Rev Esp Cardiol. 2020;73(5):383–392

Original article

Predictors and outcomes of heart failure after transcatheter aortic valve implantation using a self-expanding prosthesis

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Article history:
Received 29 November 2018
Accepted 26 June 2019
Available online 26 September 2019

Keywords:
Heart failure
Transcatheter aortic valve implantation
Nutritional risk

A B S T R A C T

Introduction and objectives: The purpose of this analysis was to assess the incidence, predictors and prognostic impact of acute heart failure (AHF) after transcatheter aortic valve implantation (TAVI) using a self-expanding prosthesis.
Methods: From November 2008 to June 2017, all consecutive patients undergoing TAVI in our center were prospectively included in our TAVI registry. The predictive effect of AHF on all-cause mortality following the TAVI procedure was analyzed using Cox regression models.
Results: A total of 399 patients underwent TAVI with a mean age of 82.4 ± 5.8 years, of which 213 (53.4%) were women. During follow-up (27.0 ± 24.1 months), 29.8% (n = 119) were admitted due to AHF, which represents a cumulative incidence function of 13.2% (95%CI, 11.1%-15.8%). At the end of follow-up, 150 patients (37.59%) had died. Those who developed AHF showed a significantly higher mortality rate (52.1% vs 31.4%; HR, 1.84; 95%; CI, 1.14-2.97; *P* = .012). Independent predictors of AHF after TAVI were a past history of heart failure (*P* = .019) and high Society of Thoracic Surgeons score (*P* = .004). We found that nutritional risk index and chronic obstructive pulmonary disease were strongly correlated with outcomes in the AHF group.
Conclusions: TAVI was associated with a high incidence of clinical AHF. Those who developed AHF had higher mortality. Pre-TAVI AHF and high Society of Thoracic Surgeons score were the only independent predictors of AHF in our cohort. A low nutritional risk index and chronic obstructive pulmonary disease were independent markers of mortality in the AHF group.

Predictores e impacto pronóstico de la insuficiencia cardiaca tras el implante percutáneo de válvula aórtica con una prótesis autoexpandible

Palabras clave:
Insuficiencia cardiaca
Implante percutáneo de válvula aórtica
Riesgo nutricional

R E S U M E N

Introducción y objetivos: El objetivo es analizar la incidencia, los predictores y el impacto pronóstico de la insuficiencia cardiaca (IC) aguda tras el implante percutáneo de una válvula aórtica (TAVI) con una prótesis autoexpandible.
Métodos: Desde 2008, se incluye prospectivamente en nuestro registro de TAVI a todos los pacientes sometidos a TAVI en nuestro centro. Se analizan los factores pronósticos determinantes de IC aguda, y la relación con la mortalidad mediante modelos de regresión de Cox.
Resultados: Se sometieron a TAVI 399 pacientes, con una media de edad de 82,4 ± 5,8 años, de los que 213 (53,4%) eran mujeres. Durante el seguimiento (27,0 ± 24,1 meses), el 29,8% de los pacientes (n = 119) ingresaron en el hospital con el diagnóstico de IC aguda, lo que representa una incidencia anual del 13,2% (IC95%, 11,1-15,8%). Al final del seguimiento, habían fallecido 150 pacientes (37,59%). En el grupo de IC aguda se evidenció una tasa de mortalidad significativamente mayor (el 52,1 frente al 31,4%; HR = 1,84; IC95%, 1,14-2,97; p < 0,012). El diagnóstico previo de IC (p = 0,019) y la puntuación de la Society of Thoracic Surgeons (p = 0,004) se identificaron como predictores independientes de IC aguda tras el TAVI. Además, el índice de riesgo nutricional y la enfermedad pulmonar obstructiva crónica son los principales factores que ensombrecen el pronóstico dentro del grupo de IC aguda.

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https://doi.org/10.1016/j.rec.2019.06.006
1885-5857/

Conclusiones: El TAVI se asocia con una alta incidencia de eventos de IC aguda, lo que supone un gran impacto en la mortalidad. La IC aguda previa al implante y la puntuación de la Society of Thoracic Surgeons fueron los únicos predictores de IC aguda hallados. Un índice de riesgo nutricional bajo y la enfermedad pulmonar obstructiva crónica son potentes determinantes de mortalidad en el grupo de IC aguda.

Abbreviations

HF: heart failure
NRI: nutritional risk index
STS: Society of Thoracic Surgeons
TAVI: transcatheter aortic valve implantation

INTRODUCTION

Degenerative aortic stenosis (AS) has become the most prevalent valvular heart disease in developed countries with an increasing incidence due to progressive population aging.[1,2] Transcatheter aortic valve implantation (TAVI) has been shown to reduce mortality compared with conservative medical treatment in patients with severe AS. It is also a solid option for treating patients with high or prohibitive surgical risk, as an alternative to conventional surgical aortic valve replacement.[3,4] In addition, 2 recent studies, PARTNER 2[5] and SURTAVI,[6] demonstrated the noninferiority of TAVI vs conventional surgery in patients at intermediate risk, with superior results when the femoral approach was used.[7]

Patients selected for TAVI commonly have important comorbidities that determine the in-hospital course and can result in a higher number of postprocedure readmissions. The number of readmissions has decreased over the past few years due to increased operator expertise and fewer complications with newer devices and delivery systems. Acute heart failure (AHF) is one of the most prevalent causes of readmission in this group of patients, as reported in several series and registries.[8,9]

Risk scores have become an important tool for predicting procedural and periprocedural outcome following TAVI. The logistic EuroSCORE (European System for Cardiac Operative Risk Evaluation) was shown to overestimate the periprocedural risk in TAVI, especially in high-risk patients and was abandoned. The EuroSCORE II and the Society of Thoracic Surgeons (STS) score were proved to be more accurate for TAVI patients and are therefore currently used to estimate risk of death in patients undergoing TAVI.[10,11]

In this study, we analyzed the incidence of rehospitalization after TAVI in patients with main diagnosis of AHF and focused on the prognostic impact for our cohort. In addition, we searched for predictors of readmission due to AHF, and analyzed the factors that could modify the prognosis in this subgroup. This would help us to identify a profile of patients at high risk of complications. Intensification of medical treatment and closer follow-up may allow us to avoid readmissions, improving the quality of life of these patients.

METHODS

Population

This was an observational, single center, prospective study. We included all patients who underwent TAVI in our university hospital from November 2008 to June 2017 (n = 399) were included. All patients were selected for transcatheter replacement according to the clinical practice guideline recommendations available at the time; only patients with a life expectancy of more than 1 year and severe symptomatic aortic stenosis were included. The indication for TAVI was made according to the guidelines available at the time of inclusion. All patients had been previously discussed by a Heart Team consisting of clinical cardiologists, interventional cardiologists, and cardiac surgeons. All patients voluntarily signed consent forms before the procedure.

The major factors that contributed to the decision to perform the transcatheter procedure vs surgical aortic valve replacement were high or unacceptable surgical risk, frailty associated with older age, and technical contraindications for surgery (most frequently the presence of porcelain aorta).

Procedure

In most patients, TAVI was performed under local anesthesia and conscious light sedation. General anesthesia was used in 8% (n = 30) of procedures, when the nonfemoral arterial approach was preferred. The femoral approach was used in most procedures. When this was not feasible, axillar artery was the selected approach. We used the standard technique as described in the literature.[12]

A Medtronic biological prosthesis were implanted in most patients: CoreValve, CoreValve Evolut R or CoreValve Evolut Pro (Medtronic Inc., Minneapolis, MN, USA), depending on the availability at the time of the procedure. In a small percentage of patients, ACURATE-Neo (Symetis S.A., Ecublens, Switzerland) devices were used.

Before the intervention, 2-dimensional echocardiography and diagnostic coronary angiography were performed in all patients. As part of our routine protocol, computed tomography was used to determine aortic root anatomy and adequacy of vascular accesses. Any complication during the procedure was registered according to Valve Academic Research Consortium-2 (VARC-2) consensus document.[13]

This study was performed in accordance with the principles of the Helsinki Declaration.

Follow-up

All data related to the event were registered in the patients' electronic medical records. In our TAVI Registry, follow-up was performed using previous registries by trained cardiologists. Our protocol includes telephone calls and review of the electronic medical records. All medical interventions, hospital admissions and pharmacological treatments were reviewed. Vital status was determined by telephone calls in the absence of medical records. No patient was lost to follow-up.

Following the established protocol at least 1 follow-up echocardiogram was performed in all patients after discharge and another one 3 months later. Subsequently an annual echocardiogram was performed.

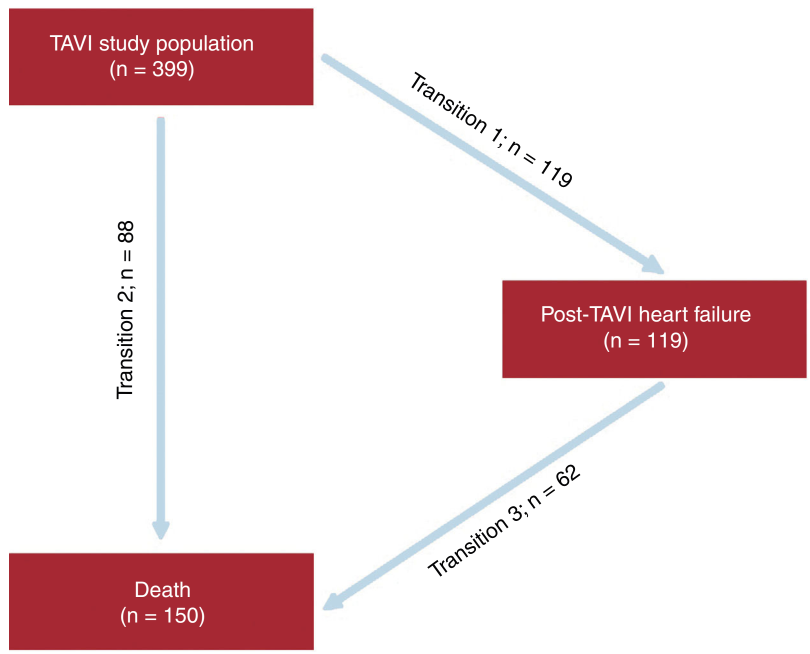

Figure 1. Heart failure-death multistate model transitions. TAVI, transcatheter aortic valve implantation.

Table 1
Baseline characteristics of the total population and of each group

Variables	Total population	HF (n = 119)	No HF (n = 280)	*P*
Clinical characteristics				
Age, y	82.4 ± 5.8	82.1 ± 5.9	82.5 ± 5.7	.543
Female sex	53.4	52.9	53.6	.908
BMI, kg/m^2	29.0 ± 5.1	28.6 ± 4.8	29.2 ±5.2	.319
Nutritional risk index	97.9 ± 7.7	98.1 ± 7.1	97.8 ± 7.9	.719
Hypertension	86.0	81.5	87.9	.095
Diabetes mellitus	27.8	31.1	26.4	.342
Dislipidemia	60.1	58.0	61.2	.566
Peripheral artery disease	12.9	13.6	12.6	.802
Coronary artery disease	40.1	42.9	38.9	.464
Prior PCI	23.4	22.7	23.7	.827
Acute heart failure before TAVI	58.4	68.9	54.0	.006
Prior stroke	12.6	12.6	12.6	.990
COPD	28.6	34.5	26.1	.090
Chronic kidney disease	49.1	50.4	48.7	.760
Dialysis	0.9	1.4	0.0	.198
NYHA functional class ≥ III	92.3	92.4	92.2	.948
ECG Parameters				
Atrial fibrillation	29.3	36.1	25.6	.042
Prior pacemaker	13.3	16.0	11.9	.290
BBB	28.6	27.2	29.3	.853
QRS duration, ms	109.6 ± 24.2	109.4 ± 22.5	109.7 ± 24.5	.917
Medications				
Loop diuretic agents	65.6	68.9	63.7	.202
Beta-blockers	30.8	25.2	34	.062
ACE inhibitors	22.5	22.7	22.3	.996
Anticoagulant agents	32.9	43.6	28.8	.039
Aspirin	57.8	55.5	59.1	.564
Oral antidiabetic drugs	21.3	20.2	21.9	.781
Statins	74.6	73.1	75.3	.695

Table 1 *(Continued)*
Baseline characteristics of the total population and of each group

Variables	Total population	HF (n = 119)	No HF (n = 280)	*P*
Laboratory data				
Hemoglobin, g/dL	12.0 ± 1.6	11.8 ± 1.6	12.0 ± 1.5	.773
Creatinine, mg/dL	1.21 ± 0.70	1.24 ± 0.49	1.18 ± 0.84	.508
Cystatin-C	1.31	1.31	1.31	.976
NT-proBNP	4913.5 ± 13 764.3	4843.1 ± 10 049.4	4942.7 ± 15 092.7	.949
Albumin, g/dL	3.7 ± 0.5	3.7 ± 0.5	3.7 ± 0.5	.936
Total cholesterol, mg/dL	156.7 ± 41.6	151.4 ± 39.0	158.7 ± 42.8	.134
Risk scores				
EuroSCORE II	6.3 ± 5.5	6.6 ± 5.6	6.1 ± 5.5	.404
STS score	6.0 ± 3.9	6.5 ± 3.9	5.8 ± 3.9	.125
TAVI implantation				
Femoral approach	94.7	92.4	95.9	.177
General anesthesia	5.6	8.4	4.1	.102
Successful implantation	99.1	99.2	99.1	.946
Radioscopy time, min	20.9 ± 22.9	23.3 ± 36.5	19.6 ± 13.6	.181
Contrast volume, mL	226.7 ± 100.5	251.2 ± 110.8	217.7 ± 93.5	.005
Post-TAVI in-hospital complications				
Vascular complications				.201
Major	5.8	6.1	5.4	
Minor	5.7	5.8	5.2	
Stroke				
Major	0.6	0.7	0.3	.376
Minor	1.8	2.4	1.1	.312
Acute kidney injury				.577
Grade 1	18.2	16.8	18.8	
Grade 2	2.1	2.5	1.8	
Grade 3	0.3	0	0.5	
Major bleeding	26.1	30.5	24.2	.191
Aortic regurgitation ≥III	3.0	1.0	4.4	.124
Pacemaker implantation	30.1	32.8	28.9	.441
Permanent BBB	27.8	33.6	24.7	.079
Troponin I peak, ng/mL	2.8 ± 9.8	2.9 ± 13.3	1.8 ± 1.9	.245
Transfusion	20.6	19.3	21.2	.678
Echocardiografic data				
LVEF groups				.561
< 40%	13.3	16.0	12.1	
40%-49%	10.3	9.2	10.7	
> 50%	76.4	74.8	77.1	
LVEDD, mm	45.3 ± 8	46.3 ± 7	45 ± 9	.246
LVESD, mm	32.2 ± 9	33.4 ± 8.9	33.1 ± 9	.779
IVS, mm	15.8 ± 4	15.7 ± 3	15.8 ± 4	.875
PWT, mm	15.1 ± 4	15.1 ± 2	14.95 ± 4	.697
Left ventricle mass, g	294 ± 98	306 ± 103	287 ± 75	.127
Aortic mean gradient, mmHg	47.6 ± 16	45.3 ± 14	48.51 ± 17	.119
Aortic peak gradient, mmHg	79 ± 23	75 ± 21	78 ± 25	.318
Aortic valve area, cm^2	0.68 ± 0.2	0.66 ± 0.19	0.69 ± 0.28	.283
Moderate-severe mitral regurgitation, %	25.7	26.1	25.6	.923
Left atrium area, cm^2	26.7 ± 6	27.8 ± 6.7	26.3 ± 6.9	.104
Pulmonary artery pressure, mmHg	47.5 ± 17.6	49.2 ± 16.8	46.6 ± 18.0	.235

ACE, angiotensin-converting enzyme; BBB, bundle branch block; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ECG, electrocardiogram; IVS, interventricular septum; LVEDD, left ventricular end diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end systolic diameter; NYHA, New York Heart Association; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PCI, percutaneous coronary intervention; PWT, posterior wall thickness, STS, Society of Thoracic Surgeons; TAVI, transcatheter aortic valve implantation.
Values are expressed as percentage for categorical data and mean ± standard deviation for continuous data.

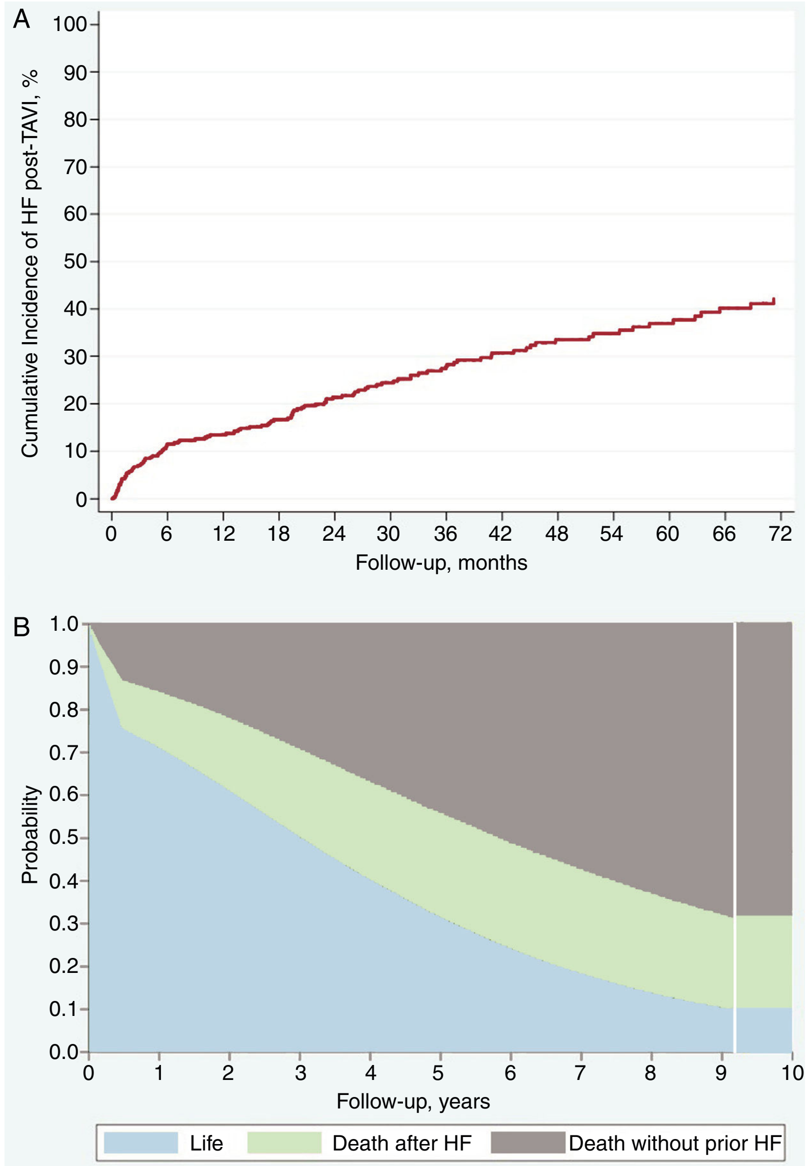

Figure 2. Cumulative incidence of HF after TAVI (A) and mortality according to HF (B). HF, heart failure; TAVI, transcatheter aortic valve implantation.

Study variables

AHF was defined following the available practice guidelines at the time of recruitment,[14] based on clinical and radiological data. The nutritional risk index (NRI) was calculated as 1.519 × serum albumin (g/L) + 41.7 × (actual body weight [kg]/ideal body weight [kg]), using the modified formula for the elderly by Bouillanne et al.[15] Ideal body weight was determined using the Lorentz formula:[15] height (cm) −100 −([height (cm) − 150]/4) for men, or height (cm) −100 −([height (cm) −150]/2.5) for women. If the ratio of measured body weight (kg) to ideal body weight (kg) was ≥ 1, the assigned value was 1, as previously described.[15,16] The NRI was calculated using the body weight measured on the day of the TAVI procedure, and the albumin value was obtained from the blood sample performed the day before the procedure. Based on NRI values, we classified the patients into 4 groups: no nutritional risk (NRI > 100), mild nutritional risk (97.5 ≤ NRI < 100), moderate nutritional risk (83.5 ≤ NRI < 97.4), and severe nutritional risk (NRI < 83.5). To simplify the model, we obtained 2 risk categories after the combination of the following: no and mild nutritional risk, and moderate and severe nutritional risk.

The presence and severity of paravalvular aortic regurgitation was assessed using transthoracic echocardiography. Transesophageal echocardiography was performed in those patients with a suboptimal acoustic window.

Statistical analysis

The statistical analysis was performed with SPSS version 22.0 and Stata version 13. Baseline characteristics according to the development of post-TAVI heart failure (HF) during follow-up are described using number and percentage for categorical data and mean ± standard deviation for continuous data, respectively. Differences in characteristics were assessed by using chi-square tests and 2-sample Student *t* tests.

Table 2
Results of the multivariate analysis

Predictor	T1: TAVI to HF hospitalization			T2: TAVI to death			T3: HF hospitalization to death		
	C-statistic: 0.69 (0.63-0.74)			C-statistic: 0.84 (0.79-0.89)			C-statistic: 0.69 (0.59-0.79)		
	HR	95%CI	*P*	HR	95%CI	*P*	HR	95%CI	*P*
Age, y	0.97[a]	0.93-1.01[a]	.082[a]	0.96[a]	0.92-1.01[a]	.075	1.03	0.98-1.10	.236
Female sex	1.10	0.70-1.73	.685	1.21	0.67-2.20	.530	0.64	0.32-1.29	.213
NRI	0.99	0.96-1.02	.510	0.98	0.95-1.01	.149	0.93[b]	0.89-0.97[b]	.002[b]
Hypertension	0.86	0.53-1.40	.537	0.86	0.44-1.69	.657	1.44	0.68-3.01	.338
PAD	1.00	0.51-1.96	.999	2.31[b]	1.10-4.85[b]	.027[b]	0.61	0.19-2.03	.426
Prior heart failure	1.66[b]	1.09-2.54[b]	.019[b]	1.08	0.66-1.78	.755	1.70	0.89-3.25	.107
COPD	1.07	0.71-1.63	.739	1.49	0.87-2.54	.146	2.35[b]	1.15-4.80[b]	.018[b]
AF	1.43[a]	0.95-2.14[a]	.085[a]	1.09	0.63-1.88	.775	1.66	0.90-3.05	.104
LVEF $<$ 40%	1.06	0.60-1.86	.848	2.54[b]	1.14-5.62[b]	.022[b]	1.06	0.44-2.55	.892
Moderate-severe MR	0.83	0.55-1.25	.369	1.36	0.81-2.27	.240	1.78[a]	0.94-3.38[a]	.079[a]
Pulmonary pressure, mmHg	1.01	0.99-1.02	.357	1.03[b]	1.02-1.05[b]	$<$ .001[b]	1.00	0.98-1.02	.962
Creatinine, mg/dL	1.08	0.75-1.55	.687	1.07	0.72-1.57	.744	1.01	0.50-2.02	.981
NT-proBNP	1.01	0.99-1.02	.841	1.00	0.99-1.01	.995	1.00	1.00-1.01	.713
STS	1.09[b]	1.03-1.15[b]	.004[b]	1.09[b]	1.02-116[b]	.009[b]	0.97	0.89-1.05	.424
Nonfemoral approach	1.84	0.80-4.24	.149	2.55[b]	1.01-6.42[b]	.047[b]	2.40	0.61-9.41	.210
Contrast volume, mL	1.01	0.99-1.02	.250	1.01[a]	1.00-1.01[a]	.060[a]	1.00	0.99-1.00	.843
Aortic regurgitation $>$ III	1.36	0.41-2.31	.252	2.21[a]	0.91-5.36[a]	.078[a]	4.87	0.44-15.14	.197
Permanent BBB	1.35	0.90-2.03	.149	1.02	0.61-1.71	.943	0.92	0.52-1.63	.785
Pacemaker implantantion	1.14	0.75-1.74	.547	0.63	0.34-1.14	.127	1.24	0.67-2.30	.486
AKI	0.46	0.75-1.89	.464	0.78	0.44-1.39	.403	1.55	0.76-3.20	.230
Transfusion	0.85	0.51-1.43	.549	2.38[b]	1.36-4.16[b]	.002[b]	0.64	0.29-1.44	.281

95%CI, 95% confidence interval; AF, atrial fibrillation; AKI, acute kidney injury; BBB, bundle branch block; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; NRI, nutritional risk index; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PAD, peripheral arterial disease; STS, Society of Thoracic Surgeons; TAVI, transcatheter aortic valve implantation.
[a] Values with statistical *trend* toward significance ($P > .05$ and $< .10$).
[b] Statistically significant values.

The association between post-TAVI HF and mortality was evaluated by Cox proportional hazards regression analyses with “post-TAVI HF” as a time-varying covariate. Results were graphically shown with Kaplan-Meier curves. Because HF hospitalization and death are semicompeting risks in which death precludes a subsequent HF hospitalization but death can still occur after a HF hospitalization, an illness-death, acyclic, multistate model was used.[17] In this model, all participants were in the initial state of “discharge after TAVI” and were at risk of a HF hospitalization (transition 1) or death without a preceding HF hospitalization (transition 2). In addition, those who were hospitalized for HF were also at risk for death after a HF hospitalization (transition 3) (Figure 1). The illness-death regression model using Weibull parametrization was developed to model the effect of covariates on the cause-specific hazards of the 3-state transitions with separate (stratified) nonparametric baseline hazards for transitions into the “post-TAVI HF” state and into the “death” state. All variables associated with post-TAVI HF based on $P < .05$ in the univariate analyses were included in a multivariate model, together with those with clinical relevance. Hazard ratios (HR) were calculated with 95% confidence intervals (95%CI).

RESULTS

Baseline characteristics, incidence, and predictors of AHF after TAVI

A total of 399 patients with severe AS underwent TAVI and were included in our registry between 2008 and 2017. The mean age of the cohort was 82.4 ± 5.8 years, and 53.4% (n = 213) were women.

Table 1 shows the baseline characteristics of the total population and of each group, including medical history, echocardiographic features, procedural details and in-hospital outcomes.

After a mean follow-up period of 27 ± 24.1 months and median of 21 months [interquartile range 6.5-40.7], 119 patients (29.82%) were admitted with a final diagnosis of AHF (cumulative incidence function 13.2%; 95%CI, 11.1%-15.8%) (Figure 2A). The average time until presentation of HF after the procedure was 20.9 ± 21.3 months with a median of 16.1 months [interquartile range 3.2-32.2]; 39.5% of AHF episodes (n = 47) occurred during the first 6 months after valve implantation.

The results of the multivariate analysis are shown in Table 2. Prior to the procedure, AHF episodes and high STS score were the only independent predictors of postprocedure AHF. There was no difference between groups in left ventricular ejection fraction (not even when we stratified according to the latest HF guidelines classification)[18].

Prognostic impact of HF post-TAVI

During follow-up, 150 deaths occurred in our cohort: 31 patients (20% of total deaths) during the first 30 days and 119 during the remaining follow-up (Figure 2B). The factors associated with higher mortality are summarized in Table 3 (univariate) and Table 2 (multivariate; Table 2 and Table 3 for with and without AHF during follow-up, respectively). After adjustment for these factors, AHF was a strong independent predictor of mortality (HR, 1.84; 95%CI, 1.14-2.97; $P < .12$), with almost twice the mortality rate in comparison with those without follow-up AHF (Figure 3).

Table 3
Factors associated with higher mortality

Variables	HR	95%CI	P
Age, y	0.99	0.97-1.01	.460
Female sex	0.91	0.66-1.26	.577
BMI, kg/m²	0.97	0.93-1.00	.085
NRI	0.97	0.95-0.98	< .001
Hypertension	1.06	0.70-1.62	.767
Diabetes	0.96	0.67-1.39	.849
Peripheral arterial disease	1.60	1.07-2.40	.023
Coronary arterial disease	1.21	0.87-1.66	.254
Prior heart failure	1.45	1.03-2.03	.030
COPD	1.16	0.82-1.65	.392
Chronic kidney disease	1.29	0.94-1.78	.118
Atrial fibrillation	1.37	0.97-1.94	.073
LVEF groups			
< 40%	1.28	0.78-2.12	.330
40-49%	1.10	0.69-1.77	.673
> 50%	ref	ref	
Moderate-severe mitral regurgitation	1.49	1.05-2.10	.024
Pulmonary pressure, mmHg	1.01	1.01-1.02	.001
Hemoglobin, g/dL	0.90	0.80-1.00	.057
Creatinine, mg/dL	1.22	1.03-1.44	.019
NT-proBNP	1.00	1.00-1.01	.096
Euroscore II	1.02	0.99-1.04	.183
STS score	1.04	1.01-1.08	.027
Femoral approach	0.54	0.31-0.94	.030
TAVI normoposition	1.19	0.92-1.53	.185
Aortic regurgitation > III	2.70	1.48-4.90	.001
Permanent BBB	0.98	0.69-1.39	.912
Pacemaker implantation	0.98	0.69-1.40	.929
Vascular complication	1.02	0.79-1.27	.984
Stroke	1.312	0.58-2.97	.516
Troponin I peak	0.17	0.1-41.6	.533
AKI	1.58	1.08-2.30	.017
Major bleeding	1.13	0.79-1.62	.504
Transfusion	1.91	1.32-2.76	.001
Follow-up heart failure	1.94	1.32-2.56	<.001

95%CI, 95% confidence interval; AKI, acute kidney injury; BBB, bundle branch block; BMI, Body mass index; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; LVEF, left ventricular ejection fraction; NRI, nutritional risk index; NT-proBNP, N-terminal pro-B-type natriuretic peptide; ref, reference group; STS, Society of Thoracic Surgeons; TAVI, transcatheter aortic valve implantation.

Mortality predictors in the post-TAVI HF group

Among the 119 patients who developed HF during follow-up, 62 (52.1%) died, with an average time between the first HF event and death of 25.7 ± 16.7 months, and a median of 16.8 months [interquartile rage 7.0-35.5]. Table 4 shows the predictive factors for mortality in this patient subgroup. Univariate analysis of patients readmitted with AHF who died showed that these patients were older, with a higher rate of AF and kidney failure, were at higher risk of malnutrition (assessed by NRI), and had increased values of N-terminal pro-B-type natriuretic peptide. Statistically significant differences in echocardiographic measurements were found only for mitral regurgitation greater than moderate and aortic regurgitation grade III or higher. In the multivariate analysis (Table 2 and Table 3), we only identified reduced NRI (HR, 0.93; 95%CI, 0.89-0.97; *P* = .002) and chronic obstructive pulmonary disease (HR, 2.35; 95%CI, 1.15-4.80; *P* = .018) as variables significantly associated with higher mortality (Figure 4).

DISCUSSION

In our TAVI registry, we gathered data from a single high-volume center expert in TAVI and included 399 TAVI patients. To our knowledge, this is the first study that assesses the incidence, prognostic impact, and predictive factors for hospital admission due to AHF following TAVI with the CoreValve device. The main findings of our study are as follows: *a)* there was a high incidence of AHF episodes requiring hospital admission, most of them with preserved ejection fraction, and up to 5-years of follow-up; *b)* those patients who developed AHF after TAVI had higher mortality and were associated with pre-TAVI hospital admissions for AHF and high STS score, and *c)* poor NRI and chronic obstructive pulmonary disease were independent mortality predictors in patients who developed AHF.

Incidence of hospital admission due to AHF

Several studies and registries have shown a high readmission rate in patients after TAVI.[19] The rate of early (within 30 days) readmission ranged from 4.0% to 17.9%, and was higher in those patients who underwent TAVI through a transapical approach. The readmission rate during the first year post-TAVI was as high as 50% of patients, mostly for noncardiovascular causes. A study by Nombela-Franco et al.[20] reported an incidence of 43.9% for all-cause readmissions up to 1 year after TAVI. Among them, 58.9% were admitted for noncardiovascular causes (mainly due to pre-existing comorbidities) and 41.1% for cardiac causes, mainly AHF (23.3%). Similar results were reported by Durand et al., [21] with 1-year total readmission rate and for AHF of 52.2% and 24.1%, respectively. Of note, in both studies the valve used was the SAPIEN device. Our registry, which mainly examined patients receiving the CoreValve device, shows similar results: 30% of our population was admitted due to AHF during follow-up, less than a half of these admissions being during the first year after the procedure (46.2%).

Prognostic impact of hospital admission due to AHF

At the end of follow-up, 150 patients had died (37.59%). Our results are similar to previous published data by Avanzas et al.[22]: that group also remarked on the relevance of admission due to HF in TAVI patients, highlighting 92.6% of deaths after an admission. There are scarce reports on the determinants and prognosis of AHF after TAVI. As far as we know, the study by Durand et al.[21] was pioneer in reporting the impact of AHF on mortality after TAVI. Among patients discharged from hospital, the rate of all-cause mortality was 13.7% at 1-year, and was 31.4% after a mean follow-up period of 27.2 + 0.7 months. Readmission due to AHF after TAVI was strongly associated with higher mortality at 1 year (24.2% vs 10.4%, *P* < .0001) and at the end of follow-up (50.0% vs 25.6%, *P* < .0001). Our results are fairly similar. After a mean follow-up period of 27 ± 24.1 months, mortality in patients admitted due to AHF was 52.1% vs 31.4% (HR, 1.84; 95%CI, 1.14-2.97; *P* < 0012). Nombela-Franco et al.[20] also assessed the impact of early hospital admission on mortality, with a mean follow-up similar to that one in our study. Their reported mortality rate at 2 years was significantly increased in those patients who were admitted within 30 days after TAVI compared with those who were not readmitted (30.2% vs 19.2%; *P* = .002). Approximately 30% to 50% of the readmissions were related to cardiovascular causes, mostly AHF, and had a major prognostic impact on mortality.

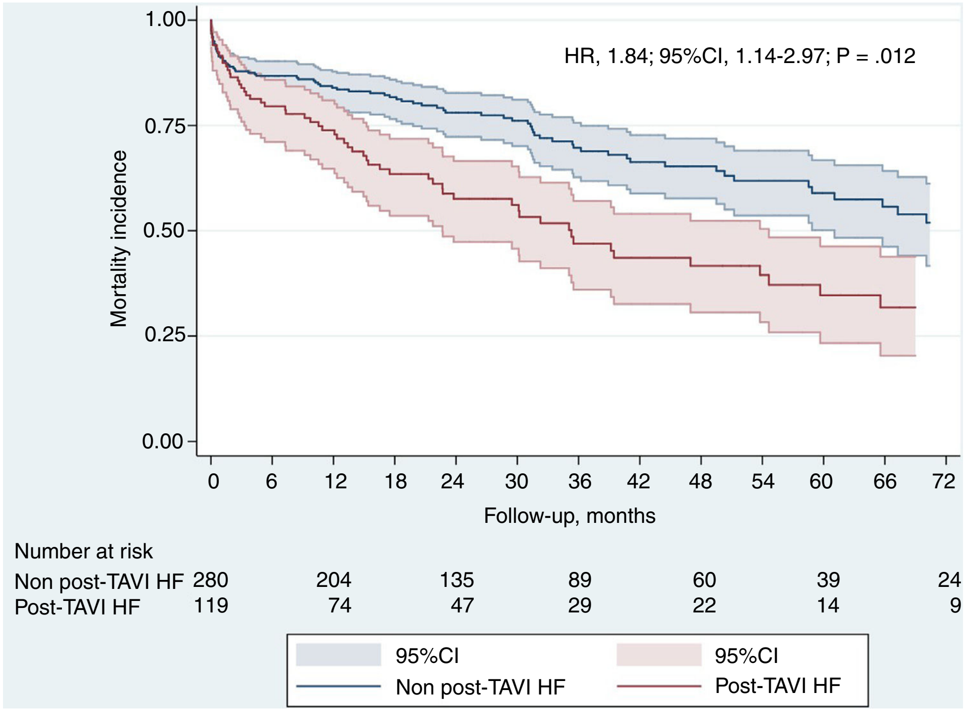

Figure 3. Adjusted survival Kaplan-Meier curves of TAVI patients based on follow-up 95%CI, 95% confidence interval; HF, heart failure; HR, hazard ratio; TAVI, transcatheter aortic valve implantation.

Table 4
Predictive factors for mortality in the subgroup of patients developing HF during follow-up

Variables	HR	95%CI	*P*
Age, y	1.04	1.00-1.08	.059
Female sex	0.71	0.43-1.15	.167
BMI, kg/m^2	0.95	0.90-1.01	.102
NRI	0.94	0.91-0.97	< .001
Hypertension	1.11	0.58-2.14	.744
Diabetes mellitus	0.76	0.43-1.36	.352
PAD	0.73	0.35-1.51	.399
CAD	1.46	0.88-2.43	.140
Prior HF	1.06	0.64-1.77	.812
COPD	0.70	0.41-1.22	.210
Chronic kidney disease	1.87	1.11-3.14	.018
Atrial fibrillation	1.17	0.701.97	.546
LVEF groups			
< 40%	1.38	0.6-3.02	.419
40-49%	1.27	0.49-3.30	.610
> 50%	ref	ref	ref
Moderate-severe MR	1.62	0.94-2.80	.082
PAP, mmHg	0.99	0.97-1.01	.250
Hemoglobin, g/dL	1.03	0.88-1.20	.675
Creatinine	1.29	0.87-1.91	.209
NT-proBNP	1.01	1.01-1.02	< .001
Aortic regurgitation >III	2.26	1.58-3.24	< .001
Pacemaker implantation	1.58	0.97-2.57	.069
Follow-up HF during first year post-TAVI	0.88	0.52-1.47	.618

95%CI, 95% confidence interval; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CAD, coronary arterial disease; HF, heart failure; HR, hazard ratio; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; NRI, nutritional risk index; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PAD, peripheral arterial disease; ref, reference group; PAP, pulmonary artery pressure; TAVI, transcatheter aortic valve implantation.

Predictive factors for hospital admission for AHF

Two independent factors were identified as predictors for AHF after the index discharge: an episode of hospital admission for AHF before TAVI implantation and high risk measured by STS score. Durand et al.[21] found 4 independent predictors for AHF: low aortic mean gradient before TAVI, postprocedural blood transfusion, severe persistent postprocedural pulmonary hypertension, and left atrial dilatation, of which only 2 were procedure-related. In this study, a previous episode of AHF before TAVI failed to achieve statistical significance in the multivariate analysis. Baron et al.[23] reported the impact of aortic valve gradient on the outcomes of TAVI in a large series of patients (n = 11 292); low aortic valve gradient (< 40 mmHg) was associated with higher mortality (HR, 1.21; 95%CI, 1.11 - 1.32; *P* < .001) and higher rates of AHF (HR, 1.52; 95%CI, 1.36-1.69; *P* < .001) with no effect of LVEF. We observed no significant impact for pre-TAVI aortic valve gradient or for LVEF. These discrepancies may be explained by demographic and clinical differences between the populations.

In our registry, despite pulmonary arterial pressure being higher in the group that developed AHF after TAVI, it did not have an impact on prognosis in our cohort. Several publications showed that pulmonary hypertension before TAVI is frequent and increases mortality after TAVI.[24,25] Patients with persistent severe pulmonary hypertension after TAVI have worse prognosis than those with a decrease in pulmonary artery systolic pressure below 60 mmHg (2-year mortality rate 50.0% vs 18.6%, *P* = .001). It was postulated that right heart catheterization could therefore aid in Heart Team decision-making.

Major bleeding and transfusion is frequent following TAVI and was associated with an increased risk of early and late mortality.[26] Durand et al.[21] observed that severe bleeding and, particularly, the need for transfusions were independent predictors of admission due to AHF after TAVI. In our cohort the need for transfusions was not associated with increased AHF, but it was a marker of higher mortality after implantation.

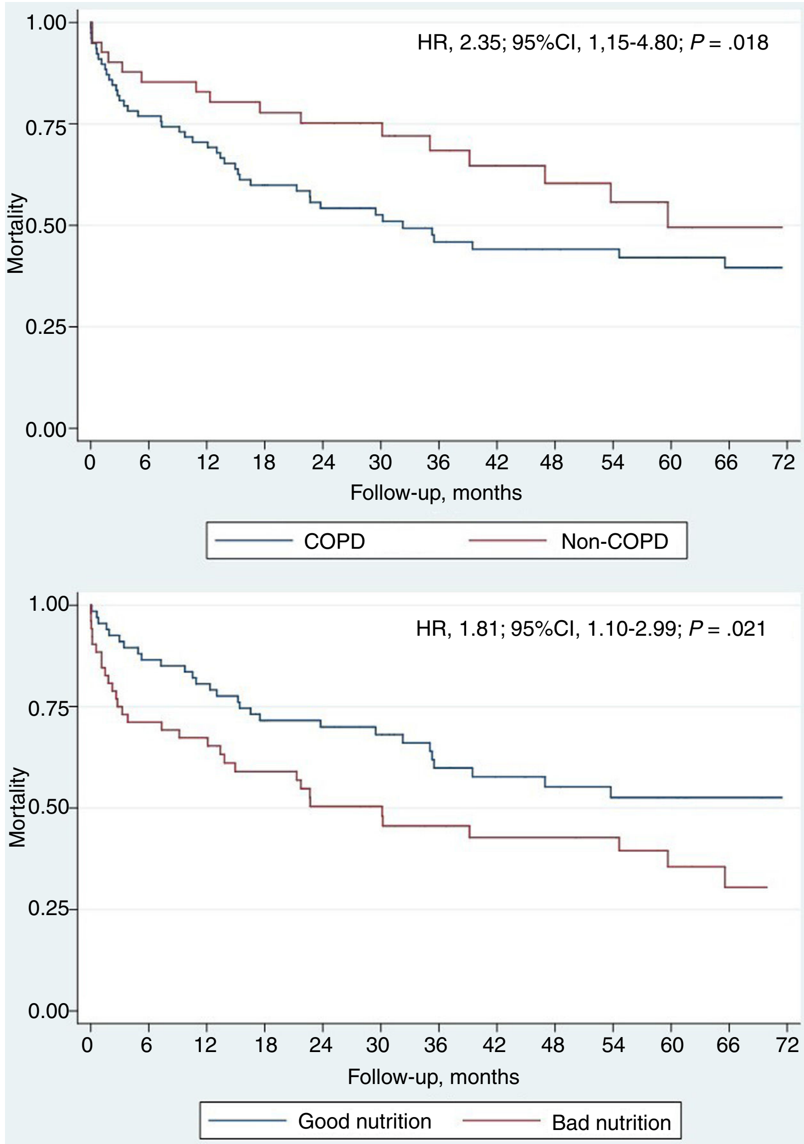

Figure 4. Adjusted survival Kaplan-Meier curves for independent predictors of mortality in patients with heart failure after transcatheter aortic valve implantation. 95%CI, 95% confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio.

Predictive factors for mortality in patients with AHF: the role of NRI

NRI and chronic obstructive pulmonary disease after valve implantation were found to be key elements influencing the prognosis of this group of patients. Our results show for the first time how nutritional status assessed by using NRI is a powerful independent prognostic factor. NRI is a validated tool for estimating the risk of undernutrition in various populations. The NRI shows a strong correlation with mortality, adverse events and deterioration of functional capacity, which is superior to that achieved using body mass index and albumin separately.[27–30] Malnutrition is highly prevalent and has been reported to be an independent risk factor for clinical events in HF. A large proportion of patients hospitalized for HF have moderate to severe malnutrition, and low NRI is associated with more readmissions and higher mortality in patients with AHF, as well as with higher mortality in patients with chronic HF.[27–30] A relationship between classic nutritional status markers, such as body mass index and hypoalbuminemia, and prognosis after TAVI (with a J-shape curve) has been established in previous studies.[31]

Assessment of malnutrition risk must be part of the geriatric assessment of patients who undergo TAVI and plays a determining role in frailty status. The potential use of the NRI for early identification of patients at risk of malnutrition who are under assessment for TAVI could be highly relevant in daily clinical practice. Such patients could potentially benefit from interventions to improve their nutritional status prior to undergoing the procedure. Larger studies are needed to validate NRI within a geriatric and frailty score, alone or as a part of other predictive scores for events after TAVI.

Chronic obstructive pulmonary disease is common in HF patients, and its presence in those with systolic dysfunction is associated with an increased burden of comorbidities, lower use of evidence-based HF medications, longer hospital stays, and increased in-hospital noncardiovascular mortality.[32]

CONCLUSIONS

The proportion of patients who develop AHF after TAVI is high, and prior AHF status has an important prognostic significance.

There is a need to identify subgroups of patients at higher risk in order to optimize their status prior to the procedure. In our study, patients with a previous history of AHF and high STS score were more prone to develop AHF during follow-up. Closer surveillance of these patients, with targeted and intensive medical treatment, could be helpful to try to reduce readmissions due to HF and improve their prognosis. In view of our results, intervention programs on the nutritional status of patients who develop AHF after TAVI and who are at risk of malnutrition could also improve their survival. In our study, as in previous studies, few factors have been identified as predictors of AHF. Future efforts should focus on the search for more predictors of AHF and evaluate whether an intervention during follow-up, such as optimization of medical therapy or nutritional status, has an impact on the prognosis of this subgroup of patients.

ACKNOWLEDGMENTS

To Manuela Sestayo for her outstanding help with language editing.

CONFLICTS OF INTEREST

R. Trillo Nouche is a proctor for Medtronic.

WHAT IS KNOWN ABOUT THE TOPIC?

- The evidence on HF after TAVI is scarce. Previous studies have observed the adverse impact of HF on post-TAVI prognosis, but the number of well recognized predictive factors is still very low.

WHAT DOES THIS STUDY ADD?

- To our knowledge, this is the study to assess the incidence, prognostic impact, and predictive factors for hospital admission due to AHF following TAVI with the CoreValve device.
- In our cohort, 2 potent prognostic determinants were found: a previous history of AHF and high STS score.
- Our results also show for the first time how nutritional status, assessed using NRI, is a powerful independent prognostic factor in this subgroup of patients, suggesting that this index could be included in the evaluation of candidates for TAVI.

REFERENCES

1. Carabello BA, Paulus WJ. Aortic stenosis. *Lancet.* 2009;373:956–966.
2. Vahanian A, Otto CM. Risk stratification of patients with aortic stenosis. *Eur Heart J.* 2010;31:416–423.
3. Leon MB, Smith CR, Miller DC, et al. Transcatheter aortic valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med.* 2010;363:1597–1607.
4. Smith CR, Leon MB, Miller DC, et al. Transcatheter versus surgical aortic valve replacement in high-risk patients. *N Engl J Med.* 2011;364:2187–9218.
5. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic valve replacement in intermediate-risk patients. *N Engl J Med.* 2016;374:1609–1620.
6. Reardon MJ, Van Mieghem NM, Popma. et al. Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients. *N Engl J Med.* 2017;376:1321–1331.
7. Thourani VH, Kodali S, Makkar RR, et al. Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis. *Lancet.* 2016;387:2218–2225.
8. Barbanti M, Petronio S, Ettori F. 5-Year Outcomes After Transcatheter Aortic Valve Implantation With CoreValve Prosthesis. *JACC Cardiovasc Interv.* 2015;8:1084–1091.
9. Franzone A, Pilgrim T, Arnold N, et al. Rates and predictors of hospital readmission after transcatheter aortic valve implantation. *Eur Heart J.* 2017;38:2211–2217.
10. Stähli BE, Tasnady H, Luscher TF, et al. Early and late mortality in patients undergoing transcatheter aortic valve implantation: comparison of the novel EuroScore II with established risk scores. *Cardiology.* 2013;126:15–23.
11. Piazza N, Wenaweser P, Van Gameren M, et al. Relationship between the logistic EuroSCORE and the Society of Thoracic Surgeons Predicted Risk of Mortality score in patients implanted with the CoreValve ReValving system-a Bern-Rotterdam Study. *Am Heart J.* 2010;159:323–329.
12. Grube E, Schüler G, Buellesfeld L, et al. Percutaneos aortic valve replacement for severe aortic stenosis in high risk patients using the second-and current third-generation self-expanding CoreValve prosthesis: device success and 30-day clinical outcome. *J Am Coll Cardiol.* 2007;50:69–76.
13. Kappetein AP, Head SJ, Genereux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *J Am Coll Cardiol.* 2012;60:1438–1454.
14. Nishimura RA, Otto CM, Bonow R, et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation.* 2017;135:e1159–e1195.
15. Bouillanne O, Morineau G, Dupont C, et al. Geriatric Nutritional Risk Index: a new index for evaluating at-risk elderly medical patients. *Am J Clin Nutr.* 2005;82:777–783.
16. González-Ferreiro R, Muñoz-García AJ, López-Otero D, Avanzas P. Nutritional risk index predicts survival in patients undergoing transcatheter aortic valve replacement. *Int J Cardiol.* 2019;276:66–71.
17. Upshaw JN, Konstam MA, van Klaveren D, Noubary F, Hugging GS, Kent DM. Multi state model to predict heart failure hospitalizations and all-cause mortality in outpatients with heart failure with reduced ejection fraction: model derivation and external validation. *Circ Heart Fail.* 2016;9:e003146.
18. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). *Developed with the special contribution of the Heart Failure Association (HFA) of the ESC Eur J Heart Fail.* 2016;18:891–975.
19. Urena M, Webb JG, Eltchaninoff H, et al. Late cardiac death in patients undergoing transcatheter aortic valve replacement: incidence and predictors of advanced heart failure and sudden cardiac death. *J Am Coll Cardiol.* 2015;65:437–448.
20. Nombela-Franco L, Trigo M, Morrison-Polo G, et al. Incidence Causes, and Predictors of Early (≤ 30 Days) and Late Unplanned Hospital Readmissions After Transcatheter Aortic Valve Replacement. *JACC Cardiovasc Interv.* 2015;8:1748–1757.
21. Durand E, Doutriaux M, Bettinger N, et al. Incidence Prognostic Impact, and Predictive Factors of Readmission for Heart Failure After Transcatheter Aortic Valve Replacement. *JACC Cardiovasc Interv.* 2017;10:2426–2436.
22. Avanzas P, Pascual I, Muñoz-García AJ, et al. Long-term follow-up of patients with severe aortic stenosis treated with a self-expanding prosthesis. *Rev Esp Cardiol.* 2017;70:247–253.
23. Baron SJ, Arnold SV, Herrmann HC, et al. Impact of ejection fraction and aortic valve gradient on outcomes of transcatheter aortic valve replacement. *J Am Coll Cardiol.* 2016;67:2349–2358.
24. Lucon A, Oger E, Bedossa M, et al. Prognostic implications of pulmonary hypertension in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation: study from the FRANCE 2 registry. *Circ Cardiovasc Interv.* 2014;7:240–247.
25. Malouf JF, Enriquez-Sarano M, Pellikka PA, et al. Severe pulmonary hypertension in patients with severe aortic valve stenosis: clinical profile and prognostic implications. *J Am Coll Cardiol.* 2002;40:789–795.
26. Généreux P, Cohen DJ, Mack M, et al. Incidence Predictors, and Prognostic Impact of Late Bleeding Complications After Transcatheter Aortic Valve Replacement. *J Am Coll Cardiol.* 2014;64:2605–2615.
27. Aziz EF, Javed F, Pratap B, et al. Malnutrition as assessed by nutritional risk index is associated with worse outcome in patients admitted with acute decompensated heart failure: an ACAP-HF data analysis. *Heart Int.* 2011;6:e2.
28. Yoshihisa A, Kanno Y, Watanabe S, et al. Impact of nutritional indices on mortality in patients with heart failure. *Open Heart.* 2018;5:e000730.
29. Barge-Caballero E, García-López F, Marzoa-Rivas R, et al. Prognostic value of the nutritional risk index in heart transplant recipients. *Rev Esp Cardiol.* 2017;70:639–645.
30. Al-Najjar Y, Clark AL. Predicting outcome in patients with left ventricular systolic chronic heart failure using a nutritional risk index. *Am J Cardiol.* 2012;109:1315–1320.
31. González-Ferreiro R, Muñoz-García AJ, López-Otero D, et al. Prognostic value of body mass index in transcatheter aortic valve implantation: A J-shaped curve. *Int J Cardiol.* 2017;232:342–347.
32. Mentz R, Fiuzat M, Wojdyla M, et al. Clinical characteristics and outcomes of hospitalized heart failure patients with systolic dysfunction and chronic obstructive pulmonary disease: findings from OPTIMIZE-HF. *Eur J Heart Fail.* 2012;14:395–403.