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Correlation of NT-pro BNP Levels with Right Ventricular Parameters in Heart Failure due to Mitral Stenosis

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Abstract

Purpose: Mitral stenosis (MS) is a common valvular heart disease that often causes heart failure (HF). The right ventricle (RV) is frequently involved in MS, which contributes to clinical outcomes in patients. NT-pro BNP (N-terminal pro-B-type natriuretic peptide) is a widely used biomarker in the diagnosis and prognosis of heart failure. However, its relationship with RV parameters in patients with HF due to MS remains insufficiently explored. This study aimed to explore the correlation between NT-pro BNP levels and right ventricular parameters in patients with mitral stenosis.
Methodology: A total of 40 outpatient subjects with severe MS were included in this study. NT-pro BNP examination was performed using the ELISA method. RV parameter assessment was performed using echocardiography by assessing TAPSE (function) and RV basal diameter (dimension).
Results: RV function parameters (TAPSE) and NT-pro BNP showed a significant weak correlation (r=0.324; p=0.041). RV dimension parameters and NT-pro BNP did not show a significant relationship. Patients with RV dysfunction had greater increases in NT-pro BNP levels compared to patients with normal RV function (6441.25±773.18 vs 7671.87±788.72 pg/mL; p=0.172).
Applications/Originality/Value: Provides valuable insights into the pathophysiology of right heart involvement in MS and provides clinicians with potential biomarkers for early identification of RV dysfunction in MS patient population.

Introduction

Mitral stenosis (MS) is a valve heart disease commonly found in developing countries (Press and Hoke, 2011; Watkins et al., 2017). This disease is mainly caused by rheumatic fever, which causes the narrowing of the mitral valve and progresses to heart failure (Peters et al., 2020). The narrowing of the mitral valve impedes blood flow from the left atrium to the left ventricle, leading to increased left atrial pressure and subsequent pulmonary hypertension (Silbiger, 2021). Over time, this increased pressure can lead to right ventricular (RV) dysfunction as the right heart works to cope with the increased afterload (Goransson et al., 2022; Taamallah et al., 2022).

In individuals with mitral stenosis, right ventricular dysfunction is a significant predictor of morbidity and mortality (Sari and Soesanto, 2024). In this regard, various biomarkers and imaging modalities are used to assess the right ventricle dysfunction. Among these biomarkers, N-terminal pro B-type natriuretic peptide (NT-pro BNP) has emerged as a sensitive indicator of heart failure, reflecting the myocardial stress that occurs during the development of valvular heart disease (Samiei et al., 2020). The main cause of NT-pro BNP's release is elevated ventricular wall tension, and it may be used as a noninvasive indicator to assess the degree of heart failure, including right ventricular dysfunction (Pradhan et al., 2020; Safi et al., 2017).

The relationship between NT-pro BNP levels and RV parameters, including RV size and function remains an area of ongoing investigation. Several studies have established that elevated NT-pro BNP correlates with poor outcomes in heart failure and left ventricular dysfunction, its role in predicting RV dysfunction in the context of mitral stenosis is less well understood. Understanding this correlation may improve clinical decision-making by providing a noninvasive tool to predict RV involvement and guide treatment strategies in patients with MS.

This study aimed to explore the correlation between NT-pro BNP levels and right ventricular parameters in patients with MS. By evaluating this relationship, we hope to provide valuable insights into the pathophysiology of right heart involvement in MS and provide clinicians with a potential biomarker for early identification of RV dysfunction in this patient population.

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Method

This study included outpatients diagnosed with severe MS due to Rheumatic Heart Disease (RHD) at Panti Rahayu and Permata Bunda Hospitals in Purwodadi, Indonesia. The following inclusion criteria were used: planimetric mitral valve area less than 1.5 cm^2 on echocardiography (Ganesan, 2017; Pandian et al., 2023) with morphology indicating RHD (calcification and fusion of the valve leaflets and commissures, and limited valve mobility).

This study excluded patients with hemodynamic instability or severe acute decompensation, defined by ascites, signs and symptoms of cardiogenic/hypovolemic shock, or congestion manifested by crackles in more than one-third of the lung fields. Patients with other moderate to severe mitral and aortic valve diseases, pregnancy, and lactation were also excluded.

The levels of NT-pro BNP were measured using the enzyme-linked immunosorbent assay (ELISA) technique. This biomarker examination was conducted at the Sebelas Maret University biomedical laboratory.

The right ventricular parameters measured in this study consisted of RV functional and dimensional parameters. Right ventricular function was measured using the Tricuspid annular systolic plane excursion (TAPSE) method via echocardiography. TAPSE is defined as the lateral displacement of the TV annulus during systole by M-mode echocardiography (Aloia et al., 2016). TAPSE is considered abnormal if the value is <17 mm. TAPSE is closely related to RV ejection fraction (RVEF) and is a strong prognostic marker in PH and other heart diseases (Aloia et al., 2016). RV dimension is calculated by measuring the basal diameter of the RV on the apical 4-chamber view on echocardiography, with normal values being 25–41 mm (Zaidi et al., 2020).

Results and Discussion

This study involved 40 outpatients who met the study criteria. The subjects in this study were mostly female and had an average age of 52.50 ± 8.85 years. All subjects had atrial fibrillation and high NT-pro BNP levels (6933.5 ± 3558.41 pg/mL). Detailed descriptions of the baseline characteristics of the subjects are described in Table 1.

Table 1. Baseline characteristics

Characteristics	All subjects (n=40)
Demography and comorbidities	
Age, years	52.50±8.85
Female, n (%)	35 (87.5%)
Body Mass Index (BMI), kg/m2	22.01±3.01
Atrial fibrillation (%)	40 (100%)
Hypertension, n (%)	4 (10.0%)
Type 2 diabetes, n (%)	2 (5%)
Coronary artery disease, n (%)	0 (0%)
Smoker, n (%)	3 (7.5%)
Creatinine, mg/dL	1.03±0.44
Estimated glomerular filtration rate (eGFR), mL/ mL/min/1,73 m2	65.00±25.29
N-terminal prohormone of brain natriuretic peptide (NT-pro BNP), pg/mL	6933.5±3558.41
Echocardiography parameters	
MVA planimetry, cm^2	0.76±0.13
LA diameter, mm	54.74±9.38
RV dimension basal diameter, mm	34.69±5.76
Left ventricular internal end-diastolic diameter (LVIDd), mm	47.07±6.83
Mean pressure gradient mitral, mmHg	12.81±4.52
Systolic pulmonary artery pressure, mmHg	17.30±5.93
LVEF, %	55.75±9.44
TAPSE, mm	18.11±5.55
Pulmonary hypertension probability (intermediate to high), %	33 (82.5%)

This study found that there was a significant weak correlation between NT-pro BNP and RV function parameters (TAPSE). While there was no significant relationship between NT-pro BNP and RV dimension parameters. Detailed descriptions of correlation between NT-pro BNP and RV function parameters are described in Table 2.

Table 2. Correlation of NT-pro BNP with RV parameters

	r	p-value
NT-pro BNP with RV dimension	-0,149	0.360
NT-pro BNP with TAPSE	0.324	0.041

There was a higher increase in NT-pro BNP levels in the group of patients with RV dysfunction (TAPSE <17 mm) compared to those with normal RV function (6441.25±773.18 vs 7671.87±788.72 pg/mL) although the value was not significant (p=0.172). Comparison between groups based on RV function can be seen in figure 1.

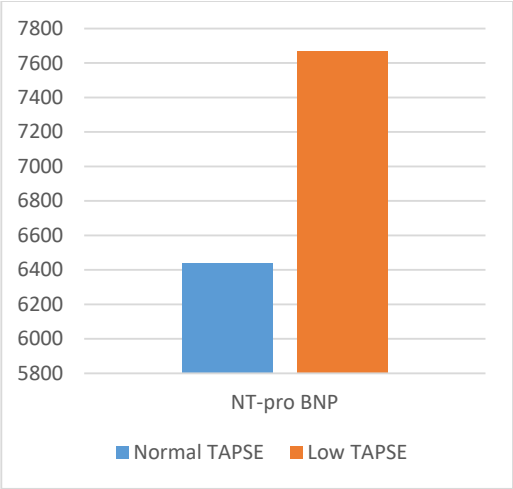

Figure 1. NT-pro BNP levels based on RV functions

It is well recognized that the survival, exercise capacity, and clinical symptoms of patients with mitral stenosis (MS) are significantly influenced by right ventricular (RV) function. Increased left atrial pressure, alterations in the pulmonary arteriolar vasculature, rheumatic process, myocardial and hemodynamic variables, pulmonary arterial hypertension, and right and left ventricular interaction are some of the causes of RV dysfunction (Sari and Soesanto, 2024). These conditions cause stress on the RV myocardial wall and theoretically will cause an increase in NT-pro BNP levels. This increase in NT-pro BNP levels should also better reflect the stress conditions in the RV because hemodynamically the Left Ventricular (LV) in MS is relatively low hemodynamic stress due to blood flow limitation caused by mitral valve stenosis.

However, in this study, only a weak correlation was found in the correlation analysis of NT-pro BNP levels and RV function through TAPSE examination. Longitudinal RV function parameters such as TAPSE are parameters that are often affected by increased afterload in rheumatic MS, even before significant pulmonary hypertension appears. This is due to the dominant longitudinal RV contraction in physiological conditions, so that changes in afterload will have an impact on RV function (Khan et al., 2019; Ladányi et al., 2024). However, TAPSE measurement depends on the load and image angle. In tricuspid regurgitation, pseudo-normalization can also occur due to additional load (Aloia et al., 2016). TAPSE can only assess the longitudinal function of the RV-free basal wall, and not the global RV function (Damy et al., 2012). Until now, there is no single parameter that can truly describe the global RV function (Sari and Soesanto, 2024).

This study also found no significant relationship between RV dimensions and NT-pro BNP levels. In addition to causing hemodynamic stress and leading to impaired function, RV overload conditions due to the MS process in the left heart will also result in an increase in RV dimensions. However, this was also not proven in this study.

The NT-pro BNP source in MS cases is still being studied. Several recent studies, for example, have revealed that although the LV does not experience hemodynamic stress, fibrosis was found in the LV wall which could be from the inflammatory stress process due to RHD (Elen et al., 2018). This stress condition may cause an increase in NT-pro BNP.

According to other studies, NT-pro BNP can be produced in locations other than the myocardial ventricles. Khare and Dwivedi (2016) discovered a relationship between left atrial dysfunction assessed using tissue doppler-derived strain/strain

rate (S/Sr) and NT pro BNP levels in patients with mitral stenosis who had percutaneous balloon mitral valvuloplasty (PMBV) (Khare and Dwivedi, 2016). From this study, NT-pro BNP level can also be used to predict improvement in left atrial function after PMBV. In another study by Inoue et al (2000) in patients with lone atrial fibrillation, it was observed that NT-pro BNP concentrations were elevated in blood samples collected from the coronary sinus compared to those obtained from the aorta or the anterior interventricular vein (AIV). The samples from the coronary sinus serve as indicators of the levels present in the atrium (Inoue et al., 2000). Based on these facts, it is still possible that other components such as the LV and left atrium play a role in increasing NT-pro BNP levels, so this study only found a weak correlation between NT-pro BNP levels and RV function. Based on the findings and limitations of this study, it is still necessary to measure other RV parameters as well as LV and LA parameters for further analysis.

Conclusions

In this study, a significant weak correlation was found between NT-pro BNP values and RV function parameters, but no correlation was found between NT-pro BNP and RV dimension parameters. Higher levels of NT-pro BNP were found in patients with decreased RV function, although the values were not significantly different.

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References

Aloia, E., Cameli, M., D'Ascenzi, F., Sciaccaluga, C., Mondillo, S., 2016. TAPSE: An old but useful tool in different diseases. Int J Cardiol. https://doi.org/10.1016/j.ijcard.2016.10.009

Damy, T., Kallvikbacka-Bennett, A., Goode, K., Khaleva, O., Lewinter, C., Hobkirk, J., Nikitin, N.P., Dubois-Randé, J.L., Hittinger, L., Clark, A.L., Cleland, J.G.F., 2012. Prevalence of, associations with, and prognostic value of tricuspid annular plane systolic excursion (TAPSE) among out-patients referred for the evaluation of heart failure. J Card Fail 18, 216–225. https://doi.org/10.1016/j.cardfail.2011.12.003

Elen, E., Atmadikoesoemah, C.A., Kasim, M., 2018. Effect of Myocardial Fibrosis on Left Ventricular Function in Rheumatic Mitral Stenosis: A Preliminary Study with Cardiac Magnetic Resonance. Indonesian Journal of Cardiology 38, 202–206. https://doi.org/10.30701/ijc.v38i4.785

Ganesan, G., 2017. How to Assess Mitral Stenosis by Echo - A Step-by-Step Approach. Journal of the Indian Academy of Echocardiography & Cardiovascular Imaging 1, 197–205. https://doi.org/10.4103/jiae.jiae

Göransson C, Vejlstrup N, dan Carlsen J. 2022. Clinically important changes in right ventricular volume and function in pulmonary arterial hypertension assessed with cardiac magnetic resonance imaging. Pulm Circ. 12(3):e12097.

Inoue, S., Murakami, Y., Sano, K., Katoh, H., Shimada, T., 2000. Atrium as a source of brain natriuretic polypeptide in patients with atrial fibrillation. J Card Fail 6, 92–96. https://doi.org/10.1016/s1071-9164(00)90010-1

Khan, I., Shahbaz, A., Iqbal, M., Khan, A.R., Riaz, W., Sayyed, M.S., Khan, K., 2019. Tricuspid annular plane systolic excursion is correlated with poor outcome in surgery for rheumatic heart valvular disease. ARYA Atheroscler 15, 130–135. https://doi.org/10.22122/arya.v15i3.1688

Khare, R., Dwivedi, S., 2016. NT-ProBNP as a Potential Marker of Left Atrial Dysfunction in Rheumatic Mitral Stenosis: Correlation with Left Atrial Function after PBMV. J Heart Valve Dis 25, 613–618.

Ladányi, Z., Eltayeb, A., Fábián, A., Ujvári, A., Tolvaj, M., Tokodi, M., Choudhary, K.A., Kovács, A., Merkely, B., Vriz, O., Lakatos, B.K., 2024. The effects of mitral stenosis on right ventricular mechanics assessed by three-dimensional echocardiography. Sci Rep 14. https://doi.org/10.1038/s41598-024-68126-y

Pandian, N.G., Kim, J.K., Arias-Godinez, J.A., Marx, G.R., Michelena, H.I., Chander Mohan, J., Ogunyankin, K.O., Ronderos, R.E., Sade, L.E., Sadeghpour, A., Sengupta, S.P., Siegel, R.J., Shu, X., Soesanto, A.M., Sugeng, L., Venkateshvaran, A., Campos Vieira, M.L., Little, S.H., 2023. Recommendations for the Use of Echocardiography in the Evaluation of Rheumatic Heart Disease: A Report from the American Society of Echocardiography. Journal of the American Society of Echocardiography 36, 3–28. https://doi.org/10.1016/j.echo.2022.10.009

Peters F, Karthikeyan G, Abrams J, et al. 2020. Rheumatic heart disease: current status of diagnosis and therapy. Cardiovascular diagnosis and therapy. 10(2):305.

Pradhan, N.M., Mullin, C., Poor, H.D., 2020. Biomarkers and Right Ventricular Dysfunction. Crit Care Clin. https://doi.org/10.1016/j.ccc.2019.08.011

Press, D. & Hoke, T. 2011. The worldwide epidemiology of acute rheumatic fever and rheumatic heart disease. Clinical Epidemiology, 1(434): 67–84.

Safi, M., Bayat, F., Ahmadi, Z., Shekarchizadeh, M., Khaheshi, I., Naderian, M., 2017. The change in NT-pro-BNP and post-PTMC echocardiography parameters in patients with mitral stenosis. A pilot study. Rom J Intern Med 55, 75–81. https://doi.org/10.1515/rjim-2017-0005

Samiei, N., Zolfaghari, R., Sanati, H., Tabrizi, R.R., Zahedmehr, A., Firouzi, A., 2020. NT-probnp in mitral stenosis: Can it be a predictor of hemodynamic status? Iranian Heart Journal 21, 98–104.

Sari, N.M.A.W., Soesanto, A.M., 2024. Right ventricular function in mitral stenosis: plays a fundamental role. J Echocardiogr. https://doi.org/10.1007/s12574-024-00663-x

Silbiger, J.J., 2021. Advances in Rheumatic Mitral Stenosis: Echocardiographic, Pathophysiologic, and Hemodynamic Considerations. Journal of the American Society of Echocardiography 34, 709-722.e1. https://doi.org/10.1016/j.echo.2021.02.015

Taamallah K, Jabloun TY, Guebsi M, et al. 2022. Subclinical right ventricular dysfunction in patients with mitral stenosis. J Echocardiogr. 20:87–96

Watkins, D.A., Johnson, C.O., Colquhoun, S.M., Karthikeyan, G., Beaton, A., Bukhman, G., Forouzanfar, M.H., Longenecker, C.T., Mayosi, B.M., Mensah, G.A., Nascimento, B.R., Ribeiro, A.L.P., Sable, C.A., Steer, A.C., Naghavi, M., Mokdad, A.H., Murray, C.J.L., Vos, T., Carapetis, J.R. & Roth, G.A. 2017. Global, Regional, and National Burden of Rheumatic Heart Disease, 1990 2015. New England Journal of Medicine, 377(8): 713–722.

Zaidi, A., Knight, D.S., Augustine, D.X., Harkness, A., Oxborough, D., Pearce, K., Ring, L., Robinson, S., Stout, M., Willis, J., Sharma, V., 2020. Echocardiographic assessment of the right heart in adults: A practical guideline from the British Society of Echocardiography. Echo Res Pract. https://doi.org/10.1530/ERP-19-0051