Tricuspid valve replacement: an appraisal of 45 years of experience

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ABSTRACT

Objectives

This study provides an overview of the change over a 45-year time period in the characteristics and outcome of patients with tricuspid valve disease undergoing surgical tricuspid valve replacement (TVR).

Methods

The characteristics and outcomes of all consecutive TVRs from November 1972 to November 2017 at Erasmus MC were collected retrospectively. A logistic regression analysis was conducted to identify the significant predictors of 30-day mortality. Multivariable Cox regression analysis was used to identify the potential risk factors of patient outcome and the effect of time on these factors.

Results

Ninety-eight patients with tricuspid valve dysfunction underwent 114 consecutive TVRs at a mean age of 50.1 ± 17.2 years (68.5% female). Aetiology changed over time from predominantly functional regurgitation (42.9% in 1972-1985) to predominantly carcinoid heart disease (47.7% in 2001-2017). Early mortality declined significantly from 35% in 1972–1985 to 6.7% in 2001–2017 ($P < 0.001$). Over time, the hazard ratio of late mortality decreased for higher New York Heart Association class, lower preoperative haemoglobin, and high central venous pressure and increased for the presence of preoperative leg oedema, higher creatinine and alkaline phosphatase. The late survival was 43.8% ± 5.89% at 10 years and was comparable among eras ($P = 0.44$). The cumulative incidence of reoperation at 10 years was 14.1% (2.3–26.0) in biological valves and 4.9% (0.1–10.3) in mechanical valves ($P = 0.25$).

Conclusions: Patient characteristics, potential risk factors and patient outcome changed considerably over time in patients undergoing TVR. Notably, there was a shift in aetiology, completely altering the patient population and their characteristics.

ABBREVIATIONS

HR	**Hazard ratio**
RV	**Right ventricular**
TVR	**Tricuspid valve** replacement

INTRODUCTION

Tricuspid valve disease can be classified into functional or structural valve disease. Almost 85% of patients have functional tricuspid valve disease [1], which is related to tricuspid annular dilation and leaflet tethering in the setting of right ventricular (RV) remodelling due to pressure and/or volume overload. Since there is no structural damage, patients are usually eligible for annuloplasty [2, 3]. Tricuspid valve replacement (TVR) is consequently only reserved for advanced stages of functional tricuspid valve disease with severe tethering [2–4]. The second group, consisting of 15% of the population, with structural tricuspid valve disease repair is often not feasible [1, 3, 5]. Possible causes of structural tricuspid regurgitation (TR) are infective endocarditis, rheumatic heart disease, carcinoid syndrome, myxomatous disease, endocardial fibrosis, Ebstein's anomaly and congenitally dysplastic valves, thoracic trauma and iatrogenic valve damage [3]. Compared with aortic or mitral valve replacement surgery, the prevalence of TVR is considerably lower, compromising only 0.7– 2.0% of all valve operations [6, 7]. TVR is, therefore, a relatively rare intervention, only indicated when the repair is not feasible and for those with structural tricuspid valve disease.

Patients with tricuspid valve disease are usually asymptomatic for prolonged periods of time before RV dysfunction or failure develops [4, 5]. Patients referred for TVR are therefore usually either severely disabled by cardiac disease or have undergone previous cardiac procedures [3]. Accordingly, patients undergoing TVR tend to be at higher risk and operative outcomes have traditionally been poor [1, 4]. Operative mortality after TVR has in the past few decades declined despite worsening risk factors, reported to range from 7.7% to 37% [1, 4, 5, 8–17].

Mortality and morbidity rates after TVR have been previously reported [1]. However, a descriptive study describing how these outcomes and risk factors changed over timeis lacking. In this study, we review the change in patient presentation, outcome and risk factors for TVR in a single-centre retrospective cohort study, spanning nearly 5 decades.

METHODS

Patients

We retrospectively reviewed the hospital records for all patients who underwent TVR at our institution, Erasmus MC, between November 1972 and November 2017. Ninety-eight con-

secutive patients with tricuspid valve dysfunction undergoing TVR were identified. In total, 98 patients underwent 114 TVRs, either as an isolated procedure or in combination with another procedure. The population was divided into 3 eras: 1972–1985, 1986–2000 and 2001–2017. Approval was obtained from the institutional medical ethical committee to conduct this study (MEC-2017-135). Informed consent was waived. The final choice of prosthesis type was at the discretion of the attending surgeon. In the case of carcinoid heart disease, a mechanical prosthesis was implanted.

Outcomes

Main outcomes were early (30-day) and late mortality. Secondary outcomes were thromboembolism, bleeding events, endocarditis and reoperation, defined according to the criteria of Akins et al. [18]. Patients were followed until the end of follow-up, death or reoperation. Vital status was checked in the Dutch civil registry on 27 January 2019.

Statistical analysis

Continuous variables were presented as mean ± standard deviation (Gaussian) and as median with interquartile range (non-Gaussian). Categorical data were presented as percentages. Normality was tested using the Shapiro–Wilk test. Comparisons were made with the analysis of variance (ANOVA) or Kruskal–Wallis test in case of a non-Gaussian distribution. Categorical data were compared with the χ^2 test or Fisher's exact test, in case of a cell frequency of <5. Potential predictors of 30-day mortality were identified using a univariable logistic regression analysis.

Both overall mortality and late mortality were calculated and presented as Kaplan–Meier estimates, and log-rank tests were used to compare groups. Unexpected bleeding, valve thrombosis and reoperation were considered a competing risk with mortality and Fine and Gray [19] competing risk models were used to calculate cumulative incidences. Gray's tests were used to quantify significant differences between biological and mechanical valve prostheses. Kaplan–Meier plots for survival were estimated by using individual patients undergoing TVR, whereas the cumulative incidence plots were estimated by using individual tricuspid valve procedures. Change in the weight of the risk factors over time for late mortality (>30 days) was assessed using a multivariable Cox regression analysis, including the risk factor, the year of surgery and the interaction term between these two. Violations of proportional hazard assumption for this Cox regression were checked by using the Schoenfeld residuals. Duration of follow-up was calculated with the inverse Kaplan–Meier method [20]. Completeness of follow-up is calculated with the modified Clarks method (*C) [21]. Statistical analysis was done in R (R Foundation for Statistical Computing, Vienna, Austria, macOS, version 1.1.463) with the use of the 'glm', 'tableone', 'survival', 'survminer' and 'cmprsk' packages.

RESULTS

Follow-up

The mean follow-up of hospital survivors was 24.7 years (range 0.06–40.5 years), with a clinical follow-up completeness of 86.0% (*C). The survival follow-up was 100% (*C) complete. The cumulative total follow-up was 694.78 patient-years.

Patient characteristics

In total, 98 patients underwent 114 consecutive TVR. Sixty-one were female patients (68.5%) with a mean age of 50.1 ± 17.2 years (range 5.4–70.1 years). Table 1 presents the baseline characteristics of these patients. The underlying diseases of these patients included functional (*n* = 20), prosthesis thrombosis (*n* = 4), valve pannus (*n* = 2), repair failure (*n* = 20), endocarditis (*n* = 3), Ebstein's anomaly (*n* = 2), carcinoid (*n* = 27), complex congenital disease (*n* = 3),

Table 1: Baseline characteristics of patients undergoing tricuspid valve replacement

Era	1972–1985	1986–2000	2001–2017	*P*-value
n	**40**	**29**	**45**	
Age (years), median (IQR)	53.23 (35.16–59.03)	53.95 (41.80–60.17)	52.54 (45.39–62.18)	0.593[a]
Female, *n* (%)	22 (59.5)	15 (68.2)	24 (61.5)	0.794[b]
BMI (kg/m^2), median (IQR)	21.09 (19.84–22.62)	22.41 (21.28–23.87)	23.62 (21.43–27.23)	0.008[a]
NYHA, *n* (%)				0.003[c]
I	0 (0.0)	0 (0.0)	2 (5.6)	
II	5 (12.5)	2 (6.9)	9 (25.0)	
III	19 (47.5)	19 (65.5)	23 (63.9)	
IV	16 (40.0)	8 (27.6)	2 (5.6)	
Hepatomegaly, *n* (%)	26 (78.8)	21 (80.8)	19 (45.2)	0.002[b]
Prior cardiac surgery, *n* (%)	25 (62.5)	22 (75.9)	21 (46.7)	0.040[b]
Prior TV related surgery, *n* (%)	7 (17.5)	17 (58.6)	17 (37.8)	0.002[b]
Concomitant surgery, *n* (%)				
Isolated TVR	4 (10.0)	8 (27.6)	15 (33.3)	0.029[c]
PVR	0 (0.0)	7 (24.1)	19 (42.2)	<0.001[c]
AVR	10 (25.0)	5 (17.2)	1 (2.2)	0.004[c]
MVR	25 (62.5)	6 (20.7)	5 (11.1)	<0.001[c]
CABG	2 (5.0)	2 (6.9)	1 (2.2)	0.626[c]
Other	7 (17.5)	14 (48.3)	24 (53.3)	0.001[b]
Aetiology: functional, *n* (%)	18 (47.4)	1 (3.6)	1 (2.3)	<0.001[c]
Urea (mmol/l), median (IQR)	9.45 (6.35–12.80)	7.25 (5.57–10.45)	6.90 (5.20–10.10)	0.276[a]
Creatinine (µmol/l), median (IQR)	85.00 (75.50–99.50)	82.00 (67.00–101.00)	92.00 (69.00–110.00)	0.495[a]

structural valve deterioration of biological prosthesis (n = 12), rheumatic (n = 13), unknown (n = 4) and others (n = 4). Distribution of aetiology changed considerably over time (Fig. 1). Functional tricuspid valve regurgitation decreased significantly over time [18 (45.0%) patients in the first era and 2 (2.7%) patients in the 2 later eras, $P < 0.001$]. Cardiopulmonary bypass time decreased significantly over time ($P = 0.011$). A total of 74 mechanical valves (74.9%) were implanted, proportionally increasing significantly over time ($P < 0.001$). All procedural characteristics are shown in Table 2.

Table 1: Baseline characteristics of patients undergoing tricuspid valve replacement (continued)

Era	1972–1985	1986–2000	2001–2017	*P*-value
Albumin (g/l), median (IQR)	43.00 (35.00–47.00)	44.00 (40.00–46.00)	41.50 (35.00–45.00)	0.242[a]
ASAT (U/l), median (IQR)	27.00 (22.00–31.00)	24.00 (16.00–29.00)	31.00 (24.75–41.00)	0.010[a]
ALAT (U/l), median (IQR)	17.00 (14.00–-25.00)	18.00 (13.00–24.00)	22.00 (17.00–36.00)	0.107[a]
ALP (U/l), median (IQR)	58.00 (43.50–83.00)	72.00 (59.00–162.00)	120.00 (85.00–201.00)	<0.001[a]
Hb (mmol/l), median (IQR)	8.05 (7.50–9.38)	7.30 (6.80–8.60)	7.90 (6.70–8.60)	0.071[a]
Ht, median (IQR)	0.40 (0.36–0.45)	0.37 (0.34–0.40)	0.38 (0.34–0.43)	0.041[a]

[a] Kruskal–Wallis.
[b] χ^2 test.
[c] Fisher's exact test.
ALAT: alanine aminotransferase; ALP: alkaline phosphatase; ASAT: aspartate aminotransferase; AVR: aortic valve replacement; BMI: body mass index; CABG: coronary artery bypass graft; Hb: haemoglobin; Ht: haematocrit; IQR: interquartile range; MVR: mitral valve replacement; NYHA: New York Heart Association; PVR: pulmonary valve replacement; TV: tricuspid valve; TVR: tricuspid valve replacement.

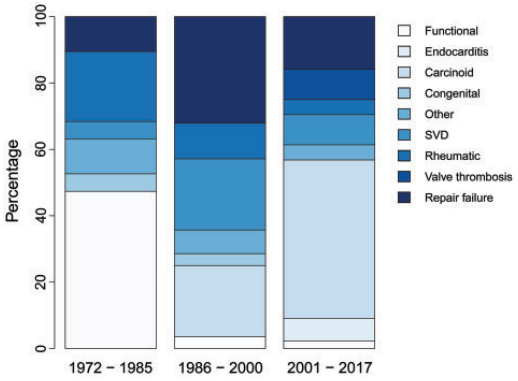

Figure 1: Stacked barplot of different valve aetiologies in 3 eras. SVD: structural valve deterioration.

Early outcomes

In total, 18 (20.2%) patients died within 30 days after TVR. Early mortality declined significantly over time [14 (35.0%) patients in the first era, 1 (3.4%) patient in the second era and 3 (6.7%) patients in the last era, $P < 0.001$]. The causes of early mortality included: heart failure ($n = 10$), thromboembolism ($n = 1$) or others ($n = 7$). The admission duration also decreased significantly from 25.0 days in 1972 to 11.5 days in 2017 ($P < 0.001$). In addition, intensive care unit stay decreased significantly from 7.5 to 2.0 days in 2017 ($P < 0.001$) (Table 2).

Using logistic regression, several determinants were significantly associated with higher 30-day mortality (Table 3). Among others, an earlier era [hazard ratio (HR) 0.29, 95% CI 0.13–0.59; $P = 0.002$] and biological prostheses (HR 0.21, 95% CI 0.07–0.58; $P = 0.004$) were associated with higher 30-day mortality.

Table 2: Procedural characteristics, postoperative outcomes and morbidity described by Akins et al. of patients undergoing tricuspid valve replacement

Era	1972–1985	1986–2000	2001–2017	*P*-value
n	**40**	**29**	**45**	
ACC (min), median (IQR)	110.00 (79.00–147.00)	71.00 (53.00–133.00)	99.00 (65.75–130.50)	0.099[a]
CPB (min), median (IQR)	185.00 (152.50–265.50)	134.00 (105.25–210.25)	140.00 (120.50–191.25)	0.011[a]
Early reopening, *n* (%)	4 (10.0)	1 (3.4)	9 (20.0)	0.108[b]
Mechanical valve prosthesis, *n* (%)	7 (17.5)	23 (79.3)	44 (97.8)	<0.001[c]
Types, *n* (%)				
SJM	1 (2.6)	21 (72.4)	43 (97.7)	<0.001[b]
Hancock	30 (76.9)	2 (6.9)	0 (0.0)	<0.001[b]
Other	8 (20.5)	6 (20.7)	1 (2.3)	0.011[b]
Early mortality (<30 days), *n* (%)	14 (35.0)	1 (3.4)	3 (6.7)	<0.001[b]
Admission duration (days), median (IQR)	25.00 (15.50–35.00)	16.00 (12.50–22.00)	11.50 (10.00–16.25)	<0.001[a]
ICU stay (days), median (IQR)	7.50 (5.75–18.50)	5.00 (4.00–9.00)	2.00 (2.00–3.00)	<0.001[a]

[a] Kruskal–Wallis.
[b] Fisher's exact test.
[c] χ^2 test.
ACC: aortic cross-clamp time; CPB: cross-pulmonary bypass time; ICU: intensive care unit; IQR: interquartile range; SJM: Saint Jude Medical.

Table 3: Univariable logistic regression for early mortality (<30 days) for patients undergoing tricuspid valve replacement

Covariate	Odds ratio (95% confidence interval)	*P*-value
Era	0.294 (0.13–0.59)	0.002
Year of surgery	0.922 (0.87–0.97)	0.026
Age	1.003 (0.97–1.04)	0.822
Female gender	0.47 (0.15–1.43)	0.182

Table 3: Univariable logistic regression for early mortality (<30 days) for patients undergoing tricuspid valve replacement (continued)

Covariate	Odds ratio (95% confidence interval)	*P*-value
Prior TV operation	0.45 (0.12–1.38)	0.193
BMI	0.963 (0.84–1.1)	0.581
Diabetes mellitus	3.5 (0.83–13.26)	0.070
NYHA	2.187 (0.99–5.25)	0.065
ACC	1.011 (1–1.02)	0.439
CPB	1.015 (1.01–1.02)	0.04
Mechanical prosthesis	0.206 (0.07–0.58)	0.004
Dose furosemide	1.011 (1–1.02)	0.014
Dose bumetanide	0.897 (0.41–1.28)	0.665
Concomitant surgery		
AVR	4.3 (1.27–13.92)	0.090
MVR	6 (2.1–18.9)	0.015
PVR	0.167 (0.01–0.88)	0.001
CABG	1.353 (0.07–9.86)	0.792
High CVD	1.236 (0.36–4.92)	0.744
Leg oedema	0.809 (0.2–2.78)	0.744
Atrial fibrillation	2.302 (0.79–7.7)	0.144
Diuretic use	0.685 (0.2– -2.7)	0.556
Aetiology: functional	5.333 (1.74–16.41)	0.003
Prosthesis type		
SJM	0.172 (0.05–0.53)	0.004
Hancock	6.46 (2.2–20.76)	0.001
Other	0.841 (0.12–3.47)	0.831
Urea (mmol/l)	1.139 (1.02–1.27)	0.018
Creatinine (µmol/l)	1.015 (1–1.03)	0.035
Albumin (g/l)	0.954 (0.88–1.03)	0.226
ASAT (U/l)	1.026 (1–1.06)	0.076
ALAT (U/l)	1.016 (1–1.04)	0.103
ALP (U/l)	0.996 (0.99–1)	0.319
Hb (mmol/l)	0.705 (0.44–1.09)	0.130
Ht	0.001 (0–8.61)	0.141

ACC: aortic cross-clamp time; ALAT: alanine aminotransferase; ALP: alkaline phosphatase; ASAT: aspartate aminotransferase; AVR: aortic valve replacement; BMI: body mass index; CABG: coronary artery bypass graft; CPB: cross-pulmonary bypass time; CVD: central venous pressure; Hb: haemoglobin; Ht: haematocrit; MVR: mitral valve replacement; NYHA: New York Heart Association; PVR: pulmonary valve replacement; SJM: Saint Jude Medical; TV: tricuspid valve.

Late outcomes

Eighty patients died during the total follow-up period (18 early and 62 late deaths). The 1-, 5-, 10- and 15-year survival rates were 77.1% ± 4.30%, 56.5% ± 5.22%, 36.9% ± 5.23% and 22.5%

± 4.79%, respectively, and are shown in Fig. 2A. The linearized occurrence rate of late death was 8.9%/year. The 1-, 5-, 10- and 15-year survival rates excluding early mortality were 90.0% ± 3.36%, 65.6% ± 5.50%, 43.8% ± 5.89% and 26.7% ± 5.55%, respectively (Fig. 2B). Causes of late death include heart failure (*n* = 16), non-cardiac related death (*n* = 8), bleeding (*n* = 4), infection (*n* = 4), endocarditis (*n* = 1) and unknown (*n* = 20). When compared over the 3 time periods, the 1-, 5-, 10- and 15-year survival rates did not differ significantly (*P* = 0.44) (Fig. 2C).

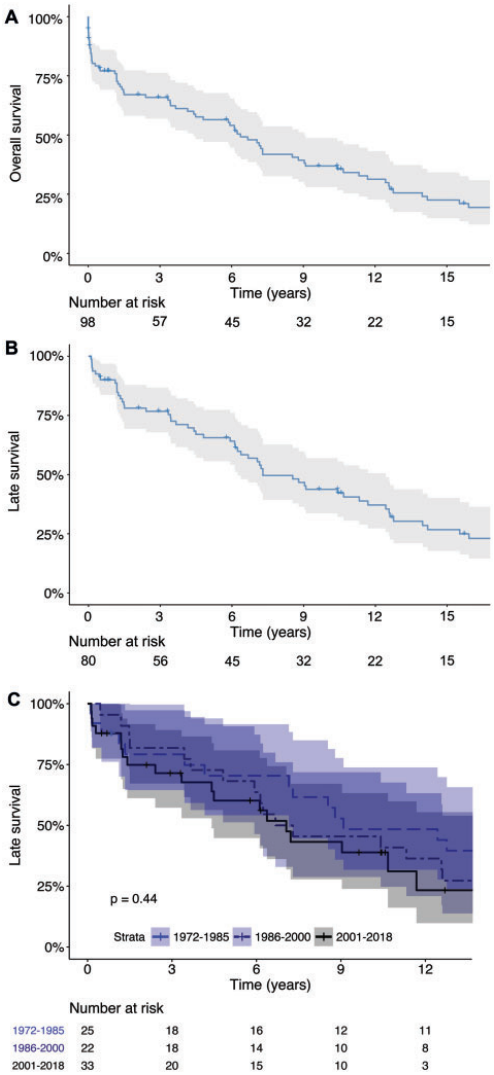

Figure 2: (A) Kaplan–Meier plot of survival (early + late) per patient after tricuspid valve replacement. (B) Kaplan–Meier plot of late survival per patient after tricuspid valve replacement. (C) Kaplan–Meier plot of late survival per patient after tricuspid valve replacement stratified to era.

Furthermore, there was no difference between the survival rate for mechanical and biological prosthesis implantations (*P* = 0.20).

There were 16 TVR reoperations in 13 different patients during the follow-up period [linearized occurrence rate (LOR): 2.4%/ year]. In 9 (36.5%) out of 16 reoperations, a patient had a biological prosthesis previously, whereas 7 (62.5%) reoperations were done in patients with a previous mechanical prosthesis. In patients with a prior mechanical prosthesis, indications for reoperation were valve thrombosis (*n* = 4), pannus (*n* = 2) and subvalular stenosis (*n* = 1). In patients with a prior biological prosthesis, indications for reoperation were structural valve deterioration (*n* = 7) and non structural valve deterioration (NSVD) (*n* = 2). Cumulative incidence of reoperation was comparable between patients receiving a mechanical- and biological valve prosthesis (*P* = 0.25) (Fig. 3). There were also no significant differences in reoperation when mechanical versus bioprosthetic valve replacement was compared over the 3 time periods (*P* = 0.71).

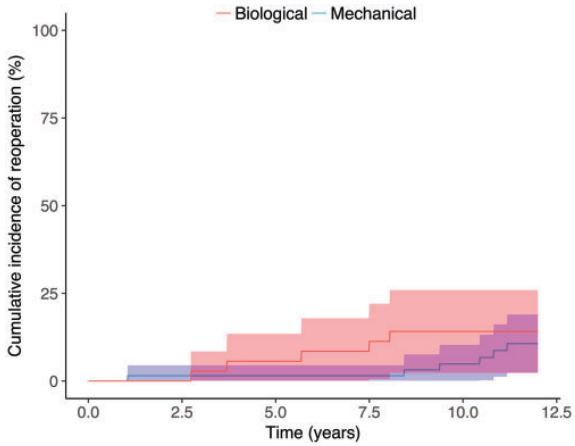

Figure 3: Cumulative incidence of freedom from reoperation after tricuspid valve replacement, mechanical compared to biological valve prosthesis (per procedure).

A bleeding event occurred in 17 patients, and 6 patients had tricuspid valve thrombosis during the follow-up period. Cumulative incidence of bleeding (*P* = 0.14) and valve thrombosis (*P* = 0.072) were comparable between patients receiving a mechanical and biological valve prosthesis (Fig. 4A and B). Four patients had endocarditis at 0.25, 4.57, 4.81 and 6.23 years after initial TVR.

Change in risk factors late mortality

Multivariable Cox regression identified multiple risk factors with either an increased or decreased HR in interaction with time. Over time the HR of late mortality decreased for New York

Heart Association, preoperative haemoglobin and high central venous pressure and increased for preoperative leg oedema, alkaline phosphatase and creatinine (Table 4).

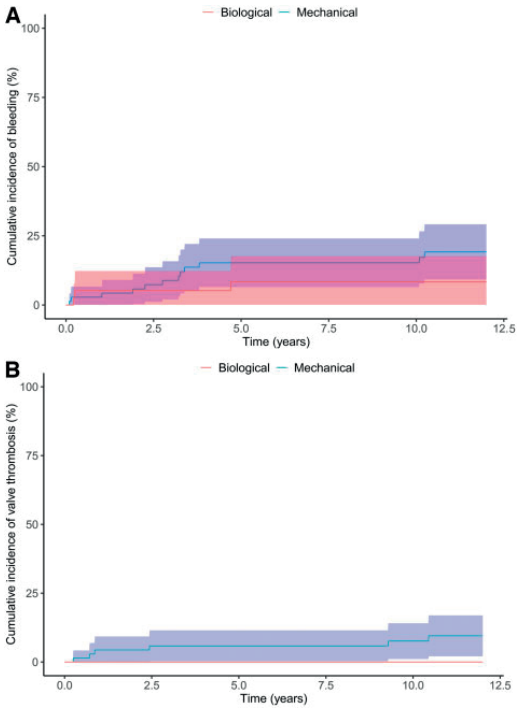

Figure 4: Cumulative incidence of (A) bleeding and (B) valve thrombosis after tricuspid valve replacement, mechanical compared to biological valve prosthesis (per procedure).

Table 4: Cox regression models of late mortality for different risk factors in patients undergoing tricuspid valve replacement

	Variables		**Year**		**Interaction term**	
	Hazard ratio (95% confidence interval)	***P*-value**	**Hazard ratio (95% confidence interval)**	***P*-value**	**Hazard ratio (95% confidence interval)**	***P*-value**
Age	1.02 (0.98–1.06)	0.418	0.93 (0.83–1.03)	0.161	1.00 (0.99–1.00)	0.120
Female gender	1.33 (0.39–4.57)	0.647	1.02 (0.97–1.06)	0.478	0.99 (0.94–1.04)	0.727
Prior TV operation	0.75 (0.17–3.30)	0.71	1.03 (1.00–1.06)	0.021	0.98 (0.93–1.04)	0.556
BMI	0.93 (0.77–1.12)	0.431	0.89 (0.76–1.05)	0.161	1.01 (1.00–1.01)	0.133
NYHA 3–4	9.96 (1.21–82.07)	0.033	1.09 (1.02–1.17)	0.013	0.92 (0.85–0.99)	0.022
Diabetes mellitus	0.02 (0–8.06)	0.206	1.00 (0.97–1.03)	0.853	1.19 (0.98–1.44)	0.078

Table 4: Cox regression models of late mortality for different risk factors in patients undergoing tricuspid valve replacement (continued)

	Variables		Year		Interaction term	
Admission duration	1.07 (1.02–1.12)	0.01	1.06 (1.00–1.12)	0.05	1.00 (0.99–1.00)	0.24
ACC	1.01 (1–1.02)	0.136	1.03 (0.98–1.09)	0.243	1.00 (0.99–1.00)	0.368
CPB	1.01 (1–1.02)	0.034	1.06 (0.98–1.15)	0.176	1.00 (0.99–1.00)	0.371
Mechanical prosthesis	0.98 (0.18–5.44)	0.981	1.01 (0.9–1.15)	0.840	1.00 (0.88–1.14)	0.979
Concomitant surgery						
AVR	1.71 (0.42–7.04)	0.456	1.02 (0.99–1.04)	0.297	1.00 (0.92–1.09)	0.990
MVR	5.14 (1.37–19.29)	0.015	1.03 (1.00–1.07)	0.056	0.94 (0.88–1.01)	0.086
PVR	0.16 (0.01–2.14)	0.165	1.00 (0.97–1.03)	0.823	1.06 (0.98–1.16)	0.139
CABG	0.91 (0.02–48.28)	0.965	1.01 (0.98–1.03)	0.582	1.04 (0.91–1.2)	0.565
High CVD	6.4 (1.4–29.22)	0.017	1.05 (1.00–1.1)	0.053	0.94 (0.89–1.00)	0.045
Leg oedema	1.06 (0.3–3.75)	0.931	0.98 (0.94–1.02)	0.236	1.06 (1.00–1.11)	0.045
Diuretic use	1.97 (0.41–9.6)	0.4	1.01 (0.95–1.08)	0.695	0.99 (0.93–1.06)	0.821
Atrial fibrillation	2.54 (0.43–14.95)	0.302	1.04 (0.98–1.1)	0.211	0.97 (0.91–1.04)	0.427
Aetiology: functional	5.04 (0.63–40.01)	0.126	1.03 (1.00–1.06)	0.086	0.94 (0.78–1.14)	0.524
Urea (mmol/l)	1.05 (0.85–1.29)	0.662	1.00 (0.92–1.08)	0.925	1.00 (0.99–1.01)	0.392
Creatinine (µmol/l)$_{per\ 50}$	1.11 (0.38–3.16)	0.846	0.94 (0.87–1.01)	0.111	1.03 (1.00–1.07)	0.043
Albumin (g/l)	0.99 (0.89–1.09)	0.796	1.07 (0.91–1.25)	0.415	1.00 (1.00–1.00)	0.564
ASAT (U/l)	1.02 (0.98–1.05)	0.407	1.00 (0.94–1.06)	0.954	1.00 (0.99–1.00)	0.652
ALAT (U/l)	1.01 (0.95–1.07)	0.796	1.00 (0.95–1.06)	0.896	1.00 (0.99–1.00)	0.892
ALP (U/l)$_{per\ 50}$	0.79 (0.54–1.15)	0.220	0.97 (0.93–1.01)	0.157	1.01 (1.00–1.02)	0.019
Hb (mmol/l)	1.56 (0.96–2.52)	0.072	1.28 (1.09–1.5)	0.003	0.97 (0.95–0.99)	0.003

Each model contained the risk factor, year of surgery and its interaction term.

ACC: aortic cross-clamp time; ALAT: alanine aminotransferase; ALP: alkaline phosphatase; ASAT: aspartate aminotransferase; AVR: aortic valve replacement; BMI: body mass index; CABG: coronary artery bypass graft; CPB: cross-pulmonary bypass time; CVD: central venous pressure; Hb: haemoglobin; MVR: mitral valve replacement; NYHA: New York Heart Association; PVR: pulmonary valve replacement; TV: tricuspid valve.

DISCUSSION

This study presents the change in outcomes and risk factors over time for patients undergoing TVR in a single-centre retrospective cohort. We found that early mortality decreased significantly and that the prevalence and weight of risk factors changed considerably during our 45-year experience with TVR.

Early outcomes

Early outcomes after TVR have improved significantly over the past several decades [1, 9, 12–14, 22]. The 30-day mortality risk in this study of 20.2% appears to be high, nevertheless is comparable to mortality risks reported in other TVR series, ranging from 7.7% to 37% [1, 4, 5, 8–17]. However, when stratified into the era, the mortality rate during this study period declined significantly [4.1% ($P < 0.001$) after 1986], indicating that early surgical outcomes of TVR improved considerably.

This decline in early mortality and improvement in other early outcomes are probably multifactorial in nature. First, the distribution of patient aetiology changed considerably over time in this series. Prior to 1985, most patients who underwent TVR had functional tricuspid or rheumatic valve disease; thereafter, this shifted to patients having mainly carcinoid disease. The decline in the indication functional TR probably may also be attributed due to the fact that this is more aggressively treated with annuloplasty during left-sided valve surgery, following the publication of Dreyfus et al. [23]. Improved living conditions, nutrition, access to medical care and penicillin use have changed the epidemiology of rheumatic heart disease greatly [24]. The number of patients with carcinoid heart disease receiving TVR increased significantly. This may have several causes, one being that the threshold in the treatment of carcinoid heart disease with TVR has lowered, making the procedure more prevalent [25]. Another cause for the increase in patients with carcinoid heart disease receiving TVR is that Erasmus MC has profiled itself in the Netherlands as a centre of expertise for patients with carcinoid disease in need of TVR. We started implanting a mechanical prosthesis in these patients and did not change our practice following satisfactory results and following reports of accelerated structural valve deterioration in biological prostheses, even though other centres did change their practice [26, 27].

Second, the most common cause for early mortality was low cardiac output (55.6%), comparable to other studies [5]. Since the seventies, there have been made substantial advances in myocardial protection and perioperative care, which may have reduced the incidence of myocardial failure during the early postoperative period. Treatment of low cardiac output syndrome also improved considerably over time [5, 8, 9, 28, 29]. Furthermore, intervention with TVR before the development of RV failure could have reduced early death after TVR.

We noted several predictors for early mortality. The use of a mechanical prosthesis ($P = 0.004$) and the concomitant placement of a pulmonary valve replacement ($P = 0.001$) were

associated with a significant reduction in early mortality. However, these interventions were mainly performed in later eras and, therefore, it is most likely the case that the use of a mechanical prosthesis or the concomitant placement of a pulmonary valve replacement in itself is not responsible for this reduction in early death. It is presumably a confounder of the aforementioned era. Likewise, mitral valve replacement ($P = 0.015$) and aortic valve replacement ($P = 0.090$) were associated with an increase in early mortality. Similarly, these operations were mainly performed in earlier eras and could therefore probably only be partially accountable for the higher early mortality in early eras.

Late outcomes

Kaplan–Meier estimates of 10-year patient survival in our series were 43.8% and comparable to other studies, which reported 10-year survival estimates between 33% and 52% [7, 9, 12, 22]. Strikingly, we did not find any difference in late mortality when stratified to different eras. This might be due to the change in the aetiology and a shift in patient selection throughout the years, which negate the era effect. Several interaction terms were found to be significant in our Cox regression model. This could either indicate that the weight of the risk factors has changed throughout the years, or that simply distribution of these risk factors has become different over the years.

The cumulative incidence for both bleeding and valve thrombosis showed no significant difference between mechanical and biological valve prostheses. Other reports showed comparable results [7, 13, 15, 17]. In addition, our results showed no difference in freedom from reoperation between mechanical and biological valve prostheses, in agreement with other reports [5, 11, 13]. Valve choice should, therefore, be made in a multidisciplinary team taking into account expected lifespan, patient characteristics and informed patient preferences.

Strengths and limitations

Strengths of this study include the duration of follow-up and long inclusion period, which have made it possible to investigate the change in outcomes and risk factors over time. Our study has a couple of limitations mainly being a retrospective observational study in a single centre with all of the inherent limitations of such investigations. Furthermore, due to multiple testing of several variables, it is possible that some statistically observed differences were found by chance. Lastly, TVR is performed rarely, resulting in a small sample size, which prohibited extensive modelling in our patient population.

CONCLUSION

In this study a shift in aetiology over time from primarily functional valve disease to predominantly patients with carcinoid heart disease was observed, completely altering the patient population and their characteristics.

REFERENCES

1. Veen KM, Etnel JRG, Takkenberg J. Tricuspid valve disease—surgical outcome. In: Soliman OI, ten Cate FJ (eds). Practical Manual of Tricuspid Valve Diseases, Vol. 1. Cham, Switzerland: Springer, 2018.
2. Antunes MJ, Rodriguez-Palomares J, Prendergast B, De Bonis M, Rosenhek R, Al-Attar N et al.; on behalf of the ESC Working Groups of Cardiovascular Surgery and Valvular Heart Disease. Management of tricuspid valve regurgitation: position statement of the European Society of Cardiology Working Groups of Cardiovascular Surgery and Valvular Heart Disease. Eur J Cardiothorac Surg 2017;52: 1022–30.
3. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ et al.; ESC Scientific Document Group. 2017 ESC/EACTS guidelines for the management of valvular heart disease. Eur Heart J 2017;38:2739–91.
4. Kilic A, Saha-Chaudhuri P, Rankin JS, Conte JV. Trends and outcomes of tricuspid valve surgery in North America: an analysis of more than 50,000 patients from the Society of Thoracic Surgeons database. Ann Thorac Surg 2013;96:1546–52; discussion 52.
5. Chang BC, Lim SH, Yi G, Hong YS, Lee S, Yoo KJ et al. Long-term clinical results of tricuspid valve replacement. Ann Thorac Surg 2006;81: 1317–23; discussion 23–4.
6. Rizzoli G, Vendramin I, Nesseris G, Bottio T, Guglielmi C, Schiavon L. Biological or mechanical prostheses in tricuspid position? A metaanalysis of intra-institutional results. Ann Thorac Surg 2004;77:1607–14.
7. Ratnatunga CP, Edwards MB, Dore CJ, Taylor KM. Tricuspid valve replacement: UK Heart Valve Registry mid-term results comparing mechanical and biological prostheses. Ann Thorac Surg 1998;66:1940–7.
8. Filsoufi F, Anyanwu AC, Salzberg SP, Frankel T, Cohn LH, Adams DH. Long-term outcomes of tricuspid valve replacement in the current era. Ann Thorac Surg 2005;80:845–50.
9. Van Nooten GJ, Caes F, Taeymans Y, Van Belleghem Y, Francois K, De Bacquer D et al. Tricuspid valve replacement: postoperative and longterm results. J Thorac Cardiovasc Surg 1995;110:672–9.
10. Nakano K, Koyanagi H, Hashimoto A, Ohtsuka G, Nojiri C. Tricuspid valve replacement with the bileaflet St. Jude Medical valve prosthesis. J Thorac Cardiovasc Surg 1994;108:888–92.
11. Kawano H, Oda T, Fukunaga S, Tayama E, Kawara T, Oryoji A et al. Tricuspid valve replacement with the St. Jude Medical valve: 19 years of experience. Eur J Cardiothorac Surg 2000;18:565–9.
12. Dalrymple-Hay MJ, Leung Y, Ohri SK, Haw MP, Ross JK, Livesey SA et al. Tricuspid valve replacement: bioprostheses are preferable. J Heart Valve Dis 1999;8:644–8.
13. Munro AI, Jamieson WR, Tyers GF, Germann E. Tricuspid valve replacement: porcine bioprostheses and mechanical prostheses. Ann Thorac Surg 1995;60(Suppl 2):S470–3; discussion S3–4.
14. Rizzoli G, De Perini L, Bottio T, Minutolo G, Thiene G, Casarotto D. Prosthetic replacement of the tricuspid valve: biological or mechanical? Ann Thorac Surg 1998;66(Suppl 6):S62–7.
15. Scully HE, Armstrong CS. Tricuspid valve replacement. Fifteen years of experience with mechanical prostheses and bioprostheses. J Thorac Cardiovasc Surg 1995;109:1035–41.
16. Nakano K, Ishibashi-Ueda H, Kobayashi J, Sasako Y, Yagihara T. Tricuspid valve replacement with bioprostheses: long-term results and causes of valve dysfunction. Ann Thorac Surg 2001;71:105–9.

17. Van Nooten GJ, Caes FL, Francois KJ, Taeymans Y, Primo G, Wellens F et al. The valve choice in tricuspid valve replacement: 25 years of experience. Eur J Cardiothorac Surg 1995;9:441–6. discussion 6–7.
18. Akins CW, Miller DC, Turina MI, Kouchoukos NT, Blackstone EH, Grunkemeier GL et al. Guidelines for reporting mortality and morbidity after cardiac valve interventions. Ann Thorac Surg 2008;85: 1490–5.
19. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. J Am Stat Assoc 1999;94:496–509.
20. Xue X, Agalliu I, Kim MY, Wang T, Lin J, Ghavamian R et al. New methods for estimating follow-up rates in cohort studies. BMC Med Res Methodol 2017;17:155.
21. Wu Y, Takkenberg JJ, Grunkemeier GL. Measuring follow-up completeness. Ann Thorac Surg 2008;85:1155–7.
22. Carrier M, Hebert Y, Pellerin M, Bouchard D, Perrault LP, Cartier R et al. Tricuspid valve replacement: an analysis of 25 years of experience at a single center. Ann Thorac Surg 2003;75:47–50.
23. Dreyfus GD, Corbi PJ, Chan KMJ, Bahrami T. Secondary tricuspid regurgitation or dilatation: which should be the criteria for surgical repair? Ann Thorac Surg 2005;79:127–32.
24. Carapetis JR, McDonald M, Wilson NJ. Acute rheumatic fever. Lancet 2005;366:155–68.
25. Ito T, Lee L, Jensen RT. Carcinoid-syndrome: recent advances, current status and controversies. Curr Opin Endocrinol Diabetes Obes 2018;25: 22–35.
26. Connolly HM, Schaff HV, Abel MD, Rubin J, Askew JW, Li Z et al. Early and late outcomes of surgical treatment in carcinoid heart disease. J Am Coll Cardiol 2015;66:2189–96.
27. Ridker PM, Chertow GM, Karlson EW, Neish AS, Schoen FJ. Bioprosthetic tricuspid valve stenosis associated with extensive plaque deposition in carcinoid heart disease. Am Heart J 1991;121:1835–8.
28. Jones JM, O'Kane H, Gladstone DJ, Sarsam MAI, Campalani G, MacGowan SW et al. Repeat heart valve surgery: risk factors for operative mortality. J Thorac Cardiovasc Surg 2001;122:913–18.
29. Stocker CF, Shekerdemian LS. Recent developments in the perioperative management of the paediatric cardiac patient. Curr Opin Anaesthesiol 2006;19:375–81.