Rev Port Cardiol. 2014;33(11):699–706

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

ORIGINAL ARTICLE

High levels of high-sensitivity C-reactive protein and uric acid can predict disease severity in patients with mitral regurgitation

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Received 29 July 2013; accepted 31 March 2014
Available online 11 November 2014

KEYWORDS
High-sensitivity C-reactive protein;
Mitral regurgitation;
NYHA class;
Uric acid

Abstract
Introduction: Both high-sensitivity CRP (hs-CRP) and uric acid (UA) levels are known to be increased in heart failure patients and are associated with poorer functional capacity and adverse outcome. The role of these markers in patients with mitral regurgitation (MR) is less clear. The aim of this study was to assess the relationship between hs-CRP, UA and organic MR. We also assessed whether hs-CRP and UA levels are correlated with symptoms of MR, severity of MR, LV remodeling and outcome during follow-up.
Methods: A total of 200 consecutive patients (87 men [43.5%]; mean age 61.6±12.5 years) with moderate or severe isolated and organic MR were included in the study. All the patients were assessed clinically and were managed and treated with standard medical therapy according to evidence-based practice guidelines. Patients were categorized according to New York Heart Association (NYHA) functional class. We assessed and graded the severity of MR using a multi-parametric approach. hs-CRP was measured with chemiluminescent immunometric assay using an IMMULITE® 1000 autoanalyzer (Siemens, Germany). Serum UA levels were analyzed using a Cobas® 6000 autoanalyzer (Roche Diagnostics, Mannheim, Germany).
Results: Mean UA levels increased significantly with NYHA class: 4.46±1.58 mg/dl for patients in NYHA class I, 5.91±1.69 mg/dl for class II, 6.31±2.16 mg/dl for class III and 8.86±3.17 mg/dl for class IV ($p<0.001$). Mean UA levels also increased significantly with increased severity of MR (moderate 5.62±1.9 mg/dl, moderate to severe 5.56±1.2 mg/dl, severe 7.38±3.4 mg/dl, $p<0.001$). There was a significant correlation between UA level and left ventricular end-diastolic diameter ($r=0.40$; $p<0.001$), left ventricular end-systolic

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diameter (r=0.297; p=0.001) and left ventricular ejection fraction (LVEF) (r=0.195, p=0.036), whereas hs-CRP was not correlated with these parameters. In multivariate Cox proportional hazards analysis LVEF, NYHA class and UA levels were the only independent predictors of death. *Conclusion:* UA and hs-CRP levels can help identify patients with asymptomatic moderate or severe mitral regurgitation. UA levels may be useful to assess the extent of left ventricular remodeling and in the optimal timing of mitral valve surgery in certain subsets of patients.

PALAVRAS-CHAVE
Proteína C-reativa de alta sensibilidade;
Regurgitação mitral;
Classe da NYHA;
Ácido úrico

Níveis elevados de proteína C-reativa de alta sensibilidade e de ácido úrico podem prever a severidade da doença em pacientes com regurgitação mitral

Resumo
Introdução: É conhecido que tanto a proteína C-reativa de alta sensibilidade (PCR-as) como o ácido úrico (AU) estão elevados nos doentes com insuficiência cardíaca e, estão associados a pior capacidade funcional e a pior prognóstico. O papel destes marcadores nos doentes com regurgitação mitral (RM) é menos claro. O objetivo deste estudo foi o de avaliar a relação entre PCR-as, o AU e a RM orgânica. Também avaliamos se os níveis de PCR-as e de AU estão correlacionados com os sintomas da RM, com a severidade da RM, com a remodelagem do ventrículo esquerdo (VE) e com o prognóstico, durante o seguimento clínico.
Métodos: Um total de 200 pacientes consecutivos (86 homens (43,5%); idade média 61,6±12,5 anos) com RM orgânica isolada, moderada ou severa, foram incluídos no estudo. Todos os doentes foram avaliados clinicamente e tratados com a terapêutica médica *standard* de acordo com a prática da medicina baseada na evidência e com as *Guidelines*. Os doentes foram classificados de acordo com a classe funcional da *New York Heart Association* (NYHA). Avaliamos e classificamos a gravidade da RM utilizando o modelo multiparamétrico. A PCR de alta sensibilidade foi quantificada com o teste imunométrico quemilumeniscente, usando um Autoanalizador IMMULITE® 1000 (Siemens, Germany). Os níveis séricos de AU foram determinados usando o Autoanalizador COBAS série 6000 (Roche® Diagnostics, Mannheim, Germany).
Resultados: Os níveis médios de AU aumentaram significativamente com a classe da NYHA: 4,46±1,58 mg/dl para Classe I da NYHA, 5,91±1,69 mg/dl para a classe II da NYHA, 6,31±2,16 mg/dl para Classe III da NYHA e 8,86±3,17 mg/dl para Classe IV da NYHA (p<0,001). Os valores médios do AU também aumentaram de forma significativa com o aumento da severidade da RM (moderada=5,62±1,9 mg/dl, moderada a severa=5,56±1,2 mg/dl, severa=7.38±3.4 mg/dl, p<0.001). Foi encontrada uma correlação significativa entre os níveis de AU e o DDVE (r=0.40; p<0.001, Figure 5), DSVE (r=0,297; p=0,001) e FEVE (r=0,195, p=0,036), enquanto a PCR-as não se correlacionou com esses parâmetros. Na análise multivariável de Cox, a FEVE, a classe da NYHA e os níveis de AU foram os únicos fatores preditivos independentes de morte.
Conclusão: Os níveis de AU e de PCR-as podem ajudar a distinguir os doentes com RM moderada a severa assintomática, dos sintomáticos. Os níveis de AU podem ser úteis na determinação da extensão da remodelagem ventricular e do tempo mais adequado para a realização da cirurgia da válvula mitral, em determinados grupos de doentes.

Introduction

Primary mitral regurgitation (MR) covers all etiologies in which intrinsic lesions affect one or several components of the mitral valve apparatus.[1] Surgery is recommended in patients with chronic severe MR if they have any symptoms or in asymptomatic patients with left ventricular (LV) dysfunction.[1] When guideline indications for surgery are reached, early surgery is associated with better outcomes, since the development of even mild symptoms by the time of surgery is associated with deleterious changes in cardiac function after surgery.[2,3] However, difficulties in detecting early LV dysfunction, accurately assessing the severity of valve involvement, or recognizing early cardiac symptoms often make it difficult to determine the optimal timing of mitral valve surgery.[4] In many patients, the development of symptoms is clear, but in others, symptoms are difficult to assess because of inactivity. In some patients, it may also be unclear whether symptoms are related to severe MR or to comorbidities.[5,6]