



## ***Tricuspid Regurgitation Improvement in Relation to the Amount of Pulmonary Artery Pressure Reduction***

I was interested in the study conducted by Dr. Zoroufian et al.,<sup>1</sup> in which they conclude, “the improvement in tricuspid regurgitation (TR) severity is directly correlated with the amount of pulmonary artery systolic pressure (PAPs) reduction after mitral balloon valvotomy (MBV)” and propose a moderately sensitive and specific cut-off point for PAPs change in the prediction of TR improvement. This conclusion is based on the post-MBV result, in which patients with TR severity improvement showed a greater decrease in PAPs following MBV than did those with unchanged or worsened TR grade ( $p$  value  $< 0.034$ ).

I believe the conclusion is not properly substantiated because there is a great mismatch between the groups and the paper fails to consider the possible influence of confounders. Based on their findings, the ejection fraction (EF) was significantly lower in patients who showed a worsening in the TR grade after intervention. Likewise, as it is accurately noticed in the discussion, right ventricular dilation is a common cause of functional TR,<sup>2, 3</sup> and mitral stenosis (MS) severity<sup>4</sup> has been indicated as a significant different variable in the comparison of patients with and without TR improvement following MBV. A comparison of the demographic data, which are highly associated with PAPs,<sup>5</sup> is also ignored in the current study. Taken together, I think there is a need to a comprehensive comparison of the demographic variables and echocardiographic measurements between the patients according to the TR change; and thereafter, all the significant variables in the univariate comparison (such as primary/secondary or/and changes in PAPs, right ventricular dimension [RVD], EF level, and possibly some demographic variables) along with the other possible confounders (initial MS grade or mitral valve area [MVA], MS severity change, or MVA increase) should be entered into the multivariable logistic model to identify the independent predictors of TR improvement. Finally, the associations of the independent predictors with TR improvement in the final model should be expressed as odds ratios (OR) with 95% CIs.

Furthermore, although PAPs  $> 35$  and PAPs  $\geq 25$  are mentioned as the definitions for pulmonary artery hypertension (PAH) according to the referred citations,<sup>6-8</sup> it is not definitely obvious what criteria are employed by the authors to define PAH. As I looked through the references, I did not find PAPs  $> 35$  as a definition for PAH. It was just mentioned that the upper limit value of PAPs in a normal population is 30mmHg. Accordingly, 28% of the normal

population had PAPs  $> 30$  mmHg in a study conducted by Berndan et al.<sup>5</sup> Moreover, even  $37 \leq \text{PAPs} \leq 50$  mmHg is considered a suggestive but not definite criterion for the presence of PAH.<sup>7</sup> Based on the current guidelines, mean PAP  $\geq 25$  mmHg (but not mean PAPs as it is written in the paper) at rest as assessed by right heart catheterization (RHC) is mentioned as a diagnostic criterion for PAH.<sup>6, 7</sup> After all, in regard to the aim of the study, it seems there is no need to use such a definition, and the use of PAPs as a quantitative variable for the subsequent analysis would lead to more accurate results.

The purpose of this letter is to point out some pitfalls which are generally ignored by the investigators and weaken the final conclusion. I hope it may be helpful.

## ***References***

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## **Tricuspid Regurgitation Improvement in Relation to the Amount of Pulmonary Artery Pressure Reduction: reply**

We appreciate Dr. H. Sadeghian's well-advised comments on our paper, entitled "Tricuspid regurgitation improvement in relation to the amount of pulmonary artery pressure reduction".<sup>1</sup> Dr. H. Sadeghian expresses concerns regarding the conclusions of the paper and the definition of pulmonary artery hypertension.

This study was aimed, as the manuscript title clearly reflects, to analyze whether the amount of changes in pulmonary artery systolic pressure (PAPs) can affect the changes in tricuspid regurgitation severity. It is well established that pulmonary hypertension is an important cause of functional tricuspid regurgitation and PAPs is a strong determinant of functional tricuspid regurgitation (TR) severity.<sup>2, 3</sup> In addition, right ventricle dilation and dysfunction may result in functional TR, and functional TR can secondarily be associated with left ventricle dysfunction and mitral valve disease (both mitral stenosis and regurgitation).<sup>4-6</sup> We studied a sample of patients with mitral stenosis who underwent mitral balloon valvoplasty (MBV). Our analysis was on the basis of the fact that in these patients, functional TR has been a consequence of increased PAPs secondary to severe mitral stenosis; the higher the severity of mitral stenosis (MS), the higher the PAPs and the higher the severity of TR grade. The increased PAPs is expected to decline following MBV. In the mentioned study, we presented a possible cut-off point for the amount of PAPs reduction showing TR severity improvement; and

the ROC (receiver-operating characteristic) analysis, which demonstrated a cut-off point of  $\geq 19$  mmHg reduction in PAPs with a 71.9% specificity and 52.7% sensitivity, might show at least a one-grade regress in TR severity.<sup>1</sup> It is deserving of note that we did not claim that we would aim either to identify the predictors of TR improvement or to find out the factors in association with PAPs. It is obvious that the determination of the predicting factors for the improvement of TR severity or the factors associated with increased PAPs (none of them was the aim of this study) requires a large sample size. Hopefully in the near future with a large study population, we will be able to present all the potential predicting factors for TR severity improvement in patients suffering from TR for any reasons, not just organic MS and its severity (our biostatistician whose name is revered amongst the co-authors approved the above remarks). We believe that Dr. H. Sadeghian is also aware that factors such as initial MS grade, mitral valve area, and MS severity change all affect TR severity improvement through changes in the pulmonary artery pressure and no one can claim that these factors directly affect the tricuspid valve in the right heart side.

With respect to pulmonary artery hypertension, we agree that in the references cited in the paper, PAPs  $> 35$  mmHg is defined as elevated PAPs. We found it reasonable to use this cut point to define pulmonary artery hypertension in the same manner as many other studies.<sup>7-10</sup> We would believe that if every investigator is restricted to define the study variables as guidelines, no new findings and conclusions can be added to our knowledge and future guidelines. In this study, we grouped the patients based on PAPs  $> 35$  mmHg so as to report only the frequency of the patients with pulmonary artery hypertension. We applied PAPs as a continuous variable in determining the cut-off value of the amount of PAPs reduction in relation with TR severity improvement, which means that even changing the definition would not influence the achieved cut-off point.

Finally, we should stress that all the patients with right ventricular dysfunction were excluded from the study. Also, no difference was found between the men and women regarding changes in PAPs and TR severity. These should have been mentioned in the method section, and we are grateful to have the opportunity to explain it in this reply.

We hope these lines will allow the esteemed readers to better understand the views mentioned.

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