

# Minimally invasive mitral valve replacement is a safe and effective surgery for patients with rheumatic valve disease

## A retrospective study

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### Abstract

The aim of the study was to evaluate the treatment of minimally invasive mitral valve replacement (MIMVR) through a right minithoracotomy for patients with rheumatic mitral valve disease.

From February 2009 to December 2016, 360 patients with rheumatic mitral valve disease underwent mitral valve replacement by the same surgeon. Among them, 150 patients accepted MIMVR through a right minithoracotomy, whereas the other 210 accepted a traditional median sternotomy. After matching by patients by age, sex, EuroSCORE, New York Heart Association (NYHA) classification, renal and liver function, and degree of mitral valve disease, we selected 224 patients for analysis in our retrospective study.

In the MIMVR group (112 patients), the aortic cross-clamp time (ACC time) ( $55.25 \pm 2.18$  minutes) was significantly longer than that in the control group (112 patients;  $36.05 \pm 1.40$  minutes) ( $P < .0001$ ). In contrast, the cardiopulmonary bypass time (CPB time) was shorter in the MIMVR group than in the control group ( $61.13 \pm 2.57$  vs  $78.65 \pm 4.05$  minutes, respectively,  $P < .0001$ ). Patients who accepted MIMVR surgery had less drainage 24 hours postoperation ( $324.10 \pm 34.55$  vs  $492.90 \pm 34.05$  mL,  $P < .0001$ ) and had less total drainage ( $713.46 \pm 65.35$  vs  $990.49 \pm 67.88$  mL,  $P < .0001$ ) than those who underwent median sternotomy. Thirty-two percent of patients in the MIMVR group needed a blood transfusion ( $1.35 \pm .28$  units of red blood cells,  $155.36 \pm 33.43$  mL plasma), whereas 67.0% of the control group needed a blood transfusion ( $2.15 \pm .24$  units of red blood cells,  $287.50 \pm 33.54$  mL plasma) ( $P_{\text{transfusion}} < .001$ ,  $P_{\text{cell}} = .029$ ,  $P_{\text{plasma}} = .006$ ). In total, 5 deaths occurred during the perioperative period; 3 occurred in the MIMVR group. The average hospital stay was significantly shorter in the MIMVR group than that in the control group ( $6.56 \pm .23$  vs  $8.53 \pm .59$  days,  $P = .003$ ).

MIMVR, an effective and safe treatment approach for patients suffering from rheumatic mitral valve disease, is associated with less trauma and a faster recovery. It is a better choice for treating simple rheumatic mitral valve disease.

**Abbreviations:** ACC = aortic cross-clamp (time), AF = atrial fibrillation, AHA = American Heart Association, AR = aortic valve regurgitation, AS = aortic valve stenosis, CKD = chronic kidney disease, CPB = cardiopulmonary bypass (time), HBP = high blood pressure, LAD = left atrial diameter, LVEDD = left ventricular end-diastolic dimension, LVEF = left ventricular ejection fraction, MIMVR/MI = minimally invasive mitral valve replacement, MR = mitral valve regurgitation, NYHA = New York Heart Association, PAH = pulmonary arterial hypertension, TB = total bilirubin, TEE = transesophageal echocardiography, TR = tricuspid regurgitation, TTE = transthoracic echocardiography.

**Keywords:** minimally invasive, mitral valve replacement, retrospective study, rheumatic valve disease

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## 1. Introduction

Rheumatic valve disease is the most common heart disease in China, and it primarily affects the mitral valve. Rheumatic fever increases valve thickness and contracture, making valvuloplasty more difficult than replacement.<sup>[1]</sup> Traditional mitral valve surgery via a median sternotomy is safe and effective, but it results in a high degree of trauma and a long incision.<sup>[2]</sup> In the last 2 decades, a minimally invasive (MI) technique has been used widely in cardiac surgery.<sup>[3,4]</sup> Its prominent advantage in postsurgery recovery and the small incision required makes patients prefer it over a traditional incision.<sup>[4,5]</sup> However, dispute still exist regarding the safety of a MI approach.<sup>[6]</sup> Furthermore, due to the low prevalence of rheumatic valve disease in the western world, few articles have focused on patients with rheumatic fever.<sup>[7]</sup> We conducted a retroactive study to evaluate the safety and efficacy of minimally invasive mitral valve replacement (MIMVR) for treating rheumatic heart disease in China.

**Table 1**  
**Preoperation data.**

	Control	MI	P
Male/female	24/88	16/96	.111
Age, y	53.21	53.37	.914
Euroscore	3.55	3.71	.524
Creatinine, $\mu\text{mol/L}$	71.12	68.39	.295
TB	13.796	13.244	.463
NYHA			
I	1 (.9%)	3 (2.7%)	1.000
II	40 (35.7%)	32 (28.6%)	
III	64 (57.1%)	74 (66.1%)	
IV	7 (6.3%)	3 (2.7%)	
HBP	11 (9.8%)	14 (12.5%)	.336
CKD	1 (.9%)	2 (1.8%)	.500
AF	82 (73.2%)	52 (46.4%)	<.001*
AVB	0 (0%)	1 (.9%)	.500

AF = atrial fibrillation, AVB = atrioventricular block, CKD = chronic kidney disease, HBP = high blood pressure, NYHA = New York Heart Association, TB = total bilirubin.

\* P value <.05.

## 2. Methods

### 2.1. Patient selection

Between February 2009 and December 2016 at Zhongshan Hospital, 360 patients (67 men, 293 women; mean age  $53.81 \pm 10.73$  years) underwent mitral valve surgery by the same surgeon excluding those undergoing aortic valve replacement at the same time). One hundred fifty of these patients underwent a lateral right minithoracotomy using a nonsternotomy MI technique; the rest underwent a traditional sternotomy incision. Data from all patients were retrospectively reviewed. This study was approved by Ethics Committee of Zhongshan Hospital Fudan University.

### 2.2. Data matching

Because this is a retrospective study, we used a propensity score matching system to make the data for the 2 groups comparable. Patient age, EuroSCORE, New York Heart Association (NYHA) classification, ejection fraction, creatinine and total bilirubin levels, and degree of mitral valve disease were set as covariates. After matching, 112 patients remained in both groups. Preoperative clinical and echocardiographic characteristics are listed in Table 1.

### 2.3. Surgical techniques

The standard procedure for pure mitral valve replacement thoracotomy through a conventional median incision will not be covered in this article.

MIMVR through a right thoracotomy incision (simplified description of the procedure): Patients underwent MI surgery with double-lumen endotracheal intubation after intravenous anesthesia combined with general anesthesia, and their right side was elevated at  $30^\circ$ . After disinfection and draping were performed, each female patient's right breast was pushed up and inward to make her skin under the breast tense, with sterile protective film fixed to it. Establishing the in vitro pathway: First, venous and arterial access was established through a right inguinal incision, and the top of the chamber housing was placed in the superior vena cava opening to ensure the smoothness of the venous system. Appropriate arterial intubation was based on the thickness of the femoral artery and the body mass index value

(18–24F). Incision establishment: A 4 to 6 cm incision was opened layer by layer in the chest anterolaterally to the right of the fourth intercostal space. A lap-protector was placed, and left-lung ventilation was conducted. The thoracoscope was inserted near the anterior axillary line of the third intercostal space into the chest with  $\text{CO}_2$  input. A pericardial longitudinal incision was made under direct vision, extending to the head side and reflexed when reaching the aorta, with the pericardium suspended. Extracorporeal circulation was started, and Chitwood occlusion forceps were inserted into the chest to block the ascending aorta through the fourth intercostal space; the drainage tube of the left atrium perforated the chest through the right midaxillary line between the fifth and sixth intercostal space. 4-0 Prolene was used for the purse-string suturing of the aorta. A long aortic perfusion needle was inserted into the aorta, and antegrade perfusion of Zhongshan 3A cardioplegia fluid containing blood (prepared by our hospital) was performed. After electrocardiograph monitoring showed that electrocardiac activity had stopped, the interatrial groove was freed, the left atrial incision was made parallel to the interatrial groove, and the left atrial drainage tube was inserted. A left atrial retractor was placed and stretched to the surface for fixation through the perforation into the prothorax, and the left atrial incision was retracted in the direction of the sternum. At the same time, the operating table was moved to the left side to expose the mitral valve. Endoscopic surgical instruments were used to remove the damaged mitral valve with the assistance of the thoracoscope, and the mitral valve was sutured intermittently (1 mechanical valve was produced by Soria, 1 by Carbon, and the others by St. Jude Corporation; biological valves were produced by St. Jude, Medtronic, and Edward). After examination of the valve location and the opening and closing performance of the valve leaf, the left atrial incision was sutured continuously. Pacing wires were sutured on the surface of the right ventricle according to the contraction condition of the heart. Retrograde cardioplegia perfusion through the tube was initiated for venting, and the anesthesiologist ventilated the lungs with air to keep the lung lobes full and to relieve the occlusion of the ascending aorta. Cardiopulmonary bypass was stopped gradually and bleeding was stopped; a chest drainage tube was inserted through the hole for the left atrium drainage tube, and the chest was closed.

The tricuspid valvuloplasties that were conducted all involved tricuspid valve C-type annular rings (Sorin Co Ltd/Baisiren Co Ltd); radiofrequency ablation of atrial fibrillation (AF) was always performed via unipolar radiofrequency ablation.

### 2.4. Analysis

All data were analyzed using SPSS 24 (IBM Corp 1989–2016). All measurements between the 2 groups were analyzed via analysis of variance; enumeration data were analyzed via chi-square analysis. Differences with  $P < .05$  were considered significant in all cases.

### 2.5. Follow-up

All but 4 patients were followed to the present.

## 3. Results

### 3.1. Preoperative data

After matching, preoperative data were nearly the same in the 2 groups (Tables 1 and 2). The mean age was 53.37 years in the MI group and 53.21 in the control group. There were 16 male

**Table 2****Preoperation echo (transthoracic echocardiography 3 days before surgery).**

	Control	MI	P
Left ventricular ejection fraction (LVEF, %)	65.19	65.11	.918
Left atrial diameter (LAD, mm)	53.29	54.21	.290
Left ventricular end-diastolic dimension (LVEDD, mm)	47.66	48.25	.471
Mitral valve stenosis (MS, grade 0–5)	3.65	3.49	.453
Mitral valve regurgitation (MR, grade 0–5)	1.91	1.76	.477
Tricuspid regurgitation (TR, grade 0–5)	1.95	1.18	<.001*
Pulmonary arterial hypertension (PAH, grade 0–5)	2.38	1.88	.022*
Aortic valve stenosis (AS, grade 0–5)	.03	.01	.315
Aortic valve regurgitation (AR, grade 0–5)	.61	.50	.133

\*  $P < .05$ .

patients in the MI group (14.3%) and 24 in the control (median sternotomy) group (21.4%,  $P = .111$ ). The mean preoperative EuroSCORE was 3.63 (MI, 3.72 vs mitral valve stenosis, 3.55;  $P = .524$ ). The NYHA functional class was the same in the 2 groups. More than 50% of the patients (77/71) were in NYHA class III or IV. AF was present in 134 patients (59.8%); 82 of whom belonged to the control group, which was significantly more than that in the MI group. The mean preoperative degree of TR (tricuspid regurgitation) in the control group was  $1.95 \pm 1.15$  (grade 0–5), and in the MI group, it was  $1.18 \pm 1.11$ . The mean left ventricular ejection fraction (LVEF) was  $65.15\% \pm 3.9\%$ . Level of stenosis and recurrent of the mitral valve were evaluated via TTE (transthoracic echocardiography), according to AHA (American Heart Association) guidelines. The mean mitral valve stenosis grade was 3.65 in the control group and 3.49 in the MI group, whereas the recurrent grade was 1.91 in the control group and 1.76 in the MI group. To avoid bias caused by aortic valve operation, we did not accept patients who had undergone a double valve replacement operation; thus, the aortic valves were healthy in both groups. Some patients' TTE showed moderate aortic valve regurgitation, but the TEE (transesophageal echocardiography) examinations performed during the operation showed only mild or no regurgitation. These patients did not accept aortic valve operation and were therefore included in this study.

The control group displayed a prominent advantage in the aortic cross-clamp time,  $36.05 \pm 14.80$  vs  $55.25 \pm 23.11$  minutes, and a disadvantage in cardiopulmonary bypass (CPB) time,  $78.65 \pm 42.89$  vs  $61.13 \pm 27.16$  minutes (Table 3). This difference could be attributed to the fact that it is easier to close 1 interatrial groove incision than 2 incisions on the septal and right atrial walls. The valve size was approximately 27, the most common size of mitral valves in China. Two control group patients died in the perioperative period; one suffered a sudden heart stoppage; the other's left ventricular muscle was damaged. Three patients died in the MI group; 2 of them died of cardiac rupture and another died of bleeding and heart failure. A comparison of the results shows that the MI method has a huge advantage in the first 24 hours regarding drainage, total drainage, in-hospital time, and the need for a blood transfusion. Patients who accepted MI surgery had less drainage 24 hours postoperation ( $324.10 \pm 34.55$  vs  $492.90 \pm 34.05$  mL,  $P = .001$ ) and had less total drainage ( $713.46 \pm 65.35$  vs  $990.49 \pm 67.88$  mL,  $P = .004$ ) than those who underwent a median sternotomy. Thirty-three percent of patients in the MI group needed a blood transfusion ( $1.35 \pm .28$  units of red blood cells,  $155.36 \pm 33.43$  mL plasma), whereas 67.0% of the control group needed a blood transfusion ( $2.15 \pm .24$  units of red blood cells,  $287.50 \pm 33.54$  mL plasma) ( $P_{\text{transfusion}} < .001$ ,

**Table 3****Perioperation data show significant advantage of postoperation recovery in minimally invasive group.**

	Control	MI	P
Aortic cross-clamp time (ACC, min)	36.05	55.25	<.001*
Cardiopulmonary bypass time (CPB, min)	78.65	61.13	<.001*
Valve size	26.74	27.43	.107
Mechanical ventilation, h	17.43	12.55	.253
ICU time, h	31.90	27.67	.454*
In-hospital time, day	8.53	6.65	.003*
First 24 hours drainage, mL	492.90	324.10	.001*
Total drainage, mL	990.49	713.46	.004*
Blood transfusion (n)	75 (67.0%)	38 (33.9%)	<.001*
Red blood cell, unit	2.15	1.35	.029*
Plasma, mL	287.50	155.36	.006*
Tricuspid valvuloplasty (TVP, n)	38 (33.9%)	10 (8.9%)	<.001*
Atrial fibrillation ablation (n)	39 (35.5%)	16 (14.3%)	<.001*
Death (n)	2 (1.8%)	3 (2.7%)	.500
Reventilation (n)	1 (.9%)	2 (1.3%)	.500
Reoperation (n)	1 (.9%)	2 (2.0%)	.500
Pneumothorax (n)	0	4 (3.6%)	.061
Hydrothorax (n)	18 (16.1%)	6 (5.4%)	.008*
Renal insufficiency (n)	6 (5.5%)	7 (6.3%)	.5
Incision infection (n)	0	2 (1.8%)	.249

\*  $P < .05$ .

$P_{\text{cell}} = .029$ ,  $P_{\text{plasma}} = .006$ ). The average hospital stay was significantly shorter in the MIMVR group than in the control group ( $6.65 \pm .23$  vs  $8.53 \pm .59$  days,  $P = .003$ ). Four patients in MI group suffered pneumothorax, and 2 developed an incision infection. More patients in the control group had hydrothorax (moderate or worse) than in the MI group (18 vs 6,  $P = .008$ ) (Table 3).

Short-term follow up (3-month postoperation TTE) showed no difference in the 2 groups (Table 4). Kaplan–Meier survival analysis showed no significant difference between all rheumatic valve disease patients undergoing MIMVR and those undergoing traditional mitral valve replacement ( $P = .748$ ) (Fig. 1).

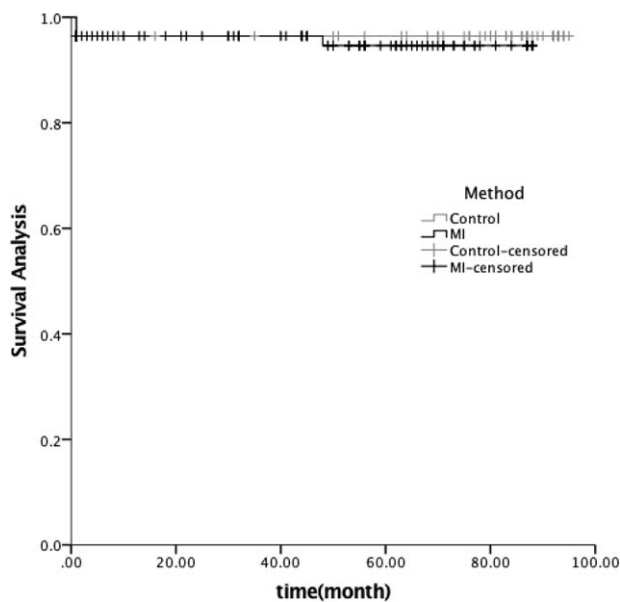
#### 4. Discussion

Rheumatic heart disease is an autoimmune disease that is common among the Chinese population; the prevalence in China is much higher than that in Europe, America, Japan, and other countries and regions. With the improvement in living standards and healthcare in recent years, the prevalence of rheumatic fever and rheumatic heart disease has drastically decreased, but these conditions still account for a large proportion of patients with

**Table 4****3-Month postoperation echo (transthoracic echocardiography).**

	Control	MI	P
LVEF, %	62.51	62.28	.821
LAD, mm	47.46	47.41	.962
LVEDD, mm	45.60	46.08	.562
MS (grade 0–5)	.30	.25	.157
MR (grade 0–5)	.02	.00	.494
TR (grade 0–5)	.92	.89	.597
PAH (grade 0–5)	1.16	1.12	.646

LAD = left atrial diameter, LVEDD = left ventricular end-diastolic dimension, LVEF = left ventricular ejection fraction, MI = minimally invasive, MR = mitral valve regurgitation, MS = mitral valve stenosis, PAH = pulmonary arterial hypertension, TR = tricuspid regurgitation.



**Figure 1.** Kaplan–Meier survival analysis showed no significant difference between all patients with rheumatic valve disease undergoing minimally invasive mitral valve replacement and those undergoing traditional mitral valve replacement ( $P=.748$ ). control = traditional median incision group, MI = minimally invasive group.

valvular lesions who need surgery. Rheumatic heart disease usually involves multiple valves. Typical rheumatic valvular lesions are thick and have adhesion and calcification of valve leaves, leading to hemodynamic abnormalities, primarily valve stenosis. Long-term mitral valve stenosis results in enlargement of the left atrium; increased pulmonary circulation resistance; symptoms such as coughing, chest tightness, and difficulty breathing; further impact on the right side of the heart; and enlargement of the right side of the heart. These factors can lead to AF, tricuspid insufficiency and systemic circulation congestion, which contribute to edema in both lower limbs and mitral facies. Because of the chronic course of rheumatic diseases and their indistinct early symptoms, when patients seek medical care for symptoms including chest tightness, wheezing, and edema in both lower limbs, they usually already have moderate (or worse) mitral stenosis, and valve replacements are therefore generally required to reconstruct the damaged valve leaves.

Traditional mitral valve replacement includes a median sternotomy, followed by successively opening the pericardium, the wall of the right atrium, and the atrial septum to the left atrium, which requires good visibility of the operation, and then proceeding with the valve replacement. It has been shown to have reliable efficacy and safety after decades of use.<sup>[2]</sup> Because of the large numbers of incisions and associated trauma, there are many complications, including a high amount of drainage, more blood transfusions and wound infections after operation, a poor sternal joint, and an incision scar on the prothorax.<sup>[4]</sup> Because some patients are unwilling to undergo surgery, their treatments are delayed. In recent years, the rapid development of MI surgery has resulted in this technique becoming more popular. MI surgery is more easily accepted by patients because of the small incision, minimal trauma and quick recovery. MI surgeries include MIMVR, valve replacement via thoracoscopy, robot-assisted valve replacement, valve replacement through a right-side small incision via thoracoscopy, and other procedures. Valve replace-

ment through a small incision in the right side of the chest via thoracoscopy is widely used because of the surgical approach and equipment costs.<sup>[7–9]</sup> We have adopted this procedure at our hospital since February 2009 and have used it to successfully treat more than 300 cases. To rule out the interference of numerous factors, a total of 360 simple mitral valve replacements performed by the same highly skilled surgeon at our hospital from February 2009 to December 2016 were reviewed; of these, 150 were MI surgeries.

Before data matching, the average age of all 360 patients was 53.81, with an average age of 51.4 years old in the MI group and 54.8 in the control group ( $P=.024$ ). We have observed that relatively young patients were more willing to have MI surgery when choosing different surgical methods. The majority (80%) of the patients were women; this was consistent with epidemiological results that show that rheumatic heart disease is more likely to occur in women. To achieve comparable data sets, we used age, EuroSCORE, LVEF, NYHA classification of cardiac function, degree of valve disease, pulmonary function, and renal function as matching covariates; data for both groups were matched and filtered. The preoperative baseline data in both groups after matching were nearly the same.

At present, the safety and efficacy of valve replacement through a small incision in the right side of the chest is still controversial. Some researchers argue that aortic blocking time and degree of extracorporeal circulation are high in MIMVR and that this may risk damage to multiple organs in patients, hence, increasing the risk of mortality and multiple organ failure.<sup>[10]</sup> However, our results disagree with this point of view; there was precisely a 19-minute disparity in the aortic occlusion time, but there was a 17-minute shortage in the extracorporeal circulation time between the methods. If a senior surgeon performed the surgery with the assistance of an experienced group, there would likely be no difference in operation times between MI surgery and conventional surgery. The rates of perioperative period mortality and incidence of postoperative complications, such as newly developed renal insufficiency and AF, were similar for the 2 methods.

In addition, the 24-hour drainage volumes after operation and postoperative total drainage volume in the MI group were significantly lower than that in the conventional group, and the percentage of patients receiving blood transfusions and the volume of blood required were lower in the MI group. Mechanical ventilation time and residence time in the surgical care unit in the MI group were lower than those in the conventional group but with no significant difference. Postoperative total hospital stays for the MI group was significantly shorter than for the conventional group; this was consistent with studies performed at other centers.<sup>[4]</sup> A reduction in the postoperative blood volume and a shortening of the length of the hospital stay could not only reduce blood transfusion reactions but also alleviate shortages of blood and reduce bed transfers in large center hospitals in our country. The reasons for the reduced blood requirements and shorter stays were most likely associated with the MI incision, minimal traction of tissue in the operation, and less tissue damage. However, the incidence of pneumothorax in the MI group was higher than that in the conventional group and was related to the surgical approach. The pleura is not opened during a median sternotomy unless there is a pleural cavity adhesion or a partial sternotomy incision. Follow-up examinations showed that the efficacy and stability of the mitral valve replacement in the MI group was the same as in the conventional group. Heart function recovery after the operation



was the same between the 2 groups; neither perivalvular leakage nor mitral regurgitation occurred.

The results of our study also reveal some weaknesses in MI surgery; there were 41 patients with moderate and severe TR, 38 of which underwent tricuspid valvuloplasty to shrink the ring of the tricuspid valve. There were 20 patients with moderate and severe TR, and only 10 underwent tricuspid valvuloplasty. More than half of the patients had left and right AF in both groups, and 39 patients in the conventional group underwent radiofrequency ablation, whereas only 16 underwent this procedure in the MI group. The closeness or resection rate of the left atrial appendage in patients with AF was lower in the MI group than that in the conventional group. Follow-up results showed no influence on the median prognosis because a small operation space limited combined surgery. Certainly, with the gradual development of MI surgery, an appropriate MI approach and improved equipment, these weaknesses could be solved.

MI surgery poses little damage to the bone and the structure of the chest, but the soft tissue through which the approach is made was thick, and the pain after the operation was no less than from a median sternotomy. A specific soft tissue distractor was used to reduce soft tissue tears; in addition, we attempted to insert a local indwelling anesthetic drug pump into the wound and obtained good effects in relieving pain after the operation. Hemostasis required 1 complete lung ventilation when extracorporeal circulation stopped; therefore, pulmonary function evaluation was required before the operation.<sup>[11]</sup> A recent study demonstrated that for patients who needed a second surgery for mitral valve replacement with a history of mitral valvuloplasty through a conventional incision or coronary artery bypass grafting, MI surgery through a right side of the chest incision was a good choice.<sup>[12]</sup> One patient received mitral valvuloplasty in our hospital 10 years ago and was admitted to the hospital again because of severe mitral valve stenosis; this patient recovered after MIMVR. Unlike in a traditional surgery with a large drainage volume and slow recovery, the endotracheal tube was removed on the first day after the operation, with a total drainage volume of 560 mL before the tube was removed. He was discharged on the sixth day. A follow-up at 18 months after discharge showed good mitral valve function, with an LVEF of 69% and no occurrence of infarction or renal insufficiency.

There were 2 limitations in the current study. Bias existed in the retrospective study itself; selection bias was difficult to eliminate in the 2 groups compared with a prospective study. Although patients undergoing surgery in the 2 groups were matched, we could not guarantee total consistency in the preoperative data. We chose relatively young patients with a mild disease who attached significance to the incision size in deciding to undergo

MI surgery. Patients who received a simple mitral valve had a relatively good recovery and relatively good heart function before surgery. Short- and median-term follow-up were not sufficient to compare the outcomes of the 2 methods. Follow-up projects were not meticulous enough; patients in the MI group appeared to adapt to normal life more quickly than patients in the conventional group, but we did not have enough evidence to fully support this observation. Quantifiable data that reflect life status could help resolve these questions.

## 5. Conclusions

Our study indicates that the safety and efficacy of MIMVR are consistent with the results of conventional surgery, with the advantages of a small incision, minimal trauma, and quick recovery. It is the first choice for patients with rheumatic mitral valve disease due to its association with reduced blood transfusion volume and decreased hospitalization time.

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