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Mitral darlığı olan hastalarda perkütan valvüloplastinin sağ kalp fonksiyonları üzerine uzun dönem etkisinin doku Doppler görüntüleme ile değerlendirilmesi

Evaluation of the long-term effect of percutaneous balloon valvuloplasty on the right ventricular function using tissue Doppler imaging in patients with mitral stenosis

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ÖZET

Amaç: Bu çalışmada, perkütan mitral balon valvüloplastinin (PMBV) sağ kalp fonksiyonları üzerine uzun dönem etkisini doku Doppler görüntüleme yöntemi işe araştırdık.

Çalışma planı: Çalışmaya başarılı PMBV yapılan 27 hasta alındı. Tüm hastalara işlemden 24 saat önce triküspit halkası dış yanından renkli doku Doppler görüntüleme kaydını içeren ekokardiyografi incelemesi yapıldı. İşlemden 24 saat ve 6 ay sonra aynı inceleme tekrarlandı.

Bulgular: İşlem sonrası 24. saatte S dalga hızında ve A' dalga hızında anlamlı artış izlendi (sırasıyla, S dalga hızı için 9.52±1.85 cm/sn ve 10.92±1.20 cm/sn, p=0.012; A' dalga hızı için -10.44±2.64 cm/sn ve -11.73±2.05 cm/sn, p=0.029). E' dalga hızında ve E'/A' oranında anlamlı değişim izlenmedi (her ikisi için de p>0.05). Altıncı ayda S dalga hızının işlemden hemen sonraki ile benzer ve işlem öncesine göre ise daha yüksek olduğu gözlendi (9.52±1.85 cm/sn ve 10.69±1.72 cm/sn, p=0.023). A' dalga hızının ise geç dönemde erken döneme göre azaldığı ve işlem öncesinden anlamlı farklı olmadığı bulundu (-10.44±2.64 cm/sn ve -10.74±2.63 cm/sn, p>0.05). E' dalga hızında işlem öncesi dönem-

ABSTRACT

Objectives: We investigated the long-term effects of percutaneous mitral balloon valvuloplasty (PMBV) on the right ventricular function using tissue Doppler imaging.

Study design: Twenty-seven patients who underwent successful PMBVs were enrolled in the study. Echocardiographic examination, including color tissue Doppler imaging, was done from the lateral tricuspid ring 24 hours before the intervention. The echocardiographic examination was repeated 24 hours, and 6 months after the intervention.

Results: At 24 hours after the intervention, significant increases were observed in S, and A' wave velocities (9.52±1.85 cm/s vs. 10.92±1.20 cm/s, p=0.012; -10.44±2.64 cm/s vs. -11.73±2.05 cm/s, p=0.029, respectively). E' wave velocity and E'/A' ratio did not change significantly (p>0.05 for both). At 6. postprocedural month, S wave velocity was similar to the value in the early postoperative period, but higher than the baseline level (9.52±1.85 cm/s vs. 10.69±1.72 cm/s, p=0.023). However, A' wave velocity in the late postoperative period was decreased compared to the early period and was not

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le karşılaştırıldığında geç dönemde görülen artış anlamlı bulundu (-7.85±1.54 cm/sn ve -9.21±1.81 cm/sn, p=0.046).
Sonuç: Perkütan mitral balon valvüloplasti ile sağ ventrikül sistolik fonksiyonları erken dönemde düzelmekte ve bu düzelme uzun dönemde benzer şekilde devam etmektedir. Sağ ventrikül diyastolik fonksiyonlarında erken dönemde düzelme görülmez iken geç dönemde düzelme gözlenmektedir. Sağ atriyum sistolik fonksiyonları ise erken dönemde düzelirken uzun dönemde işlem öncesi değerlere geri dönmektedir.

significantly different from the baseline level (-10.44±2.64 cm/s vs. -10.74±2.63 cm/s, p>0.05). The increase in E' wave velocity in the late period when compared to the baseline level was found to be statistically significant (-7.85±1.54 cm/s vs. -9.21±1.81 cm/s, p=0.046).
Conclusion: Right ventricular systolic function improved in the early period, and this improvement was seen to continue in the late post-PMBV period.. Diastolic function did not improve in the early period, but did improve in the late period. Right atrium systolic function improved in the early period; however, in the late period, levels returned to baseline levels.

Abbreviations:

A'	Late diastolic filling (A -wave)
TD	Tissue Doppler
E'	Early diastolic
MS	Mitral stenosis
MR	Mitral regurgitation
PAP	Pulmonary artery pressure
PHT	Pressure half-time -
PMBV	Percutaneous mitral balloon valvuloplasty
RMD	Rheumatic mitral valve stenosis
S	Systolic

Rheumatic mitral valve stenosis (RMSV) is a valvular disease frequently seen in adults which becomes apparent as a sequela of rheumatic carditis (RMD) experienced during childhood.[1] Mitral stenosis [MS]which develops as a result of thickening, and restricted mobility of mitral valve leaflets, prevents entry of blood flow from the left atrium into the left ventricle, and increases pressure, and volume of left atrium, pulmonary vascular bed, and right heart chambers.[2] Untreated patients can present with irreversible right ventricular failure in the long-term. Percutaneous mitral balloon valvuloplasty (PMBV) is recommended as a first-line treatment for eligible caases with its higher success, and lower complication rates .[1,3-5]

The effect of successful PMBV on the left atrial, and ventricular functions has been investigated using both conventional, and also echocardiographic, and Doppler ultrasonographic methods.[6-10] Only a few studies have investigated its effect on the right ventricular systolic, and diastolic functions.[11-18] Limited data are available concerning the long-term effects of PMVB on the right ventricular functions.[14,15]

In this study, long-term alterations in the right heart systolic, and diastolic functions were evaluated using tissue Doppler imaging methods in patients who underwent PMBV with the indication of RMD.

PATIENTS AND THE METHOD

Study plan, and patient selection

Consecutive patients who gave their informed consent for participation in the study among those who had undergone successful PMBV with the indication of RMD in our clinic between December 2006, and February 2008 were included in this prospective cohort study. The physician who monitored the patients, also selected eligible patients for PMBV following evaluation of clinical, and echocardiographic data. Approval of local ethics committee was obtained for the conduction of the study. The patients were

informed about the study in detail, and their written consent forms were obtained.

Before the procedure comprehensive echocardiographic examination including Doppler US was performed on 27 patients whose consent forms were obtained. Then. echocardiographic examinations were repeated 24 hours, and 6 months after the procedure, and the findings obtained were compared.

Exclusion criteria

The patients with coronary artery disease, lower (< 50 %) ventricular ejection fraction, non-sinus rhythm, aortic failure worser than second –degree disease, moderate degrees of aortic valve stenosis (maximal pressure gradient > 20 mm Hg), tricuspid regurgitation (TR) more severe than second degree TR, and organic tricuspid disease, connective tissue disease which is known to result in pulmonary hypertension, chronic pulmonary disease, previous history of pulmonary embolism, and pregnant women were not enrolled in the study.

Echocardiographic examination

Echocardiographic examination was performed with the patient laying in the left oblique position using General Electric Vingmed system 5, (Horten, Norway) echocardiograph with a 2.5 MHz probe. In compliance with the guidelines, during 2-D echocardiographic, and color-Doppler US examinations parasternal long-, and short axis apical 2-, 3-, and 4-chamber views were obtained from all patients [19-21] Flow rates were examined using pulsed or continuous wave Doppler US. Valvular areas was measured using both planimetric, and pressure half - time (PHT) methods.

All patients underwent transesophageal echocardiographic examinations. Valvüler structures were evaluated with Wilkins scoring system.[22] For the determination of systolic pulmonary artery pressure (PAP), parameters of tricuspid regurgitation jet, and estimated right atrial pressure were used based on previously reported relevant method, and resting systolic PAP > 40 mm Hg was accepted as a criterion for pulmonary hypertension.[23] After acquisition of images from apical 4-chamber views, inclination angle of the US probe, gain, and depth were decreased as far as possible to obtain color Doppler (DD) images from lateral mitral, and tricuspid rings. On DD images systolic (S), early diastolic (E'), and late diastolic wave velocities (A') were measured. S wave velocity of the lateral tricuspid ring lower than 6 cm/sec was considered as right ventricular systolic dysfunction.[23] The examinations performed were entered in a digital database. Analyses were performed after the procedure (off-line) using Echopac 6.5 (EchoPac Mac, GE) software program.

Mitral balloon valvuloplasty

Percutaneous mitral balloon valvuloplasty was performed using Inoue technique under the guidance of transthoracic echocardiography. İmmediately before, and after the procedure, pulmonary artery, left atrial, and systemic pressures were measured using invasive methods. Following the procedure, valvular area $\geq$ 15 cm^2 or at least 50 % increase in the valvular area, development of valvular disease less severe than second-degree mitral regurgitation were accepted as criteria for successful intervention.

Statistical analysis

During the evaluation process of the results obtained from the study, for statistical analysis SPSS (Statistical Package for Social Sciences) 11.5 program was used. The normality of distribution of data was assessed by Kolmogorov-

Smirnov goodness of fit test. All data were expressed as mean ± standard deviation. Results obtained before, and 24 hours after the procedure were compared with those detected at post-PMBV 6 months were compared individually using paired sample t-test. Correlations between parametric, and non-parametric data were analyzed using Pearson correlation analysis, and Spearman 's rank correlation coefficient, respectively. $p<0.05$ was considered to be significant.

Table 1. Comparison of early/long-term echocardiographic data retrieved before, and after percutaneous mitral balloon valvuloplasty (PMBV)

Parameters	Pre-PMBV	Post-PMBV early period	Post-PMBV long-term	*p*
Mitral valve area planimetric (cm^2)	1,08±0,22	1,85±0,26*	1,76±0,33	**<0,001**
Mitral valve area	1,02±0,19	1,81±0,29*	1,74±0,24	**<0,001**
Pressure half -time				
Peak pressure gradient (mm Hg)	23,22±6,32	10,13±2,23*	12,91±2,84#	**<0,001**
Mean pressure gradient (mm Hg)	13,33±4,39	4,84±1,43*	6,17±1,59#	**<0,001**
Mitral regurgitation	10 (37)/9 (33)/7 (26)/1 (4)	4 (15)/6 (22)/14 (52)/3 (11)*	0/10 (37)/13 (48)/4 (15)	0,011
None/trace/1/2 (%)				
Systolic pulmonary artery pressure (mm Hg)	50,81±12,91	33,85±8,59*	36,12±5,62	**0,001**
Tricuspid regurgitation None/trace/1/2 (%)	1 (4)/ 16 (59)/ 6 (22)/ 4 (15)	4 (15)/ 15 (56)/ 5 (19)/ 3 (11)	3 (11)/ 13 (48)/ 6 (22)/ 5 (19)	0,589
Left atrial diameter (cm)	4,32±0,68	3,88±0,58*	4,06±0,62#	<0,015
Tricuspid ring S wave velocity (cm/sec)	9,52±1,85	10,92±1,20*	10,69±1,72	0,023
Tricuspid ring É wave velocity (cm/sec)	-7,85±1,54	-8,29±1,85*	-9,21±1,81	0,046
Tricuspid ring Á wave velocity (cm/sec)	-10,44±2,64	-11,73±2,05*	-10,74±2,63	0,620
Tricuspid ring É/ Á ratio	0,75±0,46	0,71±0,24	0,85±0,25	0,341

p value: in comparisons between early, and late post-PMBV periods

* Statistically significant difference between before, and immediately after PMBV

Statistically significant difference between early, and late post-PMBV periods

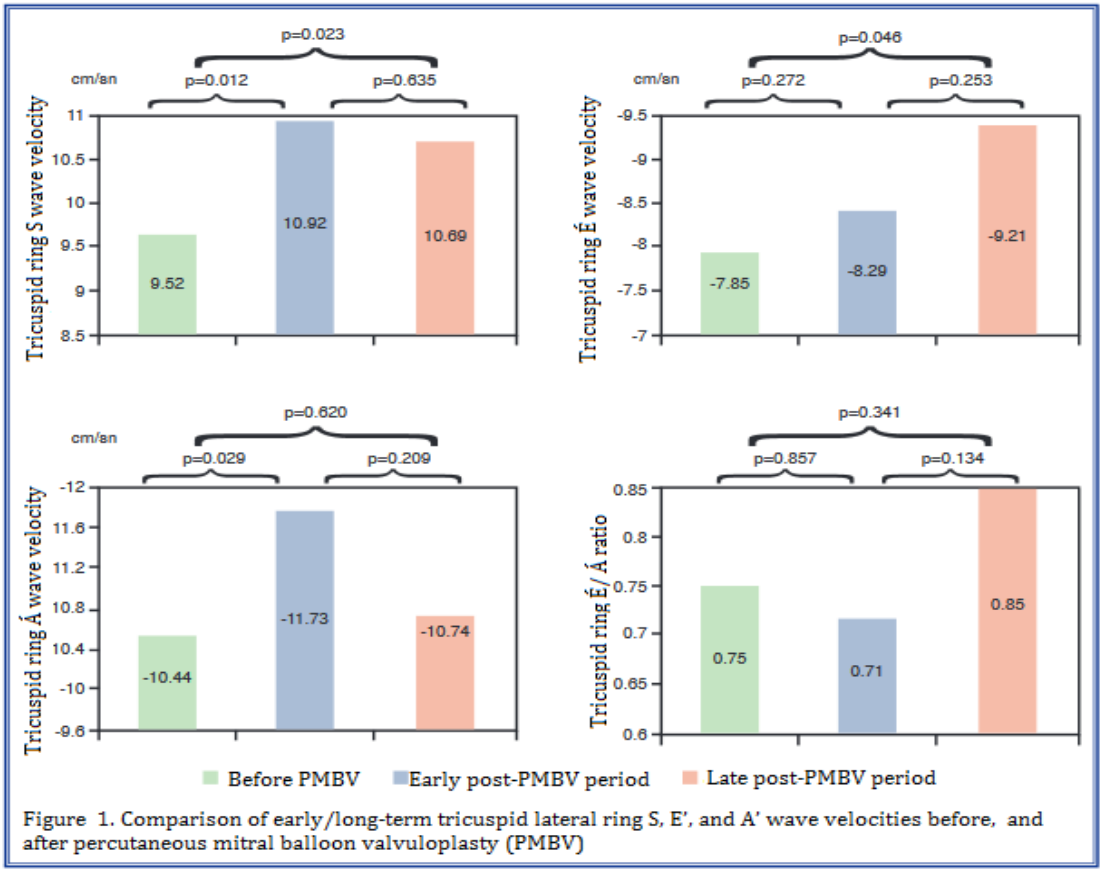

Figure 1. Comparison of early/long-term tricuspid lateral ring S, E', and A' wave velocities before, and after percutaneous mitral balloon valvuloplasty (PMBV)

RESULTS

During the enrolment period of the study, 52 patients underwent successful PMBV operations. Among them, 27 patients who agreed to participate in the study were evaluated. (23 female, and 4 male patients with a mean age of 33 ± 9 years). Mean Wilkins score of the patients was 7.1±1.2, None of the patients received any drug effective on cardiovascular system before PMPV, and during the follow-up period. The patients had pulmonary hypertension (n=20) or right ventricular systolic dysfunction (n=4). In our study significant increase in valvular area, and the degree of MR, and decrease in diameter of the left atrium, systolic pulmonary artery pressure, maximum, and mean mitral valve pressure gradient were observed. ($p<0.05$). A significant change in the degree of tricuspid regurgitation did not take place (Table 1). Significant increases in tricuspid valve S, and A' wave velocities were detected at postprocedural 24. hours when compared with baseline levels (9.52±1.85 cm/sec and 10.92±1.20 cm/sec, respectively, p=0.012; -10.44±2.64 cm/sec, and -11.73±2.05 cm/sec, respectively. p=0.029) (Table 1, Figure 1). Changes in E' wave velocity, and E'/A' ratio were not significant ($p>0.05$) (Figure 1).

At 6.months, increase in the valvular area, and decreases in the right atrial diameter, systolic PAP, and mitral pressure gradient still maintained their significance. Though increase in the degree of MS was still at a significant level, degree of tricuspid regurgitation was comparable to preprocedural baseline values (Table 1). Tricuspid ring S wave velocity continued to stay at high levels

relative to baseline values (9.52±1.85 cm/sec, and 10.69±1.72 cm/sec, respectively. p=0.023) but comparable to postprocedural values (Table 1, Figure 1). A' wave velocities decreased again at sixth months and returned to their baseline values. (-10.44±2.64 cm/sec, and -10.74±2.63 cm/sec, respectively. p=0.620) (Table 1, Figure 1). E' wave velocity was detected to be significantly higher than preprocedural values (-7.85±1.54 cm/sec, and -9.21±1.81 cm/sec, respectively. p=0.046) (Table 1, Figure 1).

In postprocedural short, and long- term comparisons, variations in the valvular area, and PAP weren't significant (planimetric mitral valve area=1.85±0.26, and 1.76±0.33, p=0.149, respectively; systolic PAP=33.85±8.59, and 36.12±5.62, respectively. p=0.759). Though at an insignificant level, left atrial diameter increased (3.88±0.58, and 4.06±0.62, respectively; p=0.073), while a significant increase was observed in mitral pressure gradients (mean mitral pressure gradient: 4.84±1.43, and 6.17±1.59, respectively: p=0.004). Significant variations were not also detected in the degree of mitral, and tricuspid regurgitations (for both, p>0.05). A significant difference in tricuspid S, E' ve A' wave velocities, and E'/A' ratio was not detected. (for all, p>0.05) (Table 1, Figure 1).

Between preprocedural S wave velocity, and valvular area a significant, but with resting systolic PAP an inverse but insignificant correlations were detected (r=0.444, p=0.044, and r=-0.425, respectively. p=0.063) (Figure 2). Preprocedural E' , was directly correlated with PHT, while a moderate but an inverse correlation existed between E' , and the resting systolic PAP (sırasıyla r=0.578, p=0.006 and r=-0.565, p=0.015, respectively) (Figure 2). However A' wave velocity did not correlate with any of conventional echocardiographic parameters neither before nor after the procedure (p>0.05).

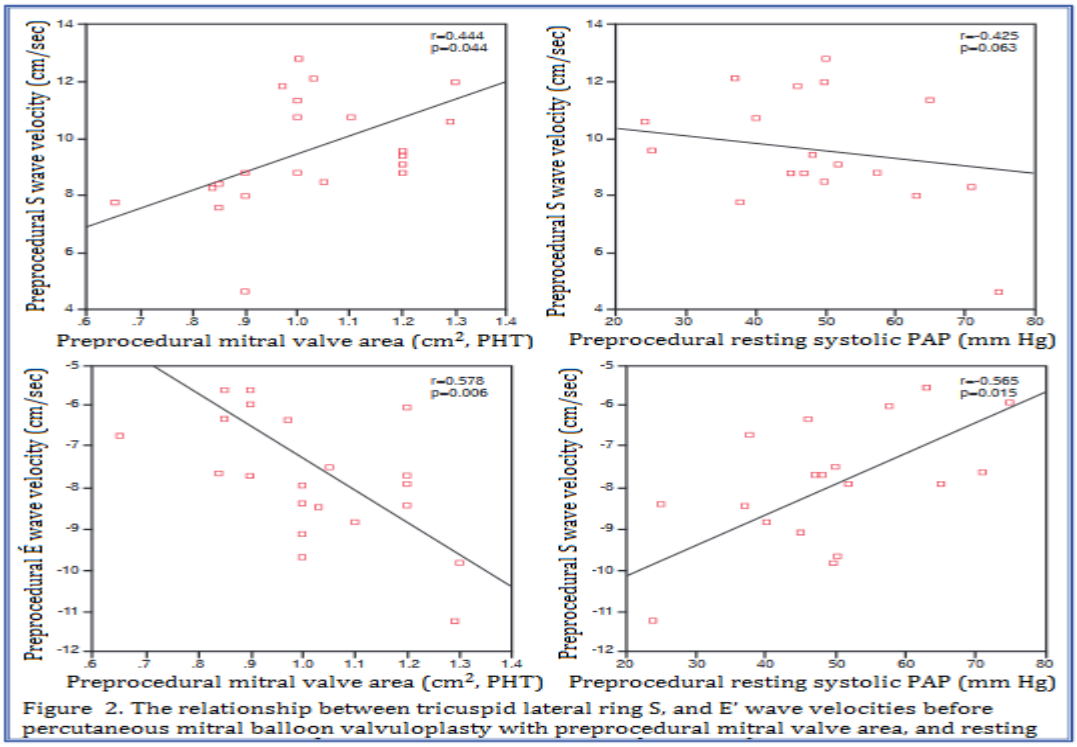

Figure 2. The relationship between tricuspid lateral ring S, and E' wave velocities before percutaneous mitral balloon valvuloplasty with preprocedural mitral valve area, and resting

DISCUSSION

This study has demonstrated that in patients who underwent PMBV, right ventricular systolic functions recovered at an early period which maintain similarly in the long-term. While, diastolic functions improves only in the long-term.

In various studies performed in patients with RMD, following successful PMBVs, a prominent symptomatic improvement together with recovery of the left atrial, and ventricular functions, and drop in the pulmonary artery pressure have been demonstrated. [1-10] Because of difficulties encountered in its evaluation, in research studies similar to clinical applications right ventricular functions have been overlooked for years. However, previous studies have shown impairment in the right ventricular functions which was associated with manifestation of symptoms. [24-26] More importantly, right ventricular functions have been demonstrated to be an indicator of clinical end-point [15,27] Sade et al.[27] evaluated right ventricular functions before application of PMBV using various methods including tissue Doppler imaging. In this study, the authors detected associations between right ventricular functions with systolic PAP, and indicated that impaired right ventricular functions correlated with poor prognosis during an average follow-up period of 20 months. Similarly, Mahfouz et al..[15] reported that during an average of 42 months, combined end-point of development of atrial fibrillation, and restenosis, progressive pulmonary hypertension, deterioration of functional class, and stroke were more frequently seen in patients with ventriculsr dysfunction. In patients who underwent successful PMBV, early phase improvements in the right ventricular systolic functions have been demonstrated using various imaging techniques.[11-14] Burger et al.[13] evaluated right ventricular functions before, and 1-2 days after PMBV during resting conditions, and exercise using thermodilution methods. . In this study, investigators demonstrated that following successful PMBV procedure, right ventricular ejection fraction increases significantly during both resting state, and exercise. The investigators could not find any correlation between right ventricular ejection fraction, and mitral valve area, however they disclosed an inverse, but significant correlation between pulmonary vascular resistance, and right ventricular ejection fraction Mohan et al.[14] evaluated Tei index, and right ventricular functions. The investigators couldn't find a change in the early post-PMBV, on the contrary during nearly a year-long follow-up they reported significant improvements. Arat et al. evaluated right ventricular functions[16] , and investigated the impact of preprocedural PAP on the recovery of the right ventricular functions after PMBV procedure. Before, and 48 hours, and 3 months after the procedure, echocardiographic evaluations were performed. In the evaluation of all patients, they couldn't detect any significant change in the tricuspid ring S, E' ve A' wave velocities at 48 hours, and 3 months after the procedure. However in the evaluation of the group without pulmonary hypertension, they detected a significant increase in S wave velocities during the early post-PMVB period which persisted in the long- term. As an indicator of diastolic function, tricuspid ring E'/A' ratio declined in the third month relative to baseline values in patients with pulmonary hypertension. However, the authors also reported that in patients without pulmonary hypertension E'/A' ratio did not change throughout this period.[16] Based on the interpretations of the

investigators, PMBV applied before development of pulmonary hypertension provides comparatively greater improvement in longitudinal functions of the right ventricle. Mahfouz et al.[15] evaluated right ventricular systolic functions with S wave velocity, and diastolic functions with E'/A' ratio. They reported improvements both in systolic, and diastolic functions on the first postoperative day following a successful PMBV operation.[15] In another article of the same group of investigators [17] right ventricular systolic functions were evaluated with S wave velocity, and tricuspid annular plane systolic excursion (TAPSE), while diastolic functions with E'/A' ratio. In this article in the early post-PMBV period, improvements in the systolic, and diastolic functions were demonstrated, however during one year of follow-up, though not specifically enumerated, the authors reported persistence of the beneficial effects of PMBV. In the same study, long-term effects of pulmonary artery stiffness on the right ventricular functions, and tricuspid regurgitation were analyzed. As a result of examinations performed before, and 6, and 12 months after the procedure, the investigators demonstrated that in the group of patients whose right ventricular functions permanently improved, and tricuspid regurgitation regressed, pulmonary artery stiffness were significantly decreased. The investigators advocated that even though adequate mitral valvular area had been ensured, persistence of tricuspid regurgitation, and right ventricular dysfunction might be related to increased pulmonary artery stiffness, and they also emphasized the importance of early intervention.[17] Another study with a long-term follow-up was performed by Hamdy[18] et al. In this study right heart functions were evaluated by Tei index derived from the lateral side of the tricuspid ring. In the study where six-month follow-up of the patients was performed, significant improvements were reported in Tei index in 39, and 62 % of the patients at 3. months, respectively. The authors indicated that improvements were not related to valvular area, and pulmonary artery pressure, however they didn't report any other predictive factor.[18]

However in our study decline in PAP, and a significant increase in S wave velocity were found during the early post-PMBV period. At the 6.month controls, we noted maintenance of decline in the resting PAP, and increase in S wave velocity. Since right ventricle works for a long time against a higher afterload diastolic functions might deteriorate. Recovery of the diastolic functions in the early post-PMBV period is not expected. In the long run, since right ventricle works against a lower afterload, recovery of myocardial structure, and improvement in the diastolic functions are anticipated. In our study, any change did not occur in the E' wave velocities in the early phase which we evaluated as an indicator of diastolic function, however a significant increase was detected in the long run. We think that this phenomenon might contribute to the recovery of the symptoms in the long term. . Even though left ventricular systolic functions are within normal limits, experience we gained from the patients with clinical symptoms of heart failure showed us the importance of diastolic functions on the emergence of symptoms. Besides, previously performed studies which demonstrated positive, and significant correlation between right ventricular diastolic functions with functional capacities of patients with MS., is supporting this interpretation.[24,25] The outcomes of this study remind us to

consider the impact of the right ventricular diastolic functions in the evaluation of the symptoms of the patients with MS. In our study, A' wave velocities increased significantly after the procedure, while at sixth month controls it didn'differ significantly from preprocedural values. The importance of the right atrial functions have not been investigated very much in patients with mitral stenosis. Observation of improvement in the early postprocedural period, contrary to an increase in standard deviation in the long term suggests predominancy of individual differences between patients. This condition can be evaluated with various mechanisms (1) conditioning of the right atrium struggling against relatively higher afterload, (2) increase in the A' wave velocity which represents atrial conditioning induced by rapid drop in the afterload after the procedure, (3) however in the long run right atrium works against lower afterload which decreases the level of atrial conditioning with resultant deceleration of A' wave However because of the limited number of patient population, potentially influential factors can not be analyzed. Since measurements were made only during the resting state, data obtained couldn't reach the level of significance.

Degree of tricuspid regurgitation is also influential on the right ventricular functions. In previous studies, discrepant data have been reported about the decrease in the severity of tricuspid regurgitation after a successful PMBV .[11,17] The impact of successful PMBV on preprocedural pulmonary artery stiffness has been indicated.[17] However, in our study significant decrease in the degree of tricuspid valve leakage did not occur. Lack of statistically significant decrease in the amount of leakage might stem from our semi-quantitative assessment. In other words, if a quantitative method like planimetric measurement were used, a significant difference might be detected.. Still scarce number of patients might effect the absence of statistically significant difference

As mentioned above, diverse outcomes have been reported in various studies related to early, and long-term improvements in systolic, and diastolic functions Potential reasons for these diverisities might be related to the differences in baseline level of pulmonary hypertension,[16] pulmonary arterial stiffness,[17] remodelling in the pulmonary vascular bed,[28] and degrees of right ventricular systolic, and diastolic dysfunctions. Besides these discrepancies might be related to differences in the evaluation methods of systolic, and diastolic functions, timing of measurements, volemic loads during measurements [29], and pecularities related to investigators.

Limitations of the study

Failure to evaluate functions of the right heart using another method (cardiac MR etc.) is a deficiency of the study. None of the methods used for the evaluation of functions of the right heart is immune from limitations.[23,29] However the efficacy, and relative reliability of tissue Doppler imaging have been demonstrated. Besides follow-up study design minimized these limitations. Because of limited number of patients, and restricted follow-up period, the factors influential on these variations could not be revealed completely. Besides all of these data belong to the measurements done during resting period, however measurements performed in patients with mitral stenosis during exercise will be more valuable.

Conclusions

Percutaneous mitral balloon valvuloplasty improves right ventricular systolic

functions in the early postoperative period which are maintained at the same level in the long term. However, any improvement is not observed in the right ventricular diastolic functions in the early postoperative period, contrarily they ameliorate in the long term. However right atrial systolic functions improve in the early postoperative period, and return to preprocedural baseline values in the long term. Investigation of influential factors on these alterations in a larger-scale patient population, and especially measurements performed during exercises will yield more valuable information.

Conflict of interest: None declared

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