Research Paper Medical science

Relation Between NT-ProBNP and Left Ventricular Filling Pressures in Chronic Heart Failure Patients with Preserved Ejection Fraction

Rayna Tasheva, MD | Department of Cardiology, Second MHAT – Sofia, Bulgaria

ABSTRACT

Natriuretic peptides reflect ventricular pressure in patients with chronic heart failure. We assumed that NT-proBNP levels correlate with indices of LV diastolic function by tissue Doppler imaging.Materials and methods: The study subjects consisted of 56 hospitalized patients with preserved ejection fraction. Doppler recordings of the mitral inflow and tissue Doppler imaging of the mitral annulus were obtained. All recruited subjects underwent coronary angiography (CAG) and invasive measurement of LVEDP. Plasma NT-proBNP levels were measured immediately before the invasive procedure. Results:Significant positive correlation between NT-proBNP and LVEDP, as well as between NT-proBNP and E/e'ratio was observed (p=0.003, p= 0,001 respectively). Conclusion: The combination of NT-proBNP levels along with E/E' ratios from tissue Doppler imaging may be a better predictor of elevated LV filling pressures in patients with suspected diastolic dysfunction.

KEYWORDS | Natriuretic peptides, left ventricular filling pressures

Introduction

Diastolic heart failure affects approximately 50% of patients presenting with signs and symptoms of heart failure[4, 6]. Data suggest that 5-year mortality from diastolic heart failure is high and comparable to systolic heart failure [6]. Despite improvements in therapy, the prognosis of patients with chronic heart failure with preserved EF remains poor.

Different noninvasive diagnostic tools are applied for the assessment of diastolic function and left ventricular filling pressures. Echocardiography is the most frequently used method for the evaluation of diastolic dysfunction. The transmitral and pulmonary venous flow velocities obtained by pulsed wave Doppler echocardiography and mitral annular velocities by tissue Doppler imaging are the most useful parameters used for the assessment of diastolic dysfunction [5,8]. Several studies demonstrated close correlation between LVEDP and E/E'ratio. However, there are a number of clinical settings in which annular velocity measurements and the E/é ratio may not provide a reliable estimate of filling pressures and should not be used as the sole data in drawing conclusions about LV diastolic function.

This necessitated a search for noninvasive markers of elevated LVEDP and the wide use of natriuretic peptides in the diagnosis of heart failure. Several clinical and epidemiological studies have demonstrated a direct relationship between increasing plasma concentrations of natriuretic peptides and decreasing left ventricular functions [1,3] .However the role of NT-proBNP in the diagnosis of diastolic heart failure is contentious.

The aim of present research was to investigate the correlation between NT-proBNP and LVEDP in patients with chronic heart failure and compare it with the results of echocardiographic assessment of diastolic function.

Materials and methods:

This study was conducted in Department of cardiology, Second MHAT – Sofia, Bulgaria and was approved by the local ethics committee. The study included patientswith preserved EF who were referred to coronary care unit for assessment of coronary artery disease.Patients with acute coronary syndromes were excluded. All patients with history of hematological, neoplastic, renal, liver, or thyroid diseases, and patients with infections and autoimmune diseases were excluded from the study, as well as patients with stroke and recent myocardial infarction (< 3 months).

A total number of 56 patients (34 men and 22 women) were recruited. Demographic data, medical treatment and history were obtained from the hospital record. Doppler recordings of the mitral inflow and tissue Doppler imaging of the mitral annulus were obtained. Lateral Tissue Doppler signals were used for the estimation of left ventricular diastolic function and E/e'ratio. Venous blood samples were obtained from participants before CAG for determining NT-proBNP levels. The serum level of NT-proBNP was determined using the technique of Enzyme Linked Fluorescent Assay - ELFA (VIDAS NT-proBNP automated test for use on the VIDAS instrument). All recruited subjects underwent coronary angiography (CAG) and invasive measurement of left ventricular end-diastolic pressure.

Patients were allocated to a control group (N=21), comprising patients without symptoms of heart failure, with preserved ejection fraction and E/e'ratio< 8 or to a CHF group (N=35), comprising patients with symptomatic heart failure, preserved ejection fraction and E/E'ratiofrom 9 to 14 and > 15. Patients with E/E'ratio in the "grey zone" were included in the study only if their LAVI was > 38 ml/m^2.

Statistical Analysis

Clinical variables were normally distributed and expressed as mean ± standard deviation (SD). Unpaired student's t-test was used to evaluate differences in normally distributed continuous variables between the two groups. Correlation analysis between variables of the study was made by means of rho correlation coefficient r for continuous variables. The difference in variables were evaluated by the ANOVA test followed by a Bonferroni post-hoc test. P values < 0,05 were considered to be statistically significant.All calculations were made using SPSS statistical software for Windows (version 19.0).

Results

Table 1 shows the baseline characteristics of the study population. The CHF group included 35 patients aged 52 to 84 (mean 66.7 ± 7.5 years). 65.7 %(23) of patients in the group were men and 34.3% (12) were women. The control group included 21 patients, mean age was 59 ± 5.7 years. 52, 4 %(11) of them were men and 47, 6% (10) were women.

Table 1. *Characteristics of the study population. Risk profile of participants in both groups*

	CHF (n= 35)	Control group (n=21)
Arterial hypertension	88.6% (31)	71.4% (15)
Diabetes mellitus	28.6% (10)	28.6% (6)
Smokers	37.1 % (13)	57.1% (12)
Dyslipidemia	45.7% (16)	52.4% (11)
BMI > 25 kg/m^2)	11.4% (4)	52.4% (11)
Family history of CAD	40% (14)	42.9% (9)

Each patient underwent echocardiographic assessment of left ventricular ejection fraction, Doppler recordings of mitral inflow and TDI of the mitral annulus. Tissue Doppler E', A' and S' were derived from the lateral mitral-annular border. In patients with E/e' ratio from 9 to 14 LAVI was measured. The echocardiography was performed immediately before the NT-proBNP samples collection. According to the E/e'ratio the patients were allocated to a control group (E/e'< 8) and CHF group with E/e' ratio9-14 and LAVI > 38 ml/m^{2}and E/e'> 15.

Immediately after the echocardiography venous blood samples were obtained from participants for determining NT-proBNP levelsbefore the invasive measurement of LVEDP.

Serum NT-proBNP levels were significantly higher in the CHF group compared to the control group (432,60 ± 366,61 pg/ml vs 192,04 ± 95,17 pg/ml, p= 0,005). Invasive measurement of LVEDP showed significantly higher filling pressures in the CHF group14,11 ± 4,7 mmHg vs. 10,42 ± 1.8mmHg in the control group (p=0,003).

In the control group no correlation between NT-proBNPlevels and E/e'ratio was observed (p=0,181), neither between LVEDP end E/e' ratio (p=0,248). In the CHF group, however, there was a positive correlation between LVEDP and E/e'(p=0,003) and between E/e'and NT-proBNP levels. (Figure 1 and 2).

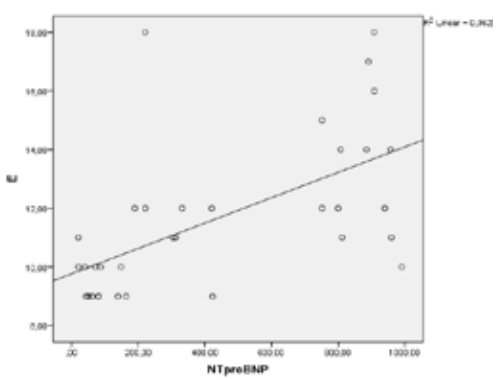


Figure 1. Correlation between NT-proBNP and E/e'ratio in CHF patients with preserved EF

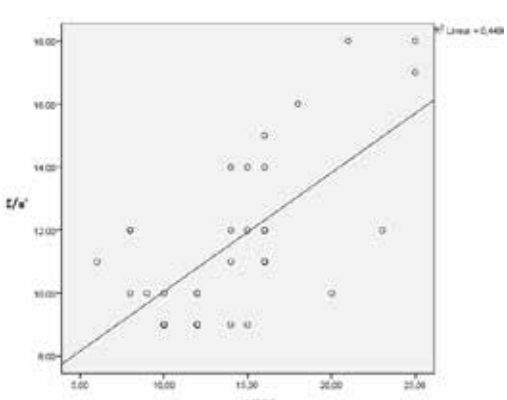


Figure 2. Correlation between LVEDP and E/e' ratio in CHF patients with preserved EF

In the chronic heart failure group with preserved EF, the subgroup of patients with E/e'ratio in the "grey zone" is problematic due to the fact that the E/e' ratiois uninformative of left ventricular filling pressures. No correlation between LVEDP and E/e'is observed in this subgroup (p=0,241). However, in these patients with symptomatic CHF and E/e' 9-14 a positive correlation between NT-proBNP levels and E/e' ratio was found (p=0,001). Also there was a positive correlation between NT-proBNP and LVEDP (p=0,001) (Fig.3).

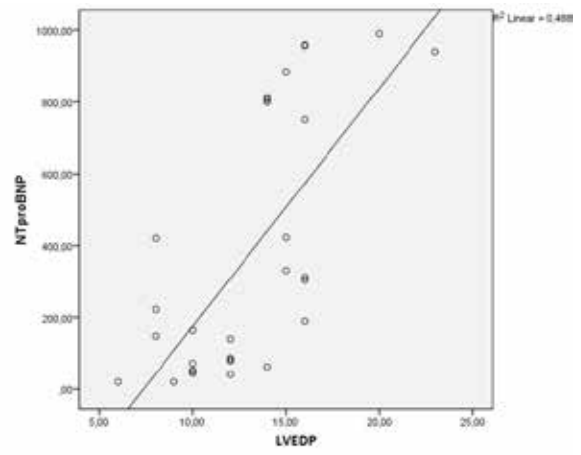
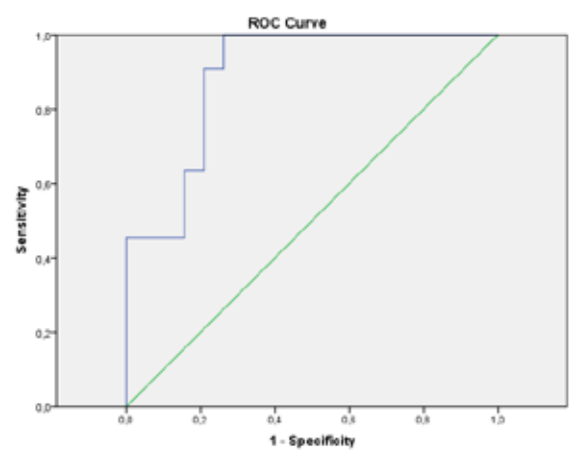


Fig.3. Correlation between NT-proBNP and LVEDP in patients with E/e' ratio in "grey zone" – 9-14

The ROC curve analysis (Fig.4) shows that NT-proBNP levels > 300 pg/ml are 90% sensitive and 40% specific for elevated left ventricular filling pressures in patients with diastolic heart failure and E/e' from 9 to 14. NT-proBNP measurement in these patients can be used for establishing the diagnosis of heart failure.



AUC – 0,890, p=0,001

Figure 4. ROC Curve. Analysis of specificity and sensitivity for elevated LVEDP in patients with HFpEF and E/e' 9-14

Discussion

Heart failure with preserved ejection fraction is one of the major problems in contemporary cardiology not only because of the difficulties in the diagnostic process but also because of the poor prognosis and high mortality rates.Diagnosis of HFpEF is frequently challenging, especially in patients with several comorbidities. The low sensitivity and specificity of heart failure symptoms and signs as well as their often milder manifestation in patients with preserved EF can make the diagnosis very difficult, especially in the early stages. There is no quanti-

tative criteria for the estimation of heart failure. The sole hemodynamic criterion to objectify the presence of the clinical syndrome is elevated LVEDP, which is practically inaccessible with noninvasive methods and its invasive measurement severely limits its use in routine clinical practice.

Different noninvasive diagnostic tools are applied for the assessment of diastolic function and left ventricular filling pressures. Echocardiography is the most frequently used noninvasive method for the evaluation of diastolic dysfunction and elevated left ventricular filling pressures. However, there are a number of clinical settings in which echocardiographic measurements may not provide a reliable estimate of filling pressures. One major drawback of E/e' ratiofor assessment of LVEDP is the big number of patients in the "grey zone" from 9 to 14. In these cases measurement of NT-proBNP serum levels can be useful for establishing the diagnosis of HFpEF. According to our data, there is a positive correlation between NT-proBNP and invasively measured LVEDP in patients with chronic heart failure and preserved ejection fraction, especially when the E/e' is uninformative.

Conclusion

The combination of NT-proBNP levels along with E/E' ratios from tissue Doppler imaging may be a better predictor of elevated LV filling pressures in patients with suspected diastolic dysfunction.NT-proBNP can be used as a predictor of increased LVEDP in patients with preserved EF and uninformative E/e' ratio (9-14).

REFERENCES

1. Groenning BA, Nilsson JC, Sondergaard L, Kjaer A, Larsson HB, Hildebrandt PR. Evaluation of impaired left ventricular ejection fraction and increased dimensions by multiple neurohumoral plasma concentrations. Eur J Heart Fail. 2001;3:699-708. | 2. Kasner M, Westermann D, Steendijk P, Gaub R, Wilkenshoff U, Weitmann K, et alUtility of Doppler echocardiography and tissue Doppler imaging in the estimation of diastolic function in heart failure with normal ejection fraction: a comparative Doppler-conductance catheterization study. Circulation 2007;11:637-47. | 3. McDonagh TA, Robb SD, Murdoch DR, Morton JJ, Ford I, Morrison CE, et al. Biochemical detection of left-ventricular systolic dysfunction. Lancet.1998;351:9-13. | 4. Mosterd A, Hoes AW. Clinical epidemiology of heart failure. Heart 2007;93:1137–1146. [PubMed: 17699180] (80) | 5. Myreng Y, Smiseth OA, Risøe C. Left ventricular filling at elevated diastolic pressures: relationship between transmitral Doppler flow velocities and atrial contribution. Am Heart J. 1990;119(3 Pt 1):620-6. | 6. Redfield MM, et al. Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. JAMA 2003;289:194–202. [PubMed:12517230] (98) | 7. Rivas-Gotz C, Manolios M, Thohan V, Nagueh SF. Impact of left ventricular ejection fraction on estimation of left ventricular filling pressures using tissue Doppler and flow propagation velocity. Am J Cardiol 2003;91:780-4. | 8. Thomas JD, Choong CY, Flachskampf FA, Weyman AE. Analysis of the early transmitral Doppler velocity curve: effect of primary physiologic changes and compensatory preload adjustment. J Am Coll Cardiol 1990;16:644-55.