Rev Port Cardiol. 2016;35(5):253–260

Revista Portuguesa de Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

ORIGINAL ARTICLE

Prevalence, predictors and prognosis of ventricular reverse remodeling in idiopathic dilated cardiomyopathy

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Received 8 July 2015; accepted 21 November 2015
Available online 23 April 2016

KEYWORDS
Dilated cardiomyopathy;
Reverse remodeling;
Prognosis

Abstract
Introduction: Cardiac remodeling is manifested as changes in size, shape and function of the heart. We studied the prevalence, prognosis and predictors of left ventricular reverse remodeling (LVRR) in idiopathic dilated cardiomyopathy (IDCM) after optimized medical therapy.
Methods: A total of 113 IDCM patients were followed for 7.1±5.6 years. LVRR was defined as an increase of 10 units in ejection fraction (EF) and decrease in left ventricular diastolic diameter (LVDD), in the absence of resynchronization therapy.
Results: Baseline EF was 27±8% and LVDD index was 37.1±6.3 mm/m^2. LVRR occurred in 34.5% within 22.6 months. Final EF was 47.5±10.1%, LVDD index was 30.2±3.9 mm/m^2. LVRR was associated with better NYHA class (I–II) and lower BNP ($p<0.01$) and all patients were alive.

Univariate predictive factors of LVRR ($p<0.05$) were mild hypertension, atrial fibrillation, ventricular hypertrophy on ECG, absence of left bundle branch block, shorter QRS duration, higher hematocrit, lower LVDD index, higher peak oxygen uptake efficiency (VO_2/log 10[VE]) and lower dVE/VCO_2/VO_2, treatment with angiotensin-converting enzyme inhibitors (ACEI)/angiotensin receptor blockers (ARB) and use of maximal doses of ACEI/ARB and beta-blockers. Multivariate regression analysis showed that higher doses of ACEI/ARB (OR: 0.32, 95% CI 0.11–0.92) were independently associated with LVRR. Non-transmural late enhancement on cardiac MRI was not a predictor of LVRR.
Conclusions: LVRR occurred in one third of IDCM patients, especially in those with mild hypertension and with less advanced disease, who may have benefited from maximal drug titration.

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http://dx.doi.org/10.1016/j.repc.2015.11.014

PALAVRAS-CHAVE
Miocardiopatia dilatada;
Remodelagem reversa;
Prognóstico

Prevalência, preditores e prognóstico da remodelagem reversa na miocardiopatia dilatada idiopática

Resumo
Introdução: A remodelagem ventricular é caracterizada por alterações no tamanho, forma e função do coração. Estudámos a prevalência, o prognóstico e os fatores preditores de reversão da remodelagem do ventrículo esquerdo (RRVE) na miocardiopatia dilatada idiopática (MCDI), após a terapêutica farmacológica otimizada.
Métodos: Cento e treze doentes foram seguidos durante 7,1±5,6 anos. A RRVE foi definida como um aumento de dezunidades da fração de ejeção (FE) e diminuição do diâmetro diastólico do VE (VED), na ausência de terapêutica de ressincronização.
Resultados: A FE basal foi de 27±8% e o VED de 37,1 ± 6,3 mm/m^2. A RRVE ocorreu em 34,5% dentro de 22,6 meses. A FE final foi de 47,5 ± 10,1%, o VED *index* foi de 30,2±3,9 mm/m^2. A RRVE associou-se a melhor classe NYHA (I-II), menor BNP e a mortalidade nula.

Os preditores de RRVE foram hipertensão arterial (ligeira), fibrilhação auricular, hipertrofia ventricular esquerda (no ECG), ausência de bloqueio de ramo esquerdo, menor duração do QRS, maior hematócrito, menor VED *index*, melhor eficiência de oxigénio no pico do exercício (VO2/LG10[VE]), um menor DVE/VCO2/VO2, uso de IECA/ARA-II e uso de doses máximas de IECA/ARA-II e bloqueadores-β. Na análise multivariada o uso de doses máximas de IECA/ARA-II (OR: 0,32, 95% CI 0,11-0,92) foi um preditor independente. A presença ou extensão do realce tardio na RMN cardíaca não foi preditora de RRVE.
Conclusão: A RRVE ocorreu num terço dos pacientes MCDI, naqueles com hipertensão ligeira e com doença menos avançada, que poderão ter beneficiado da máxima titulação dos fármacos.

Introduction

Cardiac remodeling is defined as genome expression resulting in molecular, cellular and interstitial changes and manifested clinically as changes in size, shape and function of the heart.[1] The progression of heart failure (HF) is associated with left ventricular (LV) remodeling, which manifests as gradual increases in LV end-diastolic and end-systolic volumes, wall thinning, and a change in chamber geometry to a more spherical, less elongated shape, with a progressive decrease in ejection fraction (EF).

When ventricular remodeling is advanced, it begins to be self-sustaining and capable of driving disease progression, regardless of the patient's neurohormonal status. This may explain why medical therapies lose their effectiveness in end-stage HF, and why some device-based therapies (cardiac resynchronization and mechanical ventricular assistance), which can affect LV remodeling, are beneficial.

The overall importance of ventricular remodeling as a pathogenic mechanism and prognostic determinant is not clear. Some drug therapies and cardiac devices that increase the survival of patients with HF can slow, and in some cases even reverse, certain parameters of remodeling. Controversially, as in the case of etanercept[2] and in cardiac resynchronization,[3,4] reverse remodeling has not translated into increased survival. Additionally, the molecular mechanisms of reverse remodeling have not been fully elucidated.

Left ventricular reverse remodeling (LVRR) is characterized by a decrease in LV dimensions, normalization of LV shape and improvement of systolic function.

A significant prevalence of recovery of LV function in patients with dilated cardiomyopathy (DCM) has been reported.[5] However, such studies included patients with new-onset DCM like acute myocarditis, and other reversible causes of DCM, such as peripartum and alcohol-related DCM. The mechanisms underlying LVRR in such situations appear to be different from those involved in chronic idiopathic DCM.

The aim of this prospective study was to assess recovery of LV function and reversal of ventricular remodeling in patients with chronic idiopathic DCM, after optimized medical therapy. We set out to assess its prevalence, to identify its predictors and to determine whether it was associated with better prognosis.

Methods

The study included consecutive adult patients with idiopathic DCM (left ventricular diastolic diameter [LVDD] >33 mm/m^2 in men, >32 mm/m^2 in women) between 2000 and June 2012 followed in an HF clinic, diagnosed less than 24 months previously and with two initial values of left ventricular ejection fraction (LVEF) of <0.40 more than one year apart.

We excluded DCM patients with secondary etiologies, including a history of myocardial infarction or angina, those with ischemia or significant coronary disease on coronary angiography, a history of moderate or severe hypertension, at least moderate primary mitral or aortic valvular disease, heavy alcohol use (>100 g/day), chemotherapy-induced and peripartum cardiomyopathy, acute HF with biopsy positive