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Surgical treatment of isolated tricuspid valve endocarditis: Midterm data

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Abstract

Background: Isolated tricuspid valve endocarditis (TVE) is a rare disease which is managed medically in most patients. Only in specific cases, surgical intervention becomes necessary. Hence, data about surgical outcomes are sparse. This study reports on the operative experience in patients with isolated TVE over a period of 20 years.

Methods: We retrospectively analyzed 32 patients with isolated TVE who underwent surgery from February 2001 to June 2021 at the German Heart Centre Munich.

Results: Thirty-day mortality was 3.1%. Overall survival was 89.9± 5.5% at 1 year and 76.9 ± 8.5% at 5 years. Cumulative incidence for reoperation was 11.1 ± 6.0% at 5 years. Four patients (12.5%) were treated for recurrent endocarditis. Tricuspid valve repair (TVr) was achieved in 16 patients (50%). If the subvalvular apparatus (n = 10) was involved, tricuspid valve replacement was performed more frequently.

Conclusions: Mortality in patients with isolated TVE undergoing cardiac surgery is high. In half of the cases, TVr was achieved but was less likely in patients with affected subvalvular apparatus.

KEYWORDS
endocarditis, surgery, tricuspid valve

1 | INTRODUCTION

Isolated tricuspid valve endocarditis (TVE) is a rare disease, accounting for up to 10% of all cases of heart valve endocarditis.[1] However, the prevalence is increasing in recent years.[2] This trend is attributed to an increase in medical device implantation, including pacemakers and defibrillators, usage of vascular hemodialysis catheters, and intravenous (i.v.) drug abuse.[3,4]

I.v. antibiotics are the treatment of choice for isolated right-sided IE. Over half of the patients respond well to this approach.[5,6] Surgical therapy is rare and thus, little has been reported on the outcome of surgical procedures. In the present study, we report our single-center

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experience with surgical intervention for isolated TVE over the last 20 years.

2 | METHODS

This study presents a retrospective analysis of all consecutive patients who underwent tricuspid valve (TV) surgery due to isolated TVE at the German Heart Centre Munich between February 2001 and June 2021. Patients' data were identified from our internal clinical database. All medical reports, including operative protocols, in-hospital and outpatient notes were reviewed. Patients with concomitant procedures were excluded. The study was approved by the Institutional Review Board of the Technical University of Munich (Number: 356/21).

2.1 | Endpoints

The primary endpoint of this study was all-cause mortality after TV surgery due to TVE. Secondary endpoints were the rate of reinfection, reoperation, and recurrence of tricuspid regurgitation (TR) in patients with TV repair (TVr).

2.2 | Follow-up

Patients were contacted via telephone calls and were asked to report upon reinfection, reoperation, and recurrent regurgitation. Furthermore, the family physicians and/or referring cardiologists were contacted to obtain the latest echocardiographic findings. All evaluations were carried out according to standard techniques recommended by the current guidelines. TR was graded as none/trivial (0+), mild (1+), moderate (2+), or severe (3+) according to the recommendations for the echocardiographic assessment of native valvular regurgitation from the European Association of Cardiovascular Imaging.[7]

2.3 | Statistical analysis

Statistical analysis was performed with the Statistical Package for Social Science (SPSS Inc., version 25) for Windows and R statistical software language (R Foundation for Statistical Computing, version 3.6.1). Comparisons between groups were performed using the Student *t*-test for normally distributed variables and the Wilcox rank-sum test for not normally distributed variables. Comparison between the groups was performed using either one-way analysis of variance with post hoc Dunnett-T3 test for parametric variables or Kruskal–Wallis test for nonparametric variables. Survival was reported using the Kaplan–Meier method. Correlation was measured using a χ^2-test. Differences in the endpoints were evaluated using the log-rank Mantel–Cox test and the Cumulative Incidence Analysis following the Gray test including hazard ratio with 95% confidence intervals (CIs). A probability value less than 0.05 was considered to be statistically significant. All data are represented as mean ± standard deviation or as median.

3 | RESULTS

3.1 | Patient characteristics

A total of 32 patients (22 male; 68.8%) were operated between 2001 and 2021 with an average age of 47.8 ± 18.2 years. Clinical and demographic data are summarized in Table 1. Ten patients (31.2%) were operated from 2001 to 2010, and 22 patients (68.8%) from 2011 to 2021 (Figure 1). Based on the underlying etiology of the TVE the patients could be divided into the following groups: cardiac device (*n* = 12), i.v. drug use (*n* = 11), and others (*n* = 9). In the course

TABLE 1 Baseline characteristics

Baseline data	All	Cardiac device	I.v. drug abuse	Other
Patients	*n* = 32	*n* = 12	*n* = 11	*n* = 9
Age (years)	47.8 ± 18.2	65.2 ± 13.8	32.8 ± 5.8	42.8 ± 13.8
Male	22 (68.8%)	8 (66.7%)	7 (63.6%)	7 (77.8%)
Diabetes mellitus	1 (3.1%)	1 (8.3%)	0	0
Sinus rhythm	27 (84.4%)	9 (75%)	9 (81.8%)	9 (100%)
Serum creatinine (mg/dl)	1.2 ± 0.7	1.3 ± 0.6	1.1 ± 0.7	1.3 ± 0.9
Serum bilirubine (mg/dl)	1.0 ± 1.2	1.3 ± 1.2	1.0 ± 1.5	0.4 ± 0.3
Hepatitis C	7 (21.9%)	0	7 (63.6%)	0
NYHA	3.2 ± 0.9	3.3 ± 0.8	3.1 ± 1.1	3.2 ± 0.7
Preoperative intubation	2 (6.3%)	0	2 (18.2%)	0

Note: Data are presented as *n* (%) or mean ± SD.

Abbreviations: i.v., intravenous; NYHA, New York Heart Association.

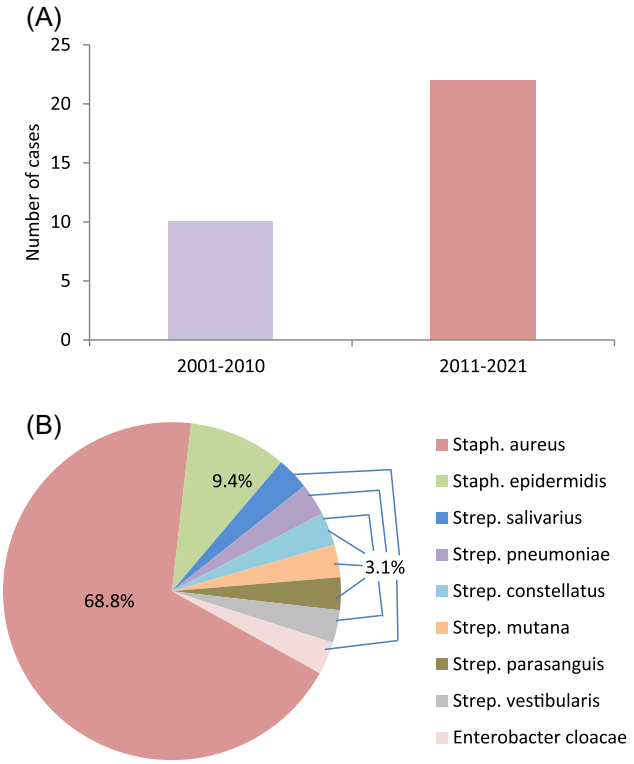

FIGURE 1 (A) Increase of case numbers over time. (B) Overview of causative organisms

of screening for infectious foci in the group "others," three patients were diagnosed with lower respiratory tract infection and one patient with pyelonephritis. The infectious focus could not be identified in five patients. Patients with implanted cardiac devices were significantly older (65.2 ± 13.8 years) compared to patients with i.v. drug use (32.8 ± 5.8 years; $p < .001$), and patients with other reasons for endocarditis (42.8 ± 13.8 years; $p = .005$).

Upon admission, 25 patients (78.1%) presented in New York Heart Association (NYHA) class III or IV. Two patients (6.3%) with i.v. drug abuse required intubation due to respiratory distress before referral to surgery. Two patients (6.7%) were on hemodialysis before surgery ($n = 1$, i.v. drug abuse group; $n = 1$, group with other reasons for endocarditis). All cases of hepatitis C (21.9%) were to be found in the group of i.v. drug users (seven out of nine patients; $p < .001$). No patient had HIV infection.

3.2 | Causative organism

Preoperative blood culture allowed the identification of the causative organism in all patients (Figure 1B). *Staphylococcus aureus* was the most common pathogen (n= 22; 68.8%), two of these cases resulted from methicillin-resistant *S. aureus* (MRSA). Of the 17 patients, who had a CT thorax before surgery 10 patients (58.8%) had pulmonary septic emboli. In 70% of these cases, the underlying pathogen was *S. aureus*.

3.3 | Indication for surgery

TV surgery was indicated due to vegetation size greater than 20 mm in 16 patients (50%), right heart failure due to severe TR in 9 patients (28.1%), and persisting infection defined as bacteremia over 7 days despite antibiotic treatment in 7 patients (21.9%).

3.4 | Operative data

All operations were performed through median sternotomy on cardiopulmonary bypass with bicaval and ascending aortic cannulation. Myocardial protection was achieved using cold (4°C) crystalloid cardioplegia (Bretschneider solution) ($n = 24$; 75%) or warm blood cardioplegia ($n = 4$; 12.5%). Four procedures (12.5%) were performed on beating heart. In patients with cardiac device infection, the foreign material was removed.

Most surgical procedures were performed as urgent or emergent ($n = 24$; 75%). The mean bypass time was 97.7 ± 37.8 min with a mean cross-clamp time of 49.5 ± 33.4 min. Mean bypass and cross-clamp time showed no significant difference in-between the groups ($p = .238$ and $p = .069$, respectively; Table 2). Further details on the operative procedure are summarized in Table 2.

3.5 | Type of surgery

TVr was achieved in 16 patients (50%) using annuloplasty ($n = 14$) and/or leaflet repair techniques ($n = 12$). Annuloplasty was performed using the DeVega suture technique ($n = 1$) or ring devices (Medtronic Contour 3D™, $n = 11$; Edwards MC3™, $n = 2$). Leaflet repair was done via patch plasty (autologous pericardium, $n = 4$; CardioCel®, $n = 2$) or direct suture of a lesion ($n = 6$).

Thirteen patients (40.6%) received a bio-prosthetic valve replacement, and three patients (9.4%) a mechanical valve replacement. The etiological causes in patients receiving a mechanical prosthesis were i.v drug abuse ($n = 1$) and others ($n = 2$).

There was no significant difference in the rates of valve repair ($p = .371$) or replacement with bio-prosthetic ($p = .072$) or mechanical valves ($p = .174$) in-between the different etiological groups. Patients with cardiac device associated IE tended to have more bio-prosthetic valve replacements than the other groups ($p = .072$) (Table 2).

The involvement of the subvalvular apparatus significantly correlated with valve replacement ($\chi^2 = 5.24$, $p = .022$). The subvalvular apparatus was infected in 50% ($n = 8$) of patients receiving valve replacement, compared to 12.5% of patients ($n = 2$) receiving TVr. Four patients (12.5%) showed no vegetation on the leaflets at the time of surgery, 12 patients (37.5%) had one affected leaflet, and 8 patients each had two (25%) or three (25%) affected leaflets. TVr was performed in 62.5% ($n = 10$) of cases where no or one leaflet was affected, compared to 37.5% ($n = 6$) of cases where two or three leaflets were involved ($\chi^2 = 2.00$, $p = .157$).

TABLE 2 Operative data and postoperative course

Operative and postoperative data	All	Cardiac device	I.v. drug abuse	Other	
Nonelective surgery	24 (75%)	11 (91.7%)	8 (72.7%)	5 (55.6%)	$p = .178$
Cardiopulmonary bypass time (min)	97.7 ± 37.8	86.2 ± 33.7	96.5 ± 27.2	114.6 ± 50.1	$p = .238$
Cross-clamp time (min)	49.5 ± 33.4	32.1 ± 29.4	59.1 ± 33.9	60.9 ± 31.1	$p = .069$
TV repair	16 (50.0%)	4 (33.3%)	7 (63.6%)	5 (55.6%)	$p = .371$
TV replacement, biological	13 (40.6%)	6 (66.7%)	3 (27.3%)	2 (22.2%)	$p = .072$
TV replacement, mechanical	3 (9.4%)	0	1 (9.1%)	2 (22.2%)	$p = .174$
Hospital stay (days)	21.8 ± 18.8	24.1 ± 27.2	16.8 ± 9.3	24.7 ± 13.8	$p = .576$
ICU stay (days)	11.1 ± 16.0	15.3 ± 21.8	7.0 ± 9.8	10.4 ± 12.8	$p = .474$
Ventilation time (h)	159.7 ± 362.7	245.5 ± 484.3	104.9 ± 244.1	112.3 ± 308.5	$p = .599$

Note: Data are presented as *n* (%) or mean ± SD.

Abbreviations: ICU, intensive care unit; TV, tricuspid valve.

3.6 | Postoperative course

The patients needed a mean ICU stay of 11.1 ± 16.0 days with an average duration of assisted respiration of 159.7 ± 362.7 h (median 14 h). Five patients (15.6%) needed temporary tracheotomy. There was no difference in-between the groups. Six patients (18.75%) required postoperative hemodialysis. The mean hospital stay was 21.8 ± 18.8 days with no difference in-between the groups ($p = .576$) (Table 2).

3.7 | Survival

Mean follow-up was 4.6 ± 4.9 years. Overall survival was 89.9 ± 5.5% at 1 year and 76.9 ± 8.5% at 5 years. For the cardiac device group, overall survival was 81.5 ± 11.9% and 69.8 ± 14.9% after 1 and 5 years, for the i.v. drug abuse group 90.0 ± 9.5% and 72.0 ± 17.8%, and for the others 100% and 87.5 ± 11.7%, respectively ($p = .777$) (Figure 2). One patient died 9 days after surgery due to sepsis, resulting in a 30-day mortality of 3.1%. There was no significant difference in survival in patients with TVr compared to tricuspid valve replacement (TVR) ($p = .500$).

3.8 | Reinfection and reoperation

After discharge four patients (12.5%) had to be treated for recurrent endocarditis. Three patients presented with reinfection of the reconstructed TV ($n = 2$) or the prosthetic valve ($n = 1$), and one patient with new endocarditis of the mitral valve. All of these patients were i.v. drug users and required reoperation. Reoperation was performed after a mean of 766.5 ± 980.5 days ranging from 84 to 2197 days. Cumulative incidence for reoperation of the TV was 11.1± 6.0% at 5 years (Figure 3).

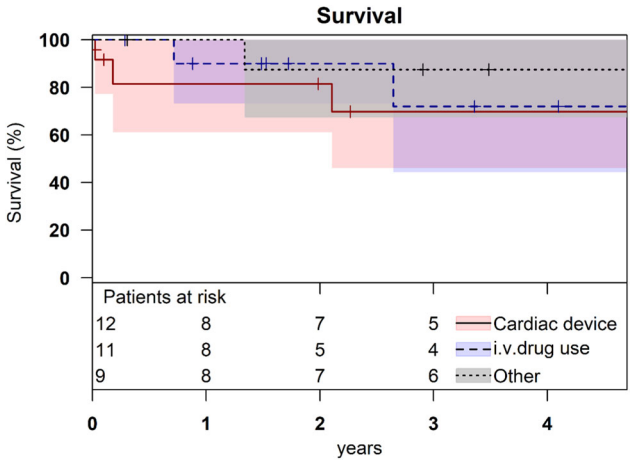

FIGURE 2 Survival of patients with different etiological causes

3.9 | Echocardiographic data

Preoperative echocardiogram showed normal mean left ventricular ejection fraction (LV-EF) (56.1 ± 11.1%). Right ventricular ejection fraction (RV-EF) was reduced in 36% of the patients. The majority of the patients (75%) presented with a moderate to severe TR and an enlarged annular diameter (41.3 ± 4.7 mm).

At follow-up, the mean LV-EF was 54.5 ± 9.8%. The majority of patients (62.5%) presented with reduced RV-EF, however, follow-up for the RV-EF was only complete in 50% of the patients ($n = 16$). At follow-up, 81.3% of patients showed no or mild TR, three patients had moderate, and one patient had severe TR. All patients with moderate to severe TR had TVr (annuloplasty ring device $n = 2$; leaflet repair with autologous pericardium $n = 1$; leaflet repair with direct suture of the lesion $n = 1$). Two of these patients developed TR due to recurrent endocarditis and were reoperated receiving biological valve prostheses.

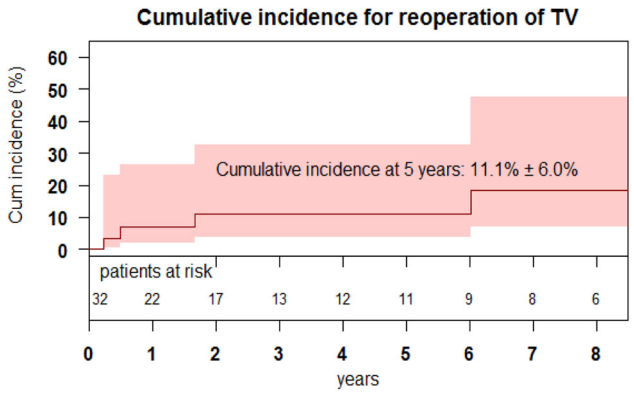

FIGURE 3 Cumulative incidence for reoperation of the tricuspid valve

4 | DISCUSSION

In the present retrospective, single-center study 32 patients were evaluated after surgical treatment for isolated TVE. In half of the patients (50%), TVr was performed. In contrast, in the other half, with extensive destruction of the leaflets and involvement of the subvalvular apparatus ($n = 10$), TVR was performed. Overall survival was 89.9 ± 5.5% at 1 year and 76.9 ± 8.5% at 5 years and cumulative incidence of reoperation was 11.1 ± 6.0% at 5 years.

4.1 | Indication and type of surgery

According to the ESC guidelines[5] surgery is indicated in patients with vegetation size larger than 20 mm, with right heart failure, or with persisting infection despite antibiotic treatment. Currently, there is a lack of data about the outcome of the different surgical indications. This data gap might be explained due to small patient numbers, as isolated TVE is a rare disease. Descriptive analysis in our cohort shows that four out of nine patients (44.4%) with right heart failure died during follow-up, while there were three deaths (18.8%) in the large vegetation group ($n = 16$) and one death (14.3%) in the persisting infection group ($n = 7$). Hence, right heart failure may increase mortality in isolated TV surgery, as has been shown previously by Dreyfus et al.[8]

Concerning the type of surgery valve repair is recommended whenever possible.[5] In our cohort, 50% of the patients were treated with TVr, 40.6% with biological, and 9.4% with mechanical valve replacement. This data is similar to a recent meta-analysis of 12 unmatched retrospective observational studies ($n = 1165$ patients) showing a median repair rate of 59%, a replacement rate with biological prostheses of 34%, and with mechanical prostheses of 7%.[9]

In a cohort of 21 patients with TVE, Renzulli et al. advised TVr in the following cases: vegetation or signs of infection on a single leaflet, or on the posterior leaflet with minimal involvement of the anterior leaflet. A multileaflet involvement is considered an indication for valve replacement.[10] However, our experience shows that also cases with multileaflet vegetation can be successfully repaired. We achieved TVr in 6 cases where two or three leaflets were affected. The decision for whether to repair or replace was mainly driven by the involvement of the subvalvular apparatus. In 50% of our patients ($n = 8$) receiving valve replacement, the subvalvular apparatus was involved, compared to 12.5% of patients ($n = 2$) with TVr.

4.2 | Recurrent TV regurgitation

Some studies show that while TVr decreases the risk of reinfection, it is associated with an increase in recurrent TR.[9] In our study, four patients developed recurrent moderate to severe TR after TVr. The diagnosis of recurrent TR was established 626 and 5 days after surgery, respectively. These two patients were treated with medical therapy following the guideline's recommendation for isolated TR in patients not undergoing left-sided valve surgery.[11]

4.3 | Recurrence of infective endocarditis

A major concern after cardiac surgery for endocarditis is reinfection.[12] Known risk factors for reinfection are the presence of prosthetic valves and continuous i.v. drug abuse.[13,14] In the previously mentioned meta-analysis Yanagawa et al. show that valve repair is associated with lower rates of reinfection (RR: 0.17, 95% CI: 0.05–0.57, $p = .004$; seven studies, 210 patients, 3 vs. 11 reinfections).[9] Potentially, the minimization of foreign material in TVr may be less prone to reinfection in the case of recurrent bacteremia. However, we did not observe this effect. In our cohort, three patients (9.4%) developed right-sided reinfection: two patients with previous TVr, and one patient with a mechanical prosthesis. TVr was performed with autologous pericardium in one patient, and with the use of an annuloplasty ring in the other patient. All of these patients had a history of illicit i.v. drug abuse, and required reoperation. Illicit i.v. drug abuse is a known risk factor for reinfection as indicated by our data and stated in the AATS guidelines.[14] The 2015 ESC guidelines recommend avoiding surgery in patients with this etiology, as reinfection might lead to reoperation resulting in higher mortality rates.[5]

4.4 | Survival

Patients with TVE undergoing cardiac surgery have reported mortality rates ranging from 4.9% and 12.5%.[8,14,15] In the present cohort, 30-day mortality was 3.1% ($n = 1$). The patient died 9 days after surgery due to septic shock. Overall survival was 89.9 ± 5.5% at 1 year and 76.9 ± 8.5% at 5 years which is slightly higher compared to other studies reporting survival rates after surgery ranging from 60% to 70% after 5 years.[14,15]

The etiology of the IE did not influence mortality in the present study ($p = .777$; Figure 2), although patients in the group with cardiac devices were significantly older (65.2 ± 13.8 years) compared to

patients with i.v. drug abuse (32.8 ± 5.8 years; $p < .001$), and other etiological causes for IE (42.8 ± 13.8 years; $p = .005$). Despite these demographics, there was no significant difference in various preoperative clinical data like cardiac, renal, and liver function in-between the three groups.

Unlike our data, Witten et al. showed that patients undergoing valve repair exhibited a better 5-year survival compared to patients undergoing valve replacement (70% vs. 30%).[14] On the other hand, data from Yanagawa et al. showed no significant difference in overall survival between valve repair and replacement after a median FU of 3.8 years.

4.5 | Causative organism

The most common causative pathogen was *S. aureus* (22 patients; 68.8%), which is consistent with other studies reporting *S. aureus* rates between 35% and 80%.[5,9,16] In general, the incidence of IE caused by *S. aureus* is increasing. Slipczuk et al. demonstrated that the percentage of *S. aureus* positive IE rose from 18.1% in the 1960s to 29.7% in the 2000s.[4] This trend is particularly alarming due to higher mortality rates associated with *S. aureus* IE of up to 22% and the increase in MRSA.[16] In our cohort two patients had an MRSA-induced IE.

S. aureus endocarditis may also be associated with higher rates of embolic events.[17] In our cohort, 17 patients received preoperative CT of the thorax. 58.8% of these patients showed pulmonary septic emboli, which in 70% of the cases were caused by *S. aureus*.

5 | CONCLUSION

Patients undergoing cardiac surgery for isolated TVE represent a heterogeneous population including cases with implanted cardiac devices as well as illicit i.v. drug abuse. Mortality remains high with no significant difference in survival in-between the different etiological groups. However, reinfection occurs predominantly in patients with i.v. drug abuse.

Valve repair was achieved in 50% of the patients. Our experience shows, that TVr can be successfully performed in patients with multileaflet involvement, but was less likely in patients with affected subvalvular apparatus.

6 | LIMITATIONS

Limitations of this study are consistent with those inherent to retrospective analysis study design. Also, the small study size may not have the statistical power to expose small effects.

CONFLICTS OF INTEREST

Ruediger Lange is a consultant, speaker, and member of the medical advisory board for Medtronic and HighLife Medical. Markus Krane is a physician proctor and a member of the medical advisory board for JOMDD, a physician proctor for Peter Duschek, and has received speakers' honoraria from Medtronic and Terumo. The other authors declare that they have no conflicts of interest.

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