ORIGINAL ARTICLE

Prevalence, Predictors and Clinical Impact of Readmission in Patients with Aortic Stenosis Evaluated by a Heart Team

Prevalencia, predictores e impacto clínico de la rehospitalización en pacientes con estenosis valvular aórtica valorados por un Heart Team

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ABSTRACT

Background: There is scarce evidence in our setting regarding the prevalence of readmission, risk factors and clinical evolution of patients with severe aortic stenosis (AS) evaluated by a Heart Team.
Objective: The aim of this study was to assess the prevalence, predictors and clinical evolution of readmission in patients with severe AS evaluated by a Heart Team.
Methods: This was an observational, single-center, retrospective cohort study including patients with severe AS evaluated by a Heart Team. Total cohort characteristics were analyzed at baseline, and after stratification according to the presence or absence of readmission during a 2-year follow-up period.
Results: Mean population age (n=275) was 83.3±6.9 years, and 51.1% were female patients. The prevalence of readmissions was 21.5%. Readmitted patients were older (85.54±6.66 vs. 82.62±6.87 years; p=0.003) and had greater prevalence of frailty (97.4% vs. 89.3%; p=0.035), surgical risk (STS score 6.11±4.79 vs. 4.72±4.12; p=0.033), and previous history of atrial fibrillation (AF) (40.7% vs. 23.6%; p=0.009), compared with non-readmitted patients. Prior AF was an independent risk factor of readmission (OR 4.59; CI 95% 1.95-10.81; p<0.001). The incidence of readmission was 33.9% for transcatheter aortic valve implantation (TAVI), 1.7% for valve replacement surgery (SAVR), and 64.4% for conservative treatment (p=0.002). At 2 years, readmission was associated with higher mortality (47.5% vs. 13.4%; p<0.001).
Conclusions: In patients with severe AS evaluated by a Heart Team, a significant incidence of readmission was observed at 2 years, and this was associated with higher mortality. Atrial fibrillation was an independent risk factor of readmissions.

Key words: Aortic stenosis - Readmission - Mortality.

RESUMEN

Introducción: En nuestro medio existe escasa evidencia sobre la incidencia de rehospitalización, factores predictores y evolución clínica de los pacientes con estenosis aórtica (EAo) grave valorados por un *Heart Team*.
Objetivos: Determinar la prevalencia, los predictores de rehospitalización y la evolución clínica de pacientes con EAo grave valorados por el *Heart Team*.
Material y métodos: Estudio unicéntrico de cohorte retrospectivo, que incluyó pacientes con EAo grave valorados por el *Heart Team*. Se analizaron las características del total de la cohorte, y según la presencia o ausencia de rehospitalización, en un seguimiento de 2 años.
Resultados: La edad promedio de la población (n=275) fue de 83,3±6,9 años, con 51,1% de sexo femenino y una incidencia de rehospitalización de 21,5%. Los pacientes rehospitalizados fueron más añosos (85,54±6,66 vs. 82,62±6,87 años; p=0,003), más frágiles (97.4% vs. 89,3%; p=0,035), con mayor riesgo quirúrgico (STS score 6,11±4,79 vs. 4,72±4,12; p=0,033), y fibrilación auricular (FA) previa (40,7% vs. 23,6%; p=0,009), en comparación con los no rehospitalizados. Se identificó la FA previa como factor de riesgo independiente de rehospitalización (OR 4,59; IC 95% 1,95-10,81, p<0,001). La incidencia de rehospitalización fue de 33,9% para el reemplazo percutáneo de válvula aórtica (TAVI), 1,7% para la cirugía de reemplazo valvular (CRVAo), y 64,4% para el tratamiento conservador (p=0,002). A 2 años, la rehospitalización se asoció a una menor sobrevida (47,5% vs. 13,4%; p<0,001).
Conclusiones: En pacientes con EAo grave valorados por un *Heart Team* se observó una significativa incidencia de rehospitalización a 2 años, que se asoció a mayor mortalidad. La FA fue un factor de riesgo independiente de rehospitalización.

Palabras clave: Estenosis aórtica- Hospitalización - Mortalidad

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INTRODUCTION

Aortic stenosis (AS) is a frequent valve disease, with an estimated prevalence of 5% in patients over 65 years old, which grows exponentially with age. (1) New therapeutic strategies have been evaluated in the last decades as alternative to conventional aortic valve replacement surgery (SAVR), such as transcatheter aortic valve implantation (TAVI), which was initially adopted for patients with prohibitive surgical risk, and is currently evaluated for high, moderate and low surgical risk. (2-4)

The Heart Team is a group of clinical cardiologists, interventional cardiologists, cardiovascular surgeons and gerontologists in charge of the integral evaluation of patients with AS who are candidates for TAVI, in order to establish the feasibility of the percutaneous procedure and discuss the individual clinical cases from different perspectives, considering clinical, gerontological and social parameters, which play an important role at the time of decision-making. (5, 6)

Beyond the therapeutic strategy selected, different parameters are contemplated at the time of baseline risk stratification, such as the probability of readmission, a factor independently associated with higher mortality during follow-up. (7)

In our setting, there is currently little evidence on the incidence of readmission, its predictive factors and the clinical evolution of patients with severe AS evaluated by a Heart Team. (8)

OBJECTIVES

The aim of this study was to analyze the prevalence and predictive factors of readmission, and its association with all-cause mortality in patients with severe AS evaluated by a Heart Team to assess TAVI indication.

METHODS

A retrospective cohort, single-center study, was carried out, including patients with severe AS, over 18 years of age, who were evaluated by the Heart Team of the Hospital Italiano de Buenos Aires after hospitalization related to their valve disease, to assess the indication for TAVI between 2016 and June 2020. Total cohort characteristics, anatomical and biochemical data, and adverse clinical events at follow-up were analyzed at baseline and after stratification according to the presence or absence of readmission, as well as the effect of readmission on all-cause mortality, with a 2-year follow-up period since the initial evaluation.

Definitions

- Readmission: defined as rehospitalization due to decompensated heart failure, requiring intravenous diuretics and 24-hour or longer hospital stay.
- Prefrailty/frailty: described according to the 5-domain Fried Frailty Scale: unintentional weight loss, exhaustion, muscle weakness, slow gait and low physical activity. The presence of one or two factors is considered "prefrailty", while three factors or more is considered "frailty". (9)
- Bleeding: the severity of hemorrhagic events was classified according to the Bleeding Academic Research Consortium (BARC), and for the present study BARC ≥3 bleeding episodes were considered. (10)
- Surgical risk: It was assessed with the Society of Thoracic Surgeons (STS) score, and was classified as low (<4 points), moderate (4-8 points) and high (>8 points). (11)

Statistical analysis

IBM SPSS 23.0 (IBM, Armonk, U.S.A.) software package was used to perform the statistical analysis. Continuous variables were expressed as mean and standard deviation, or median and interquartile range, according to their distribution. The Kolmogorov-Smirnov test or the Shapiro-Wilk test was used to analyze normality, as appropriate. Categorical variables were expressed as frequency and percentage and were analyzed using the chi-square test or Fisher´s exact test. Numerical variables were compared with Student's t test or the Mann-Whitney U test, according to their distribution. A multivariate logistic regression model was used to analyze the pre-specified variables of interest: age, body mass index (BMI), STS score, prefrailty or frailty, diabetes mellitus, chronic obstructive pulmonary disease (COPD), atrial fibrillation (AF), left ventricular ejection fraction (LVEF) and moderate/severe mitral regurgitation (MR), to identify predictive covariates of the clinical event. Overall survival analysis, associated with the presence or absence of readmission was performed using the Log-Rank test, and expressed by the Kaplan-Meier estimator. Significance was considered for type I error below 5% (two-tailed $p < 0.05$).

Ethical considerations

The present study was approved by the Ethics Committee of Hospital Italiano de Buenos Aires (#5834) and was registered in the Digital Registry of Health Investigations Platform of Buenos Aires (PRIISA BA, #3030) system. An informed consent was waived due to retrospective nature of the study.

RESULTS

A total of 275 patients were included in the study. Mean age was 83.3±6.9 years, with 51.1% female patients and a readmission incidence of 21.5% at 2 years (Table 1).

A significant burden of associated comorbidities was observed, with a prevalence of nearly 90% hypertension. Moreover, 1 out of 4 patients presented diabetes mellitus and AF, 1 out of 3 had history of congestive heart failure and virtually all the cohort analyzed presented some degree of prefrailty/frailty, with an average LVEF of almost 56% and moderate surgical risk (see Table 1).

The subgroup of readmitted patients (n=59) was older, with more frailty, higher STS score and greater prevalence of AF, compared with the subgroup of non-readmitted patients (n=216) (see Table 1).

Regarding the anatomic, functional and concomitant biochemical characteristics of AS, the subgroup of patients readmitted at follow-up presented higher coexistence of moderate to severe MR and higher systolic pulmonary artery pressure, with respect to non-readmitted patients. In turn, readmitted patients evidenced greater plasma concentration of type B natriuretic peptide (BNP), compared with non-readmitted patients (Table 2).

Table 1. Baseline characteristics

Variable	Total (n=275)	Without readmission (n=216, 78.5%)	With readmission (n=59, 21.5%)	p*
Age - mean ± SD	83.25 ± 6.88	82.62 ± 6.87	85.54 ± 6.66	0.003
Male sex – n(%)	136 (48.9)	105 (48.6)	29 (49.2)	0.941
BMI - mean ± SD	27.06 ± 4.78	27.37 ± 4.84	25.94 ± 4.49	0.015
STS - mean ± SD	4.97 ± 4.27	4.72 ± 4.12	6.11 ± 4.79	0.033
Frailty - n (%)	174/190 (91.6)	134/150 (89.3)	38/39 (97.4)	0.035
HTN - n(%)	250 (89.9)	192 (88.9)	55 (93.2)	0.330
DLP - n(%)	200 (71.9)	153 (70.8)	45 (76.3)	0.410
DM - n(%)	65 (23.4)	58 (26.9)	7 (11.9)	0.016
CAD - n(%)	97/218 (44.5)	80/182 (44.0)	17/34 (50.0)	0.515
AMI - n(%)	23/218 (10.6)	17/182 (9.3)	6/34 (17.6)	0.149
PCI - n(%)	47 (16.9)	38 (17.6)	9 (15.3)	0.672
CABG - n(%)	26 (9.4)	18 (8.3)	8 (13.6)	0.224
CHF - n(%)	72/218 (33.0)	56/182 (30.8)	15/34 (44.1)	0.128
Cancer - n(%)	55/218 (25.2)	49/182 (26.9)	6/34 (17.6)	0.254
COPD - n(%)	28/218 (12.8)	23/182 (12.6)	5/34 (14.7)	0.742
PVD - n(%)	48 (17.3)	37 (17.1)	11 (18.6)	0.786
Stroke/TIA - n(%)	28 (10.1)	20 (9.3)	6 (10.2)	0.832
Bleeding † - n(%)	30/218 (13.8)	24/182 (13.2)	6/34 (17.6)	0.490
PPM - n(%)	8/218 (3.7)	8/182 (4.4)	0/34 (0.0)	0.213
Atrial fibrillation - n(%)	78 (28.1)	51 (23.6)	24 (40.7)	0.009
ACO - n(%)	51/218 (23.4)	35/182 (19.2)	14/34 (41.2)	0.005
LVEF - mean ± SD	55.61 ± 11.21	56.38 ± 11.21	53.08 ± 10.99	0.014

* p value for the difference between subgroups with and without readmission.
† BARC bleeding events ≥3
Abbreviations: SD = Standard deviation, BMI = Body mass index [weight(kg)/height(m2)], STS = Society of Thoracic Surgeons, HTN = Hypertension, DLP = Dyslipidemia, DM = Diabetes mellitus, CAD = Coronary artery disease, AMI.= Acute myocardial infarction, PCI = Percutaneous coronary intervention, CABG: Coronary artery bypass grafting, CHF = Congestive heart failure, COPD = Chronic obstructive pulmonary disease, PVD = Peripheral vascular disease, TIA = Transient ischemic attack, PPM = Permanent pacemaker, ACO = Anticoagulant treatment, LVEF = Left ventricular ejection fraction.

Multivariate logistic regression analysis identified prior AF as an independent predictive risk factor of readmission during follow-up (OR 4.59; 95% CI 1.95-10.81; p<0.001).

The therapeutic approach strategy selected by the Heart Team was TAVI in 47.5% of cases, SAVR in 19.4% and conservative treatment in 33.1% (see Table 2).

The incidence of readmission since the index procedure was 33.9% in the subgroup of patients with TAVI, 1.7% in the subgroup with SAVR and 64.4% in the subgroup of conservative treatment, with a significant difference between subgroups (p=0.002), but without difference between TAVI and SAVR groups (p=0.234).

Finally, readmission was associated with greater accumulated incidence of all-cause mortality at the 2-year follow-up period (47.5% vs. 13.4%, Log-Rank test p<0.001) (Figure 1).

DISCUSSION

To the best of our knowledge this is the first study in our setting analyzing the long-term incidence of readmission in patients with severe AS evaluated by a Heart Team.

In agreement with data reported in the literature, our analysis evidenced a significant incidence of readmission related to greater burden of associated comorbidities. (12, 13) Readmissions in this group of patients are frequent and entail a deleterious effect in terms of adverse clinical events at follow-up, poor quality of life parameters and greater health system costs. (14, 15) A systematic review and evidence-based meta-analysis analyzing 12 cohort studies in patients with severe AS and SAVR (n=558 396) and 20 cohort studies of patients with TAVI treatment (n=109 730) demonstrated a 30-day readmission rate of 7-23% and 5-27% for SAVR and TAVI, respectively. (16) Another study with patients belonging to a database of the United States included during 2013 (n=14 325 172) observed a 30-day readmission rate of 17.2% in patients subjected to TAVI and 20.6% in those with SAVR, without significant differences between the groups analyzed after propensity score matching (p=0.28). (17) It is important to point out that there are few data on the incidence of readmission after one

Table 2. Therapeutic strategy, anatomo-functional characteristics and laboratory data

Variable	Total (n=275)	Without readmission (n=216, 78.5%)	With readmission (n=59, 21.5%)	p*
TAVI – n (%)	132 (47.5)	112 (51.9)	20 (33.9)	0.014
Conservative treatment – n (%)	92 (33.1)	53 (24.5)	38 (64.4)	<0.0001
AVRS – n (%)	54 (19.4)	51 (23.6)	1 (1.7)	<0.001
Ca score – mean ± SD	3157.80 ± 1591.55	3005.89 ± 1418.14	3667.36 ± 1954.72	0.086
Ca volume - mean ± SD	2427.00 ± 1124.12	2338.51 ± 1084.54	2776.24 ± 1238.94	0.068
Ca nodule – n (%)	88/193 (45.6)	66/149 (44.3)	20/41 (48.8)	0.609
Mod/sev MR– n (%)	86/228 (37.7)	65/189 (34.4)	20/37 (54.1)	0.024
Mod/sev TR – n (%)	57/229 (24.9)	42/189 (22.2)	14/38 (36.8)	0.056
PSP - mean ± SD	34.63 ± 14.82	33.74 ± 15.00	39.08 ± 13.46	0.018
Hct (%) - mean ± SD	37.30 ± 4.63	37.40 ± 4.47	36.83 ± 5.52	0.445
WBC (/mm3) - mean ± SD	7324.61 ± 3453.82	7361.41 ± 3632.66	7211.32 ± 2431.75	0.775
Platelets (/mm3) - mean ± SD	201 623.85 ± 58 641.88	201 944.51 ± 57 976.45	200 029.41 ± 63 977.764	0.357
Albumin (g/dL) - mean ± SD	3.89 ± 0.55	3.91 ± 0.58	3.79 ± 0.43	0.169
CA-125 (U/mL) – median (IQR)	14.30 (10.00-28.05)	13.30 (9.60-24.90)	20.25 (14.37-127.45)	0.021
CrCl (mg/dL) - mean ± SD	60.05 ± 25.38	60.08 ± 25.08	60.75 ± 26.98	0.779
Troponin (ng/mL) - median (IQR)	28.05 (16.95-47.42)	27.50 (15.55-46.87)	31.55 (19.45-82.25)	0.164
BNP (pg/mL) - median (IQR)	927.00 (344.85-3071.50)	843.95 (331.52-2878.50)	2298.50 (857.80-8504.00)	0.044

* p values for the difference between subgroups with and without readmission.
Abbreviations: SD = Standard deviation, IQR = Interquartile range, TAVI = Transcatheter aortic valve implantation, SAVR = Aortic valve replacement surgery, Ca = Calcium, Mod/sev MR = Moderate/severe mitral regurgitation, Mod/sev TR = Moderate/severe tricuspid regurgitation, PSP = Pulmonary systolic pressure, Hct = Hematocrit, WBC = Leukocytes, CA-125 = Cancer antigen 125, CrCl = Creatinine clearance [mL/min/1,73m2], BNP = B-type natriuretic peptide.

year from the index therapeutic procedure. In this context, a study including 893 consecutive patients undergoing TAVI showed a readmission rate of 43.9% at one-year follow-up, with a median time since hospital discharge to readmission of 63 days (IQR: 19-157). (7) In turn, an analysis of multicentric prospective registries of Japan (CURRENT AS, n=3815, K-TAVI, n=449) showed a lower incidence of readmission at 2 years in TAVI patients (n=449) compared with the subgroup of patients with conservative treatment (n=894), even after propensity score matching (HR 0.25, 95% CI 0.16-0.40; p<0.001). (18) In the present study, the difference observed in readmission between the different therapeutic approach strategies implemented could be due to a selection bias, with patients with greater comorbidity burden subjected to conservative treatment with higher incidence of readmission during the evolution, followed by patients undergoing TAVI and finally, by patients with less comorbidities receiving SAVR. Besides, the incidence of readmission in this last group was much lower than reported in the literature, which might confirm that this was a highly selected group and at very low risk despite having been evaluated by a Heart Team. In that sense, there was no criteria in this study for the multidisciplinary assessment of a patient. The referral to the Heart Team was decided by the treating physician, or by express request of the patient asking an evaluation for TAVI.

Atrial fibrillation was an independent predictor of readmission risk. Several studies have assessed the clinical impact of concomitant baseline comorbidities in patients with severe AS, where the occurrence of AF prior to the index therapeutic procedure was associated with greater incidence of readmission at follow-up. (15-19) A French registry including patients subjected to TAVI, with a median follow-up of 310 days (IQR 190-400) (FRANCE-2 Registry , n=39 333) observed an AF prevalence prior to the index procedure of 25.8%, and in this subgroup a greater incidence of readmission at follow-up, compared with patients without prior AF (10.1% vs. 8.6%, HR 2.02; 95% CI 1.63-2.52; p<0.001). (20) Another study including patients with TAVI (n=1139), with one-year follow-up since the index procedure, identified previous AF as a predictive risk factor of readmission (adjusted HR 1.62; 95% CI 1.09-2.40; p=0.02), which was associated with lower survival during follow-up (77.8% vs. 88%, Log-Rank test p=0.004). (21) Regarding patients with AS subjected to SAVR, a study (n=136 051) identified the presence of prior AF as an independent predictive risk factor of 30-day readmission (OR 1.24; 95% CI 1.17-1.31; p<0.001). (22) These findings agree with the evidence of the present study, where prior AF was identified as a predictive factor of readmission at follow-up, regardless of the therapeutic approach.

Finally, it was seen that readmission entailed higher total mortality at follow-up. Different studies

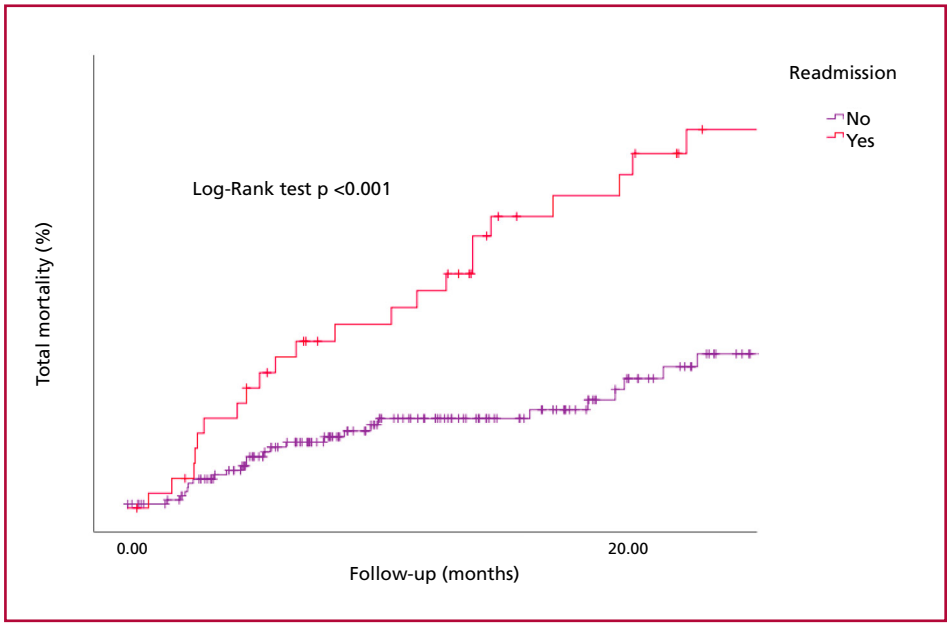

Fig. 1. Accumulated incidence of all-cause mortality, according to the presence or absence of readmission

have evaluated the deleterious clinical impact of readmission on this subgroup of patients. A study analyzing patients subjected to TAVI (n=868) observed a significantly higher risk of mortality during follow-up in the subgroup of readmitted patients, compared with non-readmitted ones (RR 4.29; 95% CI 2.86-6.42; p<0.001). (23) Similarly, another prospective study of patients with TAVI (n=720) demonstrated that the presence of readmission was significantly associated with higher total mortality at one-year follow-up, and that this decrease in survival was enhanced if readmission was caused by decompensated heart failure compared with another etiology, with 25% mortality for readmission due to decompensated heart failure, 10.9 % for readmission due to another clinical cause and 5.5% for the subgroup of non-readmitted patients (Log-Rank test p<0.0001). (12) These data agree with the observation of our study, where the subgroup of readmitted patients at follow-up presented a threefold higher mortality with respect to the non-readmitted group. However, a longer follow-up period was carried out compared with other cohorts reported in the literature, in which follow-up lasted between 30 days and one year since the index event.

This work presents some limitations related to observational studies, with biases inherent to this type of studies. Moreover, no echocardiographic data were recorded during follow-up, which could support the causes of mortality and the adverse clinical events observed, as well as no data related with the pharmacological treatment prescribed.

CONCLUSIONS

In patients with severe AS evaluated by the Heart Team for TAVI a significant incidence or readmission was observed at 2 years, similar to what is reported in the literature. Presence of AF was identified as an independent predictive risk factor of readmission. Finally, readmission was associated with higher all-cause mortality at follow-up.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material.)

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