

Left Atrial Volumes, Function and Work before and after Mitral Valve Repair in Chronic Mitral Regurgitation

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Background and aim of the study: Despite the effect of mitral valve repair in left ventricular (LV) function having been extensively studied, investigations of left atrial (LA) performance indices are minimal. This prospective study was undertaken to analyze LA volumes, function and work in patients with chronic mitral valve regurgitation (MR) who underwent mitral valve repair; the analyses were conducted both before and six months after surgery.

Methods: Twenty patients (15 males, five females; mean age 51.4 ± 12.5 years) with severe MR (grade IV) due to floppy mitral valve/mitral valve prolapse (FMV/MVP; anterior, posterior or both) underwent mitral valve repair. LA volumes, maximal at mitral valve opening (LA_{max}); minimal at valve closure (LA_{min}); and at onset of atrial systole (P-wave on ECG, LAP); and transmitral Doppler A-wave velocity were measured before and six months after surgery. LA stroke volume ($LASV = LAP - LA_{min}$); LA ejection fraction ($LAEF = LASV/LAP$); LA kinetic energy

($LAKE = 1/2 \times LASV \times 1.06$ (specific gravity of blood) $\times A^2$ (dyne·cm·10³); LA and LV dimensions and functions were assessed at the same time.

Results: NYHA functional class was improved post-operatively by at least one grade. LV systolic and diastolic dimensions were reduced significantly in all patients ($p < 0.001$). LA volumes (LA_{max} , LA_{min} and LAP) were decreased significantly in all patients ($p < 0.001$); LASV remained unchanged. LAEF and LAKE were increased significantly (both $p < 0.001$). The A-wave was also increased ($p < 0.001$).

Conclusion: Increased LA work (LAKE) after mitral valve repair, despite a decrease in LA volumes, suggests that LA muscle dysfunction was present before surgery. LA involvement may precede LV involvement. The determination of LA performance and work will help to optimize the timing of surgery in patients with FMV/MVP and MVR.

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It is well accepted today that mitral valve repair is the optimal surgical treatment in patients with severe chronic mitral valvular regurgitation (MR) due to floppy mitral valve (FMV)/mitral valve prolapse (MVP) (1-7). Important factors determining the natural history after mitral valve surgery are age, the presence of atrial fibrillation, status of left ventricular (LV) and left atrial (LA) size and function, and the type of surgery (valve replacement versus repair) (2,3,8-14). Whilst LV function has been extensively studied after mitral valve repair, indices of LA performance have not (12). This prospective study was undertaken to analyze LA volumes, function and work using a multi-dimensional approach in patients with chronic MR who had mitral valve repair, with analyses conducted both before and six months after surgery.

Clinical material and methods

Patient population

Twenty consecutive patients (15 males, five females; mean age 51.4 ± 12.5 years) with severe chronic MR (grade IV by Doppler) due to FMV/MVP who underwent mitral valve repair between October 2000 and October 2002 were studied prospectively. All patients had normal coronary arteries as determined by coronary arteriography, and were in sinus rhythm before and after the operation. Anterior leaflet prolapse was present in three patients, posterior leaflet prolapse in seven, and combined anterior/posterior leaflet prolapse in 10. Fourteen of the patients had mild dyspnea (NYHA functional class I or II), whereas six patients had more severe symptoms (NYHA class III or IV).

These patients were selected from 126 consecutive patients who underwent mitral valve repair performed by the same surgeon (A.A.P.). Only patients who fulfilled the following criteria were included in the study: (i) normal sinus rhythm; (ii) technically sat-

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isfactory mitral flow Doppler and two-dimensional (2D) echocardiography allowing accurate measurements; (iii) absence of significant coronary artery disease requiring interventional therapy; and (iv) an absence of other hemodynamically significant valvular disease. The study was approved by the local institutional ethical review committee (October 2000), and all subjects provided their informed consent.

All study patients underwent transthoracic echocardiography (TTE) and coronary arteriography before surgery. Echocardiography and Doppler echocardiography were repeated at six months after surgery. Immediate repair results were assessed in all patients by use of intraoperative transesophageal echocardiography (TEE).

Transthoracic echocardiography

M-mode and two-dimensional echocardiograms were performed with the patient in the supine and left lateral positions, using a Hewlett-Packard Model Sonos 5000 echocardiograph with a 2.5 MHz phased array transthoracic transducer in the parasternal long-axis, apical four-chamber and apical two-chamber views. An electrocardiogram was recorded simultaneously for later review in a VHS format videotape.

Left ventricular (end-systolic and end-diastolic) and LA dimensions were assessed echocardiographically both before and six months after surgery.

Pulsed-wave Doppler recordings were obtained from the apical four-chamber view. The sample volume cylinder was superimposed on the 2D image of the tips of the mitral valve leaflets, where maximal diastolic flow was recorded. The angle between the Doppler cursor and the presumed direction of the transmitral flow was estimated to be less than 20° in each subject. Care was taken to obtain the highest velocities with the best signal-to-noise ratio. Where E- and A-waves were not completely separate, the transmitral velocity (v) was defined as the perpendicular difference between the crossover point and the peak of the A-wave (11). Values were averaged from five successive beats in each subject.

The videotape was reviewed with the use of freeze-frame mode, digitized graphic pad and commercially available algorithms to determine areas and lengths from the 2D images. Left atrial area and lengths were measured at mitral valve opening (LA_{max}), mitral valve closure (LA_{min}) and at onset of atrial systole (P-wave on the simultaneously recorded electrocardiogram, LAP). Area was measured by drawing the inner lining of the left atrial walls at the specific freeze-frames with the digitized graphic pad. Left atrial length was defined as the longest line that could be drawn between the posterior LA wall and the mid-portion of the mitral valve (15,16).

Left atrial volumes

These were calculated with biplane area-length method, as described previously from the 2D echocardiography, using the formula $V = (8/3\pi L) \times A1 \times A2$, where $\pi = 3.14$, $A1$ = LA area in the four-chamber view, $A2$ = LA area in the two-chamber view, and L = the shorter of the long diameters in both planes (11,17,18).

LA stroke volume (LASV)

This was obtained by subtracting the LA_{min} from the LA volume at onset of atrial systole (LAP); the LA ejection fraction (LAEF) is the ratio of the LASV to the LA volume at onset of atrial systole (LAP).

Estimation of LA work

Peak LA kinetic energy (LAKE) was used to estimate LA work. LAKE was obtained from the mass and velocity using the formula $LAKE = \frac{1}{2} \times m \times v^2$, where $m = LASV \times \rho$ (ρ = blood density = 1.06 g/cm³) and v = transmitral Doppler A-wave velocity (11,19,20). LAKE is closely related to the LA stroke work index calculated invasively by the pressure-area relationship (19).

Surgical technique

Cardiopulmonary bypass was instituted with ascending aortic cannulation and venous bicaval cannulation with snares around the superior and inferior venae cavae. The perfusate temperature was kept at ~35°C. Intermittent antegrade and retrograde warm blood cardioplegia enriched in potassium and magnesium according to the Calafiore Protocol was used (21). The mitral valve was exposed through the superior septal approach (through the right atrium and interatrial septum and the roof of the left atrium) (22). Quadrangular resections of the posterior leaflet and the annuloplasties were performed according to Carpentier techniques (23), and the placement of synthetic chordae as described by David et al. (24). The synthetic chordae used were constructed from expanded polytetrafluoroethylene sutures (size 4-0 or 5-0). If the annular size was sufficient to allow the use of an annuloplasty ring without risk of developing mitral stenosis postoperatively, this technique was used. If the annular size was relatively small, then an annuloplasty ring was not used. The mitral annuloplasty rings used were the Physio-Ring (Carpentier-Edwards Physio Annuloplasty Ring; Baxter-Edwards Laboratories, Irvine, CA, USA), the Cosgrove-Edwards Annuloplasty System (Baxter-Edwards Laboratories), and the Annuloflex (AF800; Sulzer Carbomedics, Austin, TX, USA). The Alfieri stitch was used in four of the 20 patients; this connects the anterior mitral leaflet to the posterior leaflet, thus producing a double-orifice mitral valve (25).

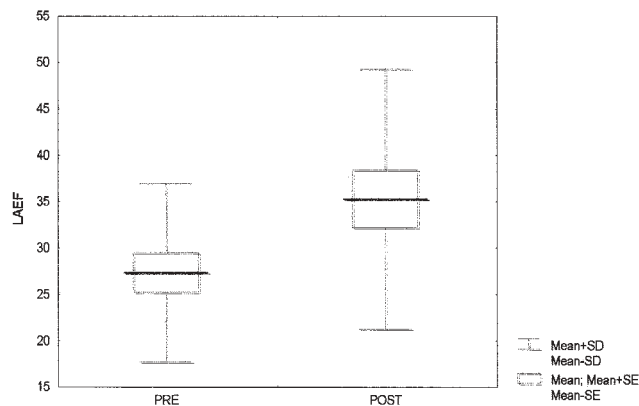


Figure 1: Left atrial ejection fraction (LAEF) before (PRE) and after (POST) mitral valve repair surgery.

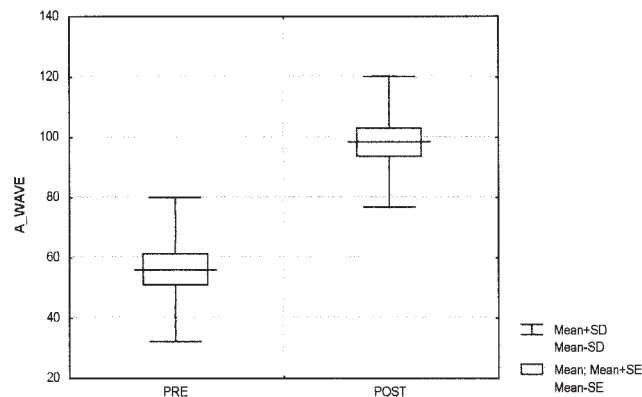


Figure 2: A-wave before (PRE) and after (POST) mitral valve repair surgery.

Table I: Valve pathology and mitral valve repair techniques used in individual patients.

Patient no.	Age/sex	Valve pathology	Mitral valve repair	Annuloplasty
1	55M	AML+PML prolapse	Synt. chordae A2/A3 + quad. resection P2	Physio 34 mm
2	45F	AML prolapse	Synt. chordae A1/A2 and A2/A3	Physio 32 mm
3	30M	AML+PML prolapse	Synt. chordae A1/A2 and A2/A3 + quad. resection P2	Cosgrove 36 mm
4	64M	PML prolapse	Quad. resection P2 + Alfieri stitch	Physio 30 mm
5	63M	AML+PML prolapse	Quad. resection P2 + Alfieri stitch	-
6	36F	PML prolapse	Quad. resection P2/P3	Physio 32 mm
7	41M	AML+PML prolapse	Alfieri	Cosgrove 34 mm
8	55F	AML+PML prolapse	Quad. resection P2 + Alfieri stitch	Cosgrove 34 mm
9	62F	AML prolapse	-	Physio 28 mm
10	64M	AML+PML prolapse	Synt. chordae A2/3	Annuloflex 36 mm
11	63M	PML prolapse	Quad. resection P2	Annuloflex 34 mm
12	39M	PML prolapse	Quad. resection P2	Annuloflex 30 mm
13	59M	AML+PML prolapse	Synt. chordae A1/A2 and A2/A3 + quad. resection P2	Annuloflex 36 mm
14	43M	PML prolapse	Quad. resection P2	Annuloflex 34 mm
15	50M	AML+PML prolapse	Synt. chordae A2/A3 + quad. resection P2/P3	-
16	45M	AML+PML prolapse	Quad. resection P2	Annuloflex 36 mm
17	36M	PML prolapse	Quad. resection P2	Annuloflex 34 mm
18	48M	PML prolapse	Quad. resection P2	Annuloflex 30 mm
19	36M	AML+PML prolapse	Quad. resection P2	Physio 32 mm
20	71F	AML prolapse	Synt. chordae A2/A3	Physio 32 mm

A1, A2, A3, P1, P2, P3: Anterior and posterior scallops, respectively.

AML: Anterior mitral leaflet; PML: Posterior mitral leaflet; Quad.: Quadrangular; Synt.: Synthetic.

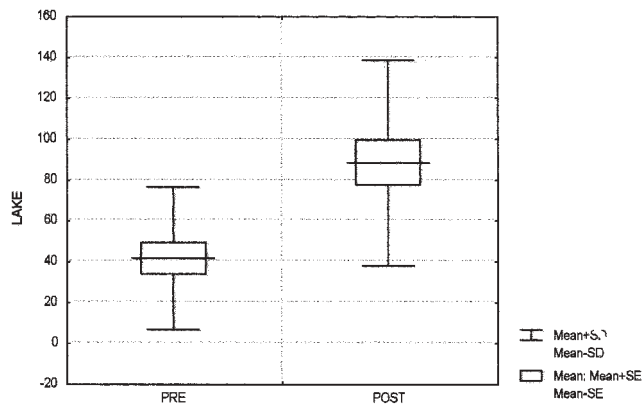


Figure 3: Left atrial kinetic energy (LAKE) before (PRE) and after (POST) mitral valve repair surgery.

Statistical analysis

Data were expressed as mean \pm SD. Comparisons of mean values between pre- and post-surgery groups of patients were performed using the paired samples *t*-test. A *p*-value <0.05 was considered to be statistically significant.

Results

All patients underwent mitral valve repair. Eighteen patients had an annuloplasty ring (14 full, four semi), 15 had quadrangular resection (posterior leaflet), seven had synthetic chordae (anterior leaflet), and four had an Alfieri stitch (between the anterior and posterior leaflets). The repair techniques used in patients are presented in Table I. All patients had preoperative and postoperative LVEF $>50\%$, and all improved symptomatically by at least one NYHA class. There was no residual mitral stenosis in any patient immediately

and six months after surgery. Among the 20 patients, three had grade 0-I residual MR immediately after surgery, but this did not show any deterioration six months later. It was unlikely that this trivial to mild residual MR had any significant effect on LA performance. The remainder of the patients did not show any MR immediately and six months after surgery.

LV and LA dimensions

LV systolic and diastolic dimensions were reduced significantly in all patients ($p <0.001$). LA dimensions were also reduced significantly at six months after surgery in all patients ($p <0.001$) (Table II).

LA volumes, function and work

LA volumes (LA_{max}, LA_{min} and LAP) were reduced significantly in all patients ($p <0.001$), though the change in LASV did not reach statistical significance (Table II). The indices of LA function, namely LAEF ($p <0.05$), A-wave ($p <0.001$) and peak LAKE ($p <0.001$), were all increased significantly at six months after surgery (Table II; Figs. 1, 2 and 3).

Discussion

Previous studies have suggested that the status of the left atrium is an important determinant of the natural history in patients with MVR (14). Left atrial size appears to be as important a predictor of outcome as LV function. LA function is complex and multi-dimensional; LA contraction due to atrial myocardial fiber shortening results in a decrease in LA volume, ejection of blood from the left atrium into the left ventricle, acceleration of blood ejected into the left ventricle, increased velocity of blood ejected into the left ventricle, and the generation of work. It has been shown in previous studies (11,26) that LA volumes and work

Table II: Left ventricular and left atrial parameters before and after mitral valve repair.*

Parameter	Preoperative	Postoperative	<i>p</i> -value
LVDD (cm)	6.50 \pm 0.67	5.49 \pm 0.58	<0.001
LVDS (cm)	3.95 \pm 0.80	3.41 \pm 0.62	<0.001
LAD (cm)	5.15 \pm 0.92	4.03 \pm 0.57	<0.001
LA _{max} (cm ³)	130.39 \pm 62.65	73.62 \pm 24.64	<0.001
LA _{min} (cm ³)	66.26 \pm 40.68	36.66 \pm 18.30	<0.001
LAP (cm ³)	87.94 \pm 44.17	54.18 \pm 20.85	<0.001
LASV (cm ³)	21.67 \pm 9.64	17.56 \pm 8.14	NS
LAEF (%)	27.19 \pm 9.63	35.15 \pm 14.03	<0.05
LAKE (kdyne-cm)	41.03 \pm 34.92	87.79 \pm 50.32	<0.001
A-wave (cm/s)	55.77 \pm 23.92	91.11 \pm 21.67	<0.001

*Values are mean \pm SD.

LA_{max}: LA volume at mitral valve opening; LA_{min}: LA volume at mitral valve closure; LA: Left atrial; LAD: Left atrial dimension; LAEF: LA ejection fraction; LAKE: LA kinetic energy; LAP: LA volume at onset of atrial systole; LASV: LA stroke volume; LVDD: Left ventricular end-diastolic diameter; LVDS: Left ventricular end-systolic diameter; NS: Not significant.

were each increased significantly in patients with chronic MR. While the LA maximal volume and stroke volume were both increased, the LAEF remained relatively unchanged. In contrast to LA volumes which were markedly increased, the A-wave velocity remained within normal range. The peak LAKE - an index of LA work - was increased in MR compared to the normal values. As LAKE is the product of LASV and A-wave velocity, the increased LAKE in chronic MR was mostly related to large LASV.

In a previous study (27), where light microscopy and ultrastructural observations were made on LA tissues obtained from patients at the time of surgery for correction of mitral valvular disease, cardiac muscle cells were found to be hypertrophied. In fibrotic areas - which were present in all left atria - the muscle cells tended to be isolated from adjacent cells and exhibited degenerative changes of varying degrees of severity. Hypertrophy was considered to lead to cellular degeneration, with a decrease or loss of contractile function. Atrial fibrillation was associated with severe cellular degeneration, the severity being greater in patients with MR than in those with mitral stenosis. Longstanding LA volume overload and increased LA work in MR may result in LA muscle dysfunction and failure. Left atrial enlargement in MR may lead to atrial fibrillation and its complications (28). The high frequency and severe consequences of the development of atrial fibrillation and its association with LA size suggest that consideration should be taken in preventing LA enlargement and incorporating LA size in the clinical decision-making process in patients with MR. Early surgery appears to prevent cardiovascular morbidity (29) and to minimize complications related to marked LA enlargement (30). In the present study, the increase in LAEF after mitral valve repair reflects the significant decrease in LA volumes after the operation, as the LASV remained unchanged. On the other hand, the postoperative increase LAKE reflected an increase in LA systolic work.

Finding the best timing for surgery in MR remains a challenge. LV dysfunction may affect even asymptomatic patients, leading to a poor long-term prognosis even after a successful mitral valve repair or replacement (9). The lack of simple parameters that could consistently predict this serious complication means that surgery cannot safely be postponed (10). Early surgery for severe MR has been suggested in asymptomatic patients with a normal LVEF to minimize the risk of postoperative ventricular failure (31). Atrial muscle dysfunction, as reflected by decreased atrial systolic function indices, exists preoperatively, even before symptoms and signs of LV failure.

Clinical implications

For many years, considerable interest has been shown in the evaluation of LA dimensions in disease

states (32). However, the measurements of LA volume does not take into consideration the complex and multi-dimensional indices of LA performance. The determination of LA work and its determining factors will better define those patients who are most likely to develop LA muscle dysfunction and failure. Interventions prior to the development of LA failure may preserve LA function and prevent the development of atrial fibrillation. The results of the present study showed that LA function and work can be measured in patients with severe MR but who have a technically adequate transthoracic echocardiogram before and after mitral valve repair. Serial measurements of LA performance and work would define the time of onset of atrial myopathy and help clinicians to better understand and manage patients with MR.

Study limitations

Although a total of 126 patients who underwent mitral valve repair was evaluated during the study period study, only a relatively small number was ultimately included due to non-fulfillment of the study criteria. In total, 38 patients were in atrial fibrillation, 12 had concomitant hemodynamically significant valvular disease other than MR, 26 had coronary artery disease, and 10 did not have technically satisfactory mitral flow Doppler and 2D echocardiography allowing accurate measurements. In addition, although the recovery of LA function may predict fewer postoperative complications, no long-term follow up of these patients was available.

In conclusion, while reconstructive mitral valve surgery in patients with severe MR due to FMV/MVP resulted in a decrease in LA size and volumes, LA work was increased postoperatively, suggesting that LA muscle dysfunction was present before surgery, and may precede LV dysfunction. The atrial myopathy which occurs in patients with severe MR prior to surgery may predispose to atrial arrhythmias and increased complications immediately or late after surgery. The degree of LA muscle dysfunction, as indicated by increased LA size and volumes and reduced LAEF and peak LAKE, should be taken into account when surgery is considered in patients with FMV/MVP/MR who are in sinus rhythm. Further definition of the LA muscle dysfunction factor, together with monitoring of LA volumes and work, may help to better define the optimal timing for reconstructive mitral valve surgery.

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