Benefit and Risk of Minimally Invasive Mitral Valve Repair for Type II Dysfunction
— Propensity Score-Matched Comparison —

Naonori Kawamoto, MD; Satsuki Fukushima, MD, PhD; Yusuke Shimahara, MD; Takuma Yamasaki, MD; Yorihiko Matsumoto, MD; Kizuku Yamashita, MD; Junjiro Kobayashi, MD, PhD; Tomoyuki Fujita, MD, PhD

Background: Despite the cosmetic benefits of the minimally invasive approach for mitral disease, the clinical benefit and risk are not fully known. We investigated the benefit and risk of minimally invasive mitral valve (MV) repair for type II dysfunction using propensity score-matched analysis.

Methods and Results: Since 2001, 602 patients have undergone MV repair for type II dysfunction (464 with conventional median sternotomy and 138 with the minimally invasive approach). One-to-one matched analysis using the estimated propensity score based on 23 factors resulted in 93 well-matched patient pairs. There was no in-hospital death in both groups. The operation time was significantly shorter (P=0.002), blood transfusion was less frequent (P=0.04), extubation at the day of surgery was more frequently performed (P=0.017), and the length of hospital stay was significantly shorter in the minimally invasive group than in the sternotomy group (P<0.0001). On postoperative (P=0.02) and 1-year echocardiography (P=0.04), ejection fraction was lower in the minimally invasive group than in the sternotomy group. There were no significant differences in postoperative cerebral infarction, aortic dissection, deep sternal infection, or mid-term outcome between the groups.

Conclusions: Standard sternotomy and the minimally invasive approach provide similar good quality of MV repair for type II dysfunction. The minimally invasive approach is more likely to contribute to fast-track perioperative treatment than the standard sternotomy approach.

Key Words: Minimally invasive mitral repair; Propensity score-matched analysis; Type II mitral valve regurgitation

Reconstructive mitral valve (MV) repair for type II MV regurgitation (MR) is currently a standardized procedure with an excellent long-term outcome.1,2 This technique has become the treatment of choice for MR. In the past 2 decades, less invasive procedures have been developed in cardiac surgery. Minimally invasive mitral surgery is being introduced in many facilities.3–5 Despite high patient satisfaction, including reduced pain and length of stay, fewer perioperative clinical complications and improved cosmetic problems, the minimally invasive approach may have problems with intraoperative myocardial and cerebral protection.5–8 Some reports have noted a higher incidence of cerebral infarction, aortic dissection, groin complications, and phrenic nerve palsy in the minimally invasive approach.6–9 Additionally, the baseline risk profiles of patients selected for the minimally invasive approach and for median sternotomy are significantly different. High-risk patients with left ventricular (LV) dysfunction, advanced age, severe heart failure, and concomitant other cardiovascular diseases are more likely to undergo median sternotomy. Therefore, comparison between the minimally invasive approach and median sternotomy in retrospective studies and randomized studies may not be available.10,11

In this study, we used propensity score-matched analysis to control for such bias, and investigated the benefit and risk of minimally invasive MV repair for type II dysfunction.

Methods

Patients
This study involved a consecutive series of 602 patients (389 men, 213 women; mean age, 62±12.8 years; range, 19–84 years) who underwent MV repair for type II severe MR using a prosthetic full ring or partial band at the present institute between January 2001 and March 2017. The data were collected from institutional medical charts and
supplemented by telephone interviews for patients who were treated by a non-local physician. Patients who had concomitant aortic valve surgery were excluded. Postoperatively, patients regularly visited the outpatient clinic of the National Cerebral and Cardiovascular Center, Osaka, Japan, who waived the need for patient review board of the National Cerebral and Cardiovascular Center for medical follow-up. This study was approved by the institutional review board of the National Cerebral and Cardiovascular Center. Osaka, Japan, who waived the need for patient consent for this retrospective study.

The minimally invasive approach through right thoracotomy was introduced in August 2011 and planned in 139 patients (minimally invasive cardiac surgery [MICS] group). The conventional full median sternotomy was planned in 463 patients (sternotomy group).

### Surgical Procedures

In minimally invasive MV repair, the patient was intubated with a double-lumen endotracheal tube. Before draping, the right internal jugular vein was cannulated with an arterial cannula, of which the size was chosen according to the physique. The patient was placed in the partial left lateral position with approximately 30° rotation from the spinal position, and the right upper arm was flexed posteriorly and set aside the chest.

Minimally invasive repair was performed via a 5–8-cm incision through the right fourth intercostal space. A soft-tissue retractor was used to limit rib spreading. Cardiopulmonary bypass was initiated through the right femoral artery and vacuum-assisted venous drainage from the right femoral vein and right internal jugular vein. A root cannula was inserted into the ascending aorta for antegrade cardioplegia. Myocardial protection was achieved with only antegrade delivery of cardioplegia. In the case of median sternotomy, myocardial protection was achieved with antegrade cardioplegia. Myocardial protection was achieved with antegrade and retrograde cardioplegia. After cardiac arrest, the left atrium (LA) was entered along the interatrial groove. A camera port was inserted into the third intercostal space with a carbon dioxide infuser. An endoscope was used for illumination, assessment of the MV, and presentation of the procedure to the operative staff.

All of the patients underwent mitral annuloplasty using a prosthetic full ring or partial band. The repair technique (resection and suture, chordal replacement, or edge-to-edge repair) depended on the leaflet involvement. The

### Table 1. MICS vs. Open MV Repair: Patient Characteristics

| Location of prolapse | MICS (n=139) | Sternotomy (n=463) | P-value | d  | MICS (n=93) | Sternotomy (n=93) | P-value | d  |
|----------------------|--------------|--------------------|---------|----|-------------|--------------------|---------|----|
| Anterior             | 19 (13.6)    | 182 (39.3)         | <0.0001 | 0.61 | 15 (16)     | 12 (12.9)          | 0.53    | 0.09 |
| Posterior            | 115 (82.7)   | 340 (73.4)         | 0.025   | 0.23 | 77 (82.8)   | 76 (81.7)          | 0.84    | 0.03 |
| Commisurism          | 18 (12.9)    | 72 (15.5)          | 0.45    | 0.07 | 11 (11.8)   | 16 (17.2)          | 0.3     | 0.15 |

Data given as n (%) or mean±SD. %FEV1, percent predicted forced expiratory volume in 1 s; AF, atrial fibrillation; ASD, atrial septal defect; BSA, body surface area; CAD, coronary artery disease; Cr, creatinine; CVD, cerebrovascular disease; d, standardized difference; DM, diabetes mellitus; EF, ejection fraction; HD, hemodialysis; HL, hyperlipidemia; HT, hypertension; LAD, left atrial diameter; LVDd, left ventricular end-diastolic diameter; LVDs, left ventricular end-systolic diameter; MICS, minimally invasive cardiac surgery; MV, mitral valve; NYHA, New York Heart Association; PAF, paroxysmal atrial fibrillation; PFO, patent foramen ovale; PSM, propensity score matching; TR, tricuspid regurgitation; TRPG, tricuspid regurgitant peak pressure gradient.
annuloplasty prosthesis size was selected according to the inter-trigone distance measured with the sizer provided, without downsizing. When the inter-trigone distance was obscure, the length of the anterior leaflet was used for selecting the prosthesis size. Water testing using a long obturator was performed by simultaneously monitoring root pressure to confirm valve competence and adequate leaflet coaptation with suitable pressure. Irrigation was stopped when the root pressure reached 60 mmHg.

Carbon dioxide field insufflation and de-airing through antegrade cannulae were routinely used to help minimize the risk of air embolus. A temporary right atrial and ventricular pacing wire was placed in all patients. In patients with concomitant tricuspid annuloplasty and the maze procedure through the minimally invasive approach, snaring was obtained by placing tourniquets around the superior and inferior venae cavae before opening the right atrium. Tricuspid valve repair with an annuloplasty ring was performed after other concomitant cardiac procedures were completed. The left-sided maze procedure was performed before the mitral procedure without LA appendage closure. The right-sided maze procedure was performed after left atriotomy closure. All maze procedures were performed using a cryoablation device. Immediately after declamping, bilateral ventilation was initiated to avoid re-expansion pulmonary edema.

**Echocardiography**

Echocardiography was performed ≤30 days before mitral surgery, ≤10 days postoperatively, and 1, 2, 3, 5, 7, 10, and 15 years postoperatively, whenever possible. On Doppler echocardiography, MR was defined as grade 0, no MR; grade 1, trivial; grade 2, mild; grade 3, moderate; and grade 4, severe. Severe MR was defined as either central jet MR >40% of the LA area, holosystolic eccentric jet MR, vena contracta >0.7 cm, regurgitant volume >60 mL, regurgitant fraction >50%, or an effective regurgitant orifice >0.40 cm². MR was classified as trivial, mild, or moderate by an expert engineer and expert doctor individually, according to the guidelines.13

Each patient’s cardiac function was assessed for residual MR, tricuspid regurgitation (TR), fractional shortening, ejection fraction (EF), LV end-diastolic diameter (LVDd) and end-systolic diameter (LVDs), mean transmural pressure gradient (mPG), LA diameter, and peak tricuspid regurgitant pressure gradient (TRPG). M-mode echocardiography was used to measure the LA diameter on images that were created via the parasternal short-axis view at the level of the aortic valve at ventricular end-systole. TRPG was defined as the right ventricular systolic pressure (systolic pulmonary artery pressure) minus central venous pressure.14 Although some patients who were treated by distant physicians were not examined on echocardiography at the present institute, clinical progress was regularly reported to this institute.

**Propensity-Score Matched Analysis**

Because baseline characteristics were different between the MICS and sternotomy groups, propensity score-matched analysis was used to compare early and mid-term outcomes between the 2 groups. Propensity scores were calculated on multiple logistic regression using the following 23 variables: sex; body surface area (BSA); age; New York Heart Association 3/4; preoperative β-blocker use; hypertension; hyperlipidemia; diabetes mellitus; percent predicted forced expiratory volume in 1s ≤70%; cerebrovascular disease; preoperative creatinine; preoperative chronic/persistent atrial fibrillation (chronic/persistent AF); thyroid disorder; coronary artery disease (CAD); patent foramen ovale/atrial septal defect; location of prolapse (anterior, posterior, or commissure leaflet prolapse); and preoperative echocardiogram parameters (LVDd, LA diameter, TRPG, TR grade ≥3, EF). Baseline characteristics in the unmatched and matched patients are listed in Table 1. Standardized differences were used to evaluate the balance between the baseline variables. C statistics (=0.86) were calculated to evaluate the goodness of fit of this model.

**Statistical Analysis**

Categorical data are presented as proportions and continuous data are expressed as mean±SD. Differences between groups were assessed using the chi-squared test.
for categorical variables, independent Student’s t-test for normally distributed continuous variables, and Mann-Whitney U-test for non-normally distributed continuous variables. Survival, freedom from reoperation, and freedom from major adverse cardiac and cerebrovascular events (MACCE) were obtained using the Kaplan-Meier method and compared between groups using the log-rank test. P≤0.05 was considered statistically significant. All statistical analyses were performed using JMP 11 (SAS Institute, Cary, NC, USA).

### Results

Patient characteristics and preoperative echocardiography are listed in Table 1. Before matching, patients in the MICS group were more frequently men (103, 74.1% vs. 286, 61.7%, P=0.007), less frequently had obstructive lung disease (7, 5% vs. 57, 12.6%, P=0.01), less frequently had AF/paroxysmal AF (AF/PAF; 23, 16.5% vs. 185, 40%, P=0.0001), less frequently had CAD (0 vs. 51, 11.0%, P<0.0001), and had a larger BSA (1.7±0.2 vs. 1.6±0.2 m², P=0.0001), younger age (54.6±10.7 vs. 62.6±12.8 years, P<0.0001), and lower prescription rate of β-blockers (61.1±11.5% vs. 80, 20.9%, P=0.04) than in the sternotomy group.

In the MICS group, 14% had anterior leaflet prolapse, 83% had posterior leaflet prolapse, and 13% had commissure leaflet prolapse. In the sternotomy group, 40% had anterior leaflet prolapse, 73% had posterior leaflet prolapse, and 15% had commissure leaflet prolapse. There were significant differences in the frequency of anterior (13.6% in the MICS group vs. 39.3% in the sternotomy group, P<0.0001) and posterior leaflet prolapse (82.7% in the MICS group vs. 73.4% in the sternotomy group, P<0.025) between the 2 groups before matching.

Patients in the MICS group had a smaller LA diameter (54.6±10.7 vs. 62.6±12.8 mm, P=0.0001), lower TRPG (25.5±12.3 vs. 32.9±14.1 mmHg, P=0.001), lower EF (61.1±6.6 vs. 62.8±8.6%, P=0.04), and lower frequency of TR ≥grade 3 (2.8% vs. 13.4%, P<0.0001) before matching.

One-to-one matched analysis using the estimated propensity score based on 23 factors resulted in 93 well-matched patient pairs. There were no significant differences in patient characteristics or preoperative echocardiography after matching (Table 1).

Surgical procedures are summarized in Table 2. Before matching, almost all of the procedures were significantly different between the 2 groups. After matching, however, the type of repair technique, and the frequency of concomitant maze procedure and coronary artery bypass grafting were similar between the 2 groups. Ring size was significantly larger (29.7±2.0 mm in the MICS group vs. 28.4±1.8 mm in the sternotomy group, P<0.0001) and the frequency of using a partial band was significantly higher in the MICS group than in the sternotomy group (86% in the MICS group vs. 67.7% in the sternotomy group, P=0.003). The rate of preoperative TR grade ≥3 was similar between the 2 groups. The number of patients with concomitant tricuspid annuloplasty, however, was smaller in the MICS group than in the sternotomy group.

Of the matched patients, in the MICS group there was a significantly shorter operation time (240.0±51.5 min in the MICS group vs. 265.5±59.2 min in the sternotomy group, P=0.002) and less frequent use of transfusion than in the sternotomy group (20% in the MICS group vs. 32.6% in the sternotomy group, P=0.04). Cardiopulmonary bypass and cardiac arrest times were not significantly different between the 2 groups.

The postoperative course before discharge in matched patients is given in Table 3. Extubation on the day of surgery was performed more frequently in the MICS group than in the sternotomy group (88.2% in the MICS group vs. 74.7% in the sternotomy group, P=0.017). Although the length of intensive care unit stay was similar between the 2 groups, the length of hospital stay was significantly shorter in the MICS group than in the sternotomy group (7.6±1.9 days in the MICS group vs. 15.3±5.1 days in the sternotomy group, P=0.0001).

Postoperative complications, including onset of deep sternal infection and in-hospital death, were not found in either of the groups. Redo mitral repair because of severe regurgitation from postero medial commissure, dissection, and renal failure was noted in 1 patient in the MICS group. Re-exploration in 1 patient and respiratory failure in 1

| Table 3. MICS vs. Open MV Repair: Postoperative Course (PSM) |
|---------------------------------|-----------------|-----------------|--------|
| **MICS** (n=93) | **Sternotomy** (n=93) | **P-value** |
| Extubation at POD 0 | 82 (88.2) | 68 (74.7) | 0.017 |
| ICU stay (days) | 1.5±0.6 | 1.6±1.0 | 0.69 |
| Hospital stay (days) | 7.6±1.9 | 15.3±5.1 | <0.0001 |
| Redo MV repair/MVR | 1 (1.1) | 0 | 0.31 |
| Aortic dissection | 1 (1.1) | 0 | 0.31 |
| Re-exploration | 0 | 2 (2.2) | 0.15 |
| Death | 0 | 0 | |
| Respiratory failure | 0 | 2 (2.2) | 0.15 |
| Renal failure | 1 (1.1) | 0 | 0.3 |
| Max Cr (mg/dL) | 1.05±0.34 | 1.06±0.31 | 0.74 |
| Groin complication | 0 | 0 | |
| Deep sternal infection | 0 | 0 | |
| Cerebral infarction | 0 | 1 (1.1) | 0.31 |

Data given as n (%) or mean ± SD. ICU, intensive care unit; MVR, mitral valve replacement; POD, postoperative day. Other abbreviation as in Table 1.
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Table 4. MICS vs. Open MV Repair: Echocardiography on PSM

|                          | MICS (n=93) | Sternotomy (n=93) | P-value |
|--------------------------|-------------|-------------------|---------|
| Postoperative echocardiography |             |                   |         |
| MR ≥2                    | 2 (2.2)     | 11 (11.8)         | 0.01    |
| EF (%)                   | 47.9±10.5   | 51.9±10.3         | 0.02    |
| LVDd (mm)                | 50.3±5.9    | 49.5±5.4          | 0.21    |
| LVDs (mm)                | 36.6±6.5    | 34.5±5.7          | 0.017   |
| LAD (mm)                 | 40.6±7.4    | 40.1±7.9          | 0.53    |
| TRPG (mmHg)              | 21.8±6.3    | 19.2±5.5          | 0.002   |
| TR ≥2                    | 11 (11.8)   | 7 (7.5)           | 0.32    |
| mPG (mmHg)               | 2.8±1.6     | 2.9±1.2           | 0.4     |
| One-year echocardiography|             |                   |         |
| MR ≥2                    | 7 (7.5)     | 7 (7.5)           | 0.9     |
| EF (%)                   | 54.8±8.0    | 58.0±8.2          | 0.04    |
| LVDd (mm)                | 47.9±5.4    | 47.6±4.3          | 0.65    |
| LVDs (mm)                | 32.4±5.1    | 31.2±4.1          | 0.11    |
| LAD (mm)                 | 39.9±7.3    | 41.1±7.7          | 0.43    |
| TRPG (mmHg)              | 21.8±6.9    | 20.8±5.8          | 0.44    |
| TR ≥2                    | 10          | 9                 | 0.87    |
| mPG (mmHg)               | 2.9±1.2     | 3.4±1.6           | 0.06    |

Data given as n (%) or mean±SD. mPG, mean transmitral pressure gradient; MR, mitral valve regurgitation. Other abbreviation as in Table 1.

During the study period, non-cardiac-related death patient were noted in the sternotomy group. Cerebral infarction occurred in 1 patient in the sternotomy group, but there were no significant differences in these complications between the 2 groups. In patients without preoperative AF, incidence of PAF before discharge was 4.3% in the sternotomy group and 9.2% in the MICS group, with no significant difference (P=0.23).

Postoperative and 1-year echocardiography in matched patients is listed given in Table 4. Although there were no significant differences in LVDd, LA diameter, mPG, or TR grade ≥2 between the 2 groups, in the MICS group the proportion of patients with MR grade ≥2 was lower (2.2% in the MICS group vs. 11.8% in the sternotomy group, P=0.01), the TRPG was significantly higher (21.8±6.3 mmHg in the MICS group vs. 19.2±5.5 mmHg in the sternotomy group, P=0.002), and LVDs was significantly larger (36.6±6.5 mm in the MICS group vs. 34.5±5.7 mm in the sternotomy group, P=0.017) than in the sternotomy group postoperatively. Furthermore, the EF was significantly lower in the MICS group than in the sternotomy group on postoperative (47.9±10.5% in the MICS group vs. 51.9±10.3% in the sternotomy group, P=0.02) and 1-year echocardiography (54.8±8.0% in the MICS group vs. 58.0±8.2% in the sternotomy group, P=0.04).

During the study period, non-cardiac-related death
MICS vs. Open Mitral Valve Repair

Discussion

In the present study, shorter operation time, lower blood transfusion rate, rapid extubation, and shorter hospital stay were considered as benefits of minimally invasive MV repair for type II dysfunction, as shown by previous reports. A shorter operation time and similar arrest time in the MICS group compared with the sternotomy group may be associated with avoidance of bleeding from the sternum to reduce the time of hemostasis.

In the present study MICS also contributed to selection of a larger size of prosthetic ring. In the MICS group, a prosthetic ring with a 1.3-mm larger diameter was used in patients with a larger BSA, leading to a relatively lower mean transmitral pressure gradient at follow-up echocar-

Figure 2. One- and 3-year freedom from reoperation rates after mitral valve repair vs. procedure type, after propensity score matching (log-rank, P=0.08). MICS, minimally invasive cardiac surgery.

Figure 3. One- and 3-year freedom from major adverse cardiac and cerebrovascular events (MACCE) after mitral valve repair vs. procedure type, after propensity score matching (log-rank, P=0.39). MICS, minimally invasive cardiac surgery.

occurred in 2 patients in the sternotomy group.

Significant difference in 1- and 3-year survival rates was found between the 2 groups (Figure 1). In the MICS group, 1 patient had MV replacement (MVR) due to infective endocarditis and 3 patients had MVR due to recurrent MR during the study period. In the sternotomy group, 2 patients had cerebral infarction and 2 patients had heart failure caused by bradycardia. One patient had angina and 2 patients had MVR due to recurrent MR during the study period. There were no significant differences in 1- and 3-year freedom from MACCE, or freedom from reoperation between the 2 groups (Figures 2,3).
diagram. Valve sizing through the endoscopic view in the MICS group was more accurate than that in the sternotomy group. A smaller mitral annuloplasty ring may cause functional mitral stenosis and late-onset AF after MV repair for type II dysfunction.\textsuperscript{15–19} Therefore, the annuloplasty ring size was significantly larger in the MICS group than in the sternotomy group. Notably, a minimally invasive approach did not significantly increase residual post-repair MR. Despite a larger prosthesis ring size in the MICS group, the frequency of postoperative MR grade ≥2 was higher in the sternotomy group than in the MICS group in the present study.

Although the benefits of MICS on pulmonary function are controversial, early initiation of ventilation immediately after aortic declamping may prevent re-expansion pulmonary edema, which leads to a shorter extubation time, in contrast to previous reports.\textsuperscript{15,20,21}

The disadvantages of MICS are difficult de-airing, risk of stroke, and risk of vascular and groin complications. The rates of postoperative complications such as stroke, deep sternal infection, groin complications, and aortic dissection were all low in the present study, which is consistent with propensity score-matched comparisons.\textsuperscript{11,15,16,20} Selection of patients is important by checking the aorta and peripheral arteries on preoperative computed tomography. Intraoperative monitoring on transesophageal echocardiography and NIRO-200NX tissue oxygenation monitor (Hamamatsu, Japan) are also important for checking the status of de-airing, aortic dissection, and ischemic legs.

Decreased cardiac function, as shown by lower EF and larger LVDs in the MICS group than in the sternotomy group, was observed after MV repair in the present study. LV dysfunction after MV repair in normal hearts has been suggested to be caused by inadequate myocardial protection or maldistribution of antegrade cardioplegia.\textsuperscript{22–25} Transient aortic regurgitation, which might be caused by retraction of the LA, might also lead to a potential risk of ischemic damage and cardiac dysfunction. Application of long-acting cardioplegia, such as del Nido cardioplegia, could be a solution to this problem.\textsuperscript{26}

The present overall 30-day mortality and 3-year survival rates were both 0%, with no significant differences between the 2 groups. Similar results were reported in other studies.\textsuperscript{10,11,20,27} The freedom from reoperation rate after minimally invasive MV repair ranges from 99% at 3 years to 91% at 4 years.\textsuperscript{27} Similarly, in the present study the 3-year freedom from reoperation rate was 96%.

**Conclusions**

The minimally invasive approach is more likely to contribute to fast-track perioperative care because of shorter operation time, less frequent use of blood transfusion, shorter extubation time, and shorter hospital stay than the standard sternotomy approach. Despite the similar short- and midterm outcomes, however, the minimally invasive approach with only antegrade delivery of cardioplegia may carry a risk of decreased cardiac function after MV repair for type II dysfunction.

**Study Limitations**

There are several limitations to our analysis. First, this analysis was retrospective and subject to multiple potential biases. Selection bias cannot be completely eliminated using a propensity score matching approach. Although 23 variables that were strongly related to outcome were included in propensity score-matching analysis, surgeon- and generation-specific factors could not be included in the analysis. The strategy for MV repair and postoperative management has not changed since 2001. Moreover, some expert surgeons have been generally in charge of MV repair through sternotomy as well as with the minimally invasive approach during the follow-up period. Therefore, we consider that the surgeon- and generation-specific factors have negligible impact on outcome. Second, mid-term and long-term outcomes were not available owing to the difference in follow-up period between the sternotomy and MICS groups. Third, the present results regarding variables such as cross-clamp time and CPB time, do not highlight the potential effect of learning curves on the success of the MV repair technique. Therefore, a longer follow-up period and larger sample size are required in the future.

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**Disclosures**

The authors declare that no conflicts of interest.

**IRB Approval**

This study was approved by the IRB of the National Cerebral and Cardiovascular Center, Suita, Japan.

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