Letter to the Editor: "Role of matrix metalloproteinases in mitral valve regurgitation: Association between the of MMP-1, MMP-9, TIMP-1, and TIMP-2 expression, degree of mitral valve insufficiency, and pathologic etiology".

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## Title Page

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To the Editor,

We read with great interest your article named "Role of matrix metalloproteinases in mitral valve regurgitation: Association between the of MMP-1, MMP-9, TIMP-1, and TIMP-2 expression, degree of mitral valve insufficiency, and pathologic etiology". The article is competent and well written. We concur with the findings that a clear correlation between the Matrix Metalloproteinases expression and the Mitral Insufficiency exists which also corresponds with the degree of severity. However, after thoroughly reviewing your article, there are a few ideas worth discussing that could enhance the quality of the overall article.

Referring to the original article, the authors mainly emphasized Matrix Metalloproteinases and their inhibitors. However, Brain Natriuretic Peptide BNP, a hormone secreted from myocardial cells is a strong

independent predictor of cardiac events. In asymptomatic degenerative mitral regurgitation, Left Ventricular longitudinal function and Left Atrial volume are the main determinants of BNP release. Measurement of BNP levels in plasma may aid in risk stratification and better management of asymptomatic patients with degenerative MR.<sup>2</sup> Furthermore, studies have shown that embolic myxomas also tend to show elevated MMP-2, MMP-9, and MT1-MMP levels and activity compared to nonembolic tumors; this was associated with an increase of extracellular matrix tumor degradation products containing glycosaminoglycans chains. These findings strongly suggest that MMPs may contribute to tumor ECM remodeling and increase the risk of embolism in cardiac myxomas. Thus, demonstrating increased activity and involvement of matrix metalloproteinases in cardiac myxoma embolism.<sup>3</sup> Additionally, MMP-2, MMP-9, and their inhibitor TIMP-1 are the most promising candidates Among signaling molecules that may have important prognostic value in Dilated cardiomyopathy, a type of heart muscle disease that causes ventricles to thin and stretch, growing larger. The MMP/TIMP ratio serves as a beneficial marker of developing fibrosis in the extracellular matrix and has prognostic value and importance in heart diseases. The activity of Matrix Metalloproteinases in tissues depends upon the presence of their tissue inhibitors. The expression of TIMP1 was decreased and the expression of MMP-1 in the myocardium was enhanced in patients with Dilated Cardiomyopathy in comparison with the normal.<sup>4</sup>

In conclusion, the study should also emphasize the measurements of Natriuretic peptide molecules such as BNP to conclude the symptoms and severity of mitral regurgitation. Screening for cancers should be considered as certain cardiac tumors also tend to increase the expression of MMPs. Inflammatory markers should also be checked as Inflammatory and viral conditions such as Viral myocarditis could also lead to increased expression of MMPs in cardiac tissues.

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