Archivos de Cardiología de México

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ORIGINAL RESEARCH ARTICLE

Calcium score association with paravalvular leakage in patients who underwent TAVR, the Mexican values

Asociación del score de calcio con fuga paravalvular en pacientes sometidos a TAVI, los valores mexicanos

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Abstract

Objective: *The objective is to determinate the association between the degree of aortic valve calcification and the presence of paravalvular leakage (PVL) in Mexican patients who underwent transcatheter aortic valve replacement (TAVR).* **Methods:** *We conducted a retrospective, analytic, cohort. Pooled data were retrospectively analyzed from the patient's files from January 2014 to July 2022. With a median follow-up of 6 months.* **Results:** *We included 83 patients. 31 (37.3%) developed residual PVL. Several factors as male gender (men 58.1% versus women 41.9% p = 0.01), higher gradients previous TAVR (mean 57 mmHg in the group with versus mean 53 mmHg in the group without PVL, p = 0.01), bigger annulus diameters and perimeters as well as reduce left ventricular ejection fraction and a degree of aortic regurgitation previous TAVR were present more frequently in the group of residual PVL. Aortic valve calcification was the only predictor after the bivariate and multivariate analysis that showed an association with the presence of PVL after TAVR. The calculated cut-off value of calcium score was 2970 Agatston units, with a sensitivity of 70% and a specificity of 60% as a predictor for PVL.* **Conclusions:** *The results are consistent with the previous data and there are no greater differences in the Mexican population. The severity of the aortic valve calcification is an independent predictor of PVL in patients who underwent TAVR.*

Keywords: *Calcium score. TAVR. Paravalvular leakage. Mexican patients.*

Resumen

Objetivo: *El objetivo es el de determinar la asociación entre el grado de calcificación de la válvula aórtica y la presencia de fuga paravalvular (FPV) en pacientes mexicanos sometidos a TAVI.* **Métodos:** *Se realizó una cohorte analítica retrospectiva. Los datos agrupados se analizaron retrospectivamente de los expedientes de los pacientes desde enero de 2014 hasta julio de 2022. Con una mediana de seguimiento de 6 meses.* **Resultados:** *Se incluyeron 83 pacientes. 31 (37,3%) desarrollaron FPV residual. Varios factores como el género masculino (hombres 58,1% vs mujeres 41,9% valor p de 0,01), mayores gradientes previo al procedimiento (media 57 mmHg en el grupo con vs media 53 mmHg en el grupo sin fuga paravalvular, valor p 0,01), diámetros de anillo y perímetros mas grandes, así como FEVI reducida y algún grado de insuficiencia aórtica previo a la TAVI se presentaron con mayor frecuencia en el grupo de FPV residual. La calcificación de la válvula aórtica fue*

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Date of reception: 08-08-2024
Date of acceptance: 17-12-2024
DOI: 10.24875/ACM.24000148

Available online: 05-03-2025
Arch Cardiol Mex. 2025;95(2):194-198
www.archivoscardiologia.com

el único predictor tras el análisis bivariado y multivariado que mostró asociación con la presencia de FPV tras el procedimiento. El valor de corte calculado del puntaje de calcio fue de 2970 AU, con una sensibilidad del 70% y una especificidad del 60% como predictor de fuga paravalvular. **Conclusiones:** *Los resultados concuerdan con los datos conocidos en estudios previos a nivel mundial, sin existir diferencias mayores en la población mexicana. La gravedad de la calcificación de la válvula aórtica es un predictor independiente de FPV en pacientes mexicanos sometidos a TAVI.*

Palabras clave: *Score de calcio. Tavi. Fuga paravalvular. Pacientes mexicanos.*

Introduction

Aortic stenosis is the most common valvular heart disease in the industrialized countries. It's a chronic disease characterized for an obstruction of the valvular plane due to degeneration of the valve and in most cases, a big amount of calcium deposits around the cusps, annulus, and left ventricular outflow tract[1,2]. The main symptoms are chest pain, syncope, exercise intolerance, and finally heart failure[3,4]. Echocardiographic assessment continues being the gold standard for diagnosis, nevertheless, Computed tomography (CT) evaluation is the cornerstone for anatomy assessment before planning the type of treatment[5,6]. Nowadays the therapeutic options include surgical aortic valve replacement (SAVR) and transcatheter aortic valve replacement (TAVR)[6,7]. Procedural complications of TAVR include vascular issues, ventricular wall perforation, paravalvular leakage (PVL), aortic regurgitation, rhythm disturbances, arrhythmias, coronary artery occlusion, myocardial infarction, cerebrovascular accident, and death. The reported incidence of PVL varies widely from 7 to 70% for mild, and 0-24% for moderate to severe leakage. Moderate or severe PVL following TAVR was associated with a threefold increase in 30-day mortality and a 2.3-fold increase in 1-year mortality[8-10]. Nevertheless, since 2016, Jones et al. reported the significance of mild aortic regurgitation in predicting mortality at 1-year following TAVR, with a percent of mortality of 7.1% in the presence of trivial regurgitation, 16.9% mild regurgitation up to 50% in moderate to severe aortic regurgitation[11].

About the associated factors for this condition, calcium score plays a main role, in making more difficult the adequate position and expansion of the valve. The Agatston units (AU) associated with more risk of presenting PVL is 3000 AU in the international literature. However, the cutoff value of the Latin-American population, specifically the Mexican one had not been established[12].

Material and methods

Study design and settings: We performed a retrospective, analytic, cohort to determinate the association of calcium score measured by CT with the presence of PVL after TAVR in the Mexican population. Pooled data were retrospectively analyzed from the patient's files from January 2014 to July 2022. With a median follow-up of 6 months.

Study population

The inclusion criteria were patients with symptomatic and severe aortic stenosis who underwent TAVR at the CMN SXXI Cardiology Hospital and have a complete medical file with a previous CT scan including calcium score. Patients with bicuspid aortic valves and those with antecedents of SAVR were excluded of the cohort.

Statistical analysis

Continues variables with normal distribution were reported as mean + standard deviation (SD) and the rest with median and ICR and compared between groups using an independent samples t-test. Categorical variables were reported in absolute and relative frequencies, the bivariate analysis was performed with the x^2 test or Fisher's exact test. Hosmer-Lemeshow was used for the multivariate logistic regression analysis with the inside criteria $p \leq 0.20$ and outside $p > 0.05$.

Results

The analysis included 83 patients from January 2014 to July 2022. We identify 31 patients (37.3%) with residual PVL. The demographic and clinic characteristics of the two groups (with and without PVL) are shown in table 1. The mean age in the residual PVL group was 78 ± 7.8 years, compared with the group without PVL with a mean age of 82 ± 4 years, p = 0.06. TAVR was performed more frequently in women, nevertheless, the PVL was reported more commonly in men (58.1%) than women (41.9%), respectively, with a p = 0.01. All the other demographic characteristics did not manifest any significant differences.

Table 1. Baseline demographic and clinic characteristics

Baseline characteristic	With PVL (n = 31)	Without PVL	p
Gender			
Male	18 (58.1%)	16 (30.8%)	0.01
Female	13 (41.9%)	36 (69.2%)	0.01
Age (years)	78 (71-85)	82 (78-86)	0.06
Weight (kg)	67 (61-78)	63 (68-72	0.09
Height (cm)	160 (150-165)	156 (150-162)	0.31
BMI	26 (24.8-28.6)	25.2 (22.7-27.3)	0.16
Hypertension	21 (67.7%)	34 (64.5%)	0.51
Diabetes	8 (25.8%)	15 (28.8%)	0.48
Dyslipidemia	9 (29%)	20 (38.5%)	0.26
Tobacco	11 (35.5%)	16 (30.8%)	0.41
COPD	4 (12.9%)	8 (15.4%)	0.34
IHD	4 (12.9%)	8 (15.4%)	0.51
NYHA class			
I	2 (6.5%)	2 (3.8%)	0.87
II	20 (64.5%)	33 (63.5%)	0.87
III	9 (29%)	16 (30.8%)	0.87
IV	0 (0%)	1 (19%)	0.97

BMI: body mass index; COPD: chronic obstructive pulmonary disease; IHD: ischemic heart disease; PVL: paravalvular leakage.

Table 2. Echocardiographic characteristics

Characteristic	With PVL (n = 31)	Without PVL (n = 52)	p
LVEF (%)	56 (45-58)	65 (59-70)	0.002
AOVA (cm^2)	0.58 (0.4-0.7)	0.57 (0.4-0.7)	0.92
V MAX (m/s)	4.5 (4.2-4.9)	4.5 (4.1-4.9)	0.88
MG (MmHg)	57 (47-64)	53 (43-61)	0.01
AR	27 (87.1%)	32 (61.5%)	0.01
Mild	17 (54.8%)	27 (51.9%)	0.08
Moderate	7 (22.6%)	5 (9.6%)	0.08
Severe	3 (9.7%)	0 (0%)	0.08
AR > moderate	10 (32.3%)	5 (9.5%)	0.01
sPAP	39 (33-50)	39 (35-46)	0.84

LVEF: left ventricular ejection fraction; AOVA: aortic valve area; MG: mean gradient; AR: aortic regurgitation; PVL: paravalvular leakage.

About the echocardiographic findings (Table 2), PVL showed differences according to left ventricular ejection fraction (LVEF), being more common in patients with a range of LVEF of 45-60%, mean 56% versus the patients with a LVEF range of 61-70%, mean of 65%, with a p = 0.002. Higher means gradients (47-64 mmHg, mean 57 mmHg in the group with versus 43-61 mmHg, mean 53 mmHg in the group without PVL, p = 0.01) and the presence of a degree of aortic regurgitation previous of the procedure were associated with residual PVL.

Pre-procedure CT-Scan characteristics reported higher aortic annulus diameters and perimeters as well as LVOT being more frequent in the PVL group (Table 3). According to the calcium score, the CT values were reported from 929 to 8398 AU, with a mean of 3191 AU. In the PVL group, these values were grater, with a mean of 3428 AU versus 2727 AU in with and without PVL groups, respectively. ROC curve analysis showed a cut-off calculated value of 2970 AU as a predictor of residual PVL in the population (Table 4 and Fig. 1).

About the type of prothesis, 30.1% of the patients underwent EVOLUT R valve, followed by 21% who underwent SAPIEN 3, 26% EVOLUT PRO, and < 1% of the patients underwent PORTICO, SAPIEN XT, ACCURATE NEO, CORE VALVE, and LOTUS, with no significant differences in the presence of PVL according to the type of prothesis. Only the size of the valve was associated with the development of PVL, leading to grater sizes in the PVL group.

We performed a multivariate analysis adjusted to gender and LVEF, finding the presence of a higher degree of aortic valve calcification as the only independent variable associated with the development of PVL (Table 5).

Discussion

In this study, 31 of 83 patients (37.3%) experienced residual PVL following TAVR, of which 14 (45%) were classified as moderate residual PVL and 1 (3.2%) as severe. Larroche et al. demonstrated that 6.5% of complications following TAVR were due to residual PVL, while Chamandi et al. showed that 21% of patients undergoing TAVR exhibited residual PVL, and Salem et al. documented a 30% incidence of residual PVL in patients undergoing aortic valve replacement.

In addition, this study documented a calcium index ranging from 929 AU to 8398 AU with a mean of 3428 AU (1650-4664), significantly higher than those without residual PVL, which had a mean of 2727 AU (1659-3999) with a p = 0.02. The calculated cut-off value was 2970, with a sensitivity of 70% and a specificity of 60%. This suggests that larger calcium deposits interfere with the

Table 3. CT scan characteristic

Characteristic	With PVL (n = 31)	Without PLV (n = 52)	p
AO annulus			
Minimum diameter (mm)	22.6 (19.1-23)	20.5 (18.8-22.6)	0.10
Maximum diameter (mm)	26.6 (24.9-27.7)	25.2 (23.6-27)	0.03
Perimeter (mm)	78.3 (70.9-85.5)	73.1 (69-77.9)	0.03
Area (mm^2)	480 (386.520)	415.8 (350-46)	0.052
LVOT			
Minimum diameter (mm)	21.8 (9.8-23.8)	19.6 (17.8-21.2)	0.002
Maximum diameter (mm)	26.5 (24-28.8)	25.3 (23.8-28)	0.41
Perimeter	75.3 (69-84)	71.9 (66.2-79.3)	0.08
Area	444 (380-543)	383 (330-471.4)	0.02
LM ostium	14 (12-15)	12.4 (11.2-14)	0.08
RCA ostium	16 (15.2-19)	15 (12.2-17)	0.01
Calcium distribution			
Asymetric	24 (77.4%)	40 (76.9%)	0.59
Symetric	7 (22.6%)	12 (33.1%)	0.59
AO annulus calcification			
NO	2 (6.5%)	9 (17.3%)	0.20
Mild	13 (41.9%)	27 (51.9%)	0.20
Moderate	13 (41.9%	14 (26.9%)	0.20
Severe	3 (9.7%)	2 (3.8%)	0.20
LVOT calcification			
NO	13 (41.9%)	32 (61.5%)	0.14
Mild	14 (45.2%)	13 (25%)	0.14
Moderate	4 (12.9%)	0 (0%)	0.14
Severe	0 (0%)	0 (0%)	0.14
AO valve calcification			
NO	0 (0%)	2 (3.8%)	0.07
Mild	5 (16.1%)	5 (9.6%)	0.07
Moderate	9 (29%)	28 (53.8%)	0.07
Severe	17 (54.8%)	17 32.7%)	0.07
Calcium Score (AU)	3428 (1650-4664)	2727 (1650-3999)	0.02

AO: aortic; LVOT: left ventricular outflow tract; LM: left main; AU: agatston units; RCA: right coronary artery; CT: computed tomography.

Table 4. Procedure characteristics

Characteristic	CON FPV (n = 31)	SIN FPV (n = 52)	p
Vascular access			
Right femoral artery	25 (80.6)	36 (62.9%)	0.44
Left femoral artery	6 (14.4%)	15 (28.8%)	0.44
Other	0 (0%)	1 (1.9%)	0.44
Prothesis			
Sapien XT	2 (6.5%)	2 (3.8%)	0.07
Evolut R	12 (38.7%)	13 (25%)	0.07
Evolut pro	8 (25.8%)	10 (19.2%)	0.07
Sapien 3	6 (19.4%)	16 (30.8%)	0.07
Acurate ENO	0 (0%)	5 (9.6%)	0.07
Acurate NEO 2	0 (0%)	1 (1.9%)	0.07
Lotus	0 (0%)	2 (3.8%)	0.07
Portico	3 (9.7%)	0 (0%)	0.07
Core valve	0 (0%)	3 (5.8%)	0.07
Prothesis size	29 (26-29)	26 (25-27)	< 0.01
Peak – peak gradient (mmHg)	60 (45-82)	60 (47-80)	0.96
Residual gradient (mmHg)	3 (0-5)	2 (0-4)	0.11
Pre-dilatation	23 (74.2%)	25 (48.1%	0.02
Posdilatation	14 (45.2%)	2 (3.8%)	< 0.001

positioning and release of the prosthesis. The results of this study are consistent with Larroche et al. who documented that the calcium score is higher in patients with significant residual PVL, and also with Van Mieghem et al. who documented that a calcium score > 3000 AU increases the risk of residual PVL following TAVR. In contrast, Guimaraes et al. documented that residual PVL had a low incidence regardless of the calcium index. The differences in the results with this study could be attributed to the fact that Guimaraes et al. used only balloon-expandable valves (SAPIEN 3 valve, Edwards Lifesciences) during their procedures, which have shown better sealing of the aortic annulus, reducing the incidence of residual PVL regardless of the degree of aortic calcification.

Conclusion

Among patients underwent TAVR in the present times, PVL continues being a frequent complication in the

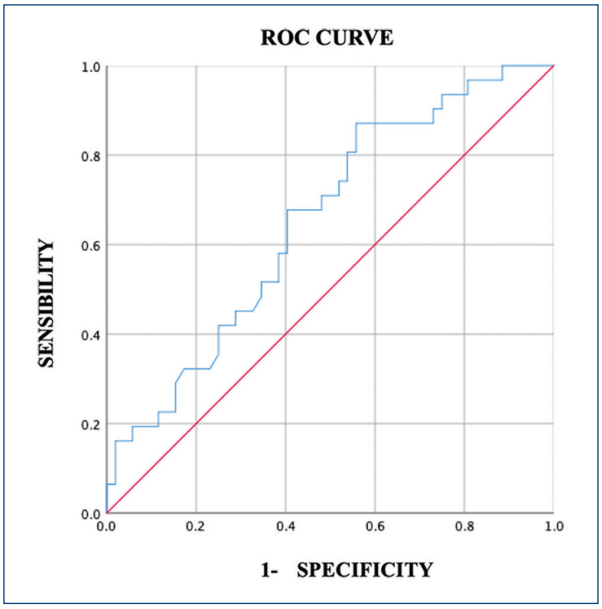

Figure 1. ROC curve.

Table 5. Bivariate and multivariate analysis

Characteristic	Simple model OR IC 95% P	Adjusted model OR IC 95% P (LVEF and gender)
LVEF %	0.93 (0.89-0.98), 0.001	-
Prothesis size	1.2 (1.0-1.5), 0.005	1.18 (0.9-1.4) 0.09
Gender	3.1 (1.2-7.85), 0.01	-
Pre-dilatation	3.1 (1.1-8.2), 0.02	2.3 (0.81-6.5) 0.12
Aortic valve calcium	14.2 (1.2-13.8), 0.004	3.9 (1.11-14.3) 0.03
Annulus perimeter	1.07 (1.0-1.1), 0.01	1.0 (0.9-1.0), 0.66
LVOT area	1 (1.0-1.1), 0.02	1.0 (0.9-1.0) 0.23

LVEF: left ventricular ejection fraction; LVOT: left ventricular outflow tract.

broad spectrum of actual prothesis available. Several factors are implicated in the development of residual PVL, including calcification of the aortic valve, with a cutoff value described in the international literature of 3000 AU, confirming that the severity of the aortic valve calcification (Cutoff-Calcium Score 2970 UA- Mexican People) in an independent predictor of PVL in patients underwent TAVR. The results shown here are consistent with the previous data and there are no greater differences in the Mexican population compared with the rest of the countries already studied. Up to our knowledge, this is the only study analyzing the predictors for PVL in the Latin American (Mexican) population, and it can help to generalize the possible behavior in this group of patients who are treated in other countries.

Funding

None.

Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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