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Short communication

Sudden cardiac death in inherited cardiomyopathy

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ABSTRACT

Cardiomyopathy is an important cause of sudden cardiac death particularly in adolescents and young adults. The risk of sudden cardiac death varies between individual cardiomyopathies and is dependent on the severity of disease, age and gender. Although rare in cardiomyopathies, a fundamental aspect of clinical management is a systematic and thorough clinical assessment to identify the small number of individuals who are at risk and who can be protected with prophylactic ICD therapy.

1. Introduction

Sudden cardiac death (SCD) can be defined as an unexpected death from cardiac causes within 1 h of symptom onset with or without known cardiac disease. Sudden cardiac death (SCD) accounts for approximately 25% of all cardiovascular deaths worldwide and in most cases is attributable to coronary artery disease [1]. Most evidence suggests that it is usually caused by ventricular arrhythmia (VA) and less commonly by bradyarrhythmia with conduction abnormalities [1].

Non-ischaemic causes of SCD are more prevalent in young adults and inherited conditions such as channelopathies or cardiomyopathies are evident in up to 50% of families of young victims of SCD [2]. Cardiomyopathies are a diverse group of disorders characterised by structural and functional abnormalities of the heart muscle that are unexplained by coronary artery disease, hypertension or valvular disease [3]. They are grouped into morphological and functional subtypes, each of which can be caused by genetic and non-genetic mechanisms.

The risk of SCD varies between cardiomyopathies and is dependent on the severity of disease, age and gender. The approach to primary prevention of SCD varies and is supported by variable levels of evidence between diseases. We briefly consider current evidence of SCD prevention in the most common cardiomyopathy subtypes.

2. Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is defined by increased left ventricular (LV) wall thickness that is not explained solely by abnormal loading conditions [4]. Screening studies suggest a population prevalence of 1 in 500 although the number of diagnosed cases is much less [3,4]. HCM can lead to early death due to heart failure (HF), stroke or SCD and is usually inherited as an autosomal dominant trait caused by mutations in genes encoding cardiac sarcomeric proteins. Rarer causes of HCM include metabolic and mitochondrial disorders, congenital malformations and endocrinopathies [4].

Contemporary reports show an overall cardiovascular mortality in HCM of 2% per year with an SCD incidence of 0.8% per year that peaks in early adulthood [5]. Different arrhythmias are responsible but the most frequent is spontaneous ventricular fibrillation (VF) [1,4].

Several clinical features are associated with SCD including non-sustained ventricular tachycardia (VT), severe LV hypertrophy, unexplained syncope, family history of SCD and abnormal blood pressure response to exercise [4]. Patients with none of these "major" risk factors are generally at low risk for SCD whereas those with multiple risk factors are considered candidates for an ICD [4]. The 2014 ESC guidelines on HCM recommended an individualised approach to risk estimation that takes into account the unique contribution of each clinical risk factor (HCM RISK–SCD) as seen in Fig. 1 [4,6]. With the exception of abnormal blood pressure response, the model uses the same risk factors recommended in previous guidelines with the addition of left atrial diameter, LV outflow tract gradient and patient age. These are integrated into an on-line calculator that can be used to estimate a five year risk of SCD [http://www.doc2do.com/hcm/webHCM.html].

Survivors of VF or sustained VT are at very high risk of subsequent lethal cardiac arrhythmias and should all receive an ICD for secondary prevention [7]. For primary prophylaxis, ESC guidelines recommend that patients with a five year risk ≥ 6% should be considered for ICD therapy [4]. ICDs may also be appropriate in people with an intermediate risk of 4–6% in the ESC model [4].

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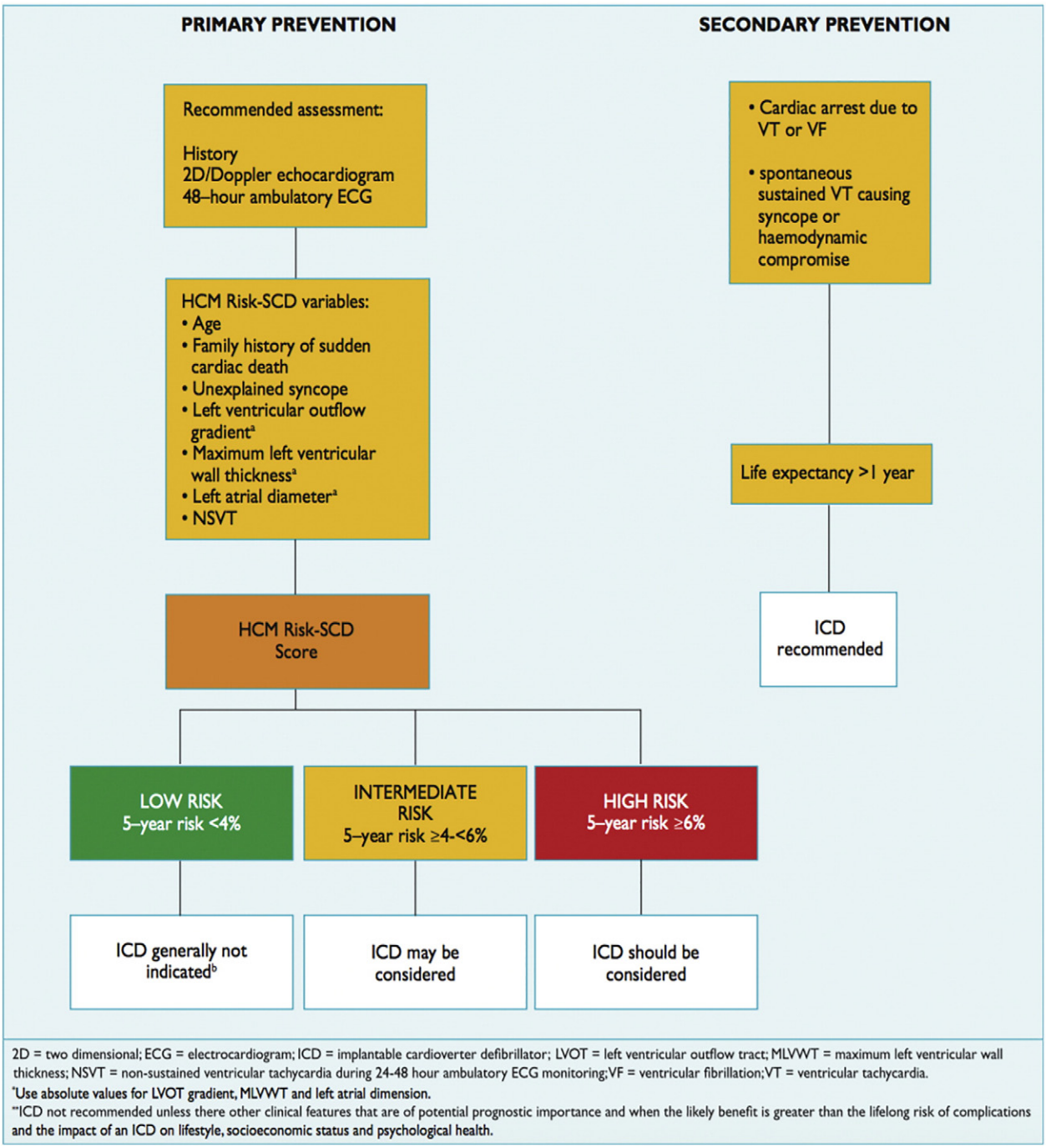

Fig. 1. Flowchart for ICD consideration in hypertrophic cardiomyopathy. The flowchart illustrates a systematic approach to management using the HCM Risk-SCD model and organizing individuals based on their SCD risk estimate at 5 years [4].

3. Dilated cardiomyopathy (DCM)

Dilated cardiomyopathy (DCM) is defined as LV dilatation with systolic dysfunction in the absence of abnormal loading conditions or coronary artery disease significant to cause ventricular dysfunction [3]. It has a prevalence of 1 in 2500 and is familial in at least 25% of cases [8]. Causative mutations occur in genes encoding proteins in the cytoskeleton, sarcomere, nuclear membrane and intercalated discs with other causes including myocarditis, metabolic and mitochondrial disease [1]. The major causes of cardiovascular death in DCM are progressive HF and SCD secondary to ventricular arrhythmia or, less commonly, bradyarrhythmia. All-cause mortality in DCM has improved substantially with the use of conventional HF medications and device therapy as seen in Fig. 2 [9]. Many non-invasive parameters have been suggested as predictors of SCD, but in a recent meta-analysis of 45 studies, functional and electrocardiographic parameters provided only modest discrimination between high and low risk patients [10].

A number of trials have compared ICD therapy alone or in combination with cardiac resynchronization therapy against placebo or amiodarone in patients with DCM [11,12]. For secondary prophylaxis, all guidelines recommend ICD implantation, although only three small trials (Antiarrhythmics vs Implantable Defibrillators (AVID), the Cardiac Arrest Study Hamburg (CASH), and the Canadian Implantable Defibrillator Study (CIDS)) have examined ICD therapy in patients with a history of resuscitated cardiac arrest or symptomatic VT [11]. For primary prophylaxis, ESC guidelines recommend an ICD in patients with DCM,