Combined Mitral and Aortic Valve Procedure via Right Mini-Thoracotomy versus Full Median Sternotomy

Insights from a Single-Center Study of Propensity-Matched Data

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Summary

Data involving combined mitral and aortic valve procedure via the right mini-thoracotomy approach are very limited. This single-center propensity-matching study aimed to evaluate early clinical outcomes of patients who underwent combined mitral and aortic valve procedure via right mini-thoracotomy versus full median sternotomy.

From January 2013 to December 2016, 926 eligible patients in our center were identified for this study. After propensity score-matching, 91 pairs of patients were entered into a RT group (right mini-thoracotomy surgery) or a FS group (full median sternotomy surgery). In-hospital and follow-up clinical outcomes were investigated and analyzed.

Patients in the RT group received similar surgical mortality as patients in the FS group (1.1% versus 2.2%, $P > 0.05$). Patients in the RT group as compared with the FS group were less likely to receive postoperative new onset of atrial fibrillation and red cell transfusion (11.0% versus 25.3%, $P = 0.012$; 17.6% versus 37.4%, $P = 0.003$, respectively), but they shared similar incidences of other major postoperative morbidity. Patients in the RT group as compared with the FS group experienced 6-minute longer aortic cross-clamping times and 9-minute longer cardiopulmonary bypass times, but received shorter intensive care unit stay and postoperative hospitalization time. No repeat valve operation, peri-prosthetic leak, or moderate or severe mitral valve regurgitation following valvuloplasty were observed in either group before discharge and also within one year of surgery.

In primary, isolated, combined mitral and aortic valve procedure, a right mini-thoracotomy approach may be utilized with accepted early clinical outcomes, and may be considered as a feasible alternative to the approach of full median sternotomy.

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Key words: Minimally invasive cardiac surgery, Surgical mortality, Major postoperative morbidity

Conventional cardiac valve surgery via a full median sternotomy has so far been the standard therapy for cardiac valve diseases. The term “minimally invasive” refers to a small incision in the chest wall. Over the past two decades, minimally invasive cardiac surgical techniques have been increasingly adopted with the goal of reducing the invasiveness of the surgical procedure and to offer the same quality, safety, and results as the standard procedure.¹⁾ Since the mid-1990s, several minimally invasive approaches for single valve procedure, such as anterolateral right mini-thoracotomy, partial sternotomy, right parasternal approach, and transverse sternotomy have been introduced and used with increasing frequency, showing some benefits by comparison with ap-

proach of the full median sternotomy approach.²⁻⁶⁾

Despite the described advantages of minimally invasive approaches, the uptake of these in the real world has been slow. In the USA and Europe, only 5%-10% of isolated aortic valve replacements were performed over the last decade using a minimally invasive approach.⁷⁻⁹⁾ Also, data involving combined mitral and aortic valve procedure via minimally invasive approaches were very limited.¹⁰⁾ The reasons for this surgical reluctance were multifactorial and included a lack of established training programs, the perception that success with the technique is limited to more proficient surgeons, and with a fear of deleterious patient outcomes, especially during the learning curve. Also, early studies showing difficulties in air

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removal, inadequate mediastinal and pleural drainage, increased risk of para-valvular leak and higher reoperation rates.^{11,12)} Nevertheless, continuous advances in refining surgical techniques and advances in peri-operative management have led to efficiency and safety that have been at least equivalent to conventional surgery in their high volume, specialized centers.¹³⁾ With the recent breakthrough of percutaneous valve interventions, the role of minimally invasive surgery is now more than ever prompted to expand in the practice of daily cardiac valve surgery.¹³⁾

This single-center study evaluated early outcomes of patients who underwent combined mitral and aortic valve procedure with or without tricuspid annuloplasty via right mini-thoracotomy versus a propensity-matched series of patients who underwent combined mitral and aortic valve procedure with or without tricuspid annuloplasty via full median sternotomy, and aimed to test the hypothesis that combined mitral and aortic valve procedure via right mini-thoracotomy is a safe and reproducible procedure that is associated with accepted early clinical outcomes, comparable to that of combined mitral and aortic valve procedure via full median sternotomy.

Methods

Patients: From January 2013 to December 2016, the documents of consecutive patients in our institute who received primary, isolated, combined mitral and aortic valve procedure with or without tricuspid annuloplasty were reviewed. The exclusion criteria were previous cardiac or thoracic surgery, emergency surgery, active infective endocarditis, cardiogenic shock, and undergoing concomitant cardiac surgical procedures (including coronary artery bypass grafting, aortic surgery, or Maze procedure). Also, patients receiving other minimally invasive approaches other than right mini-thoracotomy approach were excluded.

All included patients were divided into a RT group (patients who received valve surgery via right mini-thoracotomy) and a FS group (patients who underwent valve surgery via full median sternotomy). Baseline characteristics between the two groups were investigated and analyzed.

To reduce the effects of treatment selection bias and potential confounding, propensity score matching was used to adjust for differences in baseline characteristics. Propensity scores were created to quantify the likelihood of a given patient receiving minimally invasive multi-valve surgery via right mini-thoracotomy. Bivariate analyses were conducted to examine differences in baseline characteristics between patients in the RT group and patients in the FS group. Propensity scores were then calculated using a multivariate logistic regression model based on the following characteristics: older age; gender; obesity; recent smoking; coronary artery disease; hypertension; diabetes mellitus; chronic obstructive pulmonary disease; prior cerebro-vascular accident; renal dysfunction; etiology; enlarged left ventricle; atrial fibrillation; impaired left ventricular function (left ventricular ejection fraction < 45%); and NYHA III-IV. Pairs of patients who underwent

multi-valve surgery via right mini-thoracotomy and also full median sternotomy were derived using greedy 1:1 matching with a caliper of width 0.2 of standard deviation of the logit of the propensity score. Every patient in the RT group was matched with a patient in the FS group by the closest propensity score (within 0.030). The quality of the match was assessed by comparing selected pre-treatment variables in propensity score-matched patients using the standardized mean difference.

Surgical techniques: Surgery in the RT group was performed under general anesthesia with double-lumen endotracheal intubation. Soft pads were put under the right side of the patient's body with an inclination of 30-45°. Defibrillation electrode pads were placed behind the right scapula and on the 5th intercostal space of left anterior axillary line. Cardiopulmonary bypass was established utilizing a femoral platform under transesophageal echocardiographic guidance. Femoral artery cannulation was performed for arterial perfusion. Inferior vena cava (IVC) cannulation was inserted in the femoral vein, and superior vena cava cannulation was performed by the anesthesiologist in the internal jugular vein. For combined mitral and aortic valve procedure without tricuspid annuloplasty, a 5-6 cm arc-shaped incision was performed over the 3rd intercostal space, starting at the right edge of sternum and extending laterally. For combined mitral and aortic valve procedure with tricuspid annuloplasty, the incision was made at the right 3rd to 4th intercostal space starting at the right edge of the sternum and was extended laterally. The right internal mammary artery was dissected. After vacuum-assisted cardiopulmonary bypass was established, a left ventricular vent was placed through the right superior pulmonary vein. The ascending aorta was cross-clamped using a *Chitwood* clamp via a separate stab incision. The surgical field was flooded with carbon dioxide at a flow of 0.5 L/minute. Myocardial protection was achieved using cold blood cardioplegic solution at 4 °C and in a ratio of 1:4 via root or direct coronary antero-grade perfusion combined with intermittent coronary sinus retrograde perfusion. The cold blood cardioplegia was infused into the aortic root if there was no aortic valve regurgitation, or was delivered into the left and right coronary artery through a Y bifurcated catheter in the case of aortic regurgitation. The coronary sinus was cannulated under direct vision after right atrium was opened or under the guidance of transesophageal echocardiography. The initial dose of antero-grade cardioplegia infused was at 20 mL/kg; thereafter, the retrograde cardioplegia solution was re-infused every 30 minutes at a dose of 10 mL/kg. Right atrium and atrial septal incisions were performed for mitral valve procedure. If exposure of mitral valve was difficult, the incision was extended upwards to the left atrial roof. After mitral valve procedures were completed, aortic valve surgery was begun. The aortic valve was exposed through an oblique or transverse aortotomy. The decision to implant mechanical prosthetic valve or bio-prosthetic heart valve was influenced by each patient's demographic and clinical profile (i.e., age, peptic ulcer bleeding, size of aortic valve annulus), but the choice was ultimately left to discretion of each individual patient. The size of prosthetic valve was based on intraoperative actual measured

values. It was very important to implant a sufficiently large prosthesis in adult patients undergoing aortic valve replacement surgery. Mitral and aortic valve implantation was conducted with a double-armed 2-0 poly (ethylene terephthalate) suture with gasket and an interrupted mattress suturing technique. Afterward, tricuspid annuloplasty was performed via the right atrial incision.

Patients in the FS group received full median sternotomy under general anesthesia with single-lumen endotracheal intubation. Direct aortic cannulation was conducted in ascending aorta. Superior and IVC intubations were also conventional. The left side of the heart was vented through the right superior pulmonary vein. Myocardial protection was obtained with combined antero-grade and retrograde cardioplegia solution. Right atrium and atrial septal incisions were conducted for mitral and tricuspid valve procedure, and an aortic root incision was conducted for aortic valve procedure.

Clinical outcomes: In-hospital clinical outcomes included surgical mortality¹⁴⁾ and the occurrence of repeat valve procedure, para-valvular leak, moderate or severe valve regurgitation following valvuloplasty, and major postoperative morbidity. Major postoperative morbidity including circulatory morbidity (i.e., low cardiac output syndrome and new onset of atrial fibrillation), pulmonary complications (prolonged mechanical ventilation of more than 24 hours, re-intubation), acute renal failure requiring hemodialysis, stroke, reoperation for bleeding, and wound infection.¹⁵⁻¹⁷⁾ Also, cardiopulmonary bypass and aortic cross-clamping times, total amount of drainage, red cell transfusion, and lengths of intensive care unit (ICU) stay, as well as postoperative hospital stay were recorded.

Follow-up clinical outcomes included all-cause mortality and the occurrence of repeat valve procedure, para-valvular leak, and moderate or severe valve regurgitation following valvuloplasty.

Statistical analysis: This study protocol was approved by the ethics committee of the Zhongshan Hospital Fudan University, and was in accordance with the Declaration of Helsinki. Peri-operative data were obtained from our institutional database and were reviewed using a standard data collection form. Follow-up data were obtained by telephone and clinic visit. Data collection was performed by trained staff (two people). The trained staff, however, were not informed of the purpose of this study.

Normally distributed continuous variables were expressed as the mean $\pm$ standard deviation and were compared between groups using the Student's *t*-test. Non-normally distributed continuous variables were expressed as median and were compared between groups with the Wilcoxon rank sum test. Categorical variables were expressed as frequency distributions and single percentages and were compared between groups using χ^2 test or Fisher's exact test, when appropriate. The impacts of grouping (the RT group versus the FS group) as independent factors on surgical mortality and major postoperative morbidity were evaluated by multivariable logistic regression analysis using the backward method. A value of two-sided *P* less than 0.05 was considered statistically significant. Statistical analysis was performed with SPSS statistical package version 22.0 (SPSS Inc., Chicago, IL,

USA).

Results

Study population: From January 2013 to December 2016, a total of 1360 patients who received combined mitral and aortic valve procedure with or without tricuspid annuloplasty in our center were identified. Among them, 376 patients were excluded (previous cardiac or thoracic surgery in 46, emergency surgery in 25, concomitant coronary artery bypass grafting in 91, concomitant aortic surgery in 86, concomitant Maze procedure in 128), another 58 patients who received valve surgery via other minimally invasive approaches (including partial median sternotomy in 46 and right parasternal approach in 12) were also excluded, which left 926 eligible patients for data analysis. According to the surgical approach, 926 of the included patients were entered into either the RT group (*n* = 98) or the FS group (*n* = 828). No emergent conversion from right mini-thoracotomy to full median sternotomy during surgery was observed.

Baseline characteristics of the entire cohort are shown in Table I. Patients in the RT group as compared with the FS group were younger and less likely to have history of chronic obstructive pulmonary disease, and had lower proportions of female and obesity. Also, patients in the RT group had a higher left ventricular ejection fraction and had lower proportions of left ventricular dysfunction (left ventricular ejection fraction of < 45%) and congestive heart failure (NYHA III-IV) by comparison with patients in the FS group. Also, the RT group as compared with the FS group had significantly lower EuroSCORE (European System for Cardiac Operative Risk Evaluation) II score and Society of Thoracic Surgeons (STS) score.

Using matching propensity scores, the area under the receiver operating characteristic curve for the multivariate logistic regression model was 0.76 (95% confidence interval [CI]: 0.66-0.84, *P* = 0.019). The Hosmer-Lemeshow goodness-of-fit for this model was 6.54 (*P* = 0.812). Finally, 91 pairs of patients were successfully established in a 1:1 ratio. As presented in Table II, there were no significant differences between the two matched groups with regard to all baseline variables. As shown in the Figure, all the absolute standardized differences after matching were <10%, indicating an adequate balance.

Operative data: Patients in the RT group as compared with the FS group had longer cardiopulmonary bypass and aortic cross-clamping times but shorter operation times before matching (112.2 $\pm$ 13.1 minutes versus 102.8 $\pm$ 12.5 minutes, *P* < 0.001; 79.4 $\pm$ 11.6 minutes versus 72.4 $\pm$ 11.7 minutes, *P* < 0.001; 4.0 $\pm$ 0.3 hours versus 4.1 $\pm$ 0.4 hours, *P* = 0.017, respectively). Intraoperative transesophageal echocardiography immediately after discontinuation of cardiopulmonary bypass showed that no para-valvular leak was found, and all regurgitation degrees after valvuloplasty were $\leq$ 1+.

After propensity score-matching, patients in the RT group as compared with the FS group had significantly longer aortic cross-clamping and cardiopulmonary bypass times (79.5 $\pm$ 12.5 minutes versus 72.9 $\pm$ 11.8 minutes, *P* < 0.001; 112.5 $\pm$ 12.9 minutes versus 103.5 $\pm$ 12.2 min-

Table I. Characteristics of the Entire Cohort Before Matching

	RT group (n = 98)	FS group (n = 828)	P value
Demographics			
Age (years old)	58.6 ± 6.5	61.6 ± 7.0	< 0.001
Older age (age > 65 years)	21 (21.4%)	300 (36.2%)	< 0.001
Gender (Female)	30 (30.6%)	345 (41.7%)	0.035
Obesity (BMI > 30 kg/m ²)	4 (4.1%)	91 (11.0%)	0.033
Recent smoking	36 (36.7%)	265 (32.0%)	0.345
Concomitant diseases			
Coronary artery disease	2 (2.0%)	10 (1.2%)	0.490
Hypertension	23 (23.5%)	182 (22.0%)	0.737
Diabetes mellitus	9 (9.2%)	104 (12.6%)	0.334
COPD	2 (2.0%)	84 (10.1%)	0.009
Prior cerebro-vascular accident	7 (7.1%)	51 (6.2%)	0.704
Renal dysfunction	2 (2.0%)	35 (4.2%)	0.296
Preoperative cardiac status			
Etiology			
Rheumatic valve disease	62 (63.2%)	493 (59.5%)	0.206
Degenerative valve disease	27 (27.6%)	203 (24.5%)	
Other	9 (9.2%)	132 (16.0%)	
Atrial fibrillation	10 (10.2%)	101 (12.2%)	0.566
LVEDD (mm)	57.8 ± 9.6	58.7 ± 7.8	0.293
Enlarged left ventricles	11 (11.2%)	127 (15.3%)	0.280
LVEF (%)	58.7 ± 7.6	56.1 ± 6.1	< 0.001
> 45%	83 (84.7%)	623 (75.2%)	0.049
35-45%	15 (15.3%)	175 (21.2%)	
< 35%	0	30 (3.6%)	
NYHA class			
I-II	33 (33.7%)	243 (29.3%)	0.046
III	65 (66.3%)	538 (65.0%)	
IV	0	47 (5.7%)	
EuroSCORE II (%)	4.0 ± 0.9	4.5 ± 1.2	< 0.001
STS (%)	6.9 ± 1.2	7.7 ± 2.1	< 0.001
Operative data			
CPB time (minutes)	112.2 ± 13.1	102.8 ± 12.5	< 0.001
ACC time (minutes)	79.4 ± 11.6	72.4 ± 11.7	< 0.001
Operation time (hours)	4.0 ± 0.3	4.1 ± 0.4	0.017
Surgical procedure			
AVR + MVR	49 (50.0%)	322 (38.9%)	< 0.001
AVR + MVP	10 (10.2%)	6 (0.7%)	
AVR + MVR + TVP	30 (30.6%)	359 (43.4%)	
AVR + MVP + TVP	9 (9.2%)	141 (17.0%)	

RT group indicates patients who received multi-valve surgery via right mini-thoracotomy approach; FS group, patients who underwent multi-valve surgery via full median sternotomy; BMI, body mass index; COPD, chronic obstructive pulmonary disease; LVEDD, left ventricular endo-diastolic diameter; LVEF, left ventricular ejection fraction; NYHA class, New York heart assessment functional classification; EuroSCORE II, European System for Cardiac Operative Risk Evaluation II; STS, Society of Thoracic Surgeons; CPB, cardiopulmonary bypass; ACC, aortic cross-clamping; AVR, aortic valve replacement; MVR, mitral valve replacement; MVP, mitral valvuloplasty; and TVP, tricuspid valvuloplasty. LVEDD > 65mm defined enlarged left ventricles.

utes, $P < 0.001$, respectively). Patients in the RT group had a slightly shorter operation time, but no significant difference was found. The proportion of surgical procedure was comparable between the two score-matching groups.

In-hospital outcomes: In-hospital clinical outcomes after matching are presented in Table III. No repeat valve operation, peri-prosthetic leakage, or moderate or severe mitral valve regurgitation was observed in either group. Al-

though patients in the RT group as compared with the FS group had a slightly lower incidence of surgical mortality, no significant difference was found between the two matching groups (1.1% versus 2.2%, $P = 1.000$). Patients in the RT group as compared with the FS group had significantly lower incidences of new onset of atrial fibrillation and red cell transfusion after matching (11.0% versus 25.3%, $P = 0.012$; 17.6% versus 37.4%, $P = 0.003$, respectively). No significant differences were found between

Table II. Preoperative and Operative Data in Two Propensity Matched Groups

	RT group (n = 91)	FS group (n = 91)	P value
Demographics			
Age (years old)	58.9 ± 6.4	59.4 ± 6.8	0.610
Older age (age > 65 years)	19 (20.9%)	22 (24.2%)	0.595
Gender (Female)	27 (29.7%)	30 (33.0%)	0.632
Obesity (BMI > 30 kg/m ²)	4 (4.4%)	7 (7.7%)	0.351
Recent smoking	32 (35.2%)	30 (33.0%)	0.754
Concomitant diseases			
Coronary artery disease	2 (2.2%)	2 (2.2%)	1.000
Hypertension	21 (23.1%)	20 (22.0%)	0.859
Diabetes mellitus	8 (8.8%)	10 (11.0%)	0.619
COPD	2 (2.2%)	3 (3.3%)	1.000
Prior cerebro-vascular accident	6 (6.6%)	5 (5.5%)	0.756
Renal dysfunction	2 (2.2%)	3 (3.3%)	1.000
Preoperative cardiac status			
Etiology			
Rheumatic valve disease	58 (63.7%)	56 (61.5%)	0.945
Degenerative valve disease	25 (27.5%)	26 (28.6%)	
Other	8 (8.8%)	9 (9.9%)	
Atrial fibrillation	9 (9.9%)	11 (12.1%)	0.635
LVEDD (mm)	57.9 ± 9.5	58.3 ± 8.2	0.761
Enlarged left ventricles	10 (11.0%)	11 (12.1%)	0.817
LVEF (%)	58.5 ± 7.5	58.1 ± 6.5	0.701
> 45%	78 (85.7%)	75 (82.4%)	0.548
35-45%	13 (14.3%)	15 (16.5%)	
< 35%	0	1 (1.1%)	
NYHA class			
I-II	30 (33.0%)	29 (31.9%)	0.601
III	61 (67.0%)	61 (67.0%)	
IV	0	1 (1.1%)	
EuroSCORE II (%)	4.1 ± 0.9	4.2 ± 1.0	0.479
STS (%)	7.0 ± 1.1	7.2 ± 1.3	0.264
Operative data			
CPB time (minutes)	112.5 ± 12.9	103.5 ± 12.2	< 0.001
ACC time (minutes)	79.5 ± 12.5	72.9 ± 11.8	< 0.001
Operation time (hours)	4.0 ± 0.4	4.1 ± 0.3	0.058
Surgical procedure			
AVR + MVR	48 (52.7%)	46 (50.5%)	0.187
AVR + MVP	8 (8.8%)	2 (2.2%)	
AVR + MVR + TVP	28 (30.8%)	32 (35.2%)	
AVR + MVP + TVP	7 (7.7%)	11 (12.1%)	

Abbreviations same as Table I.

the two matching groups in major postoperative morbidity other than new onset of atrial fibrillation and red cell transfusion. Also, as compared with the FS group, the RT group had significantly lower amount of drainage and shorter lengths of ICU stay as well as shorter lengths of postoperative hospital stay (477.6 ± 82.5 mL versus 863.1 ± 109.2 mL, $P < 0.001$; 37.6 ± 7.3 hours versus 48.3 ± 8.2 hours, $P < 0.001$; 6.2 ± 1.5 days versus 7.6 ± 1.9 days, $P < 0.001$, respectively).

The impacts of grouping (the RT group versus the FS group) on surgical mortality and major postoperative morbidity are presented in Table IV. Grouping (the RT group versus the FS group) was not found to be an independent risk factor for surgical mortality in multivariable logistic regression analysis (OR = 0.534, 95% CI 0.084-5.115, $P = 0.958$). Grouping was not found to be an independent risk factor for major postoperative morbidity

other than postoperative new onset of atrial fibrillation and red cell transfusion. In multivariable logistic regression analysis, the risk of postoperative new onset of atrial fibrillation in the RT group was 0.412 times (95%CI 0.212-0.836, $P = 0.017$) that in the FS group, and the risk of red cell transfusion in the RT group was 0.428 times (95% CI 0.213-0.761, $P = 0.005$) that in the FS group.

Follow-up outcomes: A total of 169 patients (86 in the RT group and 81 in the FS group) received one-year follow up. No all-cause mortality was recorded in either group and no repeat valve procedure, para-prosthetic valve leak, or moderate or severe valve regurgitation after valvuloplasty occurred in either group.

Discussion

The important findings of this single-center, propen-

Figure. Absolute standardized differences for baseline covariates before and after matching.

Table III. Early Clinical Outcomes in the Two Matching Groups

Clinical outcomes	RT group	FS group	P value
In-hospital			
Surgical mortality	1 (1.1%)	2 (2.2%)	1.000
Low cardiac output	3 (3.3%)	6 (6.6%)	0.497
New onset of AF	10 (11.0%)	23 (25.3%)	0.012
Prolonged mechanical ventilation	16 (17.6%)	10 (11.0%)	0.204
Re-intubation	2 (2.2%)	3 (3.3%)	1.000
Acute renal failure	1 (1.1%)	3 (3.3%)	0.621
Stroke	1 (1.1%)	2 (2.2%)	1.000
Re-operation for bleeding	1 (1.1%)	2 (2.2%)	1.000
Wound infection	1 (1.1%)	3 (3.3%)	0.621
Total amount of drainage (mL)	477.6 ± 82.5	863.1 ± 109.2	< 0.001
Red cell transfusion	16 (17.6%)	34 (37.4%)	0.003
ICU stay (hours)	37.6 ± 7.3	48.3 ± 8.2	< 0.001
Postoperative hospital stay (days)	6.2 ± 1.5	7.6 ± 1.9	< 0.001
Repeat valve operation	0	0	
Para-valvular leak	0	0	
Moderate or severe valve regurgitation	0	0	
Follow-up			
All-cause mortality	0	0	
Repeat valve operation	0	0	
Para-valvular leak	0	0	
Moderate or severe valve regurgitation	0	0	

AF indicates atrial fibrillation; and ICU, intensive care unit.

sity score-matched study were as follows: 1) patients in the RT group received a similar surgical mortality as patients in the FS group; 2) patients in the RT group as compared with the FS group were less likely to receive postoperative new onset of atrial fibrillation and red cell

transfusion, but received similar incidences of other major postoperative morbidity; 3) patients in the RT group experienced longer aortic cross-clamping and cardiopulmonary times, but shorter ICU stay and postoperative hospitalization time by comparison with patients in the FS group; 4)

Table IV. Impacts of Grouping on Early Adverse Events

	OR	95%CI	P value
Surgical mortality	0.534	0.084-5.115	0.958
Low cardiac output	0.513	0.167-2.239	0.464
New onset of AF	0.412	0.212-0.836	0.017
Prolonged mechanical ventilation	1.758	0.758-4.244	0.224
Re-intubation	0.715	0.148-4.541	0.894
Acute renal failure	0.426	0.133-3.694	0.571
Stroke	0.543	0.244-4.751	0.912
Re-operation for bleeding	0.604	0.268-4.215	0.839
Wound infection	0.356	0.103-3.549	0.661
Red cell transfusion	0.428	0.213-0.761	0.005

OR indicates odds ratio; CI, confidence interval; and AF, atrial fibrillation.

no repeat valve operation, para-valvular leak, or moderate or severe mitral valve regurgitation following valvuloplasty was observed in either group before discharge and within one year of surgery.

Operative safety is considered the most important factor to evaluate when a patient is considering a minimally invasive procedure. Evaluation of the surgical mortality was considered mandatory. One of the most important findings of this study was that patients who underwent minimally invasive multi-valve procedure via right mini-thoracotomy received a similar surgical mortality as patients who underwent conventional multi-valve procedure via full median sternotomy, without adverse events (including repeat valve operation, para-valvular leak, and moderate or severe mitral valve regurgitation following valvuloplasty). This evidence was in line with the results of most of the propensity-matched studies.¹⁸⁻²¹⁾ This study further proved that the operative approach (right mini-thoracotomy versus full median sternotomy) had no impact on surgical mortality.²²⁾ Also, this study reported a surgical mortality of 1.1% for minimally invasive multi-valve procedure and 2.2% for multi-valve procedure via full median sternotomy, which were far below the surgical mortality of 9.7%-13.2% reported in previous studies.²³⁾ It might be possible that the low surgical mortality in the current series was directly related to high valve surgery volume (more than 2000 cases of valve procedure annually in our center).

Another important finding was that patients who underwent multi-valve procedure via right mini-thoracotomy were less likely to receive postoperative new onset of atrial fibrillation and red cell transfusion by comparison with full median sternotomy. This propensity-matched study found that patients in the RT group as compared with the FS group had a significantly lower incidence of new onset of atrial fibrillation, and reported that the risk of postoperative new onset of atrial fibrillation in the RT group was 0.365 times the equivalent risk in the FS group. A possible explanation for low incidence of new onset of atrial fibrillation was that limited heart manipulation and trauma, particularly in cases of minimally invasive surgery via right mini-thoracotomy, was associated with a reduction in the incidence of postoperative atrial fibrillation.^{12,24)} However, the relative benefit of minimally invasive valve surgery on postoperative atrial fibrillation remains debated in the literature. Some studies have re-

ported a lower rate of postoperative atrial fibrillation with the use of minimally invasive surgery when compared to full median sternotomy with an absolute reduction of between 28% and 50%.¹³⁾ Nevertheless, other studies have failed to find any association.¹³⁾ In addition, this study showed a significantly lower amount of drainage in the RT group but a similar incidence of reoperation for bleeding between the two groups, and found that the risk of red cell transfusion in the RT group was 0.358 times that in the FS group. Many studies have reported a lower need for transfusion (25% to 50% reduction) with minimally invasive valve surgery when compared with surgery with full median sternotomy.¹³⁾ Most series have reported a similar rate of re-intervention for bleeding between both groups.^{13,25)} Those evidences mentioned above were in line with the results from this study.

In this study, patients who received invasive multi-valve procedure via right mini-thoracotomy underwent significantly longer aortic cross-clamping and cardiopulmonary bypass times as compared to conventional multi-valve procedure via full median sternotomy. This study reported over 6-minute longer aortic cross-clamping times and 9-minute longer cardiopulmonary bypass times in the RT group as compared with the FS group. This finding was consistent with that in most of the literature. A possible explanation for that was the fact that combined mitral and aortic valve procedure via right mini-thoracotomy was more complex, more technically demanding, and provided limited exposure through right mini-thoracotomy by comparison with that through full median sternotomy. Nevertheless, a statistically significant increase in cardiopulmonary bypass-related adverse effects was not observed in the RT group. In the elderly and high-risk population, however, longer cardiopulmonary bypass and cross-clamping times were of particular concern as they were well-known independent risk factors for adverse outcomes.²⁶⁾ This should be taken into consideration in patient selection for minimally invasive multi-valve procedure via right mini-thoracotomy approach. Shorter ICU stay and postoperative hospitalization time under condition of similar age and comorbidities based on propensity score-matching data suggested that rehabilitation seemed to occur faster with minimally invasive multi-valve procedure via right mini-thoracotomy as compared with conventional multi-valve procedure via full median sternotomy.²⁷⁾ These results are in line with evidences from the majority of previous stud-

ies.

Previous studies have suggested that minimally invasive valve surgery via right mini-thoracotomy is associated with a higher incidence of postoperative cerebrovascular events.^{12,28)} The reason may be that high atherosclerotic burden in the aortic arch and descending aorta may play a crucial role in the incidence of postoperative cerebrovascular accident when using retrograde perfusion, especially in elderly patients. By contrast, this study reported a similar incidence of stroke. A possible explanation for this difference was that patients who received minimally invasive multi-valve surgery via retrograde perfusion were younger and with lower atherosclerotic burden in the aortic arch and descending aorta in this study. Also, no differences in the incidences of re-intubation and prolonged mechanical ventilation were found in this study between the two groups. These results were in line with evidences of the majority of previous studies.¹³⁾

Suitability of patients for combined mitral and aortic valve procedure via right mini-thoracotomy was based on preferences of individual surgeons and on discussion with the patient, as this was still considered a novel procedure. It is important to keep in mind that minimally invasive surgery for combined mitral and aortic valve procedure via right mini-thoracotomy was not indicated for all patients. Essentially, where patients had no history of sternotomy or thoracotomy and if a computed tomography scan showed more than half of the ascending aorta to be on the right with respect to the right sternal border at the level of the main pulmonary artery, and if the distance from the ascending aorta to the sternum was less than 10 cm, they were considered to be suitable candidates. Nevertheless, patients with NYHA heart failure class IV, severe left ventricular systolic dysfunction (left ventricular ejection fraction of < 35%), severe ventilator disturbance of pulmonary function, significant impairment of liver and/or renal function, and excessive obesity may not be suitable candidates. At Cardiovascular Center of Fudan University Zhongshan Hospital, where right mini-thoracotomy valve procedure was introduced in 2009 and has now become a common practice over the years with an annual procedure volume of over 400 cases, the procedure of combined mitral and aortic valve procedure via right mini-thoracotomy was conducted only by surgeons highly experienced in cardiac valve surgery (annual valve procedure volume of over 100 cases) who had been engaged in cardiac surgery for over 10 years and who had received relevant training for minimal invasive cardiac surgery.

Note that retrograde perfusion via femoral cannulation was identified to be one independent risk factor for stroke.^{9,29)} The atherosclerotic burden in the aortic arch and descending aorta may play a crucial role in the incidence of postoperative cerebrovascular accident when using retrograde perfusion. Also, retrograde aortic dissection is a rare complication that is reported in up to 0.2% of patients.¹³⁾ In order to avoid these complications, cannulation of the ascending aorta should be the preferential approach, which allowed for a more direct and physiological flow, and retrograde perfusion may be a viable option for younger patients without vascular disease. Additionally,

another concern with minimally invasive multi-valve surgery was that of obtaining adequate exposure. In circumstances where adequate exposure cannot be obtained, minimally invasive surgery may need to be converted to a full median sternotomy. The conversion rate of minimally invasive surgery to full median sternotomy is 1.0%-4.0% during single valve procedure, but data for conversion rate of minimally invasive multi-valve surgery to full median sternotomy were very rare.^{30,31)} In the present study, adequate exposure of operative field was obtained in all patients, and no patients required conversion to a median sternotomy.

This study had some potential limitations. Firstly, although using propensity score matching, this study was only a single-center, clinical observational study with a small sample size, which may influence the generalizability. Confounds and selection biases among the two groups that were unobserved cannot be eliminated. Also, this study showed that adverse event rate was very low in both groups, and also showed that no significant differences were found between the two approaches in terms of surgical mortality and major postoperative morbidity, other than new onset of atrial fibrillation, which may be related to a small sample size. A final determination would need a prospective, multi-center study involving larger sample size. Secondly, all of the included minimally invasive multi-valve surgeries were performed via a right mini-thoracotomy approach, and cannot be extrapolated to represent outcomes that may be obtained from other minimally invasive approaches. The results should be viewed as an observational study of a consecutive series of right mini-thoracotomy multi-valve surgeries, and as supportive of the hypothesis that right mini-thoracotomy approach may be an alternative option to full median sternotomy for multi-valve surgery. Finally, this study did not report the medium and long-term follow-up results. The medium and long-term outcomes need further observation.

Conclusions

This single-center, propensity-matched study showed that, in patients requiring combined mitral and aortic valve procedure with or without tricuspid annuloplasty, a right mini-thoracotomy approach may be utilized with acceptable early clinical outcomes. In some categories of patients it may be considered as a feasible alternative to the conventional full sternotomy approach.

Disclosures

Conflicts of interest: None.

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