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Relationship of Tricuspid Repair at the time of Left Ventricular Assist Device Implantation and Survival

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Abstract

Purpose—Tricuspid regurgitation contributes to right ventricular failure (RVF) and is associated with worse clinical outcomes in patients undergoing Left Ventricular Assist Device (LVAD). However, whether tricuspid valve repair (TVR) at the time of LVAD implantation improves outcomes is not clear.

Methods—We identified all patients undergoing initial implantation of a long-term continuous flow LVAD at our institution from 3/2006 to 8/2011. We assessed the impact of TVR on survival and incidence of RVF using Kaplan-Meier curves and proportional hazards regression adjusted for age, gender, baseline tricuspid regurgitation, RV function, MELD score, albumin, and indication (bridge vs. destination).

Results—A total of 101 patients were included in the analysis, of which 14 patients underwent TVR concomitant LVAD. All TVR patients had moderate or severe baseline regurgitation. Crude survival was not different between groups. In multivariable models adjusted for confounding factors, TVR showed a significant association with improved survival (HR=0.1, p=0.049). Adjusted models showed no difference in RVF.

Conclusions—In this cohort of patients TVR at the time of LVAD implantation appears associated with better survival. Additional larger studies are needed to verify the effect of TVR at the time of LVAD implantation, and whether it should be utilized more frequently.

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Conflicts of Interest:

RB- Thoratec (Research) Heartware (Research)

CW- Thoratec (Research)

JM- Thoratec (Research) Heartware (Research)

DL- Thoratec (Research and Speaking) Heartware (Research).

Keywords

Tricuspid Valve Insufficiency; Cardiac Valve Annuloplasty; Heart Failure; Heart; Artificial

INTRODUCTION

The use of continuous flow left ventricular assist devices (LVADs) as bridge and destination therapy for patients with end stage heart failure is growing rapidly as overall outcomes improve.¹⁻³ Despite the positive effects of LVADs on patient mortality, acute and chronic right ventricular failure after LVAD implantation remains a major postoperative complication.⁴ In one report examining implantation of continuous flow LVADs as bridge therapy, 22% of the patients experienced post implant RV dysfunction.⁵ Severe RV dysfunction often results in the need for mechanical RV support or prolonged inotropic support.⁵ Tricuspid regurgitation (TR) is common in patients with RV dilation and dysfunction (almost 50%), and significant pre-operative TR has been associated with longer post-LVAD inotropic support, longer hospital stays and a trend towards greater mortality.^{6,7} LVAD implantation itself may cause an acute increase in TR, possibly by volume over loading the RV.⁸

Given the risk associated with TR and the crucial importance of RV function after LVAD,^{6,9} tricuspid valve repair (TVR) is often considered concomitantly with LVAD implantation. The decision to perform concomitant TVR is obvious in extreme cases; however, many patients have moderate or less severe TR, and importantly the actual assessment of TR severity can vary over time. Other considerations include the concern that TR may worsen after LVAD, as well as the incremental increase in surgical risk by adding to the procedure complexity. Indeed, there is data to suggest that additional procedures performed at the time of LVAD implantation were associated with worse outcomes,¹⁰ but also data indicating that TVR may be beneficial in the setting of LVAD placement. In order to better illuminate the effect of TVR on post-LVAD outcomes, we assessed the association of concurrent TVR during LVAD implantation on the incidence of right heart failure and overall post-LVAD patient mortality.

METHODS

Subjects

The records of all patients who underwent implantation of long term continuous flow LVADS (HeartMate II or HeartWare HVAD) between March 2006 and August 2011 at our institution were reviewed. Clinical data from all available sources were retrospectively reviewed and collected. Operative notes were reviewed to determine if patient underwent TVR at the time of LVAD. All LVAD implantations were performed on cardiopulmonary bypass and without cardioplegic arrest (unless concomitant aortic valve repair replacement was indicated). Tricuspid valve repair was performed with an annuloplasty band (MC3 Edwards ring) in all cases. Baseline characteristics including demographics, pre-operative TR severity, RV function, mean pulmonary artery pressure (mPAP) and MELD scores were noted, and outcomes assessed. The primary endpoint of study was survival, and the

secondary endpoint of interest was incident of RVF after the procedure. RVF was defined as placement of right-sided mechanical support or intravenous inotrope infusion for greater than 2 weeks. The decision to perform TVR for each patient was based on assessment by the operating surgeon at the time of LVAD implantation.

Echocardiography

Preoperative echocardiograms were reviewed and compared to echocardiograms in the immediate post-operative period. A trans-esophageal echocardiogram was also performed during the procedure. All echocardiograms were performed by using standard clinical protocols and interpreted by staff cardiologists at Henry Ford Hospital. The severity of TR and right ventricular dysfunction before LVAD implantation was based on a graded scale of 0 to 3 for the following: none or trace (0), mild (1), moderate (2), and severe (3).

Statistical Analysis

Categorical data are presented as counts and proportions. Continuous variables are expressed as a mean $\pm$ standard deviation (SD). Variables were compared using Student *t* tests or Chi-square tests, as appropriate. Kaplan-Meier survival curves and proportional hazards regression modeling were used to compare survival times between groups using all subjects. A secondary analysis of proportional hazards regression was performed restricted to subjects with baseline TR greater than mild. Logistic regression was used to compare the incidence of RVF between groups. Multivariable models were adjusted for baseline characteristics previously demonstrated to be associated with survival or specified as important potential confounders. These covariates were age, gender, baseline tricuspid regurgitation, RV function, creatinine, albumin, and indication (bridge vs. destination). For all analyses, a *p* value of <0.05 was considered statistically significant. All analyses were performed in SAS version 9.1.3 (SAS Institute, Cary, North Carolina).

RESULTS

101 patients with chronic heart failure underwent implantation of a CF-LVAD at our institution during the study period, of which 14 underwent concomitant TVR. Table 1 shows baseline characteristics for the two groups. All patients who underwent TVR at the time of LVAD implantation had moderate or severe TR at baseline. Forty patients in the LVAD alone group had moderate or severe TR ($n = 3$ with severe). Seven patients in the TVR group (50%) had at least moderately reduced RV function before surgery, compared to 36 patients (41.4%) in the LVAD alone group. The mean age for LVAD patients undergoing TVR was 54 ± 15.3 years with 10 (10%) males and 4 (4%) females, while those who did not undergo TVR had a mean age of 53.2 ± 11.2 , with 65 (64%) males and 22 (22%) females. Devices were implanted as a bridge to transplantation (BTT) in 62 patients and as destination therapy (DT) in 39 patients. Pre-operative serum creatinine, bilirubin, MELD scores, and mean PAP were similar between the groups. Interestingly SGPT differed between groups ($p=0.005$) but SGOT did not. The LVAD implant was complicated by reoperation in 17 patients (19.5%) from the no-TVR group, compared to 2 patients (14.3%) in the TVR group (all except one for bleeding). There was one incidence of device malfunction that required re-operation in the no-TVR group.

Among patients undergoing LVAD without TVR, 76 (87.4%) survived till discharged, while this was 13 (92.9%) in the TVR group (Table 2). Kaplan-Meier survival curves are shown in Figure 1 and did not differ statistically ($p=NS$). After adjustment for possible confounders (age, gender, indication, TVR, baseline RV function, baseline albumin and baseline MELD score) and established predictors of survival post LVAD, TVR showed a significant association with improved survival ($HR=0.1$, $p=0.049$). A sub-group analysis was performed just on patients with moderate or severe tricuspid regurgitation prior to LVAD implantation ($n=54$). This was essentially consistent with the primary analysis revealing protective association (HR for TVR 0.064) of borderline statistical significance ($p=0.065$).

In terms of perioperative RVF, 12 patients (13.8%) in the no-TVR group had RVF post-implant, while 4 patients (28.6%) in the TVR group suffered this, trending towards more RVF in these high-risk subjects ($OR=1.77$, $p=0.43$). However, after adjustment for potential confounders this trend reversed ($OR=0.68$, $p=0.7$), particularly among patients who survived to hospital discharge ($OR=0.29$, $p=0.28$).

DISCUSSION

In our study there is a statistically significant higher survival for the TVR group after adjusting for confounders, though no effect on post-operative RVF was seen. Our results could be viewed as consistent with previous studies that have shown no increase in mortality with concomitant TVR at the time of LVAD implantation,¹¹ and suggest a possible benefit.¹²

Most patients undergoing LVAD implantation have some right heart dysfunction in addition to left heart failure. TR is a common finding in patients with heart failure,¹³ and the incidence of pre-operative TR in LVAD patients was reported to be as high as 50%.¹⁴ Piacentino et al. demonstrated that TR is not reduced immediately after LVAD implantation and is in fact, associated with adverse clinical outcomes post-operatively. While some investigators have argued that as LV failure resolves after LVAD implantation the accompanying decrease in LA pressure and pulmonary congestion decreases RV afterload and improving tricuspid insufficiency¹⁵ there is little evidence that simply reducing RV afterload resolves TR.¹⁶ In addition, increased flow from the LVAD can lead to increased preload returning to the RV, negatively affect RV geometry, and may thus exacerbate tricuspid insufficiency and RVF.

Traditionally, there was some reluctance to repair TR in patients with advanced cardiomyopathy to avoid the acute increase in RV afterload that can occur after TVR. Concern existed that this may lead to acutely increased RV dysfunction as the incompetent tricuspid valve could serve as a 'pop-off' valve, decreasing RV afterload. However, Krishnan et al questioned the pop-off hypothesis and demonstrated no increase in peri-operative mortality, and similar post-operative outcomes in patients who underwent TVR and those who did not.¹⁷ In other studies as well, concomitant tricuspid procedures, in contrast to aortic procedures, have not been associated with an increase in early post-operative mortality.¹⁰ Some more recent studies have demonstrated varying results pointing to at least as good¹¹ or improved^{14,18} clinical outcomes in patients who underwent

concomitant TVR with LVAD implantation, with which our data agree. It is worth noting that our findings of better survival were not mediated via reduced RVF in the perioperative setting. This could be interpreted as showing inconsistency of the data, but alternatively it is possible that the benefit of TVR occurs over a longer period of time. Our existing data do not provide a window into long term incidence of RVF.

Our study has additional limitations worth noting when interpreting the data. This is a modest sized, retrospective review. Thus all potential selection bias can never be eliminated, though we have tried to mitigate this by adjusting for known confounders. The number of patients that underwent repair were relatively small, though our cohort size appears typical of single center LVAD studies. As a result the statistical power of the analysis is limited. However, the main effect size was large, indicating that while there is certainly noise and the HR is overestimated, there is also likely an important signal of possible effect. Regardless, our findings should be interpreted quite conservatively, and further studies with more patients and longer follow-up are needed.

Conclusions

Our results show that concomitant TVR with LVAD implantation in patients with moderate or severe TR appears associated with improved survival and trends towards less RVF. Additional larger observational studies are required to further describe this association, and ultimately a randomized study of subjects with mild to moderate TR would be needed to establish the utility of concomitant TVR at the time of LVAD implantation.

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Figure 1.
Comparison of Kaplan Meier survival between patients who underwent TVR versus those who did not undergo TVR.

Table 1

Baseline Clinical Characteristics of LVAD Patients

Variable	LVAD Alone	TVR
Numbers	87	14
Mean Age (Years)	53.2 ± 11.2	54 ± 15.3
Gender		
Male	65 (64.4%) ²	10 (9.9%) ²
Female	22 (21.8%) ²	4 (4.0%) ²
Race		
Caucasian	53 (52.5%) ²	10 (9.9%) ²
African American	34 (33.7%) ²	4 (4.0%) ²
Indication		
BTT % (N)	61% ()	64 % ()
DT % (N)	39% ()	36 % ()
Etiology of HF		
Ischemic CM	32 (31.7%) ²	2 (2.0%) ²
NIDCM	55 (54.5%) ²	12 (11.9%) ²
RV EF at baseline (echo)		
Normal/mildly reduced		
Moderately reduced		
Severely reduced		
Tricuspid Regurgitation		
None/Mild		
Moderate/Severe		
BSA	2.02 ± 0.27 ¹	1.91 ± 0.27 ¹
BMI	28.74 ±	25.74 ±
Albumin	3.28 ± 0.47 ¹	3.04 ¹ ± 0.64 ¹
DM	41 (40.6%) ²	5 (5.0%) ²
HTN	78 (77.2%) ²	12 (11.9%) ²
Creatinine	1.34 ± 0.46 ¹	1.61 ± 0.66 ¹
COPD*	16 (15.8%) ²	3 (3.0%) ²
Mechanical ventilation	13 (12.9%) ²	5 (5.0%) ²
Reoperation	17 (16.8%) ²	2 (2.0%) ²
SGOT	37.90 ±	32.71 ±
SGPT	46.82 ±	21.00 ±

Table 2

Outcomes of patients undergoing LVAD with TVR vs. those without TVR.

Variable	LVAD (no TVR)	LVAD + TVR
Re-operation Required	17 (19.54%)	2 (14.29%)
Survived to discharge	76 (87.36%)	13 (92.86%)
Length of stay (post-implant)		
RVF post LVAD	12 (13.80%)	4 (28.57%)
Median Survival (days)		