Concomitant tricuspid valve repair in left ventricular assist device implantation may increase the risk for temporary right ventricular support but does not impact overall outcomes

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Abstract

Objectives

Tricuspid valve repair in left ventricular assist device implantation continues to pose a challenge and may impact the occurrence of early and late right heart failure. We investigated the effects of concomitant tricuspid repair on clinical outcomes.

Methods

A retrospective, multicentre study enrolled adult patients who received continuous-flow left ventricular assist devices between 2005 and 2017 and compared those who received concomitant tricuspid valve repair to those who did not. Primary outcomes were early right heart failure necessitating temporary ventricular assist devices and right heart failure-related rehospitalizations requiring inotropic or diuretic treatment.

Results

Out of 526 patients who underwent left ventricular assist device implantation, 110 (21%) received a concomitant tricuspid valve repair. Those patients were sicker, and most had moderate or severe tricuspid regurgitation. A significantly higher incidence of temporary right ventricular assist devices was observed in the group with concomitant tricuspid valve repair (18% vs. 11%, P=.049), with a significantly elevated risk for temporary right heart assist device (sHR 1.68 [95% CI 1.04-2.72], P=.037). After adjusting for confounders, no significant differences were found in the incidence of and risk for most clinical outcomes, including right heart failure-related rehospitalizations (P=.891) and death (P=.563).

Conclusions

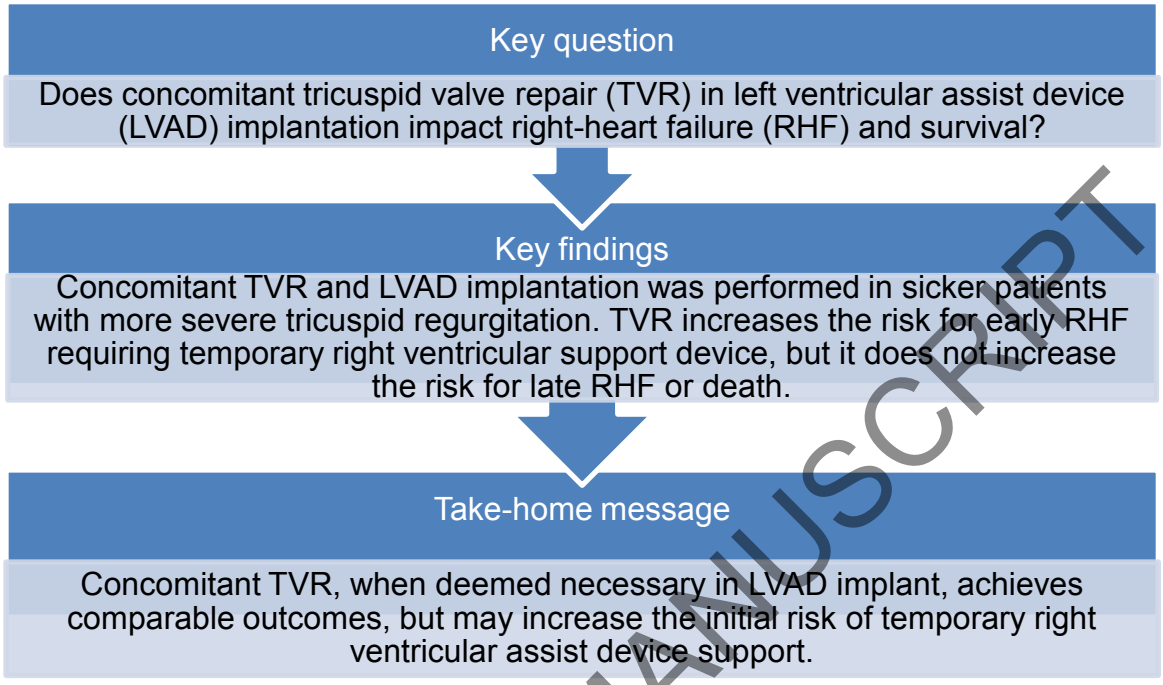
Concomitant tricuspid valve repair, when deemed necessary in left ventricular assist device implantation, may increase the risk of early right heart failure requiring a temporary right ventricular assist device but does not impact the incidence or risk of death or rehospitalizations due to late right heart failure.

Keywords

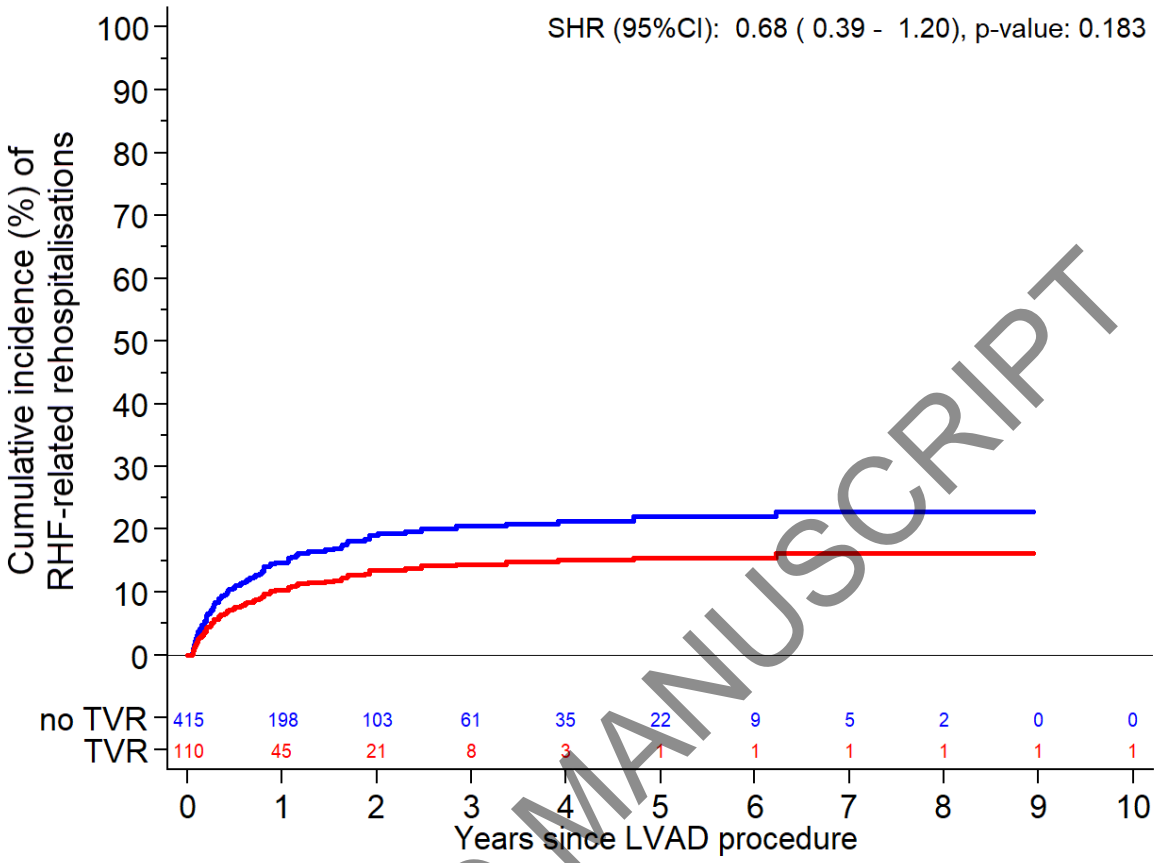
Left Ventricular Assist Device, Tricuspid Valve Repair, Advanced Heart Failure, Right Heart Failure, Rehospitalization

Graphical Abstract

Visual Abstract



Central Image



Introduction

Left ventricular assist device (LVAD) support is an established therapy for end-stage advanced heart failure (HF) (1). However, complications related to LVAD support remain high, and long-term survival is often limited by right heart failure (RHF), occurring in 10% to 40% of patients (1-7). While some risk factors have been identified to help predict and treat RHF following LVAD implantation, it remains unclear how tricuspid regurgitation (TR) impacts the occurrence of RHF and other outcomes (8-16). Thus, we sought to investigate the impact of concomitant tricuspid valve repair (TVR) and LVAD implantation on postoperative outcomes.

Patients and Methods

Study Design. A retrospective, multicentre study was conducted at three tertiary centres.

Inclusion criteria. All adult patients who underwent primary implantation of a HeartMate II (HMII; Abbott, Chicago, IL, USA), HeartMate 3 (HM3; Abbott, Chicago, IL, USA), or HeartWare HVAD (HVAD; Medtronic, Minneapolis, MN, USA) between January 2005 and June 2017 were screened.

Exclusion criteria. Patients were excluded if they received other LVAD devices, a definite biventricular assist device (BiVAD), or a total artificial heart (TAH).

Study period. The follow-up duration included the time from device implantation until death, heart transplantation, device explant, recovery, or lost-to-follow-up, whichever occurred first.

Study grouping. Patients were grouped according to receiving concomitant TVR or not (TVR group vs. non-TVR group). The study did not investigate the indication for performing TVR. Instead, the decision to perform TVR was based on surgeon discretion and included tricuspid ring annuloplasty or DeVega annuloplasty. TV replacement was not performed in any of the included patients.

Primary Outcomes. These included *early RHF*, defined as right ventricular (RV) failure requiring a temporary right-sided ventricular assist device (tRVAD), and *late RHF*, defined as RHF-related rehospitalizations requiring inotropic or diuretic therapy.

Secondary endpoints. These included death and heart transplantation as competing events and rehospitalizations due to device-related major adverse events (MAE) and device-related minor adverse events (AEs). MAEs were defined as pump thrombosis (i.e., outflow graft twist), device malfunction (excluding pump thrombosis), and ischemic or haemorrhagic stroke. AEs were gastrointestinal bleeding (GIB), cardiac arrhythmia, major infection (excluding driveline infections), and driveline infections. Further exploratory endpoints included reinterventions, defined as pump-/outflow graft-exchange, driveline revision, other device-related reoperation, non-device-related cardiac reoperations, and others. For multiple events, each event was seen as a driver for rehospitalisation. Further exploratory endpoints included echocardiographic parameters, including the most recent echocardiographic status before LVAD implantation (baseline echo) and all available postoperative echocardiographic follow-ups.

Data Collection: Data were collected from electronic health records and organized in a central, online database using Research Electronic Data Capture software (REDCap, v11.0.3, Vanderbilt University, Nashville, TN, USA).

Ethics. The study conformed to the principles outlined in the Declaration of Helsinki. The local ethics committees approved the research (Bern 2018-01469, Freiburg 458/18, Houston HSC-MS-20-00510) and waived written informed consent.

Statistical Analysis. The STROBE checklist was used for reporting observational studies. Categorical data are summarized as counts and percentages, and groups were compared using Fisher's, chi-squared, or Student's t tests, as appropriate. Survival analysis techniques were used for time-to-event data with restricted mean survival times of each endpoint calculated at the last follow-up (with 95% confidence interval [CI]). TVR versus non-TVR

groups were compared using Cox regressions and hazard ratios (HR) with 95% CI. P-values from Wald tests are reported. In the time-to-event analysis, heart transplantation and death were considered competing risks for the other secondary outcomes (Fine and Gray models). Recurring events were analysed using robustified Poisson regressions with the offset time under observation and are reflected as incidence risk ratios (IRR) with 95% CI. Adjusted models were constructed by identifying confounders of rehospitalisation due to RHF (chosen from the univariable competing risk regression models including predictors with P<.2) and assuming modal values in case of missing data. The identified confounders included gender, obstructive sleep apnea (OSAS), diabetes, previous mitral valve (MV) surgery or MitraClip (Abbott, Chicago, IL, USA), and device strategy. Other variables were omitted due to prevalence of missing baseline values (LV ejection fraction (LVEF), mitral regurgitation (MR), and TR). The need for tRVAD was analyzed using the Mantel-Haenszel method with; reporting risk ratios and 95% CI with chi-squared tests. To reduce for time bias, the linear effect of "year" was added to the adjusted model. The echocardiographic parameters were analysed with logistic regressions with concomitant tricuspid annuloplasty, years since LVAD implantation and years since LVAD squared as predictors, which included cluster robustification for the patient identifier, to reduce the bias of selective mortality of the "non-improvers". Two- and single-sided P-values <.05 were considered significant for primary and secondary outcomes, respectively. Statistical analyses were performed in Stata/IC17.0 (StataCorp., College Station, TX, USA).

Results

Baseline Demographics and Operative Details

A total of 526 subjects were included in this study. Concomitant TVR was performed in 110 patients (20.9%) (Table 1, Figure S5), with the majority of LVAD implants occurring after 2012 (86.9% of implants). The mean age was 54.5±1.6 years, with similar baseline demographics in the TVR and non-TVR groups, with a few exceptions (Table 1). In short, the TVR group had more male patients, more comorbidities, less severe Interagency Registry for

Mechanically Assisted Circulatory Support (INTERMACS) scores of ≥4, and a higher incidence of preoperative moderate or severe TR and MR. Median sternotomy was performed in most patients (97.7%), and longer cardiopulmonary bypass (CPB) times were observed in the TVR group.

Outcomes Analysis

The follow-up included a cumulative 862.9 patient-years, with a median follow-up time of 464 days (interquartile range [IQR] 147-961) per patient. The mean hospitalization duration was 32.3±28.8 days (P=.719). The primary endpoint of tRVAD support occurred in 18.2% (20/110) of the TVR group but in only 10.8% (45/416) of the non-TVR group (P=.049). The majority of tRVAD support was immediate/non-delayed (P=.034) (Tables 1, 2). The median duration of tRVAD support was 16 days (IQR 10-32; P=.931). In the unadjusted model, patients with TVR had significantly elevated risks for tRVAD support (sHR 1.68 [95% CI 1.04-2.72], P=.037), but no risk increase was found after adjusting for confounders (P=.346) .

RHF-related rehospitalizations accounted for 21.2% of all first rehospitalizations, after a median of 152 days (IQR 62-385; P=.795) (Figure 1, Tables S1, S2), and a calculated rate of 0.16 (95% CI 0.14-0.19) events per patient year. No significant difference in RHF-related rehospitalizations was found after tricuspid repair (P=.183), and a Forrest plot subanalysis found no identifiable risk factor in the investigated parameters for RHF-related rehospitalizations (Table 2, Figures 1, 2, S6).

The median follow-up time of alive patients was 591 days (IQR 147-961; n=303). The cumulative competing risk analysis (Figures 1, 2) shows no significant differences between the groups. Heart transplantation was performed in 143 patients (40.5%) after a median 424 days (IQR 219-743) (Figures 1, 2, S1). Death occurred in 199 patients (56.3%) after a median 194 days (IQR 38-913). The Kaplan-Meier unadjusted estimator for survival at 30 days, 90 days, and 1 year was 91.6%, 83.3%, and 76.9%, respectively (P=.984; Figures 1, 2).

When considering all rehospitalisations irrespective of the cause (1515 rehospitalisations in 356 patients; Table S1), a lower incidence and unadjusted risk reduction was observed in the TVR group (P=.021), but no significance was found in the adjusted model (P=.314; Table 2). No significant differences were found in all other investigated causes of rehospitalisation (Tables 2, S1, Figure 2) or any device- or cardiac-related reinterventions (Tables 2, S1, S2, S3, Figure S3).

A subanalysis of echocardiographic changes one year after LVAD implantation found significant improvement in LVEF>10% (P=.002), irrespective of TVR (Table S2, Figure S4). A protective effect for significant reduction of TR grade ≥1 was observed in the TVR group (unadjusted odds ratio 0.03 [95% CI 0.00-0.22], P<.001) (Table S3); also shown in the linear prediction model for TR in TVR group (Figure S4).

Discussion

Patients in the TVR group had a significantly elevated incidence of early RHF, necessitating tRVAD support. However, after adjusting for identified confounders, no evidence was observed for elevated risk of tRVAD support. Further late RHF-related rehospitalizations and all-cause-mortality were similar between groups. This conforms to existing findings in this field (14-16).

Our data suggest that concomitant TVR and LVAD implantation (i) increases the risk for early RVF and (ii) it does not seem to reduce mortality or rehospitalizations for RHF. However, this should be interpreted with respect to the inherent differences between groups. Patients in the TVR group had more comorbidities, underwent more concomitant procedures, and had more severe TR than the non-TVR group. Thus, while concomitant tricuspid annuloplasty was associated with a higher incidence of and risk for early RHF necessitating tRVAD support, it did reduce TR severity without worsening the outcomes in death and RHF-related rehospitalizations.

We know that late RHF is associated with worse outcomes and elevated mortality in LVAD patients, and the idea behind concomitant TVR is to reduce the overall occurrence of RHF leading to those outcomes (15, 17, 18). Other studies of non-advanced HF populations that undergo concomitant TVR and left-sided heart surgery do not demonstrate reduced overall mortality; however, the procedure reduces symptoms for congestive HF, without increasing perioperative mortality (19). Veen et al. showed that the severity of TR is reduced over time after a successful LVAD implantation (15). In addition, Barac et al. evaluated the durability of successful TR reduction after concomitant TVR in LVAD implantation and found that 37.8% of patients had a TVR failure within six months of LVAD support (15), and the authors concluded that TVR failure was an independent predictor of late RHF (P<.001). Our study was not designed to assess the durability of TVR, limiting our ability to compare our findings. Still, we observed a significantly lower risk for deterioration of TR ≥1 grade compared to baseline (OR 0.03 [95% CI 0.00-0.21], P<.001) in the TVR group. Furthermore, the linear model showed reductions from moderate/severe TR to none/mild TR after concomitant tricuspid annuloplasty; no such change was observed in the non-TVR group. While this is an important observation, the results should be interpreted carefully, as 50% of baseline TVRs are missing.

One of the pathophysiological mechanisms for early RV failure is the initial worsening of TR after LVAD implantation due to leftward interventricular septal shift, and increased preload for the RV generated by the LVAD, ultimately leading to increased RV wall stress and consecutive RV failure (7, 9). While tRVAD support is the treatment of choice, an anticipated and direct tRVAD is associated with superior outcomes compared to a delayed one (20-24). Overall, tRVAD support occurred in 12.4%, consistent with existing data. The most commonly used tRVAD devices included CentriMag (Abbott, St Paul, MN, USA), Levitronix (Levitronix, Zurich, Switzerland) with or without an oxygenator, followed by the use of RV-ECMO. While we did not differentiate between the different devices, the mean duration of support in those who were weaned off RVAD support was comparable between groups, and

similar to length of tRVAD support described elsewhere. Therefore, it remains important to identify patients at risk for early RVF.

Previously identified predictors of RHF, such as pulmonary hypertension, severe TR/MR and inotropic and mechanical circulatory support, are commonly included in several risk scores to predict RV failure after LVAD implantation – such as Michigan (25), Utah (2), Pittsburgh (26), and the EuroMACS risk scores (27), with varying C-statistics between 0.70-0.87. However, these are rarely used in clinical reality; instead, it is often the surgeon's discretion whether to perform TVR and to implant a direct tRVAD support. This decision-making for TVR could not be included in the study due to retrospective design. As some variables were either not collected or had high levels of missing values, we were unable to use these risk scores or include some of the known predictors in the adjusted model, thereby increasing selection and treatment bias. However, since the mean duration of tRVAD support along with the 30-day, 90-day and 1-year mortality were non-different between the groups, these data suggest that those with concomitant TVR had comparable outcomes (late RHF and survival), despite initially having a higher occurrence of tRVAD support.

An important factor to consider is that treatment strategies in the USA and Europe differ, mostly due to regulatory reasons. An example is the use of a calcium sensitizer, levosimendan, which is not available in the USA, but it was readily and routinely used by the two European study centres. A recent study showed a significant reduction in HF-related rehospitalizations in advanced HF patients with intermittent levosimendan infusions (28). However, as our study did not differentiate between inotropic or diuretic agents used during rehospitalizations or during index hospitalization, we are unable to investigate this effect and adjust for a potential treatment bias between centres.

Late RHF is an important predictor of overall survival in LVAD patients, and it is associated with worse quality of life, more frequent rehospitalizations, and worse survival (29). Rich et al. found that late RHF developed in 8% of LVAD patients after a median of 480 days post-LVAD implantation and had a significantly lower 1-year survival compared to those without

late RHF (P<.001) (29). Takeda and colleagues showed that 11% of LVAD patients developed late RHF after a median of 99 days after discharge (30). The incidence of RHF-related rehospitalizations in our study was higher (21.2%) and occurred earlier (median 152 days), but while the absolute incidence of late RHF was lower in the TVR group (16% vs. 23%), this difference was non-significant. Nonetheless, this study was not designed to compare outcomes of those who develop RHF, but instead investigated for the effect of concomitant TVR on the occurrence of RHF. In fact, the difference between groups was non-significant for the incidence, incidence rate, frequency of events per patient year, and for risk of late RHF-related rehospitalizations, or death. In addition, as the median time to first RHF rehospitalisation did not differ between groups, there seems to be no protective effect from TVR on late RHF. This is further supported by the observation that no significant difference was observed in overall mortality.

Our study is subject to the inherent limitations of observational research, in particular, potential confounders due to systemic baseline differences between the TVR and non-TVR groups, inherently leading to possible differences in respective outcomes. Time bias can occur over long observational period, which covered a shift in two devices, and a gradual shift from a less aggressive approach to treat TR, to a more aggressive one. Most devices were HMII, which were gradually replaced with the newer HVAD and HM3 devices that became available in 2011 and 2016, respectively. The HMII was less commonly implanted in the TVR group, but it still accounted for the majority of device implants. Similarly, even though a significantly higher distribution of patients with TVR received the HM3, these were associated with a shorter observation period, as the HM3 has only been available since 2016. Most centres have adopted a more aggressive approach to perform concomitant TVR and LVAD over time. Therefore, a subanalysis was performed to investigate for the effect of time bias per year, but no large effect of time was observed on the investigated outcomes (Figure S5, Table S5). Unfortunately, the study site identifier was not included in analyses; thus, it remains a potential confounder. The median follow-up time was 464 days; thus, our

results are robust for 1-year follow-up. However, careful interpretations is warranted for later outcome probabilities.

Additionally, we did not investigate all AEs (i.e., renal impairment, transfusion requirement, etc.) during the index hospitalization; instead, we focused on those that either led to a reintervention or rehospitalization. This might create a bias in those with poor outcomes during the index hospitalizations. However, the overall occurrence of rehospitalizations due to investigated AEs was comparable to other studies after adjusting for confounders. These confounders were identified to be statistically significant. While other confounders were identified (LVEF, MR and TR), these had too many missing values and could not be considered for adjustment. Conversely, reporting results from parameters with many missing data needs to be interpreted carefully. For example, a large number of baseline echocardiographic parameters are missing (Table 1); thus, the ability to correct for the differences between the groups was limited.

An important limitation is missing information regarding the indication for TVR, which techniques were used, how aggressive the ring downsizing was, how residual the TR was after repair, and other chosen medical therapies. We know that these factors influence not only the patency of tricuspid repair but also the risk for early RHF. Most advanced HF patients have a failing LV and a weak RV. A residual TR might be beneficial for preventing RHF after LVAD implantation, where pathophysiological LVAD increases the RV preload and decreases RV compliance. A tight TV after repair may result in increased RV afterload by closing the back door for the weakened RV, ultimately leading to RV failure. Unfortunately, we could not consider these variabilities due to the retrospective design; these factors should be included in future prospective studies. Because this study was based on all available patients, a formal a priori sample size and power calculation were not performed. Hence, our results do not support causal inferences or give conclusions and recommendations but should be interpreted in terms of associations.

Conclusion

In conclusion, patients who undergo concomitant TVR and LVAD implantation may be associated with an elevated risk for early RHF, necessitating the use of a tRVAD. Still, no significant differences were found regarding rehospitalizations for late RHF or death. Prospective, randomized non-inferiority trials are needed to investigate further.

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Funding Statement

None.

Conflict of Interest Statement

MM has received a non-profit fellowship grant from the Novartis Foundation for Medical-Biological Research. DR is a consultant and proctor for Abbott. Other authors declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions Statement

MM drafted and edited the manuscript and led the analysis; MM, MKJ, JB and TPL contributed to data collection and refinement, and were responsible for obtaining IRBs approvals from their respective institutions. DH contributed to data refinement and led the statistical analysis. FB, RR, IDG, LH, MS and DR significantly edited the manuscript and oversaw the study from design to completion. DR significantly edited the manuscript and supervised the work and submission. All authors agree to be accountable for the content of the work.

Figure Legends

Figure 1. Cumulative incidence for death (A) and RHF-related rehospitalizations (B).

Figure 2. Cumulative first event up to five years as competing event for death, heart transplantation, RHF-related rehospitalizations, no events, and censored patients.

Tables

Table 1. Baseline Data. Legend: LVAD (left ventricular assist device); TVR (tricuspid valve repair); INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support); RVAD (right ventricular assist device).

	LVAD/-TVR (N=416)	LVAD/+TVR (N=110)	p-value	Missing (%)
Age [years]	54.5 (±12.6)	55.0 (±12.6)	0.740	0
Gender (male)	200 (48%)	83 (75%)	<0.001	0
Hypertension	329 (79%)	78 (71%)	0.074	0
Diabetes mellitus	154 (37%)	23 (21%)	0.001	1 (0.2%)
Obstructive sleep apnea	93 (22%)	15 (14%)	0.047	2 (0.4%)
Renal insufficiency	201 (48%)	54 (49%)	0.915	1 (0.2%)
Reoperation	113 (27%)	24 (22%)	0.327	3 (0.6%)
Previous MitraClip	5 (1%)	10 (9%)	<0.001	0
Aetiology				0
ischemic cardiomyopathy	196 (47%)	35 (32%)	0.005	
non-ischemic dilatative cardiomyopathy	174 (42%)	66 (60%)	0.001	
Other	46 (11%)	9 (8%)	0.484	
Left ventricular end-diastolic diameter [mm]	68.2 (±12.0)	71.7 (±9.8)	0.017	108 (20.5%)
Tricuspid annular plane systolic excursion [mm]	15.2 (±5.2)	14.2 (±4.3)	0.181	334 (63.4%)
Mitral regurgitation			<0.001	37 (7.0%)
none	40 (10%)	16 (15%)	0.226	
mild	233 (61%)	19 (18%)	<0.001	
moderate	87 (23%)	41 (39%)	0.002	
severe	24 (6%)	30 (28%)	<0.001	
Tricuspid regurgitation			<0.001	268 (50.9%)
none	28 (18%)	0	<0.001	
mild	72 (46%)	16 (16%)	<0.001	
moderate	47 (30%)	42 (41%)	0.084	
severe	9 (6%)	45 (44%)	<0.001	
INTERMACS Stage			<0.001	0
1	169 (41%)	33 (30%)	0.047	
2	95 (23%)	17 (15%)	0.115	
3	84 (20%)	11 (10%)	0.012	
4	30 (7%)	25 (23%)	<0.001	
5	19 (5%)	9 (8%)	0.151	
6	16 (4%)	12 (11%)	0.007	
7	3 (1%)	3 (3%)	0.109	
Strategy			<0.001	0
Bridge-to-decision therapy	54 (13%)	34 (31%)	<0.001	
Bridge-to-transplant therapy	189 (45%)	51 (46%)	0.914	

Destination therapy	173 (42%)	25 (23%)	<0.001	
Device Type			<0.001	0
HeartMateII	265 (64%)	56 (51%)	0.016	
HeartMate3	49 (12%)	31 (28%)	<0.001	
HeartWare HVAD	102 (25%)	23 (21%)	0.453	
Cardiopulmonary bypass time [min]	88.8 (±41.3)	127.7 (±48.3)	<0.001	56 (10.6%)
Full sternotomy	404 (97%)	110 (100%)	0.131	1 (0.2%)
TVR	0 (0.0%)	110 (100%)	<0.001	0
Mitral valve repair/replacement	14 (3%)	4 (4%)	0.776	0
Aortic valve repair/replacement	22 (5%)	13 (12%)	0.029	0
Coronary artery bypass grafting	15 (4%)	6 (5%)	0.411	0
Other	133 (32%)	80 (73%)	<0.001	0
Hospitalization duration [days]	32.1 (±29.2)	33.9 (±25.4)	0.719	204 (38.7%)
Temporary RVAD*	45 (11%)	20 (18%)	0.049	0
Direct	37 (9%)	18 (16%)	0.034	0
Delayed	8 (2%)	2 (2%)	1.000	0
Change to definitive biventricular assist device	3 (1%)	3 (3%)	0.109	0

*Depicted are counts (% of non-missing data) or means (±1 standard deviation). P-values from Fisher's test (2 x 2 table) or chi-square tests (n x 2 table) or t-test (continuous parameter). *Post-operative primary endpoint*.

Table 2. Primary and secondary endpoints accounting for competing risk (first events only). Legend: LVAD (left ventricular assist device); TVR (tricuspid valve repair)

	LVAD/-TVR	LVAD/+TVR	LVAD/+TVR vs. LVAD/-TVR		LVAD/+TVR vs. LVAD/-TVR	
	N = 416	N = 110	sHR (95% CI)	p-value	aHR (95% CI)	adj. p-value
Primary Endpoints						
Temporary right ventricular assist device *	45 (10.8%)	20 (18.2%)	*1.68 (1.04-2.72)	*0.037	*1.28 (0.76-2.16)	*0.346
Rehospitalisation for right heart failure	79 (22.8%)	14 (16.1%)	0.68 (0.39-1.20)	0.183	1.04 (0.57-1.89)	0.891
Secondary Endpoints						
Death	162 (56.3%)	37 (56.2%)	1.00 (0.70-1.42)	0.984	0.89 (0.61-1.31)	0.563
Heart transplantation	118 (41.0%)	25 (38.9%)	0.94 (0.60-1.45)	0.767	1.06 (0.69-1.65)	0.781
Rehospitalisations:						
Pump thrombosis	21 (6.2%)	7 (8.4%)	1.38 (0.59-3.24)	0.459	1.01 (0.36-2.80)	0.986
Device malfunction	66 (20.1%)	11 (13.9%)	0.67 (0.35-1.26)	0.215	0.69 (0.35-1.37)	0.285
Ischemic stroke	43 (12.7%)	7 (8.4%)	0.65 (0.29-1.44)	0.285	0.78 (0.32-1.86)	0.572
Haemorrhagic stroke	6 (1.9%)	1 (1.3%)	0.68 (0.08-5.82)	0.728	0.70 (0.07-7.27)	0.767
Gastrointestinal bleeding	85 (24.2%)	15 (17.2%)	0.68 (0.40-1.18)	0.173	0.92 (0.54-1.59)	0.778
Infection	114 (32.8%)	21 (24.9%)	0.72 (0.45-1.14)	0.165	0.88 (0.54-1.41)	0.584
Driveline infection	41 (11.7%)	17 (19.3%)	1.73 (0.99-3.05)	0.056	1.40 (0.77-2.54)	0.269
Arrhythmia	58 (16.5%)	11 (12.6%)	0.74 (0.39-1.41)	0.363	1.00 (0.53-1.92)	0.990
Other	202 (57.3%)	27 (30.8%)	0.43 (0.29-0.63)	<0.001	0.59 (0.40-0.87)	0.008
Reinterventions:						
Pump/outflow-graft exchange	92 (26.7%)	16 (19.3%)	0.69 (0.41-1.18)	0.176	0.72 (0.40-1.30)	0.274
Driveline revision	63 (19.4%)	14 (18.9%)	0.97 (0.54-1.75)	0.914	1.20 (0.66-2.17)	0.557
Other device-related	65 (20.1%)	14 (18.9%)	0.93 (0.52-1.68)	0.816	1.15 (0.63-2.09)	0.643
Cardiac non-device related	298 (77.9%)	72 (75.3%)	0.93 (0.72-1.19)	0.546	1.18 (0.89-1.55)	0.244
Other	168 (48.4%)	26 (31.1%)	0.56 (0.37-0.85)	0.006	0.76 (0.49-1.17)	0.207

Number of first events occurring before the competing event/total nr. of first events (Cumulative incidence % from Nelson-Aalen estimator under competing risk with death and heart transplantation). Note that death is under competing risk with heart transplantation and vice versa. Only the first event per patient of each event (sub)type is counted.
**Mantel-Haenszel risk ratio stratified by strategy with 95% confidence intervals, p-value from chi-square test and homogeneity test. One patient died during LVAD operation.*

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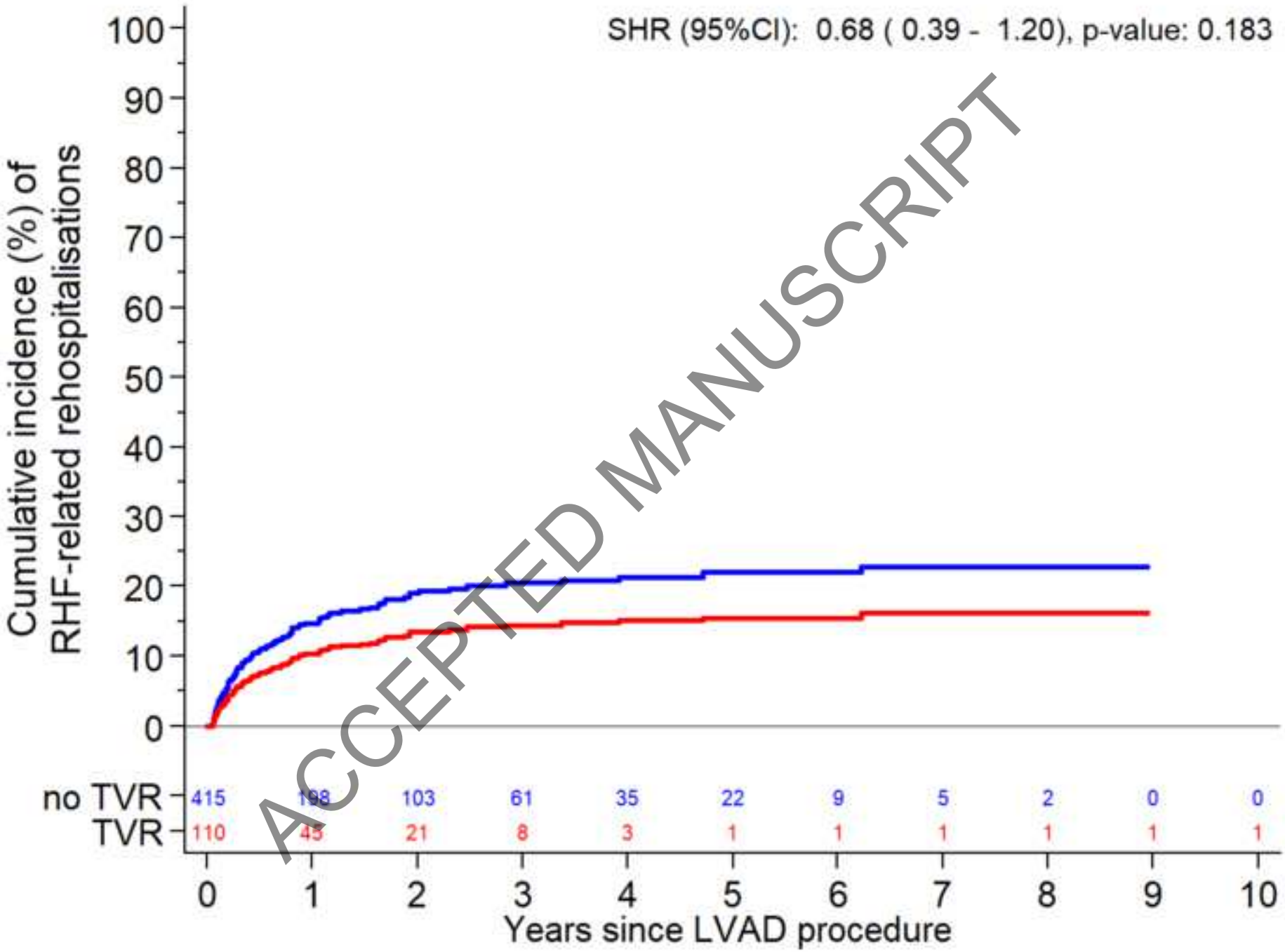
Central image



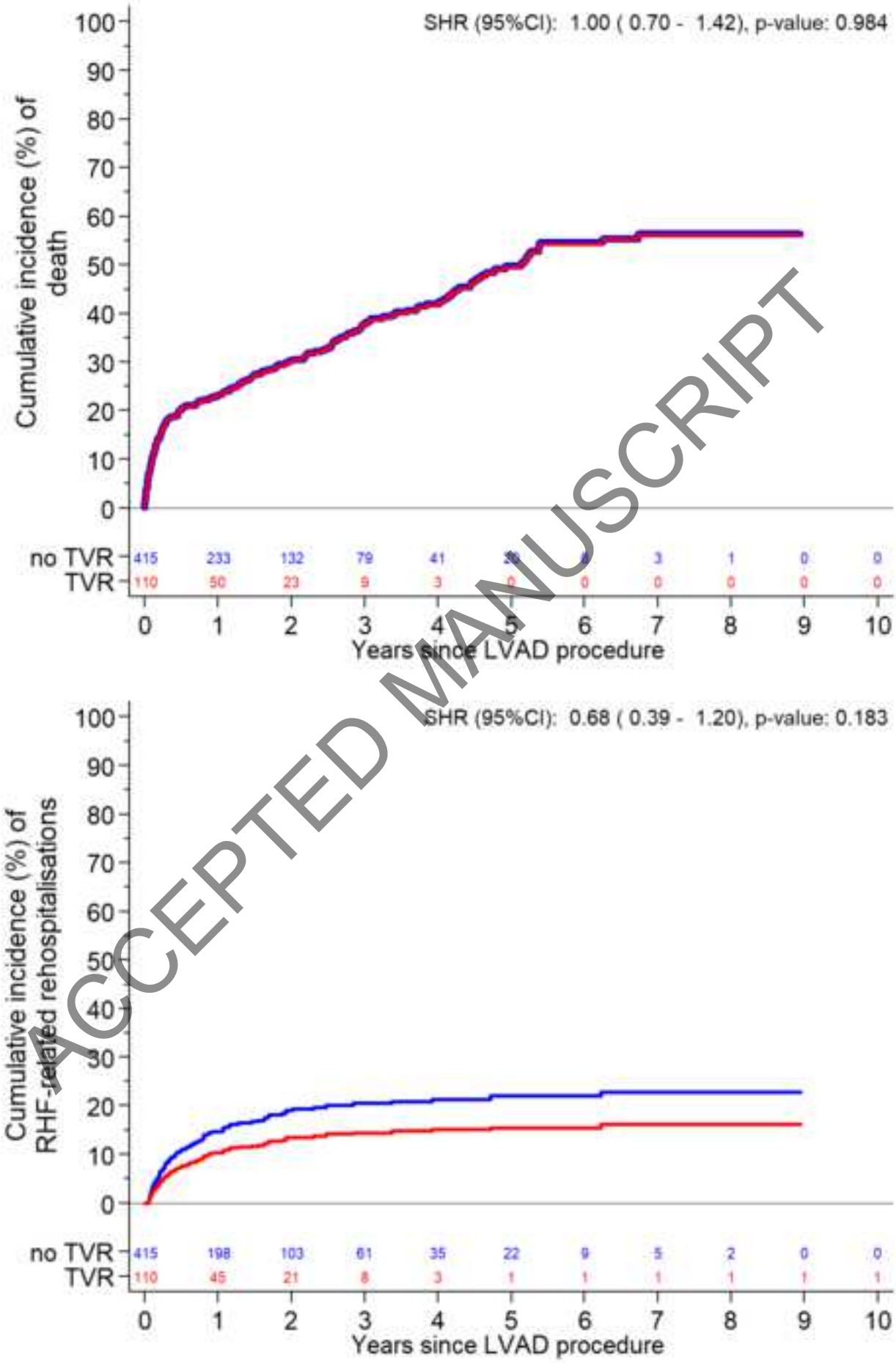


Figure 2