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ORIGINAL ARTICLE

Potential use of Brain Natriuretic Peptide in patients with asymptomatic significant mitral stenosis

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KEYWORDS

Brain Natriuretic Peptide;
Rheumatic mitral stenosis;
Exercise echocardiography;
Balloon commissurotomy

Abstract *Objective:* To evaluate the ability of BNP to identify a subset of patients with asymptomatic significant rheumatic MS, who get symptoms on stress exercise testing.
Methods: Seventy asymptomatic patients with significant rheumatic MS (MVA $\leqslant 1.5\ cm^2$) were included in the study. All patients underwent resting echo-Doppler study, exercise echocardiography and BNP level assessment pre- and one week post-balloon dilatation (for group I patients who had PMC).
Patients were divided into two groups. Group I included 33 patients who became symptomatic on exercise and had low exercise capacity. Group II included 37 patients who were asymptomatic on exercise and had reasonable exercise capacity.
Results: BNP level in group I was 92 ± 12 compared to 40 ± 10 pg/ml in group II, $P < 0.001$. Post PMC, BNP in group I significantly decreased (92 ± 12, compared to 31 ± 9 pg/dl, $P < 0.001$). LA dimension was significantly different between both groups (50 ± 2.9 in group I compared to 46 ± 3.1 mm in group II, $P < 0.001$). Post-exercise SPAP was 72 ± 12 in group I compared to 46 ± 13 mmHg in group II, $P < 0.001$. Post-exercise MV gradient was 28 ± 9

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; AF, atrial fibrillation; ANP, Atrial Natriuretic Peptide; AS, aortic stenosis; BNP, Brain Natriuretic Peptide; EF, ejection fraction; ESC, European Society of Cardiology; LA, left atrium; MR, mitral regurgitation; MS, mitral stenosis; MVA, mitral valve area; NT-Pro-BNP, N terminal-pro brain natriuretic peptide; PAP, pulmonary artery pressure; PMC, percutaneous mitral commissurotomy; SPAP, systolic pulmonary artery pressure; WMA, wall motion abnormality.

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compared to 20 ± 12 mmHg, $P = 0.002$. BNP significantly correlated with post-exercise SPAP ($r = 0.635$; $P < 0.001$). Area under the ROC curve for BNP as a predictor of low exercise capacity and development of symptoms on exercise was 0.98 [CI 95% 0.96–1.0]. When using a cutoff value of 55 pg/mL for BNP, sensitivity was 93.9% and specificity was 91.9%.

Conclusion: BNP may be used to approach asymptomatic patients with significant MS. BNP may identify a subset of patients with exercise-induced clinical and echo-Doppler criteria that meet the contemporary guidelines for intervention.

1. Introduction

Current European Society of Cardiology (ESC) guidelines for management of valvular heart diseases (2012), recommend doing percutaneous mitral commissurotomy (PMC) for patients with clinically significant mitral stenosis (MS) (mitral valve area $\leqslant 1.5\ cm^2$) with suitable valve scores if patients are symptomatic. In asymptomatic patients, intervention is justified for those who become symptomatic on exercise testing and those who had low exercise capacity [achieve < 5 Metabolic Equivalents (METs)].[1]

Rheumatic valvular heart diseases continue to be a major health problem in developing countries. Mitral stenosis is one of the most frequently encountered rheumatic valvular heart disease affections.[2,3] Regular follow up for patients with significant mitral stenosis is crucial to take the proper decision of intervention in the proper time (either surgical replacement or alternatively balloon commissurotomy if the valve morphology is suitable). It is frequently encountered that rheumatic MS patients describe equivocal symptoms. Due to the long latent period between onset of the initial rheumatic valvular affection and development of significant mitral stenosis, it is difficult for the treating physician to truly identify patients with symptoms that could be attributed to either hemodynamically significant stenosis or non cardiac dyspnea. Some patients have a sedentary life style that may result in physical deconditioning and subsequently exertional symptoms. On the other hand, other patients who are considered asymptomatic adapt their level of exertion and thereby do not get symptoms. Symptomatic status is mainly subjective, and hence a better risk stratification objective tool is required to be implemented in regular follow up of rheumatic MS patients.[4]

Several studies have reported an association between natriuretic peptides and severity of mitral stenosis.[5] Other studies have remarked a significant drop of Brain Natriuretic Peptide (BNP) post PMC.[5,6]

The predominant cardiac source of Atrial Natriuretic Peptide (ANP) is the atria, while the ventricles are the main source of BNP, although both can be synthesized in either chamber.[7–10] Both ANP and BNP are released into the circulation following primarily myocyte stretch. ANP release is more closely related to increased left atrial pressure while BNP release is more dependent on increased left ventricular pressure.[11,12,10,13–16]

In previous studies, a strong correlation between plasma BNP level and left atrial area suggested atrial secretion of BNP in MS. This was supported by evidence for synthesis of BNP by atrial myocytes in response to chronic increase in wall stress and co-storage of BNP with ANP in atrial granules.[14]

In valvular heart diseases, BNP serum level was found to be related to functional class and prognosis, particularly in aortic stenosis (AS) and mitral regurgitation (MR). In patients with chronic asymptomatic MR, several studies suggested the value of elevated BNP levels and a change in BNP as predictors of outcome. A cut-off BNP value $\geqslant 105$ pg/ml determined in a derivation cohort was prospectively validated in a separate cohort and helped to identify asymptomatic patients at higher risk of developing heart failure, LV dysfunction or death on mid-term follow-up.[17] Another study found that low-plasma BNP had a high negative predictive value and might be helpful for the follow-up of asymptomatic organic MR patients.[18]

The aim of our study was to evaluate the ability of a single baseline BNP level assessment to truly identify an important subset of asymptomatic clinically-significant rheumatic MS patients (with suitable valve scores for PMC) whose exercise stress criteria (clinical and echo-Doppler) meet the ESC contemporary guidelines for intervention.

2. Patients and methods

In this single center study, seventy asymptomatic patients with clinically significant rheumatic mitral stenosis (MVA $\leqslant 1.5\ cm^2$ and $> 1\ cm^2$) were prospectively included. All patients had suitable mitral valve scores for percutaneous dilation (mitral valve scores of $\leqslant 8$). All patients had a resting systolic pulmonary artery pressure < 50 mmHg. All patients underwent treadmill exercise testing and post-exercise echo-Doppler study. Patients were divided into two groups based on symptomatic status on exercise and exercise capacity. Group I included 33 patients who were symptomatic on exercise and had low exercise capacity (< 5 METs).[19] Group II included 37 patients who were asymptomatic on exercise and had a reasonable exercise capacity (> 5 METs).

Exclusion criteria were poor echocardiography window, significant renal impairment, presence of ischemic heart disease by history or resting wall motion abnormality (WMA) on echo-Doppler study, previous cardiac surgery or valve intervention, coexistent heart muscle disease or other valvular lesion (if graded more than mild) or inability to exercise (inability to walk on treadmill).

This study was carried out in the Cardiology Department, Faculty of Medicine, Zagazig University Hospitals, in the period from July 2011 to November 2013. All patients gave an informed consent to participate in the study.

2.1. BNP measurement

All samples were collected by veni-puncture into EDTA tubes within 2 h of obtaining the baseline echocardiogram and one week after PMC (for group I). The blood samples were kept at room temperature and analyzed within 4 h of sampling