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ORIGINAL ARTICLE

The role of biomarkers in dilated cardiomyopathy: Assessment of clinical severity and reverse remodeling

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KEYWORDS
Biomarkers;
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Abstract
Introduction: Biomarkers in dilated cardiomyopathy (DCM) reflect various pathobiological processes, including neurohormonal activation, oxidative stress, matrix remodeling, myocyte injury and myocyte stretch. We assessed the role of biomarkers in clinical and echocardiographic parameters and in left ventricular (LV) reverse remodeling (LVRR).
Methods: In this prospective study of 50 DCM patients (28 men, aged 59±10 years) with LV ejection fraction (LVEF) <40%, LVRR was defined as an increase of >10 U in LVEF after optimal medical therapy.
Results: Baseline LVEF was 25.4±9.8% and LV end-diastolic diameter (LVEDD)/body surface area (BSA) was 34.2±4.5 mm/m^2. LVRR occurred in 34% of patients within 17.6±15.6 months. No correlation was found between B-type natriuretic peptide (BNP), 25-hydroxyvitamin D (25(OH)D), CA-125, high-sensitivity C-reactive protein (hs-CRP), lipoprotein(a) [Lp(a)], noradrenaline, adrenaline, renin or aldosterone and LVRR. Patients in NYHA class III or IV, with pulmonary congestion or ankle edema, had higher CA-125, cystatin C, BNP and hs-CRP levels ($p<0.05$). CA-125 was correlated with BNP ($r=0.61$), hs-CRP ($r=0.56$) and uric acid ($r=0.52$) (all $p=0.01$). BNP correlated directly with LVEDD ($r=0.49$), LV volumes ($r=0.51$), pulmonary artery systolic pressure (PASP) ($r=0.43$) and E/e′ ($r=0.31$), and was inversely correlated with LVEF ($r=-0.50$) and e′ velocity ($r=-0.32$) ($p<0.05$). CA-125 was positively correlated with left atrial volume/BSA ($r=0.46$), E/A ratio ($r=0.60$) and PASP ($r=0.49$) ($p<0.05$).

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Conclusions: No correlation was found between biomarkers and LVRR, but CA-125, BNP and hs-CRP were predictors of clinical severity and congestion. BNP correlated with parameters of systolic and diastolic dysfunction, while CA-125 correlated with measures of diastolic dysfunction.

PALAVRAS-CHAVE
Biomarcadores;
Miocardiopatia dilatada;
Remodelagem reversa

O papel dos biomarcadores na miocardiopatia dilatada – avaliação de gravidade clínica e remodelagem reversa

Resumo
Introdução: Os biomarcadores na miocardiopatia dilatada (DCM) refletem vários processos fisiopatológicos: ativação neuro-hormonal, stresse oxidativo, remodelagem da matriz extracelular, lesão e estiramento miocitários. Procurámos associar biomarcadores com parâmetros clínicos, ecocardiográficos e com a reversão da remodelagem do ventrículo esquerdo (LVRR).
Métodos: Estudo prospetivo de 50 doentes com DCM (28 homens, idade 59±10 anos) com fração de ejeção ventricular esquerda (LVEF) <40%. A LVRR definiu-se como aumento>10 U da LVEF, após a terapêutica médica otimizada.
Resultados: A LVEF basal foi de 25,4±9,8% e o diâmetro do VE (LVD)/BSA de 34,2±4,5 mm/m^2. A LVRR ocorreu em 34%, em 17,6±15,6 meses. Não houve correlação entre BNP, 25-OH-vit D, CA 125, hsCRP, Lp(a), noradrenalina, adrenalina, renina, aldosterona e LVRR. Doentes em classe NYHA (III-IV), com congestão pulmonar ou edema periférico apresentaram níveis mais elevados de CA 125, cistatina C, BNP e hsCRP (p<0,05). O CA 125 correlacionou-se com níveis de BNP (r=0,61), hsCRP (r=0,56) e ácido úrico (r=0,52) (p=0,01). O BNP relacionou-se diretamente com LVD (r=0,49), volume VE (r=0,51), PSAP (r=0,43), razão E/e′ (r=0,31); e inversamente com LVEF (r=-0,50) e vel. e′ (r=-0,32) (p<0,05). O CA 125 correlacionou-se com o volume AE/BSA (r=0,46), razão E/A (r=0,60) e PSAP (r=0,49) (p<0,05).
Conclusões: Não houve correlação entre biomarcadores e LVRR, contudo, o CA125, BNP e hsCRP foram preditores de gravidade clínica e de congestão. O BNP relacionou-se com parâmetros de disfunção sistólica e diastólica, enquanto o CA 125 se relacionou com medidas de disfunção diastólica.

Introduction

Heart failure (HF) is a major public health burden and is often a clinically silent process, with progressive cardiac remodeling that eventually leads to symptomatic presentation late in the course of disease progression. The severity and prognosis of HF vary substantially, ranging from mild disease that is easily managed with neurohormonal blockade to advanced illness requiring mechanical support or heart transplantation.[1] Physicians use biomarkers as additional tools to aid clinical diagnosis and treatment and to identify high-risk subjects.[2]

The progression of HF is complex and is driven by multiple biological processes, including inflammation, oxidative stress, neurohormonal activation, vascular remodeling, myocyte injury, and renal impairment.[3] Current guidelines recommend testing B-type natriuretic peptide (BNP) or N-terminal pro-BNP (NT-proBNP).[4]

The progression of 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 elliptical shape, with a continuous decrease in LV ejection fraction (LVEF).[5] When ventricular remodeling is advanced, it is self-sustaining, leading to disease progression, regardless of neurohormonal status.

However, in some situations, there may be LV reverse remodeling (LVRR), characterized by decreases in LV dimensions, normalization of LV shape and improvement of systolic function.

In this work, we set out to find associations between biomarkers and clinical severity and echocardiographic parameters. We also sought predictors of LVRR after optimal pharmacological therapy. We used available biomarkers that reflect diverse biological pathways in HF: adrenaline, noradrenaline, plasma renin, aldosterone and BNP (neurohormonal activation), high-sensitivity C-reactive protein (hs-CRP), cancer antigen CA-125 (inflammation), uric acid and lipoprotein(a) [Lp(a)] (oxidative stress), creatinine and cystatin C (renal function), and 25-hydroxyvitamin D