Laimoud and Fouly
The Cardiothoracic Surgeon (2023) 31:19
https://doi.org/10.1186/s43057-023-00110-0

The Cardiothoracic Surgeon

RESEARCH

Open Access

Outcomes of tricuspid valve regurgitation after heart transplantation; a single center retrospective cohort study

Mohamed Laimoud[1,2*] and Mohamed Fouly[3]

Abstract

Background Tricuspid valve regurgitation (TR) of the donor's heart is a common problem that can develop immediately after cardiac transplantation. There is still little data about its impact on clinical outcomes. We aimed to evaluate the short-term and 1-year effects of significant TR after heart transplantation. We retrospectively analyzed 120 patients who underwent elective orthotopic heart transplantation between 2011 and 2022. According to the postoperative TR, the patients were divided into insignificant (n= 106) and significant (n= 14) TR groups.

Results Patients with significant TR were younger [median age: 38 (Q1- Q3: 36- 39) vs. 49 (35- 55) years, p=0.037] and had a higher prevalence of nonischemic cardiomyopathy (85.71% vs. 42.45%, p=0.003) and donor female gender (35.7% vs. 19.8%,p=0.021). The patients with significant TR had a longer ICU stay [19 (14-27) vs. 11 (9-14) days, p=0.001], more frequent acute kidney injury (57.14% vs. 32.08%, p=0.023), and continuous renal replacement therapy (14.3% vs. 5.66%, p=0.031), with higher 30-day mortality (7.14% vs. 1.9%, p=0.046) and 1-year mortality (14.3% vs. 2.8%, p=0.022) compared to patients with insignificant TR. The degree of TR significantly decreased during the follow-up [β: -0.18 (95% CI: -0.25 to -0.10); p<0.001]. All patients with TR were managed medically without surgical interventions. Logistic multivariable regression revealed that nonischemic heart disease (OR: 3.41,95% CI: 1.31-41.2, p=0.024) and female donor (OR:1.56, 95%CI: 1.13-25.3, p=0.013) independently predicted significant postoperative TR.

Conclusions Significant TR was associated with early mortality and morbidities with prolonged hospitalization. The degree of TR significantly decreased during the first year after transplantation.

Keywords Tricuspid regurgitation, Heart transplantation, Survival

Background

Tricuspid valve regurgitation (TR) is the most common valvular lesion after orthotopic heart transplantation (OHT), with a reported wide incidence (19%-84%) [1–4]. The wide variability in the incidence of posttransplant TR could be attributed to the different designs and populations of the involved studies and the timing of TR diagnosis. Significant TR was linked to decreased survival post-transplantation [3, 5], and several authors recommended prophylactic tricuspid repair; however, no clinical evidence supports this practice [4]. The dynamic state of postoperative TR and response to medical therapy make it difficult to approach and predict the outcomes and survival.

Little data have evaluated the effect of post-transplant TR, and the outcomes are affected by the center volume and experience [4]. We aimed to report the incidence of TR in our transplantation center and its impact on patient outcomes. The primary outcome was 30-day and 1-year mortality, and the secondary outcomes included ICU length of stay, occurrence of acute kidney injury

*Correspondence:
Mohamed Laimoud
m.laimoud@cu.edu.eg; mlaimoud@kfshrc.edu.sa
[1] King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia
[2] Critical Care Medicine department, Cairo University, Cairo, Egypt
[3] Cardiothoracic Surgery Department, Cairo University, Cairo, Egypt

(AKI), and need for continuous renal replacement therapy (CRRT).

Methods

Study design and data collection

The study was a retrospective cohort enrolling patient who underwent orthotopic heart transplantation in a tertiary referral center between October 2011 and January 2022. The study was approved by the ethical committee and given a reference number (2181238). Patients who underwent emergency transplantation or died within the first week after surgery were excluded. Donors with any degree of TR were excluded from this study.

The variables and outcomes

The data were collected from electronic hospital records. The preoperative variables included age, body mass index, gender, underlying heart disease, laboratory variables (creatinine, bilirubin, hemoglobin, and albumin), and right heart catheterization (RHC) data. From RHC, we reported direct measurements of systolic, diastolic, and mean pulmonary artery pressures (PAP). The transpulmonary gradient (TPG) was calculated as the mean PAP - mean pulmonary capillary wedge pressure (PCWP). Pulmonary vascular resistance (PVR) was calculated as TPG divided by cardiac output [6].

Echocardiographic assessment

The assessment of the degree of TR was performed by echocardiographer cardiologists. According to the guidelines, the degrees of TR were none, mild, moderate, or severe [7]. Grading of TR was done using the regurgitation jet area and the width of vena contracta. Assessment of right ventricular function was done using tricuspid annular plane systolic excursion (TAPSE). The enrolled patients were divided into two groups: the significant TR group included moderate or severe TR, and the insignificant TR group included less than moderate degrees of TR.

Statistical analysis

Data were presented as the median (interquartile range) for continuous data and frequency and percent for dichotomous data. According to the normality distribution, continuous data were compared with Student's t test or the Mann–Whitney test. Dichotomous data were compared with the chi-squared or Fisher exact test. The change in the degree of tricuspid regurgitation was evaluated with ordinal logistic mixed effects regression. The coefficient (β) and its confidence intervals were reported. Multiple logistic regression was used to identify factors affecting the occurrence of postoperative tricuspid regurgitation. Significant factors in the univariable analysis were introduced into a multivariable analysis. Stata 17 was used (Stata Corp- College Station- TX), and a p value of <0.05 was considered significant.

Results

Baseline characteristics

The study cohort included 120 adult patients who received bi-caval orthotopic heart transplantation. The median age was [49 (35- 55) vs. 38 (36- 39) years, p=0.037], and the nonischemic underlying cardiomyopathy was (42.45% vs. 85.71%, p=0.003) in the insignificant and significant TR groups, respectively. The two groups had no statistically significant differences regarding other preoperative clinical, laboratory, or pulmonary hemodynamics. The studied variables of the donors were comparable in both groups except higher frequency of female gender donor in the significant TR group (Tables 1 and 2).

Tricuspid regurgitation

Among the 14 patients with significant TR, one had severe right ventricular failure (RVF) and died during the hospital admission. Another two patients with RVF did not improve and continued to have significant RVF and died during the first year after transplantation. For the remaining 11 patients, the degree of tricuspid regurgitation significantly decreased during the follow-up [β: -0.18 (95% CI: -0.25 to -0.10); p<0.001]. Among the patients with postoperative insignificant TR, 17 patients (16.04%) developed severe TR after three months and then regressed in 13 (12.3%) patients after one year, and only 4 (3.8%) patients continued to have severe TR. All patients with TR were managed medically without surgical interventions. Logistic multivariable regression revealed that nonischemic heart disease (OR: 3.41,95% CI: 1.31-41.2, p=0.024) and female donor (OR:1.56, 95%CI: 1.13-25.3, p=0.013) were the independent predictors of significant postoperative TR. Although preoperative age, PVR, and TPG were significantly different between the two groups by univariable analysis, they were insignificant in the logistic regression analysis (Table 3). The data of postoperative RHC and RV functions were summarized in Table 4.

Perioperative data

The patients with significant TR had longer ICU stays [19 (14-27) vs. 11(9-14) days, p=0.001], more frequent AKI (57.14% vs. 32.08%, p=0.023), and CRRT (14.3% vs. 5.66%, p=0.031), with higher 30-day mortality (7.14% vs. 1.9%, p=0.046) and 1-year mortality (14.3% vs. 2.8%, p=0.022) compared to patients with insignificant TR (Table 5 and Fig. 1).

Table 1 Baseline characteristics of patients with and without significant tricuspid regurgitation after heart transplantation

Variables	All patients (*n*=120)	Insignificant TR (*n*= 106,88.3%)	Significant TR (*n*= 14,11.7%)	*p*-value
Age (years)	45(36-53)	49 (35- 55)	38 (36- 39)	0.037
Male gender (n, %)	76(63.3%)	69 (65.09%)	7 (50%)	0.271
BMI (kg/m^2)	28.02(25.6-30.2)	28(24.8-31.2)	27.6(25.6-30.4)	0.81
Hypertension (n, %)	49(40.8%)	45 (42.45%)	4 (28.57%)	0.395
Diabetes mellitus (n, %)	62(51.7%)	58 (54.72%)	6 (42.86%)	0.403
Ischemic heart disease (n, %)	63(52.5)	61 (57.55%)	2 (14.29%)	0.003
Nonischemic heart disease (n, %)	57(47.5)	45 (42.45%)	12 (85.71%)	
Hemoglobin (mg/dl)	97(89-113)	97(91-117)	98(89-114)	0.067
Serum creatinine(μmol/L)	92(68-103)	83(71-116)	98(87-124)	0.1
Serum bilirubin (μmol/L)	8.6(3.9-13.4)	7.8(6.6-17.4)	8.4(6.3-12.4)	0.09
Serum albumin (g/L)	36(34-38.4)	38(34.4-40.2)	37.3(35-38)	0.85
sPAP (mmHg)	35(31-37)	34(30-36)	38(32-41)	0.08
dPAP (mmHg)	21(17-25)	20(17.5-22)	23(20-28)	0.078
Mean PAP (mmHg)	25(21-31)	24.5(22-27)	27(23-31)	0.056
PVR (WU)	2.61(1.97-3.15)	2.34(1.91-3.21)	2.64(2.46-3.24)	0.039
TPG (mmHg)	10(8-13.5)	10 (8-13.2)	11(9-14)	0.041
Pre-operative mechanical ventilation (n, %)	15(12.5)	13(12.3)	2(14.3)	0.53
Pre-operative inotropes (n, %)	36(30)	31(29.2)	5(35.7)	0.71

BMI Body mass index, *sPAP* Systolic pulmonary artery pressure, *dPAP* Diastolic pulmonary artery pressure, *mPAP* Mean pulmonary artery pressure, *TPG* Transpulmonary gradient, *PCWP* Pulmonary capillary wedge pressure, *PVR* pulmonary vascular resistance, *WU* Wood unit.

Data were presented as median (interquartile range) or numbers and percentages

Table 2 The studied variables of the donors

Variables	All patients (*n*=120)	Insignificant TR (*n*= 106)	Significant TR (*n*= 14)	*p*-value
Age (years)	37.3(26-41)	37(25.3-39)	36.4(28-43.6)	0.82
Female gender (n, %)	26(21.7)	21(19.8)	5(35.7)	0.021
BMI (kg/m^2)	26.4(24.6-30.2)	26.1(24.2-29.6)	26.7(24.5-30.1)	0.71
Inotropic support (n, %)	66(55)	57(53.8)	9(64)	0.16
Donor-recipient BMI mismatch (n, %)	44(36.7)	38(35.8)	6(42.9)	0.16
Cause of brain death (n, %)				
Trauma	26(21.7)	22(20.8)	4(28.6)	0.64
Cerebrovascular stroke	94(78.3)	84(79.2)	10(71.4)	

Table 3 Multivariable logistic regression for postoperative significant TR

Variables	OR	95% CI	*p*-value
Age	0.82	0.63-4.87	0.27
Nonischemic heart disease	3.41	1.31-41.2	0.024
Female donor	1.56	1.13-25.3	0.013
Pre-operative PVR	1.26	0.71-8.24	0.38
Pre-operative TPG	1.21	0.82-6.83	0.47

OR Odds ratio, *CI* Confidence interval, *TPG* Transpulmonary gradient, *PVR* Pulmonary vascular resistance

Discussion

The main findings in our cohort were that 11.7% of patients had postoperative significant TR and were younger with more frequent nonischemic cardiomyopathy and more female donors than patients with insignificant TR. Published studies have reported differences regarding the incidence, risk factors, and predictors of posttransplant TR. Bishawi et al. [8] studied 542 patients post-OHT and reported the occurrence of significant TR in 21% of patients without differences in age, BMI,

Table 4 The postoperative RHC and echocardiographic variables

Variables		Insignificant TR	Significant TR	*P* value
sPAP (mmHg)		36(30.4-37.8)	42(38-43.4)	0.051
dPAP (mmHg)		19(16-22.4)	22(19-26)	0.064
Mean PAP (mmHg)		28(24.6-26.4)	32(25-38.2)	0.06
PVR(WU)		1.82(1.61-3.01)	2.15(1.81-3.54)	0.052
TPG (mmHg)		11.2(8.7-12.6)	11.9(9.3-14.7)	0.042
RV function at 1 month (n,%)	Mild dysfunction	54/106(50.9)	3/14(21.4)	0.034
	Moderate dysfunction	48/106(45.3)	8/14(57.1)	
	Severe dysfunction	4/106(3.8)	3/14(21.4)	
RV function at 3 months (n,%)	normal	30/104(28.8)	2/13(15.4)	0.081
	Mild dysfunction	43/104(41.3)	5/13(38.5)	
	Moderate dysfunction	29/104(27.9)	4/13(30.7)	
	Severe dysfunction	2/104(0.96)	2/13(15.4)	
RV function at 6 months (n,%)	normal	52/102(50.98)	4/12(33.3)	0.47
	Mild dysfunction	34/102(33.3)	5/12(41.7)	
	Moderate dysfunction	16/102(15.7)	2/12(16.7)	
	Severe dysfunction	0/102(0)	1/12(8.3)	
RV function at1year (n,%)	normal	60/101(59.4)	6/11(54.5)	0.87
	Mild dysfunction	27/101(26.7)	4/11(36.4)	
	Moderate dysfunction	14/101(13.8)	1/11(9.1)	
	Severe dysfunction	0/101(0)	0/11(0)	

RHC Right heart catheterization, *RV* Right ventricle, *sPAP* Systolic pulmonary artery pressure, *dPAP* Diastolic pulmonary artery pressure, *mPAP* Mean pulmonary artery pressure, *TPG* Transpulmonary gradient, *PVR* Pulmonary vascular resistance, *WU* Wood unit

Table 5 Perioperative data and outcomes in patients with and without significant tricuspid valve regurgitation after heart transplantation

Variables	All patients (*n*=120)	Insignificant TR (*n*= 106)	Significant TR (*n*= 14)	*p*-value
Cardiopulmonary bypass time (minutes)	136(126-140)	132 (129- 139)	138 (128- 141)	0.637
Ischemic time (minutes)	203(168-228)	201(164-234)	194(182-241)	0.31
ICU stay(days)	14(12-21)	11(9-14)	19(14-27)	0.001
Acute kidney injury (n, %)	42(35)	34(32.08)	8(57.14)	0.023
CRRT (n, %)	8(6.7)	6 (5.66%)	2 (14.3)	0.031
30-day mortality	3(2.5)	2(1.9)	1(7.14)	0.046
1-year mortality	5(4.2)	3(2.8)	2(14.3)	0.022

CRRT Continuous renal replacement therapy, *AKI* Acute kidney injury, *ICU* Intensive care unit, *sPAP* Systolic pulmonary artery pressure, *dPAP* Diastolic pulmonary artery pressure, *mPAP* Mean pulmonary artery pressure, *TPG* Transpulmonary gradient, *PVR* Pulmonary vascular resistance, *WU* Wood unit.

Data were presented as median (interquartile range) or numbers and percentages

or operative variables between patients with and without TR. Algarni et al [4] studied 30 patients post heart transplantation and reported occurrence of significant TR in 37% of the patients studied. López-Vilella et al. [3] studied 1009 patients with OHT and reported a 19.8% incidence of significant postoperative TR, and the patients with significant TR were statistically younger without gender differences but with frequent female donors compared to those without significant TR. Recipient female gender was a statistically insignificant variable while donor female gender was significantly more frequent in the significant TR group in our cohort, which was similar to López-Vilella et al. [3], who reported that recipient gender was insignificantly different; however, donor-female gender and donor-recipient sex mismatch were statistically significant predictors of significant TR. Recipient female gender was more frequent (p=0.001) in the significant TR group, and donor male gender was

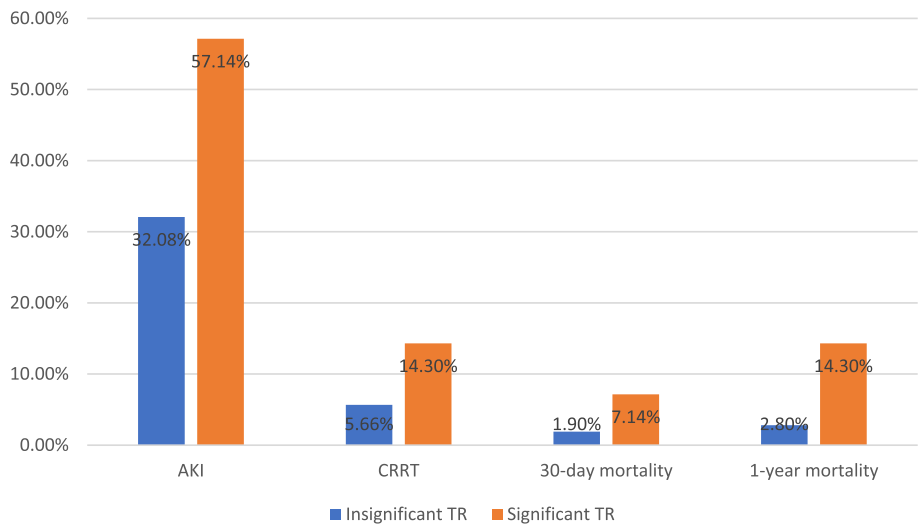

Fig. 1 Outcomes of the patients studied according to TR

associated with a decreased risk of postoperative TR [hazard ratio: 0.4; 95% CI: 0.25-0.66]. Female gender was linked to rapid TR progression in a study that enrolled 946 patients with functional TR [9].

The pre-OHT cardiomyopathy was significantly different in our cohort, and the patients with significant TR had a higher frequency of nonischemic cardiomyopathy. Moreover, nonischemic cardiomyopathy predicted postoperative TR (OR: 3.41,95% CI: 1.31-41.2, p=0.024). Our finding was consistent with previous reports [3, 4, 7] and this could be explained by donor-recipient heart size mismatch in patients with dilated cardiomyopathy. In logistic regression model, nonischemic cardiomyopathy was a predictor of postoperative significant TR. Although age, TPG, and PVR were statistically significant between the two groups in the univariable analysis, they were insignificant in the multivariable logistic regression model. TPG and PVR are frequently used as parameters of pulmonary vascular remodeling but cannot differentiate reversible from fixed pulmonary vascular changes [10].

According to our cohort, significant TR was associated with worse outcomes, prolonged ICU stay, and higher mortality than patients with insignificant TR. Our results are similar to those of Bishawi et al. [8], who linked significant TR with prolonged ICU stay, renal dysfunction, and 1-year mortality. López-Vilella et al. [3] reported a significant association between postoperative significant TR and decreased survival. In other reports, significant TR was linked to different worse outcomes and greater mortality [5, 11–14]. Prophylactic tricuspid valve annuloplasty during OHT was recommended and was performed in a few studies to avoid worse outcomes [15–17]. Marelli and colleagues modified inferior vena cava anastomosis to decrease TR by using a flap from the recipient right atrium (RA) to augment the donor RA wall [15]. The modified bicaval technique was associated with a short ICU stay and eliminated significant TR for one year [15]. Greenberg and colleagues analyzed 330 patients with OHT; 52.4% had a donor TV repair and found no significant benefit or harm regarding mortality, hemodialysis, or tricuspid valve procedures after OHT [16].

Jeevanandam and colleagues conducted a small randomized controlled trial and compared 30 patients with OHT to 30 patients with OHT with DeVega tricuspid annuloplasty [17]. The group with annuloplasty had a shorter reperfusion time, lower mortality, and better right ventricular performance than those without annuloplasty. At the 1-year follow-up, the tricuspid annuloplasty group showed less TR, without a difference in renal function compared to the OHT without annuloplasty group. The study had significant limitations, including underpower and different surgeons; one surgeon performed OHT with tricuspid annuloplasty, and another performed OHT without annuloplasty [17]. In our cohort, at the 1-year follow-up, the TR degree decreased without tricuspid valve procedures. Bishawi et al. [8] reported the improvement of TR over time. Similarly, Algarni et al [4] reported improvement of TR with medical therapy after 6 months of transplantation.

In summary, TR is not a benign postoperative finding, as significant TR was associated with early mortality and morbidities with prolonged hospitalization. The degree of TR significantly decreased during the first year after transplantation.

Limitations of the study

The study was a retrospective cohort with a relatively small number of patients. The study missed data about rejection and long-term survival analysis. Furthermore, it is a single-center experience, and the results may not be generalized to other institutions. The study is also limited by the small number of patients with TR, making the recognition of factors affecting post-transplant TR not feasible.

Conclusions

Significant TR was associated with early mortality and morbidities with prolonged ICU stay. The degree of TR significantly decreased during the first year after transplantation.

Abbreviations

AKI	Acute kidney injury
CRRT	Continuous renal replacement therapy
ICU	Intensive care unit
RHC	Right heart catheterization
TR	Tricuspid regurgitation
TPG	Transpulmonary gradient
OHT	Orthotopic heart transplantation
PAP	Pulmonary artery pressure
PVR	Pulmonary vascular resistance

Acknowledgements

Not applicable.

Authors' contributions

ML and MF participated in study design, data collection, statistical analysis, and manuscript writing.

Funding

The authors did not receive any funds for the study nor publication.

Availability of data and materials

The data of the study is available with the corresponding author.

Declarations

Ethics approval and consent to participate

The study was approved by the ethical committee of King Faisal Heart Center, was given a reference number (2181238) and waived from a specific consent as there is no personal identifiable data or photos.

Consent for publication

Not applicable.

Competing interests

The authors declare that there is no competing interest.

Received: 28 July 2023 Accepted: 18 September 2023
Published online: 25 September 2023

References

1. Mielniczuk L, Haddad H, Davies RA, Veinot JP (2005) Tricuspid valve chordal tissue in endomyocardial biopsy specimens of patients with significant tricuspid regurgitation. J Heart Lung Transplant 24:1586–90
2. Wong RC, Abrahams Z, Hanna M et al (2008) Tricuspid regurgitation after cardiac transplantation: an old problem revisited. J Heart Lung Transplant. 27(3):247–52. https://doi.org/10.1016/j.healun.2007.12.011. (PMID: 18342744)
3. López-Vilella R, Paniagua-Martín MJ, González-Vílchez F, et al. Epidemiological Study of Tricuspid Regurgitation After Cardiac Transplantation. Does it Influence Survival? Transpl Int. 2022 Mar 21;35:10197. https://doi.org/10.3389/ti.2022.10197. PMID: 35387398; PMCID: PMC8979064.
4. Algarni KD, Arafat AA, Pragliola C, et al. Tricuspid Valve Regurgitation After Heart Transplantation: A Single-Center 10-year Experience. J Saudi Heart Assoc. 2020;32(2):213-218. https://doi.org/10.37616/2212-5043.1058
5. Anderson CA, Shernan SK, Leacche M et al (2004) Severity of intraoperative tricuspid regurgitation predicts poor late survival following cardiac transplantation. Ann Thorac Surg 78:1635–42
6. Galie N, Humbert M, Vachiery JL et al (2016) ESC Scientific Document Group. 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension: the Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Heart J 37:67–119
7. Rudski LG, Lai WW, Afilalo J et al (2010) Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr 23:685–713 (quiz 786–8)
8. Bishawi M, Zanotti G, Shaw L, et al. Tricuspid Valve Regurgitation Immediately After Heart Transplant and Long-Term Outcomes. Ann Thorac Surg. 2019 ;107(5):1348-1355. https://doi.org/10.1016/j.athoracsur.2018.10.065. Epub 2018 Dec 5. PMID: 30529215; PMCID: PMC7256852.
9. Prihadi EA, van der Bijl P, Gursoy E et al (2018) Sex differences in progression of tricuspid regurgitation: results from a large-scale echocardiographic study. Circulation 136:A16542
10. Tedford RJ, Beaty CA, Mathai SC et al (2014) Prognostic value of the pretransplant diastolic pulmonary artery pressure–to–pulmonary capillary wedge pressure gradient in cardiac transplant recipients with pulmonary hypertension. J Heart Lung Transplant 33(3):289–97
11. Aziz M, Saad RA, Burgess MI et al (2002) Clinical significance of tricuspid valve dysfunction after orthotopic heart transplantation. J Heart Lung Transplant 21:1101–8
12. Marelli D, Esmailian F, Wong SY et al (2009) Tricuspid valve regurgitation after heart transplantation. J Thorac Cardiovasc Surg 137:1557–9
13. Chan MC, Giannetti N, Kato T et al (2001) Severe tricuspid regurgitation after heart transplantation. J Heart Lung Transplant 20:709–17
14. Sahar G, Stamler A, Erez E et al (1997) Etiological factors influencing the development of atrioventricular valve incompetence after heart transplantation. Transplant Proc 29:2675–6
15. Marelli D, Silvestry SC, Zwas D et al (2007) Modified inferior vena caval anastomosis to reduce tricuspid valve regurgitation after heart transplantation. Tex Heart Inst J 34:30–5
16. Greenberg J, Teman NR, Haft JW et al (2018) Association of donor tricuspid valve repair with outcomes after cardiac transplantation. Ann Thorac Surg 105:542–7
17. Jeevanandam V, Russell H, Mather P et al (2004) A one-year comparison of prophylactic donor tricuspid annuloplasty in heart transplantation. Ann Thorac Surg 78:759–66 (discussion 765–6)

Publisher's Note