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Original Article

Acute and short term effects of successful mitral valvuloplasty on net atrio ventricular compliance and its correlation with clinical outcome

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ABSTRACT

Aim of the study: Patients undergoing successful balloon mitral valvuloplasty (BMV) have variable improvement in New York Heart Association (NYHA) functional class (FC), exercise capacity (EC) and regression of systolic pulmonary artery pressure (sPAP). Improvement in net atrioventricular compliance (Cn), one of the major determinants of above factors is not routinely assessed. Aim of present study was to assess the change in Cn after successful BMV and its correlation with above factors.

Methods: 50 patients of very severe mitral stenosis in sinus rhythm who underwent successful BMV have been studied. NYHA FC, 6 min walk test (6 MWT) and echocardiographic evaluation was done 24 h before and at 2 weeks, 12 weeks and 24 weeks after BMV. Echocardiographic parameters of patients with improvement in NYHA class of $\geq$2 (group A) were also compared with those with improvement in NYHA class of $\leq$1 (group B).

Results: Following successful BMV, there was progressive improvement in Cn upto 12 weeks with no further significant improvement till 24 weeks. Change in Cn showed very good correlation with change in NYHA class [$r = 0.62$, $p < 0.01$], 6 MWT [$r = 0.30$, p0.03] and regression of sPAP assessed at 12 weeks and was maintained upto 24 weeks. Change in MVA did not show any correlation with above factors. Group B patients had significantly lower Cn post BMV as compared to group A patients inspite of comparable MVA and trans valvular gradients.

Conclusion: Improvement in Cn following BMV has good correlation with clinical improvement. So Cn should also be assessed along with MVA to better predict clinical outcome.

1. Introduction

Balloon mitral valvuloplasty (BMV) is the treatment of choice in patients of severe mitral stenosis (MS) with suitable anatomy. At present severity of MS is classified based on the mitral valve area (MVA).[1] The most commonly accepted criteria for successful BMV is an increase in MVA to $\geq$1.5 cm^2 or $\geq$ 50% increase from baseline without the development of significant mitral regurgitation (MR).[2,3] But this improvement in MVA per se does not lead to uniform clinical improvement in all patients.

Despite similar mitral valve area, significant discrepancies are observed in the New York Heart Association (NYHA) functional class (FC) and exercise capacity of patients with MS.[4] This is due to variation in the degree of pulmonary arterial hypertension that develops in patients of MS despite comparable valve area and transmitral gradient. Pulmonary artery pressure is not uniquely determined by the stenotic lesion itself but by a combination of hemodynamic parameters.[5] Left atrial compliance plays a crucial role in the occurrence of pulmonary hypertension and symptoms.[6]

The term compliance is used to describe how easily a chamber of the heart or lumen of a blood vessel expands when it is filled with a volume of blood. Left atrial compliance is defined as change in left atrial volume divided by the change in pressure.[7] In patients of isolated MS the left ventricular compliance is usually assumed to be normal. The net atrioventricular compliance (Cn) denotes compliance characteristics of both the chambers, atrium and ventricle as a single unit and can be easily assessed non-invasively by echocardiography.[8] Hence in patients of isolated MS, an abnormal Cn reflects abnormality of the left atrial compliance.[9] But it has been found that about one-third of patients of MS have reduced left ventricular compliance.[10] Hence we assessed left ventricular end diastolic pressure (LVEDP) at the time of BMV and patients with

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raised LVEDP (>12 mm of Hg, a marker of altered left ventricular compliance) were excluded from the study.

Patients of MS with low Cn have been reported to be more symptomatic (higher NYHA FC) with higher systolic pulmonary artery pressure (sPAP) compared to those with higher Cn inspite of comparable mitral valve area and trans mitral gradient.[4]However the effect of BMVon Cn has not been well studied. Two studies[3,11] have reported about significant improvement in Cn acutely after successful BMV while one study[12] assessed change in Cn over a period of 24 weeks. To the best of our knowledge, no study till date has assessed the correlation of change in Cn following successful BMV with clinical outcome over a 24 week period (change in NYHA FC or exercise capacity).

As Cn is not routinely assessed following BMV, we studied change in Cn in patients of very severe MS in sinus rhythm serially after successful BMV. Our primary aim was to assess the change in Cn following successful BMV over a period of 24 weeks and its correlation with parameters of clinical outcome i. e change in NYHA FC of dyspnoea, change in exercise capacity assessed by 6 min walk test (6 MWT), along with regression of hemodynamic burden reflected by fall in sPAP (assessed at 2 weeks, 12 weeks and 24 weeks). Secondary aim of the study was to compare the conventional echocardiographic indices of MS along with Cn in patients showing good clinical response, defined as improvement in NYHA class of dyspnoea by$\geq$ 2 (Group A) to those showing poor clinical response, defined as improvement in NYHA class by$\leq$ 1 (Group B).

1.1. Patient population

A total of 50 patients of isolated very severe MS (MVA $\leq$ 1 cm^2) in sinus rhythm who underwent successful BMV between Jan 2018 to July 2019 were included. Exclusion criteria for the study were a) patients having absolute contraindications for BMV (persistent left atrial/left atrial appendage thrombus, severe bicommissural calcification) b)more than mild mitral or aortic regurgitation c)aortic stenosis d)organic tricuspid valve disease e) left ventricular dysfunction f) atrial fibrillation g) inability to calculate sPAP from tricuspid regurgitation jet h)technically unsuccessful BMV i)pregnancy j)concomitant hypertension k)documented coronary artery disease l)patients with LVEDP >12 mm of Hg assessed invasively at time of BMV.

2. Study procedure

All subjects gave written informed consent for participation in the study. Eligible patients underwent baseline clinical assessment, 12 lead electrocardiogram, 6 MWT as a measure of exercise capacity, and echocardiographic evaluation. Clinical evaluation for NYHA FC, exercise capacity by 6 MWT and echocardiography was again done at 2 weeks, 12 weeks and 24 weeks after BMV.

2.1. Echocardiographic and doppler evaluation

Studies in all patients were performed by two operators unaware of each other's results or other data. Echocardiography was done on the day before BMV, immediately after BMV (to assess for procedural success and complications) and at 2 weeks, 12 weeks and 24 weeks after BMV.

All patients underwent echocardiography using IE 33 Philips with 3.5 MHz transducer. All values and measures were obtained at rest with the patient in left lateral position. All the echocardiographic measurements were done at resting heart rate of 70–80/min and average of 5 cycles were used to calculate the indices. The left ventricular ejection fraction (LVEF) was calculated using Simpson's formula, based on measurements of the end-diastolic volume and end-systolic volume in apical four-chamber view.

The mitral valve area was measured by planimetry from two dimensional images in parasternal short axis view. The sPAP was derived from the tricuspid regurgitant jet velocity, using the simplified Bernoulli equation and adding a constant value of 10 mm of Hg for right atrial pressure to it. The left atrial postero-anterior dimension was measured from the parasternal long-axis view. The total Wilkins score along with Wilkins subvalvular score were carefully assessed in every patient.

Cn was calculated from mitral E wave deceleration rate (dV/dt) and MVA by continuity equation as proposed by Flachskampf FA et al.[8]

$$Cn = 1270 \times (MVA/E\ dv/dt)\ (ml/mmHg)$$

Intraobserver and interobserver variability were calculated by dividing the difference of the two sets of measurements by the mean of two observations.

The echocardiography of 20 patients were repeated to assess the intraobserver variability.

3. Statistical analysis

The data was analysed by using statistical software SPSS version 20. The normality of continuous variables was tested by Shairo Wilk test. For comparison between the two groups Student's *t*-test was applied for continuous variables. The categorical variables were analyzed using Chi-square/Fisher's exact test. The correlation of Cn with parameters of clinical success and sPAP was analysed by Pearson and Spearman test as appropriate. The percentage change was determined for all the parameters and change was compared in the two groups by Student's *t*-test or Mann Whitney *U* test. All the pre and post BMV variables were compared by the paired Student's *t*-test or Wilcoxon singed rank test. Analysis of covariance was applied taking baseline value as a covariate only for those post variables for which baseline value was found to be significant. *P*-value of less than 0.05 was considered as significant.

4. Results

Our study population comprised of 50 patients and their demographic profile, clinical characteristics and baseline echocardiographic features are described in Table 1.

Prior to BMV, LVEDP was assessed in all the patients and mean LVEDP was 9.12 ± 0.99 mm of Hg. The mean left atrial pressure prior

Table 1
Baseline characteristics of the study population (n = 50).

Age (yrs)	30.04 + 5.63
Females n (%)	34 (68.0%)
NYHA functional class[a]	3 (3–3)
NYHA II	0
NYHA III n (%)	43 (86%)
NYHA IV n (%)	7 (14.0%)
6MWT (meters)	266.96 ± 47.95
Wilkins score[a]	8 (7–8)
MVA (cm^2)	0.73 ± 0.09
Mean TMG (mmHg)	15.32 ± 2.23
Cn (ml/mm of Hg)	4.66 ± 0.89
sPAP (mmHg)	60.36 ± 7.70

Values are expressed as mean ± SD.
NYHA: New York Heart Association, TMG: Trans mitral gradient, sPAP: systolic pulmonary artery pressure.
MVA: mitral valve area, Cn: Net atrioventricular compliance.
[a] Values are expressed as median with interquartile range.

to BMV was 25.66 ± 3.01 mm of Hg with significant fall to 14.38 ± 1.26 mm of Hg ($p < 0.01$) after BMV, associated with a slight increase in LVEDP as compared to baseline (9.32 ± 1.02 mm of Hg, $p = 0.02$). However none of the patients had increase in LVEDP to greater than 12 mm of Hg following BMV.

Following successful BMV there was significant improvement in NYHA FC, exercise capacity i. e increase in 6 MWT along with regression of sPAP. There was concurrent increase in MVA assessed by planimetry along with decrease in mean TMG. Cn also improved significantly following BMV (Table 2).

Serial assessment of parameters over a period of 24 weeks showed progressive improvement in 6 MWT and Cn till 12 weeks post BMV as compared to baseline. No statistically significant improvement in 6 MWT and Cn was noticed beyond 12 weeks. Similarly sPAP showed progressive decrease over period of 12 weeks as compared to baseline with no further decrease beyond that period (Table 2).

Change in Cn at 2 weeks as compared to baseline showed significant correlation with change in NYHA FC ($r = 0.46$, $p < 0.01$), 6 MWT ($r = 0.35$, $p = 0.01$) and sPAP ($r = 0.68$, $p < 0.01$) (Table 3). Similar correlation was observed between change in Cn and change in NYHA FC, 6 MWT and sPAP assessed at 12 weeks (Figs. 1 and 2) and 24 weeks post BMV as compared to baseline (Table 3).

However change in MVA assessed at 12 weeks as compared to baseline did not show any correlation with improvement in 6 MWT, NYHA FC or regression of sPAP (Table 4).

On subgroup analysis, 34 (68%) patients had significant improvement in NYHA functional class by≥ 2 (Group A) while the rest of the patients (Group B) had marginal improvement by only one FC or no improvement at 12 weeks post BMV as compared to baseline. Distribution of their demographic profile, clinical

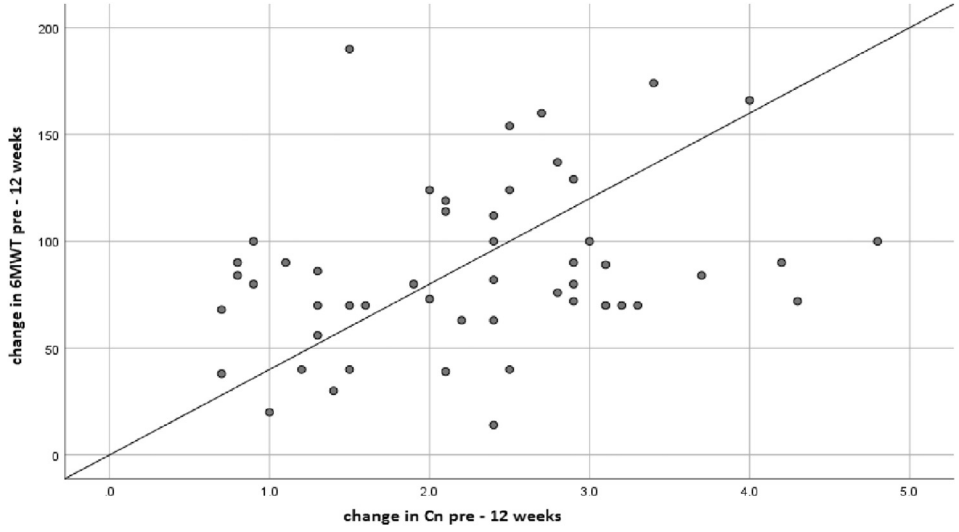

Fig. 1. Scatter plot between the change in Cn and change in 6 MWT. There was positive correlation between the change in 6 MWT (post minus pre) and change in Cn (post minus pre) value, indicating higher change in Cn is associated with greater improvement in 6 MWT.

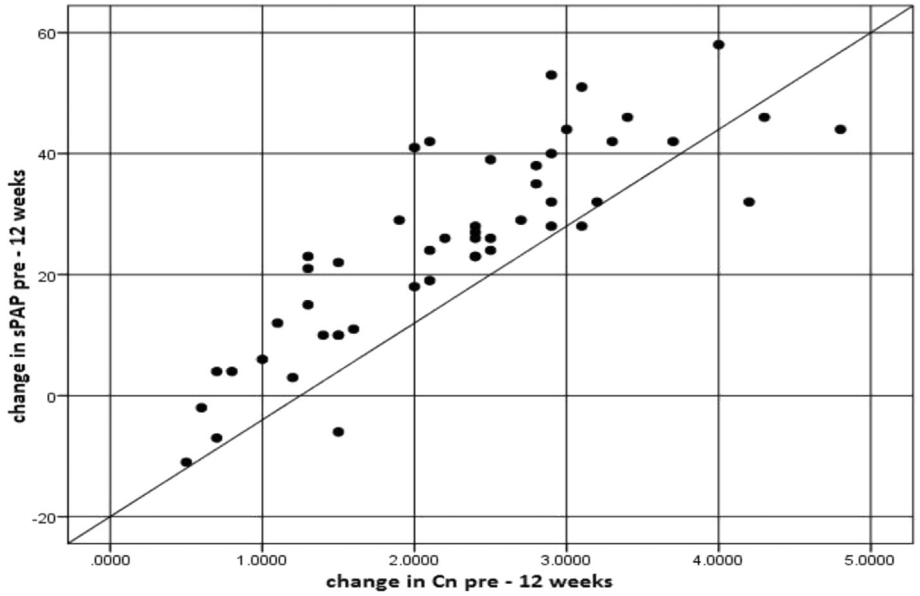

Fig. 2. Scatter plot between change in Cn and Change in sPAP. There was positive correlation between the change in sPAP (pre minus post) and change in Cn (post minus pre) value, indicating higher change in Cn is associated with greater fall in sPAP.

Table 2
Comparison of pre and post BMV variables in the study population.

	Pre BMV	Post BMV At 2 weeks	Post BMV At 12 weeks	Post BMV At 24 weeks
NYHA functional class[e,a]	3 (3–3)	2 (2–3)[b]	1 (1–2)[b,c]	1 (1–2)[b,c]
6 MWT (meters)	266.96[d] 47.95	315.48[d] 51.49[b]	354.00[d] 58.65[b,c]	358.58[d] 60.58[b,c]
MVA (cm^2)	0.73[d] 0.09	1.54[d] 0.15[b]	1.53[d] 0.16[b]	1.52[d] 0.16[b]
Mean TMG (mmHg)	15.32[d] 2.23	6.60[d] 2.80[b]	6.78[d] 1.90[b]	6.06[d] 1.37[b,d]
Cn (ml/mm of Hg)	4.66[d] 0.89	6.00[d] 1.25[b]	6.91[d] 1.37[b,c]	6.92[d] 1.35[b,c]
sPAP (mmHg)	60.36[d] 7.70	42.32[d] 13.34[b]	35.16[d] 13.48[b,c]	35.12[d] 13.69[b,c]

Values are expressed as mean [d] standard deviation.
NYHA: New York Heart Association, 6 MWT: 6 min walk test, TMG: Trans mitral gradient.
sPAP: systolic pulmonary artery pressure, MVA: mitral valve area, Cn: Net atrioventricular compliance.
[a] Values are expressed as median with interquartile range.
[b] ndicates $p < 0.05$ in comparision with pre BMV.
[c] ndicates $p < 0.05$ in comparision with post BMV at 2 weeks.
[d] ndicates $p < 0.05$ in comparision with post BMV at 12 weeks.
[e] Wilcoxon Signed ranked test.

Table 3
Correlation of change in Cn with change in clinical and echocardiographic parameters.

	pre-post at 2 weeks		pre-post at 12 weeks		pre-post at 24 weeks	
	Correlation coefficient	*P* value	Correlation coefficient	*P* value	Correlation coefficient	*P* value
NYHA functional class [a]	0.46	**<0.01**	0.62	**<0.01**	0.47	**<0.01**
6 MWT (meters)	0.35	**0.01**	0.30	**0.03**	0.29	**0.04**
MVA (cm^2)	0.06	0.61	0.13	0.34	0.01	0.92
Mean TMG (mmHg)	0.01	0.93	0.16	0.42	0.24	0.08
sPAP (mmHg)	0.68	**<0.01**	0.84	**<0.01**	0.73	**0 < 0.01**

NYHA: New York Heart Association, TMG: Trans mitral gradient, sPAP: systolic pulmonary artery pressure.
MVA: mitral valve area, 6 MWT: 6 min walk test, Cn: Net atrioventricular compliance. Statistically significant values have been entered in bold.
[a] Spearman correlation.

Table 4
Correlation of change in MVA (post at 12 weeks minus pre) with change in clinical and hemodynamic Parameters.

	Correlation coefficient	*P* value
NYHA functional class	0.06	0.67
6 MWT (meters)	0.02	0.83
sPAP (mmHg)	0.12	0.39

NYHA: New York Heart Association, sPAP: systolic pulmonary artery pressure, 6 MWT: 6 min walk test.
MVA: Mitral valve area.

characteristics and baseline echocardiographic features are described in Table 5.

The mean left atrial pressure (25.82 ± 3.22 mm of Hg in group A vs 25.31 ± 2.46 mm of Hg in group B, $p = 0.94$) and the LVEDP (9.11 ± 0.99 mm of Hg in group A vs 9.12 ± 0.98 mm of Hg in group B, $p = 0.90$) prior to BMV were comparable in both the groups. Following BMV there was significant fall in mean left atrial pressure in group A (14.02 ± 1.21 mm of Hg, $p < 0.01$) and group B (15.12 ± 1.05 mm of Hg, $p < 0.01$) as compared to the baseline. There was also significant difference in post BMV left atrial pressure between group A and group B ($p < 0.01$). However there was no significant difference in post BMV, LVEDP between the two groups (9.29 ± 1.07 mm of Hg vs 9.37 ± 0.92 mm of Hg, $p = 0.67$).

Following BMV at 12 weeks as compared to baseline, MVA, and mean TMG were comparable in both the groups (Table 6). However, Cn [7.39 ± 0.92 vs 5.48 ± 1.18 mm of Hg, $p < 0.01$] was significantly higher in group A as compared to group B, resulting in significantly lower sPAP in group A compared to group B (Table 6). The percentage improvement of Cn in group A was also significantly higher than group B and best cutoff value of percent change in Cn for predicting good clinical outcome was 36.87% with sensitivity of 91.2% and specificity of 68.7% (area under curve: 0.858, Confidence Interval: 0.75–0.96) (Fig. 3).

Table 5
Comparison of baseline demographic and Echocardiographic features between patients with good (Group A) and poor clinical outcome (Group B) assessed at 12 weeks post BMV.

	Group A (34)	Group B (16)	*P* value
Age (years)	30.09 ± 5.69	29.94 ± 5.69	0.83
Females (no.)	25 (73.52%)	9 (56.25%)	0.37
Wilkins score[a,b]	7 (6–8)	8 (8–8)	0.57
6MWTdistance (meters)	272.65 ± 46.58	254.88 ± 50.07	0.70
MVA planimetry (cm^2)	0.73 ± 0.10	0.71 ± 0.09	0.33
Mean TMG (mmHg)	15.32 ± 2.17	15.31 ± 2.44	0.85
Cn (ml/mm of Hg)	4.92 ± 0.69	4.06 ± 0.99	**0.04**
sPAP (mmHg)	61.82 ± 8.29	57.25 ± 5.27	0.38

Values are expressed as mean ± SD. Statistically significant values have been entered in bold.
NYHA: New York Heart Association, 6 MWT: 6 min walk test TMG: Trans mitral gradient, sPAP: systolic pulmonary artery pressure MVA: mitral valve area, 6 MWT: 6 min walk test, Cn: Net atrioventricular compliance.
[a] Mann Whitney *U* test.
[b] values are expressed as median with interquartile range.

Table 6
Comparison of post BMV parameters at 12 weeks between groups with good (Group A) and poor clinical outcome (Group B).

	Group A ($n = 34$)	Group B ($n = 16$)	*P* value
MVA (cm^2)	1.50 ± 0.15	1.52 ± 0.16	0.71
Mean TMG (mmHg)	6.56 ± 2.03	7.19 ± 2.28	0.45
Cn (ml/mm of Hg) [a]	7.39 ± 0.92	5.48 ± 1.18	**<0.01**
sPAP (mmHg)	28.19 ± 10.91	48.81 ± 10.34	**<0.01**
6 MWT (meters)	355.19 ± 52.16	312.31 ± 54.62	**0.02**
% change in Cn	67.01 ± 37.64	32.32 ± 14.16	**<0.01**

TMG: Trans mitral gradient, sPAP: systolic pulmonary artery pressure MVA: mitral valve area, 6 MWT: 6 min walk test, Cn: Net atrioventricular compliance. Statistically significant values have been entered in bold.
[a] Analysis of covariance.

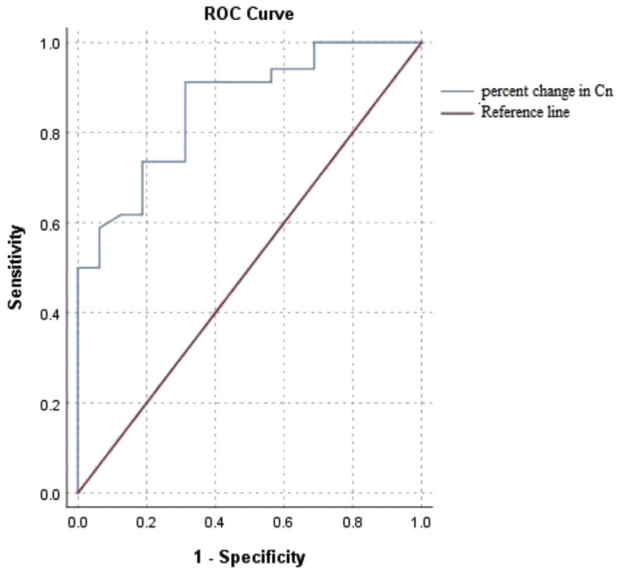

Fig. 3. Receiver-operating characteristic curve for Cn in predicting good clinical outcome. AUC: 0.858, $p < 0.001$, CI: 0.75–0.96. The best cutoff value of percent change in Cn for outcome prediction was, 36.87% with a sensitivity of 91.2% and a specificity of 68.7%. AUC indicates area under the curve; and CI, confidence interval.

The inter and intra observer variability for different echocardiographic parameters like Cn and sPAP were assessed. For Cn, inter and intra observer variability was 0.5 ± 0.2 percent and 0.3 ± 0.1 percent respectively. For sPAP, inter and intra observer variability was 2.3 ± 1.4 percent and 2.9 ± 1.6 percent respectively.

5. Discussion

BMV has evolved as a safe and effective procedure to relieve the obstruction in patients of MS with suitable valve morphology. But successful procedure presently assessed by echocardiography (defined as final MVA $\geq$ 1.5 cm^2 or $\geq$ 50% increase from baseline without significant MR) does not produce uniform degree of clinical improvement in all patients. Despite a similar increase in MVA, patients may have variable improvement in NYHA FC and exercise capacity.[13,14,15] Increased MVA and decreased transmitral valve gradient do not correlate well with clinical outcome.[16]

In patients of MS low atrial compliance is associated with higher FC, higher sPAP and poorer exercise capacity.[4,17] However Cn is not routinely assessed in patients of rheumatic MS. In our study, there was a significant improvement in Cn acutely following BMV which is in agreement with two studies which assessed the acute effects of BMV on Cn.[3,11] Cn has also shown a very good correlation with sPAP.[4,9,17,18] Our study results are in agreement with these studies. Following BMV, PA pressure regresses over 24 weeks. Progressive improvement in Cn after successful BMV may be an important factor responsible for sPAP regression.[12]

Our study has shown that following successful BMV there is a progressive improvement in Cn upto 12 weeks, associated with significant reduction of sPAP with no further significant improvement thereafter. In our study, a very good correlation was also seen between change in Cn with improvement in NYHA FC and exercise capacity along with regression of sPAP over a period of 24 weeks post BMV compared to baseline. Rajib et al also showed that post BMV Cn significantly correlated with NYHA FC assessed after BMV at 72 h.[3] Our study also showed good correlation between improvement in Cn and NYHA FC assessed after BMV at 2 weeks with further improvement uptill 12 weeks. At baseline 43 (86%) patients were in NYHA class III and 7 (14%) were in class IV. At the end of 2 weeks after BMV 18 (36%) were in class III, 24 (48%) were in class II and 8 (16%) were in class I. With progressive improvement in Cn and fall in sPAP at end of 12 weeks, 1 (2%) was in class III, 20 (40%) were in class II and 29 (58%) were in class I. After 12 weeks till 24 weeks, neither further improvement in NYHA FC nor deterioration was seen in the study population.

In our study change in MVA did not show any correlation with improvement in NYHA FC, 6 MWT or regression of sPAP.

We compared the baseline echocardiographic parameters in patients with good clinical outcome to those with poor clinical outcome. In spite of comparable MVA and trans mitral gradient at baseline, Cn was significantly lower in patients with poor clinical outcome compared to those with good clinical outcome. Similarly following BMV (inspite of comparable MVA and TMG) Cn was significantly lower and sPAP was significantly higher in patients with poor clinical outcome. Studies have shown a negative correlation of Cn with sPAP which inturn is inversely correlated with exercise capacity.[19,20,21] Hence in our study, patients of group B with lower Cn were in higher FC with poorer exercise capacity than group A patients. Patients with poor clinical outcome did not only have significantly lower Cn at baseline (suggestive of stiffer atria with more fibrosis)[18] than those with good clinical outcome but the extent of improvement in Cn post successful BMV was also significantly less.

So while the extent of increase in MVA (MVA $\geq$1.5 cm^2) is a predictor of procedural success, the extent of improvement in Cn is a predictor of clinical success (improvement in NYHA FC and exercise capacity). Hence, we feel that apart from anatomical assessment of MVA, parameters like Cn should also be routinely evaluated in patients undergoing BMV to better predict the clinical outcome.

6. Study limitations

Pressure gradients and flow data were assessed by echocardiography and were not correlated with invasively derived measurements. In the current study, Cn was derived from echocardiographic examinations performed at rest and represent resting Cn only.

7. Conclusion

We found improvement in Cn following BMV to have significant correlation with clinical improvement. Increase in MVA or reduction in mean TMG did not correlate with clinical improvement. Hence change in Cn should also be assessed along with MVA to better predict clinical outcome following successful BMV.

Declaration of competing interest

All the authors declare that they have no conflicts of interest with respect to the present submission.

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