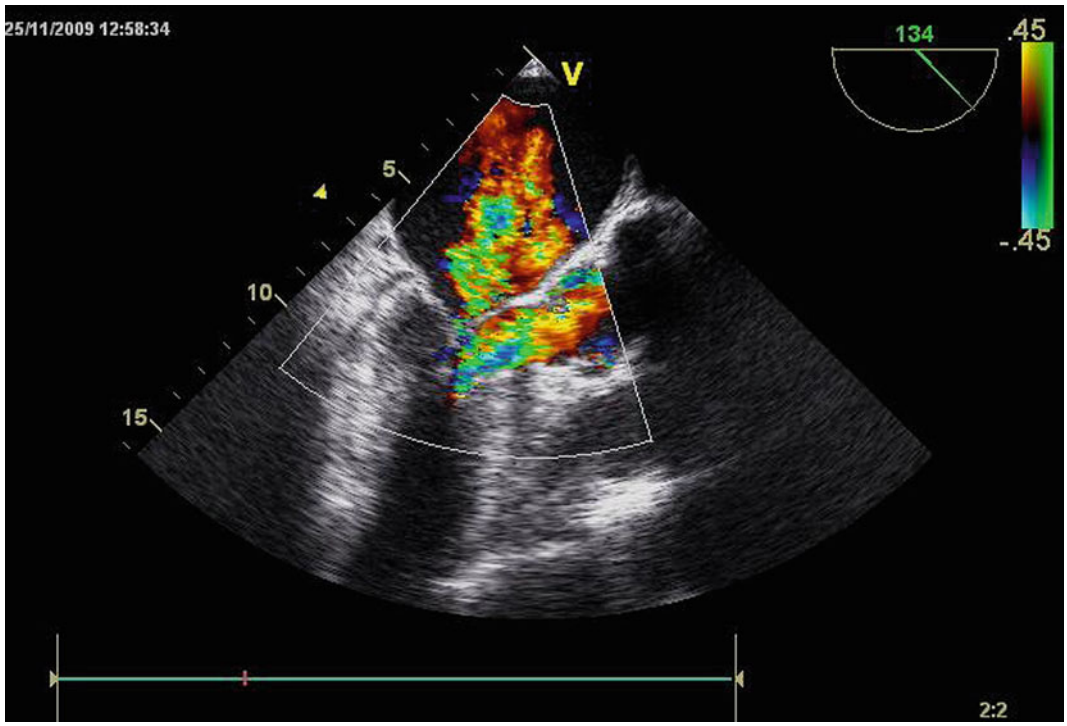

Fig. 13.3 Mitral regurgitation and systolic anterior motion in hypertrophic cardiomyopathy

and specificity for identifying LV pre-A pressure greater than 15 mmHg. However, that ratio shows only a modest correlation when related to mean left atrial pressure, although this parameter identifies patients with low exercise capacity.

TDI has been investigated in the preclinical diagnosis of HCM, but additional data are needed to determine TDI velocity values that provide the highest diagnostic accuracy.

Differential diagnosis of HCM includes:

- LV hypertrophy due to hypertension: LV hypertrophy in HCM is asymmetrical, whereas that of LV hypertrophy caused by hypertension has a concentric appearance.
- LV hypertrophy in athletes: the criteria that may be utilized to support the diagnosis of pathological HCM are LVOT obstruction, impaired diastolic function, enlarged left atrium, family history, left bundle branch block, and ST-segment depression.

The management of HCM, in addition to β-blockers, includes surgical septal miectomy (if the LVOT gradient is greater than 50 mmHg) or percutaneous alcohol septal ablation. The abnormal insertion of papillary muscle may contribute to mitral regurgitation, requiring a more extended septal myectomy or mitral valve replacement. Intraoperative echocardiography is used to check:

- Residual gradient across the LVOT
- Iatrogenic ventricular septal defect
- SAM of the mitral valve
- Residual mitral regurgitation

Echocardiography can provide important information for the appropriate diagnosis of HCM; however, it cannot distinguish conditions based on myocyte hypertrophy from those in which LV mass and wall thickness are increased by interstitial infiltration or intracellular accumulation of metabolic substrates. Cardiac

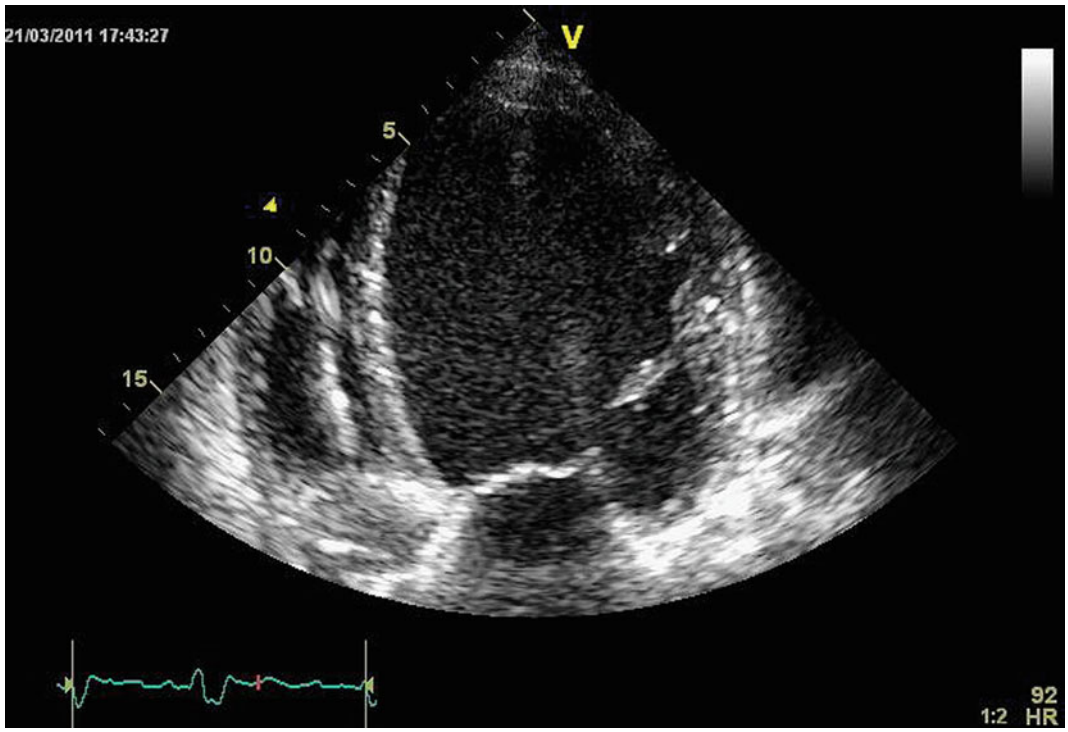

Fig. 13.4 Dilated left ventricle in dilatative cardiomyopathy

magnetic resonance imaging may help in the diagnosis, even if the final diagnosis in some specific conditions can only be obtained by myocardial biopsy.

13.3 Dilated Cardiomyopathy

DCM is a primary myocardial disease characterized by differing degrees of LV dysfunction and dilatation in the absence of chronic increased afterload (e.g., aortic stenosis or hypertension) or volume overload (e.g., mitral regurgitation).

Although there are many different causes of DCM, in most cases it is idiopathic. DCM may be a final consequence of a variety of pathways, such as hypertension, ischemia, severe valvular disease, myocarditis, endocrine or congenital heart disorders, toxins, chemotherapy, and LV noncompaction. In the absence of these etiological factors, DCM may occurs as a result of gene mutations.

Echocardiography not only facilitates evaluation of strict diagnostic criteria, but also provides us with a comprehensive assessment of cardiac anatomy, pathophysiological changes, and hemodynamics.

The following are echocardiographic features of DCM:

- Ventricular dilation. The left ventricle is considered dilated if its end-diastolic volume is more than 117% of the predicted value, corrected for age and body surface area (Fig. 13.4).
- Severe ventricular dysfunction. Typically LV fractional shortening is less than 20% and LV ejection fraction is less than 35%.
- Functional mitral regurgitation with a central jet.
- Dilatation of the mitral annulus associated with an increase of the annulus dimensions.
- Tethering of both mitral leaflets by displaced papillary muscles. The degree of tethering is reflected in the angle between each leaflet and the annular plane, the height between the

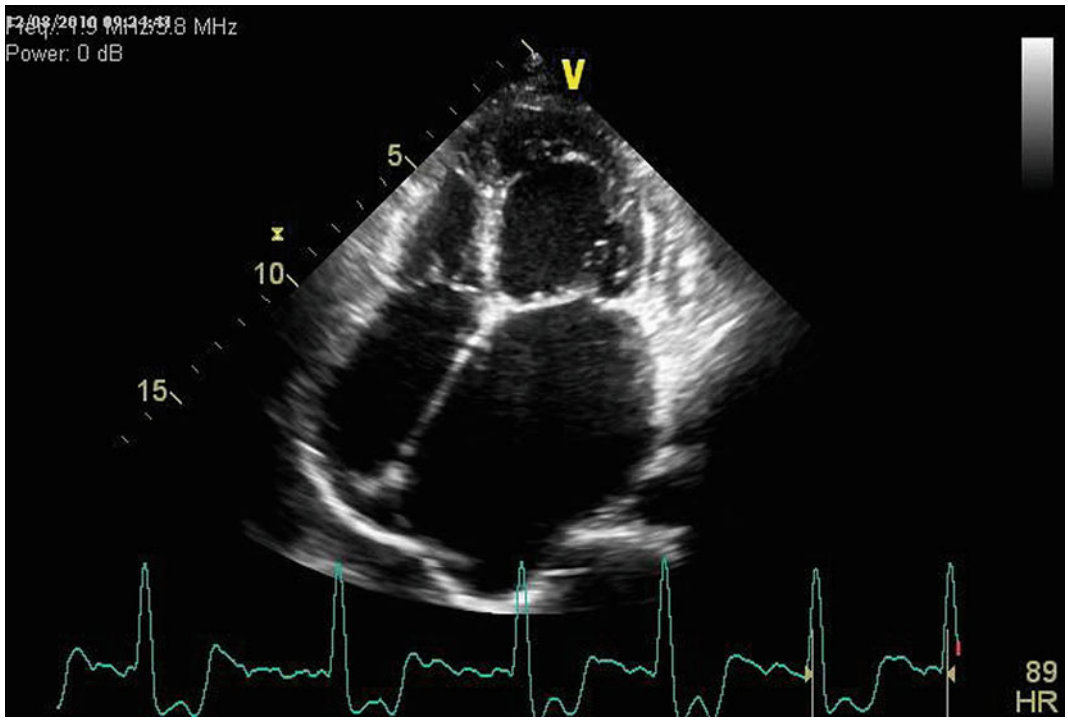

Fig. 13.5 Restrictive cardiomyopathy

annular plane and leaflet point of coaptation, and the tenting area bordered by the annular plane and the two leaflets.

- Functional tricuspid regurgitation.

The differential diagnosis includes ischemic heart disease and primary mitral valve disease: in both conditions there is a low ejection fraction, but in DCM there is a dilated mitral annulus, abnormal papillary muscle angle, leaflet tethering, and absence of severe leaflet disease, e.g., rheumatic disease, flail, or prolapse.

13.4 Restrictive Cardiomyopathy

RCM is characterized by increased stiffness of the myocardium, normal or reduced ventricular diastolic volumes, normal or mildly increased wall thickness, and preserved systolic function. Unlike the other cardiomyopathies, which are classified according to morphological criteria, RCM is a functional classification. The classic echocardiographic features include:

- A small (not dilated neither hypertrophied) left ventricle
- Marked dilatation of both atria (Fig. 13.5)
- Normal systolic function in the absence of a pericardial disease
- Mild to moderate mitral and tricuspid valve regurgitation
- Increased pulmonary pressures
- Pulmonary venous flow showing a blunted S wave and pronounced diastolic and atrial waves (with sinus rhythm)
- A restrictive filling pattern, as transmitral velocity is characterized by a rapid but ill-sustained ventricular filling on pulsed wave Doppler echocardiography (E wave), little or no late ventricular filling (A wave), an *E*/*A* ratio greater than 2 and the deceleration time of the E wave shortened to less than 150 ms

However, as in the case of HCM, transmitral velocity in the early stage of RCM is reduced; when compliance of the heart decreases the left atrial pressure increases, leading to pseudonormalization of the diastolic pattern and then to a restrictive pattern. The early mitral tissue Doppler velocity may be a more reliable guide to LV filling pressure as the E/E' ratio increases with the severity of the disease. In RCM—unlike in constrictive pericarditis—E' is blunted and this reduction is consistent with the finding that RCM is a disease of the myocardium.

Systemic amyloidosis is a disorder of protein metabolism in which abnormal extracellular protein material is deposited in organs and tissue. Primary amyloidosis involves the heart in 90% of cases, and cardiac amyloidosis is the commonest cause of RCM: interstitial infiltration of the atria and ventricles leads to a firm and rubbery consistency of the myocardium. Secondary amyloidosis only rarely affects the heart.

The echocardiographic features of cardiac amyloidosis include thickened RV and LV walls, granular or "sparkling" appearance of the myocardium, normal-sized or small LV, enlarged atria, depressed LV systolic and diastolic function, mild mitral regurgitation, restrictive pattern of E/A, high E/e' ratio suggestive of elevated filling pressures, and pericardial effusion in advanced disease.

Tissue Doppler echocardiography can contribute to the earlier diagnosis of amyloid infiltration of the heart. Peak systolic and early diastolic mitral annular velocities, as well as myocardial velocity gradients (strain rate) in systole and early diastole, are equally reduced in patients with or without a restrictive pattern of transmitral Doppler velocities.

13.5 Arrhythmogenic Right Ventricular Cardiomyopathy

ARVC is a syndrome characterized by myocardial disease, predominantly involving the right ventricle and associated with ventricular tachycardia arising from this chamber, syncope, and sudden death. At autopsy there is an unusual distribution of fatty and fibrotic tissue within the right ventricle, preferentially affecting the apex, the inflow tract, and the outflow tract. ARVC is a genetic cardiac disease involving genes encoding for specialized intercellular adhesion junctions known as desmosomes and thus is mechanistically distinct from either HCM or DCM.

The original descriptions of ARVC focused on the fatty replacement in the right ventricle. Replacement infers that the muscle develops normally and subsequently undergoes dysplastic degeneration with replacement of muscle by fibrous scarring and fatty tissue. There is important histologic evidence of fibrofatty involvement of the left ventricle in 30–75% of ARVC cases.

The intrinsic difficulties in making a diagnosis of ARVC are evident from the existence of the task force criteria (1994).

ECG may be useful, but only in the appropriate clinical context. Major criteria include ε waves or localized prolongation of the QRS duration (greater than 110 ms) in right precordial leads. Minor criteria include inverted T waves in right precordial leads in individuals older than 12 years in the absence of right bundle branch block.

Early diagnosis by echocardiography is difficult, because of the irregular shape and trabeculation of the normal right ventricle. However, some echocardiographic features suggestive of ARVC have been showed and include (Fig. 13.6):

- RV and RV outflow tract dilatation (diameter 30 mm)
- Trabecular derangement
- Global RV dysfunction with fractional shortening less than 32%
- RV regional wall motion abnormality, especially of the apex and anterior wall
- Focal RV aneurysms.

Echocardiographic assessment in ARVC requires considerable expertise given the complex geometry of the right ventricle, the lack of standard reference views, and the load dependence of RV function.

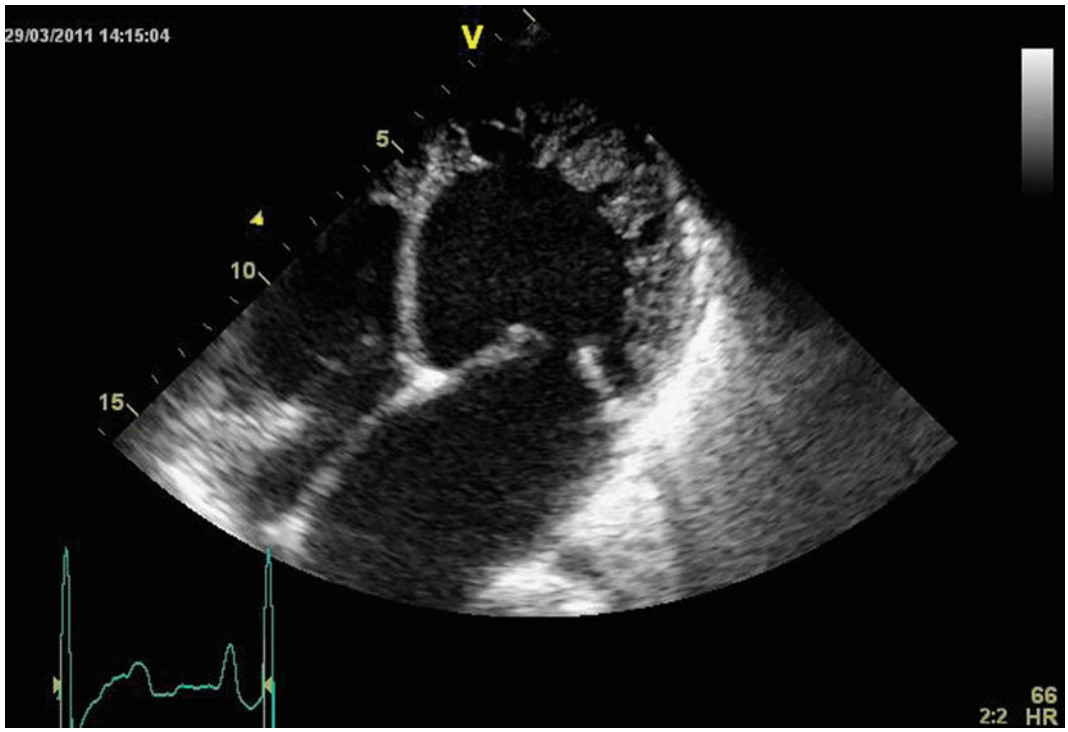

Fig. 13.6 Left ventricular noncompaction

13.6 Left Ventricular Noncompaction

LV noncompaction is a sarcomeric cardiomyopathy. Sporadic or familial adult forms are genetically distinct from X-linked infantile cases, and they are transmitted by an autosomal dominant trait. The reported prevalence is 0.014–0.05%. The major clinical manifestations in patients with reduced LV function include heart failure, arrhythmias (atrial fibrillation, ventricular tachyarrhythmias, sudden cardiac death, and Wolff–Parkinson–White syndrome in pediatric patients) and systemic embolic events. The diagnosis is often delayed (3.5–5.7 years). Echocardiography is considered the reference standard for the diagnosis, and the features includes:

- Absence of coexisting cardiac abnormalities by definition
- Typical two-layered structure of the myocardium with a thin, compacted epicardial band and a much thicker, noncompacted endocardial layer consisting of trabecular meshwork with deep endocardial spaces (with a ratio of the noncompacted layer to the compacted layer greater than 2)
- Multiple ventricular trabeculations, prominent in the middle and apical segments (Fig. 13.6)
- Predominant segmental location of the abnormality (noncompacted myocardium greater than 80%) found in the apical and mid-ventricular regions of both inferior and lateral walls
- Color Doppler evidence of deeply perfused intertrabecular recesses (not communicating with the coronary circulation, unlike for myocardial sinusoids)

Further Reading

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