Original Article

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Mid Regional Natriuretic Peptide for Predicting Prognosis of Hypertrophic Cardiomyopathy

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Abstract

Background: Hypertrophic cardiomyopathy (HCM) is a genetic disorder of cardiac myocytes that is characterized by cardiac hypertrophy, cellular disarray and interstitial fibrosis. Mutation of MYH7 and MYBPC3 encoding proteins β-myosin heavy chain and myosin binding protein C, respectively, are the two most common genes involved, together accounting for about 50% of cases. The present study was conducted to evaluate the prognostic value of MR-proANP in patients with HCM. **Subjects and Methods:** The present study was conducted at Narayana Medical College & Hospital, Chintareddy Palem, Nellore, Andhra Pradesh from July 2016 to July 2017 on 46 patients of hypertrophic cardiomyopathy of both genders. Serum NT-proBNP was measured by a two-site electrochemiluminescence immunoassay on a Roche Diagnostics E170 analyser. **Results:** The mean systolic blood pressure was 124.8 mm Hg, diastolic blood pressure was 78 mm Hg, heart rate was 68 beats/minutes, NYHA 1(n=4), NYHA 2 (n=27), NYHA 3–4 (n=15) and atrial fibrillation was 12%. The mean MR-proANP was 106 pmol/L and NT-proBNP was 540 pg/mL at the start of the study. At the end of 12 months of follow up, 15 patients had a primary end point defined as heart failure hospitalisation (n=10), heart transplant (n=3) death(n=2). Both mean MR-proANP and NT-proBNP were strongly associated with the primary end points at the end of study period with values of 1010 pmol/L and 2545 pg/ml respectively. This showed a strong association with P <0.05. **Conclusion:** Authors found that MR-proANP is a valuable biomarker for the prediction of heart failure related events in patients with HCM.

Keywords: Heart Failure, Hypertrophic Cardiomyopathy, Immunoassay

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Introduction

Hypertrophic cardiomyopathy (HCM) is a genetic disorder of cardiac myocytes that is characterized by cardiac hypertrophy, unexplained by the loading conditions; a nondilated left ventricle; and a normal or increased ejection fraction.[1] Cardiac hypertrophy is usually asymmetrical with greatest involvement most commonly of the basal interventricular septum subjacent to the aortic valve. It is occasionally restricted to other myocardial regions, such as the apex, the midportion and the posterior wall of the left ventricle. At the cellular level, cardiac myocytes are hypertrophied, disorganized, and separated by areas of interstitial fibrosis. HCM is a disorder without a distinct geographic, ethnic or sex pattern of distribution. Prevalence of HCM has been estimated at 0.16% to 0.29% in the general adult population.[2] In adults, HCM may be diagnosed by the presence of left ventricular end diastolic wall thickness >13 mm on an echocardiogram or other imaging technique. The European Society of Cardiology guidelines recommend using a left ventricular wall thickness of $\geq$15 mm in the diagnostic criteria.[3] Estimating the prevalence of HCM based on detection of cardiac hypertrophy, although clinically valuable, has many limitations.[4]

Natriuretic peptides are released from the heart due to increased myocardial wall stretch caused by volume and pressure overload. Mid-regional proatrial natriuretic peptide (MR-proANP) is the mid-regional epitope of the ANP prohormone which, like NT-proBNP, has a long circulating half-life.[5] MR-proANP may be equal or superior to BNP or NT-proBNP for diagnosis and prognosis in heart failure (HF). The present study was conducted to evaluate the prognostic value of MR-proANP in patients with HCM.

Subjects and Methods

The present study was conducted at Narayana Medical College & Hospital, ChintareddyPalem, Nellore, Andhra Pradesh from July 2016 to July 2017 on 46 patients of

hypertrophic cardiomyopathy of both genders. The patients were informed regarding the study and written consent was taken. Institutional Ethical approval was obtained from committee before starting the study.

Left ventricular hypertrophy was assessed with echocardiography according to published criteria.[4] Left ventricular end diastolic and end systolic diameters and left atrial diameters were obtained from M-Mode and two-dimensional images from the parasternal view. LVEF was calculated according to Simpson biplane method. Septal and posterior wall thicknesses were measured from the parasternal view.

Venous blood samples were collected. Samples were immediately centrifuged. Supernatant serum was stored at −80°C until the samples were analysed. Serum NT-proBNP was measured by a two-site electrochemiluminescence immunoassay on a Roche Diagnostics E170 analyser. Results were subjected to statistical analysis. P value less than 0.05 was considered significant.

Results

Table 1: Distribution of patients

Total- 46		
Gender	**Males**	**Females**
Number	26	20

Table 1 shows that out of 46 patients, males were 26 and females were 20.

Table 2: Assessment of parameters

Parameters	**Mean**
Systolic blood pressure	124.8 mm Hg
Diastolic blood pressure	78 mm Hg
Heart rate	68 beats/min
NYHA 1	4
NYHA 2	27
NYHA 3–4	15
Atrial fibrillation	12%

Table 2 shows that mean systolic blood pressure was 124.8 mm Hg, diastolic blood pressure was 78 mm Hg, heart rate was 68 beats/minutes, NYHA-1 was 4, NYHA-2 was 27, NYHA 3–4 was 15 and atrial fibrillation was 12%.

Table 3 shows that mean MR-proANP was 106 pmol/L and NT-proBNP was 540 pg/mL, LV end diastolic dimension was 46 mm, LV ejection fraction was 62 %, LV ejection fraction <50% was 40, posterior wall thickness was 12 mm, septal wall thickness was 19 mm, maximum wall thickness was 20 mm and left atrial diameter was 42 mm.

Table 3: Different variables

Variables	**Mean**
MR-proANP (pmol/L)	106
NT-proBNP (pg/mL)	540
Echocardiography data	
LV end diastolic dimension	46 mm
LV ejection fraction	62 %
LV ejection fraction <50%	40
Posterior wall thickness	12 mm
Septal wall thickness	19 mm
Maximum wall thickness	20 mm
Left atrial diameter	42 mm

Table 4: Marker values

Markers (mean)	**Start of study (n=46)**	**End of study(end point achievers n=15).**
NT-proBNP (pg/mL)	540	2545*
MR-proANP (pmol/L)	106	1010*

*P<0.05

Table 4 shows the statistically significant increase in mean values of both NT-proBNP and MR-proANP of those who achieved primary end point.

Discussion

Hypertrophic cardiomyopathy (HCM) is a genetic disorder that is characterized by left ventricular hypertrophy unexplained by secondary causes and a nondilated left ventricle with preserved or increased ejection fraction. It is commonly asymmetrical with the most severe hypertrophy involving the basal interventricular septum. Left ventricular outflow tract obstruction is present at rest in about one third of the patients and can be provoked in another third.[6] The histological features of HCM include myocyte hypertrophy and disarray, as well as interstitial fibrosis. The hypertrophy is also frequently associated with left ventricular diastolic dysfunction. In the majority of patients, HCM has a relatively benign course. However, HCM is also an important cause of sudden cardiac death, particularly in adolescents and young adults. The diagnostic and prognostic values of brain natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) are now well-

established in heart failure. In HCM, increased BNP and NT-proBNP concentrations have been associated with evidence of ventricular dysfunction, exercise intolerance, the development of heart failure and death.[7] The present study was conducted to evaluate the prognostic value of MR-proANP in patients with HCM.

In present study, out of 46 patients, males were 26 and females were 20. Begue et al,[8] compared the prognostic value of MR-proANP and NT-proBNP in HCM. Of 357 patients enrolled, the median age was 52 years. MR-proANP and NT-proBNP were both independently associated with age, weight, New York Heart Association (NYHA) class, left ventricular ejection fraction (LVEF), wall thickness and left atrial dimension. During a median follow-up of 12 months, 15 patients had a primary end point defined as death (n=2), heart transplantation (n=3), and heart failure hospitalisation (n=10). Both NT-proBNP and MR-proANP (p<10–4) were strongly associated with the primary endpoint, and the areas under the receiver operating characteristic (ROC) curves for both peptides were not significantly different. However, in a multiple stepwise regression analysis, the best model for predicting outcome was NYHA 1–2 vs 3–4, LVEF and MR-proANP.

We found that mean systolic blood pressure was 124.8 mm Hg, diastolic blood pressure was 78 mm Hg, heart rate was 68 beats/minutes, NYHA 1was 136, NYHA 2 was 148, NYHA 3–4 was 38 and atrial fibrillation was 12%. The mean MR-proANP was 106 pmol/L, NT-proBNP was 540 pg/mL, LV end diastolic dimension was 46 mm, LV ejection fraction was 62 %, LV ejection fraction <50% was 40, posterior wall thickness was 12 mm, septal wall thickness was 19 mm, maximum wall thickness was 20 mm and left atrial diameter was 42 mm.

Briguori et al,[9] reported that plasma concentration of ANP in HCM was strongly associated with left atrial function, whereas BNP was strongly associated with obstruction. Only one study, including only 40 patients, has investigated MR-proANP in patients with HCM, showing that among several biomarkers, MR-proANP was the only one associated with the extent of late gadolinium enhancement on MRI.

Geske et al,[10] reported increased plasma concentrations of BNP and NT-proBNP in patients with HCM and shown that they are associated with more left ventricular hypertrophy, more left ventricular outflow tract obstruction, left ventricular diastolic and systolic dysfunction, worse symptoms and reduced exercise tolerance. This is not unexpected, as the main source of BNP is cardiomyocytes and increased ventricular wall stress the major stimulus to its secretion.

Conclusion

Authors found that MR-proANP is a valuable biomarker for the prediction of heart failure related events in patients with HCM.

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