ORIGINAL ARTICLE

Endomyocardial Biopsy-related Tricuspid Regurgitation After Orthotopic Heart Transplantation: Single-center Experience

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Background: Damage of tricuspid valve (TV) with resultant tricuspid regurgitation (TR) induced by endomyocardial biopsy (EMB) following heart transplantation has been reported in several studies. This study tried to determine the prevalence of EMB-related iatrogenic damage over tricuspid apparatus following orthotopic heart transplantation and to evaluate its impact on the patients.

Methods: Fifty patients received orthotopic heart transplantation between July 1987 and March 2005. Eleven patients were excluded from the study due to early postoperative mortality or inadequate follow-up. The medical records of the remaining 39 patients were reviewed retrospectively for basic characteristics as well as each attempted EMB. The iatrogenic damage of tricuspid apparatus and serial change of TR were accessed with 2-D and Doppler echocardiography. The obtained data were analyzed for their statistical significance with SPSS (version 12.0).

Results: A total of 373 biopsies were performed on the 39 patients between 1987 and 2005. The follow-up duration was 42.9 ± 26.7 months. The prevalence of TR immediately following heart transplantation was 84.6%, with only 25.6% of patients having moderate or severe TR. At the end of the follow-up, the prevalence of TR increased to 92.3% and 61.5% of patients having moderate or severe TR, respectively. Eight patients (20.5%) had small chordae rupture (SCR) noted after 6.6 ± 3.2 biopsies, and 10 patients (25.6%) had flail tricuspid valve (FTV) after 5.7 ± 5.1 biopsies. Of patients with SCR, 62.5% had progression of TR, and 70% of patients with FTV showed significant TR change.

Conclusion: The prevalence of iatrogenic tricuspid apparatus damage was high in this study. It contributed to the progression of TR significantly regardless of the damage severity. Measurements should be taken for prevention of iatrogenic tricuspid apparatus damage induced by EMB. [*J Chin Med Assoc* 2007;70(5):185–192]

Key Words: endomyocardial biopsy, heart transplantation, tricuspid regurgitation

Introduction

Tricuspid regurgitation (TR) is a common finding after orthotopic heart transplantation, with a prevalence ranging from 47% to 98%.[1] The presence of significant TR has been suggested to have adverse effects on cardiac performance and may eventually lead to right-sided heart failure,[2] which presents symptoms such as fatigue and decreased exercise tolerance associated with hepatomegaly, jugular venous distension and lower-extremity edema. Such condition is refractory to medical management and therefore requires surgical therapy.[3] The cause of TR seems multifactorial, with a wide range of speculations, including: (1) distortion of right atrial geometry following mid-atrial anastomosis of donor and recipient right atrium (RA); (2) ischemic injury of the papillary muscles at the time of transplantation; (3) biopsy-induced injury to the tricuspid valve (TV) apparatus; (4) size mismatch of the donor heart and the pericardial cavity; (5) endocarditis; (6) rejection; and (7) elevation of systolic pulmonary artery pressure (SPAP) and pulmonary vascular resistance.[2,3] Among these speculations, the most widely accepted one is iatrogenic TV apparatus damage induced by endomyocardial biopsy (EMB),[1–4] which is the gold standard method for rejection detection after heart

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transplantation. If significant damage is inflicted on the chordae or leaflet of TV during the biopsy procedure, it might result in flail tricuspid valve (FTV) and cause moderate or even severe TR. This study was to determine the prevalence of TR based on the experience of our institution and to try to evaluate the likelihood of each of the previously proposed speculations of TR. We also focused on the incidence of biopsy-induced TV damage and its impact over the TR grade. We hope this information can give us clues about the most highly influencing cause of TR and help us to prevent it.

Methods

Between July 1987 and March 2005, orthotopic heart transplantations were performed in 50 patients. Eleven patients were excluded from the study group, including 6 patients who survived < 1 month (3 patients died within 7 days after heart transplantation, 2 patients died within 14 days, and 1 patient expired on the 29th day after transplantation) and 5 patients who were lost to follow-up within 3 months after transplantation. The study group thus included 39 patients who received serial right heart catheterization with EMB and echocardiography. The end point of the study for each patient was the mortality of the patient. Thirty patients (77%) were male and 9 were female (23%), with a mean age at transplantation of 46.6 ± 13.0 years (range, 21–67). Patients underwent routine right-sided cardiac catheterization and EMB at 1, 3, 6, 9, 12, 18 and 24 months after the operation and every year thereafter.[5] Once acute rejection was detected and the patient received anti-rejection therapy, an additional biopsy would be repeated 1 month after the treatment. Otherwise, the biopsies were performed as clinically indicated. The mean follow-up length was 42.9 ± 26.7 months, with a range of 6–96 months. A total of 373 biopsies were performed during our study period, with each patient receiving 9.6 ± 6.4 biopsies. The right-sided cardiac catheterization and EMB were carried out by senior cardiologists who had gained experience in such techniques. The pre-transplantation and post-transplantation hemodynamic data including SPAP and pulmonary vascular resistance index were collected with right-sided cardiac catheterization. The left and right ventricular ejection fractions were obtained with first-pass nuclide angiography by injecting Tc-99m DTPA *via* the ante-cubital vein, with data acquisition by a gamma scintillation camera. The wall motion and ejection fraction were then calculated from the data obtained.

Standard mid-atrial anastomosis versus bicaval anastomosis

We have used 2 different anastomosis techniques for heart transplantation in our institution. The standard mid-atrial anastomosis leaves generous right atrial cuffs of donor and recipient hearts. The atrial cuffs are anastomosed together with 3-0 prolene without creating a tension between anastomoses. The bicaval anastomosis method creates separate anastomoses of superior vena cavae and inferior vena cavae between donor and recipient hearts. Therefore, it leaves the structure and geometry of the donor RA intact. In this study, 19 patients received mid-atrial technique and 20 patients underwent bicaval technique. The severity of initial and late TR, incidence of iatrogenic damage and the rate of TR progression were compared between the 2 different anastomosis techniques.

EMB techniques

After obtaining a signed consent form from the patient, we carried out the procedure in our cardiac catheterization room. The right internal jugular vein was punctured and followed by guide wire and sheath introducer. A 10-cm sheath with side arm and backbleed valve was introduced over the guidewire. A Swan–Ganz catheter was inserted with its tip placed at the pulmonary artery under biplanar fluoroscopic guide (posterior–anterior and lateral view), and hemodynamic data were obtained. Under biplanar fluoroscopic guide (30° right anterior-oblique and 60° left anterior-oblique views), a bioptome was guided into the right ventricle and placed against the interventricular septum. Operators withdrew the bioptome about 1 cm and opened the jaws, and then the bioptome was readvanced into contact with endomyocardium. The jaws were closed with a brief delay to sever the tissue, and then the bioptome was withdrawn gently with its enclosed sample. The procedure was repeated to obtain 5 pieces of specimen. The sheath was removed and hemostasis achieved with direct compression over the puncture site of the right internal jugular vein. The puncture wound was covered with sterilized gauze fixed with adhesive tape. The specimens were examined and reported at the pathology laboratory of our institute. Between 1987 and 1991, biopsies were graded for rejection according to the system of Billingham of Stanford University.[6] Between 1991 and 2005, biopsies were graded for rejection according to the Working Formulation of the International Society for Heart and Lung Transplantation.[7]

Echocardiography

All patients received 2-dimensional echocardiography at 1 week after heart transplantation and on the next day following each EMB. The TVs were examined from all views for the presence of iatrogenic damage over chordae or leaflet. We defined extent of iatrogenic damage as flail tricuspid leaflet, which was defined as prolapse of leaflet of the TV with excursion of the leaflet edge and/or free chords into the RA during systole,[1] and SCR, which meant rupture of chordae was evident but excursion and prolapse of tricuspid leaflet was not noted. The degree of TR was graded according to the ratio of the maximum area of the regurgitant jet in the RA to the area of the RA itself using color-flow Doppler echocardiography.[8] We defined regurgitant jet area ratio < 10% as trivial TR, ratio 10–24% as mild TR, ratio 24–49% as moderate TR, and ratio ≥ 50% as severe TR. Change of TR grade ≥ 1 between the early and latest cardiac echogram was taken as progression of TR. Significant change of TR grade appearing simultaneously with iatrogenic damage with tricuspid apparatus was regarded as biopsy-related TR progression.

Data analysis

The data were collected retrospectively from the patients' medical records. They were analyzed with SPSS 12.0 (SPSS Inc., Chicago, IL, USA) for statistical significance. We used 2-sample *t* test for comparison of continuous variables, Fisher's exact test for categorical variables, Kaplan–Meier method for survival rate, and log-rank test for comparison of survival rate. We also used logistic regression to assess risk factors for initial and late significant TR, progression of TR grade as well as iatrogenic damage of tricuspid apparatus. The data were presented as mean ± SD unless otherwise indicated. A p value ≤ 0.05 was considered significant.

Table 1. Patient population profile of the study group

Recipient body weight (kg)	61.9 ± 11.6 (37–89)
Preoperative LVEF (%)	18.8 ± 6.6 (11–23)
Preoperative RVEF (%)	26.7 ± 9.7 (10–37)
Preoperative SPAP (mmHg)	44.5 ± 13.2 (24–69)
PVR index	381.7 ± 384.7 (45.6–1614.0)
Anastomosis technique	
Mid-atrial/bicaval	19/20
Total bypass time	180.0 ± 56.1 (110–360)
Total ischemic time	172.1 ± 53.6 (62–270)
Initial TR grade	
None–mild/moderate–severe	29/10 (74.4%/25.6%)
Late TR grade	
None–mild/moderate–severe	15/24 (38.5%/61.5%)
Postoperative SPAP (mmHg)	35.3 ± 9.8 (19–61)
Postoperative LVEF (%)	49.8 ± 10.5 (26–73)
Postoperative RVEF (%)	50.9 ± 8.8 (26–67)
Follow-up length (mo)	42.9 ± 26.7 (6–96)
Total biopsy number	9.6 ± 6.4 (1–28)
Iatrogenic damage of TV	18 (46.2%)
Number of biopsies when iatrogenic damage occurred	6.1 ± 4.3 (1–14)
Number of rejection episodes	0.6 ± 2.1 (0–10)
Symptoms of right-sided heart failure	5 (12.8%)
4-year survival	65.5%

Data displayed as mean ± SD (range) or number (%) of patients. LVEF = left ventricular ejection fraction; RVEF = right ventricular ejection fraction; TR = tricuspid regurgitation; SPAP = systolic pulmonary artery pressure; PVR = pulmonary vascular resistence; TV = tricuspid valve.

Results

Prevalence and severity distribution of TR

The characteristics of the 39 patients are summarized in Table 1. Initially, 33 of 39 patients (84.6%) were found to have TR; 23 patients (59.0%) had mild TR; 8 patients (20.5%) had moderate TR; and 2 (5.1%) had severe TR. At the end of follow-up, TR was present in 36 out of 39 patients (92.3%), and the distribution of severity shifted to mild/moderate/severe: 12 (30.8%)/16 (41.0%)/8 (20.5%). Progression of TR was noted in 14 patients (35.9%) at the end of follow-up.

Comparison between different severities of TR

We divided our patients into 2 groups according to the severity of TR at the end of follow-up. The patients in the 1st group had none to mild TR ($n = 15$), while those in the second had moderate to severe TR ($n = 24$). We collected variables, including demographic characteristics, hemodynamic characteristics, operative method and time, follow-up length, total biopsy number, iatrogenic damage of TV, number of rejection episodes, symptoms of right-sided heart failure (including hepatomegaly, jugular venous distension, and lower-extremity edema), and 4-year survival, and compared them between the 2 groups, with the results summarized in Table 2.

The moderate–severe TR group had significantly longer follow-up length (29.5 ± 16.6 months *vs.* 51.2 ± 28.7 months, $p = 0.011$), higher rate of iatrogenic damage of TV (7% *vs.* 71%, $p < 0.001$), and higher prevalence of right side heart failure (0% *vs.* 21%, $p = 0.02$). The total biopsy number also was greater in this group (6.5 ± 3.9 *vs.* 11.46 ± 7.04), and the difference also reached statistical significance ($p = 0.018$).

Table 2. Comparison between patients with different severity of tricuspid regurgitation

	None/mild	Moderate/severe	*p*
No. of patients	15	24	
Gender (M/F)	9/6	21/3	
Age (yr)	44.0 ± 13.7	48.3 ± 12.5	NS
Dilative cardiomyopathy (%)	46.7	37.5	NS
Ischemic cardiomyopathy (%)	53.3	62.5	NS
Preoperative LVEF (%)	18.6 ± 3.3	18.9 ± 8.2	NS
Preoperative RVEF (%)	25.5 ± 8.2	27.7 ± 11.0	NS
SPAP (mmHg)	43.9 ± 14.5	44.9 ± 12.9	NS
PVR (dynes s/cm^5)	360.7 ± 369.5	395.2 ± 407.4	NS
Bicaval anastomosis (%)	53%	50%	NS
Total bypass time (min)	189.5 ± 45.6	174.8 ± 61.6	NS
Total ischemic time (min)	165.1 ± 37.9	176.7 ± 64.5	NS
Postoperative SPAP (mmHg)	31.5 ± 7.3	37.4 ± 10.5	NS
Postoperative LVEF (%)	54.2 ± 10.5	47.9 ± 10.1	NS
Postoperative RVEF (%)	53.7 ± 8.3	49.6 ± 9.1	NS
Rejection episodes	0.8 ± 2.1	0.5 ± 2.0	NS
Follow-up length (mo)	29.5 ± 16.6	51.2 ± 28.7	0.011
Total biopsy number	6.5 ± 3.9	11.5 ± 7.0	0.018

Data displayed as mean ± SD or number (%) of patients. LVEF = left ventricular ejection fraction; RVEF = right ventricular ejection fraction; NS = not significant; SPAP = systolic pulmonary artery pressure; PVR = pulmonary vascular resistance.

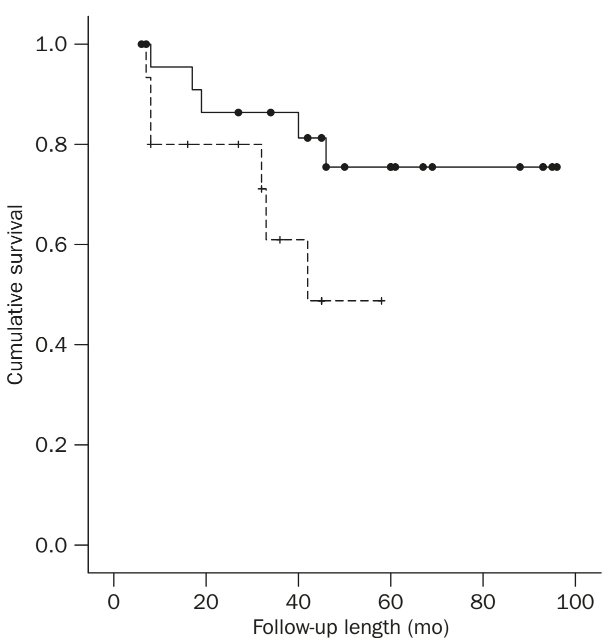

Figure 1. Survival curves of different tricuspid regurgitation (TR) grades. The upper straight line represents patients with moderate to severe TR and the lower dotted line is the survival curve of patients with none to mild TR.

As to the survival rate, the moderate–severe TR group had 75.5% in 4-year survival, in contrast to 48.8% in the none–mild TR group, and they were not statistically different (Figure 1).

Table 3. Comparison between different anastomosis methods

	Mid-atrium	Bicaval	*p*
No. of patients	19	20	
Initial TR grade			NS
None–mild	74%	75%	
Moderate–severe	26%	25%	
Late TR grade			NS
None–mild	37%	40%	
Moderate–severe	63%	60%	
Iatrogenic damage	37%	55%	NS
Progression of TR	36%	35%	NS

TR = tricuspid regurgitation; NS = not significant.

Comparison between different anastomosis techniques

We divided the 39 patients into 2 groups according to their anastomosis technique. The 1st group consisted of 19 patients who received mid-atrial anastomosis technique and the 2nd group was composed of 20 patients who underwent bicaval anastomosis. We compared the initial and late TR grade as well as the rates of iatrogenic damage and progression of TR between the groups. All of the items we compared did not reach statistical significance. The results are summarized in Table 3.

Table 4. Comparison between patients with different severity of iatrogenic damage on tricuspid valve (TV) apparatus

	None	SCR	FTV	*p*
No. of patients	21	8	10	
Late TR grade				0.001
None–mild	67%	12%	0%	
Moderate–severe	33%	88%	100%	
Progression of TR	10%	62.5%	70%	0.001
Total number of biopsies	6.6 ± 4.0	11.6 ± 3.5	14.2 ± 9.1	0.003
Number of biopsies when damage occurred	NA	6.6 ± 3.2	5.7 ± 5.1	NS
Symptoms of right-sided heart failure	14%	0%	20%	NS
4-year survival	34.2%	100%	88.9%	0.006

Data displayed as mean ± SD, number or percentage of patients. SCR = small chordae rupture; FTV = flail tricuspid valve; NA = not available; NS = not significant.

Comparison between different severity of iatrogenic damage

The 39 patients were then divided into 3 groups according to the severity of iatrogenic damage inflicted by EMB over the TV at the end of each follow-up. Twenty-one patients did not sustain any iatrogenic damage over tricuspid apparatus, and they were members of the 1st group. Eight patients were found to have SCR and 10 patients had FTV, and they were brought under the 2nd and the 3rd groups, respectively. We compared the distribution of TR severity, the rate of TR progression, the number of total biopsies, the number of biopsies when iatrogenic damage occurred, the presence of symptoms of right-sided heart failure, and the 4-year survival rate between the 3 groups. As to the distribution of the TR grade, the no-damage group had only 33% of patients with TR grade above moderate. In contrast, 88% of patients in the SCR group and 100% of patients in the FTV group had moderate to severe TR, and the difference was statistically significant ($p = 0.001$). The no-damage group had only 10% of patients with TR progression while the SCR group had 62.5% and FTV group had 70% of patients with progressed TR grade. The difference was also significant ($p = 0.001$). The FTV and SCR groups also had significant higher number ($p = 0.003$) of total biopsies along the follow-up, with the values of 14.2 ± 9.1 and 11.6 ± 3.5, respectively. The iatrogenic damage occurred after 6.6 ± 3.2 biopsies in the SCR group and 5.7 ± 5.1 biopsies in the FTV group, and the difference was not significant between the 2 groups. The rate of symptoms of right-sided heart failure showed no difference among the 3 groups. We finally come to 4-year survival of the 3 groups. Much to our surprise, the no-damage group had only 34.2%, while the SCR group had 100% and the FTV group had 89.9% 4-year survival. We will discuss this unexpected finding in a latter section of this article. The results of comparison among the 3 groups are summarized in Table 4, and the survival curves are shown in Figure 2.

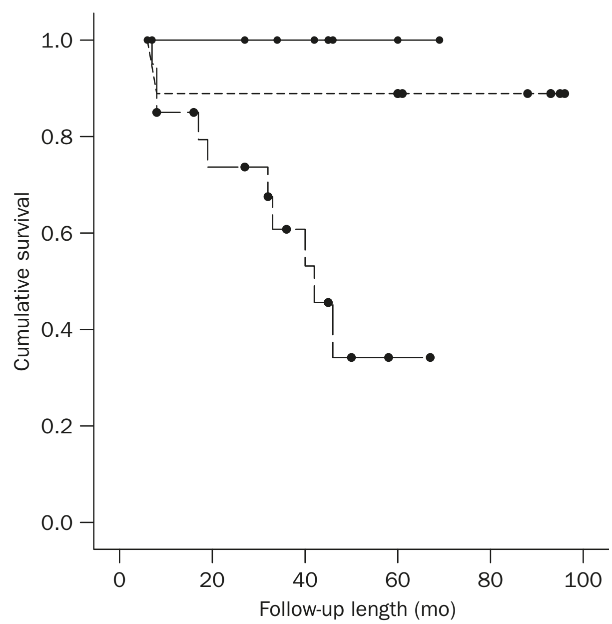

Figure 2. Survival curves of different severity of tricuspid valve (TV) damage: the upper straight line represents the small chordae rupture (SCR) group; the middle dotted line represents the flail tricuspid valve (FTV) group; the lower dashed line represents the no-damage group.

Mortality

Eleven patients expired during the follow-up period. Seven patients (63.6%) died of sepsis due to infections of various microorganisms, and 3 (27.3%) sustained acute rejection and subsequent cardiogenic shock. The remaining 1 patient expired suddenly at our institute, and the cause of mortality could not be clarified, even after autopsy.

Risk factor assessment

We calculated risk factors for initial and late significant TR, progression of TR grade as well as iatrogenic damage of tricuspid apparatus with logistic regression. However, only total biopsy number ≥ 10 reached significance as a risk factor for both iatrogenic damage of TV apparatus ($p = 0.002$), and progression of TR ($p = 0.017$). All of the risk factors we tested for both initial and late TR grade failed to reach statistical significance.

Discussion

Prevalence and severity of TR after cardiac transplantation

High prevalence of TR following orthotopic cardiac transplantation has been documented in many studies.[1–4] TR is not a rare finding in normal subjects, and the prevalence has been reported from 24% to 83%.[2,9,10] However, the severity of TR in normal subjects is mostly trivial to mild. In contrast, a significant portion of patients receiving orthotopic heart transplantation is found to have moderate to severe TR, with the percentage ranging from 5.6% to 85%.[1–4] Moreover, Hausen et al[4] noted the severity of TR progressed with time after heart transplantation in a retrospective study including 251 patients with follow-up length as long as 4 years. In this study, the prevalence of TR was 84.6% immediately after the transplantation, and it increased to 92.3% at the end of the follow-up. The proportion of patients with moderate to severe TR also increased from 25.6% to 61.5%. The results were compatible with those of other series. Therefore, prevalence and the severity of TR after orthotopic heart transplantation seem to have the tendency to progress with time.

Causes of TR

Many hypotheses have been proposed for the causes of TR after cardiac transplantation.

Hausen et al[4] proposed that if preoperative SPAP exceeds 55 mmHg and postoperative pulmonary vascular resistence (PVR) is in excess of 240 dynes s/cm^5, patients are more likely to experience early postoperative TR. However, Williams et al[2] found that early postoperative pulmonary hypertension resolved promptly in most post-transplantation patients in their study of 72 orthotopic cardiac transplant recipients.[2] In other studies, the statistical data also failed to prove the correlation between postoperative TR and preoperative SPAP as well as postoperative PVR.[4,8] In our study, no significant differences of postoperative SPAP and PVR were found between different severities of TR, and logistic regression also failed to prove SPAP and PVR as significant risk factors for early and late TR. Thus, we deem that pulmonary hypertension may not be the major cause of post-transplant TR.

At least 3 different anastomosis techniques have been applied in orthotopic heart transplantation. They are mid-atrial, bicaval, and total techniques. As mentioned earlier, mid-atrial technique connects donor and recipient atrial cuffs, and bicaval technique makes anastomoses between superior and inferior vena cavae of recipient and donor hearts. Total technique involves complete excision of recipient atria with separate bicaval end-to-end anastomoses, as well as pulmonary venous anastomoses.[11] Morgan and Edwards reviewed 39 studies related to comparison of outcome of all these 3 techniques and concluded that bicaval techniques provided anatomic and functional advantages such as decreased valvular insufficiency.[11] However, in this study, we found there was no statistical difference in the initial and late TR grades, incidence of iatrogenic damage as well as rate of TR progression. In addition, Yankah et al[3] noted the incidence of TR after Lower and Shumway technique was very low in their study of 1,124 orthotopic cardiac transplantations at the Deutsches Herzzentrum Berlin. Therefore, it is our opinion that the different anastomosis techniques of orthotopic heart transplantation may not play a key role in the development and progression of TR after orthotopic heart transplantation.

EMB was initially noted to be associated with post-transplantation TR in the early 1990s. Braverman et al[12] reported 5 patients with TV chordae rupture in a study of 81 patients receiving orthotopic heart transplantation. More reports related to iatrogenic damage of tricuspid apparatus induced by EMB were published later. We have summarized the rate of flail tricuspid and TR prevalence as well as TR severity of these studies in Table 5.[1–4,13] Williams et al[2] found the presence of FTV was frequently associated with the development of severe TR after heart transplantation. Hausen et al[4] noted significant correlation between the number of biopsy and the development of TR. In the present study, we found the presence of iatrogenic damage of tricuspid apparatus was significantly related to the presence of moderate to severe TR ($p = 0.001$) and progression of TR ($p = 0.001$). Moreover, the total biopsy number was also significantly correlated to the occurrence of iatrogenic damage ($p = 0.003$). We deem the iatrogenic damage of tricuspid apparatus induced by EMBs might

Table 5. Comparison of tricuspid regurgitation (TR) prevalence and severity between different studies

	No. of patients	TR prevalence (%)	Moderate & severe TR (%)	FTV (%)
Chan et al[1]	336	67	34	NA
Williams et al[2]	72	98	32	14
Yankah et al[3]	647	20.1	5.6	2.3
Hausen et al[4]	251	96	85	13.9
Tucker et al[13]	181	NA	33	21
This study	39	93	61	25

FTV = flail tricuspid valve; NA = not available.

be the most highly influencing factor for the development and progression of TR after heart transplantation.

Acute or chronic rejection was once suspected as a cause of TR after orthotopic heart transplantation. In our series, the rejection episodes were not statistically different between patients with different severity of TR (Table 2). Nonetheless, rejection episodes do really influence the development of TR through the necessity of more frequent EMB. At most heart transplantation institutes, additional EMB is performed if suspected rejection episodes appear. As previously mentioned, the chance of iatrogenic damage of tricuspid apparatus would increase due to this reason.

Relationship between survival and severity of TR

Hausen et al[4] noted that mortality increased with the severity of TR after orthotopic heart transplantation. Nath et al[14] studied 5,223 patients without heart transplantation for 4 years and concluded that increasing TR severity was associated with worse survival. However, the survival curve we obtained in this study was surprisingly beyond our expectations. Shown in Figures 1 and 2, the survival curves of the patients with lesser degree of TR and TV damage seemed worse than for patients with a high degree of TR and TV damage. The only explanation for this unthinkable finding lies in the cause of mortality of our subjects. Eleven patients expired during the follow-up period; 7 patients died of infection, while 3 patients died of acute rejection. Most of the mortality was not directly related to right-sided heart function and the severity of TR. Conversely, the patients who survived longer would inevitably receive more EMBs and thus were more likely to sustain iatrogenic damage of tricuspid apparatus. Therefore, these survival curves just tell us that the patients who survived longer were more likely to sustain TR, but not that the TR made them live longer. We do believe that TR severity impacts survival after orthotopic heart transplantation in the long run. Nonetheless, this difference may not be obvious in our small patient group and relatively short follow-up period.

Prophylactic measurements for TV damage induced by EMB

From the literature we reviewed and the results we obtained in our series, it is our opinion that iatrogenic damage over tricuspid apparatus induced by EMB plays the key role in the progression of post-transplantation TR. Measurements for prevention of iatrogenic damage induced by EMB were tested and reported in some studies. Williams et al[2] thought the incidence of biopsy-related damage could be decreased by minimizing the number of passages of the bioptome across the tricuspid apparatus. Therefore, they used 45-cm long sheath in their routine EMB procedure and successfully reduced the incidence of FTV from 41% to 6% and mean grade of TR from 2 to 1.[1] From previous literature[4,12,15] and the results of our series, we conclude that the total number of EMBs was significantly correlated to the incidence of biopsy-related damage over TVs and chordae. Yankah et al[3] studied 647 patients receiving orthotopic heart transplantation at Deutsches Herzzentrum Berlin. They reduced the frequency of EMB with the aid of intramyocardial electrocardiography (IMEG), which is a noninvasive method to monitor the amplitude of the QRS-complex by telemetric bipolar pacemaker during the sleeping phase of a patient through a normal telephone system at home. EMBs were only arranged when doubtful IMEG and echocardiographic data emerged. They successfully reduced the frequency of EMB from 14.4 to 4.8 biopsies/patient/year. Combined with the utilization of a 45-cm long sheath bioptome, this technology decreased the rate of FTV to 2.3% and prevalence of severe TR to 2.5%. This result was outstanding compared to other studies we have reviewed here (Table 5).

Surgical management for TR after orthotopic heart transplantation

Most low-grade TR following cardiac transplantation can be left alone unless symptoms of right-sided heart failure develop. However, when severe TR and FTV are present, surgical management for TR should be considered. Messika-Zeitoun et al[16] studied 60 patients with

TR induced by FTV. They found patients with flail tricuspid were associated with increased 10-year mortality (39 ± 10%) and TR-related morbidity (75 ± 15%). Poor outcome of medical treatment was confirmed by TR-related event rate (69 ± 9%). They concluded surgical management for TR with FTV had low mortality (3%) and excellent symptomatic improvement (88%). Stahl et al[17] first reported 5 patients with severe TR and right-sided heart failure after heart transplantation receiving TV repair as well as replacement and the operations successfully improved TR grade without mortality in 1995. Yankah et al[3] also operated on 17 patients with severe TR after heart transplantation. Eleven patients received prosthetic valve replacement and 6 patients underwent TV repair. Forty percent of the patients receiving the operation were expected to survive more than 10 years. Therefore, surgical intervention should be beneficial for patients with severe TR and impending right-sided heart failure after heart transplantation.

TR is a fairly common finding in patients receiving orthotopic heart transplantation. The percentage of patients with moderate to severe TR after heart transplantation is higher compared to that of normal subjects, and it tends to increase with time. The iatrogenic damage over TV induced by EMB might play the central role in facilitating progression of TR. The incidence of damage over TV could be reduced through minimizing the frequency of EMB and utilization of 45-cm long sheath bioptome. In the face of severe TR with FTV as well as right-sided heart failure, surgical intervention on TVs has reasonable surgical mortality and provides symptomatic relief as well as survival improvement.

Study limitations

There were several limitations in our series. First, the heart transplantation team in our institute was established around 1995, and many patients who received heart transplantation before this were lost to follow-up due to inadequate education and communication with the patients after the transplantation. The patients who were excluded from the study group increased the bias of the study. Our series was a small-group study, and the follow-up lengths were only feasible for intermediate outcome analysis. Statistical biases were easily created in such condition. Therefore, the results of our study should be taken conservatively. Finally, many variables were unable to be precisely controlled, such as personnel in charge of EMB and cardiac echogram. Further prospective study with larger patient group and longer follow-up is necessary to determine whether the length of biopsy sheath and frequency are able to influence chances of iatrogenic damage of TV apparatus as well as their impact on long-term survival.

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