Decompensated Heart Failure in Patients With Aortic Valve Stenosis

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Introduction

Heart failure may be a sign of disease progression in patients with a diagnosis of severe aortic valve stenosis; it represents an adverse prognosis factor related to increased severity and entails the need to resolve the disease because, once manifested, life expectancy is poor.[1] In certain cases, the condition warrants hospitalization for the treatment of the decompensation itself and to solve the valve disease.

To date, there is almost no published literature showing the evolution of this special patient population during hospitalization due to heart failure. Therefore, the outcome of these patients is largely unknown, in terms of death, complications, days of hospitalization, use of hospital resources, and method of resolution of the valve disease in an inpatient setting.

ICBA has a multidisciplinary Heart Team engaged in the assessment, treatment, and follow-up of high-risk valve disease patients. As a result, the number of patients with this condition who receive care at the institution and are hospitalized due to several intercurrent conditions, including heart failure, is high. This represents an opportunity to study this population within the framework of heart failure-related decompensation.

The objectives of this study were to analyze the clinical features, inpatient outcome, and established treatments for patients admitted with a diagnosis of heart failure with aortic valve stenosis, and to assess patients' vital status at follow-up following discharge, based on the assigned treatments.

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Material and Methods

This is an analytical retrospective cohort study involving patients admitted to the institution with a diagnosis of decompensated heart failure and aortic stenosis pursuant to the International Classification of Diseases (ICD-10) between October 2015 and August 2018.

Population

Inclusion criteria were defined as patients aged 75 or older admitted to our institution due to decompensated heart failure who presented with severe aortic stenosis or those presenting with moderate aortic stenosis with no other reasons to justify the clinical condition (eg, significant nonrevascularized coronary artery disease), and congenital aortic stenoses of any degree of severity.

Severe AS was defined as an area <1 cm^2 and/or a maximum jet velocity $\geq$4m/s or, in the case of moderate stenosis, as an area between 1 and 1.5 cm^2 and/or a maximum jet velocity of 3-4 m/s.

The diagnosis of heart failure was defined as the presence of compatible symptoms: class III/IV dyspnea according to the Functional Classification of the NYHA, paroxysmal nocturnal dyspnea and/or fatigue with signs of congestion, chest X-ray showing capillary and venous congestion, lower limb edema, pulmonary rales, jugular vein distention, and/or hepatomegaly.

All patients whose heart failure was due to other conditions were excluded (eg, significant nonrevascularized coronary artery disease, hypertrophic cardiomyopathy, and infiltrative cardiomyopathy).

Demographic data were obtained from the medical history at admission, including age, gender, vital signs, and concomitant diseases (history of hypertension and/or hypertension treatment, dyslipidemia, diabetes mellitus, atrial fibrillation, coronary artery disease defined as prior infarction or coronary intervention, chronic obstructive pulmonary disease, and renal failure).

Following discharge, in December 2018, a follow-up was conducted through the medical history electronic system; when required, a telephone call was made to find out the patient's vital status. Two patients could not be located.

Informed consent was obtained to take part in the study. The study was approved by the Ethics Committee and the Institutional Review Board of the institution, and it was conducted in compliance with the principles of the Declaration of Helsinki.

Statistical Analysis

Categorical variables were expressed as frequencies and percentages, and continuous variables as means and standard deviations or medians, with their corresponding interquartile range (IQR), as applicable. The difference between categorical variables was estimated by means of the chi-square or Fisher's test, as applicable. Continuous variables were compared with the *t* test or Mann-Whitney test based on their distribution. Survival was assessed during follow-up by means of Kaplan-Meier curves based on the treatment received, and they were compared with the log-rank test. A significant *P* value was considered as a value <0.05. The Statistics program, version 21, was used for the statistical analysis.

Results

Out of a total of 471 patients admitted to ICBA with a diagnosis of decompensated heart failure between October 2015 and August 2018, 66 patients were identified as having aortic valve stenosis as a primary etiology causing the clinical condition. Baseline characteristics are summarized in Table 1. The score of the Society of Thoracic Surgeons (STS) was 7.5 (IQR 25-75 5-10) among the general population; 7.5 (IQR 25-75 5.3-10) for TAVIs; 4.6 (IQR 25-75 3.4-7.3) for those who underwent surgery and 8 (IQR 25-75 6-22) for those receiving medical treatment (non-intervention group); interaction value of $P = 0.003$.

Table 2 outlines the echocardiographic data. Except for 1 patient with bicuspid aorta, in all cases, the cause was sclerosis and calcification; only 1 patient had a valvular area of 1.1 cm^2 labeled as moderate with no other causes which might explain the clinical condition.

Table 1. Baseline population characteristics

Variable	Value
Male	39 patients (59%)
Age	84 (SD $\pm$ 7) years old
Diabetes	17 patients (25.8%)
Hypertension	58 patients (87.9%)
Dyslipidemia	37 patients (56.1%)
BMI	27.8 ($\pm$5)
Atrial fibrillation	24 patients (36%)
Coronary artery disease	15 patients (22.7%)
COPD	12 patients (18%)
Chronic renal failure	14 patients (21%)
STS	7.5 (IQR 25-75 5-10)

BMI, body mass index; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; STS, score of the Society of Thoracic Surgeons.

Table 2. Doppler echocardiography for the population

Variable	Value
Maximum gradient	73 (SD ± 26) mm Hg
Medium gradient	44 (SD ± 16) mm Hg
Peak velocity	4.2 (SD ± 0.85) m/s
Aortic valve area	0.6 (SD ± 0.19) cm^2
VTI	94 (SD ± 23) cm
LVEF	51% (SD ± 14)
LVEF <50%	26 patients (39%)
IVS	159 (SD ± 14) mm
PW	13.8 (SD ± 14) mm

IVS, interventricular septum; LVEF, left ventricular ejection fraction; PW, posterior wall; VTI, velocity time integral.

As regards inpatient evolution, the mean hospitalization was 16 (SD ± 11) days, the most frequent clinical presentation form was systemic congestion (86.4%, 57 patients), followed by pulmonary edema (9%, 9 patients); low cardiac output sydrome was present in 4.5% (3 patients). The rate of use of inotropes and/or vasopressors was 9.1% (6 patients); in one case, an aortic counterpulsation balloon was implanted (prior to the valvuloplasty, patient presented in shock). Eight patients (12%) underwent some kind of assisted ventilation (noninvasive ventilation and/or mechanic respiratory support). Finally, a coronary angioplasty was performed on 3 patients (4.5%), 2 within the framework of a TAVI as concomitant procedure, and another one associated with a valvuloplasty.

During hospitalization, a mortality of 12% (8 patients) was recorded. The variables associated with death were presentation with low output/shock (37.5% vs 0%, $P < 0.0001$), maximum measured troponin ($P = 0.029$, 284 ug/L IQR 25-75 87.5-537 vs 56 ug/L IQR 25-75 36-103.5), maximum measured creatinine ($P = 0.019$, 2.82 mg/dL SD ± 0.13 vs 1.68 mg/dL SD ± 1.09), STS ($P = 0.005$, 12.3 IQR 25-75 8-18.7 vs 7.1 IQR 25-75 5-10), maximum gradient ($P = 0.037$ 95 mm Hg SD ± 27 vs 71 mm Hg SD ± 26), use of inotropes ($P > 0.0001$, 62% vs 1.7%), and use of some kind of respiratory support ($P < 0.001$ 75% vs 3.4%; Table 3). Variables such as ejection fraction or aortic valve area were not associated with a poorer inpatient outcome.

During hospitalization, 7 TAVIs and 9 valve replacement surgeries were performed; 1 patient died in the postoperative period due to cardiogenic shock, with no deaths in the TAVI group. Six valvuloplasties were conducted in patients with cardiogenic shock; 1 as a bridge to a TAVI; 4 of the patients who underwent a valvuloplasty died within 12 hours following the procedure due to refractory shock. Of the patients who did not

Table 3. Variables associated with death during hospitalization

Variable	Alive (48 patients)	Deceased (8 patients)	*P* Value
Low cardiac output/ shock presentation	0%	37.5%	<0.0001
Maximum measured troponin	56 ug/L IQR 25-75 36-103.5)	284 ug/L (IQR 25-75 87.5-537)	0.029
Maximum measured creatinine	1.68 md/dL SD ± 1.09	2.82 md/dL SD ± 0.13	0.019
STS	7.1 (IQR 25-75 5-10)	12.3 IQR 25-75 8-18.7	0.005
Maximum gradient	71 mm Hg SD ± 26	95 mm Hg SD ± 27	0.037
Inotropes	1.7%	62%	<0.0001
Respiratory support	3.4%	75%	<0.0001

undergo any interventions (n = 45), 12 patients were excluded from procedures due to high clinical risk or anatomical contraindications for TAVI, and 6 patients rejected any kind of invasive procedures; 22 patients were discharged on a TAVI scheme and 5 on an aortic valve replacement scheme.

Fifty-two discharged patients were followed up (2 were lost to follow-up), with a median follow-up of 12 months (IQR 25-75: 6-23 months). During said period, 17 patients were implanted a TAVI and 5 underwent aortic valve replacement surgery. The death rate during follow-up was 34.4% (20 patients), 30% in the TAVI branch (6 patients), 15% in the surgery branch (3 patients), and 55% in the nonintervention group (11 patients).

An overall survival curve was developed based on the allocated treatment (Fig 1), which showed a higher mortality for patients who received medical treatment vs those undergoing interventions, either with a TAVI ($P = 0.003$) or with valve replacement ($P = 0.022$); there were no significant differences between TAVI and valve replacement ($P = 0.9$).

Discussion

This record shows inpatient outcomes of an extremely high clinical risk population given their underlying condition and associated comorbidities. There is very limited published literature showing the outcome of patients admitted for decompensated heart failure and aortic stenosis. It should be highlighted that dyspnea as a clinical manifestation of the disease signals a poor short-term prognosis[1] and, thus, a worse outcome is to be expected for a patient admitted for heart failure in the context of significant aortic stenosis than for those with no valve conditions.

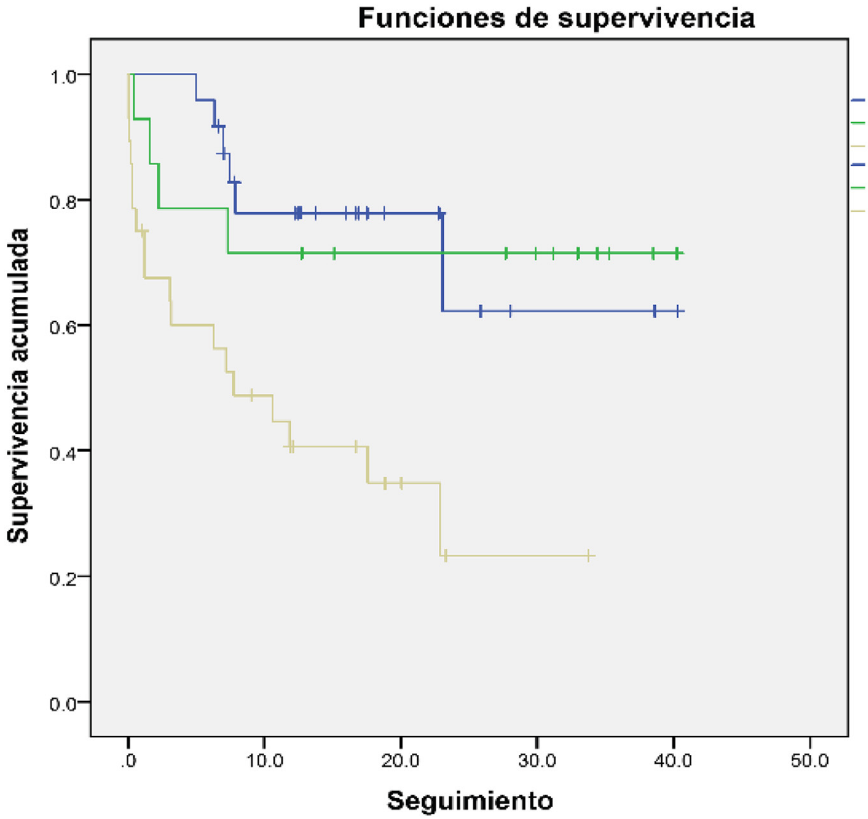

FIG 1. Survival curve based on allocated treatment. Valve replacement is shown in green, TAVI is shown in blue, and medical treatment in yellow. (Color version of figure is available online.)

With respect to the characteristics of the population, the age of presentation was higher than that observed in admission records due to decompensated heart failure: in the European registry (EORP) and in the Argentine heart failure registry, the average age was 72 and 77, respectively, vs 84 in our case history.[2,3] Instead, the age was very similar to the one described in other publications of patients admitted due to decompensated heart failure with an aortic stenosis diagnosis, such as those published by Nagao et al and[4] by Kawase et al, of 81 and 85 years of age, respectively.[5] Hospital stay was significantly longer than in the Argentine registry (15.5 days vs 5 days); there are no data regarding the average hospital stay in the publications on patients with aortic valve conditions.

In terms of comorbidities, it should be noted that the prevalence of arterial hypertension reached 87%, a much higher rate than that observed for other hospitalization publications but closer to the one published in the work by Kawase mentioned above (arterial hypertension prevalence of 88%). The prevalence of diabetes, chronic obstructive pulmonary disease, renal failure, and atrial fibrillation was similar to the one reported in general heart failure registries and to those from the publications on patients with aortic stenosis.

Hospital mortality reached 12%, higher than in the last Argentine registry, which shows a lower rate (2.5%), and in the EORP registry (3.8%), although, again, it is more similar to the cases described by Kawase, with an 11% inpatient mortality. In turn, and as a sign of higher clinical severity, low cardiac output presentation was also somewhat higher in this case: 4.5% compared with the Argentine registry mentioned above (2.5%) and with the EORP registry (2.3%).

As regards echocardiographic variables, it should be highlighted that the median LVEF was 53% (IQR 25-75 38-63), which contrasts with the median LVEF from the publications on decompensated heart failure, which were much lower (the average LVEF from decompensated heart failure records was 35%-38%). This finding is probably related to the fact that aortic stenosis only impairs the LVEF at advanced stages and is in keeping with the average LVEF published by Nagao's series, which was 55% on average. In our case histories, impairment of the LVEF, defined as a cutoff below 50% based on the European valve disease guidelines,[6] was not associated with a higher death risk. This finding contrasts with Kawase's record, where a LVEF $< 50\%$ meant a higher death risk, even though this association was observed at the 12-month follow-up. This is probably linked to the size of our population sample.

Patients who underwent a definitive treatment, whether TAVI or valve replacement, had an excellent outcome, with only one in-hospital death in the surgery group. Therapeutic decisions were made by the Heart Team, who conducted a thorough multidisciplinary screening to determine the appropriate treatment. This was reflected in the STS score, which showed lower values for the surgical group compared with the TAVIs, and even more so with the group which did not qualify for interventions. Discussion patients in a specialized Heart Team could influence the results obtained.

Valvuloplasty has been and still remains a rescue treatment which, in our study, was mainly performed on patients with severe shock who were not candidates for definitive treatment. There is still very limited literature on the evolution of patients undergoing a valvuloplasty in emergency settings. In the urgent care setting, 12-month survival is only 33%-55%.[5,7] The discouraging results from our cohort can probably be explained by the fact that the patients were admitted in cardiogenic shock to the Cath Lab, in a true emergency situation.

It should be noted that patients admitted with a severe aortic stenosis diagnosis have a high death and/or hospitalization rate at follow-up. In the above-mentioned registry by Nagao et al,[4] the 30-day and 3-year death rates were 6.5% and 50.5%, respectively. As this study shows, even following intervention, hospitalized patients have a poorer outcome than those with no admissions due to decompensated heart failure. In the subanalysis of the Spanish IDEAS registry, which included over 700 patients with aortic stenosis,[8] it was observed that those patients assigned to TAVI or to valve replacement surgery who were on stand-by for a given procedure based on the guideline recommendations and who ultimately did not undergo any interventions showed a death rate of almost 20%, which led the authors to conclude that nonintervention is an independent death risk factor for patients whose stenosis is not repaired based on the guidelines. The data from these publications are compatible with our follow-up findings, which showed an increased mortality for patients assigned to medical treatment, for whom the death rate reached 50%. This underscores that these are extremely high-risk populations who require early intervention, always based on the assessment of a multidisciplinary team. Last, the poorer evolution of TAVI patients compared with those who underwent surgery may be linked to the higher risk of the population, expressed through a higher STS score and not to the procedure itself. In fact, at the 12-month follow-up of the Partner B study, which did not discriminate patients admitted for decompensated heart failure, the death rate for TAVIs and medical treatment was 30% and 50%, respectively, with similar results to our population.[9]

Limitations

The number of patients is a limiting factor, although given that this is an understudied population, despite the limited number of patients, we believe that this work contributes to understanding the evolution of patients admitted for heart failure within the context of an aortic valve disease. We have not been able to include biomarker dosage, such as Nt-pro BNP, as a risk stratification variable. Last, the case history is restricted to a single site.

Conclusions

Individuals admitted due to decompensated heart failure with aortic valve disease are patients with higher clinical severity due to their underlying condition, but also because of their comorbidities: advanced age, high prevalence of concomitant cardiovascular risk factors and diseases comorbidities and higher presentation with low cardiac output. All of the above result in a longer hospitalization and higher hospital mortality.

Patients who received medical treatment have a high death rate during hospitalization and follow-up, which is also related to the clinical severity of the population studied.

Patient intervention, either with TAVI or with a valve replacement procedure, offers an improved prognosis both during hospitalization and follow-up.

The availability of a multidisciplinary Heart Team would seem to be beneficial, since it allows for a multidisciplinary discussion of the clinical cases to assign treatment based on each patient's clinical risk.

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