



Early and mid-term outcomes of tricuspid valve surgery in patients with functional tricuspid regurgitation induced by atrial fibrillation

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Background: The strategy of treatment for tricuspid regurgitation (TR) induced by atrial fibrillation (AF) has not been established. The aim of this study was to evaluate the outcomes of surgical treatment for TR induced by AF.

Methods: From 2000 to 2021, a total of 1,301 patients underwent tricuspid valve (TV) surgery. Among them 43 patients who diagnosed as AF induced TR were enrolled. The tricuspid valve-related events (TVRE) included cardiac death, TV reoperation, development of moderate or greater TV disease, congestive heart failure requiring re-admission, and major bleeding or thrombosis. The median follow-up duration was 42.0 months.

Results: The interval from diagnosis of AF to more than moderate TR was 61.2 months, and the interval from initial diagnosis of severe TR to surgery was 2.4 months. Concomitant Cox-maze III procedure was performed in 39 patients. The operative mortality occurred in 1 patient, and there was no permanent pacemaker implantation. Overall survival rates at 1- and 5-year were 90.6% and 79.3%, respectively. The cumulative incidence of TVRE at 1- and 5-year were 16.3% and 26.5%, respectively. The cumulative incidences of AF recurrence at 1- and 3-year in the patients with surgical ablation were 29.7% and 67.6%. The TVRE was significantly associated with the longer interval from diagnosis of severe TR to surgery (hazard ratio: 1.023, 95% confidence interval: 1.005–1.042).

Conclusions: TV surgery for TR induced by AF showed low surgical mortality and favorable mid-term outcomes. For these patients, early surgery after progress to severe TR can be helpful to decrease the occurrence of TVRE.

Keywords: Atrial fibrillation (AF); tricuspid valve regurgitation; tricuspid surgery

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Introduction

Background

Functional tricuspid regurgitation (FTR) can originate from various etiologies, in the absence of morphological defects in the tricuspid valve (TV) apparatus. According to etiology,

FTR can be categorized into two types: ventricular FTR and atrial FTR. Left-sided valvular or myocardial diseases, along with intrinsic pulmonary vascular diseases, result in pressure overload on the right ventricle (RV), leading to ventricular remodeling. This remodeling includes ventricular enlargement, displacement of papillary muscles,

leaflet tethering, and annular flattening and dilation, ultimately contributing to tricuspid regurgitation (TR), now defined as ventricular FTR (1,2). On the contrary, atrial fibrillation (AF) can induce remodeling of the right atrium (RA) without concurrent RV remodeling, subsequently enlarging the tricuspid annulus and resulting in the development of FTR, now classified as atrial FTR (3). Since several studies have demonstrated the efficacy of surgery for ventricular FTR (4,5), current guidelines suggest concurrent surgical intervention for significant TR in left-sided valve surgery (6,7). However, the clinical importance of surgical treatment of atrial FTR has been underestimated.

Rationale and knowledge gap

Although the mechanism by which remodeling the RA contributes to FTR is not yet proven precisely, AF basically deteriorates atrial and TV annular contraction, leading to RA enlargement and TV annular dilatation (8). The pathophysiology of TR induced by AF strengthens the plausibility of surgical correction, such as TV annuloplasty. However, research on TV surgery for AF-induced TR is insufficient.

Objective

This study aimed to report early and mid-term clinical outcomes of TV surgery in patients with AF-induced TR.

We present this article in accordance with the STROBE reporting checklist (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-23-1776/rc>).

Methods

The study protocol was reviewed by the Institutional Review Board (IRB) of Seoul National University Hospital and approved as a minimal-risk retrospective study that did not require individual consent (IRB approval No. 2208-151-1353). The investigation was conducted in accordance with the principles articulated in the Declaration of Helsinki (as revised in 2013), emphasizing a commitment to ethical research practices.

In this study, atrial FTR was defined as (I) isolated TV annular dilatation with RA enlargement and AF and (II) no other reasons to cause FTR, such as significant left ventricular systolic dysfunction [left ventricular ejection fraction (LVEF) <50%], left-sided valvular heart disease (\geq moderate degree), RV failure [right ventricle ejection fraction (RVEF) <35%], significant pulmonary hypertension (pulmonary arterial systolic pressure above 50 mmHg) (9), and atrial or ventricular septal defect.

From January 2000 to December 2021, 1,301 patients underwent TV surgery. In a total of 987 patients who underwent concomitant left-sided valve surgery, coronary bypass grafting, or aortic surgery, TR could be attributed to causes other than AF, those patients were excluded from the study. Among 314 patients who underwent isolated TV surgery, 48 patients who had morphological defects at TV apparatus and 212 patients with other origins of FTR than AF were also excluded. After excluding patients with missing data, 43 patients were finally enrolled in this study and those patients were reviewed by 2 physicians to confirm the presence of AF preceding TR and the absence of any other etiology besides AF (*Figure 1*). Forty-one patients (95.3%) underwent preoperative cardiac magnetic resonance imaging (CMR). CMR was performed using a 3-T system (Magnetome Skyra; Siemens Healthcare, Erlangen, Germany) with a 60-channel phased-array body surface coil. The CMR protocols have been described previously (10). The RV end-diastolic volume (RVEDV), RV end-systolic volume (RVESV), and RVEF were measured using a software program (Argus; Siemens Healthcare). Preoperative AF was classified as paroxysmal, persistent, or long-standing persistent (11), and all patients had long-standing persistent AF. The rhythm status was evaluated based on an electrocardiogram (ECG) performed

Highlight box

Key findings

- Tricuspid valve (TV) surgery for tricuspid regurgitation (TR) induced by atrial fibrillation (AF) showed low surgical mortality and favorable midterm outcomes.

What is known and what is new?

- AF-induced severe TR was a significant predictor of mortality in the patients who suffered from AF. Although isolated functional tricuspid regurgitation (FTR) and its prognosis had recently drawn more attention from physicians, surgical treatment is uncommon and there is still a lack of study regarding surgical outcomes of AF-induced TR.
- TV surgery for AF-induced TR showed not only favorable surgical morbidity and mortality but also acceptable midterm outcomes in terms of overall survival and tricuspid valve-related events (TVRE).

What is the implication, and what should change now?

- Researchers should investigate the clinical benefits of surgical treatment and find the adequate surgical timing for AF-induced TR.

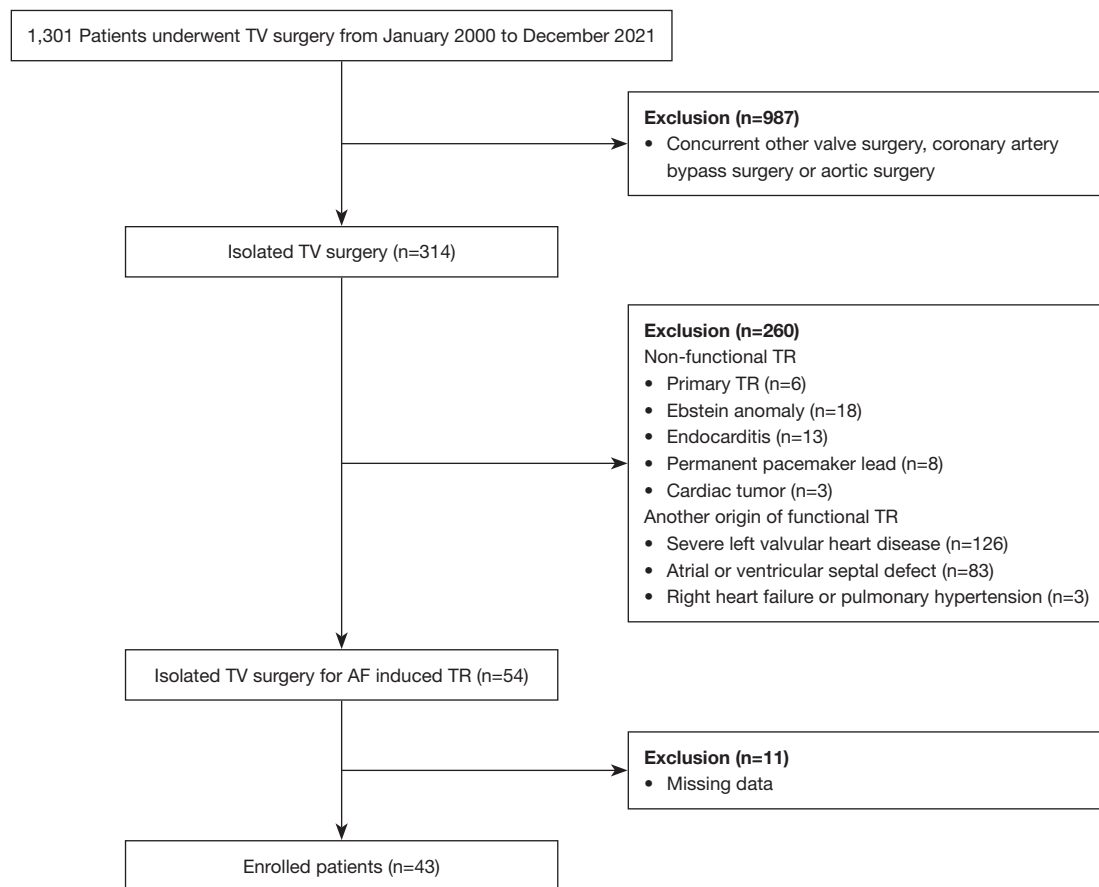


Figure 1 Summary flow diagram demonstrating patient enrollment for study. TV, tricuspid valve; TR, tricuspid regurgitation; AF, atrial fibrillation.

3 months after surgery. Postoperative AF was defined as AF, atrial flutter, atrial tachycardia, or pacing rhythm. Sinus rhythm included normal sinus and junctional rhythms.

Surgical procedures

All patients underwent full median sternotomy under moderate hypothermia and cold cardioplegic arrest, except for 1 patient with right thoracotomy. TV repair, also known as tricuspid annuloplasty (TAP), was preferred in almost all cases, however, the decision to perform a TV replacement (TVR) or TV repair was made at the discretion of the attending surgeon. Throughout the study period, 3 patients underwent direct TVR due to severely dilated annulus including septal leaflet annulus with or without leaflet thinning while another 3 patients initially underwent TV repair but subsequently required TVR because of residual TR after TAP.

For De Vega annuloplasty, annular size reduction was performed using commercially available cylindrical valve sizers with labeled sizes of 27 (actual diameter 29.5), 29 (31.5), and 31 (33.5) mm. The plication sutures, made of 3-0 extended polytetrafluoroethylene (e-PTFE), were tied down with the cylindrical size inserted into the TV orifice. For ring annuloplasty, Tri-Ad Adams tricuspid ring (Medtronic, Minneapolis, MN, USA) and MC3 annuloplasty ring (Edwards LifeScience, Irvine, CA, USA) were used during study period and were chosen based on the attending surgeon's preference. The ring size was determined based on the inter-commissural distance of the septal leaflet and the attached leaflet area originating from the anterior papillary muscle.

Evaluation of echocardiographic outcomes

All the patients underwent preoperative and postoperative

echocardiography. The severity was categorized on a scale from 0 to 4, where 0 indicated no or trivial severity, 1 indicated mild, 2 indicated moderate, 3 indicated moderate-to-severe, and 4 indicated severe. Echocardiographic follow-up examinations were carried out at the judgment of the operating surgeon or referring physician, guided by symptoms and auscultatory findings. Out of the 41 patients who survived early postoperative period, 36 underwent at least one echocardiographic examination after being discharged. The median follow-up duration of echocardiographic evaluation was 21.1 months [interquartile range (IQR): 11.8–52.6 months].

Evaluation of clinical outcomes

The study primarily focused on assessing early- and mid-term postoperative outcomes. Operative mortality was characterized by fatalities within a 30-day period following the surgery or while under hospital care. Low cardiac output syndrome (LCOS) was characterized by a cardiac index below 2.0 L/min/m² or a systolic arterial pressure below 90 mmHg, necessitating continuous infusion of inotropic agents such as dopamine or dobutamine exceeding 5 µg/kg/min, or epinephrine or norepinephrine at any rate. Acute kidney injury (AKI) was defined by the RIFLE definition (an acronym corresponding to the risk of renal dysfunction, injury to the kidney, failure of kidney function, loss of kidney function, and end-stage kidney disease) denoting a rise in serum creatinine (Cr) level of 50% or more from the baseline within 7 days after the procedure (12). Perioperative stroke referred to a stroke that presented within the initial 30 days post-procedure, characterized by a focal neurological deficit of central origin persisting over 24 hours, with or without confirmation through neuroimaging (13). Respiratory complications encompassed postoperative pneumonia and prolonged ventilator support lasting >48 hours.

Patients underwent regular postoperative follow-ups at the outpatient clinic at 3- or 4-month intervals. If they did not visit the last clinic at the scheduled time, they were contacted via telephone to confirm their condition. The clinical follow-up ended on December 31, 2022, and the follow-up completion rate was 95.3% (41/43). The follow-up duration was 42.0 months (IQR, 17.3–152.5 months) and most of the patients (n=36, 83.7%) underwent TV surgery since January 1, 2014. As for mid-term outcomes, overall survival rates and cumulative incidences of TVRE, AF recurrence, or permanent pacemaker (PPM) insertion

were analyzed. TVRE included development of moderate or severe TV disease, TV reoperation, congestive heart failure (CHF) requiring readmission, major bleeding or thrombosis, and valve-related mortality (14).

Statistical analysis

Statistical analyses were performed using R ver. 4.2.1 and IBM SPSS Statistics ver. 26. The data are expressed as mean ± standard deviation, medians with IQRs or proportions. Overall survival was analyzed using the Kaplan-Meier method. The cumulative incidence was estimated by considering death as a competing risk. The overall survival and TVRE were compared between groups using log-rank test and Fine-Gray's test. The risk factors for time-related events were analyzed using the Cox proportional hazards model. The minimal P value approach was used to estimate a cutoff value of time interval that associated with the occurrence of TVRE. Statistical significance was set at P<0.05 univariate analysis.

Results

Patient characteristics

Preoperative and operative characteristics are summarized in *Tables 1,2*, respectively. Thirty-nine (90.7%) patients had severe TR and 4 (9.3%) had moderate-to-severe TR. As for concurrent functional mitral regurgitation (FMR), 2 (4.7%) patients had mild-to-moderate MR, 16 (37.2%) had trivial or mild MR while 25 (58.1%) patients had no MR.

The interval from initial diagnosis of AF to significant TR (moderate-to-severe or greater TR) was 61.2 months (IQR, 6.4–107.1 months), and the interval from initial diagnosis of severe TR to surgery was 2.4 months (IQR, 0.8–20.9 months), respectively. Preoperative echocardiographic dimensional data and CMR data were also stated in *Table 1*.

The concomitant Cox-maze III procedure was performed in 39 patients (90.7%). For 3 patients, the Maze procedure was not indicated due to the factors such as severe pericardial adhesion, a significantly enlarged and thin RA, concurrent RV dysfunction, and various comorbidities including old age above 80. Among the entire cohort, 34 patients underwent the left atrial appendage (LAA) treatment through various technique including internal obliteration (n=7), external exclusion (n=12), or excision (n=15). Another five patients did not undergo LAA treatment because their LAAs had severe adhesions and

Table 1 Preoperative characteristics

Preoperative data	Values (n=43)
Age (years)	69.3±8.6
Gender (female)	22 (51.2)
Body surface area (mm ²)	1.67±0.18
Body mass index >25 kg/m ²	15 (34.9)
Functional class ≥3	12 (27.9)
Diabetes mellitus	15 (34.9)
Hypertension	19 (44.2)
History of stroke	6 (14.0)
Dyslipidemia	9 (20.9)
Chronic renal failure (eGFR <60 mL/min/1.73 m ²)	19 (44.2)
Coronary artery disease	4 (9.3)
Liver disease	4 (9.3)
Preoperative TR grade	
Moderate-to-severe	4 (9.3)
Severe	39 (90.7)
Echocardiographic dimensional data (n=41)	
Tricuspid valve annulus (mm)	45.5±6.5
RA area at end-systole (cm ²)	39.2±11.4
RA volume (mL)	169.1 (105.1–227.9)
Left atrium dimension (mm)	56.1±8.8
RV end-systolic area (cm ²)	16.4±4.0
RV end-diastolic area (cm ²)	27.7±8.2
Cardiac magnetic resonance data (n=41)	
RV ejection fraction (%)	48.4±8.1
RV end-systolic volume (mL)	132.3±47.4
RV end-diastolic volume (mL)	256.3±82.4
Interval from AF to significant TR (months)	61.2 (6.4–107.1)
Interval from severe TR to surgery (n=39, months)	2.4 (0.8–20.9)

Values are presented as median (interquartile range), number (percentage) or mean ± standard deviation. eGFR, estimated glomerular filtration rate; TR, tricuspid regurgitation; RA, right atrium; RV, right ventricle; AF, atrial fibrillation.

a broad base that was not suitable for both internal and external procedures. Most patients underwent TV repair (n=37, 86.0%), while 6 patients (14.0%) underwent TVR. The mean cardiopulmonary bypass (CPB) and aortic cross-

Table 2 Operative data of the study patients

Variables	Values (n=43)
Type of tricuspid valve surgery	
Repair	37 (86.0)
De-Vega annuloplasty	4 (9.3)
Ring annuloplasty	33 (76.7)
Replacement	6 (14.0)
Concomitant Cox-maze III procedure	39 (90.7)
CPB time (min)	160.6±50.7
ACC time (min)	100.4±27.5

Values are presented as number (percentage) or mean ± standard deviation. CPB, cardiopulmonary bypass; ACC, aortic cross-clamp.

clamp (ACC) times in the whole cohort were 160.6±50.7 and 100.4±27.5 min, respectively (*Table 2*).

Anticoagulation strategy during follow-up

As for anti-coagulation during follow-up, 5 patients (11.6%) without mechanical TV and free from AF were prescribed no anti-coagulation. Fifteen patients (34.9%) were on novel oral anticoagulants (NOAC) while 10 (23.3%) on anti-platelet agents such as aspirin or clopidogrel, and 7 (16.3%) on warfarin. Additionally, 5 patients (11.6%) with concurrent cerebral or coronary arterial disease received a combination of anti-platelet therapy with NOAC or warfarin.

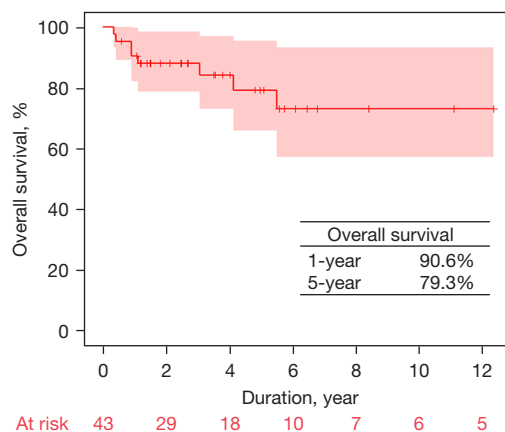
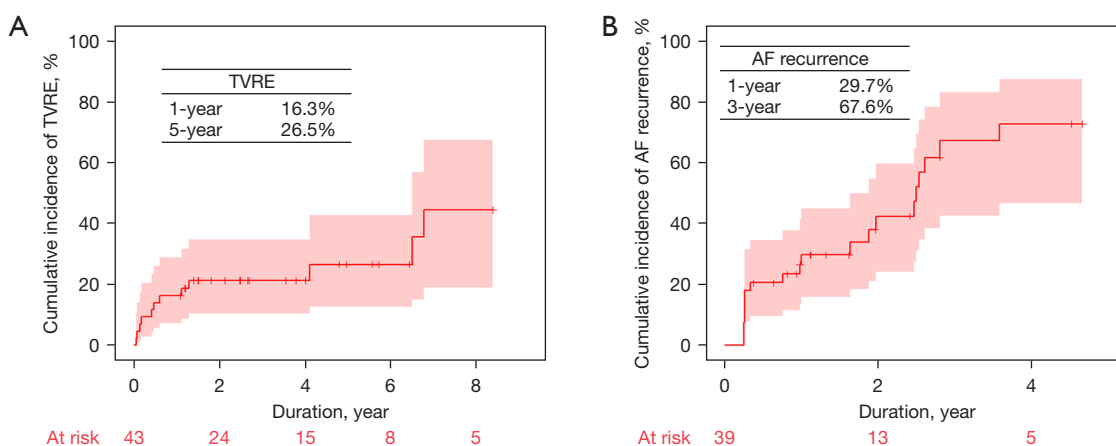
Early clinical outcomes

Operative mortality occurred in 1 patient (2.3%). The patient had been diagnosed with severe TR 9 years preoperatively and had RV dysfunction (RVEF, 33.1% on CMR) before surgery. The patient died of ventricular fibrillation arrest-associated bradycardia and electrolyte imbalance 145 days after surgery during the same hospitalization. The median length of hospital stay was 15 (IQR, 11–20) days. Two (4.7%) patients experienced low postoperative cardiac output syndrome. Reoperation for postoperative bleeding was performed in 2 patients (4.7%). Nine patients (21.0%) developed AKI, and renal replacement therapy was required in 5 patients. Perioperative stroke occurred in 2 patients (4.7%), while respiratory complications occurred in 7 patients (16.3%). No patient required PPM implantation after surgery (*Table 3*).

Table 3 Early postoperative outcomes

Early outcomes	Values (n=43)
Operative mortality	1 (2.3)
Hospital course (days)	15 [6–145]
Low cardiac output syndrome	2 (4.7)
Bleeding reoperation	2 (4.7)
AKI	9 (20.9)
AKI requiring RRT	5 (11.6)
Permanent pacemaker implantation	0
Stroke	2 (4.6)
Respiratory complication	7 (16.3)

Values are presented as number (%) or median [range]. AKI, acute kidney injury; RRT, renal replacement therapy.

**Figure 2** Overall survival in patients who underwent surgery for tricuspid regurgitation induced by atrial fibrillation.**Figure 3** Cumulative incidences of (A) TVRE, (B) recurrence of AF in patients who underwent surgery for tricuspid regurgitation induced by atrial fibrillation. TVRE, tricuspid valve related events; AF, atrial fibrillation.

The TR grade was significantly improved after surgery from 3.8 ± 0.4 to 0.6 ± 0.8 ($P < 0.001$). Two patients had moderate or greater postoperative residual TR. One patient with severe TR improved to trivial TR 11 months after surgery, and the other patient with moderate TR improved to mild TR 66 months after surgery, without additional TV procedures.

Mid-term clinical outcomes

Late death occurred in seven patients. The 1- and 5-year overall survival rates were 90.6% and 79.3%, respectively (Figure 2). The cumulative incidences of TVRE at 1- and 5-year were 16.3% and 26.5%, respectively (Figure 3A).

Four patients who underwent TAP developed moderate ($n=3$, 7.0%) or moderate-to-severe ($n=1$, 2.3%) TR, and two of these patients were readmitted due to CHF. One patient in the TVR group underwent reoperation because of structural bioprosthetic valve degeneration, approximately 40 months after the first surgery while 2 patients in the TAP group underwent reoperation of TVR with concomitant mitral valve repair due to recurred TR along with newly developed significant MR. During follow-up, bleeding events occurred in two patients, but there were no embolic events, including thromboembolic stroke (Table 4). The cumulative incidences of AF recurrence at 1- and 3-year in patients who underwent concurrent Cox maze

Table 4 Mid-term postoperative outcomes

Midterm outcomes	Values (n=42)
Late mortality	7 (16.7)
Cardiac death	2 (4.8)
PPM insertion	6 (14.3)
Recurrence of AF after Cox-maze III procedure (n=39)	20 (51.3)
Recovery to sinus rhythm, free from PPM	15 (38.5)
TV re-operation	3 (7.1)
Development of moderate or severe TV disease	4 (9.5)
Congestive heart failure requiring re-admission	2 (4.8)
Major bleeding or thrombotic events	2 (4.8)

Values are presented as number (%). AF, atrial fibrillation; PPM, permanent pacemaker; TV, tricuspid valve.

III procedures (n=39) were 29.7% and 67.6%, respectively (Figure 3B). The cumulative incidence of PPM insertion at 1- and 3-year were 4.7% and 17.1%, respectively.

The interval from the diagnosis of severe TR to surgery was not associated with overall survival (P=0.48), but was significantly associated with TVRE (hazard ratio: 1.023, 95% confidence interval: 1.005–1.042). The cutoff value of interval from the diagnosis of severe TR to surgery for predicting the TVRE was 23.1 months.

Outcomes in patients with sinus rhythm

During follow-up, sinus rhythm was maintained in 20 patients. There was no long-term mortality in patients with sinus rhythm, and the cumulative incidence of TVRE was 10% at 3 years. While there was a significant difference in overall survival between patients with sinus rhythm and those without sinus rhythm (P=0.01, Figure S1A), there was no significant difference in the incidence of TVRE between patients with sinus rhythm and those without sinus rhythm (P=0.45, Figure S1B).

Discussion

Key findings

The present study demonstrated that TV surgery for AF-induced TR showed favorable surgical morbidity and mortality, as well as acceptable mid-term outcomes in terms of overall survival and TVRE. AF-induced TR usually originates from a dilated and posteriorly displaced TV

annulus, accompanied by RA enlargement and RV eccentric dilatation (15,16). Several studies have shown that severe AF-induced TR is a significant predictor of mortality in patients with AF (17-20). Although more attention has recently been drawn to isolated FTR and its prognosis, surgical treatment is uncommon, and there is still a paucity of research on the surgical outcomes of AF-induced TR (21).

Strengths and limitations

Previous studies on isolated TV surgery have reported an operative mortality rate of approximately 10% (22-24); however, this study showed a very low mortality rate. Early surgical referral can affect these favorable early clinical outcomes by physicians. In our study, the median interval from severe TR to surgery was just 2.4 months. In the follow-up results, a longer duration from diagnosis of severe TR to surgery was also associated with a higher incidence of TVRE, although this analysis was only performed using univariate analysis. Further large-sample studies are required to elucidate the clinical effect of surgical referral timing on AF-induced TR.

Comparison with similar research

The risk factors attributed to recurrent AF or significant TR were not analyzed in the present study because of the small sample size. Wang *et al.* reported that a high tethering height >6 mm and RV sphericity index are independent risk factors for the recurrence of AF or TR in AF-induced TR (25). Because RV dilatation can result in displacement of the papillary muscles and leaflet tethering (26), it is important to consider intervention before the RV is severely dilated in patients with AF-induced TR.

Explanations of findings

Despite the significance of surgery for isolated FTR, the reluctance of physicians towards surgery might be due to the critical morbidity and mortality associated with TV surgery, based on previous studies. However, previous studies on TV surgery included patients with heterogeneous etiologies and inadequate timing of surgery (22,27).

The AF recurrence rate was very high in this population, compared with that in other studies that reported the results of the Cox-maze III procedure. This high recurrence rate can be attributed to the long duration of AF. Although the median interval from AF to significant TR was 61.8 months

in this study, this value could have been underestimated because of the missing records of the first diagnosis of AF. Although the recurrence rate of AF was high, there was no thromboembolic stroke during follow-up. Decreasing the AF burden using the Cox maze procedure and LAA treatment can lead to favorable clinical outcomes (28).

Implications and actions needed

Current guidelines recommend surgical intervention for ventricular FTR originating from left valvular heart disease at the time of left-sided valve surgery or in symptomatic patients (6,7). However, there is no consensus regarding the optimal surgical timing for AF-induced TR. As patients with AF-induced TR are less likely to have RV dysfunction or a history of cardiac surgery than patients requiring TV surgery, more favorable operative outcomes are expected, as in this study. Therefore, further studies should be performed to evaluate the clinical benefits of surgical treatment and to determine the appropriate surgical timing for AF-induced TR.

Limitations

The present study has several limitations. First, this was a single-center, retrospective, non-comparative observational study. Therefore, the number of patients included in the study is not sufficient to draw comprehensive conclusions, particularly in terms of conducting detailed research on surgical techniques, such as a comparison between TV repair and replacement. The further comparative studies according to surgical techniques or origin of TR should be performed. Second, the study period was long because isolated TV surgery for AF-induced TR was not prevalent. Although the surgical technique did not change during the study period, changes in the medical system may have affected the results. Third, although isolated TV surgery can be performed safely through minimally invasive procedures (29), most surgeries in the present study were conducted via median sternotomy because the concomitant Maze procedure can increase the complexity of surgery for patients with atrial FTR. Further studies regarding surgical approaches for these patients are needed to assess more effective strategies.

Conclusions

TV surgery for TR induced by AF has shown low surgical

mortality and favorable mid-term outcomes. In addition, this study showed the possibility of improving surgical outcomes in these patients through early surgery after progression to severe TR. Further studies are needed to improve the clinical outcomes of surgery in patients with AF-induced TR.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://jtd.amegroups.com/article/view/10.21037/jtd-23-1776/rc>

Data Sharing Statement: Available at <https://jtd.amegroups.com/article/view/10.21037/jtd-23-1776/dss>

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-23-1776/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board (IRB) of Seoul National University Hospital (IRB approval No. 2208-151-1353), and individual consent for this retrospective analysis was waived.

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