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Reversed right ventricular remodeling and improved functions after percutaneous mitral valve clipping

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Abstract: Background: Percutaneous mitral valve clipping (PMVC) is being used successfully in the management of severe functional mitral regurgitation (MR) in patients with high surgical risk. However, the impact of (PMVC) on right ventricular volumes and functions is not clear.

Aim:

The aim of the present study was to assess the impact of (PMVC) (in both short and intermediate terms) on right ventricular (RV) volumes and functions using trans-thoracic echocardiography . **Methods:**

The study population included 37 patients with severe (MR), and congestive heart failure who were at high surgical risk. The mean age was 61±14 years. Nine (24.3%) were males. (PMVC) was successfully done for all patients All had clinical and echocardiographic follow up at 6 and 12-months post (PMVC) .

Results: MR showed significant improvement after (PMVC) . MR was less than grade II in 29 (78 %) of patients at 6 months and persisted at 12 months (P = 0.0001). Similarly, tricuspid regurgitation (TR) showed marked improvement. Severe (TR) was seen in 29 patients (78%) before), but decreased to 7 patients (18.9%) after (PMVC) (P=0.004). Left ventricular ejection fraction (LVEF) improved from 32.63±13.35% at base line to 36.31±13.28 % at 6 months(P=0.003). This was maintained at 12 months (35.38±91%) Table 1 shows the changes in RV end diastolic volume (RVDV), RV end systolic volume (RVSV) , RV ejection fraction

(RVEF), Tricuspid annulus plane systolic excursion(TAPSE), RV longitudinal systolic function by tissue Doppler imaging(TDI) as well as peak systolic pulmonary artery pressure (PASP). **Conclusion:**

(PMVC) induced a significant reverse remodeling of RV by decreasing both (RVDV) and (RVSV) Moreover, it improved longitudinal RV systolic function as well as (RVEF). This was maintained up to one year follow up.

Keywords: *Right Ventricular, Remodeling , Percutaneous, Mitral Valve Clipping*

Echo data at baseline, and at follow up

	Baseline	6m	12m	P value
TAPSE cm	**1.7±0.57**	**2.0±0.7**	**1.9±0.6**	**0.001**
TDI S cm/s	**10.5±2.3**	**13.9±3**	**12.2±2.7**	**0.005**
RVEF %	**34.1±9.9**	**42.3±12.8**	**45±18.3**	**0.001**
RVDV ml	**58±20.8**	**50.9±20.7**	**52.9±31.9**	**0.008**
RVSV ml	**39.9±16.9**	**32.4±20.4**	**31±22.4**	**0.004**
PSAP mmHg	**50.4±13.9**	**42.7±13.6**	**42.3±13.3**	**0.03**

TAPSE: Tricuspid annulus plane systolic excursion, TDI S´: Peak lateral tricuspid annulus systolic velocity by tissue Doppler imaging, RVEF : Right ventricular ejection fraction, RVDV: Right ventricular end diastolic volume, RVSV: Right ventricular end systolic volume, PASP: Peak pulmonary artery systolic pressure.

Introduction

Mitral regurgitation (MR) represents the second most common valvular disease in Europe[1] .This pathology evolves, over many years, allowing the heart to adapt to a chronic volume overload, leading to significant hemodynamic, and structural changes.

In chronic severe MR, the remodeling of left heart may lead to the development of significant pulmonary hypertension in almost half of the patients [2& 3]. The increase in right ventricular (RV) afterload at first induces remodeling of RV and right atrium (RA) .Afterwards, it leads to decreased contractile performance and to RV dysfunction that affects patient´s prognosis.

Right ventricular (RV) ejection fraction (EF) is depressed in patients with chronic organic MR[2& 4]. RV systolic performance is influenced by pulmonary artery systolic pressure (PASP). [4&5]. In organic MR, elevated PASP increases RV afterload and is thought to elicit progressive RV failure, particularly in patients with disproportionate pulmonary hypertension (PH) [6].

Percutaneous mitral valve repair (PMVR) which was FDA approved in 2013 has been shown to be associated with a favorable left ventricular (LV) reverse remodeling and with clinical outcomes in high-risk patients with severe MR[7]. However, nowadays, scarce data, are available on reverse remodeling and right ventricular functions, after PMVR

Aim of the work

The aim of the present study was to assess the impact of Mitral Valve Clipping (in both short and intermediate terms) on right ventricular (RV) dimensions and function using trans-thoracic echocardiography.

Patients and Methods

The study included 37 consecutive patients who underwent Percutaneous Mitral valve Repair (PMVR) with Mitral Clip insertion in the period from April 2013 to June 2015 in Madinah cardiac center , Madinah Monawara, KSA. PMVR was decided after heart team meeting where these patients were deemed as high surgical risk The team also assessed valve anatomy to check the suitability for Mitral Clip treatment according to the EVEREST anatomic eligibility criteria. [8 &9].

Patients were selected if they had severe functional or degenerative mitral regurgitation and met the most recent indications for intervention from American College of Cardiology (ACC)/ and American Heart Association (AHA) joint task force recommendations regarding therapy of valvular heart disease R?.

All echocardiograms were assessed by an independent echocardiographic laboratory. Mitral regurgitation was evaluated according to American society of echocardiography (ASE) guidelines by the use of quantitative (regurgitant volume, and regurgitant fraction) and qualitative (color Doppler and pulmonary venous flow) criteria [10].

Patients were on stable guideline optimized heart failure medication, Associated CAD was treated by PCI (percutaneous angioplasty and stent implantation) 3 months before, (PMVR) , if applicable.
Clinical and echocardiographic follow-up through office visits were carried out at 6 and 12 months after (PMVR).

Inclusion Criteria

1-Candidates for mitral valve repair as shown by echocardiography.
2- Symptomatic patients with moderate to severe (3+) or severe (4+) chronic mitral valve regurgitation (functional or degenerative) , with LVEF >25% and LVID-s ≤55 mm
3-Asymptomatic patients with one or more of the following:
A-LVEF >25% to 60%
B-LVID-s ≥40 to 55 mm
C-Pulmonary hypertension defined as pulmonary artery systolic pressure >50 mm Hg at rest or >60 mm Hg with exercise.

Exclusion Criteria

1-MR due to changes caused by endocarditis, rheumatic heart disease
2-Recent myocardial infarction
3-Mitral valve orifice area <4 cm2
4- Severe renal insufficiency (GFR <30 ml /min.)
5-Previous mediastinal surgery
6-Short life expectancy less than one year

Methods

All patients in this study were subjected to the following:

1-History taking

Detailed history taking with special emphasis as regards history of endocarditis and rheumatic heart disease for exclusion. Detailed analysis of the degree of heart failure symptoms. especially NYHA functional class.
Assessment of surgical risk and eligibility for Mitral Clip therapy.

2-Clinical examinations

General examination including vital signs and local cardiac examinations with special emphasis on auscultation to assess valvular and structural heart disease, With the utmost care given to signs of CHF.

3-Laboratory investigations

All patients had the following done:
Complete blood count
Coagulation profile (PT, PTT, INR)
Cardiac markers
Kidney function tests, GFR
Blood glucose level
Liver function tests

4- Resting Electrocardiogram (ECG)

5-*Echocardiographic assessment*

All enrolled patients had transthoracic two-dimensional echocardiography (Philips i33, Philips Ultrasound, Andover, MA, USA) before the procedure, at 6 months and 1 year after the procedure.
All measures were assessed according to ASE recommendations guidelines [11].
LV volumes and ejection fraction were calculated from apical two- and four-chamber views using the modified Simpson's rule. LV internal dimensions, end-diastolic diameter and end-systolic diameters were measured at the level of the LV minor axis, approximately at the mitral valve leaflet tips, in the parasternal view, using two-

dimensional-targeted M-mode echocardiography. LA and RA volumes were measured from a single-plane apical imaging window. MR severity was visually estimated by color Doppler and grading by the vena contracta width and the PISA (proximal isovelocity surface area) method, according to the following score: 1+ (mild), 2+ (mild to moderate), 3+ (moderate to severe), or 4+ (severe). To evaluate the possible development of MV stenosis, the mitral valve area was measured by Doppler evaluation. .The modified apical four-chamber view was performed to obtain 'the right ventricle-focused view' to evaluate the RV changes in size and function.
The following parameters were measured at end diastole:
1-RV free wall thickness,
2- Basal, mid, and RV base to apex diameters.
The RV global function was evaluated in apical four-chamber view by tracing the RV area, both in systole and diastole, and calculating fractional area changes (FACs) using the following formula:
FAC = (end-diastolic area − end-systolic area)/end-diastolic area, reported in percentage.
The RV longitudinal function was obtained, in apical four-chamber view, placing an M-mode cursor through the tricuspid annulus and measuring tricuspid annular plane systolic excursion (TAPSE).
Pulsed Doppler tissue imaging, at the mitral lateral site and at tricuspid annulus respectively was acquired from the apical four-chamber view to measure the following parameters:
Systolic velocity (Sm), early diastolic (Em), and atrial contraction peak velocities.
All measurements were performed on three consecutive cycles if the patient would be in sinus rhythm and on 10 consecutive cycles in case of atrial fibrillation and the mean value was calculated.
Systolic pulmonary artery pressure (SPAP) was determined from peak tricuspid regurgitation jet velocity, using the simplified Bernoulli equation and combining this value with an estimate of the RA pressure: SPAP = $4 \times (V)^2$ + RA pressure, where V is the peak velocity (in m/s) of the tricuspid valve regurgitation jet. RA pressure was estimated from inferior vena cava diameter and with respiratory changes according to the guidelines [11].

Statistical analysis

Categorical variables as age and sex were presented as frequencies and percentages. Continuous variables were presented as mean± SD. For continuous variables, paired comparison between baseline, 6-month and 12 months follow-up was performed with a Wilcoxon signed-rank test. The comparison of a single group over different points of time was achieved by the Friedman two-way ANOVA with Bonferroni's post-tests.
Correlations between the echocardiographic measurements were tested, and only those statistically significant have been reported, providing the Spearman correlation coefficient. A P-value of, 0.05 was considered statistically significant. All data were processed using the Statistical Package for Social Sciences, version 15 (SPSS, Chicago, IL, USA).

Results

A total number of 37 consecutive patients underwent Percutaneous Mitral valve repair with Mitral Clip system were studied in MCC Madinah Monawarah KSA over a period of two years from April 2013 to June 2015.
The mean age was 61 ± 14 years old. There were 9 males (24%) and 28 females (76%). Twenty one patients (56.8%) were diabetic. Twenty two patients were hypertensive (59.5%). Six patients (16.2%) were in AF .Twenty five patients had history of CHF (67.6%). However, 97.3 % (36 patients) had NYHA III/IV either at the time of the procedure or as a past history. Thirteen patients (35.1%) had pulmonary artery systolic pressure (PASP) > 60 mmHg. Twenty patients (54 %) had CAD with history of PCI and stent implantation. Four patients (10.8%) had chronic obstructive pulmonary disease (COPD),and 7 patients (18.9%) had chronic renal impairment with serum creatinine>170 mmol/l.(Table 1)
PMVR was successfully completed in all the 37cases. One clip was deployed in 14 patients . Eleven patients needed two clips, while only one patient needed three clips .

Echocardiographic data

Mitral Regurgitation Parameters

Regarding Mitral regurgitation, the following parameters showed significant improvement; MR severity, vena contracta (VC), proximal isovelocity surface area radius (PISA r), and proximal isovelocity surface area(PISA), All these changes were maintained at 6 as well as 12 months.(Table 2)

MR severity

All the patients had MR grade ≥ III before insertion of Mitral Clip , Twenty nine patients (78.38%) had MR less than 2 after the procedure. Mitral regurgitation was less than grade II in the 29 patienta at 12 month follow up(P = 0.0001).

Vena Contracta

In the same context, vena contracta improved from 0.69±0.17 cm at baseline to 0.37±0.18 cm at 6 months, and 0.40± 0.25 cm at 12 months (P = 0.0001).

PISAr and PISA

PISAr showed reduction from 0.96±0.29 cm at baseline to 0.38±0.28 cm at 6 months, Further reduction was noted at 12 months as 0.30±0.29 cm (P 0.0001).

PISA showed similar changes form 201.00±177.02 cm^2 at baseline to 105.33± 118.52 cm^2 at 6 months with further reduction at 12 months to be 83.95± 104.21cm^2 (P0.0001)

Mitral Valve Mean Pressure Gradient (MPG)

Mean mitral valve gradient increased from 3.01± 1.99 mmHg at baseline to 5.71± 3.12 mmHg at 6 months and 6.20±2.81 mmHg at 12 months. No patient had gradient 10 mmHg or more (P=0.0001).

Right Ventricular function

The following parameters showed significant improvement at 6 months, and at 12 months, compared to baseline values : Tricuspid annular plane systolic excursion (TAPSE), tissue Doppler imaging at lateral tricuspid annulus (TDI), right ventricular ejection fraction (RVEF), RV systolic and RV diastolic volumes, and pulmonary artery systolic pressure(PASP).

On the other hand, right ventricular wall thickness (RVWT), basal diameter (RVBD), and mid diameter showed non-significant improvement. (Table 3)

TAPSE

The tricuspid annular plane systolic excursion (TAPSE) improved from 1.73 ±0.57 cm at base line to 2.02 ±0.70 cm at 6 months, this improvement was still maintained at 12 months (1.87±0.63cm). (P = 0.0001) (Table 3 , figure 1).

TDI

In the same context, the systolic velocity at the lateral tricuspid annulus examined by tissue Doppler imaging (TDI-RV-Sm) improved from 10.50 ±2.33 cm at baseline to 11.98 ±3.02 cm at 6 months , and 11.24 ±2.72 cm at 12 months respectively (P= 0.005) (table 4) (figure 2).

RV EF

Similarly, right ventricular ejection fraction (RVEF), showed significant improvement, from 34.19 ±9.94 % at baseline, to 42.35 ±12.82 % at 6 months. It showed further improvement to 45.08 ±18.39 % at 12 months (P= 0.001).

Right Ventricular Volumes

Right ventricular diastolic volume improved from 56.05 ±20.86 ml at baseline to 54.91 ±28.73 ml at 6 months and 52.90 ±31.91 ml at 12 months respectively. (P= 0.008).Right ventricular systolic volume decreased from 39.41 ±16.99 ml at base line to 37.44 ±20.47 ml at 6 months, and was 31.06 ±22.49 ml at 12 months. (P=0.004).(Figure3)

Pulmonary Artery Systolic Pressure (PASP)

Pulmonary artery systolic pressure (PASP) also showed significant improvement from 50± 13.92 mmHg at baseline, to 45.73±15.67 mmHg, at 6 months with further decrease to 42.33±16.32 mmHg at 12 months. (P=0.036) (Figure4)

RV Diameters

Right ventricular wall thickness (RVWT) was 0.69 ±0.13 cm at baseline, 0.71±0.11cm at 6 months, and 0.6±80.13 at 12 months respectively (P= 0.062).Right ventricular basal diameter was 4.04±0.82 cm at baseline, 4.19±0.77 cm at 6 months, and 4.08±0.78 cm at 12 months respectively (P= 0.034). Right ventricular mid diameter was 2.73±0.66 cm at baseline, 2.99±0.79 cm at 6 months, and 3.04±0.86 cm at 12 months respectively (P =0.129) .

Left Ventricular Ejection Fraction (LVEF)

Left Ventricular Ejection Fraction (LVEF) improved from 32.63±13.35% at base line to 36.31±13.28 % at 6 months. This was maintained at 12 months (35.38±91%) (P=0.003).

Tissue Doppler measurement at the mitral valve annulus

TDI at lateral mitral valve increased from 4.73 ±1.89 cm/s at base line to 5.28 ±1.93cm/s at 6 months and 4.84 ±1.81cm/s at 12 months respectively. (P=0.004).

S ´at medial annulus was 7.29 ±3.01 cm/s base line. It showed improvement to 8.23 ±2.84 cm/s at 6 months , and was maintained at 12 months as 8.52 ±3.11 cm/s (P=0.001).

Left ventricular volumes

Left ventricular diastolic volume (LVDV) was 201.44 ±70.81ml at baseline and was 191.73 ±61.67ml at 6 months .It dropped to 180.54 ±69.18 ml at 12 months follow up (P= 0.123). Left ventricular systolic volume was at baseline 138.83 ±128.85 ml. It dropped to 126.22 ±124.65 ml at 6 months and 123.09 ±117.67 ml at 12 months respectively.(P= 0.381).

Left and Right atrial Volumes

Left atrial volume (LAV) showed non significant change .It was 68.47 ±25.36 ml at baseline .At 6 months, it showed almost no change (68.61 ±38.16 ml), while it showed some decrease at 12 months 67.05 ±36.69 ml (P=0.154) .

Right atrial volume (RAV), showed mild improvement from 54.12 ±34.41 ml at base line to 53.89 ±33.46 ml at 6 months, with further improvement to be 52.30 ±31.74 ml at 12 months (P=0.029). (Table 4)

Severity of tricuspid regurgitation

Number of patients with severe TR was 29 patients before insertion of MitraClip (78%), this number decreased to 7 patients after insertion (18.9%) (P=0.004) .The number of patients with mild and moderate TR increased from 8 patients (21.6%) before insertion to 30 patients after insertion (81%). This change persisted at 12 months (P = 0.0001) .

NYHA class

In addition to the improvement of MR and LV function, NYHA class improved significantly .At baseline ,36 patients had NYHA class III / IV (97.3%) . The latter was seen only in 7 patients (18.92%) at 6 months, and in 9 patients (24.32%) at 12 months respectively (P =0.003).

Laboratory Investigations

Among all the laboratory investigations done to the patients before and after the procedure, only INR, and albumin showed significant change at 6 months and was maintained at 12 months.

At base line INR was 1.33±0.33.It improved to 1.18±0.27 at 6 months and 1.19±30 at 12 months respectively .P=0.003).

Albumin was 2.71±0.45 gm/dl at baseline, improved to 3.16± 0.43 gm/dl at 6 months and was 3.12± 0.46 at 12 months respectively (P=0.004).

All other labs did not show any significant change.

Table 1 : Baseline data before PMVR

	Mean	SD
Age, years	61	14
	Count	%
Male gender	9	24.3%
Diabetes mellitus	21	56.8%
Hypertension	22	59.5%
Atrial fibrillation	6	16.2%
Chronic obstructive pulmonary disease	4	10.8%
Serum creatinine >170 mmol/Dl	7	18.9%
Coronary artery disease	20	54.1%
congestive heart failure	25	67.6%
NYHA functional class III/IV	36	97.3%
SPAP >= 60 mmHg	13	35.1%

NYHA: New York heart association dyspnea classification, *PASP* Pulmonary Artery Systolic Pressure.

Table 2., Effect of PMVR on MR (Echo Parameters)

	Baseline	6m	12m	Sig
Vena contracta cm	0.69 ±0.17	0.37 ±0.18	0.40 ±0.25	0.000
PISA r cm	0.69 ±0.29	0.38 ±0.28	0.30 ±0.29	0.000
PISA cm^2	201.00 ±177.02	105.33 ±118.52	83.95 ±104.21	0.000
MPG mmHg	3.01 ±1.99	5.71 ±3.12	6.20 ±2.81	0.000
MR <2	0.00 (0.00%)	29.00 (78.38%)	29.00 (78.38%)	0.000

MR:Mitral regurgitation. PISA: proximal isovelocity surface area .PISA r: : proximal isovelocity surface area radius.MPG:Mean pressure gradient

Table 3.,Echocardiographic data of RV at baseline,6 months and at one year

	Baseline	6m	12m	Sig
TAPSE cm	1.73 ±0.57	2.02 ±0.70	1.98 ±0.63	0.000
TDI cm/s	10.50 ±2.33	10.98 ±3.02	10.24 ±2.72	0.005
RV EF %	34.19 ±9.94	42.35 ±12.82	45.08 ±18.39	0.000
RVDV ml	56.05 ±20.86	54.91 ±28.73	52.90 ±31.91	0.008
RVSV ml	39.41 ±16.99	37.44 ±20.47	31.06 ±22.49	0.004
PASP mmHg	50.49 ±13.92	45.73 ±15.67	42.33 ±16.32	0.036
RV WTH cm	0.69 ±0.13	0.71 ±0.11	0.68 ±0.13	0.062
RV BD cm	4.04 ±0.82	4.19 ±0.77	4.18 ±0.78	0.034
RV MD cm	2.73 ±0.66	2.99 ±0.79	3.04 ±0.86	0.129

, *TAPSE* annular plane systolic excursion, *TDI* tissue Doppler imaging, *RV EF* Right ventricular ejection fraction, *RVDV* Right ventricular diastolic volume, *RVSV* Right ventricular systolic volume, *PASP* Pulmonary artery systolic pressure,*RV WTH* Right ventricular wall thickness, *RV BD* Right ventricular basal diameter, *RVMD* right ventricular mid-diastole.

Table4 Echocardiographic data of LV ,RA and MR

	Baseline	6m	12m	Sig
LVDV ml	201.44 ±70.81	191.73 ±61.67	180.54 ±69.18	0.123
LVSV ml	138.83 ±128.85	126.22 ±124.65	123.09 ±117.67	0.381
EF %	32.63 ±13.35	36.31 ±13.28	35.38 ±13.91	0.003
TDV M. LAT cm/s	4.63 ±1.89	5.28 ±1.93	4.99 ±1.81	0.004
TDV M. MED cm/s	7.29 ±3.01	8.23 ±2.84	8.52 ±3.11	0.001
LAV ml	68.47 ±25.36	68.61 ±38.16	67.05 ±36.69	0.154
RAV ml	54.12 ±34.41	53.89 ±33.46	52.30 ±31.74	0.029
Vena contracta cm	0.69 ±0.17	0.37 ±0.18	0.40 ±0.25	0.000
PISA r cm	0.69 ±0.29	0.38 ±0.28	0.30 ±0.29	0.000
PISA cm ^{2}	201.00 ±177.02	105.33 ±118.52	83.95 ±104.21	0.000
MPG M mmHg	3.01 ±1.99	5.71 ±3.12	6.20 ±2.81	0.000
MR <2	0.00 (0.00%)	29.00 (78.38%)	29.00 (78.38%)	0.000

LVDV left ventricular diastolic volume, *LVSV* left ventricular systolic volume, *LVEF* left ventricular ejection fraction, *TDV M. LAT* tissue Doppler velocity at lateral mitral annulus, *TDV M. MED* tissue Doppler velocity at medial mitral annulus, *LAV* left atrial volume, *RAV* right atrial volume, *PISA r* proximal isovelocity surface area radius, *PISA* proximal isovelocity surface area, *MPG M* mean pressure gradient mitral valve, *MR* mitral regurgitation.

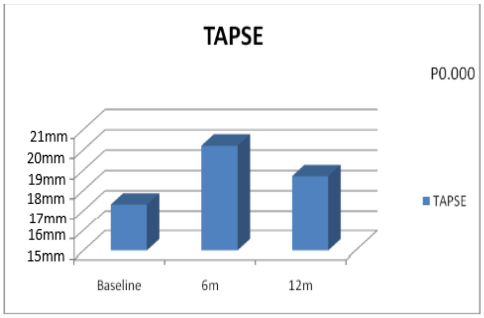

Fig.1. TAPSE :Tricuspid annulus plane systolic excursion. At baselie,after 6 and 12 months

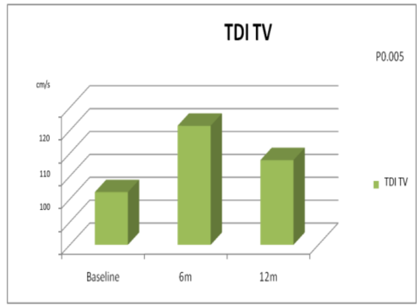

Fig.2. TDI TV, TDI TV tissue Doppler imaging at lateral tricuspid annulus.

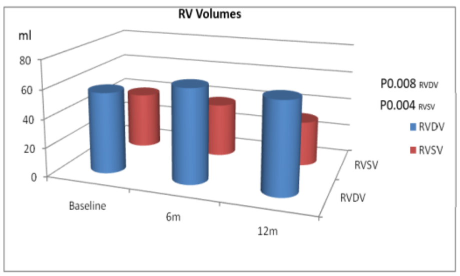

Fig.3:, RVDV Right ventricular diastolic volume

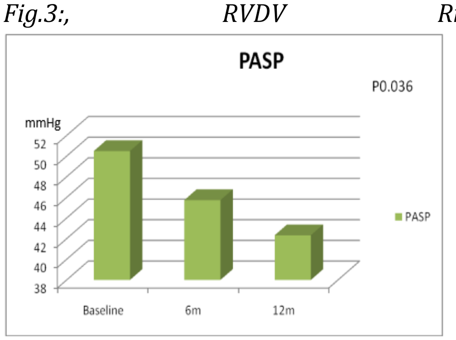

Fig.4. PASP, PASP Pulmonary Artery Systolic Pressure.

Discussion

In this study, we included 37 high surgical risk patients with severe MR to evaluate the impact of percutaneous mitral valve clip insertion on pre-existing RV dysfunction and its remodeling. In such patients with severe MR regurgitation who could not have surgery due to high surgical risk, percutaneous mitral valve repair (PMVR) using Mitral Clip device has evolved as a promising interventional tool for MV repair. This procedure has been demonstrated to be feasible and safe leading to reduction in MR severity. has been shown to be associated with a favorable left ventricular (LV) reverse remodeling and improvement in clinical status and quality of life [7,8,9].

However, until recently, no solid data on right cardiac chambers reverse remodeling and function, after PMVR, has been available [12].

The results of our study showed significant improvement of right ventricular function with improvement of right ventricular volumes after (PMVR) . It also showed improvement of pulmonary artery systolic pressure (PASP) and decreased severity of tricuspid regurgitation. Improvement of left ventricular function and volumes were also noted, and, most importantly, the significant improvement of mitral regurgitation parameters. This was associated with concomitant clinical improvement of heart failure and NYHA functional class.

Right ventricular function

We found significant improvement of RV function at 6 months and 12 months compared to baseline. This can be explained by improvement of afterload and reduction of pulmonary artery systolic pressure (PASP) caused by correction of MR and improvement of LV function. The latter might also result in improvement of RV function through interventricular dependence.

Our results match literature as it is known that the natural history of MR, eventually, leads to right ventricular failure, the latter improves after correction of mitral regurgitation [13, 14].

Usually, right ventricular failure in mitral regurgitation is secondary to of pulmonary hypertension (P. HPN). The presence of P. HPN (defined as a systolic pressure >50 mm Hg at rest or >60 mm Hg with exercise) even in absence of symptoms is class IIA is an indication for surgery or intervention in MR according to the previous and the latest ESC and ACC/AHA guidelines of 2021[15,16,17].

However, the results from Ohno et al., opposed ours regarding RV functions, although it matched our results regarding the improvement in MR, TR, and NYHA functional class. They studied 146 cases and with MitraClip insertion for treatment of MR. Their results showed non significant change, in TAPSE at baseline, and at 12 months. .However, they did not give any explanation for that.

Improvement of right ventricular function in our study was reflected as marked improvement of RV Ejection Fraction, with significant improvement of Trans Annular Plane Systolic Excursion (TAPSE), and S´wave in tissue Doppler Imaging (TDI) of lateral tricuspid annulus. This indicates that the improvement of right ventricular function and right ventricular ejection fraction is mainly an improvement of longitudinal function. RV contraction actually consists of three steps. In the first step tricuspid annulus moves toward the apex, then apex moves toward the infundibulum in the second step. Then the third step is radial contraction of the RV free wall towards the interventricular septum which is the last and least important component[19].

This could indicate that MR correction improves the longitudinal function represented by the first two steps which are more important than radial contraction. It could be possible that these two steps are more affected by PASP which is improved after MR correction.

Our results support the fact that reduction in LV filling pressure obtained after MitraClip implantation results in a positive effect on the hemodynamics of the right side of the heart through reduction of PASP[20]. Follow up at 6-months and 12 months, showed significant reduction in PASP and significant increase in longitudinal RV systolic function (increase in TAPSE and RV S′TDI) in all patients with baseline RV dysfunction. These findings support the fact that RV performance is influenced by elevated PASP, which is a common finding in severe chronic MR. Reduced or normalized PASP after mitral valve repair could, at least in part, be the mechanism of the observed improvement of RV impairment in such patients [20, 21].

RV outcome after MitraClip procedure is not yet clearly defined [22,23]. In significant MR, complex interaction between the remodeled and enlarged left ventricle, septal performance, and PASP results in RV dysfunction [24].

In the same context, as per Haddad et al., There is continuity between right and left ventricles at the level of myofiber layer. Together with the pericardium and the inter-ventricular septum it helps interventricular dependence, this can help understanding how failure of one ventricle affects the other. Actually ,the left ventricle is responsible for 20% to 40% of RV contractile performance[19]. This can also participate in the mechanism of right ventricular function improvement . Godino et al studied 60 patients from 2008 to 2014 to evaluate the impact of RV dysfunction in patients with moderate–severe functional mitral regurgitation (FMR) successfully treated with MitraClip. Their results matched our results as it showed marked improvement of RV function at 6 months. However, their main objective was to study the outcome of mitral clip insertion in patients with RV dysfunction. For attaining this aim, they divided patients into two groups, one with normal right ventricular function (38 patients) and the other with impaired right ventricular function (21patients), the second group showed marked improvement of RV dysfunction .
On the same line results from Giannini et al 2013 matched ours. They studied 35 patients to investigate the changes of left and right ventricular (RV) dimensions and function after MitraClip implantation in high-risk surgical patients with severe functional mitral regurgitation (MR).They concluded that MitraClip implantation induces a significant reverse remodeling of the right ventricle, with a significant reduction in PASP .Moreover,a significant increase in longitudinal RV systolic function was noted.

PASP

Our study showed marked improvement of Pulmonary Artery Systolic Pressure (PASP) at 6 months that was maintained at 12 months .This matches well with literature.
Reduction in LV filling pressure obtained after MitraClip implantation mostly resulted in reduction of PASP[20].
Our results were supported by those from the 2014 multinational registry which was done to present a real-world overview of Mitral Clip use in Europe on a total of 628 patients, MitraClip insertion resulted in marked improvement of PASP from 46.0 ±14.5mmHg at baseline to 40.2 ± 11.7mmHg after insertion (P= 0.001) [25].
In addition, our results are supported by the results of Gaemperli et al,. who used right ventricular catheterization to assess immediate hemodynamic changes after percutaneous PMVR in fifty patients with severe MR. They reported immediate reduction of mean pulmonary artery pressure (mPAP) from 29±12mmHg before insertion to 24±6 mm Hg after insertion (P 0.013) [26].
On the other hand results from Siegel et al., opposed our results. They studied 107 patients with right heart catheterization and echocardiography immediately before and after MitraClip insertion. They mentioned that mean pulmonary artery pressure was not decreased , on the contrary it showed (non significant) increase from 23.5±11.9 mmHg to 23.8±7.7 mmHg (P 0.806) [27].
They explained these results by the trans mitral gradient associated with the creation of the double orifice valve and reduction of the MV area from 6.0 ± 1.3 cm2 to 3.6 ± 1.2 cm2 with a small increase in the MV gradient from 1.7 ±0.9 mm Hg to 4.1±2.2 mm Hg by TTE Doppler follow up within 1.2 ± 6.8 days following MitraClip insertion [27].
In our study no patients developed severe iatrogenic mitral stenosis and the reduction in PASP was significant.

Right ventricular volumes

Both RVDV and RVSV improved at 6 months with further improvement at 12 months (P0.008) for RVDV, and (P0.004) for RVSV.
This results are logic and go with literature as RV EF is calculated according to fractional area change method, so it is the result of manipulating these figures and it changes according to the change of these values.

Right ventricular diameters

In our results no change regarding RV wall thickness and RV diameters (basal and mid diameters2) was detected.,. However, this would not cause any discrepancy with improvement of RV function and volumes as it is mentioned before that, improvement in RV function was mainly in longitudinal function represented by TAPSE and TDI from the lateral tricuspid annulus.

The lack of change in RV thickness and dimensions could be explained in view of irreversible histological changes in ventricular wall due to long standing hemodynamic changes. Whether longer periods of follow up can lead to different findings this needs to be answered in future studies.

Assessment of Left Ventricular function

We found significant improvement in Left Ventricular Ejection Fraction (LVEF) .

Similarly there was a significant improvement in tissue Doppler measurement at the mitral valve reflecting a better improvement of longitudinal function of left ventricle.

This matches the literature as shown by many researchers. (Gainnini et al 2013[22], the results of Taramsso et al in 2014[28],and Scandura et al., [7])

Left and Right atrial Volumes

Left atrial volume (LAV) showed almost no change at 6 months and some change at 12 months that was non significant (P0.154). On the other hand, right atrial volume (RAV), showed mildly significant improvement from at 6 months follow up, with further improvement at 12 months (P=0.029).

This can be explained by the histo-pathological changes including fibrosis that take place in both atria in response to hemodynamic changes caused by mitral regurgitation. These changes could be irreversible and more resistant to remodeling in Lt. atrium because of longer duration and the thicker muscle of the Lt. atrium. It is also important to note that the later the intervention, the more difficult remodeling will be [7], Attizani et al., [32] as they concluded similar results.

Conclusion

Our study showed that successful MitraClip implantation in patients with FMR and RV dysfunction yields significant improvement of RV function represented in improvement of TAPSE, TDI TV, as well as RV volumes, RA. atrial diameter, MR severity, LV function and NYHA class at short and intermediate term follow-up.

References

1. Vahanian, A., Baumgartner, H., Bax, J., et al., 2007a. Guidelines on the management of valvular heart disease. Revista espanola de cardiologia, 60, 1e.
2. Borer, J. S. & Bonow, R. O. 2003. Contemporary approach to aortic and mitral regurgitation. Circulation, 108, 2432-2438.
3. Mclaughlin, V. 2004. Rich S. Pulmonary hypertension. Curr Probl Cardiol, 29, 575-634.
4. Le Tourneau T, Deswarte G, Lamblin N, et al., 2013. Right ventricular systolic function in organic mitral regurgitation: impact of biventricular impairment. circulation 2013.
5. Morrison D, Goldman S, Wright AL, et al., 1983. The effect of pulmonary hypertension on systolic function of the right ventricle. Chest. 1983; 84:250–257.
6. Alexopoulos, D., Lazzam, C., Borrico, S., et al., 1989. Isolated chronic mitral regurgitation with preserved systolic left ventricular function and severe pulmonary hypertension. Journal of the American College of Cardiology, 14, 319-322.
7. Scandura, S., Ussia, G. P., Capranzano, P., et al., 2012. Left cardiac chambers reverse remodeling after percutaneous mitral valve repair with the MitraClip system. Journal of the American Society of Echocardiography, 25, 1099-1105.
8. Feldman, T., Wasserman, H. S., Herrmann, H. C.,et al., 2005. Percutaneous mitral valve repair using the edge-to-edge technique: six-month results of the EVEREST Phase I Clinical Trial. J Am Coll Cardiol, 46, 2134-40.
9. Feldman, T., Foster, E., Glower, D. et al., 2011. Percutaneous repair or surgery for mitral regurgitation. New England Journal of Medicine, 364, 1395-1406.
10. Zoghbi W.A., Sarano M.E., Foster E., et al., 2003. Recommendations for evaluation of the severity of native valvular regurgitationwith two dimensional and doppler echocardiography. Journal of the American society of Echocardiography 7, 777-802.
11. Bonow R.O., Otto C.M., Carabello B. A. , et al 2014. AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.J Am Coll Cardiol. 2014 Jun, 63 (22) e57–e185.

12. Godino, C., Salerno, A., Cera, M.,et al., 2016b. Impact and evolution of right ventricular dysfunction after successful MitraClip implantation in patients with functional mitral regurgitation. IJC Heart & Vasculature, 11, 90-98.
13. Foltz, B., Hessel 2ND, E. & Ivey, T. 1984. The early course of pulmonary artery hypertension in patients undergoing mitral valve replacement with cardioplegic arrest. The Journal of thoracic and cardiovascular surgery, 88, 238-247.
14. Tempe, D. K., Hasija, S., Datt, V., et al., 2009. Evaluation and comparison of early hemodynamic changes after elective mitral valve replacement in patients with severe and mild pulmonary arterial hypertension. Journal of cardiothoracic and vascular anesthesia, 23, 298-305.
15. Nishimura, R. A., Otto, C. M., Bonow, R. O., et al.,2014. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. The Journal of thoracic and cardiovascular surgery, 148, e1-e132.
16. Grigioni, F., Clavel, M.-A., Vanoverschelde, J.-L., et al., 2018. The MIDA Mortality Risk Score: development and external validation of a prognostic model for early and late death in degenerative mitral regurgitation. European heart journal, 39, 1281-1291.
17. Ono, M. 2021. Updating guidelines: When is the best timing of upgrading recommendation for an emerging technology? : SAGE Publications Sage UK: London, England.
18. Ohno, Y., Attizzani, G. F., Capodanno, D., et al., 2014. Association of tricuspid regurgitation with clinical and echocardiographic outcomes after percutaneous mitral valve repair with the MitraClip System: 30-day and 12-month follow-up from the GRASP Registry. European Heart Journal–Cardiovascular Imaging, 15, 1246-1255.
19. Haddad, F., Hunt, S. A., Rosenthal, D. et al., 2008. Right ventricular function in cardiovascular disease, part I. Circulation, 117, 1436-1448.
20. Grose, R., Strain, J. & Yipintosoi, T. 1983. Right ventricular function in valvular heart disease: relation to pulmonary artery pressure. Journal of the American College of Cardiology, 2, 225-232.
21. Goldstone, A. , Chikwe, J., Pinney, S., et al., 2011. Incidence, epidemiology, and prognosis of residual pulmonary hypertension after mitral valve repair for degenerative mitral regurgitation. The American journal of cardiology, 107, 755-760.
22. Gianninni, C., Petronio, A. , De Carlo, M., et al., 2013. Integrated reverse left and right ventricular remodelling after MitraClip implantation in functional mitral regurgitation: an echocardiographic study. European Heart Journal–Cardiovascular Imaging, 15, 95-103.
23. Van Riel, A.C. KirstenB.D.,Rianne H.A.,et al., 2014. Percutaneous Mitral Valve Repair Preserves Right Ventricular Function. Journal of the American Society of Echocardiography, 27, 1098-1106.
24. Juilliere, Y., Barbier, G., Feldmann, L., et al., 1997. Additional predictive value of both left and right ventricular ejection fractions on long-term survival in idiopathic dilated cardiomyopathy. European heart journal, 18, 276-280.
25. Nickenig, G., Estevez-loureiro, R., Franzen, O., et al., 2014. Percutaneous mitral valve edge-to-edge repair: in-hospital results and 1-year follow-up of 628 patients of the 2011–2012 Pilot European Sentinel Registry. Journal of the American College of Cardiology, 64, 875-884.
26. Gaemperli, O., Moccetti, M., Surder, D., et al., 2012. Acute haemodynamic changes after percutaneous mitral valve repair: relation to mid-term outcomes. Heart, 98, 126-132.
27. Siegel, R. J., Biner, S., Rafique, A. M., et al., 2011. The acute hemodynamic effects of MitraClip therapy. Journal of the American College of Cardiology, 57, 1658-1665.
28. Taramasso, M., Maisano, F., Latib, A., et al., 2014. Clinical outcomes of MitraClip for the treatment of functional mitral regurgitation. EuroIntervention: journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology, 10, 746-752.
29. Bozdag-turan, I., Paranskaya, L., Birkemeyer, R., et al., 2014. Percutaneous Mitral Repair with the Mitral Clip System in Patients with Mild-to-Moderate and Severe Heart Failure: A Single-Centre Experience. Cardiovascular therapeutics, 32, 66-73.
30. Glower, D. , Kar, S., Trento, A., et al., 2014. Percutaneous mitral valve repair for mitral regurgitation in high-risk patients: results of the EVEREST II study. Journal of the American College of Cardiology, 64, 172-181.
31. Baldus, S., Schillinger, W., Franzen, O., et al., 2012. MitraClip therapy in daily clinical practice: initial results from the German transcatheter mitral valve interventions (TRAMI) registry. European journal of heart failure, 14, 1050-1055.
32. Attizzani, G., Ohno, Y., Capodanno, D., et al.,2015b. Extended Use of Percutaneous Edge-to-Edge Mitral Valve Repair Beyond EVEREST (Endovascular Valve Edge-to-Edge Repair) Criteria: 30-Day and 12-Month Clinical and Echocardiographic Outcomes From the GRASP (Getting Reduction of Mitral Insufficiency by Percutaneous Clip Implantation) Registry. JACC: Cardiovascular Interventions, 8, 74-82.