



IMPACT OF LEFT VENTRICULAR VOLUME OVERLOAD AND SYSTOLIC PULMONARY ARTERY PRESSURE ON RIGHT VENTRICULAR SYSTOLIC FUNCTION IN PATIENTS WITH CHRONIC PRIMARY MITRAL AND AORTIC REGURGITATION USING THREE DIMENSIONAL ECHOCARDIOGRAPHY

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ABSTRACT

Background: To compare the effects of left ventricular volume(LV) overload due to chronic organic mitral(MR) or aortic valve(AR) regurgitation on RV shape and function.

Methods: We studied 40 patients with moderate-severe or severe primary MR (60±19 years, 52% were men) and 20 patients with moderate or severe AR (53±18 years, 81% were men). Three-dimensional 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 RV eccentricity index .

Results: LV end-diastolic volume (EDVi) was significantly larger in the patients with AR than those with MR. RV EF and RV FAC were lower in pts with AR than in those with MR. RV eccentricity index was significantly higher in the AR group (2.5±0.6 vs 2.1±0.5, p=0.003). In both groups, LV EDVi showed positive correlations with RV shape (RV eccentricity: r= 0.693 for AR and r=0.399 for MR; p<0.001) and negative correlations with RV function (RV EF: r= -0.545 for AR and r=- 0.383 for MR, p <0.001; RV FAC: r=-0.816 for AR and r=-0.647 for MR, p<0.001).Moreover, LV sphericity index showed negative correlations with RV function (RVFAC: r= -0.512 for MR and r=-0.608 for AR,P=0.001;RV EF:r=-0.408 for MR and r=-0.469, P=0.004) and positive correlation with the RV shape (RV eccentricity index,r= 0.39 for MR and r=0.511, P<0.001) .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.

Conclusions: 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.

Keywords: Left ventricle- Mitral regurgitation- Aortic regurgitation-Right ventricle.

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,^(1,2) 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).⁽³⁻⁵⁾ 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.⁽⁶⁾ However, Elevation of PASP secondary to isolated aortic valve regurgitation (AR) is less common than with other valve lesions.⁽⁷⁾ 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:

Forty patients with moderate-severe or severe organic mitral valve regurgitation and twenty patients with moderate or severe aortic valve regurgitation were included in this study.

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.

RV function was estimated by:1) tricuspid annular plane systolic excursion (TAPSE), 2)fractional area change (FAC)..

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.

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 χ^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, figure 1,2). Both LV end-diastolic volume (EDVi) and end-systolic volume (ESVi) were significantly larger in the patients with AR than those with MR. LV EF was significantly lower in AR group than in MR group.(table 2,3).

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

	MR group (n= 40)	AR group (n=20)	P value
Male (%)	52	81	0.004
Age (y)			
Min-Max	60 \pm 14	53 \pm 18	0.008
Mean \pm SD	20-89	19-83	
BSA (m2)	1.8 \pm 0.2	1.9 \pm 0.2	0.1
HR (Beats/min)	71 \pm 13	71 \pm 11	0.326
Blood pressure			
Systolic (mmHg)	126 \pm 16	134 \pm 20	<0.001*
Diastolic(mmHg)	75 \pm 7	62 \pm 8	<0.001*
Atrial fibrillation(%)	8	3	
NYHA II(%)	75	80	
NYHA III-IV (%)	22	15	

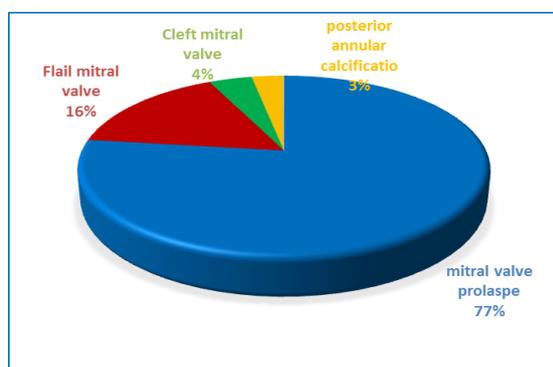


Figure (1): Etiology of MR

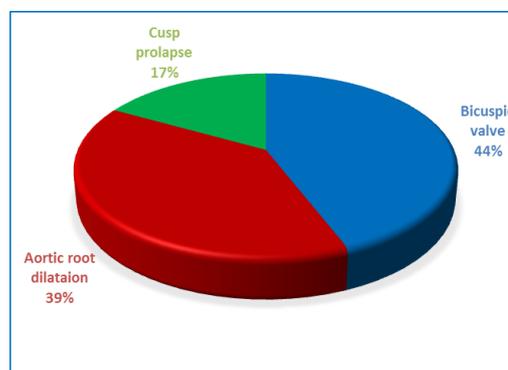


Figure (2) Etiology of AR

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

LV geometry and function	MR (n=40)	AR(n=20)	P value
3D LVEDV (ml)	137±38	205±84	<0.001
3D LVESV (ml)	50±17	97±59	<0.001
3D LVEDVi (ml/m ²)	78 ± 20	106 ± 36	<0.001
3D LVESVi (ml/m ²)	29 ± 8	50 ± 28	<0.001
LV EF (%)	62 ± 6	54 ± 10	<0.001
LV sphericity index	0.49±0.10	0.53±0.11	<0.001

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

RV geometry and function	MR (n=40)	AR(n=20)	P value
TAPSE (mm)	18±4	19±4	0.09
RV EDVi (ml/m ²)	51 ± 13	59 ± 12	<0.001
RV ESVi (ml/m ²)	28 ± 9	31 ± 9	0.245
RV FAC (%)	37±9	34±9	0.04
RV EF (%)	43 ± 7	40 ± 6	0.032
RV eccentricity index	2.1±0.5	2.5±0.6	0.003

Pathophysiologic correlates of RV geometry and function: (Table 4)

In univariate analysis, LV EDVi showed significant 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, $p<0.001$).

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, $P<0.001$).

Regarding correlation with strain in both groups, in the AR group, LV GLS and peak RV LS showed significant positive correlation with RV EF but the MR group, only peak RV LS and mid septal RV LS showed significant positive correlation with RV EF.

Predictors of RV remodelling in LV overload: (Table 5)

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. However, RV EF, FAC and eccentricity index changes occur independent on PASP values.

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						
3D LV EDVi (ml/m ²)	-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 LS (%)	0.356*	0.004*	0.004	0.974	0.131	0.306
Mid septal LS (%)	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
AR group						
3D LV EDVi (ml/m ²)	-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 LS (%)	0.230	0.178	0.230	0.178	0.104	0.546
Mid septal LS (%)	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 $p \leq 0.05$

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 (ml/m2)	-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
LV EF (%)	-0.059	0.746	0.457	-0.217	0.099
F=31.395* p<0.001* R ² =0.572					
RV EF (%)	B	t	Sig.	95% C.I	
				Lower	Upper
3D LV EDVi (ml/m2)	-0.074	2.782*	0.007*	-0.126	-0.021
sPAP (mmHg)	-0.089	1.829	0.071	-0.185	0.008
LV sphericity index	-15.285	2.022*	0.046*	-30.295	-0.274
LV EF (%)	0.101	1.236	0.219	-0.061	0.264
F= 10.340* p<0.001* R ² = 0.306					
RV eccentricity index	B	t	Sig.	95% C.I	
				Lower	Upper
3D LV EDVi (ml/m2)	0.011	6.530	<0.001*	0.008	0.015
sPAP (mmHg)	0.005	1.692	0.094	-0.001	0.012
LV sphericity index	0.465	0.937	0.035*	-0.520	1.451
LV EF (%)	-0.002	-0.434	0.665	-0.013	0.008
F= 22.934* p<0.001* R ² =0.494					

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 $p \leq 0.05$

DISCUSSION

LV size and shape affect RV function and geometry .First ,the LV acts on RV function through the interventricular septum.⁽⁸⁾Septal contraction contributes to both RV and LV functions and is regarded as one of the major determinants of RV performance.⁽⁹⁾ 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.⁽¹⁰⁾ 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.⁽¹¹⁾

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.^(12,13) 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. ⁽⁶⁾ Moreover, elevated PASP >45 mmHg was detected in 30-40% of the patients referred for MV surgery.⁽⁴⁻⁶⁾

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.⁽¹⁴⁾ 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 > 65 mm.⁽¹⁵⁾

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 > 45 mmHg 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.⁽¹⁶⁾ Moreover, In dogs with congestive heart failure related to severe MR, LV enlargement compresses and flattens the RV, thereby, impairing RV function.⁽¹⁷⁾ In AR, an experimental animal study concluded that LV sphericity index predicts LV systolic dysfunction in aortic regurgitation.⁽¹⁸⁾

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.⁽¹⁹⁾ 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 impair 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 was 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.^(20,21)

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.

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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