Outcomes after surgery for functional tricuspid regurgitation: a systematic review and meta-analysis

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Aims

This study aims to provide a contemporary overview of outcomes after tricuspid valve (TV) surgery for functional tricuspid regurgitation (TR).

Methods and results

The literature was systematically searched for papers published between January 2005 and December 2017 reporting on clinical/echocardiographic outcomes after TV surgery for functional TR. A random effects meta-analysis was conducted for outcome variables, and late outcomes are visualized by pooled Kaplan–Meier curves. Subgroup analyses were performed for studies with a within-study comparison of suture vs. ring repair and flexible vs. rigid ring repair. Eighty-seven publications were included, encompassing 13 184 patients (mean age: 62.1 ± 11.8 years, 55% females). A mitral valve procedure was performed in 92% of patients. Pooled mean follow-up was 4.0 ± 2.8 years. Pooled early mortality was 3.9% (95% CI: 3.2–4.6), and late mortality rate was 2.7%/year (95% CI: 2.0–3.5), of which approximately half was cardiac-related 1.2%/year (95% CI: 0.8–1.9). Pooled risk of early moderate-to-severe TR at discharge was 9.4% (95% CI: 7.0–12.1). Late moderate-to-severe TR rate after discharge was 1.9%/year (95% CI: 1.0–3.5). Late reintervention rate was 0.3%/year (95% CI: 0.2–0.4). Mortality and overall (early and late) TR rate were comparable between suture vs. ring annuloplasty (14 studies), whereas overall TR rate was higher after flexible ring vs. rigid ring annuloplasty (6 studies) (7.5%/year vs. 3.9%/year, $P = 0.002$).

Conclusion

This study shows that patients undergoing surgery for functional tricuspid regurgitation (FTR) have an acceptable early and late mortality. However, TR remains prevalent after surgery. The results of this study can be used to inform patients and clinicians about the expected outcome after surgery for FTR and can results serve as a benchmark for the performance of emerging transcatheter TV interventions.

INTRODUCTION

Functional tricuspid regurgitation (FTR) is the most common form of tricuspid valve (TV) disease. Functional tricuspid regurgitation is the result of changes in the tricuspid annular geometry caused by dilatation of the right ventricle in the absence of structural valve abnormalities. In most, FTR is caused by left-sided heart disease and subsequent pulmonary hypertension.[1] Historically, FTR was believed to be benign and to resolve after the left-sided heart disease was corrected.[2] However, recent research shows that FTR is an ongoing process, which can even worsen if left untreated[3–5] and that the presence of TV regurgitation is associated with impaired long-term survival.[6] Therefore, latest guidelines recommend TV surgery in patients undergoing left-sided valve surgery if severe FTR is present and/or when annulus dilatation exceeds 40mm.[7,8] Whenever feasible, the TV is repaired with either a suture or ring annuloplasty. Optimal patient selection with current techniques remains controversial. Additionally, new transcatheter technologies for treating FTR are already on the horizon.[9] In this light a comprehensive overview of both clinical and echocardiographic outcomes is warranted, which is currently lacking in the literature. This systematic review of the literature and meta-analysis aims to provide a contemporary overview of outcomes after surgery for FTR. Furthermore, we analysed studies specifically addressing ring vs. suture annuloplasty and flexible vs. rigid ring annuloplasty.

METHODS

Search strategy

To establish an overview of reported outcome, we conducted a systematic literature search according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[10] On 13 December 2017, Embase, Medline, Web of science, Cochrane, and Google scholar were searched by a biomedical information specialist (search terms are available in Supplementary material online, Text S1). The search was limited to studies that were published after 1 January 2005. Two researchers (K.M.V. and J.R.G.E.) independently reviewed abstracts and full texts. We included observational studies and randomized controlled trials that reported on outcome after surgery for FTR in humans with a sample size ≥20 patients and were published in English. Studies solely reporting on primary TV disease or studies with a mix of patients with FTR and primary TV disease without extractable data on patients with FTR were excluded. In case of multiple publications on overlapping study populations, the publication with the greatest total follow-up in patient-years and/or overall completeness of data was included for each outcome of interest separately. In case of disagreement, an agreement was negotiated.

Data extraction

Microsoft Office Excel 2011 (Microsoft Corp., Redmond,WA, USA) was used for data extraction. If total follow-up in patient-years was not reported, it was calculated by multiplying the number of patients with the mean follow-up (or median follow-up, if the mean was not provided). Outcomes were recorded according to the guidelines described by Akins et al.[11] Early mortality was defined as either hospital mortality or 30-day mortality. A sensitivity analyses were performed for studies reporting 30-day mortality. Extracted baseline characteristics and outcomes are provided in Supplementary material online, Table S1. Early tricuspid regurgitation (TR) was defined as moderate-to-severe TR at discharge echocardiogram. Late TR was defined as number of patients that progressed from none-to-mild at discharge to moderate-to-severe at last follow-up. Overall TR was defined as moderate-to-severe TR at last follow-up (early TR plus late TR).

Statistical analyses

Sample sized weighted pooled baseline patient and procedural characteristics were calculated. Event risks (early) and rates (late) were pooled using inverse variance weighting. Outcomes were pooled on a logarithmic scale, because the Shapiro–Wilk test revealed a skewed distribution among the majority of outcomes. Outcomes were pooled in a random effects model using the Der Simonian and Laird method to estimate the between-study variance.[12] In case, a particular event was reported not to occur, we assumed that 0.5 patient experienced the event for pooling purposes (continuity correction). Subgroup analyses were conducted of studies comparing ring vs. suture annuloplasty and flexible vs. rigid ring annuloplasty, in which risk ratios (RRs) and mean differences (MDs) were calculated for baseline characteristics and outcomes, a random model was used to pool outcomes and a fixed model was used to pool baseline characteristics.[12] We did not use continuity correction in subgroup analyses and if only two studies reported the variable of interest or had zero events, no pooling of RR/MD was performed. The Cochrane Q statistic and I^2 were used to assess heterogeneity. Potential causes of heterogeneity in early/late mortality and early TR were explored by investigating the association of all baseline patient characteristics and operative details listed in Supplementary material online, Table S3 by means of univariable random effects meta-regression. The influence of potential publication bias on pooled outcome was investigated by conducting sensitivity analyses by temporarily excluding the smallest quartile (by sample size). Microsoft Office Excel 2011 was used to conduct the random effects meta-analyses and R (Version 3.3.3, Vienna, Austria, using the Open Meta Analyses interface) for the univariable meta-regression analyses. Comprehensive meta-analysis (Biostat, Englewood, USA) was used to pool RRs and MDs from studies included in the subgroup analyses. A *P*-value of <0.05 was considered significant.

We visualized the survival and freedom from late TR in pooled KM curves derived from the original published KM curves using the method described by Guyot et al.[13] Published Kaplan–Meier curves were digitized and an estimate of the individual patient time-to-event data was then extrapolated from the digitized curve co-ordinates, assuming a constant rate of censorship between each time point at which the number of patients at risk was specified.[12] We used Engauge Digitizer 9.7 to create a list of co-ordinates of the KM curve and employed an in-house developed algorithm written in R language (Version 3.3.3) to reconstruct the original patient data. The mortality of the general population was obtained for the pooled median year of intervention among included studies (2006) and for the regions that the majority of the included study population originated from (North America, 41% of patients; Europe, 23% of patients; and Japan 16% of patients).

RESULTS

The literature search resulted in 11 707 publications. After applying inclusion and exclusion criteria 87 studies were included for analysis, of which 14 publications compared ring vs. suture annuloplasty and six compared flexible vs. rigid ring annuloplasty (Figure 1) (Supplementary material online, References S1–S87). In 18 of the 87 included publications only a subgroup or part of the outcomes could be extracted in order to prevent overlapping study populations (Supplementary material online, Table S2).

Study and patient characteristics

Individual study characteristics are presented in Supplementary material online, Table S2. In total, 13 184 patients with a mean age of 62.1 ± 11.8 years (55% females) were included, encompassing 41 874 patient-years of total follow-up. In total, 10 418 patients had late follow-up, resulting in a mean pooled follow-up of 4.0 ± 2.8 years. Pooled patient and procedural characteristics are presented in Table 1. Al least one concomitant procedure was performed in 98.7% of patients, usually a mitral valve procedure (92.6%).

Clinical outcomes

Early and late outcomes are presented in Table 2. Heterogeneity was high in all outcome measures, except for late valve-related mortality, late pacemaker implantation, and reintervention (Table 2). Unvariable meta-regression identified several potential sources of heterogeneity. These were older mean age and higher proportion concomitant coronary artery bypass graft (CABG) associated with higher early mortality risk; older mean age, higher proportion concomitant CABG, higher CPB, and aortic cross clamp (ACC) time associated with higher late mortality rate (Supplementary material online, Table S3). Sensitivity analysis did not reveal major changes in pooled outcomes when studies with a sample size lower than 25th percentile were temporarily excluded, nor did 30-mortality differ from early mortality (3.9% vs. 3.9%; Supplementary material online, Table S4). Twenty-five studies reported a Kaplan–Meier curve encompassing 7531 patients in total (Supplementary material online, References S1–S25), which could be pooled (Figure 2). Survival at 1, 3, and 8 years was 87.7%, 80.9%, and 64.5%, respectively.

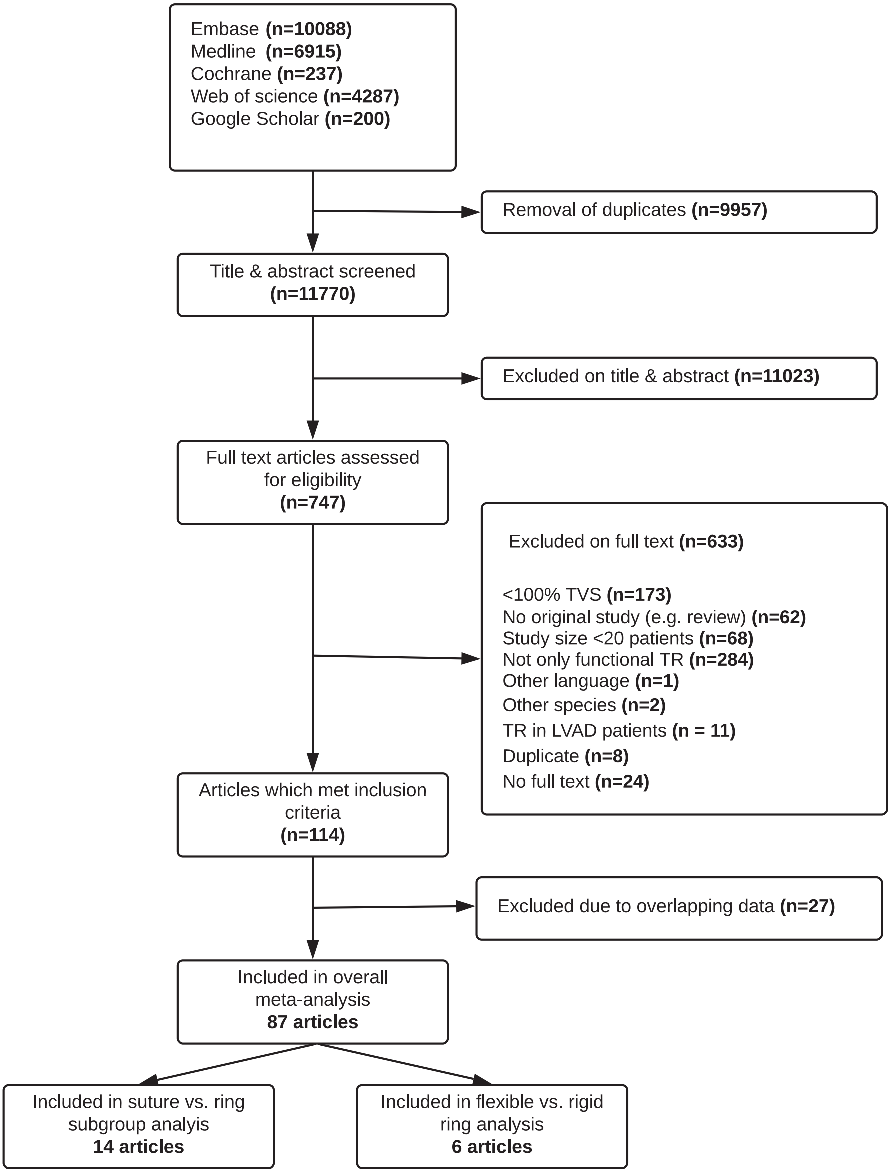

Figure 1. A flow chart of included studies.

Tricuspid regurgitation

Pooled risk of early moderate-to-severe TR is 9.4% (Table 2). Possible sources of heterogeneity in early TR risk were higher proportion of moderate-to-severe TR at baseline and higher proportion of patients with diabetes (Supplementary material online, Table S3). Twenty-four studies reported both early and late moderate-to-severe TR, of which two had to be excluded due to large discrepancy in number of patients with a discharge echocardiogram compared to a follow-up echocardiogram. Pooled estimate of late TR is 1.9%/year and overall TR rate (early and late combined) was 3.5%/year (Table 2).

In total, 18 studies presented a KM curve reporting freedom from moderate-to-severe TR, encompassing 4138 patients in total (Figure 3A). Overall freedom from TR at 1, 3, and 5 years was 92.9%, 89.4%, and 84.9%. Seventeen studies reported a KM curve in which it was distinguishable whether patients underwent suture or ring annuloplasty, encompassing 4046 patients in total (Figure 3B). Eight studies reported on a KM on flexible/rigid rings encompassing 1727 patients

(Figure 3C).

Table 1. Pooled baseline characteristics

Characteristics	Pooled proportion (*n* = 13 184)	Range	N studies reported
Age (years)	62.1 ± 11.8	25.1–72.5	75
Female (%)	55.5	17.6–90	72
NYHA III–IV (%)	58.5	16.1–100	47
AF (%)	60.7	20.0–100	58
≥ Moderate TR (%)	78.5	0.0–100	57
LVEF (%)	51.8 ± 13.5	28.5–65.0	57
PAPs (mmHg)	48.6 ± 14.2	35.3–76.9	42
TV repair[1] (%)	98.6	0.0–100	75
Suture repair[2]	22.6	0.0–100	72
Ring repair[2]	77.4	0.0–100	72
TV replacement[1] (%)	1.4	0.0–100	75
MV procedure (%)	92.6	16.9–100	75
MV repair[3]	40.9	0.0–100	58
MV replacement[3]	59.1	0.0–100	59
AV procedure (%)	20.9	0.0–64.9	66
CABG (%)	16.6	0.0–58.8	66
CPB time (min)	148 ± 61	45–256	52
ACC time (min)	101 ± 39	35–168	47

ACC, aortic cross-clamp; AF, atrial fibrillation; AV, aortic valve; CABG, coronary artery bypass graft; CPB, cardio pulmonary bypass; LVEF, left ventricular ejection fraction; MV, mitral valve; NYHA, New York Heart Association; PAPs, systolic pulmonary artery pressure; TR, tricuspid regurgitation; TV, tricuspid valve.
[1]Percentage of patients with reported technique.
[2]Percentage of patient with reported TV repair.
[3]Percentage of patient with reported MV procedure.

Table 2. Pooled outcomes

Outcomes	Pooled estimate (95% CI)	Heterogeneity (I^2)	*N* studies reported
Early outcome (%)			
Early mortality	3.9 (3.2–4.6)	62.6	73
Early pacemaker implantation	3.2 (2.1–5.0)	83.0	27
AKI	4.8 (3.6–6.5)	86.0	26
LCOS	7.4 (5.5–9.9)	71.8	19
Early re-exploration	5.5 (4.4–6.9)	87.1	34
Early moderate-to-severe TR	9.4 (7.0–12.3)	90.5	35
Late outcome (%/year)			
All-cause mortality	2.7 (2.0–3.5)	92.9	46
Cardiac mortality	1.2 (0.8–1.9)	88.9	32
Valve-related mortality	0.7 (0.5–0.9)	21.0	26
Late pacemaker implantation	0.8 (0.5–1.3)	27.5	7
Late admission HF	2.1 (0.8–5.4)	94.8	9
Late reintervention[a]	0.3 (0.2–0.4)	14.1	34
Overall moderate-to-severe TR[b]	3.5 (2.1–6.0)	96.5	24
Late moderate-to-severe TR	1.9 (1.0–3.5)	95.1	22

AKI, acute kidney injury; HF, heart failure; LCOS, low cardiac output syndrome; TR, tricuspid regurgitation.
[a]Only containing tricuspid valve reinterventions.
[b]Combining late and early TR.

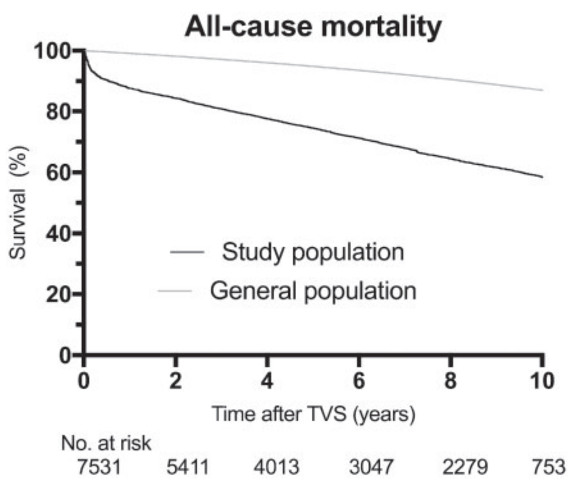

Figure 2. Pooled Kaplan–Meier curve of overall survival (both early and late).

Suture repair vs. ring repair

In total, 14 studies focused on ring repair vs. suture repair (Supplementary material online, References S7, S10, S12, S20, S32, S36–S44) encompassing 1425 patients (ring) and 586 patients (suture). Pooled baseline characteristics were comparable between patients; except for age and pulmonary systolic artery pressure which was both higher in the ring group (Table 3). Cardiopulmonary bypass (CPB) time of patients undergoing suture annuloplasty was on average 9.2 min shorter compared to patients undergoing ring annuloplasty (Table 4). Early mortality risk and late mortality rate were comparable (Table 3). Furthermore, early TR, overall TR, and late reintervention were comparable (Table 3). Only two studies reported both early and TR at last follow-up, hence pooled late TR could not be computed. Forest plots of all outcomes are presented in Supplementary material online, Figures S1–S7.

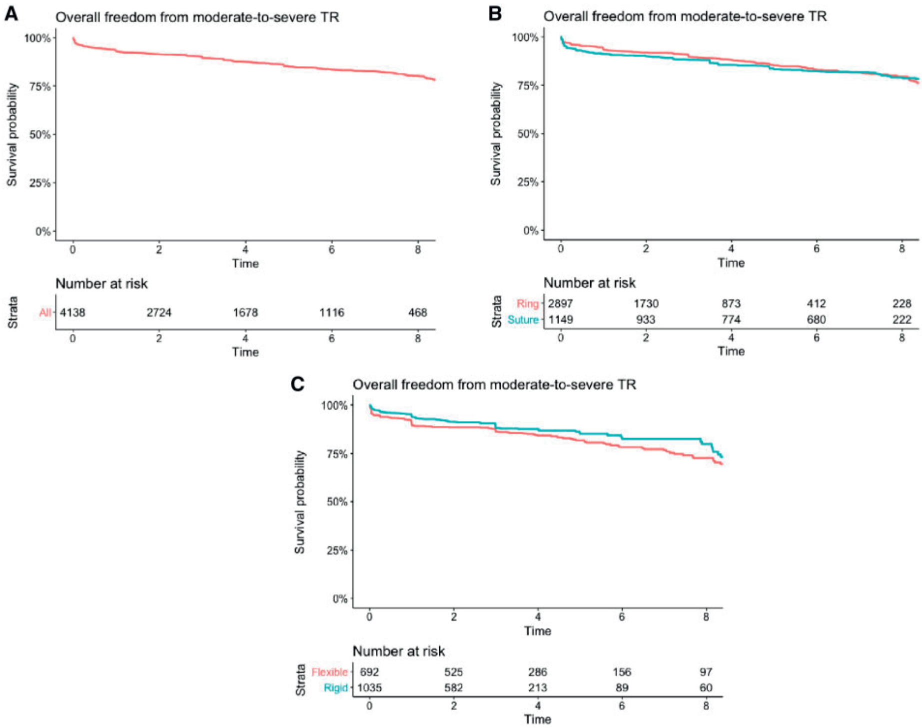

Figure 3. Pooled Kaplan–Meier curve overall freedom from moderate-to-severe tricuspid regurgitation (both early and late) (A) and with either a suture or a ring repair (B) and a flexible ring or a rigid ring (C). TR: Tricuspid regurgitation.

Flexible vs. rigid ring repair

In total, six studies focused on flexible vs. ring repair encompassing 749 (flexible) and 745 (rigid) patients (Supplementary material online, References S13, S18, S28, S30, S35, and S36). On average, patients receiving a rigid ring were older, had less atrial fibrillation, and were more frequently in New York Heart Association Class III–IV (Table 4). cardiopulmonary bypass times and early/late mortality and late mortality were comparable between groups (Table 4).One study reported early pacemaker implant, which was comparable (3% vs. 2%).[14] Three studies reported early TR, which was comparable in all studies.[15–17] Overall TR rate was significantly higher in the flexible group (7.5%/year) vs. the rigid group (3.9%/year, *P*=0.002) (Table 4). Late TV re-intervention was comparable; however, only in two studies patients underwent late TV reintervention.[14,15] In two other studies, no TV interventions were performed.[16,17] Four studies reported ring dehiscence: one study found higher incidence of ring dehiscence in the rigid ring group,[15] whereas the three other studies no ring dehiscence was noted in both groups.[17–19] Forest plots of all outcomes are presented in Supplementary material online, Figures S8–S11.

Table 3. Pooled baseline characteristics and outcomes of studies with a within-study comparison of ring vs. suture repair

	Ring (*n* = 1425)	95% CI	Suture (*n* = 586)	95% CI	RR/MD	95% CI	*P*-value
Baseline characteristics							
Age (years)	57.8	57.1–58.8	55.9	55.3–56.5	-1.2	-2.1 to -0.3	0.010
Female	56.6	53.5–59.4	56.9	54.2–59.6	1.02	0.96–1.09	0.564
NYHA III–IV	66.0	62.9–69.0	65.2	62.4–67.9	1.04	0.99–1.08	0.127
AF	62.9	59.8–66.0	61.5	58.4–64.5	0.99	0.94–1.03	0.631
LVEF (%)	50.3	49.8–50.8	46.7	46.3–47.2	0.31	-0.40 to 1.01	0.396
PAPs (mmHG)	49.5	49.0–49.9	48.3	47.8–48.7	1.00	0.34–1.67	0.003
≥ Moderate TR	76.5	73.1–79.6	77.2	73.7–80.3	1.01	0.99–1.3	0.517
MV procedure	89.5	87.0–91.6	90.3	88.2–92.7	1.00	0.98–1.02	0.803
AV procedure	22.2	19.6–25.0	22.3	19.8–24.9	1.03	0.87–1.21	0.757
Outcomes							
CPB time (min)	145	113–177	134	106–162	9.2	4.5–14.0	>0.001
Early mortality	2.5	2.3–4.6	2.5	1.6–3.9	1.21	0.75–1.96	0.427
Late mortality[a]	1.7	0.9–3.3	2.6	0.2–3.4	0.67	0.33–1.35	0.264
Late reintervention[a]	0.2	0.1–0.4	0.3	0.2–0.5	1.25	0.53–2.94	0.604
Early TR	10.2	4.3–22.8	6.8	2.8–15.3	0.82	0.61–1.01	0.179
Overall TR[a]	4.3	2.1–8.3	6.3	1.2–28.1	0.98	0.72–1.33	0.889

AV, aortic valve; CPB, cardiopulmonary bypass; LVEF, left ventricular ejection fraction; MD, mean difference; MV, mitral valve; NYHA, New York Heart Association; PAPs, systolic pulmonary artery pressure; RR, risk ratio; TR, tricuspid regurgitation.
[a]Rate ratios instead of risk ratios.

Table 4. Pooled baseline characteristics and outcomes of studies with a within-study comparison of flexible ring vs. rigid ring repair

	Flexible ring (*n* = 749)	95% CI	Rigid ring (*n* = 745)	95% CI	RR/MD	95% CI	*P*-value
Baseline characteristics							
Age	64.8	64.1–65.5	66.2	65.6–66.7	-1.02	-1.95 to -0.09	0.032
Female	55.3	51.7–55.8	54.2	50.6–57.7	1.03	0.94–1.13	0.527
NYHA III–IV	61.6	54.2–68.4	71.6	63.0–79.2	0.89	0.80–1.0	0.045
AF	56.1	52.0–60.0	54.0	50.1–57.8	1.13	1.04–2.81	0.005
LVEF	54.1	53.5–54.8	54.9	54.0–55.8	-0.77	-1.87 to 0.32	0.167
≥ Moderate TR	63.2	55.7–70.1	71.1	65.0–77.5	1.02	0.98–1.07	0.304
MV procedure	88.0	83.1–91.6	90.7	86.5–93.8	0.99	0.96–1.03	0.707
AV procedure	31.6	25.2–38.7	26.4	21.0–32.6	1.13	0.82–1.55	0.456
Outcomes							
CPB time	136	100–173	145	107–184	-5.5	-11.4 to 0.3	0.063
Early mortality	6.4	3.2–12.5	6.0	3.6–10.1	1.21	0.65–2.24	0.543
Late mortality[a]	4.4	0.5–28.2	3.8	1.2–11.2	1.74	0.91–3.33	0.093
Late reintervention[a]	0.3	0.1–0.8	0.3	0.1–0.7	—[b]	—[b]	—[b]
Early TR	3.6	1.9–6.6	2.5	0.4–12.5	—[b]	—[b]	—[b]
Overall TR[a]	7.5	2.7–19.1	3.9	1.4–10.5	1.83	1.24–2.74	0.002
Ring dehiscence	0.0	0.0–0.0	0.9	0.5–1.7	—[b]	—[b]	—[b]

AV, aortic valve; CPB, cardiopulmonary bypass; LVEF, left ventricular ejection fraction; MD, mean difference; MV, mitral valve; NYHA, New York Heart Association; PAPs, systolic pulmonary artery pressure; RR, risk ratio; TR, tricuspid regurgitation.
[a]Rate ratios instead of risk ratios.
[b]No pooling attempt was made, since only two studies reported non-zero events.

DISCUSSION

In this study, we provide a comprehensive overview of outcomes after TV surgery for FTR in the light of emerging transcatheter TV interventions. To the best of our knowledge, this is the first comprehensive review and meta-analysis of outcomes after surgery for FTR. We noted acceptable early and late mortality, nevertheless early and late TR remain prevalent. Subgroup analyses revealed a significantly higher rate of overall TR of flexible rings compared to rigid rings. The results of this study can be used to inform patient and clinicians about the expected outcome after surgery for FTR. Furthermore, these data can be used for microsimulation models.[20] In addition, these results can be used as benchmark for the performance of emerging transcatheter TV interventions.

Patient and study characteristics

Patient characteristics varied considerably among studies. Interestingly, some studies included exclusively patients without moderate-to-severe FTR at baseline.[21,22] These studies investigated the 'prophylactic' approach of surgery for FTR in which only annular dilation is present, originally presented by Dreyfus et al.,[3] who proposed a cut-off of 70 mm intraoperatively, which was later converted to 40 mm on echocardiography. Nevertheless, this concept has been debated, especially since no specific evidence exist for 70–40 mm conversion, or the initial 70 mm cut-off.[3,23] Nearly all patients underwent a concomitant procedure, usually a mitral valve procedure. This indicated that the main cause of FTR in the included studies is left-sided heart disease. In only four studies patients underwent TV replacement for FTR, reflecting the preference for TV repair in this population. Notwithstanding, the current consensus is that TV replacement is preferred in case of very severe functional TR, with severe tethering.[24]

Early outcomes

Early mortality is acceptable in this patient population (3.9%) and studies with higher mean age and proportion of concomitant CABG reported higher mortality risks. Prior research has shown that TV surgery during left-sided valve surgery does not increase perioperative risk and even seems to protect against cardiac-related mortality compared to patients that did not undergo concomitant TV surgery.[25] Early pacemaker implantation (3.2%) is comparable with other large cohorts.[26,27] This may indicate that TV surgery does not add extra risk for pacemaker implant. Notwithstanding, other studies identified TV surgery as risk factor for post-operative pacemaker implant or noted high incidence of pacemaker implantation after TV surgery.[28–30] Jouan et al.[28] mentioned the close proximity of TV annular septal segment to the atrioventricular node may increase the risk of damage to the latter during TV interventions.

Late outcome

Our Kaplan–Meier analysis illustrates that mortality hazard is higher in the early post-operative period and becomes relatively stable thereafter. Compared to the general population, the survival in the study population is impaired. This is mainly due to the early morality, but late mortality is also higher compared to the general population. Studies with higher mean age, higher CPB/ACC time, and higher proportion of CABG reported higher rates of late mortality. Approximately half of the observed mortality can be attributed to cardiac causes, which is roughly two times higher compared to the general USA population.[31] Late re-intervention rate of the TV is low (0.3%/year) and little heterogeneity is present, indicating re-intervention is low uniformly among studies.

Tricuspid regurgitation

The incidence of early moderate-to-severe TR is relatively high (9.3%) and studies with a higher proportion moderate-to-severe TR at baseline reported higher risks of early moderate-to-severe TR, explaining partly the heterogeneity in this outcome. Interestingly, the type of repair (suture vs. ring) was not associated with risk of early TR upon univariable meta-regression. After the hospital period some patients develop late TR (1.9%/year), indicating a suboptimal durability. This rate does not correspond to the reintervention rate, meaning that only a part of the patients with early/late TR are reoperated. This can partly be explained by the fact that mortality risk after re-intervention of the TV is high, especially after late referral if right ventricular failure has already developed.[24,32,33]

Subgroup analyses

On average there were statistically significant differences between the suture group and the ring group [age, systolic pulmonary artery pressure (PAPs)]. Nevertheless, these differences are small (age: 1.2 years, PAPs: 1.0 mmHg) and may not be clinically relevant. Mortality and postoperative TR rates were comparable between ring vs. suture repair. In regard to early mortality and TR rate, this is in disagreement with a prior meta-analysis by Parolari et al.[34] focusing solely on the comparison ring vs. suture. Several factors may have contributed to this disagreement. Firstly, the prior meta-analysis did not exclude studies with primary TR. Secondly, the prior metaanalysis also compared studies without a within-study comparison of suture vs. ring, and variations in study populations between studies may have contributed to the observed differences in TR rates. Thirdly, two studies included in our TR rate analyses utilized the modified De Vega technique, with multiple pledgets, which is associated with better outcome than classical De Vega with two pledgets on the ends (Supplementary material online, References S12, S38, and S40). This technique was not used in the studies included in the prior systematic review.

In studies, comparing flexible rings vs. rigid rings a higher TR rate in the flexible ring group was noted. This is in agreement with a prior systematic review only including studies comparing flexible rings vs. rigid rings, regardless of TV disease aetiology.[35]

Future perspectives

The threshold to perform concomitant TV surgery has become increasingly lower.[1] Indeed, untreated TR does seem to be associated with impaired mortality.[6] Nevertheless, prediction of progression of TR after left-sided valve surgery remains difficult. In order to adequately address FTR multiple approaches are possible. Firstly, one can become even more liberal in performing concomitant TV surgery or optimize selection criteria for concomitant TV surgery by investigating longitudinal evolution of TR after left-sided valve surgery. Another approach emerges with the rise of transcatheter TV devices. One may be more conservative during the initial left-sided valve surgery and treat late TR using transcatheter tricuspid valve devices. Nevertheless, these devices are still in development and no evidence exists whether late percutaneous intervention of TR is beneficial. Future studies have to elucidate whether late transcatheter intervention is equivalent to earlier concomitant surgical intervention.

Limitations

This is a systematic review and meta-analysis of mainly retrospective observational studies. Therefore, inherent limitations of pooling such studies apply to this study.[36] Secondly, publication bias may be present which can potentially lead to underestimation of the estimates. We did not assess publication bias using funnel plots, as funnel plots do not allow for meaningful interpretation in case of absolute risk outcomes because of substantial methodological limitations, which may in itself give rise to funnel plot asymmetry.[37] Furthermore, heterogeneity was present in most outcomes which may lead to inaccurate results. Nevertheless, we conducted a thorough examination of heterogeneity by meta-regression. Linearized occurrence rates assume a constant hazard over time, while in fact most of the distribution of events may be time related.[38] Therefore, a pooled KM analyses was performed, illustrating the distribution of time-to-event. Inconsistencies in the reporting of TR and loss to echocardiographic follow-up among the included studies may have introduced uncertainty. Unfortunately, important variables, such as TV tethering, were not frequently reported in the primary studies.

CONCLUSION

This comprehensive systematic review with meta-analysis provides an overview of outcomes after surgery for FTR, which is in most cases performed concomitantly to left-sided valve surgery. It illustrates an acceptable early and late mortality, while early and late TR risk and rate are still suboptimal. These results can be used as benchmark for the performance of emerging transcatheter TV interventions.

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SUPPLEMENTARY MATERIAL

Contents

SUPPLEMENTARY TEXT 1: SEARCH TERMS

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(‘tricuspid valve’/de OR ‘Ebstein anomaly’/exp OR ‘tricuspid valve disease’/exp OR ‘tricuspid valve prosthesis’/de OR ‘tricuspid valve repair’/de OR ‘tricuspid valve replacement’/de OR (tricuspid* OR ((right-atrioventricul*) NEAR/3 valv*) OR Ebstein*):ab,ti) AND (‘surgery’/de OR surgery:lnk OR ‘cardiovascular surgery’/de OR ‘heart surgery’/exp OR ‘tricuspid valve prosthesis’/de OR ‘tricuspid valve repair’/de OR ‘tricuspid valve replacement’/de OR ‘surgical technique’/de OR ‘surgical mortality’/de OR ‘postoperative period’/de OR (surger* OR surgic* OR operati* OR prosthe* OR bioprosthe* OR graft* OR homograft* OR allograft* OR transplant* OR homotransplant* OR allotransplant* OR repair* OR replace* OR implant* OR correct* OR valvotom* OR valvuloplast*):ab,ti) AND (‘observational study’/exp OR ‘cohort analysis’/exp OR ‘longitudinal study’/exp OR ‘retrospective study’/exp OR ‘prospective study’/exp OR ‘health survey’/de OR ‘health care survey’/de OR ‘epidemiological data’/de OR ‘case control study’/de OR ‘cross-sectional study’/de OR ‘correlational study’/de OR ‘population research’/de OR ‘family study’/de OR ‘major clinical study’/de OR ‘multicenter study’/de OR ‘comparative study’/de OR ‘follow up’/de OR ‘clinical study’/de OR ‘clinical article’/de OR ‘clinical trial’/exp OR ‘controlled study’/de OR ‘randomization’/exp OR ‘intervention study’/de OR ‘open study’/de OR ‘community trial’/de OR ‘review’/exp OR ‘systematic review’/exp OR ‘meta analysis’/de OR (((observation* OR epidemiolog* OR famil* OR comparativ* OR communit*) NEAR/6 (stud* OR data OR research)) OR cohort* OR longitudinal* OR retrospectiv* OR prospectiv* OR population* OR (national* NEAR/3 (stud* OR survey)) OR (health* NEAR/3 survey*) OR ((case OR cases OR match*) NEAR/3 control*) OR (cross NEXT/1 section*) OR correlation* OR multicenter* OR multi-center* OR follow-up* OR followup* OR clinical* OR trial OR random* OR review* OR meta-analy*):ab,ti) NOT ([animals]/lim NOT [humans]/lim) NOT ([Conference Abstract]/lim OR [Letter]/lim OR [Note]/lim OR [Editorial]/lim) AND [english]/lim

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(“Tricuspid Valve”/ OR “Ebstein Anomaly”/ OR “Tricuspid Valve Stenosis”/ OR “Tricuspid Valve Prolapse”/ OR “Tricuspid Valve Insufficiency”/ OR (tricuspid* OR ((right-atrioventricul*) ADJ3 valv*) OR Ebstein*).ab,ti.) AND (“Surgical Procedures, Operative”/ OR surgery.xs. OR “Cardiovascular Surgical Procedures”/ OR exp “Cardiac Surgical Procedures”/ OR “postoperative period”/ OR (surger* OR surgic* OR operati* OR prosthe* OR bioprosthe* OR graft* OR homograft* OR allograft* OR transplant* OR homotransplant* OR allotransplant* OR repair* OR replace* OR implant* OR correct* OR valvotom* OR valvuloplast*).ab,ti.) AND (“observational study”/ OR exp “Cohort Studies”/ OR “Health Surveys”/ OR “Epidemiologic Studies”/ OR “Case-Control Studies”/ OR “Cross-Sectional Studies”/ OR “multicenter study”/ OR “comparative study”/ OR “clinical study”/ OR exp “clinical trial”/ OR “Controlled Before-After Studies”/ OR “Random Allocation”/ OR “review”/ OR “meta-analysis”/ OR (((observation* OR epidemiolog*

OR famil* OR comparativ* OR communit*) ADJ6 (stud* OR data OR research)) OR cohort* OR longitudinal* OR retrospectiv* OR prospectiv* OR population* OR (national* ADJ3 (stud* OR survey)) OR (health* ADJ3 survey*) OR ((case OR cases OR match*) ADJ3 control*) OR (cross ADJ section*) OR correlation* OR multicenter* OR multi-center* OR follow-up* OR followup* OR clinical* OR trial OR random* OR review* OR meta-analy*).ab,ti.) NOT (exp animals/ NOT humans/) NOT (letter OR news OR comment OR editorial OR congresses OR abstracts).pt. AND english.la.

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((tricuspid* OR ((right-atrioventricul*) NEAR/3 valv*) OR Ebstein*):ab,ti) AND ((surger* OR surgic* OR operati* OR prosthe* OR bioprosthe* OR graft* OR homograft* OR allograft* OR transplant* OR homotransplant* OR allotransplant* OR repair* OR replace* OR implant* OR correct* OR valvotom* OR valvuloplast*):ab,ti)

Web of science

TS=(((tricuspid* OR ((“right atrioventricul*”) NEAR/2 valv*) OR Ebstein*)) AND ((surger* OR surgic* OR operati* OR prosthe* OR bioprosthe* OR graft* OR homograft* OR allograft* OR transplant* OR homotransplant* OR allotransplant* OR repair* OR replace* OR implant* OR correct* OR valvotom* OR valvuloplast*)) AND ((((observation* OR epidemiolog* OR famil* OR comparativ* OR communit*) NEAR/5 (stud* OR data OR research)) OR cohort* OR longitudinal* OR retrospectiv* OR prospectiv* OR population* OR (national* NEAR/2 (stud* OR survey)) OR (health* NEAR/2 survey*) OR ((case OR cases OR match*) NEAR/2 control*) OR (cross NEAR/1 section*) OR correlation* OR multicenter* OR multi-center* OR follow-up* OR followup* OR clinical* OR trial OR random* OR review* OR meta-analy*))) AND DT=(article) AND LA=(english)

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Tricuspid surgery|surgical|operative|prosthetic|bioprosthesis|repair|replacement observational|cohort|longitudinal|prospective|trial

Supplementary Table 1: Extracted outcome and baseline variables

Baseline variables	Outcomes
Age	Cardio-pulmonary bypass time
Sex	Aortic clamp time
NYHA class	Early mortality
Left ventricle ventricular function	Early pacemaker implantation
Systolic pulmonary artery pressure	Early low cardiac output syndrome
TR grade at baseline	Acute kidney failure
Atrial fibrillation	Early reopening
Diabetes mellitus	Residual moderate-to-severe TR (= TR at discharge)
TV repair	Late mortality
- Ring	Cardiac mortality
o Flexible ring	Valve related mortality
o Rigid ring	Late pacemaker implantation
- Suture repair	Late admission for heart failure
o De Vega	Late reintervention
o Kay	Overall TR (TR at last echocardiogram)
TV replacement	
- Biological prostheses	
- Mechanical prostheses	
MV procedure	
- MV replacement	
- MV repair	
AV procedure	
Concomitant coronary artery bypass grafting	

NYHA: New York heart association, TR: tricuspid regurgitation, TV: tricuspid valve, MV: mitral valve, AV: aortic valve.

Supplementary Table 2: Baseline characteristics of individual studies

Author (year)	N	Follow-Up (years)	Age	Female (n,%)	≥moderate TR (n,%)	AF (n,%)	NYHA III-IV (n,%)	TV repair	TV ring repair	MV procedure
Abdelgawad (2017)[1]	20	1,0	38,9	9 (45)	20 (100)	9 (45)	15 (75)	20 (100)	20 (100)	20 (100)
Ada (2017)	43	-	56,2	27 (63)	43 (100)	24 (56)	20 (47)	43 (100)	43 (100)	35 (81)
Ariyoshi (2013)	47	4,6	66,1	32 (68)	-	44 (94)	30 (64)	47 (100)	25 (53)	47 (100)
Aykut (2011)	62	-	48,1	36 (58)	-	37 (60)	-	62 (100)	-	62 (100)
Basel (2010)	129	2,2	38,8	81 (63)	130 (100)	41 (32)	-	129 (100)	67 (52)	129 (100)
Benedetto (2012)	22	1,0	64,0	9 (41)	6 (27)	9 (41)	17 (77)	22 (100)	22 (100)	22 (100)
Bertrand (2014)[4]	-	-	-	-	32 (71)	-	-	-	-	-
Calafiore (2009)	51	5,5	63,9	9 (18)	51 (100)	20 (39)	-	51 (100)	0 (0)	51 (100)
Calafiore (2011)[4]	-	-	-	-	-	-	-	-	-	-
Cao (2014)	135	-	42,2	75 (56)	-	-	-	135 (100)	135 (100)	135 (100)
Chan (2009)	125	6,8	64,3	93 (74)	-	76 (61)	80 (64)	125 (100)	85 (68)	125 (100)
Chang (2008)	334	3,5	52,7	87 (26)	295 (88)	298 (89)	299 (90)	334 (100)	0 (0)	334 (100)
Chen (2016)	137	2,1	61,0	96 (70)	137 (100)	113 (82)	55 (40)	137 (100)	-	132 (96)
Chikwe (2015)	419	3,7	59,2	143 (34)	72 (17)	95 (23)	-	419 (100)	419 (100)	419 (100)
Choi (2017)	72	6,5	54,5	46 (64)	0 (0)	57 (79)	27 (38)	72 (100)	72 (100)	72 (100)
Choi (2016)[4]	-	-	-	-	40 (100)	-	-	-	-	-
De Bonis (2012)	140	1,8	63,8	60 (43)	134 (96)	73 (52)	71 (51)	140 (100)	140 (100)	138 (99)
De Meester (2015)	37	5,0	70,0	27 (73)	-	25 (68)	-	37 (100)	16 (43)	37 (100)
Di Mauro (2017)	541	-	54,1	303 (56)	-	-	-	-	-	541 (100)
Dreyfus (2005)	148	4,8	58,5	60 (41)	18 (12)	47,952 (32)	-	148 (100)	144 (97)	148 (100)
Filsoufi (2006)[5]	-	-	-	-	-	-	-	-	-	-
Fujita (2013)	67	-	62,7	36 (54)	52 (78)	53 (79)	19 (28)	67 (100)	67 (100)	58 (87)
Fukuda (2007)	136	3,5	65,0	83 (61)	123 (90)	36 (26)	-	136 (100)	136 (100)	61 (45)
Fukunaga (2015)	220	4,4	65,4	-	124 (56)	147 (67)	61 (28)	220 (100)	220 (100)	220 (100)

Supplementary Table 2: Baseline characteristics of individual studies (continued)

Author (year)	N	Follow-Up (years)	Age	Female (n,%)	≥moderate TR (n,%)	AF (n,%)	NYHA III-IV (n,%)	TV repair	TV ring repair	MV procedure
Gatti (2016)	527	5,2	69,6	279 (53)	325 (68)	169 (32)	337 (64)	527 (100)	449 (85)	488 (93)
Gatti (2016) [6]	-	-	-	-	-	-	-	-	-	-
Ghanta (2007)	237	3,0	67,0	126 (53)	227 (96)	-	125 (53)	237 (100)	80 (34)	195 (82)
Giamberti (2011)	65	5,3	46,0	24 (37)	65 (100)	-	42 (65)	62 (95)	14 (23)	11 (17)
Goncu (2015) [4]	-	-	-	-	64 (100)	-	-	-	-	-
Gosev (2015)	60	4,5	67,4	31 (52)	60 (100)	-	12 (20)	-	-	45 (75)
Hata (2017)	684	2,3	65,6	404 (59)	492 (72)	524 (77)	420 (61)	684 (100)	372 (54)	609 (89)
He (2012)	39	-	49,8	28 (72)	39 (100)	-	9 (23)	39 (100)	0 (0)	39 (100)
Hou (2017)	85	2,7	52,1	38 (45)	-	18 (21)	-	85 (100)	40 (47)	85 (100)
Huang (2013)	237	6,5	61,3	85 (36)	177 (75)	86 (36)	185 (78)	237 (100)	0 (0)	212 (89)
Huang (2014) [1]	232	7,4	64,2	-	227 (98)	208 (90)	208 (90)	232 (100)	232 (100)	232 (100)
Hwang (2014) [2]	67	6,9	57,0	48 (72)	-	62 (93)	22 (33)	0 (0)	-	14 (21)
Isomura (2015)	76	3,9	68,0	46 (61)	73 (96)	53 (70)	49 (64)	76 (100)	76 (100)	64 (84)
Ito (2017)	98	3,4		52 (53)	41 (42)	76 (78)	42 (43)	98 (100)	98 (100)	87 (89)
Izutani (2010)	117	2,0	72,5	71 (61)	111 (95)	89 (76)	-	117 (100)	117 (100)	102 (87)
Jeong (2010) [10]	-	-	-	-	-	-	35 (34)	-	-	84 (82)
Jeong (2017)	123	7,3	53,7	75 (61)	-	95 (77)	-	123 (100)	74 (60)	-
Jouan (2016)	88	3,0	60,7	41 (47)	28 (32)	35,991 (41)	-	88 (100)	88 (100)	88 (100)
Jung (2010)	219	3,0	54,2	154 (70)	216 (99)	180 (82)	108 (49)	219 (100)	219 (100)	198 (90)
Kara (2013)	93	2,1	54,3	50 (54)	-	55 (59)	81 (87)	93 (100)	34 (37)	93 (100)
Kawaura (2015) [1]	56	-	67,6	28 (50)	56 (100)	40 (71)	9 (16)	56 (100)	56 (100)	56 (100)
Khallaf (2016) [3]	62	1,0	33,0	39 (63)	-	-	-	62 (100)	0 (0)	62 (100)
Koppers (2013)	89	1,3	69,0	47 (53)	-	-	-	89 (100)	89 (100)	89 (100)
Kunova (2015)	43	4,6	-	26 (60)	34 (79)	36 (84)	31 (72)	43 (100)	0 (0)	36 (84)

Supplementary Table 2: Baseline characteristics of individual studies (continued)

Author (year)	N	Follow-Up (years)	Age	Female (n,%)	≥moderate TR (n,%)	AF (n,%)	NYHA III-IV (n,%)	TV repair	TV ring repair	MV procedure
Lee (2016)	91	7,6	49,0	51 (56)	-	72 (79)	23 (25)	91 (100)	60 (66)	-
Lin (2012)	45	6,8	49,0	33 (73)	45 (100)	40 (89)	45 (100)	11 (24)	0 (0)	-
Lin (2014)	399	3,3	46,4	211 (53)	391 (98)	184 (46)	254 (64)	399 (100)	157 (39)	394 (99)
Maghami (2016)	216	2,8	69,0	150 (69)	216 (100)	104 (48)	93 (43)	216 (100)	216 (100)	198 (92)
Masherbauer (2013)	46	5,2	-	-	-	-	-	-	-	193 (420)
Meng (2015)	69	1,7	51,7	-	45 (65)	69 (100)	-	69 (100)	40 (58)	-
Muller (2011)	25	-	-	-	-	-	-	25 (100)	-	25 (100)
Murashita (2014) [3]	42	9,1	64,0	24 (57)	25 (60)	36 (86)	29 (69)	42 (100)	0 (0)	42 (100)
Naqshband (2010)	83	5,1	27,0	43 (52)	83 (100)	52 (63)	23 (28)	83 (100)	0 (0)	83 (100)
Navia (2012) [9]	91	3,0	69,0	51 (56)	91 (100)	34 (37)	32 (35)	91 (100)	64 (70)	84 (92)
Navia (2010) [7]	2277	-	68,0	1376 (60)	2116 (96)	1549 (68)	1133 (50)	2277 (100)	1856 (82)	2097 (92)
Patel (2016)	25	1,0	40,0	11 (44)	10 (40)	12 (48)	20 (80)	25 (100)	25 (100)	25 (100)
Pettinari (2016)	260	2,1	68,0	119 (46)	-	97 (37)	133 (51)	-	-	235 (90)
pfanmuller (2013)	441	3,4	68,7	257 (58)	-	287 (65)	-	441 (100)	419 (95)	441 (100)
Pfannmüller (2012)[6]	-	-	-	-	-	-	-	-	-	-
Pradhan (2011)[8]	23	0,3	25,1	14 (61)	-	11 (48)	21 (91)	23 (100)	0 (0)	23 (100)
Ratschiller (2015)	415	2,0	70,1	195 (47)	400 (96)	285 (69)	318 (77)	415 (100)	415 (100)	319 (77)
Ren (2015)	74	2,8	48,4	63 (85)	52 (70)	-	71 (96)	74 (100)	40 (54)	74 (100)
Rhashwan (2017)	50	2,2	42,6	38 (76)	48 (96)	23 (46)	24 (48)	50 (100)	50 (100)	50 (100)
Risteski (2016)	37	4,8	67,0	9 (24)	25 (68)	12 (32)	-	37 (100)	-	37 (100)
Ro (2013)	431	5,4	53,3	279 (65)	281 (65)	303 (70)	-	431 (100)	-	431 (100)
Roshanali (2010)	210	-	55,4	133 (63)	-	151 (72)	-	210 (100)	105 (50)	185 (88)
Sharma (2016)[7]	117	-	-	-	-	-	-	117 (100)	-	117 (100)
Shi (2012)	70	6,6	61,2	15 (21)	12 (17)	27 (39)	-	70 (100)	0 (0)	70 (100)

Supplementary Table 2: Baseline characteristics of individual studies (continued)

Author (year)	N	Follow-Up (years)	Age	Female (n,%)	≥moderate TR (n,%)	AF (n,%)	NYHA III-IV (n,%)	TV repair	TV ring repair	MV procedure
Shinn (2016)	296	7,4	71,0	188 (64)	-	174 (59)	224 (76)	296 (100)	148 (50)	296 (100)
Šmíd (2010)	45	0,3	71,3	27 (60)	-	-	-	45 (100)	45 (100)	45 (100)
Song (2016)	50	2,0	46,6	25 (50)	0 (0)	-	41 (82)	50 (100)	-	50 (100)
Sorabella (2015)	272	3,1	70,3	165 (61)	-	172 (63)	-	272 (100)	250 (92)	236 (87)
Takano (2016)	52	11,7	61,9	33 (63)	25 (48)	30 (58)	-	52 (100)	52 (100)	52 (100)
Teman (2014)	63	2,3	65,4	45 (71)	-	-	-	57 (90)	57 (100)	63 (100)
Toporcer (2017)	54	-	58,9	24 (44)	-	-	-	54 (100)	-	54 (100)
Utsunomiya (2017)	97	-	66,0	56 (58)	97 (100)	-	-	97 (100)	97 (100)	65 (67)
Verdonk (2017)	165	-	61,0	105 (64)	86 (52)	89 (54)	132 (80)	165 (100)	165 (100)	165 (100)
Wang (2016)	106	2,9	57,1	56 (53)	106 (100)	-	91 (86)	106 (100)	106 (100)	106 (100)
Wang (2013)	60	2,6	45,3	31 (52)	55 (92)	-	48 (80)	60 (100)	0 (0)	53 (88)
Yeates (2014)	22	3,9	65,2	15 (68)	22 (100)	-	10 (45)	22 (100)	-	22 (100)
Yilmaz (2006)	25	1,5	36,3	-	25 (100)	20 (80)	-	25 (100)	0 (0)	-
Yoda (2011)	136	1,5	64,7	56 (41)	101 (74)	-	-	136 (100)	136 (100)	115 (85)
Zientara (2015)	22	-	67,0	12 (55)	22 (100)	15 (68)	-	22 (100)	22 (100)	22 (100)

1 Only ring cohort extracted
2 Only replacement cohort extracted
3 Only suture subgroup extracted
4 Only echocardiographic data extracted
5 Only KM curve extracted
6 Only included in flexibe vs rigid ring subgroup analyses
7 Only hospital mort extraxted
8 Other outcomes than hosp mort extracted
9 Other outcomes than hosp mort extracted and late outcomes extracted
10 Only outcomes not in Jeong (2017)

Supplementary Table 3: Meta-regression estimates

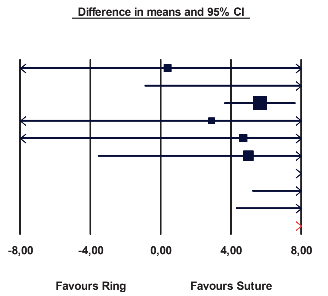
Covariate	Outcome measure		
	Early mortality (OR [95% CI], p value)	Overall late mortality (HR [95% CI], p value)	TR at discharge
Age	1.01 (1 to 1.01) p <0.001	1.62 (1.25 to 2.12) p<0.001	0.9 (0.7 to 1.14) p= 0.376
Female	1 (0.85 to 1.19) p= 0.962	1.08 (0.87 to 1.35) p= 0.48	1.21 (0.9 to 1.62) p= 0.214
NYHA III-IV	0.95 (0.84 to 1.07) p= 0.446	1.06 (0.9 to 1.25) p= 0.512	0.99 (0.83 to 1.19) p= 0.916
Mean cohort	1.01 (1 to 1.02) p= 0.172	1.42 (0.67 to 3) p= 0.360	0.99 (0.99 to 1) p= 0.095
Mean CPB	1.05 (1 to 1.12) p= 0.053	1.11 (1.01 to 1.2) p= 0.024	0.97 (0.9 to 1.06) p= 0.54
Mean ACC	1.06 (0.99 to 1.15) p= 0.083	1.17 (1.04 to 1.31) p= 0.01	0.96 (0.86 to 1.07) p= 0.476
Mean LVEF	0.99 (0.72 to 1.35) p= 0.942	0.70 (0.49 to 1.01) p= 0.058	1.17 (0.82 to 1.67) p= 0.386
Prior cardiac surgery	1.07 (0.97 to 1.19) p= 0.195	1.15 (0.76 to 1.75) p= 0.511	0.9 (0.7 to 1.15) p= 0.387
AF	0.94 (0.84 to 1.06) p= 0.362	0.88 (0.73 to 1.05) p= 0.154	1 (0.84 to 1.2) p= 0.969
Diabetes	1.34 (0.91 to 1.97) p= 0.136	0.76 (0.38 to 1.49) p= 0.418	2.69 (1.16 to 6.23) p= 0.02
MV procedure	0.94 (0.82 to 1.07) p= 0.345	1.12 (0.84 to 1.48) p= 0.438	1.01 (0.81 to 1.25) p= 0.953
AV procedure	1.16 (1.04 to 1.3) p= 0.006	1.15 (0.95 to 1.38) p= 0.158	0.92 (0.73 to 1.15) p= 0.479
CABG	1.26 (1.09 to 1.43) p<0.001	1.54 (1.23 to 1.92) p< 0.001	0.97 (0.79 to 1.19) p= 0.777
%moderate/severe TR at baseline	1.01 (0.92 to 1.11) p= 0.835	1.02 (0.89 to 1.17) p= 0.776	1.28 (1.15 to 1.43) p= <0.001
TV repair (vs replacement)	0.98 (0.91 to 1.05) p= 0.555	0.94 (0.84 to 1.05) p= 0.254	1.02 (0.9 to 1.16) p= 0.717
TV ring repair (vs suture)	1.03 (0.98 to 1.08) p= 0.209	1.00 (0.93 to 1.08) p= 0.912	0.99 (0.91 to 1.06) p= 0.756

Supplementary Table 4: Outcomes after Sensitivity analyses in which studies with sample size below 25th quantile are excluded

Outcomes	Pooled estimate (95% CI)	Heterogeneity	N studies reported
	Early outcome (%)		
Early mortality	3.8 (3.1 to 4.6)	I^2 = 68.9	62
30-day mortality*	3.9 (3.0 to 5.2)	I^2 = 73.2	33
Early pacemaker implantation	3.3 (2.1 to 5.2)	I^2 = 86.3	21
AKI	4.8 (3.5 to 6.6)	I^2 = 88.4	21
LCOS	6.9 (5.0 to 9.6)	I^2 = 77.4	14
Early reopening	5.4 (4.3 to 7.0)	I^2 = 89.7	27
Early moderate-to-severe TR	7.5 (5.5 to 10.3)	I^2 =90.5	26
	Late outcome (%/y)		
All-cause mortality	2.4 (1.7 to 3.3)	I^2 = 94.4	34
Cardiac mortality	1.1 (0.7 to 1.8)	I^2 = 91.4	24
Valve related mortality	0.6 (0.4 to 0.8)	I^2 = 27.7	20
Late pacemaker implantation	0.8 (0.5 to 1.5)	I^2 = 39.6	5
Late admission HF	1.7 (0.8 to 3.7)	I^2 = 89.0	8
Late reintervention[1]	0.3 (0.2 to 0.4)	I^2 = 30.3	26
Overall TR**	2.8 (1.9 to 4.0)	I^2 = 90.8	20
Late TR	1.6 (1.0 to 2.5)	I^2 = 89.7	15

CPB time

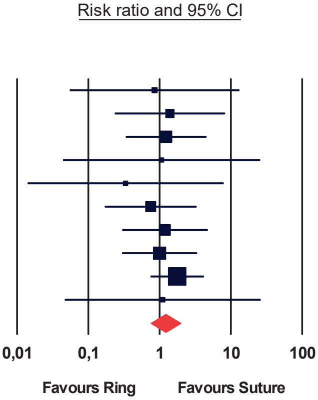
Model	Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Ren 2015	0,400	7,256	52,656	-13,822	14,622	0,055	0,956
	Huang 2014	14,000	7,608	57,876	-0,911	28,911	1,840	0,066
	Lin 2014	5,651	1,030	1,061	3,632	7,670	5,487	0,000
	Murashita 2014	2,900	9,103	82,860	-14,941	20,741	0,319	0,750
	Kara 2013	4,707	6,865	47,127	-8,748	18,162	0,686	0,493
	Hata 2017	5,000	4,370	19,094	-3,564	13,564	1,144	0,253
	Hou 2017	15,100	2,788	7,774	9,635	20,565	5,416	0,000
	Ghanta 2007	27,000	11,108	123,390	5,229	48,771	2,431	0,015
	Khallaf 2016	20,000	8,019	64,296	4,284	35,716	2,494	0,013
Random		9,236	2,420	5,858	4,492	13,980	3,816	0,000



Supplementary figure 1: Cardiopulmonary bypass time suture vs ring repair

Early mortality (ring vs suture)

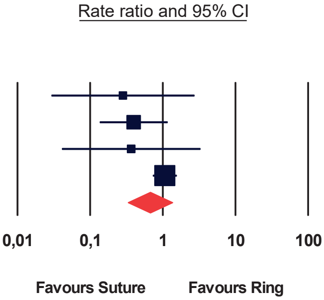
Model	Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
	Ren 2015	0,850	0,055	13,083	-0,117	0,907
	Huang 2014	1,397	0,236	8,278	0,368	0,713
	Lin 2014	1,233	0,336	4,522	0,316	0,752
	Murashita 2014	1,066	0,044	25,679	0,039	0,969
	Goncu 2015	0,333	0,014	7,889	-0,681	0,496
	Shinn 2016	0,750	0,171	3,293	-0,381	0,703
	Hata 2017	1,192	0,301	4,728	0,250	0,802
	Roshanali 2010	1,000	0,298	3,353	0,000	1,000
	Ghanta 2007	1,766	0,748	4,171	1,297	0,194
	Khallaf 2016	1,105	0,047	26,032	0,062	0,950
Random		1,214	0,752	1,960	0,794	0,427



Supplementary figure 2: Early mortality, suture vs ring repair

Late mortality (ring vs suture)

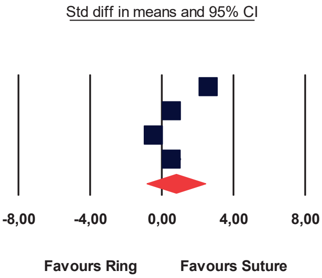
Model	Study name	Rate ratio	Lower limit	Upper limit	Z-Value	p-Value
	Ren 2015	0,283	0,029	2,722	-1,093	0,275
	Murashita 2014	0,398	0,136	1,164	-1,682	0,092
	Kara 2013	0,367	0,041	3,284	-0,896	0,370
	Hata 2017	1,068	0,733	1,556	0,342	0,732
Random		0,670	0,331	1,354	-1,116	0,264



Supplementary figure 3: Late mortality, suture vs ring

Residual TR continuous (ring vs suture)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Huang 2014	2,589	0,128	0,016	2,338	2,840	20,203	0,000
Murashita 2014	0,538	0,182	0,033	0,181	0,894	2,957	0,003
Hata 2017	-0,472	0,078	0,006	-0,625	-0,320	-6,068	0,000
Khallaf 2016	0,526	0,271	0,073	-0,005	1,057	1,942	0,052
	0,796	0,834	0,695	-0,838	2,430	0,954	0,340

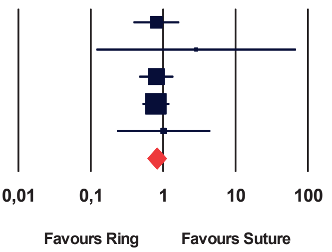


Supplementary figure 4: Residual TR (as continuous variable) suture vs ring

Residual TR catagorical (ring vs suture)

Model	Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
	Huang 2014	0,806	0,390	1,664	-0,584	0,559
	Meng 2015	2,860	0,120	68,229	0,649	0,516
	Hata 2017	0,805	0,469	1,381	-0,787	0,431
	Ghanta 2007	0,795	0,520	1,215	-1,061	0,289
	Khallaf 2016	1,016	0,231	4,469	0,021	0,983
Random		0,817	0,608	1,097	-1,344	0,179

Risk ratio and 95% CI

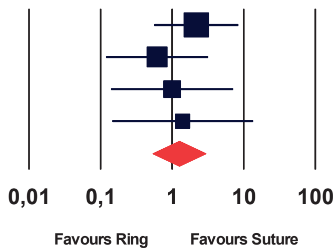


Supplementary figure 5: Residual TR moderate-to-severe (as categorical variable), suture vs ring

Late re-intervention (ring vs suture)

Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
Huang 2014	2,172	0,563	8,383	1,125	0,261
Lin 2014	0,617	0,120	3,168	-0,578	0,563
Shinn 2016	1,000	0,141	7,086	0,000	1,000
Hata 2017	1,404	0,146	13,485	0,294	0,769
	1,253	0,535	2,938	0,519	0,604

Risk ratio and 95% CI

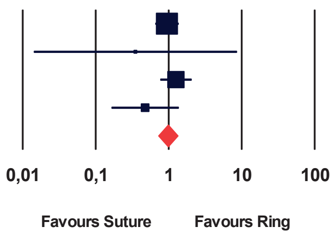


Supplementary figure 6: Late reintervention rate, suture vs ring

Overall TR rate (ring vs suture)

Model	Study name	Rate ratio	Lower limit	Upper limit	Z-Value	p-Value
	Huang 2014	0,947	0,657	1,365	-0,290	0,772
	Meng 2015	0,350	0,014	8,592	-0,643	0,520
	Hata 2017	1,258	0,769	2,058	0,915	0,360
	Khallaf 2016	0,476	0,165	1,372	-1,374	0,170
Random		0,978	0,721	1,328	-0,140	0,889

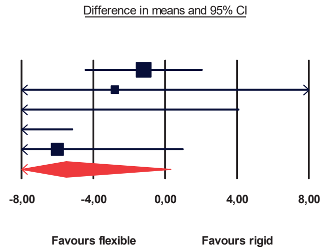
Rate ratio and 95% CI



Supplementary figure 7: Overall TR rate, suture vs ring

CPB time (flexible vs rigid ring)

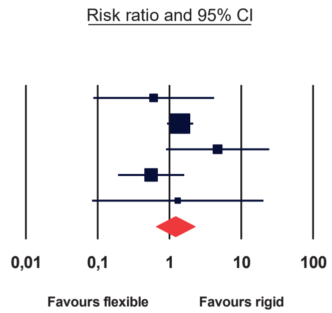
Model	Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Lin 2014	-1,200	1,669	2,787	-4,472	2,072	-0,719	0,472
	Pfannmüller 2012	-2,800	7,644	58,430	-17,782	12,182	-0,366	0,714
	Gatti 2016	-11,000	7,716	59,531	-26,122	4,122	-1,426	0,154
	Ito 2017	-26,000	10,645	113,316	-46,864	-5,136	-2,442	0,015
	Wang 2016	-6,000	3,579	12,806	-13,014	1,014	-1,677	0,094
Random		-5,526	2,972	8,830	-11,350	0,298	-1,860	0,063



Supplementary figure 8: Cardiopulmonary bypass time, flexible vs rigid

Early mortality (flexible vs rigid ring)

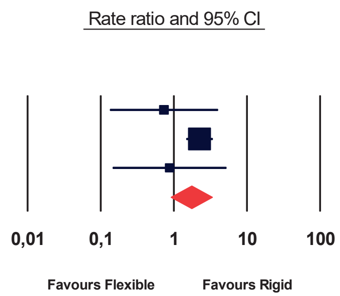
Model	Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
	Lin 2014	0,602	0,087	4,161	-0,514	0,607
	Pfannmüller 2012	1,406	0,928	2,131	1,609	0,108
	Izutani 2010	4,686	0,899	24,413	1,834	0,067
	Gatti 2016	0,556	0,193	1,598	-1,090	0,276
	Wang 2016	1,304	0,084	20,303	0,190	0,850
Random		1,210	0,655	2,239	0,609	0,543



Supplementary figure 9: Early mortality, flexible vs rigid ring

Late mortality (flexible vs rigid ring)

Model	Study name	Rate ratio	Lower limit	Upper limit	Z-Value	p-Value
	Izutani 2010	0,733	0,134	4,000	-0,359	0,719
	Gatti 2016	2,247	1,485	3,400	3,831	0,000
	Wang 2016	0,874	0,146	5,229	-0,148	0,882
Random		1,742	0,912	3,329	1,681	0,093

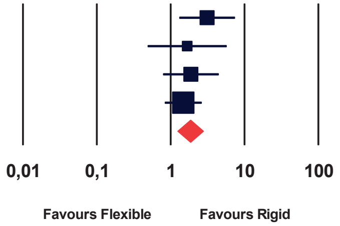


Supplementary figure 10: Late mortality, flexible vs rigid ring

Overall TR rate (flexible vs rigid ring)

Model	Study name	Rate ratio	Lower limit	Upper limit	Z-Value	p-Value
	Izutani 2010	3,116	1,313	7,394	2,577	0,010
	Gatti 2016	1,674	0,490	5,719	0,822	0,411
	Ito 2017	1,878	0,791	4,458	1,430	0,153
	Wang 2016	1,482	0,836	2,629	1,346	0,178
Random		1,843	1,241	2,738	3,029	0,002

Rate ratio and 95% CI



Supplementary figure 11: Overall TR rate, flexible vs rigid ring

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