ORIGINAL ARTICLE

Old Age Alone is not a Limitation for Surgical Aortic Valve Replacement

La edad avanzada en forma aislada no constituye una limitación para el reemplazo valvular aórtico quirúrgico

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ABSTRACT

Background: Surgical aortic valve replacement (SAVR) is the reference treatment in patients with symptomatic severe aortic valve disease. However, according to international scores, transcatheter aortic valve implantation (TAVI) is currently an alternative in different risk patients, and some guidelines consider TAVI as a preferable procedure in elderly patients.
Objectives: The aim of this study was to assess SAVR morbidity and mortality risk and results in adult patients, classified according to age as >75 years or ≤75 years.
Methods: A retrospective study was performed on 228 consecutive patients undergoing SAVR between January 1, 2011 and December 31, 2020 for symptomatic severe aortic valve disease. Among the total number of patients operated on, 46 (16%) were >75 years (Group 1, G1) and 182 (84%) were ≤75 years (Group 2, G2). Patients with concomitant coronary heart disease, bacterial endocarditis or other associated valve diseases were excluded from the analysis.
Results: Group 1 patients had greater risk of surgical morbidity and mortality analyzed by validated risk scores: ArgenSCORE 1.55 (IQR 0.99-3.33) vs 1.08 (IQR 0.68-2.23), p = 0.02 and STS score 2.33 (IQR 1.57-3.23) vs. 0.94 (IQR 0.72-1.44), p = 0.0001, with respect to G2, while no significant differences were found for EuroSCORE II: 2.37 (IQR 1.19-3.61) vs. 1.83 (IQR 1.16-3.04), p = 0.2. Overall mortality was 1.7% (G1: 2.1% vs. G2: 1.6%, p=NS), with no perioperative stroke or acute myocardial infarction (AMI).
Conclusions: The low number of deaths, stroke and AMI observed suggests that the selected treatment for these patients was adequate, with excellent results and without significant differences between these two age groups.

Key words: Aortic valve stenosis – Aortic valve replacement – Symptomatic aortic valve disease

RESUMEN

Introducción: El reemplazo quirúrgico de la válvula aórtica (REEAO) en pacientes con valvulopatía aórtica grave sintomática, es el tratamiento definido como el de referencia. Sin embargo, el implante valvular aórtico transcatéter (TAVI) se posiciona actualmente como una alternativa en pacientes de diferentes riesgos según los scores internacionales. Algunas guías consideran al TAVI como el procedimiento preferible en los pacientes añosos
Objetivos: Conocer el riesgo y resultados de morbimortalidad del REEAO en pacientes adultos clasificados según la edad en mayores de 75 años, o de 75 años o menos.
Materiales y métodos: Estudio retrospectivo sobre 228 pacientes consecutivos intervenidos mediante REEAO entre el 1 de enero de 2011 y el 31 de diciembre de 2020 por valvulopatía aórtica grave sintomática. Del total de pacientes operados, 46 (16%) eran mayores de 75 años (Grupo 1, G1) y 182 pacientes (84%) tenían 75 años o menos (Grupo 2, G2). Se excluyeron pacientes con enfermedad coronaria concomitante, endocarditis bacteriana u otras valvulopatías asociadas.
Resultados: Los pacientes del G1 tenían mayor riesgo de morbimortalidad quirúrgica analizado por scores de riesgo validados: ArgenSCORE de 1,55 (RIC 0,99-3,33) vs 1,08 (RIC 0,68-2,23), p = 0,02 y STS score de 2,33 (RIC 1,57-3,23) vs. 0,94 (RIC 0,72-1,44), p = 0,0001, con respecto al G2; no se encontraron en cambio diferencias significativas en el EuroSCORE II : 2,37 (RIC 1,19-3,61) vs. 1,83 (RIC 1,16-3,04), p = 0,2.
La mortalidad registrada global fue del 1,7% (G1: 2,1% vs. G2: 1,6% , p ns); no se observaron accidente cerebrovascular (ACV) ni infarto agudo de miocardio (IAM) perioperatorios.
Conclusiones: La escasa presentación de muerte, ACV e IAM sugiere que el tratamiento seleccionado para estos pacientes fue adecuado, con excelentes resultados sin diferencias entre los dos grupos etarios.

Palabras clave: Estenosis valvular aórtica - Reemplazo valvular aórtico - Valvulopatía aórtica sintomática

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Abbreviations

AMI	Acute myocardial infarction
AS	Aortic stenosis
HUA	Hospital Universitario Austral
MACE	Major adverse cardiovascular events
SAVR	Surgical aortic valve replacement
STS	Society of Thoracic Surgeons
TAVI	Transcatheter aortic valve implantation

INTRODUCTION

Symptomatic aortic valve disease is more frequently diagnosed in elderly people, and it is clear that valve replacement improves quality of life and life expectancy. (1, 2) In the last decade, transcatheter aortic valve implantation (TAVI) has emerged as a valuable alternative to surgical valve replacement (SAVR) in a selected spectrum of patients with symptomatic severe aortic stenosis (AS). Safety and efficacy of TAVI was initially established for patients at high surgical risk evaluated by the Society of Thoracic Surgeons mortality predictors with a score >8%. The high-risk PARTNER and US CoreValve studies according to STS, showed comparable clinical results with both techniques. (3, 4) The role of TAVI in intermediate risk patients (STS score 4%-8%) were later investigated in the PARTNER 2 and SURTAVI studies, demonstrating noninferiority of TAVI in this population of patients compared with surgery. (5, 6)

Recent evidence from controlled, randomized trials comparing TAVI with SAVR in low-risk patients with symptomatic severe AS, have been the starting point for the new 2020 American College of Cardiology/American Heart Association medical practice guideline, recommending as Class 1 level of evidence A SAVR and TAVI in low-risk patients over 65 years of age. (7)

Clearly risk assessed by STS has identified the possibility of performing any of the two procedures with similar results in its different score levels. The purpose of this study was to evaluate current morbidity and mortality results in a series of consecutive patients undergoing SAVR, analyzed according to preoperative STS score, EuroSCORE and ArgenSCORE.

Inclusion criteria

The study included all patients >18 years of age with SAVR indication (isolated or additionally requiring aortic annulus enlargement, an ascending aorta procedure or atrial fibrillation ablation) consecutively operated on at Hospital Universitario Austral (HUA) from January 1, 2011 to December 31, 2020. Patients with combined SAVR and myocardial revascularization surgery, infective endocarditis or any other valve disease were excluded from the analysis.

METHODS

This was a retrospective cohort study of patients undergoing SAVR according to the inclusion and exclusion criteria. An exclusive database was created for this study (all the variables analyzed are enclosed) with data collection from HUA electronic clinical histories.

The primary endpoint was major adverse cardiovascular events (MACE) defined as the composite of death, stroke or acute myocardial infarction (AMI) within 30 days of SAVR procedure.

Variables were defined as follows:

Stroke: Focal or diffuse brain injury confirmed by clinical findings and computed tomography study with sequel at patient discharge.

AMI: Development of persistent new Q waves in the electrocardiogram of at least 0.04 msec in two or more consecutive leads or decreased R wave voltage above 25% in precordial leads, increase of more than 10 times normal troponin levels or wall motion abnormalities in the echocardiogram consistent with electrocardiographic findings.

Need for permanent pacemaker: Due to new conduction blockades in the immediate postoperative period and despite awaiting 7 days for improvement.

Mediastinitis: Clinical signs with positive cultures confirmed in surgical mediastinal toilette.

Kidney failure: Increase in creatinine level above 50% baseline value.

Shock: Need for at least 24-hour inotropic support in case of low cardiac output defined by systolic blood pressure <90 mmHg, cold and pallid skin, poor capillary filling, obnubilation and oliguria, cardiac index <2.2 L/min/m2, pulmonary capillary pressure >18 mmHg, as well as need for inotropic agents for sustained hypotension due to vasodilation or hypovolemia.

Prolonged mechanical respiratory assistance: Need for 24-hour or more postoperative mechanical respiratory assistance.

Surgical bleeding: Need for reoperation due to mediastinal hemorrhage secondary to cardiac tamponade or bleeding above 500 mL in the first 6 hours.

The preoperative surgical condition was classified into two groups: scheduled or elective or non-scheduled or non-elective procedures.

The following scores were used to validate preoperative morbidity and mortality risk: ArgenSCORE, (8) STS score (9) and EuroSCORE. (10)

Ethical considerations

The registry was approved by the Evaluation and Ethics Independent Committee of HUA, which waived the need for an informed consent, as no sensible data or clinical follow-up were required (according to the Habeas Data law 25326 on Protection of Personal Data).

Statistical analysis

Qualitative variables are presented as percentages. Quantitative variables are expressed as mean and standard deviation or median and interquartile range, according to normal or non-normal distribution. Chi-square, Student's t, Wilcoxon or Mann Whitney tests were used as appropriate. Multivariate analyses were performed with linear or logistic regression analysis according to the characteristic of the dependent variable (quantitative or qualitative) and following

tests' assumptions. Statistical significance was considered for $p<0.05$.

RESULTS

Among a total of 228 consecutive patients who underwent SAVR between January 2011 and December 2020, 46 patients (16%) were >75 years (Group 1, G1) and 182 patients (84%) were ≤75 years (Group 2, G2). Table 1 shows preoperative baseline characteristics. Group 1 patients had greater presence of hypertension (89.1% vs. 71.9% p=0.01), diabetes (32.6% vs. 17.5% p=0.02), dyslipidemia (76 % vs. 52.7% p=0.004), permanent pacemaker (8.6% vs. 1.6% p = 0.01), cancer (23.9% vs. 6% p=0.002) and pulmonary artery pressure >50 mmHg, while G2 patients presented more frequently severe aortic regurgitation (4.3% vs. 15.3% p=0.01).

Group 1 patients had higher risk of surgical morbidity and mortality compared with G2, analyzed by validated risk scores: ArgenSCORE 1.55 (IQR 0.99-3.33) vs. 1.08 (IQR 0.68-2.23), p=0 .02 and STS score 2.33 (IQR 1.57-3.23) vs. 0.94 (IQR 0.72-1.44), p=0.0001. On the other hand, no significant differences were found for EuroSCORE II: 2.37 (IQR 1.19-3.61) vs. 1.83 (IQR 1.16-3.04), p=0.2, Table 1).

Overall mortality was 1.7% with no significant difference between both groups (G1: 2.1% vs. G2: 1.6% p=NS), and no perioperative stroke or acute myocardial infarction (AMI) were observed.

In multivariate analysis, mean valve gradient measured by Doppler echocardiography was the only predictor of morbidity adjusted for gender, age and ejection fraction (OR=0.95; 95% CI 0.91-0.99; p=0.01).

DISCUSSION

In our population of patients with severe aortic stenosis, SAVR is still an excellent option, even in patients ≥75 years. Mortality in patients undergoing SAVR in this series had an expected risk of 1.7% for the global population in accordance with the EuroSCORE II, STS score and ARGENscore. Clearly, the scarcity of major events hinders drawing final conclusions based on the segmentation of patients according to age and operative risk measured by classical surgical scores; however, we can corroborate that surgical treatment

Table 1. Preoperative variables

	Group 1 (n = 46)	Group 2 (n = 182)	Total (n = 228)	P Value
Age	78.8 ± 3.75	57.4 ± 13.8	61.4 ± 15.7	<0.0001
Male gender	27 (58.6 %)	112 (61.5 %)	139 (60.9 %)	NS
HTN	41 (89.1 %)	131 (71.9 %)	172 (75.4 %)	0.01
BMI	26.9 ± 3.2	29 ± 4.6	27.8 ± 4.4	NS
Diabetes	15 (32.6 %)	32 (17.5 %)	47 (20.6 %)	0.02
DLP	35 (76 %)	96 (52.7 %)	131 (57.4 %)	0.004
Smoking	18 (39.1 %)	67 (36.8 %)	85 (37.2 %)	NS
Angina	1 (2.1 %)	2 (1.1 %)	3 (1.3 %)	NS
Dyspnea I-II	34 (73.9 %)	144 (79.1 %)	178 (78 %)	NS
Dyspnea III-IV	10 (21.7 %)	36 (19.7 %)	46 (20.1 %)	NS
COPD	6 (13 %)	19 (10.4 %)	25 (10.9 %)	NS
CKD	5 (10.8 %)	16 (8.7 %)	21 (9.2 %)	NS
Prior PPM	4 (8.6 %)	3 (1.6 %)	7 (3 %)	0.01
Prior surgery	5 (10.8 %)	10 (5.4 %)	15 (6.5 %)	NS
Cancer	11 (23.9 %)	11 (6 %)	22 (9.6 %)	0.002
Non-elective	11 (23.9 %)	37 (20.3 %)	48 (21 %)	NS
Aortic calcium	22 (47.8 %)	85 (46.7 %)	107 (46.9 %)	NS
Valve area (cm^2)	0.76 ± 0.2	0.77 ± 0.2	0.77 ± 0.2	NS
Mean gradient (mmHg)	48.5 ± 11.9	53.8 ± 16.7	52.6 ± 15.8	NS
LVEF	58.7 ± 9	57.8 ± 11	58 ± 10.7	NS
LVEF<50 %	7 (15.2 %)	33 (18.2 %)	40 (17.5 %)	NS
SPAP >50 mmHg	6 (13 %)	8 (4.3 %)	14 (6.1 %)	0.03
Maximum velocity (m/s)	4.2 ± 0.7	4.4 ± 0.9	4.3 ± 0.9	NS
Severe AR	2 (4.3 %)	35 (19.2 %)	37 (16.2 %)	0.01
EuroSCORE	2.37 (1.19-3.61)	1.83 (1.16-3.04)	1.89 (1.19-3.12)	0.2
ArgenSCORE	1.55 (0.99-3.33)	1.08 (0.68-2.23)	1.24 (0.72-2.33)	0.02
STS score	2.33 (1.57-3.23)	0.94 (0.72-1.44)	1.15 (0.78-1.94)	0.0001

HTN: Hypertension, BMI: Body mass index, DLP: Dyslipidemia, SMK: Smoking, COPD: Chronic obstructive pulmonary disease, CKD: Chronic kidney disease, PPM: Permanent pacemaker, LVEF: Left ventricular ejection fraction, SPAP: Systolic pulmonary artery pressure, AR: Aortic regurgitation, STS: Society of Thoracic Surgeons

of severe aortic valve disease continues to be a safe and low-mortality procedure. The risk of suffering a perioperative stroke was zero in this population and there was only one event in a patient >75 years following discharge after the procedure. Clearly, the type of intervention chosen for each patient with this pathology was based on surgical risk. Although we support the concept that age is important when making decisions, survival, durability of the prosthetic valve, patient's comorbidities, life expectancy, quality of life and a comprehensive multidisciplinary discussion of the healthcare team are also a matter for debate. Among patients with the possibility of being operated on, older patients and with more comorbidities (chronic obstructive pulmonary disease, previous AMI, kidney failure, carotid artery disease, other severe valve heart diseases, permanent atrial fibrillation) are gradually seen more frequently. The discussion is not only about the aortic valve and the surgical strategy, but also about comorbidities, since the real objective is not only in-hospital survival but also long-term survival. In the last decade, TAVI has emerged as a valuable alternative to SAVR in an increasingly broad spectrum of patients with symptomatic severe AS. The safety and efficacy of TAVI was initially established in patients at high surgical risk, assessed by STS mortality predictors with a score greater than 8% in the PARTNER 1 and US CoreValve studies in high-risk STS patients (3, 4), and in recent years in patients at intermediate surgical risk (STS score 4% -8%), endorsed by the PARTNER 2 and SURTAVI studies, demonstrating the non-inferiority of TAVI compared with surgery. (5, 6)

Although this treatment alternative is an excellent option and competes directly with valve replacement surgery, it did not provide a solution for some patients with symptomatic severe AS who present at the same time other significant associated mitral or tricuspid valve disease, as well as coronary heart disease with inadequate coronary artery beds due to their fine caliber, extensive calcifications and various lesions, small or very large rings, predominant aortic regurgitation, or aneurysmal aortas, or poor peripheral vascular access to enter the valve implant.

Table 2. Intraoperative data

	Group 1 (n= 46)	Group 2 (n= 182)	Total (n= 228)	P Value
CPB time	78.5 ± 24.1	90.3 ± 36.3	87.9 ± 34.4	0.03
ACC time	61.1 ± 18.4	66 ± 21.2	66.5 ± 21.1	NS
Mini-sternotomy	13 (28.2 %)	26 (14.2 %)	39 (17.1 %)	0.02
Mechanical prosthesis	1 (2.1 %)	82 (45 %)	83 (36 %)	0.02
Biological prosthesis	45 (97.9 %)	100 (43.8 %)	145 (64 %)	0.01
Prosthesis number				
19	6 (13 %)	11 (6 %)	17 (7.4 %)	NS
21	19 (41.3 %)	65 (35.7 %)	84 (36.8 %)	NS
23	18 (39.1 %)	63 (34.6 %)	81 (35.5 %)	NS
25	3 (6.5 %)	32 (17.5 %)	35 (15.3 %)	NS
27	0	11 (6 %)	11 (4.8 %)	NS
Annulus enlargement	4 (8.6 %)	10 (5.5 %)	14 (6.1 %)	NS

CPB: Cardiopulmonary bypass, ACC: Aortic cross-clamping.

Table 3. 30-day morbidity and mortality

	Group 1 >75 years (n= 46)	Group 2 ≤75 years (n= 182)	Total (n= 228)	P Value
Death	1 (2.1 %)	3 (1.6 %)	4 (1.7 %)	NS
Stroke	0	0	0	NS
AMI	0	0	0	NS
TIA	1 (0.5 %)	0	1 (0.4 %)	NS
Pacemaker	2 (4.3 %)	5 (2.7 %)	6 (2.6 %)	NS
Inotropic agents	5 (10.8 %)	9 (4,9 %)	14 (6.1 %)	NS
Reop. for bleeding	1 (2.1 %)	3 (1.6 %)	4 (1.7 %)	NS
AF	15 (32.6 %)	47 (25.8 %)	62 (27.1 %)	NS
Dialysis	1 (2.1 %)	0	1 (0.4 %)	NS
ARF	3 (6.5 %)	6 (3.2 %)	9 (3.9 %)	NS
Mediastinitis	1 (2.1 %)	3 (1.6 %)	4 (1.7 %)	NS
MRA > 24 h	5 (10.8 %)	4 (2.1 %)	9 (3.9 %)	0.006

AMI: Acute myocardial infarction, TIA: Transient ischemic attack, Reop.: reoperation, AF: Atrial fibrillation, ARF: Oliguric acute renal failure, MRA: Mechanical respiratory assistance.

A study carried out in South America by Boissonnet et al. (11) on 1156 patients with a mean age of 81 years undergoing TAVI between 2008 and 2015 reported 12.5% 30-day mortality, 3.5% stroke and 23% need for permanent pacemaker implantation. According to the meta-analysis carried out by Borracci et al. (12) which included 494 intermediate-risk patients from our country undergoing TAVI, 30-day mortality was 4.8%. The weighted estimates of all the studies gave the following results: stroke 2.7%, AMI 1.0%, need for permanent pacemaker 24.8%, moderate or severe paravalvular leak 16.7% and major bleeding 5.5%, which are very contrasting data compared with those reported in the PARTNER 3 study (13) on 1000 low-risk patients randomized to TAVI vs. SAVR with a composite endpoint of death/stroke at 30 days of 1% vs. 3.3% (HR 0.30; 95% CI 0.11-0.83; p=0.01), respectively. The 5-year results of the OBSERVANT study (14) which included 7610 low- and intermediate-risk patients with severe aortic valve disease treated in the "real world" with TAVI and SAVR have recently came to light. In the group of patients matched according to a propensity score, a protective effect on mortality was observed for surgery compared with TAVI (48.3% with TAVI vs. 35.8% with surgery, HR 1.38; 95% CI 1.12-1.69, p=0.002). These current data of TAVI results place us in the local and international reality. Regarding the results of SAVR in Argentina, we mention another meta-analysis by Borracci et al. (15) including 1192 patients. Mortality was 3.1%, stroke 1.3%, myocardial infarction 0.4%, need for permanent pacemaker 2.7%, mediastinitis 1.4%, and reoperation for bleeding 2.6%.

The age range used to support TAVI in the new American guidelines (7) (≥65 years) is well below the mean age of the published evidence on low risk (73 years for the PARTNER 3 study and 74 years for the low-risk EVOLUT study in which the SAPIEN 3 valve was used). In none of these published works, is there a reference to support TAVI in people younger than those defined in their respective populations. We could think that the 80-year-old population would benefit from endovascular therapy; however, the 5-year mortality was statistically higher with respect to SAVR in the OBSERVANT study.

With increasing age, especially in octogenarians, another problem is added, which is frailty defined as sarcopenia, lack of strength, sensory disorder, low weight, fatigue, evaluated by universal scores such as the Frail and the Essential Frailty Toolset, which influences the postoperative period due to the difficulty in starting ventilator weaning, the inability to stand and swallowing disorders with high risk of pneumonia and prolonged hospitalization. (16-18)

For all the problems of these "new patients", the creation of a heart team was necessary in all centers in order to decide the best option and, even to rule out a surgical procedure. (19, 20)

In this cohort study, not only a low overall mortality of 1.75% stands out, and in the population >75 years of 2.17%, but also low global morbidity, with renal failure on dialysis of 0.43%; stroke 0%; AMI 0%; and indication of permanent pacemaker 2.63%.

To achieve low morbidity and mortality it is necessary to add to the experience of the surgical team, a multidisciplinary team that can correctly evaluate the patient in the preoperative period (select candidates for each procedure according not only to age and risk score, but also to adequately assess other organ damage, frailty and osteopenia) and the intraoperative management by an experienced anesthesiologist and an imaging specialist (intraoperative transesophageal color Doppler echocardiography) to assess the immediate surgical outcome. Lastly, postoperative management is essential to prevent and treat complications, mainly the presence of low cardiac output, the most serious medical complication with the worst prognosis. On the other hand, we also emphasize reducing the time of respiratory assistance and removal of intravenous lines and catheters to promptly mobilize the patient and avoid infective complications.

The well-known severity classification according to valve area must be associated with the hemodynamic behavior of the valve, mainly expressed through its gradients, to adequately interpret the stenotic behavior of the diseased valve. Valve area <1 cm^2 is a sensitive cut-off point, but the gradients are much more specific. In the present work, we can observe that the operated population had severe AS (area <1 cm^2) with high gradient (mean gradient >40 mmHg) and preserved left ventricular ejection fraction (LVEF), the classic normal flow and high gradient stenosis; in this sense, it is interesting to note that the statistically significant mean gradient reduction between both groups was the only variable that showed an association with morbidity. The relationship between mean gradient and prognosis was already described many years ago by Dr. Blase Carabello, (21) but that original description referred to poor function and low gradient clinical scenarios. Subsequently, evolution and morbidity and mortality by groups were described for both asymptomatic (22) and symptomatic (23) patients in relation to the hemodynamic behavior of the valve, and a worse prognosis was defined for patients with low gradient and low flow. However, we are not aware of the description within the same high-gradient group, in which differences characterized by its reduction (always within mean gradient values >40 mmHg) are associated with increased morbidity and mortality. Knowing the pathophysiology of aortic valve disease and its myocardial repercussion, it seems logical to think that this decrease in the gradient may be an expression of greater myocardial involvement in these patients even with preserved LVEF, since in previous works (24) and in one study of our group (25) it has been shown that different structural changes, and particularly fibrosis, are already present in relatively early stages of the disease. Consequently, we could

state that the behavior of mean gradient in these patients' follow-up can be another useful variable for the prediction of a more adverse evolution or to better assess the moment to indicate valve replacement.

CONCLUSIONS

Surgical aortic valve replacement in this patient population presented mortality in accordance with that expected by national and international scores. Low death, stroke and AMI occurrence shows that the treatment chosen for these patients was adequate and had excellent results. Patients over75 years of age did not present more postoperative events despite having more comorbidities than the younger group.

Conflicts of interest

None declared.

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

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