Original Article

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

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Abstract

Background: *Given the common concomitance of tricuspid regurgitation (TR) with significant mitral stenosis, we aimed at exploring the relation between TR severity and pulmonary artery hypertension (PAH) in patients who underwent mitral balloon valvotomy (MBV).*

Methods: *We analyzed the echocardiography data of 133 consecutive patients (82.0% female, mean age 44.68 ± 12.56 years) with different degrees of TR severity that underwent MBV between April 2006 and March 2008. The pulmonary artery systolic pressure (PAPs) > 35 mmHg was considered as PAH.*

Results: *Before MBV, 36.20% of the patients had moderate to severe TR, 92.5% PAH, and 18.0% right ventricular (RV) dilation (RV dimension ≥ 33 mm). After MBV, TR severity improved in 41.4%, worsened in 8.3%, and did not change in 50.4%. Before and after MBV, PAPs was significantly correlated with TR severity, and the mean PAPs change in patients with improved TR was significantly more than that of patients without TR improvement (p value = 0.042). Tricuspid regurgitation severity and mean PAPs (from 52.83 ± 18.82 to 35.89 ± 9.39 mmHg) decreased significantly after MBV (both p values < 0.001); this reduction was significantly correlated to the amount of PAPs decrease. A cut-off point of ≥ 19 mmHg reduction in PAPs had a specificity of 71.79% and sensitivity of 52.73% to show TR severity improvement (by Receiver-Operative-Characteristics analysis). The mean of RV dimension decreased from 28.94 ± 5.43 to 27.95 ± 4.67 mm (p value < 0.001). In contrast to patients with RV dilation, TR reduced significantly in patients without RV dilation (p value < 0.001).*

Conclusion: *Improvement in TR severity was directly correlated with the amount of PAPs reduction after MBV. More studies are needed to better define a cut-off value for PAPs reduction related to TR severity improvement.*

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Introduction

Rheumatic heart disease is the most common cause of mitral stenosis.[1] In patients with long-standing left-sided valve disease, pulmonary hypertension is commonly present, which may thus give rise to the development of tricuspid regurgitation (TR).[2] In such cases, there have been reports of up to 28% of functional TR,[3] whose development is directly associated with increased morbidity and mortality.[4] Indeed, even moderate TR negatively impacts survival, regardless of left ventricular function or pulmonary arterial pressure.[5] It is thought that secondary TR decreases or even disappears

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after surgical correction of mitral valve disease.[6] It has also been demonstrated that significant TR in patients with severe mitral stenosis and severe pulmonary artery hypertension regresses after successful mitral balloon valvotomy (MBV),[7] as pulmonary arterial pressure reduction lessens the right ventricular (RV) pressure and consequently eliminates the TR.[8]

The aim of this study was to analyze pre- and post-interventional TR severity in patients with structurally normal tricuspid valves who underwent MBV to find out whether TR severity improves after intervention. We also investigated the relation between TR severity and pulmonary artery hypertension to determine whether a reduction in pulmonary artery systolic pressure (PAPs) has an impact on TR.

Methods

We considered the echocardiography data of 170 patients with different degrees of TR severity that underwent MBV in our center between April 2006 and March 2008. From these patients, 37 were excluded due to missing data, leaving 133 patients for this study. None of the patients had tricuspid valve rheumatismal involvement. In the evaluation of TR severity, two-dimensional echocardiography with color Doppler study was done using a 3-MHZ phased array sector scanner (Vivid 3 or Vivid 7 GE, USA) within one month before and during the first month after MBV. In all standard views, including the apical 4-chamber, parasternal short axis, RV inflow, and subcostal views, TR severity was observed and graded. TR was graded as 0 for no regurgitation, 1+ for trivial, 2+ for mild, 3+ for moderate, 4+ moderately severe, and 5+ for severe regurgitation. Left ventricular ejection fraction was measured by the modified biplane Simpson method, and RV systolic function was evaluated by the tricuspid annular plane systolic excursion (TAPSE) and tissue Doppler imaging study (RVsm). Additionally, PAPs was estimated by obtaining the peak TR Doppler jet from multiple windows until peak velocities were consistent and reproducible plus right atrial pressure (which was estimated in regard to JVC size and respiratory collapse).

Pulmonary artery hypertension was defined as PAPs > 35 mmHg,[9, 10] although the current definition of pulmonary artery hypertension is based on mean PAPs > 25 mmHg.[11, 12] Left ventricular ejection fraction < 50 % and RV dimension ≥ 33 mm were considered as left ventricular systolic dysfunction and RV dilation, respectively. In addition, TR severity reduction ≥ 1 grade was defined as TR severity improvement.

Mitral balloon valvotomy was performed via the transvenous, transseptal approach from the right femoral vein in accordance with the stepwise Inoue balloon technique, as was first described by Inoue et al.[13] The Inoue balloon was passed across the atrial septum before being flow guided to the left ventricle. The septotomy was subsequently enlarged with a 14F vessel dilator before segmental inflation of the balloon was performed within the mitral valve. The balloon size was determined according to the height of the patient ([Height (cm) / 10] + 10 = recommended balloon size).[14] Immediately after the procedure, hemodynamic measurements were repeated and recorded.

The numerical variables are presented as mean ± SD (standard deviation), while the categorical variables are summarized by absolute frequencies and percentages. The continuous variables were compared using Student's t-test or one-way analysis of variance (ANOVA) across the groups defined by TR severity grade, and the categorical variables were compared using the chi-square or Fisher's exact test, when more than 20% of the contingency table cells had expected cell frequencies less than five.

The continuous variables were compared by the paired t-test, ordinal variables by the Wilcoxon signed ranks test, and categorical (binary) ones by McNemar's test, prior to and after percutaneous MBV.

The Receiver Operating Characteristic (ROC) curve analysis was performed to find an optimal cut-off point for PAPs reduction to show at least a one-grade regress in TR severity.

For statistical analysis, the statistical software SPSS version 13.0 for Windows (SPSS Inc., Chicago, IL) was used. All p values were 2-tailed, with statistical significance defined by p value ≤ 0.05.

Results

The demographic and clinical data are presented in Table 1. The study population consisted of 133 consecutive patients with different degrees of TR severity (Table 2) who underwent MBV because of significant mitral stenosis.

TR severity improved in 55 (41.4%) after MBV, whereas it remained unchanged in 67 (50.4%) and worsened in 11 (8.3%) patients. However, a small but statistically significant decrease was noted in TR severity from 2 (2, 3) [median (1st quartile, 3rd quartile)] before MBV to 2 (1, 3) thereafter (P value< 0.001).

From 48 patients with higher grades of TR severity (moderate, moderate to severe, and severe), 30 (62.5%) showed improvement, 17 (35.4%) no change, and only one (2.1%) worsening (p value < 0.001). However, the patients with lower grades of TR severity (trivial and mild) showed slightly significant TR reduction after MBV (p value = 0.073).

Prior to MBV, 92.5% of the patients had pulmonary arterial hypertension (PAPs > 35 mmHg), which decreased significantly to 44.4% after MBV (p value < 0.001). The mean PAPs reduced markedly from 52.83 ± 18.82 mmHg to

35.89 ± 9.39 mmHg after intervention (p value < 0.001).

Table 1. Patient's characteristics (n=133)

Age (y)	
Mean±SD	44.68±12.56
Range	20-85
Female gender (%)	82.0
LV function (%)	
Dysfunction (EF < 50%)	7.5
Normal (EF ≥ 50%)	92.5
EF (%)	
Mean±SD	53.87±4.87
Range	25-65
AF (%)	29.5

LV, Left ventricular; EF, Ejection fraction; AF, Atrial fibrillation

Table 2. Tricuspid regurgitation (TR) grade before and after mitral balloon valvotomy (MBV)*

TR grade	Before MBV	After MBV
No TR	0	3 (2.3)
Trivial	8 (6.0)	31 (23.3)
Mild	77 (57.9)	65 (48.9)
Moderate	30 (22.6)	21 (15.8)
Moderately Severe	11 (8.3)	10 (7.5)
Severe	7 (5.3)	3 (2.3)

*Data are presented as n (%)

Before and after intervention, PAPs was significantly correlated with TR severity: the higher the PAPs, the higher the degree of TR (both p values < 0.001).

Changes of mean PAPs in the patients with improved TR grade were significantly higher than those in the patients without TR improvement (p value = 0.034); higher rates of PAPs reduction were accompanied by higher chances of TR improvement.

The ROC curve analysis demonstrated that a cut-off point of ≥ 19 mmHg reduction in PAPs had a specificity of 71.79% and sensitivity of 52.73% to show at least a one-grade regress in TR severity.

In 86.4% of the patients with moderate to severe TR, improvement in TR severity occurred by this cut-off point. Although the patients with mild or trivial TR did not demonstrate significant improvement in TR post MBV compared to pre MBV, 34.5% of them showed TR improvement by the same cut-off point (p value < 0.001)

The mean ejection fraction was 53.87 ± 4.87% in all the study population prior to MBV.

The mean pre-procedural ejection fraction was not different between the patients with and without TR improvement. The patients who showed a worsening of TR grade after intervention had a significantly lower mean ejection fraction compared to those whose TR severity had improved or not changed (p value = 0.003 and p value = 0.002, respectively).

The mean of mitral valve peak pressure (MVPP) reduced from 19.86 ± 7.11 mmHg to 10.35 ± 3.45 mmHg. The mean of mitral valve mean pressure (MVMP) reduced from 11.98 ± 5.30 mmHg to 5.32 ± 2.51 mmHg before to after MBV, respectively. Both of these changes were statistically significant (both p values < 0.001). No relation was, however, found between the difference of mean MVPP, mean MVMP, and TR changes.

The mean RV dimension decreased from 28.94 ± 5.43 mm before to 27.95 ± 4.67 mm after MBV (p value < 0.001). Twenty-three (17.7%) patients had RV dilation (RV dimension ≥ 33 mm) before intervention, which decreased to 19 (14.6 %) after intervention. Tricuspid regurgitation grade improved in 44% of the patients without RV dilation and in 29.2% of the patients with RV dilation; these findings were not statistically significant.

The presence or absence of atrial fibrillation before MBV had no relationship with TR changes after MBV.

Discussion

This study revealed association between the amount of PAPs reduction and degree of TR severity regression after MBV in patients with significant mitral stenosis.

Right ventricular dilation due to RV ischemia or infarction, mitral valve disease, and pulmonary vascular disease is a more common cause of functional TR than primary valvular disease[15] and it has been demonstrated that the presence of TR is associated with pulmonary hypertension.[16]

Song et al.[17] reported that TR was resolved in 32% of patients who underwent percutaneous mitral valvoplasty. In their study, all the patients had significant moderate to severe TR before intervention. They showed that patients with significant functional TR had more severe mitral stenosis, which could be diminished if the transmitral pressure gradient was sufficiently relieved with percutaneous mitral valvoplasty. In the group of patients who showed resolution of TR grade, the mean PAPs reduced from 57 ± 19 before percutaneous mitral valvoplasty to 35 ± 16 mmHg at follow-up. It is worthy of note that the authors did not demonstrate any relation between the amount of PAPs reduction and TR regression.

In the Hannoush et al. investigation,[7] of 53 patients with significant TR, 27 showed TR regression after MBV. The study showed that PAPs was initially higher and decreased (from 70.7 ± 23.8 to 36.5 ± 8.3 mmHg) at follow-up in those patients. Right ventricular dimension was also significantly reduced after intervention. In contrast, Shafie et al.[8] demonstrated that in 8 patients with severe TR who underwent successful closed commissurotomy for severe mitral stenosis, no TR improvement was observed at follow-up. Also Sagie et al. reported that although RV systolic

pressure fell by more than 10 mmHg, RV dimension did not decrease and TR did not resolve after percutaneous balloon mitral valvotomy.[18]

As was mentioned above, there are some studies investigating TR severity after intervention with the aim of resolving mitral stenosis. In this study, we compared TR severity before and after MBV. Tricuspid regression occurred in 41.4% of the patients, of whom 54.5% had moderate or greater degrees of TR before intervention; there was, however, no significant TR improvement in patients with lower grades of TR before MBV (p value = 0.073).

In our study population, the mean of MVPP and mean of MVMP decreased significantly after MBV. Transmitral pressure gradient was concomitant with TR reduction, as was described before.[17] Be that as it may, there was no relation between the difference of mean MVPP, mean MVMP, and TR changes.

Berger et al.[19] reported that TR could be identified in a large number of patients with pulmonary artery hypertension, especially when PAPs rose to 50 mmHg. In their study, 39 out of 49 patients with PAPs ≥ 35 mmHg had TR, while only 2 out of 20 patients with PAPs < 35 mmHg presented with TR.

Some investigators have shown that severe functional TR with a dilated annulus can be eliminated spontaneously after reducing PAPs,[3] but other investigators have demonstrated that elevated PAPs has no significant determinable role in functional TR.[20] Most investigators currently believe that patients with mitral stenosis associated with moderate or more than moderate TR, especially when there is tricuspid valve annulus dilation, are not good candidates for percutaneous transvenous mitral commissurotomy and that they should be referred for mitral valve surgery plus tricuspid valve annuloplasty.

In the present study, before and after MBV, PAPs was significantly correlated with TR severity; higher PAPs was seen concomitantly with higher degrees of TR. After MBV, the mean PAPs and the number of patients with pulmonary artery hypertension decreased significantly; TR severity was significantly correlated to the amount of PAPs reduction after MBV. We sought to determine a cut-off point in PAPs reduction to determine how much decrease in PAPs warrants TR improvement after intervention. In the final analysis, we found out that a cut-off point of ≥ 19 mmHg reduction in PAPs had a specificity of 71.79 % and sensitivity of 52.73% to predict TR improvement. In our sample, 86.4% of the patients with higher degrees of TR and 34.5% with lower grades of TR before MBV showed TR improvement with this cut-off point.

Previous studies have revealed that the grade of TR is correlated with left ventricular ejection fraction and TR is strongly associated with RV dilation.[16, 21]

Our results showed a significant correlation between ejection fraction and TR changes only in the patients with worsened TR after intervention. On the other hand, pre MBV, ejection fraction < 50% showed a relation with worsening of TR severity after MBV.

The present study has some limitations, the most prominent amongst which is the fact that only immediate post-interventional echocardiography data were utilized. Moreover, longer follow-up periods are required to evaluate changes in TR severity and to determine cut-off points in PAPs reduction with higher specificity and sensitivity.

Conclusion

In this study, the severity of TR regressed after MBV and this regression was related to the amount of PAPs reduction. A cut-off point of ≥ 19 mmHg reduction in PAPs, with a specificity of 71.79 % and sensitivity of 52.73%, showed TR improvement after MBV. Patients with an ejection fraction < 50% at the time of MBV had a greater chance of TR severity worsening after MBV.

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