

# Right ventricular geometry and function in chronic primary mitral and aortic valve regurgitation: a three-dimensional echocardiography study.

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## Abstract

**Aims** To compare the effects of LV volume overload due to chronic organic MR or AR on RV shape and function. **Methods and results** We studied 63 patients with moderate-severe or severe primary MR and 36 patients with moderate or severe AR. 3D echocardiography of LV and RV was performed to measure volumes and EF. RV fractional area change (FAC) was calculated, and RV shape was assessed by calculating the RV eccentricity index. LV EDVi was significantly larger in the patients with AR than in those with MR. RV EF and RV FAC were lower in pts with AR than in those with MR. RV EI was significantly higher in the AR group. In both groups, LV EDVi showed positive correlations with RV EI (  $r= 0.693$  for AR and  $r=0.399$  for MR) and negative correlations (RV EF : $r= -0.545$  for AR and  $r=- 0.383$  for MR ; RV FAC:  $r=-0.816$  for AR and  $r=-0.647$  for MR, ). LV sphericity index showed negative correlations (RVFAC:  $r= -0.512$  and  $r=-0.608$  f ;RV EF: $r=-0.408$  and  $r=-0.469$  respectively ) and positive correlation with the RV EI ( $r= 0.39$  and  $r=0.511$  respectively) .LV EDVi and LV sphericity index were found to be the only independent predictors of RV eccentricity index, EF, and FAC. **Conclusions** RV remodeling in chronic LV overload due to MR or AR occurs independently on PASP values. LV size and shape are the only independent predictors of RV geometry and function. Accordingly, chronic AR has a greater impact on RV than MR

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# **Right ventricular geometry and function in chronic primary mitral and aortic valve regurgitation: a three -dimensional echocardiography study.**

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On behalf of all contributing authors, I am submitting **our original paper** entitled “**Right ventricular geometry and function in chronic primary mitral and aortic valve regurgitation: a three-dimensional echocardiography study.**”

- Our article highlights the use of 3D echocardiography in assessment of RV geometry and function in chronic primary MR and AR,
- No issues related to the journal policies.

- No conflict of interests
- All authors approved the submission
- All contents were not published and not submitted elsewhere

## **Introduction:**

Ventricular function is an important predictor of preoperative and postoperative outcome of mitral and aortic valve regurgitation. This is well known in regard to left ventricular (LV) function, which figures prominently in the clinical guidelines for surgical indications,<sup>(1,2)</sup> but it is less well known in regard to right ventricular (RV) function. The RV performance may be influenced by elevated systolic pulmonary artery pressure (PASP), which is a common finding in degenerative severe chronic mitral regurgitation (MR).<sup>(3-5)</sup> On the other side, RV systolic dysfunction can be an indirect consequence of chronic LV volume overload and, thus of enlarged LV in MR patients.<sup>(6)</sup> However, Elevation of PASP secondary to isolated aortic valve regurgitation (AR) is less common than with other valve lesions.<sup>(7)</sup> Therefore, the aim of the present study is to compare effects of LV volume overload due to chronic organic MR or AR on RV shape and function and to assess the pathophysiologic determinants of RV systolic function .

## **Methods**

### **Study population:**

Sixty-three patients with moderate-severe or severe organic mitral valve regurgitation and thirty-six patients with moderate or severe aortic valve regurgitation were included in this study. Patients with previous cardiac surgery, other significant valve disease (except for tricuspid regurgitation), previous myocardial infarction or severe lung disease were excluded.

## **2D echocardiography:**

Standard transthoracic echocardiography was performed using a Vivid E9 and Vivid E 95 ultrasound system, (GE Vingmed Ultrasound AS, Horten, Norway) equipped with a M5S 3.5-mHz transducer. M-mode, 2D, color Doppler, pulsed-wave and continuous-wave Doppler data were stored onto a dedicated workstation for off-line analysis (Echo PAC, GE Healthcare, Horten, Norway). Severity of mitral and aortic valve regurgitation was assessed according to guidelines.

RV function was estimated by 1) tricuspid annular plane systolic excursion (TAPSE), 2) fractional area change (FAC) obtained by the following formula:  $(RV \text{ end-diastolic area} - RV \text{ end systolic area}) / RV \text{ end-diastolic area} \times 100$ .

Systolic pulmonary artery pressure (PASP) was determined from the tricuspid regurgitation (TR) jet velocity using modified Bernoulli equation, and this value was combined with an estimate of the right atrial pressure by means of the diameter and collapsibility of the inferior vena cava.

## **3D echocardiography:**

An apical 3D dataset of LV and RV was obtained using a Vivid E9 or Vivid E95 equipped with a 4V probe. (GE Vingmed, Horten, Norway).

LV and RV full-volume datasets were obtained from 4 or 6 consecutive beats for adequate temporal resolution (20-40 volumes/sec).

Quantification of 3D LV volumes and EF was performed using a dedicated software (4D AutoLVQ, GE Vingmed, Norway). LV sphericity index is a quantitative parameter reflecting LV

shape, calculated as the ratio between the LV end-diastolic volume divided by the volume of a sphere, whose diameter is equal to the longitudinal LV axis measured at end-diastole.

RV volumes and EF were measured using software packages designed for volumetric analysis (TomTec Imaging Systems GmbH, Unterschleissheim, Germany). RV shape was assessed using RV eccentricity index, calculated as the ratio between RV longest lateral distance to the perpendicular distance from RV septum to free wall – at the level of LV papillary muscles.

(Figure 10)

### **Statistical analysis**

Data were expressed as mean  $\pm$  standard deviation for continuous variables and as percentages for categorical variables. Between-group comparisons were performed using Student's t-tests or  $\chi^2$  test, as appropriate. To identify pathophysiological correlates of RV function and shape, univariate linear regression analysis was carried out. Candidate variables were entered into a stepwise multivariate regression analysis to identify the independent predictors of RV changes. Statistical significance was defined as  $p < 0.05$ . Statistical analysis was performed using SPSS Version 20.0

### **Results:**

Baseline clinical and echocardiographic characteristics of the patient population are shown in table 1. Both LV end-diastolic volume (EDVi) and end-systolic volume (ESVi) were significantly larger in the patients with AR than those with MR. (Table 2). LV EF was significantly lower in AR group than in MR group. (Table 2). Pulmonary artery systolic pressure more than 45 mmHg was detected in 27% of patients with MR compared to only 8% in those with AR. (Figures 1-6).

### **RV shape and function:**

Impairment of RV systolic function (RV EF<45%) was detected in 63% of patients with AR compared to 58% of those with MR. Moreover, RV EF was significantly lower in the AR group than in MR group ( $40 \pm 6$  vs  $43 \pm 7$ ,  $p=0.03$ ). RV FAC was significantly lower in AR group when compared to MR group. ( $34 \pm 9$  vs  $37 \pm 9$ ,  $p=0.04$ ) (table 3) Tricuspid annular plane systolic excursion (TAPSE) correlated weakly with RV EF ( $r=0.24$ ,  $p=0.04$ ), that is why no significant difference was detected between both studied groups.

RV eccentricity index was significantly higher in the AR group when compared to MR group. ( $2.5 \pm 0.6$  vs  $2.1 \pm 0.5$ ,  $p=0.003$ ) (Table 3) (Figures 7-9).

Reduction in RV systolic function measured by EF and FAC has been strongly correlated with RV shape changes assessed by RV eccentricity index. ( $r=-0.45$  for RV EF and  $-0.52$  for FAC,  $p<0.001$ )

### **Pathophysiologic correlates of RV geometry and function:**

In univariate analysis, LV EDVi showed positive correlations with RV eccentricity index ( $r=0.693$  for AR and  $r=0.399$  for MR;  $p<0.001$ ) and negative correlations with RV EF (RV EF:  $r=-0.545$  for AR and  $r=-0.383$  for MR,  $p<0.001$ ) and RV FAC (RV FAC:  $r=-0.816$  for AR and  $r=-0.647$  for MR,  $p<0.001$ ). (Figures 11-13)

Moreover, LV sphericity index showed negative correlations with RV FAC ( $r=-0.512$  for MR and  $r=-0.608$  for AR,  $P=0.001$ ) and with RV EF ( $r=-0.408$  for MR and  $r=-0.469$  for AR,  $P=0.004$ ) and positive correlation with the RV eccentricity index ( $r=0.39$  for MR and  $r=0.511$  for AR,  $P<0.001$ ) (figures 14-16) .(Table 4).

On multivariable linear regression analysis, LV EDVi and LV sphericity index were found to be the only independent predictors of RV eccentricity index, EF, and FAC. (Table 5)

**Table 1: Basic clinical and echocardiographic characteristics in MR and AR patients:**

	<b>MR (n=63)</b>	<b>AR(n=36)</b>	<b>P</b>
<b>Age, years</b>	60±15	58±18	
<b>Male, n (%)</b>	33(55%)	29(80%)	
<b>BSA, m2</b>	1.8±0.2	1.9±0.2	
<b>Heart rate, bpm</b>	71±14	71±11	
<b>Systolic blood pressure, mmHg</b>	126±18	134±22	
<b>Atrial fibrillation</b>	5(8)	1(3)	
<b>Etiology of MR</b>			
<b>Mitral valve prolapse, n (%)</b>	48(77)		
<b>Flail MV, n (%)</b>	10(16)		
<b>Cleft mitral valve, n (%)</b>	3(4)		
<b>Posterior annular calcification, n (%)</b>	2(3)		
<b>Etiology of AR</b>			
<b>Bicuspid, n (%)</b>		16(44)	
<b>Aortic root dilatation, n (%)</b>		14(39)	
<b>Cusp prolapse, n (%)</b>		6(17)	
<b>≥ moderate TR, n (%)</b>	14(22)	4(11)	
<b>PASP (mmHg)</b>	33±17	27± 8	0.032
<b>mPAP (mmHg)</b>	19.8±11	15.4±5	0.043

PASP>45 mmHg	17(27)	3(8)	
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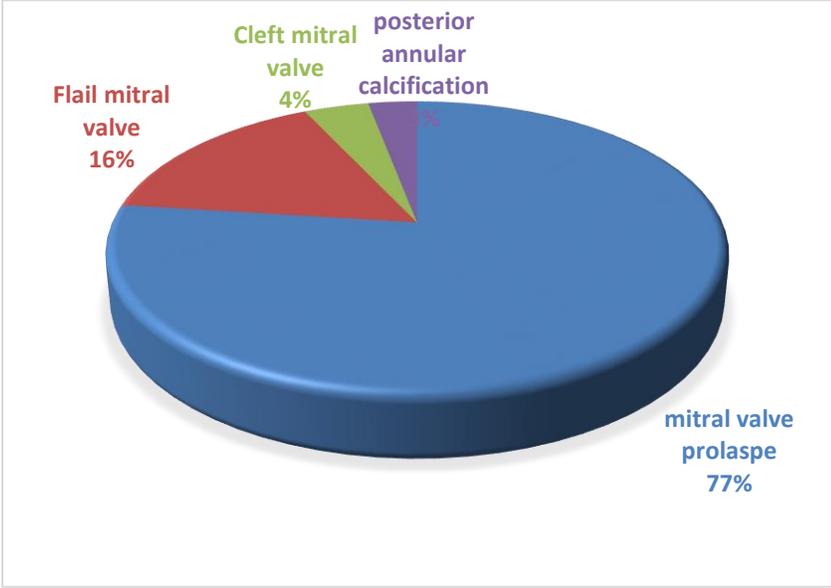


Figure 1: Etiology of mitral valve regurgitation.

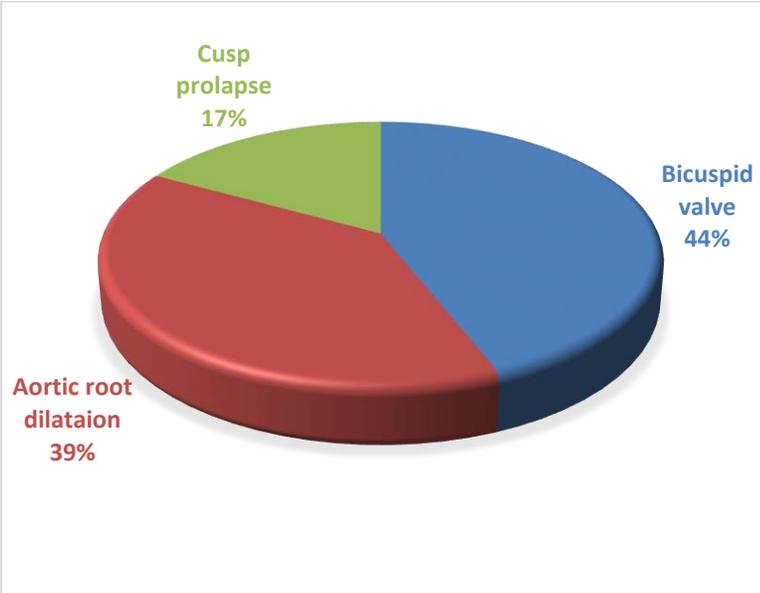
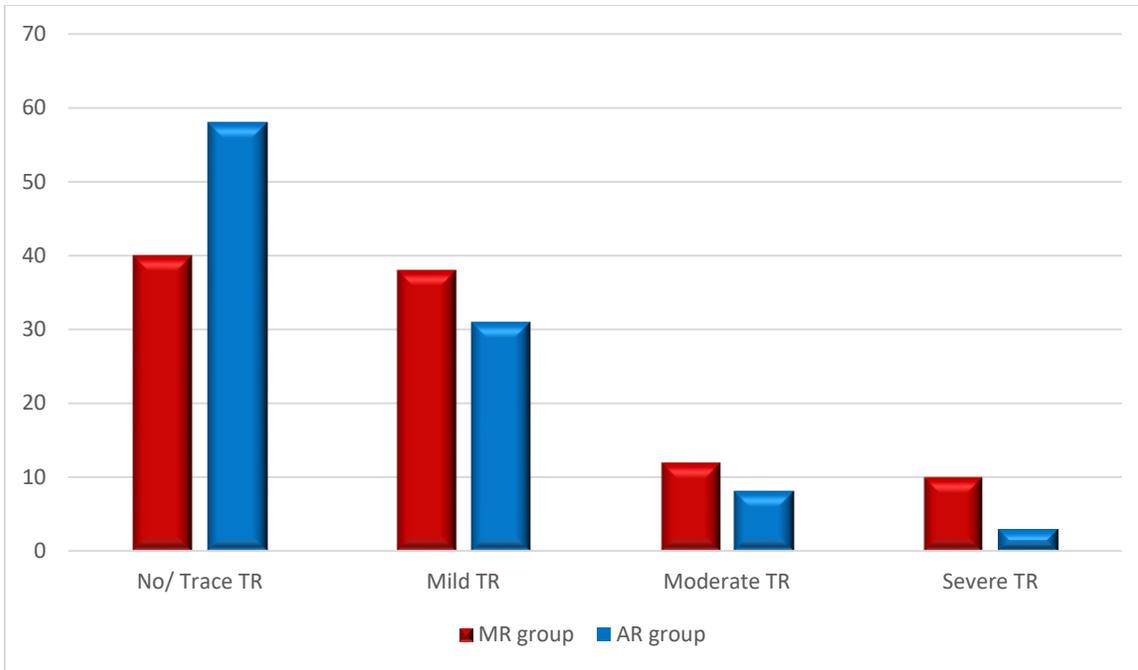
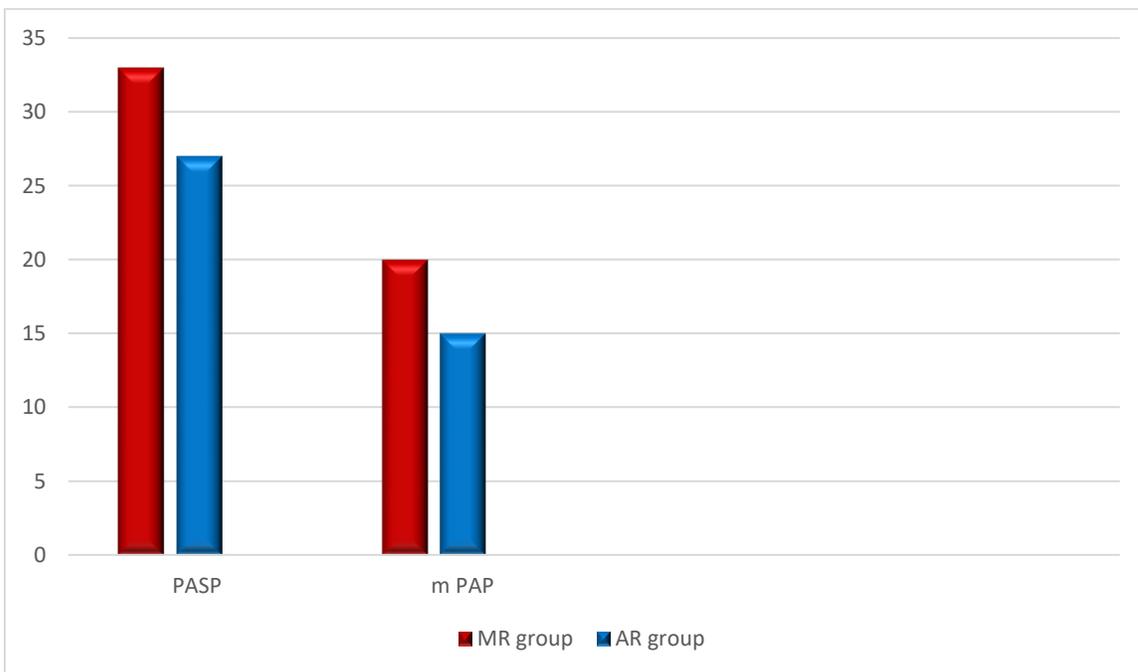


Figure 2: Etiology of aortic valve regurgitation.



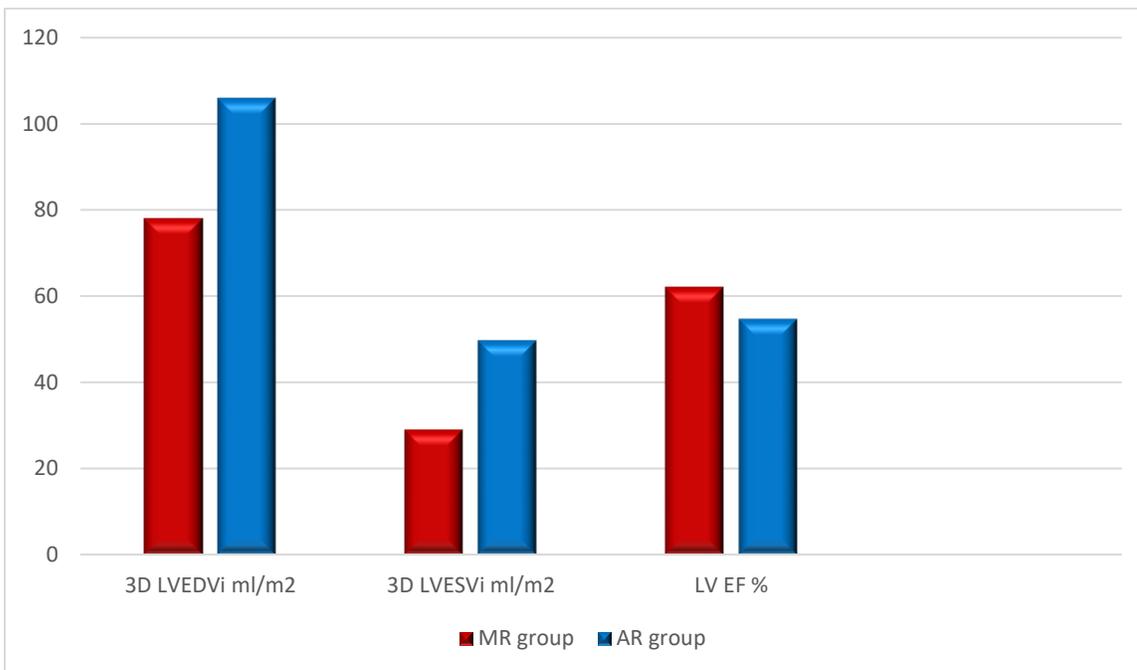
**Figure 3: TR severity in MR and AR groups.**



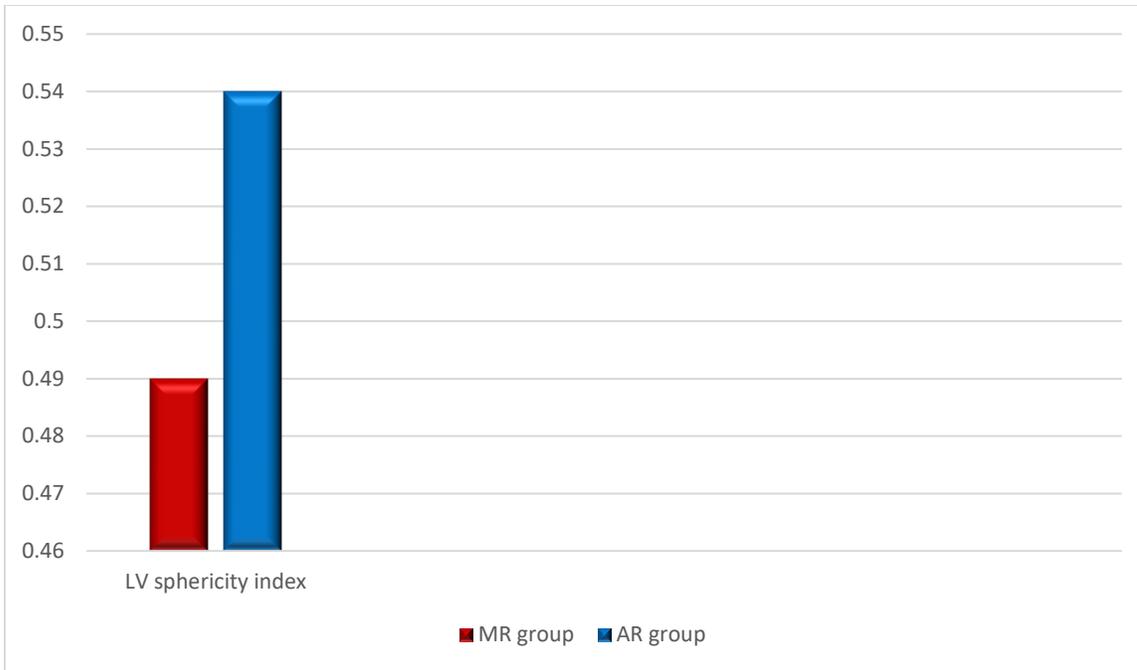
**Figure 4: comparison between both MR and AR groups according to the PAP.**

**Table 2:3D LV volumes, EF and sphericity index in MR and AR patients:**

<b>LV geometry and function</b>	<b>MR (n=63)</b>	<b>AR(n=36)</b>	<b>P value</b>
<b>3D LVEDV (ml)</b>	137±38	205±84	<0.001
<b>3D LVESV (ml)</b>	50±17	97±59	<0.001
<b>3D LVEDVi (ml/m2)</b>	78 ± 20	106 ± 36	<0.001
<b>3D LVESVi (ml/m2)</b>	29 ± 8	50 ± 28	<0.001
<b>LV EF (%)</b>	62 ± 6	54 ± 10	<0.001
<b>LV sphericity index</b>	0.49±0.10	0.53±0.11	<0.001



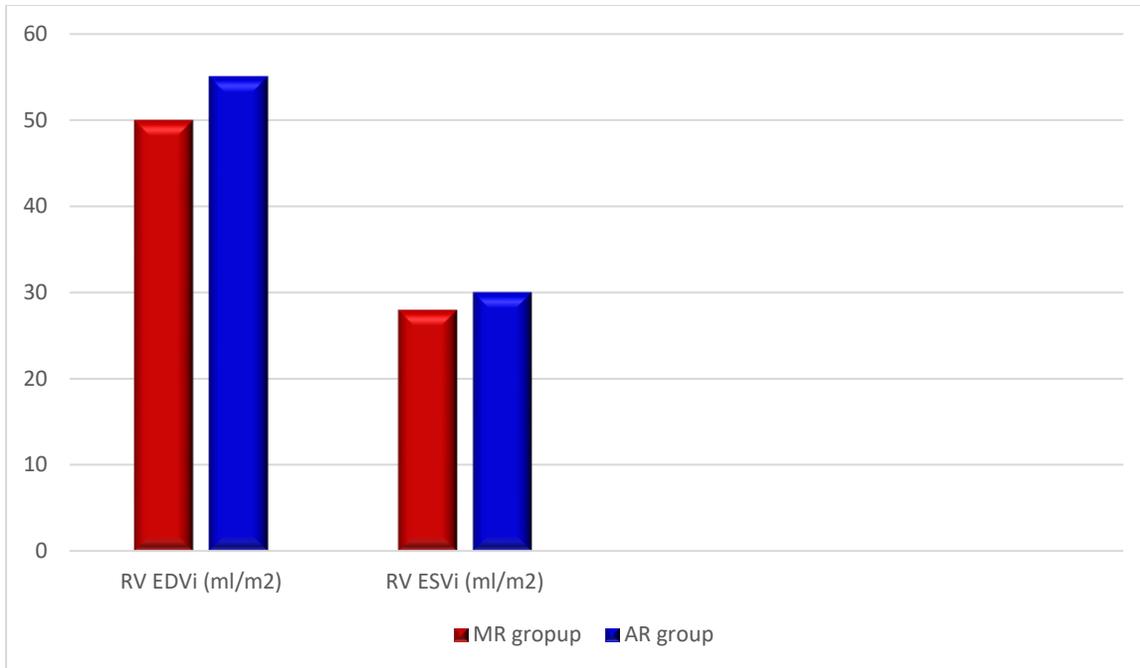
**Figure 5: Comparison between the two studied groups according to 3D LV volumes and EF**



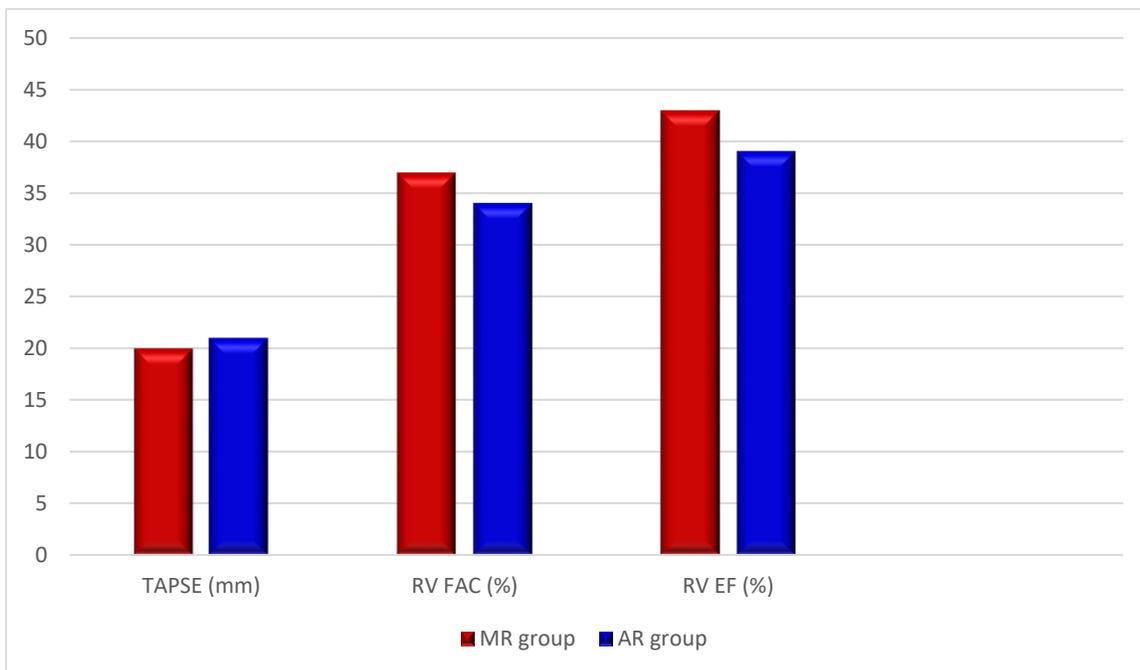
**Figure 6: Comparison between the two studied groups according to sphericity index**

**Table 3: RV volumes, function and eccentricity index in MR and AR patients:**

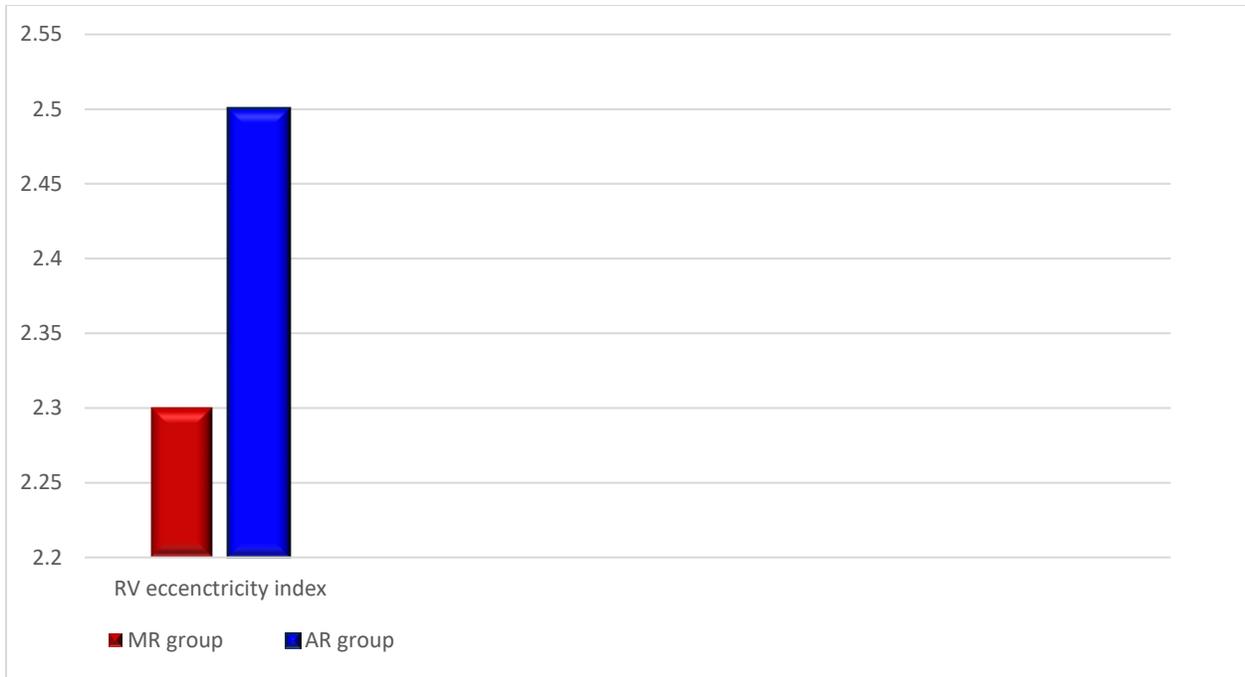
<b>RV geometry and function</b>	<b>MR (n=63)</b>	<b>AR(n=36)</b>	<b>P value</b>
<b>TAPSE (mm)</b>	18±4	19±4	0.09
<b>RV EDVi (ml/m2)</b>	51 ± 13	59 ± 12	<0.001
<b>RV ESVi (ml/m2)</b>	28 ± 9	31 ± 9	0.245
<b>RV FAC (%)</b>	37±9	34±9	0.04
<b>RV EF (%)</b>	43 ± 7	40 ± 6	0.032
<b>RV eccentricity index</b>	2.1±0.5	2.5±0.6	0.003



**Figure 7: Comparison between the two studied groups according to the RV volumes**



**Figure 8: Comparison between the two studied groups according to TAPSE, RV EF and FAC**



**Figure 9: Comparison between the two studied groups according to the RV eccentricity index.**

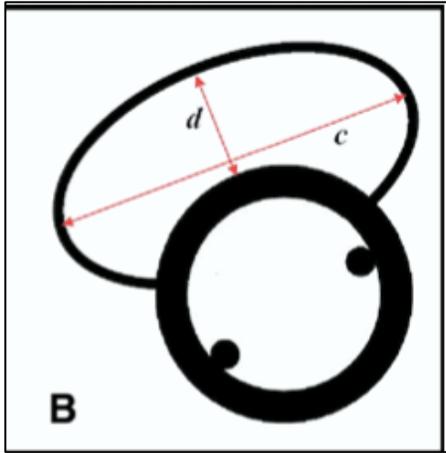
**Table 4: Correlation between different parameters and RV EF, RV FAC, and eccentricity index**

	RV					
	EF		FAC		Eccentricity index	
	r	P	r	p	r	p
MR group						

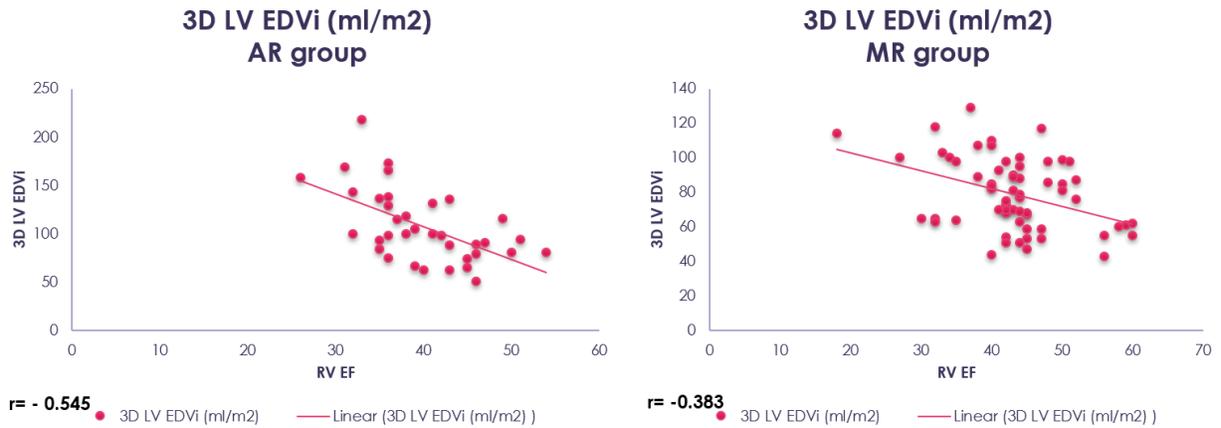
LV EDVi (ml/m <sup>2</sup> )	-0.393*	0.001*	-0.759*	<0.001*	0.591*	<0.001*
LV Sphericity index	-0.438*	<0.001*	-0.531*	<0.001*	0.441*	<0.001*
Basal septal	0.356*	0.004*	0.004	0.974	0.131	0.306
Mid septal	0.354*	0.004*	0.015	0.9070	0.200	0.116
LV GLS	0.074	0.565	0.002	0.987	-0.082	0.521
Peak RV GLS	0.484*	<0.001*	0.248*	0.050*	0.171	0.181
<b>AR group</b>						
LV EDVi (ml/m <sup>2</sup> )	-0.545-	0.001*	-0.816*	<0.001*	0.693*	<0.001*
LV Sphericity index	-0.469*	0.004*	-0.608*	<0.001*	0.511*	0.001*
Basal septal	0.230	0.178	0.230	0.178	0.104	0.546
Mid septal	0.164	0.338	0.072	0.678	0.069	0.689
LV GLS	0.526*	0.001*	0.475*	0.003*	0.489*	0.002*
Peak RV GLS	0.511*	0.001*	0.389*	0.019*	0.416*	0.012*

**r: Pearson coefficient**

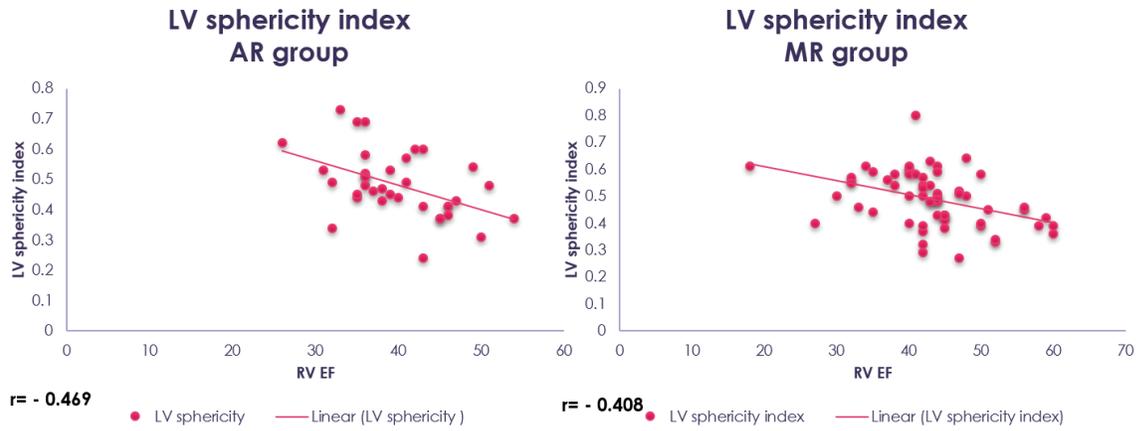
**\*: Statistically significant at  $p \leq 0.05$**



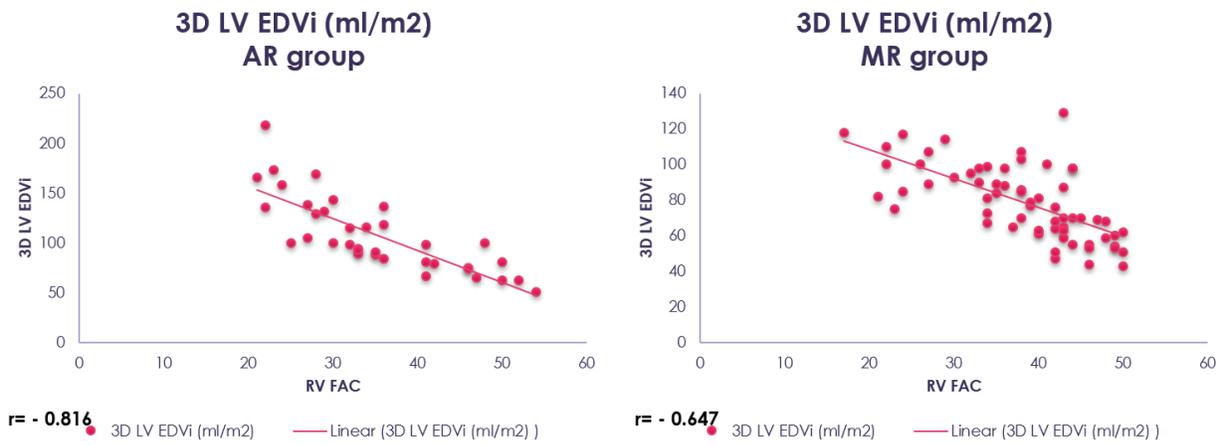
**Figure 10:** The RV eccentricity index is the ratio between RV longest lateral distance to the perpendicular distance from RV septum to free wall – at the level of LV papillary muscles.



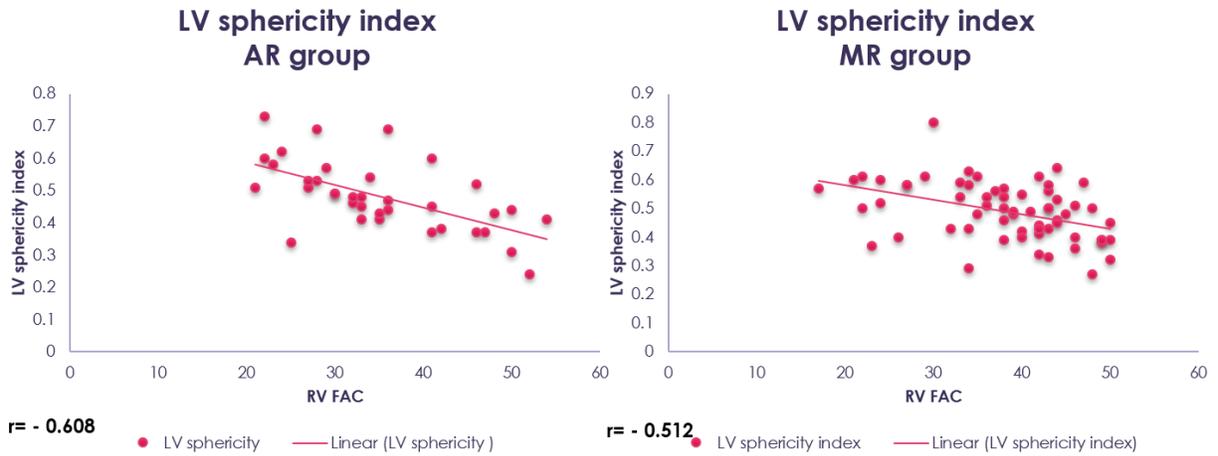
**Figure 11:** Correlation between 3D LV EDVi and RV EF in patients with AR and MR



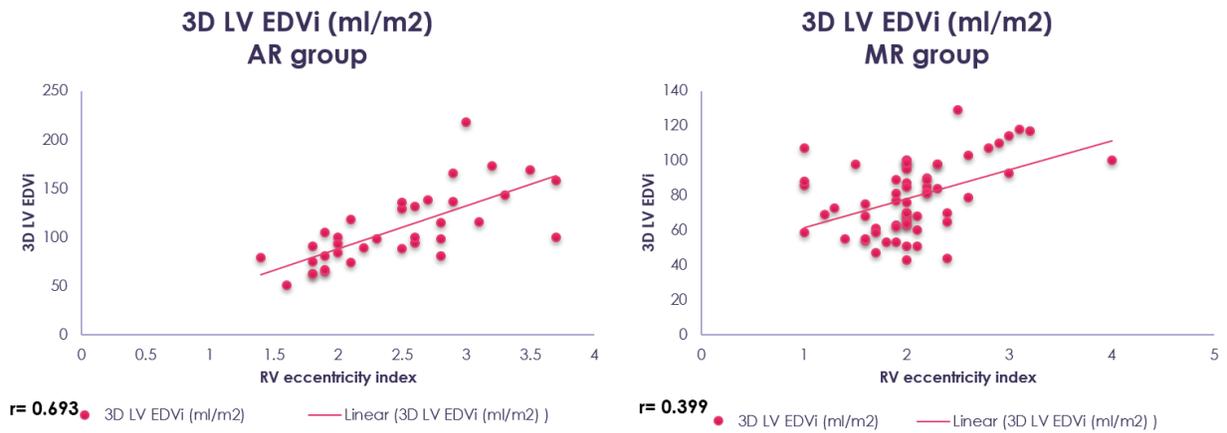
**Figure 12: Correlation between LV sphericity index and RV EF in patients with AR and MR.**



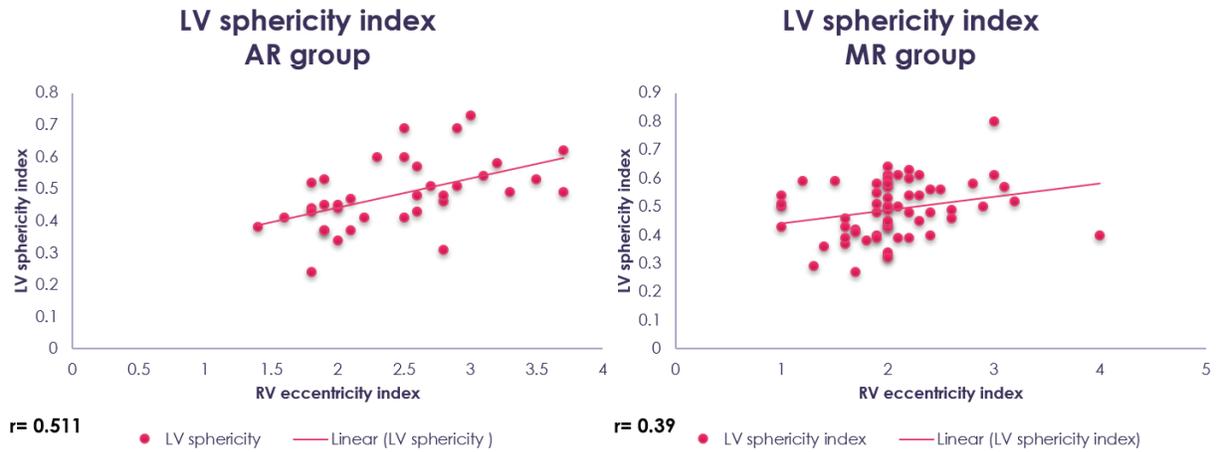
**Figure 13: Correlation between 3D LV EDVi and RV FAC in patients with AR and MR**



**Figure 14: Correlation between LV sphericity index and RV FAC in patients with AR and MR.**



**Figure 15: Correlation between 3D LVEDVi and RV eccentricity index in patients with AR and MR**



**Figure 16: Correlation between LV sphericity index and RV eccentricity index in patients with AR and MR.**

**Table 5: Echocardiographic predictors of the RV FAC, RV EF, and RV eccentricity index by multivariate analysis:**

RV FAC	B	t	Sig.	95% C. I	
				Lower	Upper
3D LV EDVi	-0.181	7.052*	<0.001*	-0.232	-0.130
sPAP (mmHg)	-0.096	2.032*	0.045*	-0.189	-0.002
LV sphericity index	-18.525	2.527*	0.013*	-33.081	-3.969

<b>LV EF (%)</b>	-0.059	0.746	0.457	-0.217	0.099
	F=31.395*	p<0.001*	R <sup>2</sup> =0.572		

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<b>RV EF</b>	<b>B</b>	<b>t</b>	<b>Sig.</b>	<b>95% C. I</b>	
				<b>Lower</b>	<b>Upper</b>
<b>3D LV EDVi</b>	-0.074	2.782*	0.007*	-0.126	-0.021
<b>sPAP (mmHg)</b>	-0.089	1.829	0.071	-0.185	0.008
<b>LV sphericity index</b>	-15.285	2.022*	0.046*	-30.295	-0.274
<b>LV EF (%)</b>	0.101	1.236	0.219	-0.061	0.264
	F= 10.340*	p<0.001*	R <sup>2</sup> = 0.306		

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<b>RV eccentricity index</b>	<b>B</b>	<b>t</b>	<b>Sig.</b>	<b>95% C. I</b>	
				<b>Lower</b>	<b>Upper</b>
<b>3D LV EDVi</b>	0.011	6.530	<0.001*	0.008	0.015
<b>sPAP (mmHg)</b>	0.005	1.692	0.094	-0.001	0.012
<b>LV sphericity index</b>	0.465	0.937	0.035*	-0.520	1.451
<b>LV EF (%)</b>	-0.002	-0.434	0.665	-0.013	0.008
	F= 22.934*	p<0.001*	R <sup>2</sup> =0.494		

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F: F test (ANOVA)

R: coefficient or regression

B: Unstandardized Coefficients

t: t-test of significance

CI: Confidence interval

LL: Lower limit

UL: Upper Limit

\*: Statistically significant at  $p \leq 0.05$

### Case (1): A 52-year-old woman, NYHA III

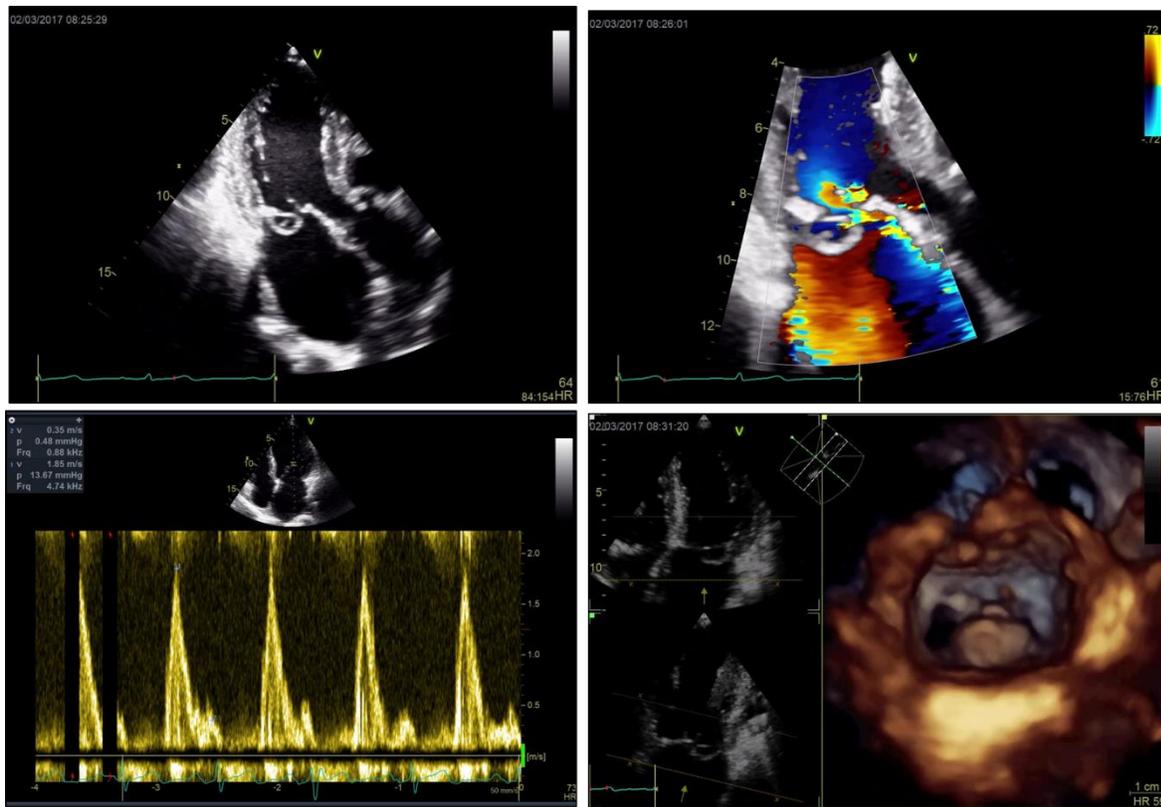


Figure 17: 2D TTE showed prolapse of the posterior leaflet with severe anteriorly directed valve regurgitation. (E wave velocity = 1.9cm/sec) .3D TTE of the mitral valve (zoomed mode, surgical view) revealed flail P2 scallop.

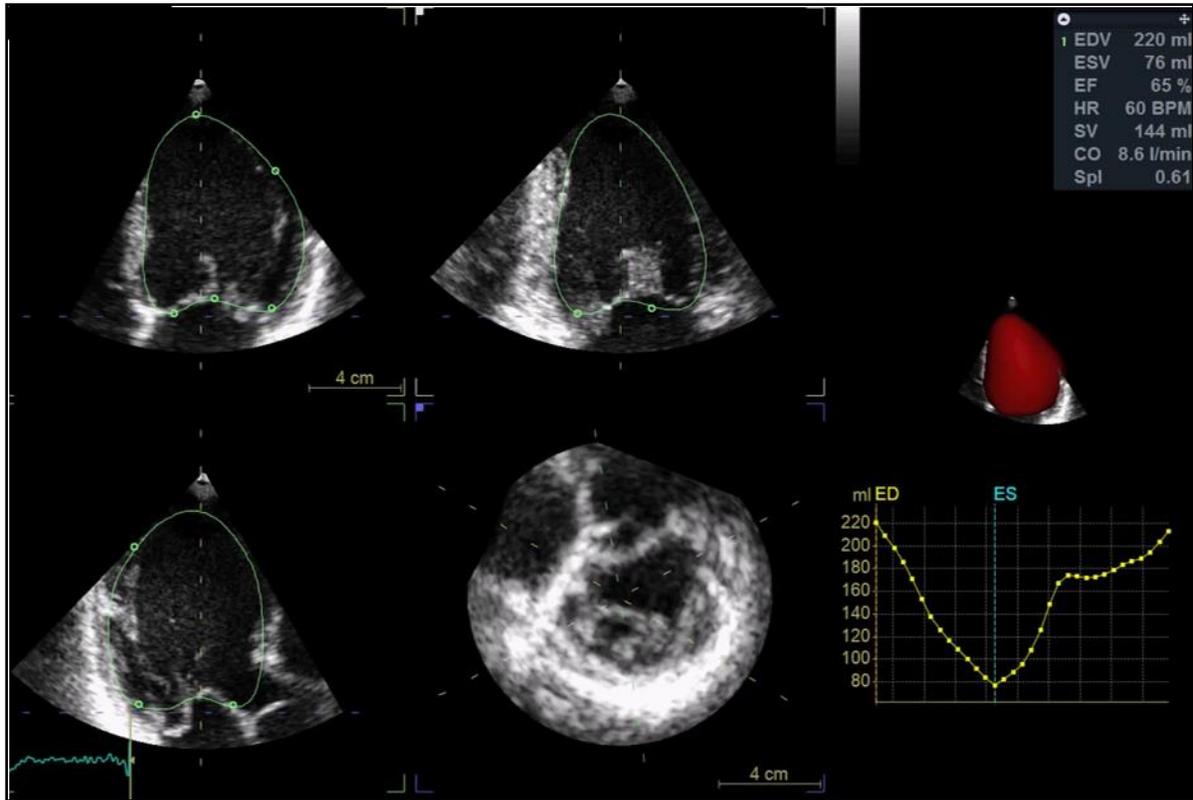


Figure 18: 3D TTE (Full volume, multibeat acquisition) of the LV revealed increased LV volumes but normal systolic function (LV EDVi= 119ml/m<sup>2</sup>, LV ESVi=42ml/m<sup>2</sup>, LV EF=65%). Sphericity index= 0.61

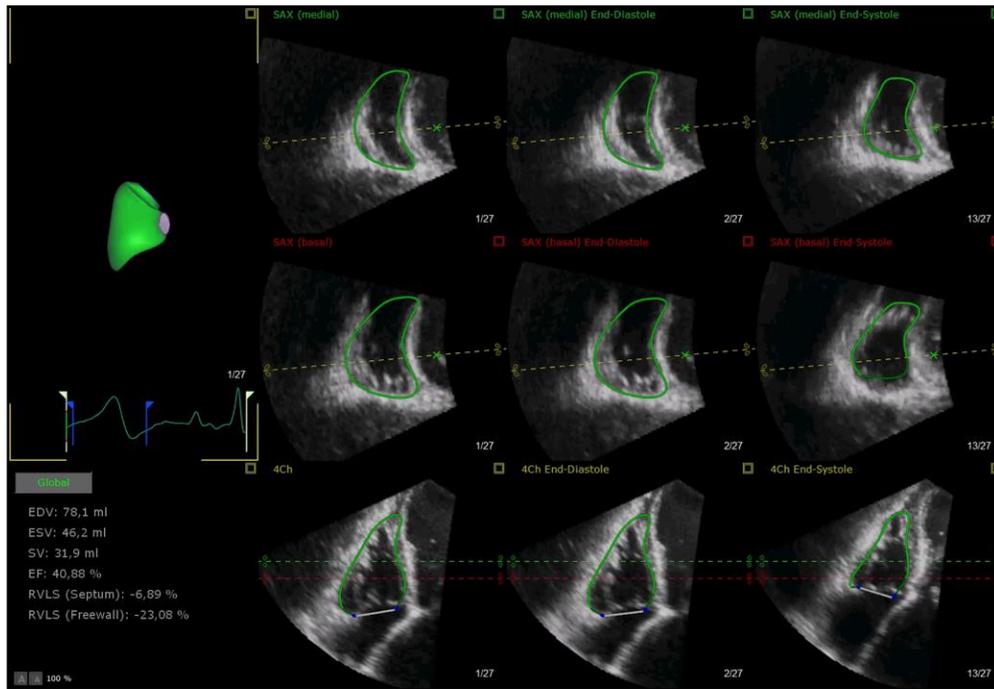


Figure 19: 3D TTE (Full volume, multibeat acquisition) of the RV showed normal RV volumes but reduced systolic function (RV EDVi=42ml/m<sup>2</sup>, RV ESVi= 25ml/m<sup>2</sup>, RV EF=40%)



Figure 20: RV eccentricity index was calculated at the LV papillary muscles as 2.8

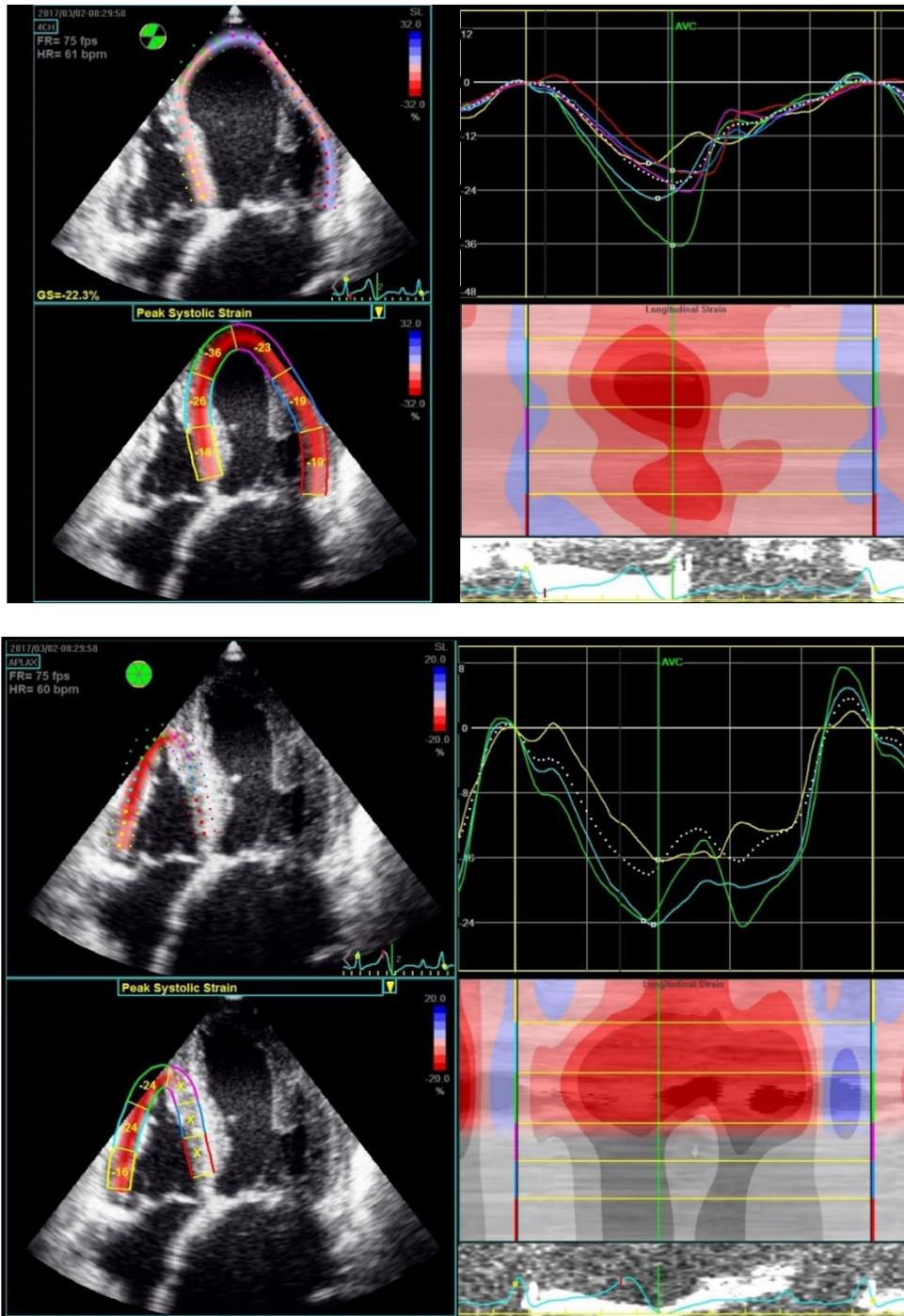


Figure 21: 2D STE of the interventricular septum and RV free wall showed average segmental and peak longitudinal strain values (peak RV LS = -21%)

**Case (2): A 28-year-old man, NYHA II.**

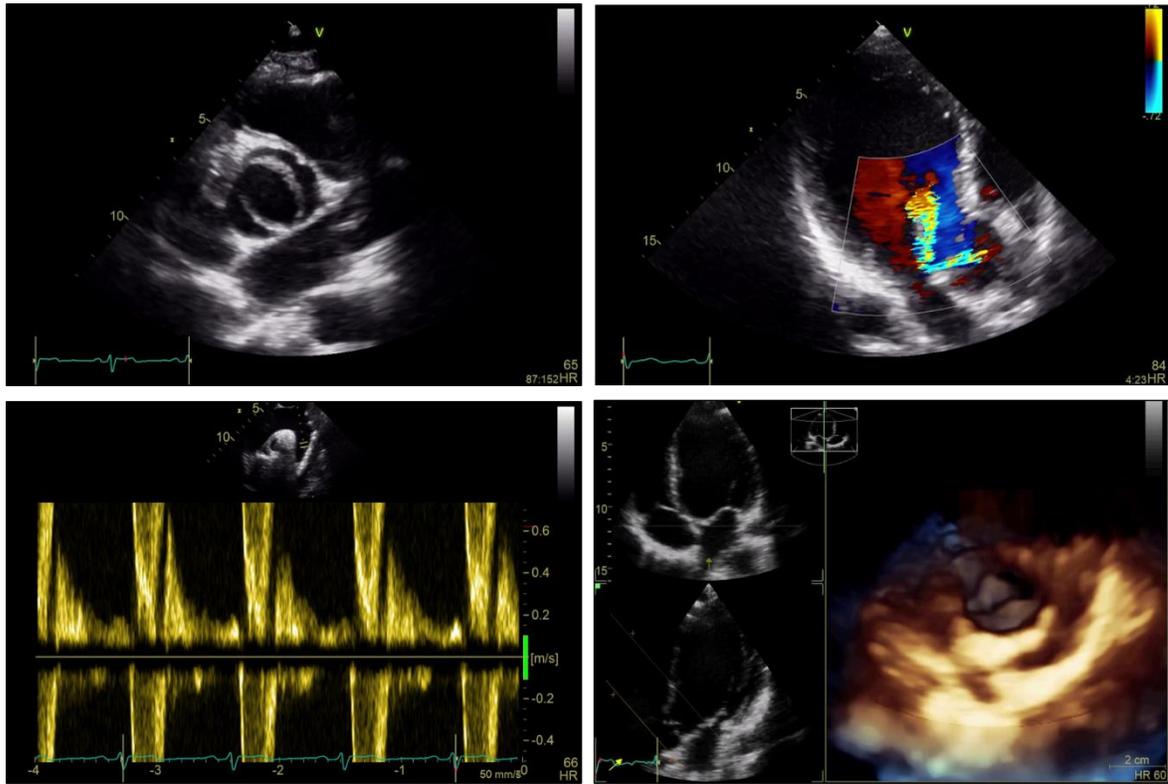


Figure 22: 2D TTE revealed bicuspid aortic valve with severe eccentric valve regurgitation. Holodiastolic flow reversal was detected in proximal descending aorta. 3D TTE of the aortic valve (LVOT perspective) confirmed a bicuspid morphology.

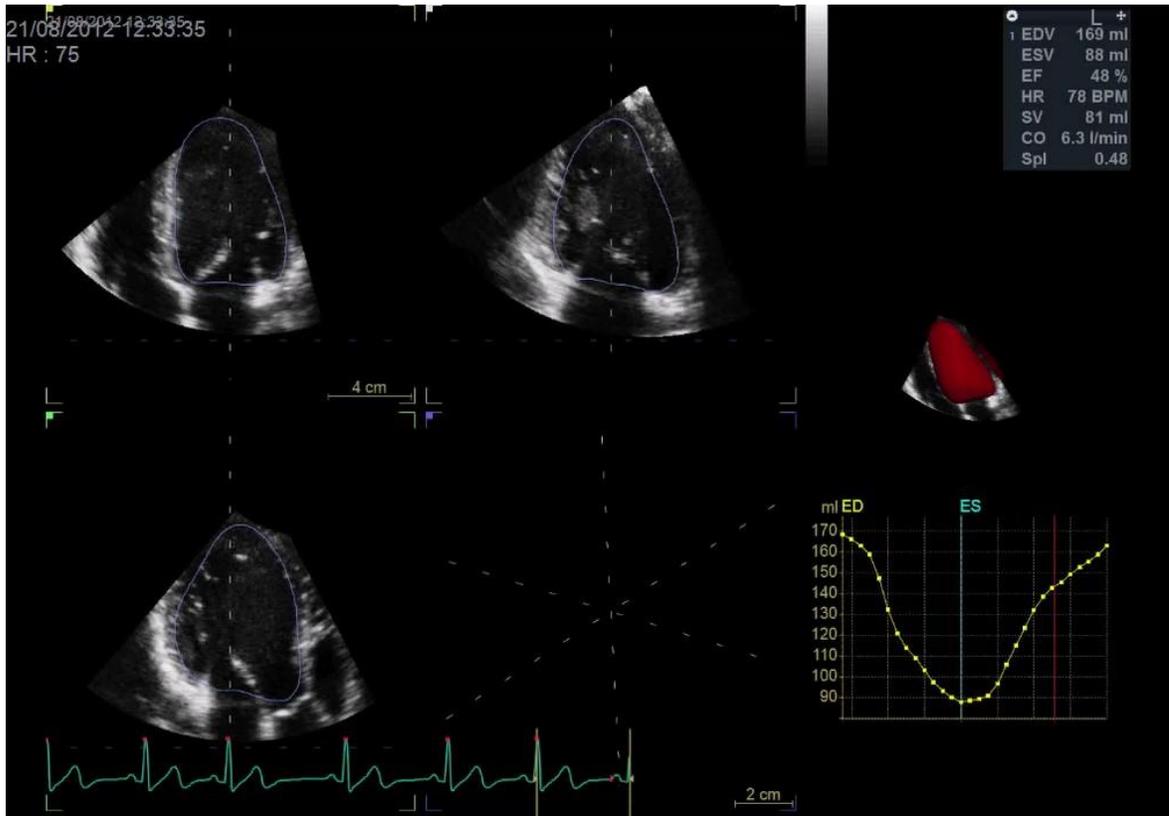


Figure 23: 3D TTE (Full volume, multibeat acquisition) of the LV revealed normal LV volumes and systolic function (LV EDVi= 76ml/m<sup>2</sup>, LV ESVi=40ml/m<sup>2</sup>, LV EF=50%). Sphericity index= 0.48

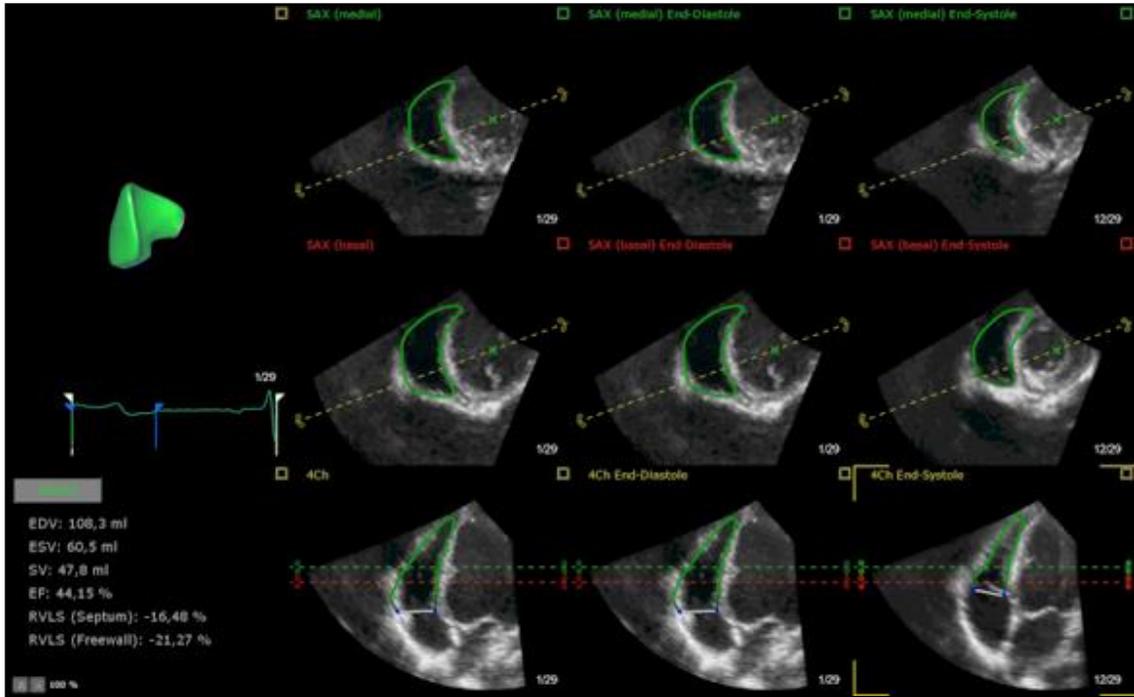


Figure 24: 3D TTE (Full volume, multibeat acquisition) of the RV showed normal RV volumes but reduced systolic function (RV EDVi=49ml/m<sup>2</sup>, RV ESVi= 27ml/m<sup>2</sup>, RV EF=45%)

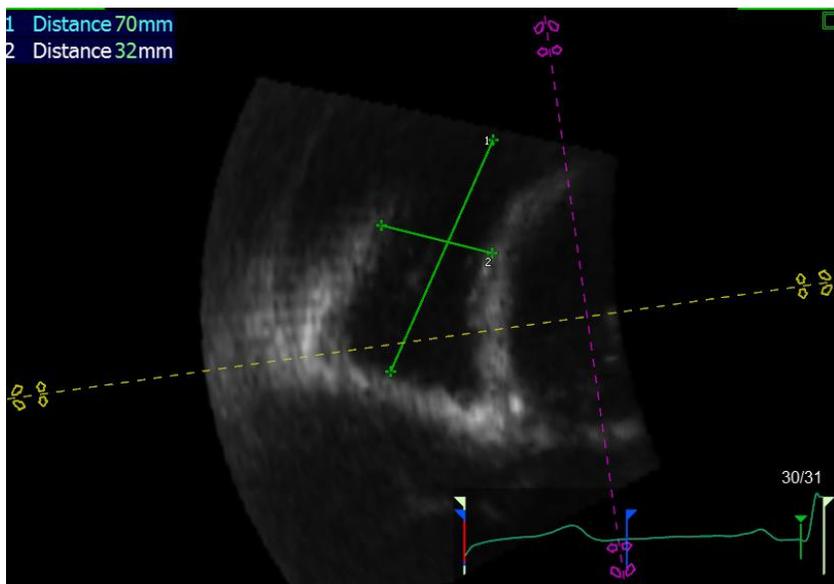


Figure 25: RV eccentricity index was calculated at the LV papillary muscles as 2.1

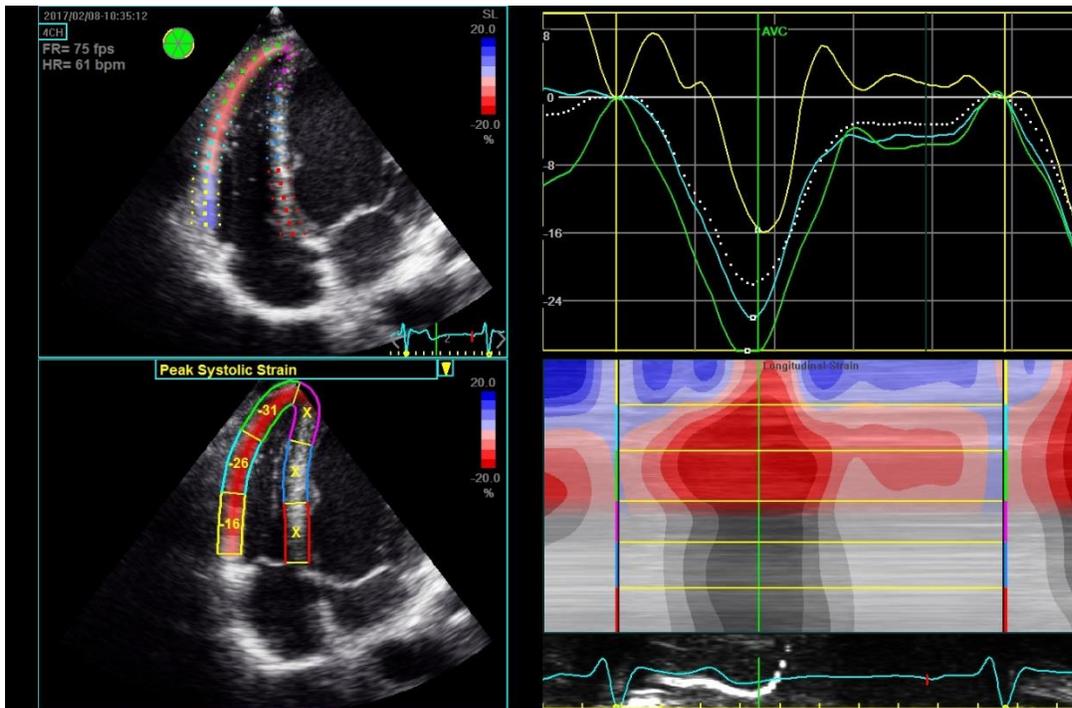
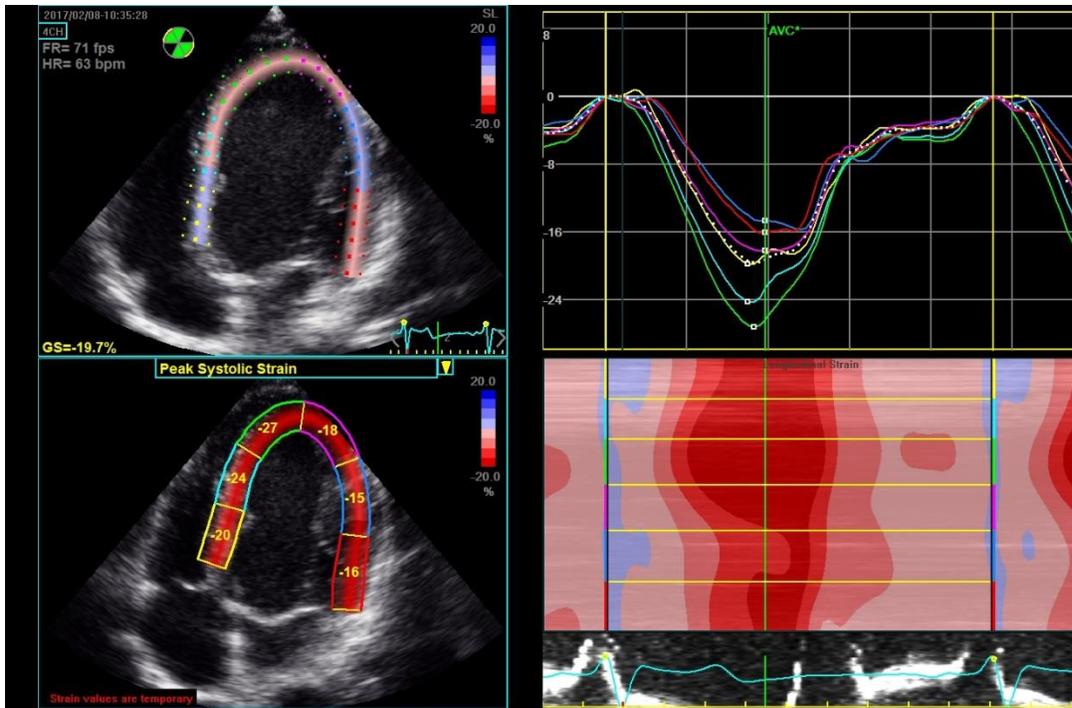


Figure 26: 2D STE of the interventricular septum and RV free wall showed reduced segmental longitudinal strain values of the LV lateral wall, However, the IVS and peak RV LS values were normal (peak RV LS = -24%)

**Post-operative follow up:** (Table 6) (Figures 27-29)

Nineteen consecutive patients undergoing elective mitral valve repair and aortic valve replacement were prospectively investigated with RV focused echocardiography, including fractional area change, tricuspid annular plane systolic excursion, RV ejection fraction. RV eccentricity index and 2-dimensional speckle tracking-derived longitudinal strain performed 12 to 24 months postoperatively.

Preoperative NYHA functional class improved in all studied patients except for 2 patients. Preoperative PASP > 50mmHg was only detected in one patient. Postoperative PASP was estimated using Bernoulli's equation in 13 patients yet, mean PASP postoperatively was 23mmHg. Postoperative LV volumes and sphericity index have declined significantly when compared to the preoperative data.

Regarding the right ventricle, persistent RV dysfunction (RV EF < 45%) was detected in 16 (68%) patients. Except for the RV eccentricity index, RV FAC, EF and TAPSE did not show significant improvement.

In addition, postoperative regional septal function and peak RV LS decreased significantly in comparison to the preoperative values.

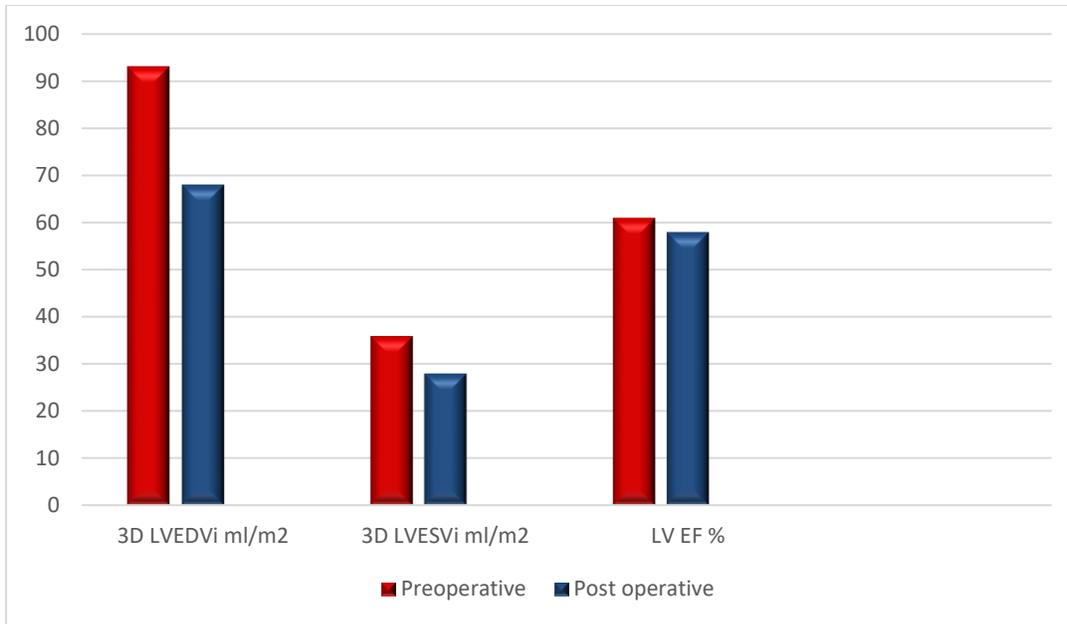
Table (6): Comparison between the pre- and postoperative data:

	Preoperative (n=19)	Postoperative (n=19)	P value
LV EDVi ml/m <sup>2</sup>	93±25	68±12	<0.001
LV EF%	61±7	58±5	0.08

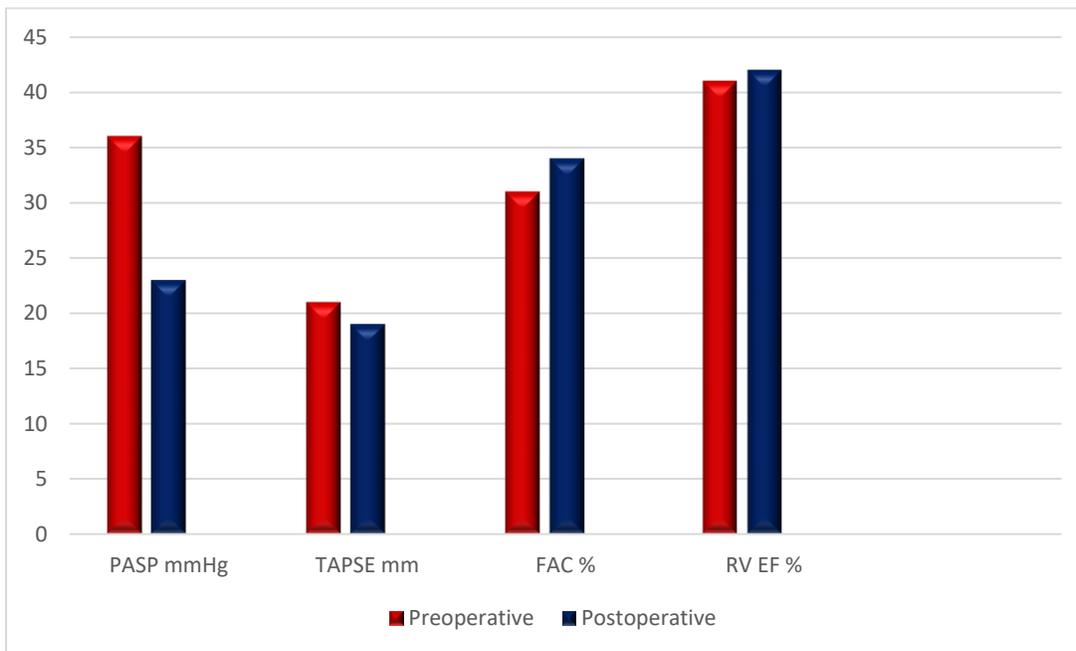
LV sphericity index	0.52±0.07	0.39±0.08	<0.001
RV EDD mm	38±7	44±11	<0.001
RV EF%	41±6	42±6	0.44
RV FAC %	31±9	34±7	0.12
TAPSE mm	22±4	19±3	0.03
RV eccentricity index	2.2±0.41	1.7±0.37	<0.001
RV basal septal LS %	-17±4	-14±3	0.009
RV mid septal LS %	-21±4	-17±3	<0.001
Peak RV LS %	-28±5	-21±3	<0.001
LV GLS%	-21±2	-18±2	<0.001

Normally quantitative data was expressed in mean ± SD and was compared using student t-test.

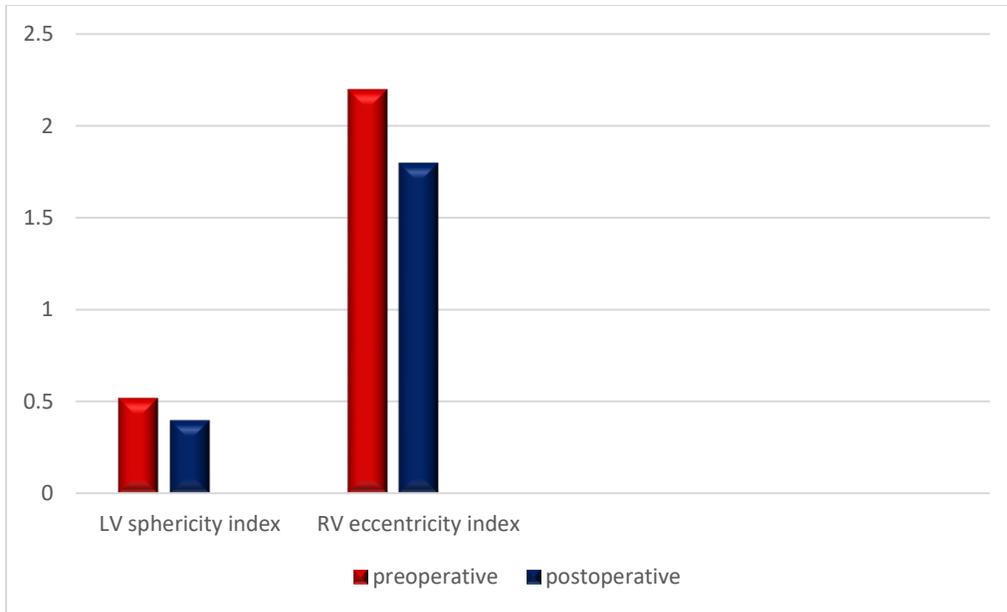
\*: Statistically significant at  $p \leq 0.05$



**Figure 27: Comparison between the studied groups according to the 3D LV volumes and LV EF.**



**Figure 28: Comparison between the studied groups according to PASP, TAPSE, FAC and RV EF.**



**Figure 29: Comparison between the studied groups according to LV sphericity index and eccentricity index.**

**Case (3): A 47-year -old man, presented with dyspnea III.**

Preoperative 2D/3D TTE showed A3 and P2 prolapse of the mitral valve with severe valve regurgitation.

**Preoperative data:**

The LV was dilated.

LV EDVi= 92ml/m<sup>2</sup>

LV ESVi= 48ml/m<sup>2</sup>

LV sphericity index: 0.62

**2D STE of IVS and RV:**

Basal septal LS = -17%

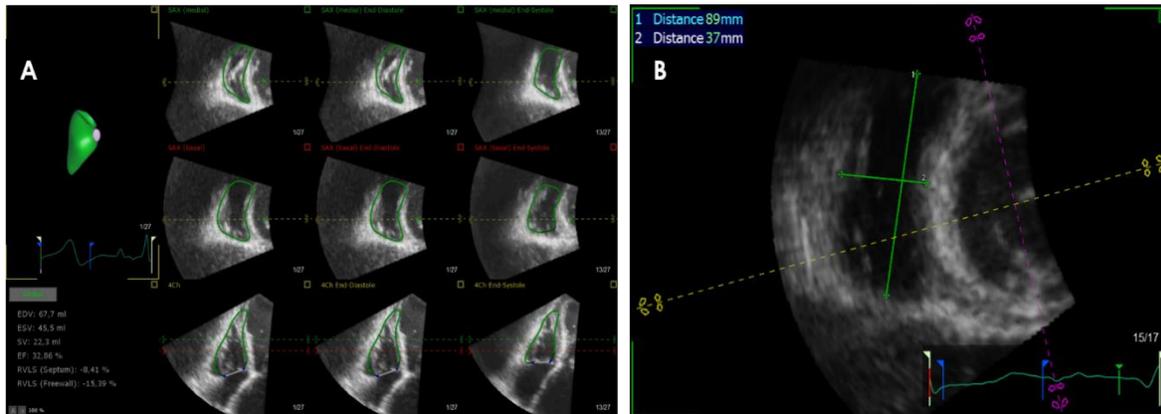
Mid septal LS= -22%

Peak RV LS= -25%.

RV EF = 32%

RV eccentricity

index=2.4



**Figure 30: 3D TTE (Full volume, multibeat acquisition) of the RV. A: preoperative RV EF was 32% and B: preoperative RV eccentricity index=2.4**

**The patient underwent mitral valve ring annuloplasty and 2 neo chords insertion. Follow up echocardiography done 6 months postoperatively.**

**Postoperative data:**

**LV volumes decreased**

LV EDVi=72ml/m<sup>2</sup>

LV ESVi= 32ml/m<sup>2</sup>,

LV sphericity index = 0.42

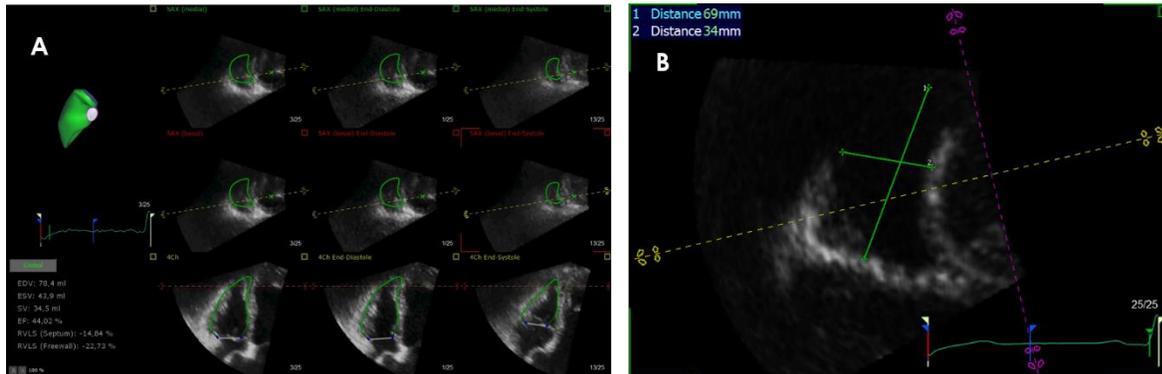
**2D STE of the IVS improved.**

Basal septal LS = -20%

Mid septal LS = -25%

**RV EF improved up to 45%.**

**RV eccentricity index=2**



**Figure 31: 3D TTE (Full volume, multibeat acquisition) of the RV. A: postoperative RV EF = 45% and B: postoperative RV eccentricity index=2**

## **Discussion:**

The aim of the present study is to assess the impact of left ventricular volume overload in patients with chronic organic MR and AR on the right ventricular shape and function and to determine the pathophysiologic determinants of RV function.

LV size and shape affect RV function and geometry .First ,the LV acts on RV function through the interventricular septum.<sup>(8)</sup>Septal contraction contributes to both RV and LV functions and is regarded as one of the major determinants of RV performance.<sup>(9)</sup> Second, both ventricles are enclosed inside relatively inextensible pericardium .Chronic LV volume overload owing to MR and AR results in eccentric hypertrophy with geometric changes of the LV .Thus, LV enlargement into more spherical shape impinges the RV with impairment of the septal function. Moreover, LV enlargement can cause septal shift to the right and this decreases the septo-free wall diameter of the RV and subsequently, increases RV eccentricity index.

Third, RV systolic function may be influenced by PASP elevation caused by primary or secondary pulmonary diseases and by left heart failure.<sup>(10)</sup> Elevated LV filling pressure and left atrial pressure induces a backward rise in pulmonary capillary wedge pressure and artery pressure. In addition to the direct effect, pulmonary vascular remodeling or abnormal vasoconstriction contributes to PASP elevation.<sup>(11)</sup>

### **RV function and pulmonary artery systolic pressure:**

The degree to which afterload, primarily a function of pulmonary artery pressure, affects RV EF is a controversial topic. In chronic organic MR, many studies have showed that RV performance is influenced by PASP with an inverse relation of RV EF to the level of PASP.<sup>(12,13)</sup> Le Tourneau et al, found an independent relation of PASP to RV EF but this relation was weak , and this

clearly suggests that PASP is not the main determinant of RV function in chronic organic MR<sup>(6)</sup>. Moreover, elevated PASP >45 mmHg was detected in 30-40% of the patients referred for MV surgery.<sup>(4-6)</sup>

In chronic AR, a recent study has shown that PASP elevation >45 mmHg was detected only in 14% of the patients who were indicated for aortic valve replacement and it was found that pulmonary hypertension was associated with high surgical risk and poor survival at three year follow up.<sup>(14)</sup> Another recent study studied the long term outcomes in patients with AR, mean value of their RV systolic pressure was 32±10 mmHg and RV systolic dysfunction was detected in only 1.5 % of the patients. However, the mean value of LV end diastolic diameter was 54±9 mm with only 11% of the patients who had severe dilatation > 65mm.<sup>(15)</sup>

Although our study revealed that RV systolic dysfunction (RV EF <45% and FAC <35%) was detected in 63 % of patients with AR and in 58% of patients with MR, PASP elevation > 45mmHg was seen only in 8% of the former and 27% of the latter.

### **RV function and left ventricular remodeling:**

LV sphericity is one of the echocardiographic indices that have been used to assess the changes in LV geometry. In chronic MR due to mitral valve prolapse, ischemic heart disease and rheumatic heart diseases that underwent mitral valve replacement, it was found that LV geometric changes assessed by LV sphericity index are independent risk factors for survival.<sup>(16)</sup> Moreover, In dogs with congestive heart failure related to severe MR, LV enlargement compresses and flattens the RV, thereby, impairing RV function.<sup>(17)</sup> In AR, an experimental animal study concluded that LV sphericity index predicts LV systolic dysfunction in aortic regurgitation.<sup>(18)</sup>

There is an important concept of ventricular interdependence between the RV and LV. Thus, the changes in pressure or volume in one chamber are likely to affect the pressure and the size of the other.<sup>(19)</sup> The explanations of this are the sharing of both ventricles by the interventricular septum (IVS), the insertion of anterior and posterior ends of the RV free wall into the IVS and encircling fibers of the pericardium. So, in chronic volume overload due to MR or AR, the LV enlarges and changes from ellipsoid into more spherical shape, thus impinges the RV and impairs the septal contraction. In our study, we found that both LV EDVi and LV sphericity index are increased in both MR and AR, but they were significantly larger in the AR group. So, upon correlation between both LV EDVi and LV sphericity index and RV systolic function assessed by RV EF and FAC, there were significant negative correlations between them in both groups with stronger correlations in patients with AR when compared to those with MR. Accordingly, AR has a greater impact on the RV function.

### **RV shape and LV remodeling:**

RV eccentricity index is a novel echocardiographic index that is designed to assess the RV shape changes. It shares the same geometric concept with LV eccentricity index that have been used in several studies to differentiate between RV pressure and volume overload.<sup>(20,21)</sup>

RV eccentricity index is described as the ratio between RV longest lateral distance to the perpendicular distance from RV septum to free wall – at the level of LV papillary muscles and it is used to explain the idea of RV impingement by the enlarged LV.

LV enlargement shifts the IVS to the right causing decrease in the RV diameter in the septo-free wall direction and more elongation in the antero-posterior direction making the RV more eccentric.

Our study revealed that RV eccentricity was significantly higher in the AR group when compared to the MR group. Upon correlation with LV EDVi and LV sphericity index, both have a significant positive correlation with RV eccentricity index, and this correlation was stronger in the AR group.

Interestingly, we have found a strong negative correlation between RV eccentricity index and both RV EF and FAC. ( $r=-0.45$  for RV EF and  $-0.52$  for FAC,  $p<0.001$ )

According to these results, AR group had more RV systolic impairment and more eccentric RV than MR group.

#### **Pathophysiologic determinants of RV geometry and function:**

Several studies have addressed the prognostic value of pre-operative pulmonary hypertension in patients undergoing surgery for MR and AR and how it is associated with increased mortality.

<sup>(4,14)</sup> In regard to RV systolic function, Le Tourneau et al, have showed that LV septal function and LV end diastolic diameter index were the pathophysiologic correlates of RV EF, and they further highlighted that PASP is only a weak determinant of RV EF in chronic organic MR. <sup>(6)</sup>

In concordance with these results, another study included 36 patients with mitral and aortic valve disease (33% of the studied patients had isolated organic MR and 25% had AR) and it showed that RV function is not a simple function of PASP at rest or during exercise and less than 25% of the variation in RV EF at rest can be explained by the variations in PASP. <sup>(22)</sup>

However, previous studies had independently reported strong inverse correlations between RV EF and PASP at rest. <sup>(23,24)</sup>.

Upon multivariate regression analysis, we have found that 3D LV EDVi and LV sphericity index are the only independent predictors of RV EF, FAC and eccentricity index. Accordingly, we concluded that RV remodeling in chronic LV volume overload owing to MR or AR occurs independent of PASP.

### **Conclusion:**

RV systolic dysfunction with EF less than 45% is a common finding in patients with chronic moderate or severe MR and AR and this can be partially explained by PASP elevation. However, RV function can be influenced by other interactions as demonstrated by the association of LV enlargement and RV EF and FAC. In relatively inextensible pericardium, LV enlargement into more spherical shape impinges the RV with impairment of the septal function. Moreover, LV enlargement can cause septal shift to the right and this reduces the distance from the RV septum to the RV free wall, causes more elongation in the antero-posterior diameter and thus increases the RV eccentricity index.

RV remodeling in chronic LV overload due to MR or AR occurs independent on PASP values.

LV size and shape are the only independent predictors of RV geometry and function.

Accordingly, chronic AR has a greater impact on RV than MR.

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