Improvement in exercise capacity and exercise hemodynamics 3 months after double-balloon, catheter balloon valvuloplasty treatment of patients with symptomatic mitral stenosis

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ABSTRACT Clinical status, exercise treadmill performance, and hemodynamics were determined in 24 patients with symptomatic mitral stenosis before catheter balloon valvuloplasty (CBV) and at 3 months follow-up. Hemodynamic determinations at rest showed that mitral CBV performed by the double-balloon technique resulted in significant immediate decreases in mean pulmonary arterial wedge pressure (28 ± 7 to 16 ± 5 mm Hg, p < .01), mean pulmonary arterial pressure (41 ± 11 to 33 ± 10 mm Hg, p < .05), and mitral valve gradient (16 ± 7 to 6 ± 3 mm Hg, p < .01), and significant increases in cardiac output (4.3 ± 1.1 to 5.0 ± 1.4 liters/min, p < .01). Mitral valve area increased from 1.0 ± 0.3 to 2.2 ± 0.7 cm² (p < .01). The mitral valve area was unchanged (2.0 ± 0.7 cm², p = NS) at 3 months. The lower pulmonary arterial wedge pressure, pulmonary arterial pressure, and mitral valve gradient persisted at 3 month follow-up catheterization. Clinical examinations showed that before CBV, 21 of 24 patients were in New York Heart Association functional class III or IV; 3 months after CBV, 22 patients were in class I or II. Before CBV, the mean exercise treadmill time was 5.9 ± 3.2 min and it had increased to 9.8 ± 2.9 min (p < .01) by the 3 month follow-up. Comparisons of hemodynamic determinations at the same exercise workload and duration before CBV and 3 months after CBV showed that despite similar heart rates and increased cardiac outputs (5.9 ± 1.7 vs 6.9 ± 1.5 liters/min, p < .01), there were significant decreases in the mean pulmonary arterial wedge pressure (42 ± 10 vs 28 ± 10 mm Hg, p < .01), mean pulmonary arterial pressure (61 ± 17 vs 42 ± 12 mm Hg, p < .01), and mitral valve gradient (27 ± 8 vs 14 ± 7 mm Hg, p < .01). Comparisons of hemodynamic determinations at symptom-limited supine bicycle exercise before and 3 months after CBV showed that the exercise time (9.1 ± 3.2 vs 17.1 ± 3.7 min, p < .01) and workload (43.0 ± 18.7 vs 58.9 ± 18.2 W, p < .01) both increased. Despite significant increases in heart rate (116 ± 23 vs 127 ± 20 beats/min, p < .01) and cardiac output (5.9 ± 1.7 vs 8.0 ± 1.5 liters/min, p < .01), the decreases in pulmonary arterial wedge pressure (41 ± 10 vs 29 ± 10 min Hg, p < .01), mean pulmonary arterial pressure (61 ± 17 vs 42 ± 11 mm Hg, p < .01), and mitral gradient (27 ± 8 vs 16 ± 5 mm Hg, p < .01) were significant. Comparisons of hemodynamic determinations at the two exercise levels 3 months after CBV (Post-CBV:Exl vs Post-CBV: Ex2) also demonstrated significant increases in heart rate (119 ± 25 vs 127 ± 20 beats/min, p < .01) and cardiac output (6.9 ± 1.5 vs 8.0 ± 1.5 liters/min, p < .01) compared with small changes in the pulmonary arterial wedge pressure (28 ± 10 vs 28 ± 9 mm Hg, p = NS) and pulmonary arterial pressure (42 ± 12 vs 42 ± 11 mm Hg, p = NS). We conclude that mitral CBV by the double-balloon technique resulted in increased mitral valve areas that persisted at 3 month follow-up and were associated with reduced symptoms, increased exercise treadmill time, increased supine exercise bicycle performance, and a significant improvement in hemodynamics both at rest and exercise; the latter provides a physiologic explanation for the observed clinical and treadmill improvement.


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are standard treatments for patients with severe rheumatic mitral valve stenosis.1–3 Catheter balloon valvuloplasty (CBV) is a relatively new treatment for patients with rheumatic mitral stenosis.4–7 In adult patients, CBV by the double balloon technique6, 7 may result in mitral valve areas similar to those achieved after closed8, 9 and open10 surgical commissurotomy in selected patients. The mechanisms of increase in mitral valve area after double-balloon CBV and after surgical commissurotomy are similar.11 Left atrial and pulmonary arterial pressures are reduced and cardiac output is increased soon after CBV.6, 7, 12, 13

To evaluate the effects of CBV in patients with mitral stenosis, we studied their clinical status, maximum exercise performance, and cardiac hemodynamics during rest and exercise before CBV and over a 3 month follow-up period.

**Methods**

Of the first 27 patients receiving isolated mitral double-balloon CBV at LAC-USC Medical Center, there was one death in a patient in functional class IV and one 73-year-old patient died of recurrent seizures at 2½ months after CBV. One patient, 82 years of age, has returned for clinical follow-up but has declined repeat cardiac catheterization and exercise studies. The clinical characteristics of the remaining 24 patients, whose data form the basis of this report, are listed in table 1. Informed consent for this study was obtained from all patients. There were 21 women and three men whose ages ranged from 22 to 70 years (41 ± 15 years, mean ± SD). Functional class was graded by the New York Heart Association criteria.14 Before CBV, 21 patients were in functional classes III or IV, and three patients were in functional class II. Seven patients were in atrial fibrillation. On chest x-ray, all patients had left atrial enlargement or pulmonary venous enlargement, 14 had interstitial edema with or without pleural effusions, and the average cardiothoracic ratio was 0.54 ± 0.07. Mitral regurgitation was judged by angiography to be mild in 10 patients and moderate in three. Eight patients had mild aortic regurgitation, four had gradients of less than 30 mm Hg.

**Table 1**

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<th>Other medical conditions</th>
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<th>Pulm. edema</th>
<th>CT ratio</th>
<th>CXR AO valve gradient (mm Hg)</th>
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**Mean ± SD**

| Age (yr) | 41 ± 15 | Pulm. edema | 0.54 ± 0.07 | CT ratio | 0.56 ± 0.11 | AO valve gradient (mm Hg) | 0.54 ± 0.07 | CAD | 0.56 ± 0.11 |

AVR = aortic valve replacement; CMC = closed mitral commissurotomy; OMC = open mitral commissurotomy; old CVA = previous cerebrovascular accident; TIA = transient ischemic attack; NSR = normal sinus rhythm; RVH = right ventricular hypertrophy; ECG = electrocardiogram; CT ratio = cardiothoracic ratio; Pulm. edema = interstitial pulmonary edema; D = dyspnea on exertion; P = paroxysmal nocturnal dyspnea; O = orthopnea; F = fatigue, weakness; E = edema; H = hemoptysis; MR = mitral regurgitation; AR = aortic regurgitation; CAD = coronary artery disease; EF = left ventricular ejection fraction; TR = tricuspid regurgitation; + = present; − = absent.

^A Angiographic regurgitation: 1 = mild; 2 = moderate; 3 = moderate to severe; 4 = severe.
across their aortic valves and none had coronary artery disease. The mean left ventricular ejection fraction was 0.55 ± 0.10 (range, 0.33 to 0.81).

Functional class was assessed before CBV and at 1 to 2 weeks and 3 months after CBV. Exercise treadmill tests were performed by the Bruce protocol before CBV and monthly after CBV for 3 months. The total exercise time and the maximum stage for each patient was recorded.

Cardiac catheterization was performed before and 3 months after CBV in all patients. Before CBV, right and left heart pressures, blood oxygen saturations, and cardiac outputs by both the thermilization and Fick methods were obtained at rest. Oxygen consumption was measured directly with a Collins spirometer. Symptom-limited supine bicycle exercise was performed during cardiac catheterization in 23 patients using single leg exercise (Siemens bicycle ergometer Model 880). The workload was started at 25 W and increased in increments of 25 W at 3 min intervals until the patient experienced fatigue or dyspnea. Patients unable to perform exercise at progressively higher work levels (due to orthopedic limitations, muscle weakness, leg cramps, etc.) were maintained at moderate workloads until the heart rate increased and the patient became dyspneic. Previous studies have shown that these stable workloads result in hemodynamic changes that reach a steady state. At this symptom-limited end point (Pre-CBV:Ex1), the workloads and times for each patient were recorded, and repeat hemodynamic determinations were obtained. After exercise, left ventricular, supravalvular aortic, and selective coronary cineangiography were performed. Immediately after CBV, resting hemodynamics and left ventricular angiography were repeated. Three months after CBV, repeat cardiac catheterization was performed. Blood oximetry determinations were performed in all patients, and Fick cardiac outputs were used where appropriate to calculate mitral valve area in six patients with atrial septal defects (Qp/Qs ranged from 1.2/1 to 1.6/1). Cardiac outputs (QOs) determined by the Fick and thermilization methods in patients without intracardiac shunts in our laboratory are highly correlated [CO (thermo) = 1.09 × CO (Fick) − 0.57, SEE = 0.07, r² = .93, p < .001, mean difference = 6.6%]. Hemodynamic determinations at 3 month follow-up were obtained at rest and again during supine bicycle exercise. Hemodynamic determinations were obtained at follow-up at the same workload and time as had been achieved before CBV and are labeled Post-CBV:Ex1. Patients then continued to exercise for longer times and at higher workloads to achieve a symptom-limited end point. Hemodynamic determinations at this point were labeled Post-CBV:Ex2. Left ventricular angiography was also repeated at rest.

Double-balloon CBV was performed from the right femoral vein as described previously in detail. In brief, two exchange guidewires with heavy duty cores and J tips of 0.038 inch diameter were used. Each wire with a preshaped curl at the distal end was placed in the apex of the left ventricle through a single transseptal puncture with a Mullins sheath or a double-lumen catheter, or through two transseptal punctures. If the procedure was performed by placing the guidewires out the left ventricular outflow tract to the descending aorta, exchange guidewires with normal core stiffness were used. Two balloon catheters (Mansfield Scientific) were selected to approximately equal the mitral valve annular diameter as determined by two-dimensional echocardiography. Balloon lengths ranged from 3 to 6 cm. The valve commissures were opened by repeatedly inflating the two balloons simultaneously.

Statistical analyses were performed by repeated-measures analysis of variance and the Student-Newman-Keuls multiple comparison test. Hemodynamic determinations at rest before CBV, immediately after CBV, and 3 months after CBV were compared. Hemodynamic determinations at exercise were compared by two separate analyses of variance: (1) exercise hemodynamics were compared at the equal workload end point (Pre-CBV:Ex1 vs Post-CBV:Ex1), and (2) all three exercise determinations were compared to analyze the symptom-limited end points (Pre-CBV:Ex1 vs Post-CBV:Ex1 and Pre-CBV:Ex1 vs Post-CBV:Ex2 and Post-CBV:Ex1 vs Post-CBV:Ex2). One elderly patient could not exercise at all and musculoskeletal disability or technical limitations precluded complete exercise determinations 3 months after CBV in eight patients. For all three of these analyses of variance, differences between the means with an overall p value (two-tailed) of less than .05 were accepted as statistically significant. Values are expressed as mean ± SD.

FIGURE 1. New York Heart Association functional class in patients with mitral stenosis before, 1 to 2 weeks after, and 3 months after CBV.

FIGURE 2. Exercise treadmill time (Bruce protocol) before and 3 months after CBV in patients with mitral stenosis.
### TABLE 2
Hemodynamics at rest before, immediately after, and at 3 months after double-balloon mitral CBV

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<th>Post CBV Heart rate (beats/min)</th>
<th>3 mo F/U Heart rate (beats/min)</th>
<th>Pre CBV Mean aorta (mm Hg)</th>
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Overall p values

- Pre CBV vs Post CBV: NS
- Pre CBV vs 3 mo F/U: NS
- Post CBV vs 3 mo F/U: NS

RA = right atrium; PA = pulmonary artery; PAW = pulmonary artery wedge; LVEDP = left ventricular end-diastolic pressure; MV Grad = mitral valve gradient.

*p < .05; **p < .01 by Student-Newman-Keuls test and repeated-measures analysis of variance.

### Results

**Changes in functional class.** Before CBV, 21 of 24 patients were in functional classes III or IV (figure 1). After an initial recovery period of 1 to 2 weeks after CBV, 22 of 24 patients experienced some improvement in their functional class; 21 patients were in functional classes I or II, and three patients were in functional class III. After 3 months of follow-up, 22 patients were in functional classes I or II. Seven patients showed some further decrease in symptoms at between 2 weeks and 3 months, and one patient showed recurrence of functional class III symptoms.

**Exercise treadmill performance.** Before CBV, the duration of exercise, as shown in figure 2, was 5.9 ± 3.2 min. The treadmill time had increased to 8.8 ± 2.5 min 1 month after CBV, to 8.9 ± 3.0 min 2 months after CBV, and to 9.8 ± 2.9 min 3 months after CBV. The mean value at each month after CBV was significantly increased when compared with the mean value before CBV by analysis of variance (p < .01); however, the differences in exercise duration at the various stages during the 3 months of follow-up were not significant. Twenty of 23 patients increased their maximum exercise level by at least 1 stage, and seven patients increased it by two or more stages (figure 2).

**Hemodynamic comparisons at rest.** Immediately after CBV, there were decreases in mitral valve gradient (from 17 ± 5 to 6 ± 3 mm Hg, p = .01), in mean pulmonary arterial wedge pressure (from 28 ± 7 to 16 ± 5 mm Hg, p < .01), and in mean pulmonary arterial pressure (from 41 ± 11 to 33 ± 10 mm Hg, p < .01). There was an increase in cardiac output (from 4.3 ± 1.1 to 5.0 ± 1.4 liters/min, p < .01) and in mitral valve...
area (from 1.0 ± 0.3 to 2.2 ± 0.7 cm², p < .01), as shown in table 2 and figures 3 to 5.

At 3 month follow-up, these significant changes persisted (table 2; figures 3 to 5). Aside from a small but significant increase in mean aortic pressure and decreases in heart rate and mean pulmonary arterial pressure, the differences between the determinations immediately after CBV and 3 months after CBV were not significantly different.

Hemodynamic comparisons during equal exercise workloads. Hemodynamics were determined during exercise before CBV (Pre-CBV:Ex1, 41 ± 18 W and 9.1 ± 3.2 min) and repeated at the same workloads and times for each patient 3 months after CBV (Post-CBV:Ex1). Comparisons of hemodynamics at this same exercise level before and 3 months after CBV showed that the heart rates were similar (116 ± 23 vs 119 ± 25 beats/min, p = NS) and cardiac output increased (from 5.9 ± 1.7 to 6.9 ± 1.5 liters/min, p < .01), mean pulmonary arterial wedge pressure decreased (from 42 ± 10 to 28 ± 10 mm Hg, p < .01), mitral valve gradient decreased (from 27 ± 8 to 14 ± 7 mm Hg, p < .01), mean pulmonary arterial pressure decreased (from 61 ± 14 to 42 ± 12 mm Hg, p < .01), and mean right atrial pressure decreased (from 13 ± 6 to 10 ± 4 mm Hg, p < .01). The changes in left ventricular end-diastolic pressure were not significant (table 3; figures 3 to 5).

Hemodynamic comparisons at maximum symptom-limited end points. Comparison of the symptom-limited determinations before (Pre-CBV:Ex1) and 3 months after CBV (Post-CBV:Ex2) showed that there were increases in exercise time (9.1 ± 3.2 vs 17.1 ± 3.7 min, p < .01), in maximum workload (43.0 ± 18.7 vs 58.9 ± 18.2 W, p < .01), in heart rate (116 ± 23 vs 127 ± 20 beats/min, p = NS), and in cardiac output (5.9 ± 1.7 vs 8.0 ± 1.5 liters/min, p < .01). In contrast, the Post-CBV:Ex2 determinations demonstrated significantly lower pulmonary arterial wedge pressures (42 ± 10 vs 28 ± 9 mm Hg, p < .01), mean pulmonary arterial pressure decreases (from 61 ± 14 to 42 ± 12 mm Hg, p < .01), mean right atrial pressure decreases (from 13 ± 6 to 10 ± 4 mm Hg, p < .01).
### Hemodynamics during supine bicycle exercise before and 3 months after double-balloon mitral CBV

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**Overall p values**

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**Comparison of Post-CBV:Ex1 with Post-CBV Ex2 determinations in patients who achieved the Post-CBV:Ex2 end point (table 3) showed that there were further increases in heart rate (119 ± 15 vs 129 ± 22 beats/min, p < .01), cardiac output (7.0 ± 1.1 vs 8.2 ± 1.5 liters/min, p < .01), and mean mitral valve gradient (14 ± 7 vs 16 ± 5 mm Hg, p < .05); however, these significant increases were associated with small changes in pulmonary arterial wedge pressure (28 ± 10 vs 28 ± 9 mm Hg, p = NS) and in mean pulmonary arterial pressure (42 ± 12 vs 42 ± 11 mm Hg, p = NS) that were not significant.

**Left ventricular angiography.** Left ventricular angiography (table 4) demonstrated that before CBV, immediately after CBV, and at 3 months after CBV the left ventricular end-diastolic volumes were 84 ± 27, 83 ± 17, and 89 ± 20 ml/m², the end-systolic volumes were 37 ± 17, 34 ± 10, and 36 ± 15 ml/m², and ejection fractions were 0.56 ± 0.11, 0.57 ± 0.08, and 0.60 ± 0.10, respectively. None of these differences were statistically significant.

Before CBV, 11 patients had no mitral regurgitation, 10 patients had 1+ mitral regurgitation, and three patients had 2+ mitral regurgitation. Immediately after CBV, there was an increase from 1+ to 2+ mitral regurgitation in one patient, a decrease from 1+ to 0 in one patient, and an increase from 0 to 1+ in five patients.
Three months after patients. Three months after CBV, mitral regurgitation had increased from 1+ to 2+ in three patients and had decreased from 2+ to 1+ in one patient and from 1+ to 0 in one patient.

Discussion

We have demonstrated that there is subjective improvement in symptoms in patients with mitral stenosis 3 months after CBV; importantly, we have objectively documented that this improvement is associated with an increase in overall exercise capacity on the maximum treadmill tests and on supine bicycle tests during cardiac catheterization. Furthermore, hemodynamic measurements during supine bicycle exercise documented that patients achieved a higher cardiac output and had significantly lower mean pulmonary arterial wedge pressures, mean pulmonary arterial pressures, and mean mitral valve gradients. These detailed hemodynamic studies during exercise testing corroborated the improvement in clinical status seen in our patients at 3 months of follow-up.

Clinical and hemodynamic improvements occurred relatively rapidly in these patients. Patients with high pulmonary arterial wedge pressures before CBV who had marked reductions in pulmonary arterial wedge pressures at CBV experienced relief of orthopnea and paroxysmal dyspnea immediately after the procedure. After a short recovery period, which included 48 hr in the hospital and 1 to 2 weeks of progressive activity at home, many patients reported a major reduction in symptoms that persisted over the 3 month follow-up period. Younger patients in functional class III often became asymptomatic, a finding also noted after recovery from surgical commissurotomy. Improvements in exercise treadmill performance objectively documented these reported reductions in symptoms. The exercise treadmill time at 1 month after CBV was

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**TABLE 3**

(Continued)

**THERAPY AND PREVENTION—VALVULOPLASTY**

**FIGURE 3.** Heart rate and cardiac output before, immediately after, and 3 months after CBV. Mean values ± SDs for each variable are shown as bar graphs with extended vertical lines. Hemodynamics obtained at rest are shown as open bars. Hemodynamics obtained at symptom-limited exercise before CBV (BEFORE CBV: Ex1, Sx LTD) and at the same exercise level 3 months after valvuloplasty (3 MONTHS AFTER CBV: Ex1) are shown as solid bars. Hemodynamics obtained at symptom-limited exercise 3 months after valvuloplasty (Ex2 Sx LTD) are shown as hatched bars.
FIGURE 3. Figure arterial wedge

TABLE 4

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p = NS for all comparisons. Abbreviations are as in table 2.

The hemodynamics at rest demonstrate a persistent increase in mitral valve area at 3 month follow-up after CBV. These data are similar to earlier studies that reported hemodynamic data at rest before and soon after closed and open mitral commissurotomy in selected surgical patients. Mean left atrial pressure, which ranged from 22 to 28 mm Hg, was reduced to the range of 16 to 19 mm Hg immediately after surgical commissurotomy. Lower left atrial and mean pulmonary arterial pressures persisted at 2 to 6 weeks after surgery, and 6 to 24 months after surgery they were associated with slight increases in cardiac output.

Average mitral valve areas increased from the 0.8 to 1.2 cm² range before surgery to the 1.2 to 2.3 cm² range several months after surgery. These areas are similar to the mitral valve area at 3

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month follow-up in our series of patients (range 1.0 to 4.0 cm², average 2.0 cm²).

Direct comparison of exercise hemodynamics before and after CBV both at similar workloads (Pre-CBV:Ex1 vs Post-CBV:Ex1) and at symptom-limited exercise (Pre-CBV:Ex1 vs Post-CBV:Ex2) showed that the pulmonary arterial wedge and mean pulmonary arterial pressures and mitral valve gradients were all significantly lower after CBV. Supine bicycle exercise hemodynamics have previously been used to describe the circulatory changes associated with mitral stenosis. However, there are a few studies that document exercise hemodynamics in operated patients with mitral stenosis. In patients with mitral stenosis who perform mild steady-state exercise, the heart rate, cardiac output, pulmonary arterial wedge pressures, and mean pulmonary arterial pressures all increase. Wade et al. studied 10 patients during supine exercise before and at 6 months after closed commissurotomy. The exercise workload was individualized for each patient according to his or her disability, but the same workload was repeated at each patient’s follow-up test. The increases in heart rate and cardiac output from rest to exercise were similar before and after commissurotomy, but after commissurotomy the pulmonary arterial wedge and mean pulmonary arterial pressures were lower both at rest and during exercise. Feigenbaum et al. studied 35 patients before and again at an average of 9 months after transventricular commissurotomy. All patients performed exercise by a standard protocol using leg exercise at a single workload. The average mitral valve area increased from 1.3 to 2.6 cm² after commissurotomy. During rest and exercise, the mean pulmonary arterial pressures, pulmonary arterial wedge pressures, and mitral valve gradients were all significantly lower at follow-up. Our results after CBV show the same pattern of improved hemodynamics at rest and exercise.

It has been emphasized that it is important to objectively document the benefits of CBV. In the present study, the beneficial hemodynamic changes demonstrated after CBV in our patients corroborate the reported improvements in symptoms and provide a physiologic explanation for the improved exercise performance during both the treadmill and supine bicycle exercise tests.

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Improvement in exercise capacity and exercise hemodynamics 3 months after double-balloon, catheter balloon valvuloplasty treatment of patients with symptomatic mitral stenosis.

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