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Clinical Research

The Relationship Between Heart-Failure Hospitalization and Mortality in Patients Receiving Transcatheter Aortic Valve Replacement

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ABSTRACT

Background: Patients who have had transcatheter aortic valve replacement (TAVR) are at risk of hospitalization during the first year postprocedure. Few studies have examined the incidence of heart-failure hospitalizations (HFH) post-TAVR and the impact this has on subsequent hospitalizations and mortality. Our aim was to determine the incidence, predictors, and mortality associated with HFH post-TAVR.

Methods: We used prospectively collected data for all patients who underwent TAVR between August 1, 2010, and March 31, 2015; 742 consecutive patients who underwent TAVR during the study period were included. Patients were followed for a minimum of 1 year post-TAVR.

Results: Mean age was 80.9 ± 8.1, and 58.2% were men. Hospitalizations post-TAVR occurred in 20% of patients at 30 days and 59.7% at 1 year. Of patients hospitalized, HFH was the primary cause of hospitalization in 25.8% and 21.4% of patients at 30 days and 1 year post-TAVR, respectively. Patients with HFH at either 30 days or 1 year

RÉSUMÉ

Introduction : Les patients qui ont eu un remplacement valvulaire aortique par cathéter (RVAC) risquent d'être hospitalisés durant la première année après l'intervention. Peu d'études ont porté sur l'incidence des hospitalisations dues à l'insuffisance cardiaque (HIC) après le RVAC et leurs répercussions sur les hospitalisations subséquentes et la mortalité. Notre objectif était de déterminer l'incidence, les prédicteurs et la mortalité associés aux HIC après le RVAC.

Méthodes : Nous avons utilisé de manière prospective les données collectées de tous les patients qui avaient subi le RVAC entre le 1er août 2010 et le 31 mars 2015; nous avons sélectionné 742 patients consécutifs qui avaient subi le RVAC durant la période à l'étude. Les patients étaient suivis durant une période minimale de 1 an après le RVAC.

Résultats : L'âge moyen était de 80,9 ± 8,1, et 58,2 % étaient des hommes. Les hospitalisations survenaient chez 20 % des patients dans les 30 jours après le RVAC et chez 59,7 % dans la 1re année après le RVAC. Parmi les patients hospitalisés, les HIC étaient la

Transcatheter aortic valve replacement (TAVR) has become a viable alternative to surgical aortic valve replacement in intermediate and high-risk patients with severe aortic stenosis.[1-5] Technological advancements in recent years with TAVR have resulted in improved periprocedural outcomes, and, as such, the focus of interest has shifted toward understanding both the short- and long-term outcomes associated with TAVR.[6-10] Hospitalization within the first year post-TAVR is common and ranges between 12% and 53%.[11-15] Recent data from the United States, using a nationwide admission database, demonstrated that of 12,221 patients with TAVR, 2188 (17.9%) had hospitalizations within 30 days.[14] This study revealed that the most frequent cause of hospital readmission within 30 days was heart failure (HF), accounting for 22.5% of all hospitalizations. To date, there has been a scarcity of data examining predictors and associated

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had higher subsequent rates of rehospitalization compared with patients who had non-HFH. Patients with HFH or non-HFH at 30 days had 1-year mortality rates of 23.1% and 21.4%, respectively, whereas those with HFH by 1 year had a higher 1-year rate of mortality compared with patients who had non-HFHs (25% vs 10.9%, *P* < 0.001).

Conclusions: HF accounts for a quarter of all hospitalizations post-TAVR and is associated with higher rates of subsequent rehospitalization and death compared with those who had non-HFH. Understanding predictors of readmissions post-TAVR will allow for better risk stratification and improve outcomes in patients receiving TAVR.

première cause d'hospitalisation chez 25,8 % dans les 30 jours après le RVAC et chez 21,4 % des patients dans la 1re année après le RVAC. Les patients ayant eu des HIC soit dans les 30 jours soit dans la 1re année avaient des taux subséquents plus élevés de réhospitalisation comparativement aux patients qui n'avaient pas eu d'HIC. Les patients qui avaient eu des HIC ou qui n'avaient pas eu d'HIC dans les 30 jours avaient respectivement des taux de mortalité dans la 1re année de 23,1 % et de 21,4 %, tandis que ceux qui avaient eu des HIC dans la 1re année avaient des taux plus élevé de mortalité dans la 1re année comparativement aux patients qui n'avaient pas eu d'HIC (25 % *vs* 10,9 %, *P* < 0,001).

Conclusions : L'IC représente un quart de toutes les hospitalisations après le RVAC et est associée à des taux plus élevés de réhospitalisations subséquentes et de décès comparativement à ceux qui n'avaient pas eu d'HIC. La compréhension des prédicteurs de réadmission après le RVAC permettra une meilleure stratification du risque et améliorera les résultats cliniques chez les patients qui reçoivent un RVAC.

mortality of patients admitted to hospitals post-TAVR beyond 30 days. This is of particular importance, given the underlying comorbidity burden of patients undergoing TAVR and the potential life-years gained by pursuing TAVR in a patient population susceptible to HF.

The main objectives of our study were to determine the incidence, predictors, and associated mortality of patients with HF hospitalization (HFH) at 30 days and 1 year after undergoing TAVR.

Methods

Data source and patient population

Clinical, echocardiographic, and laboratory data were prospectively collected in all patients with symptomatic severe aortic stenosis undergoing transfemoral and transapical TAVR between August 1, 2010 and March 31, 2015, at St. Paul's Hospital and Vancouver General Hospital, British Columbia, Canada. Patients who had unsuccessful procedures, those who died in hospital at the index TAVR procedure, non-British Columbia residents, and those who had repeat TAVR procedures within 1 year or surgical aortic valve replacement within 6 months were excluded from the analysis. Only 2 patients were excluded owing to having had TAVR procedures within 1 year or surgical aortic valve replacement within 6 months; including these patients in our analysis would not alter any of the findings significantly.

Databases

The baseline characteristics for study cohort were collected prospectively in a provincial administrative database, which was generated and maintained by Cardiac Services British Columbia (CSBC). These data were linked to the British Columbia Vital Statistics Agency (for survival analysis) and to the British Columbia Ministry of Health Discharge Abstract Database (DAD) (for hospitalization analysis). The TAVR data from St Paul's Hospital and Vancouver General Hospital were collected and maintained by dedicated nurse specialists.

Hospitalization

HFHs were identified as those hospitalizations with most responsible diagnoses of HF, using ICD-10 code I50.x. The Canadian Institute for Heath Information conducts regular chart reviews of acute care diagnostic, intervention, and other selected data elements that were previously collected and submitted to the DAD as part of its comprehensive Data Quality Program. The agreement on the assignment of the most responsible diagnosis between the DAD data and the chart review data was 93% in the 2015 to 2016 DAD reabstraction study.[16] This has also been confirmed in a HF-specific analysis in Ontario, which demonstrated 94.3% agreement.[17] Non-HFHs were those associated with any acute hospitalization for any most responsible diagnosis other than HF. Patients were divided into 3 groups: those with at least 1 hospitalization in which HF was listed as most responsible diagnosis (HFH), those with 1 or more hospitalizations that were all non-HF most responsible diagnosis hospitalizations (non-HFH), and those with no hospitalization (NH). Length of hospital stay (LOS) during the index procedure hospitalization was assessed for the 3 groups. LOS was defined as the date of the TAVR procedure to the discharge date from the index procedure hospitalization. We also examined the total number of days alive and out of hospital (DAOH) at 365 days, starting at the date of the index TAVR procedure. Rehospitalization rates were examined as events per patient year (EPPY) after a hospitalization event (HFH or non-HFH). This was defined as the total number of hospitalizations occurring, divided by the total follow-up period (in years), after the qualifying hospitalization event. The calculation of the follow-up period began from the date of discharge from the first hospitalization during 30 days or 1 year for those with hospitalizations and from the 30-day or 1-year landmark (post-discharge from index TAVR procedure) for the NH group. Given the long follow-up times we have on the cohort, those who had no hospitalizations in the first 30 days or 1 year (NH group) were still at risk for subsequent hospitalization beyond the 1 year. Interhospital transfer to another hospital was not counted as a new hospitalization. Both planned and unplanned hospitalizations were included in this analysis.

Outcomes

The primary outcomes of interest for this study were hospitalizations at 30 days and 1 year.

Statistical analysis and ethics

Results are expressed as frequencies and percentages for categorical variables and means ± standard deviation for continuous variables. Differences in baseline characteristics and procedural variables were tested with the analysis of variance (ANOVA) test for continuous variables and the Pearson χ^2 test for categorical variables. A 2-tailed P value of less than 0.05 was considered statistically significant. DAOH were summarized by simple descriptive statistics and compared across subgroups, using Wilcoxon test. Cumulative event rates were examined using the Kaplan−Meier method. Cox proportional hazard model with time-dependent covariates was used to analyse the effect of time to rehospitalization within the first year of TAVR on mortality.

Statistical analyses were performed using SAS version 9.3 (SAS Institute Inc, Cary, NC) and R version 3.3. The study was approved by the Research Ethics Board at Providence Health Care. Analysis was performed on deidentified data.

Multivariable model and time-varying analysis

All baseline variables (demographics, comorbidities, clinical factors, valve-stenosis severity, and The Society of Thoracic Surgeons [STS] score[18]) were assessed as candidate predictors of 1-year HF hospitalization. Aortic valve stenosis severity, as measured by the mean gradient, was assessed using transthoracic echocardiographic studies performed before the TAVR procedure.

Predictors identified from univariate Cox regression analysis (P value < 0.1) were included in the multivariable Cox regression model. Backward and stepwise approaches were used to retain significant predictors in the final model (P value < 0.05). The proportional hazards assumption was tested using the Schoenfeld residuals. Estimated hazard ratios (HRs) are presented with 95% confidence intervals (CIs). Cox proportional-hazards model with time-dependent covariates was used to analyse the relationship between HF hospitalization and 1-year survival. Cumulative event rates were estimated using the Kaplan−Meier method and were compared using log-rank test. A 2-tailed P value of less than 0.05 was considered statistically significant.

Results

Patient population and baseline characteristics

A total of 742 patients underwent TAVR between August 1, 2010 and March 31, 2015. After applying the exclusion criteria, 720 patients with a minimum of 1-year follow-up data were included in the cohort for this analysis (Fig. 1). The mean age for the study population was 80.9 ± 8.1 years, and 58.2% were men. There were 92 patients with HFH with a total follow-up time of 194.4 years, 338 patients with non-HFH and a total follow-up time of 824.4 years, and 290 patients with NH and a total follow-up of 782.1 years. Baseline patient characteristics for the cohort are summarized in Table 1. Compared with patients who had either NH or non-HFH, patients with HFHs had higher STS scores, more atrial fibrillation (AF), a higher prevalence of renal dysfunction (an estimated glomerular filtration rate [eGFR] of < 60 or < 30 mL/min/1.73 m^2), a left-ventricular ejection fraction LVEF of $< 35\%$, and more likely to be classified as New York Heart Association (NYHA) III/IV at baseline. Pre-TAVR aortic valve mean gradient was lower for the HFH group (36.9 ± 13.6 mm Hg) compared with non-HFH (40.7 ± 14.9 mm Hg) and NH (42.8 ± 17.9 mm Hg), $P = 0.007$.

Patients with HFH by both 30 days and 1 year had longer LOS during the index TAVR procedure hospitalization compared with the non-HFH and NH groups. In patients with hospitalization by 30 days, the HFH group had a median LOS of 7 days (interquartile range [IQR] 4, 12), compared with 5 days (IQR 3, 10) for non-HFH and 4 days (IQR 3, 7) for NH groups ($P < 0.001$). Similarly, in those with a hospitalization by 1 year, the HFH group had a median LOS of 6 days (IQR 4, 11), compared with 4 days (IQR 3, 7) for non-HFH and 3 days (IQR 2, 6) for NH groups ($P < 0.001$).

Hospitalization

By 30 days, 151 (20%) of patients had at least 1 hospitalization; of those, 39 (25.8%) had at least 1 HFH, and 112 (74.2%) had non-HFH. By 1 year, 430 (59.7%) of patients had at least 1 hospitalization, and, of those, 92 (21.4%) had at least 1 HFH, and 338 (78.6%) had non-HFH.

Rehospitalization rates. In patients with 30-day hospitalizations, those in the HFH group had subsequent rehospitalization rates for HF of 1.02 EPPY compared with 0.16 EPPY for the non-HFH group and 0.09 EPPY for the NH group ($P < 0.001$). Similarly, those in the HFH group had a subsequent all-cause rehospitalization rate of 2.33 EPPY compared with 1.97 EPPY for the non-HFH group and 0.99 EPPY for NH group ($P < 0.001$) (Fig. 2A). Patients with hospitalization at 1 year had similar findings, with the HFH group having subsequent rehospitalization rates for HF of 0.84 EPPY compared with 0.05 EPPY for the non-HFH group and 0.06 EPPY for the NH group ($P < 0.001$) (Fig. 2B). Further, in those with hospitalizations at 1 year, the rates of all-cause rehospitalizations were 2.36 EPPY for the HFH group, 1.52 EPPY for the non-HF group, and 0.51 EPPY for the NH group ($P < 0.001$).

Predictors of HF hospitalization

All baseline variables were examined using a univariate analysis (Table 2). From the univariate analysis STS score, access site, LVEF $< 50\%$, NYHA III/IV, eGFR, AF, permanent pacemaker, mean gradient and moderate/severe TR were identified as significantly different and entered the subsequent multivariate analysis. The multivariate analysis revealed 5 independent predictors of HFH within 1 year of TAVR. NYHA III/IV HF symptoms (HR 3.21, 95% CI, 1.16-8.90), AF (HR 2.34, 95% CI, 1.48-3.71), transapical access (HR 2.25, 95% CI, 1.41-3.60), eGFR < 30 mL/min (HR 2.12, 95% CI, 1.14-3.93), and STS score (per 1% increment) (HR 1.06, 95% CI, 1.01-1.11) were independent predictors of HF hospitalizations within 1 year of TAVR (Table 3).

Death

In patients who had hospitalizations within 30 days post-TAVR, 1-year mortality rates were 23.1% for the HFH

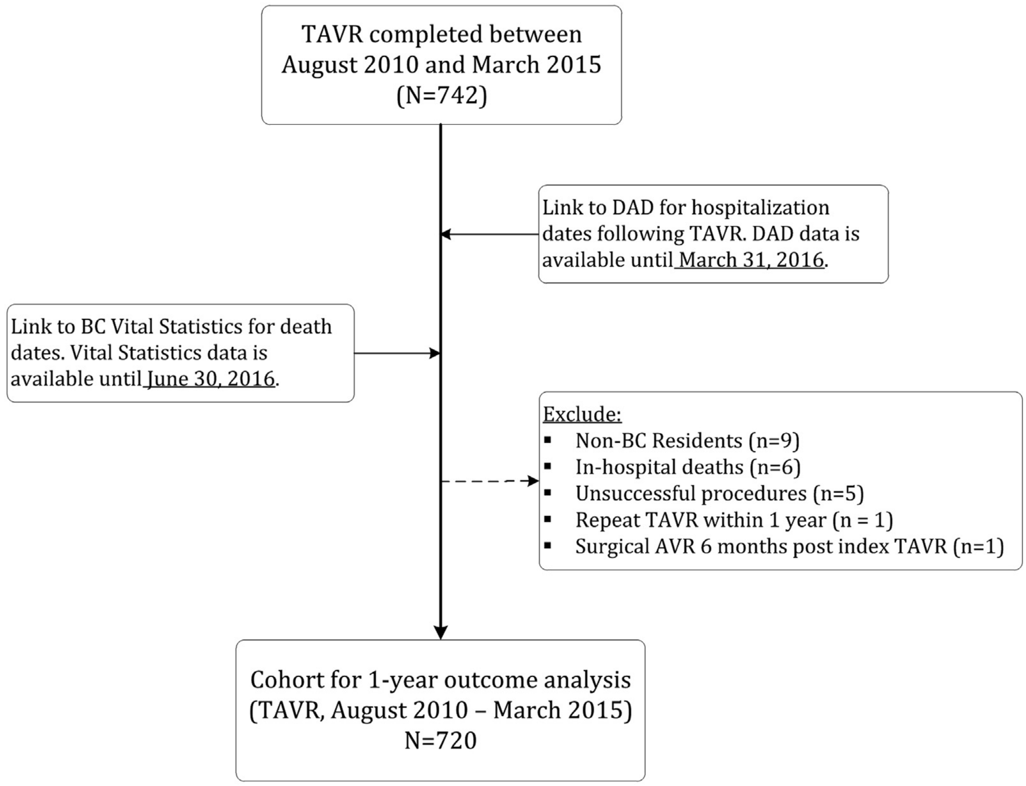

Figure 1. Cohort diagram.

group and 21.4% for the non-HFH group compared with the NH group (7.6%, $P < 0.0001$; Fig. 3A). Similarly, for those experiencing hospitalizations within the first year post-TAVR, the 1-year mortality for patients with HFH, non-HFH, and NH was 25.0%, 10.9%, and 5.5%, respectively. ($P < 0.0001$; Fig. 3B). Furthermore, the HFH group had fewer DAOH 301.7 days (IQR, 276.5, 365) compared with 337.2 days (IQR, 365, 365) for the non-HFH group and 347.4 days (IQR, 365, 365) for the NH patient groups ($P < 0.001$) during the first year post-TAVR.

Table 1. Baseline characteristics of patients with heart-failure hospitalizations, non—heart-failure hospitalizations, and no hospitalizations at 1 year

	All	HFH	Non-HF	NH	*P* value
N =	720	92	338	290	
Age	80.9 ± 8.1	81.6 ± 7.8	80.5 ± 8.3	81.2 ± 7.9	0.397
Male	419 (58.2%)	47 (51.1%)	198 (58.6%)	174 (60%)	0.314
Previous CAD	659 (91.5%)	87 (94.6%)	306 (90.5%)	266 (91.7%)	0.462
Previous MI	94 (13.1%)	10 (10.9%)	52 (15.4%)	32 (11%)	0.218
Previous OHS	200 (27.8%)	29 (31.5%)	92 (27.2%)	79 (27.2%)	0.692
Previous PCI	181 (25.1%)	21 (22.8%)	86 (25.4%)	74 (25.5%)	0.861
Previous Stroke	88 (12.2%)	14 (15.2%)	46 (13.6%)	28 (9.7%)	0.206
COPD	71 (10%)	9 (9.9%)	36 (10.8%)	26 (9.2%)	0.784
Diabetes mellitus	188 (26.1%)	28 (30.4%)	84 (24.9%)	76 (26.2%)	0.557
AF	240 (36.5%)	52 (61.2%)	101 (32.3%)	87 (33.6%)	< 0.0001
PPM	96 (13.4%)	18 (19.8%)	41 (12.2%)	37 (12.8%)	0.155
STS Score	6.9 ± 3.8	8.5 ± 4.7	6.5 ± 3.7	6.8 ± 3.6	< 0.0001
eGFR < 60	397 (55.1%)	62 (67.4%)	174 (51.5%)	161 (55.5%)	0.024
eGFR < 30	66 (9.2%)	16 (17.4%)	24 (7.1%)	26 (9%)	0.010
LVEF < 50	188 (26.1%)	31 (33.7%)	70 (20.7%)	87 (30%)	0.006
LVEF < 35	67 (9.3%)	12 (13%)	22 (6.5%)	33 (11.4%)	0.047
AVA	0.7 ± 0.4	0.7 ± 0.1	0.7 ± 0.5	0.7 ± 0.2	0.258
Mean gradient, mm Hg	41.1 ± 16.1	36.9 ± 13.6	40.7 ± 14.9	42.8 ± 17.9	0.007
NYHA III/IV	600 (83.3%)	87 (94.6%)	269 (79.6%)	244 (84.1%)	0.003
Moderate/Severe MR	35 (4.9%)	4 (4.3%)	16 (4.7%)	15 (5.2%)	0.940
Moderate/Severe TR	35 (4.9%)	9 (9.8%)	14 (4.1%)	12 (4.1%)	0.063

AF, atrial fibrillation; AMI, acute myocardial infarction; AVA, aortic valve area; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disorder; eGFR, estimated glomerular filtration rate; HFH, heart-failure hospitalization; LVEF, left ventricular ejection fraction; NH, no hospitalization; non-HFH, non—heart-failure hospitalization; MR, mitral regurgitation; NYHA, New York Heart Association; OHS, open heart surgery; PPM, permanent pacemaker; STS, Society of Thoracic Surgery; TR, tricuspid regurgitation.

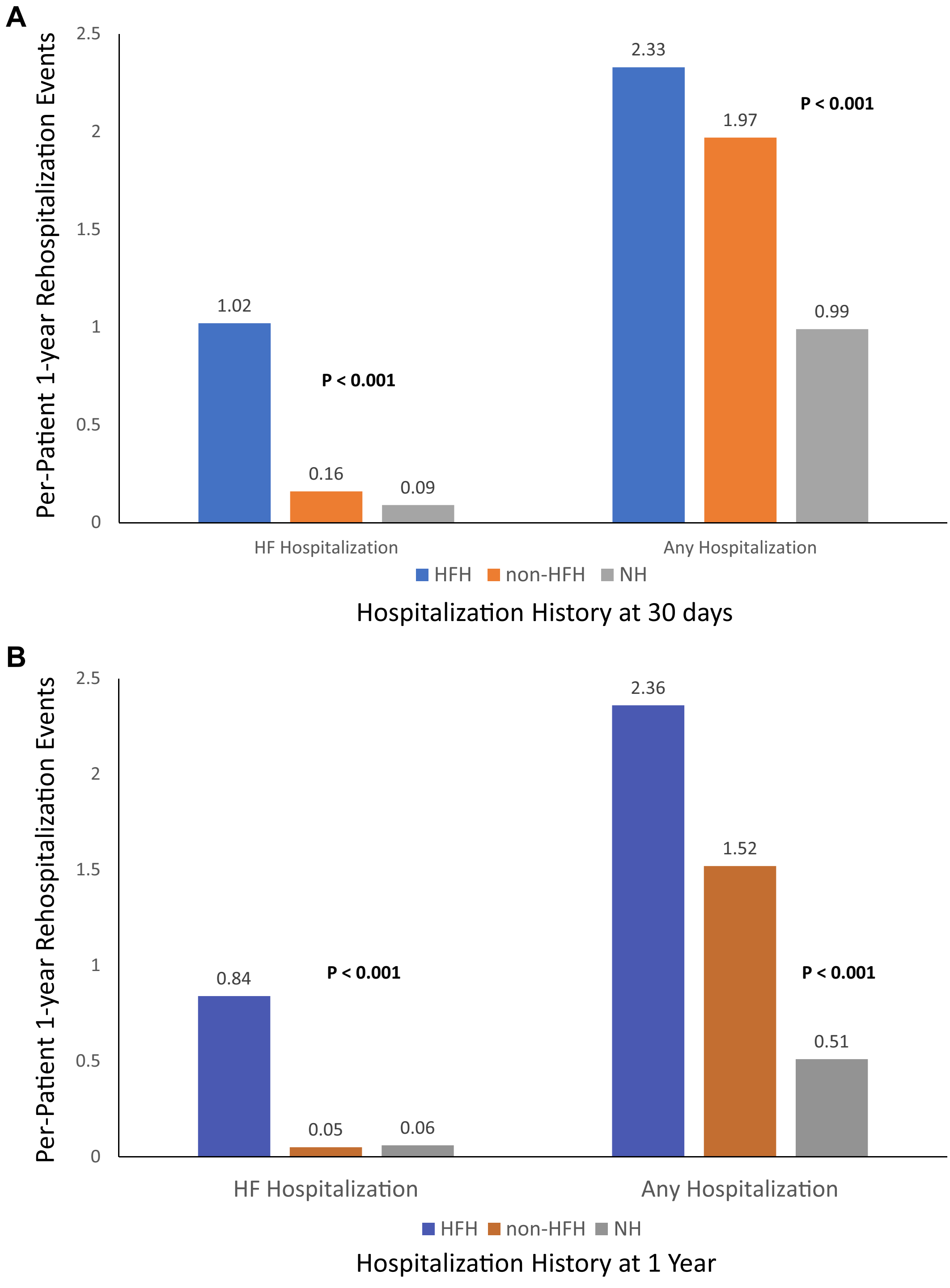

Figure 2. (**A**) Rehospitalization rates expressed as events per patient year for patients with hospitalizations at 30 days. (**B**) Rehospitalization rates expressed as events per patient year for patients with hospitalizations at 1 year.

After adjusting for time to HF hospitalization using a time-varying analysis, HFH was associated with an increased hazard of death within 1 year post-TAVR with a HR 3.17 (95% CI, 1.44-4.44) (Table 4). Increased age, male sex, and eGFR < 30 mL/min were also associated with significantly increased hazard for death.

Discussion

In this study, we show that one-quarter of all hospitalizations at 30 days and 1 year post-TAVR were attributable to HF. Furthermore, HF hospitalizations post-TAVR were associated with a higher rate of subsequent HF and non-HF rehospitalizations as well as a 3-fold increase in the hazard

Table 2. Univariate analysis of predictors for heart-failure hospitalizations at 1 year

	Univariate analysis		
Variables	*P* value	HR	95% HR confidence limits
Age	0.333	1.013	(0.987, 1.040)
Male	0.158	0.745	(0.495, 1.121)
STS score	< 0.0001	1.101	(1.058, 1.146)
Transapical access	< 0.0001	2.731	(1.788, 4.171)
LVEF < 50	0.049	1.545	(1.002, 2.380)
LVEF < 35	0.140	1.580	(0.861, 2.898)
NYHA III/IV	0.004	3.793	(1.540, 9.341)
eGFR < 30	0.002	2.350	(1.370, 4.029)
eGFR < 60	0.010	1.773	(1.146, 2.741)
Severe COPD	0.995	0.9998	(0.501, 1.986)
Diabetic	0.304	1.262	(0.810, 1.968)
AF	< 0.0001	3.035	(1.962, 4.695)
PPM	0.045	1.695	(1.012, 2.839)
Previous stroke	0.304	1.348	(0.763, 2.381)
Previous CAD	0.260	1.679	(0.382, 4.134)
Previous OHS	0.367	1.224	(0.789, 1.901)
AVA	0.195	0.486	(0.163, 1.446)
Mean gradient, mm Hg	0. 007	0.980	(0.966, 0.994)
Moderate/Severe MR (Yes)	0.913	0.945	(0.347, 2.575)
Moderate/Severe TR (Yes)	0.011	2.451	(1.232, 4.877)

AF, atrial fibrillation; AVA, aortic valve area; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disorder; eGFR, estimated glomerular filtration rate; HR, hazard ratio; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; NYHA, New York Heart Association; OHS, open heart surgery; PPM, permanent pacemaker; STS, Society of Thoracic Surgery; TR, tricuspid regurgitation.

of death at 1 year. These findings may have implications for patient selection for TAVR as well as management strategies after TAVR to increase surveillance and ensure active management plans are in place for these high-risk patients.

The overall hospitalization rate at 30 days of 20.0% in our cohort is similar to previously published reports ranging from 12.4% to 20.9%.[6,11,12,19] Only a handful of previous studies have reported the proportion of hospitalizations attributable to HF, with similar results to our own (21.9% and 22.5%).[12,14] Our 1-year all-cause hospitalization rate of 59.7%, is higher than observed in the Partner A and B populations (18.2% and 22.3%, respectively).[1,20] Whereas the Austrian TAVR registry reported an unusually low hospitalization rate of only 12%,[21] our results are similar to those reported by Nombela-Franco et al. and the large STS/ACC transcatheter valve therapy registry, which report 43.9% and 53% 1-year hospitalization rates, respectively.[6,11] This highlights the generalizability gap between real-world experience and clinical trials, which is particularly relevant when determining the effectiveness of procedure-based interventions and systems of care after procedures.

Table 3. Multivariate analysis of predictors for heart-failure hospitalization at 1 year

Parameter	HR	95% HR CI	*P* value
Age	1.008	0.978-1.038	0.613
Male	0.765	0.485-1.208	0.250
Transapical access	2.251	1.408-3.597	0.001
AF	2.343	1.481-3.707	0.0003
PPM	1.032	0.601-1.774	0.908
STS score (%)	1.06	1.008-1.114	0.023
LVEF < 50	1.155	0.704-1.894	0.568
eGFR < 30	2.116	1.138-3.933	0.018
Mean gradient, mm Hg	0.986	0.971-1.002	0.094
Moderate/severe TR	1.557	0.757-3.203	0.228
NYHA III/IV	3.21	1.158-8.895	0.025

AF, atrial fibrillation; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PPM, permanent pacemaker; TR, tricuspid regurgitation.

Understanding patient characteristics that may predict hospitalizations post-TAVR is essential in helping to reduce overall subsequent rehospitalization rates. We found that NYHA III/IV classification, AF, transapical access, eGFR < 30 mL/min/1.73 m^2, and higher STS score were all associated with a significantly higher risk for HF hospitalization at 1 year. Two recent studies have reported on both early and late predictors of hospital readmission post-TAVR.[11,15] Franzone et al. identified male gender and stage 3 renal failure as independent predictors of any hospitalization within 1 year post-TAVR, whereas in-hospital myocardial infarction and in-hospital life-threatening bleeding were shown to be predictive of cardiovascular readmissions.[15] Nombela-Franco et al. examined early (≤ 30 days) and late (> 30 days to 1 year) predictors of hospitalizations. Similar to our findings, they found a history of AF and low eGFR were significant predictors of hospital readmission within the first year.[11] Although mean gradient and LVEF were not found to be predictors of HFH, those with HFHs had significantly lower mean gradients and LVEF at baseline. These findings are suggestive of a higher proportion of patients with low-flow, low-gradient (LEF-LG) severe aortic stenosis. The concept of both LEF-LG aortic stenosis has been well established previously.[22] Intuitively, this subset of patients represent a higher-risk cohort of those undergoing TAVR. It has been shown that LV function is enhanced in patients with low LVEF undergoing TAVR.[23]

To the best of our knowledge, our analysis is the first to focus specifically on predictors for HFH in patients undergoing TAVR. In the United States nationwide readmission database, HF was the most common cardiac cause for 30-day rehospitalization following TAVR at 22.5%.[14] As such, we need to focus our efforts in better understanding patient characteristics that may result in HFH, in the hope of reducing overall cardiac-associated readmissions post-TAVR. There have been numerous studies that have examined predictors of HF readmission in the general HF population.[24,25] However, it is unknown whether similar factors predict outcomes following TAVR in which the underlying myocardial remodelling differs from the general HF population. Well-recognized predictors of HF readmissions include renal impairment, especially when occurring in the context of a HF hospitalization.[26] Several studies have also identified the relevance of comorbid noncardiac conditions—including diabetes mellitus, anemia, and pulmonary disease—in predicting HF and non-HF readmissions.[27,28] One study examined factors associated with HF readmission at 7 days and 30 days postdischarge from a HF-associated hospitalization. The study identified that discharge against medical advice, renal disease, and discharge from hospitals without specialized HF services were all predictive of subsequent HF readmission at both 7 and 30 days postdischarge. These variables remained significant even when adjusted for age, sex, and other comorbidities.[29] We also show that having a HF hospitalization at either 30 days or 1-year post-TAVR resulted

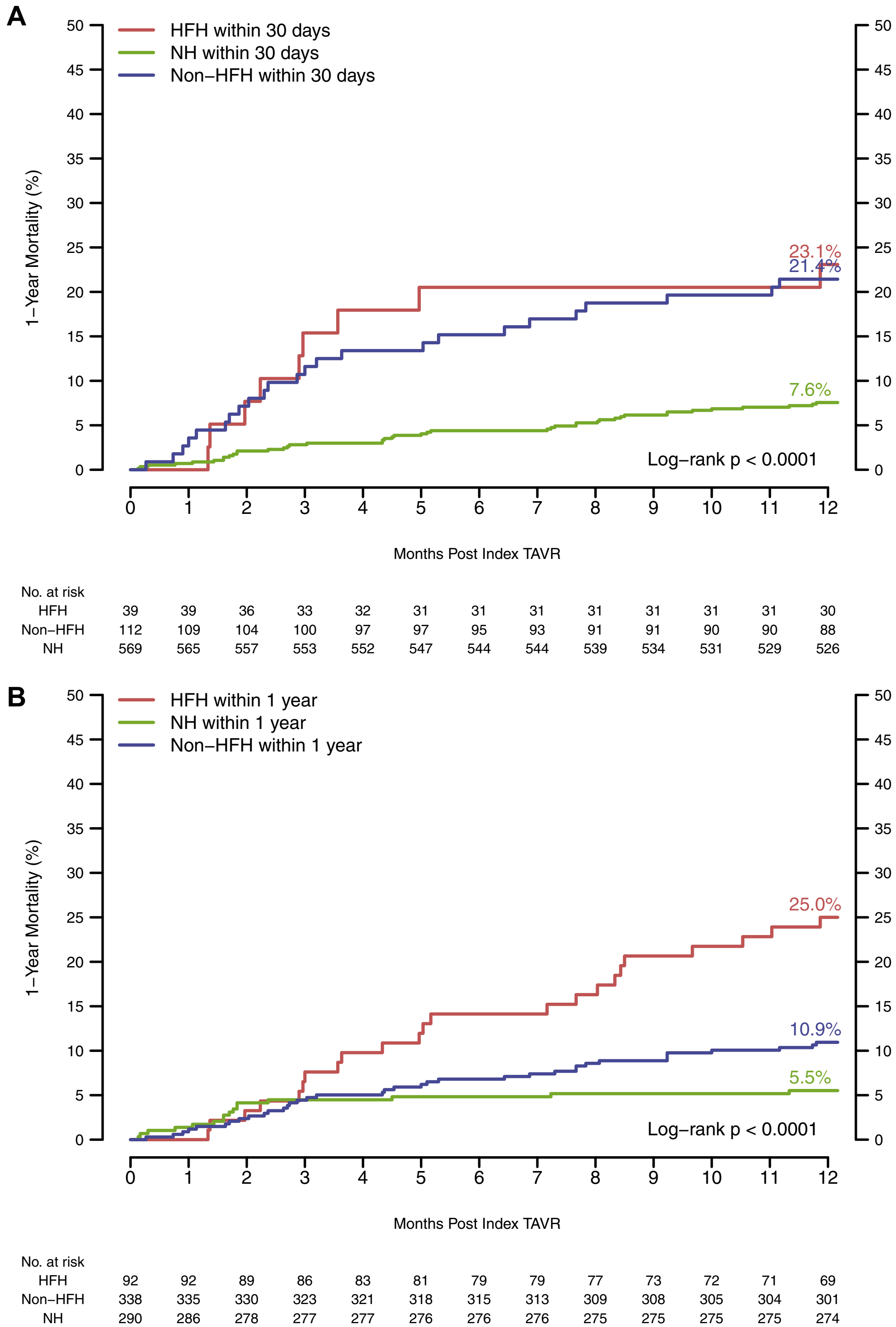

Figure 3. (**A**) One-year mortality for patients with hospitalizations at 30 days. (**B**) One-year mortality for patients with hospitalizations at 1 year. HFH, heart-failure hospitalization; NH, no hospitalization; non-HFH, non–HFH.

in a change in the trajectory of these patients and in higher subsequent HF and non-HF rehospitalizations compared with patients who had non-HF hospitalizations during the same periods. Although there are limited data examining HFH post-TAVR, our data are in agreement with studies focused on the general HF population.[30] A recent analysis from the United Kingdom found that patients hospitalized with initial HF diagnoses were 2-fold more likely to have HFH during

Table 4. Predictors of death at 1 year using time-varying analysis

Parameter	HR	95% HR CI	*P* value
HFH	3.168	2.262-4.438	< 0.0001
Age	1.026	1.005-1.048	0.014
Male	1.666	1.213-2.288	0.002
eGFR < 30	1.739	1.135-2.662	0.011

CI, confidence interval; eGFR, estimated glomerular filtration rate; HFH, heart-failure hospitalization; HR, hazard ratio.

follow-up. They identified renal impairment, diabetes, and previous HFH as major predictors of subsequent HFH.[31] A population-based analysis of 88,195 HF patients found that those with recent HFH (< 1 year) had higher mortality, unplanned HF admission, and unplanned all-cause hospitalization compared with the remote HFH patients (> 1 year).[32] Although that study was focused on a general HF population, their findings are consistent with our data that a previous HFH yields a poorer overall prognosis compared with patients who have had no previous HF hospitalizations.

We found that patients with HFH post-TAVR have significantly lower DAOH compared with those with non-HFH or NH. Unlike evaluating mortality or rehospitalization in isolation, DAOH is a measure that encompasses both of these outcomes and allows the assessment of the overall impact that HFH or non-HFH has on a patient. DAOH has become an increasingly used outcome measure in HF studies.[33] In 1 study, patients on candesartan had 24 more DAOH and a 2% mean increase in percent DAOH compared with placebo.[33] The strength of measuring DAOH is in its objectivity and ability to account for the number and duration of multiple hospitalizations.

Finally, our study is the first to show that HF hospitalization is associated with a 3-fold increased risk of death at 1 year in patients who undergo TAVR. Our 1-year mortality rates in patients with HFH within 1 year post-TAVR of 25.0% are similar to the reported 1-year mortality rate of the general population of patients admitted with HF (29.6%).[34] Considering the expense and expertise involved in pre- and periprocedural care, equal value should be placed on post-procedure care and care models that emulate the success of a multidisciplinary clinics for HF in TAVR recipients.

Our study has some notable strengths and limitations. Although this is a retrospective analysis, the TAVR registry was assembled in a prospective fashion and enrolled consecutive patients. Administrative databases were used to determine hospitalization using ICD codes and can be subjective to misclassification; however, they have been shown to highly specific. In our analysis of death rates in each subgroup, it is important to recognize that our model did not incorporate death as a competing risk factor. Patients who died without rehospitalization would be included in the NH subgroup, which may have resulted in a bias toward a higher death rate in the NH group. However, the vast majority of patients in our analysis had rehospitalizations before death. Therefore, although we recognize the limitation of not using death as a competing risk factor, we believe this had little impact on our findings and, in fact, would result in an under- rather than overestimation of rehospitalization rates. Finally, it is possible that medications may play a role in the outcome of patients receiving TAVR; however, medication data were not available.

Conclusions

With the expanding role of TAVR in patients with aortic stenosis, it is becoming increasingly important to understand predictors of hospital readmission. HF hospitalizations post-TAVR are common and account for 25% of all hospitalizations. HF hospitalizations are associated with increased risk of subsequent rehospitalizations and a 3-fold increased risk of death. Our study is the first to focus on understanding the predictors of HFH post-TAVR and the associated increase in mortality compared with non-HFH. Implementation of strategies to facilitate transition of care and improve outcomes in patients receiving TAVR and careful clinical management post-TAVR, with vigilance for HF particularly, are important to prevent HF hospitalizations and death.

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Disclosures

The authors have no conflicts of interest to disclose.

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