Cardiomyopathies

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Abstract

The cardiomyopathies are a heterogeneous collection of heart muscle disorders with diverse genetic and non-genetic aetiologies. The advent of molecular genetics and next-generation sequencing has transformed understanding of the mechanisms of disease underlying many forms of cardiomyopathy, and unlocked the prospect of personalized medicine based on knowledge of an individual's genetic variants. Current management of patients with inherited cardiomyopathies is beginning to integrate knowledge of individual genomic profiles with advances in cardiovascular imaging. This has enhanced surveillance potential for high-risk individuals and begun to facilitate diagnosis, appropriate risk stratification and prognostication. This review provides an introduction to the cardiomyopathies, focusing on hypertrophic cardiomyopathy, dilated cardiomyopathy, restrictive cardiomyopathy, arrhythmogenic cardiomyopathy and left ventricular non-compaction, giving an overview of their aetiological complexity, diagnosis and contemporary clinical management.

Keywords Arrhythmogenic right ventricular dysplasia; cardiomyopathy; dilated cardiomyopathy; genetic; hypertrophic cardiomyopathy; left ventricular non-compaction; restrictive cardiomyopathy; sudden cardiac death

Key points

- Hypertrophic cardiomyopathy is the most common monogenic cardiac disorder. It is defined by the presence of unexplained left ventricular hypertrophy and is genetically primarily a disease of sarcomeric and associated myofilament proteins
- Dilated cardiomyopathy (DCM) has a broad clinical spectrum ranging from genotype-positive, phenotype-negative disease identified on cascade screening, to a hypokinetic, non-dilated phenotype, to classical DCM with biventricular dilatation and systolic impairment
- Restrictive cardiomyopathy is rare and characterized by diastolic impairment from restrictive ventricular filling but with preserved systolic function. It results from a diverse range of infiltrative, non-infiltrative and storage disorders, whose clinical presentation is largely that of heart failure
- Arrhythmogenic cardiomyopathy is a phenotypic response to disruption of desmosomal function. It is characterized pathologically by myocyte loss and progressive fibro-fatty replacement that can involve either or both ventricles, and clinically by a high frequency of ventricular arrhythmias and propensity to sudden cardiac death
- Left ventricular non-compaction (LVNC) is characterized by prominent trabeculations of the left ventricle and a thin compacted layer with deep endomyocardial intertrabecular recesses, giving a bilayered myocardial appearance on imaging. It can be associated with neuromuscular disease and chromosomal defects, or isolated. LVNC can be complicated by thromboembolism, heart failure and sudden cardiac death from ventricular arrhythmia

Cardiomyopathies – definition and classification

Cardiomyopathies are a group of heart muscle disorders defined by structural and functional abnormalities of the ventricular myocardium not explained by obstructive coronary artery disease or abnormal loading conditions. Traditional taxonomies have classified cardiomyopathies first as primary or secondary disorders, and then based on gross morpho-functional appearances into hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), restrictive cardiomyopathy (RCM), arrhythmogenic right ventricular cardiomyopathy and, more recently, left ventricular non-compaction (LVNC). However, the practical distinction between primary and secondary cardiomyopathy can be challenging and not reflect the complexity of clinical presentation. In contrast, subdivision of the major phenotypes into familial (genetic) and non-familial (non-genetic) types informs diagnosis and management (Figure 1). Familial cardiomyopathies are largely monogenic disorders, reflecting a single-gene defect whose ultimate phenotypic expression reflects a complex interaction with modifier genes and environmental exposures.

A more comprehensive genotype–phenotype nosology has been advocated, in particular the MOGE(S) nomenclature, endorsed by the World Heart Federation.[1] The MOGE(S) descriptive classification emulates the TNM grading systems for tumours, integrating morphofunctional phenotype (M), organ/system involvement (O), genetics (inheritance pattern) (G),

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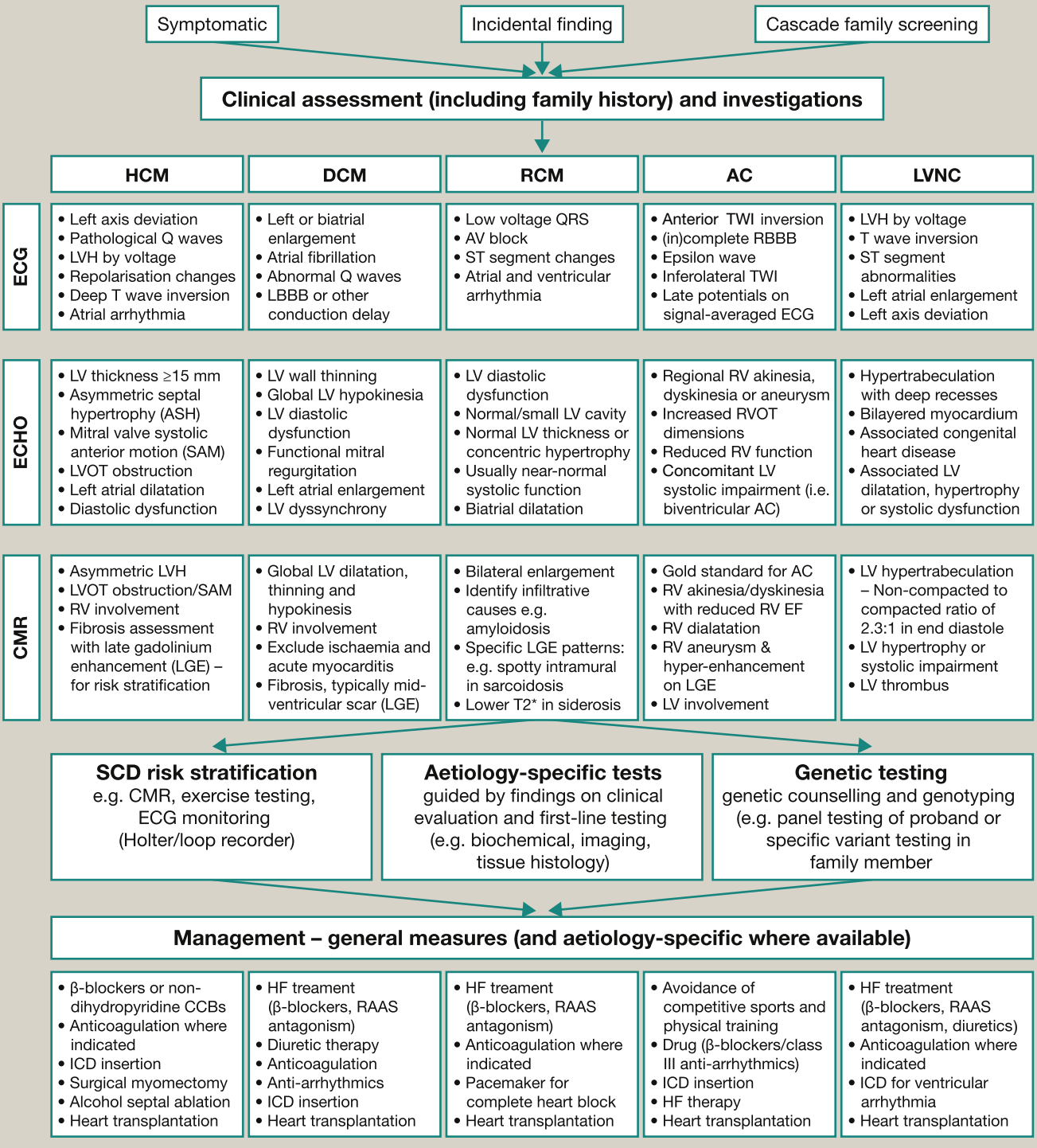
Please cite this article in press as: Chan K, et al., Cardiomyopathies, Medicine (2018), https://doi.org/10.1016/j.mpmed.2018.07.014

Overview of assessment and management of cardiomyopathies



CCB, calcium channel blocker; CMR, cardiac magnetic resonance; EF, ejection fraction; ICD, internal cardiac defibrillator; HF, heart failure; LBBB, left bundle branch block; LVOT, LV outflow tract; RAAS, Renin-angiotensin aldosterone system; RBBB, right bundle branch block; RVOT, RV outflow tract; TWI, T-wave inversion.

Figure 1

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