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Review article

Almanac 2014: cardiomyopathies

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ABSTRACT

Cardiomyopathies are myocardial disorders that are not explained by abnormal loading conditions and coronary artery disease. They are classified into a number of morphological and functional phenotypes that can be caused by genetic and non-genetic mechanisms. The dominant themes in papers published in 2012–2013 are similar to those reported in Almanac 2011, namely, the use (and interpretation) of genetic testing, development and application of novel non-invasive imaging techniques and use of serum biomarkers for diagnosis and prognosis. An important innovation since the last Almanac is the development of more sophisticated models for predicting adverse clinical events.

Contents

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Introduction

Cardiomyopathies are myocardial disorders that are not explained by abnormal loading conditions and coronary artery disease. They are classified into a number of morphological and functional phenotypes that can be caused by genetic and non-genetic mechanisms. The dominant themes in papers published in 2012–2013 are similar to those reported in Almanac 2011, namely, the use (and interpretation) of genetic testing, development and application of novel non-invasive imaging techniques and use of serum biomarkers for diagnosis and prognosis. An important innovation since the last Almanac is the development of more sophisticated models for predicting adverse clinical events.

Hypertrophic cardiomyopathy

Cardiac imaging and circulating biomarkers

Hypertrophic cardiomyopathy (HCM) occurs in one in every 500 adults and in most individuals is inherited as an autosomal dominant trait caused by mutations in cardiac sarcomere protein genes and is associated with an increased risk of sudden cardiac death (SCD), progressive ventricular dysfunction and stroke (Fig. 1) [1–3]. Diagnostic tools such as ECG and echocardiography remain fundamental to diagnosis and treatment of HCM but cardiac MRI (CMR) improves diagnostic accuracy and provides additional phenotypic information in patients with established disease (Fig. 2) [4–7]. For example, in one study, CMR identified hypertrophy in about 10% of sarcomere mutation carriers thought to have normal wall thickness by echocardiography [8]. Novel CMR sequences, such as T1 mapping, provide quantitative estimates of the myocardial extracellular volume (ECV) (and therefore a surrogate measure of interstitial fibrosis) [5] and, in one study, an increase in ECV was reported in individuals with sarcomere mutations but without LV hypertrophy [9]. These findings suggest that selective use of CMR may be helpful in family screening, particularly when they are other features consistent with HCM, such as ECG abnormalities.

The clinical relevance of myocardial scar inferred from abnormal gadolinium enhanced CMR is a recurring subject in the literature. Available data support a relation among late gadolinium enhancement (LGE), representing macroscopic focal myocardial scar, and cardiovascular mortality, heart failure death and all-cause mortality but show only a trend towards an increased risk of SCD [10,11]. ECV measured by CMR correlates with concentrations of both N-terminal pro-brain natriuretic peptide and serum biomarkers of collagen synthesis providing further evidence that myocardial fibrosis is important early in disease pathogenesis [9].

Numerous papers have investigated biomarkers as a tool for diagnosis and prognosis and have shown predicting poor outcome in patients with heart failure [12]. In a study of 772 patients with HCM, brain natriuretic peptide (BNP) was an independent predictor of morbidity in mortality [13]. In another study of 183 stable outpatients, plasma NT-proBNP was a predictor of heart failure-related events [14] and was a predictor of heart failure and transplant-related death but not sudden death or inappropriate implantable cardioverter defibrillator (ICD) shocks [15]. A further study of 183 patients reports elevated serum concentrations of high-sensitivity cardiac troponin T to predict adverse outcomes in HCM [16].

Treatment strategies

Current management of individuals with HCM focuses on prevention of SCD and stroke, relief of drug-refractory symptoms associated with LV outflow tract obstruction (LVOTO), and palliation of limiting symptoms caused by systolic or diastolic dysfunction. There have been few developments in therapy since the last Almanac, but early prophylactic β-blocker therapy in physically active patients (NYHA 1 and 2) with provokable LVOTO has been shown to be effective in reducing outflow gradients during physiological exercise [17]. Another study has confirmed the additive benefit of disopyramide in therapy of symptomatic patients with obstruction resistant to initial therapy with β-blocker or verapamil [18].

Invasive treatment of LVOTO is recommended for patients with drug-refractory symptoms. Several studies have provided new data on septal alcohol ablation (SAA) and LV septal myectomy. Over a follow-up of 5.7 years, survival following SAA in 177 patients was similar to that of patients treated with septal myectomy and a matched control population. Pacemakers were required in 20.3% in patients who underwent SAA compared with 2.3% in the surgical cohort in the 30 days following the procedure [19]. Similar results following SAA were reported in a study of 470 patients [20] in whom 10-year survival (all-cause death rate 1.2%) was 88% compared with 84% in a matched normal population (Fig. 3); the same authors also report a reduction in SCD risk factors. In a study of 239 patients, septal myectomy was associated with a reduction in syncope and increased survival [21]. Another study reports a cumulative incidence of HCM-related death of 3.3% at 5 years [22]. Finally, in 699 patients age and persistent atrial fibrillation were reported to be predictors of poorer outcome in patients undergoing surgical myectomy [23].

New data have re-examined the efficacy of dual chamber pacing for refractory symptomatic LVOTO [24,25]. In a recent Cochrane review, it was noted that all data derive from small studies and that the few randomised trials [26,27] concentrate on physiological outcome measures rather than hard clinical