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Original Article

NT pro B type natriuretic peptide levels in constrictive pericarditis and restrictive cardiomyopathy

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ABSTRACT

Background: The differentiation of constrictive pericarditis (CP) from restrictive cardiomyopathy (RCM) may be clinically difficult and may require multiple investigations. Even though brain natriuretic peptide (BNP) is shown to be higher in patients with RCM as compared to CP, the clinical utility is not fully established especially in Indian patients known to have advanced CP and myocardial involvement.

Methods and results: We measured NT-pro-BNP levels in 49 patients suspected of having either CP or RCM, diagnosed on the basis of echocardiography, computed tomography, magnetic resonance imaging, endomyocardial biopsy and cardiac catheterization data as needed. Twenty nine patients (Mean age – 26 yrs, 24 males) had CP and 20 patients (Mean age – 39 yrs, 14 males) had RCM. The median plasma NT-pro-BNP levels were significantly higher in RCM as compared to CP [1775 (208–7500) pg/ml vs 124 (68–718) pg/ml, respectively; $p = 0.001$]. A cut off value of 459 pg/ml had sensitivity, specificity and overall accuracy of 90%, 86% and 88% respectively, for differentiating CP from RCM.

Conclusions: The NT-pro-BNP levels are significantly elevated in RCM as compared to CP.

1. Introduction

Differentiation between constrictive pericarditis (CP) and restrictive cardiomyopathy (RCM) has always been a difficult task for the clinicians. The differentiation is crucial as CP is curable surgically whereas RCM needs conservative management with poor prognosis. Patients need to undergo various investigations like echocardiography including tissue Doppler, computed tomography and magnetic resonance imaging, one after the other and may require cardiac catheterization many a times to differentiate between the two conditions. An individual test is often unable to differentiate

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the two conditions, for instance, hemodynamic assessment by cardiac catheterization may miss up to one fourth of the cases of CP.[1]

Brain natriuretic peptide (BNP) is secreted from ventricular myocyte in response to ventricular overload.[2,3] Its secretion is influenced by various hemodynamic factors.[4] BNP levels are increased in various conditions like cardiac diseases (heart failure, acute myocardial infarction, hypertension with left ventricular hypertrophy), pulmonary diseases (chronic obstructive pulmonary diseases, pulmonary embolism), endocrine diseases, renal diseases and cirrhosis of liver. It is secreted as a pre-prohormone that splits into BNP and functionally inactive NT-pro-BNP. Half life of BNP is much lesser than NT-pro-BNP hence concentration of BNP are lesser.[5] The action of this peptide, like those of atrial natriuretic peptide, includes natriuresis, vasodilatation, inhibition of the renin-angiotensin-aldosterone axis, and inhibition of sympathetic nerve activity.[6]

In CP, there is no stretch on the myocardium because of the constrictive effect of the diseased pericardium, but in RCM the restrictive effect is in ventricular myocardium which produces significant atrial stretch. Due to this inherent difference in the physiology of these two conditions, the levels of BNP/NT-pro-BNP are found to be lower in CP in contrast to RCM.[7] Indian patients with CP often present late with advanced myocardial involvement and have tubercular etiology most of the time.[8] Hence, we conducted this study to evaluate the utility of NT-pro-BNP levels as a differentiating marker between Indian patients with RCM and predominantly tubercular CP.

2. Methods

All patients with a diagnosis of CP or RCM on the basis of clinical examination, echocardiography, computed tomography (CT), magnetic resonance imaging (MRI) and hemodynamic assessment were included in the study after an informed consent. CP due to radiation pericarditis and post cardiac transplant was excluded from the study. RCM due to various causes like idiopathic, endomyocardial fibrosis (EMF), amyloidosis, hemochromatosis and sarcoidosis were included in the study. Patients with features suggestive of both RCM and CP, e.g. radiation associated myopericardial involvement were excluded from the study as the basic aim of the study was to focus on the discriminatory value of NT-pro BNP for differentiating between RCM and CP. RCM patients with end stage disease and on transplant list were also excluded because multiple comorbidities associated with very advanced disease may confound the overall result of the study. End stage patients were defined as NYHA class IV patients who required hospitalization, intravenous medications and a median life expectancy of about 6 months. The study was approved by Institute's Ethics committee.

All patients suspected to have CP or RCM underwent complete clinical and echocardiographic evaluation. A 6-min walk test was done as per standard protocols. Echocardiogram was performed by a cardiologist with vast experience in this field. A comprehensive echocardiogram which included respiratory variation in mitral/tricuspid inflow velocities, atrial enlargement, septal thickness, mitral regurgitation (MR), tricuspid regurgitation (TR), TR gradient, pericardial thickness, pericardial calcification, myocardial architecture and tissue doppler was performed. Patients with primary diagnosis of CP were subjected to cardiac CT, while those with primary diagnosis as RCM were subjected to MRI/cardiac catheterization and endomyocardial biopsy for further confirmation and diagnosing the etiology of RCM. In case of diagnostic dilemma, usually a CT was done followed by MRI/cardiac catheterization if diagnosis is still elusive. CP diagnosis was finally confirmed on surgery for patients who underwent pericardiectomy.

All the patients with confirmed diagnosis of either condition on the basis of clinical evaluation, echocardiography, CT or MRI and hemodynamic assessment were enrolled in the study. The blood sample for NT-pro-BNP was obtained in the morning after at least 30-min rest. NT-pro-BNP measurement was done for all the patients using quantitative assay for NT-pro-BNP by Roche diagnostics, Basel, Switzerland.

3. Statistical analysis

Statistical analysis was performed using STATA 11.0 (College Station, Texas, USA) statistical software. Results are presented as mean (SD) when parametric tests were used, and median (IQR) when non-parametric tests were used. Student's *t*-test was done to compare the means of continuous variables. Two-sample Mann Whitney test was used to compare non-parametric variables. A p value of <0.05 was taken as significant. Nonparametric estimation of receiver operating characteristics curve was used to derive cut off values for NT-pro-BNP levels.

4. Results

We studied 49 patients with confirmed diagnosis of either RCM or CP based on various tests. No patient was excluded due to suspected radiation CP. Two patients with RCM were excluded as they were of end stage disease. All these patients were on a stable dose of standard therapy including diuretics, ACE inhibitors and beta blockers. All patients had normal renal functions. Table 1 summarizes the characteristics of the two groups of patients. Patients with CP were younger, had relatively lower hemoglobin values and higher ESR as compared to RCM. Various other parameters like duration of disease, NYHA class, extent of hepatomegaly, 6-min walk test and left ventricular (LV) function were not statistically different between the two groups. None of the patients in the CP group had atrial or ventricular enlargement on echocardiography. Similarly, none of the patients in the RCM group had pericardial thickening, calcification or effusion. Majority of patients [24 (82%)] in the CP group had significant respiratory variation in mitral/tricuspid inflow velocities while none in the RCM group had this finding. A mitral annular early diastolic velocity of >8 cm/s was seen in all patients with CP and in 3 (15%) with RCM. All patients with CP were of tubercular etiology and had completed or were receiving antitubercular treatment (ATT). In the RCM group 2 had cardiac amyloidosis,