ORIGINAL ARTICLE

Early and Long-term Outcomes of Aortic Valve Replacement Surgery in Low- and Intermediate-risk Patients

Resultados tempranos y alejados de la cirugía de reemplazo valvular aórtico en pacientes de riesgo intermedio y bajo

DANIEL NAVIA*, FERNANDO PICCININI*, MARIANO VRANCIC*, MARIANO CAMPORROTONDO*, JUAN ESPINOZA*, BRUNO SIMONETTO*, ALBERTO DORSA^, MARIANO BENZADON+

ABSTRACT

Background: With the introduction of new percutaneous techniques for the treatment of severe aortic stenosis, it is important to define which group of patients will benefit more with this new therapeutic option.
Objective: The aim of this study was to analyze the outcomes of aortic valve replacement in low/intermediate risk patients in our setting to establish a reference point for the application of this new therapeutic technology.
Methods: Early and long-term postoperative outcomes were analyzed in 520 patients over 70 years of age, with severe aortic stenosis with or without associated coronary heart disease who were operated on between January 2010 and January 2017. Four hundred and forty-five patients were identified as low risk (STS <4) and 75 as intermediate risk (STS=4-8) patients; PROM STS for the overall group of patients was 2.5.
Results: Mean population age was 76.8 ±4.7 years, and most patients were men. Total in-hospital mortality was 3.1%: 2.7% for low-risk patients and 5.3% for intermediate-risk patients. The incidence of stroke was 0.6% and the need for definitive pacemaker 3.5%. Five-year survival for low-risk patients was 88.5% vs. 67.8% for intermediate-risk patients (logrank test <0.001). At 5 years, freedom from readmission for low-risk patients and intermediate-risk patients was 91.1% and 91.9%, respectively (p=ns) and freedom from reintervention was 98.7 and 97.7%, respectively (p=ns).
Conclusion: Aortic valve replacement in low/intermediate risk patients has low incidence of in-hospital morbidity and mortality, low rate of stroke and need for definitive pacemaker, and low frequency of events at a 5-year follow-up.

Key words: Aortic Valve Stenosis - Heart Valve Prosthesis Implantation - Risk Assessment - Perioperative Period

RESUMEN

Introducción: Debido a la introducción de técnicas percutáneas para el tratamiento de la estenosis aortica severa, es importante poder definir qué grupo de pacientes se beneficiarían con esta nueva opción terapéutica.
Objetivo: Analizar los resultados de RVA en pacientes (pac) de riesgo intermedio/bajo en nuestro medio y de esta forma establecer un punto de referencia para la aplicación de esta nueva tecnología terapéutica.
Material y métodos: se analizaron los resultados postoperatorios (po) tempranos y alejados de 520 pacientes mayores de 70 años, operados con diagnóstico de estenosis aortica severa con o sin enfermedad coronaria intervenidos en el periodo comprendido entre enero 2010 y enero 2017. Se identificaron 445 pac con riesgo bajo (STS < 4) y 75 pac con riesgo intermedio (STS= 4-8), el PROM STS para el grupo total de pac fue de 2.5.
Resultados: La edad promedio del grupo total de pacientes fue de 76.8 (4.7) años con mayoría de sexo masculino. La mortalidad hospitalaria para el grupo total fue de 3,1%, siendo del 2.7% (n:445) para el grupo de pac con riesgo bajo y del 5,3%(n:75) para los pac con riesgo intermedio. La incidencia de ACV fue 0.6% y la necesidad de marcapasos definitivo del 3.5%. A 5 años la sobrevida de pac con bajo riesgo fue del 88.5% vs. 67.8% para pacientes con riesgo intermedio (Log Rank <0.001). El periodo libre de re-internación fue de 91.1% para bajo riego y de 91.0% para pac de riesgo intermedio (p=ns) y el periodo libre de re-intervención fue de 98.7% en bajo riesgo y de 97.7% en riesgo intermedio (p=ns).
Conclusión: la RVA en pacientes de riesgo intermedio/bajo presento baja incidencia de morbi-mortalidad hospitalaria, baja incidencia de ACV po y necesidad de marcapasos definitivo, con baja incidencia de eventos a 5 años de seguimiento.

Palabras claves: Estenosis de la Válvula Aórtica – Implantación de Prótesis de Válvulas Cardíacas – Medición de Riesgo - Periodo Perioperatorio

Rev Argent Cardiol 2018;86:190-195. http://dx.doi.org/10.7775/rac.v86.i3.12898

Received: 01/31/2018 – *Accepted:* 04/15/2018

Address for reprints: Dr. Daniel Navia. Blanco Encalada 1543, (1428) CABA. E-mail: donavia@icba.com.ar

* Department of Cardiac Surgery, Instituto Cardiovascular de Buenos Aires (ICBA)
^ Department of Anesthesiology, Instituto Cardiovascular de Buenos Aires (ICBA)
+ Cardiovascular Recovery Unit, Instituto Cardiovascular de Buenos Aires (ICBA)

INTRODUCTION

Aortic valve disease is the most frequent acquired valve disease in elderly patients, (1) and its growth is expected to increase due to the greater life expectancy observed in recent years. (2) Aortic valve replacement (AVR) is considered the most efficient treatment for this disease after the onset of clinical symptoms (class IA, AHA). (3)

Since the introduction of transcatheter aortic valve implantation (TAVI) in 2002, its indication has been extensively studied and extended in daily practice. (4) In the beginning, this type of treatment was limited to non-surgical high-risk patients (STS >8), and different studies showed that TAVI was superior to medical treatment regarding 2-year survival in this group of patients. (5-7)

These results, together with the mini-invasive nature of the treatment and proven safety, led interventional cardiologists to expand its indication to surgical, high-risk patients.

Further studies in high-risk patients treated with TAVI have shown that this type of percutaneous procedure can be an acceptable alternative to AVR, with comparable morbidity and mortality outcomes. (8-9)

Even though several surgical risk scores have been used to define patients at low, intermediate and high risk, the most widely accepted one is the Society of Thoracic Surgeons (STS) Predicted Risk of Mortality score (PROM). However, recent studies have demonstrated a reduction in the previously estimated rates of mortality despite the population was defined as high risk by the STS-PROM. (10-11)

The purpose of this study was thus to evaluate early and long-term outcomes of AVR in STS PROM low-risk and intermediate-risk patients in our setting, to establish a reference point to compare the results of new therapeutic alternatives in patients with severe aortic stenosis.

METHODS

Between January 2010 and January 2017, 1,115 patients with severe aortic stenosis were operated on and prospectively and consecutively entered into a general database. Among these patients, 520 underwent isolated AVR, or combined with coronary artery bypass grafting (CABG), and postoperative early and long-term outcomes were analyzed. Only patients with elective surgery and ≥70 years of age were included. Patients with pure aortic regurgitation, infective valve disease and mitral valve involvement or thoracic aortic surgery were excluded from the study. Aortic valve replacement was performed by mini-invasive technique in patients without coronary heart disease (n=136) through upper hemisternotomy in the third or fourth intercostal space, with femoral venous access performed with Seldinger technique under intraoperative transesophageal echocardiography (TEE) guidance. (12)

The primary endpoint was in-hospital mortality, postoperative stroke, need for definitive pacemaker and total length of hospital stay. The secondary endpoint was 5-year mortality and freedom from readmission and/or reintervention period. In-hospital mortality was defined as that occurring during hospitalization or within 30 days of surgery. In-hospital mortality, deep sternal wound infection (mediastinitis), postoperative acute myocardial infarction (AMI), postoperative stroke (presence of neurological deficit lasting >72 hours and/or confirmed by computed tomography), reoperation for bleeding and kidney failure requiring dialysis were evaluated. Long-term follow-up was performed to analyze survival and presence of events through direct contact with the patient, his family and his family doctor, and review of clinical records. Presence of new stroke and signs of heart failure due to prosthesis dysfunction were considered reasons for readmission and the need for valve replacement was considered to assess the freedom from reintervention period.

Patients' preoperative characteristics were expressed as mean±standard deviation, median and interquartile range (IQR) or prevalence (in percentage), as appropriate. Kaplan-Meier freedom from events survival curves were built and the differences in the time-event curves between both groups were analyzed using the logrank test.

Mean follow-up was 2.6±1.8 years and median follow-up was 2.4 years (IQR 1.1-3.8).

Ethical considerations

The Instituto Cardiovascular de Buenos Aires Ethics Committee authorized the performance of this study.

RESULTS

Among a total of 520 patients, 445 were identified as low-risk patients (STS <4) and 75 as intermediate-risk patients (STS=4-8); PROM-STS for the total group of patients was 2.5±1.2. Table 1 shows baseline characteristics of the population. Mean age for the overall population was 76.8±4.7 years, with predominance of men. In 39.8% of cases, patients presented with coronary heart disease and required CABG. Dyspnea was the most frequent symptom (47.3%) followed by angina (12.9%); 8.7% of patients were considered to be asymptomatic. Most of the patients received biological prostheses (96.5%), and the most common size used was 23-25 mm (48.5%) (Table 2).

In-hospital mortality for the total group was 3.1%: 2.7% for the low-risk group of patients (n=445) and 5.3% for the group of intermediate-risk patients (n=75). Postoperative stroke was 0.6% and the need for definitive pacemaker was 3.5%. Median hospital stay was 5 days (IQR 4-8) (Table 3). In 136 patients (26%) AVR was performed by mini-invasive technique allowing greater possibility of extubation in the operating room (p=0.01). No significant differences were found for other postoperative variables.

A long-term 5-year follow-up was conducted in 96.7% of the total group of patients, with a mean follow-up period of 2.6±1.8 years. Survival at 5 years for the low-risk group of patients was 88.5% vs. 67.8% for the intermediate group (logrank test <0.001) (Fig. 1A). Freedom from readmission at 5 years was 91.1% for the low-risk group and 91.0% for the intermediate-risk group (p=ns) (Fig. 1B). Finally, freedom from reintervention at 5 years was 98.7% for the low-risk group and 97.7% for the intermediate-risk patients (p=ns) (Fig. 1C).

Table 1. Baseline characteristics

	Low (n=445)	Intermediate (n=75)	Total (n=520)
Age (years)	76.1±4.2	81.2±4.8	76.8±4.7
Men	62.2%	49.3%	60.4%
Weight (kg)	78.6±14.7	70.1±14.7	77.4±14.9
Height (cm)	167±9	164±11	166±10
STS score	2.1±0.8	4.9 ±0.8	2.5±1.2
Dyspnea	47.0%	49.3%	47.3%
Asymptomatic	9.4%	4.0%	8.7%
Associated coronary heart disease	36.9%	57.3%	39.8%
Prior AMI	9.9%	17.3%	11.0%
Prior CABG	3.1%	9.3%	4.0%
Prior PCI	11.9%	8.0%	11.3%
Prior stroke	2.2%	8.0%	3.1%
Peripheral vascular disease	1.3%	6.7%	2.1%
Diabetes	18.2%	18.7%	18.3%
COPD	6.7%	9.3%	7.1%
Prior kidney failure	4.7%	16.0%	6.3%
LV dysfunction (mod/sev)	7.4%	13.3%	8.3%
HTN	80.4%	85.3%	81.2%
SMK or ExSMK	46.5%	34.7%	44.8%
Family history	7.2%	5.3%	6.9%

STS: Sociery of Thoracic Surgeons. AMI: Acute myocardial infarction. CABG: Coronary artery bypass grafting. PCI: Percutaneous coronary intervention. COPD: Chronic obstructive pulmonary disease. LV: Left ventricular. HTN: Hypertensiom. SMK: Smoker.

Table 2. Surgical characteristics

		Low (n=445)	Intermediate (n=75)
Type of prosthesis	Mechanical	3.1%	9.3%
	Biological	96.9%	90.7%
Prosthesis size	<19 mm	1.3%	5.3%
	19-20 mm	6.7%	13.3%
	21-22 mm	26.7%	25.3%
	23-24 mm	43.6%	42.7%
	25-26 mm	17.8%	10.7%
	≥ 27 mm	3.8%	2.7%
CPBT (minutes)		96±30	100±3.3
Extubated in the operating room		10.8%	10.2%
BMI (kg/m2)		28±7	26±4

CPBT: Cardiopulmonary bypass time. BMI: Body mass index.

DISCUSSION

The incidence of severe aortic stenosis is markedly growing in direct relationship with increasing life expectancy. It is estimated that by 2050, the population over 85 years will be above 5 million and the population over 65 years will be 88.5 million. (2) This means that the increase in symptomatic aortic stenosis among elderly patients will result in a higher number of patients requiring some type of treatment for this disease. Aortic valve replacement surgery is still the most consolidated cornerstone for the treatment of this disease, with a marked therapeutic benefit, since the mortality of the symptomatic patient is close to 25% per year. (13) In our series of surgeries for severe symptomatic aortic stenosis in the last 7 years, most patients (85%) have been low-risk, in agreement with other published experiences, (14) and the prevalence of patients > 80 years of age with severe symptomatic aortic stenosis is almost 20%. Despite this scenario, in-hospital mortality in low-risk and intermediate-risk elderly patients has decreased due to multiple factors and is coincident with results from other centers. (15) Our study included electively operated patients with or without need for CABG, with >70 years of age and STS PROM <4%. Baseline characteristics of our patients were similar to studies comparing AVR with TAVI. (16) The correlation between low and intermediate-risk and the STS score is relevant in our series.

	Low (n=445)	Intermediate (n=75)	Total (n=520)
Death	2.7%	5.3%	3.1%
Stroke	.7%	0.0%	0.6%
Dialysis	.9%	8.0%	1.9%
Reoperation for bleeding	3.4%	4.0%	3.5%
Mediastinitis	.9%	2.7%	1.2%
Ischemia or AMI	.2%	0.0%	0.2%
Low cardiac output	5.6%	10.7%	6.3%
AF	32.4%	41.3%	33.7%
Definitive pacemaker	3.8%	1.3%	3.5%
Postoperative length of stay (days, median, IQR)	5 (4-8)	7 (4-13)	5 (4-8)

Table 3. In-hospital outcomes. AMI: Acute myocardial infarction. AF: Atrial fibrillation

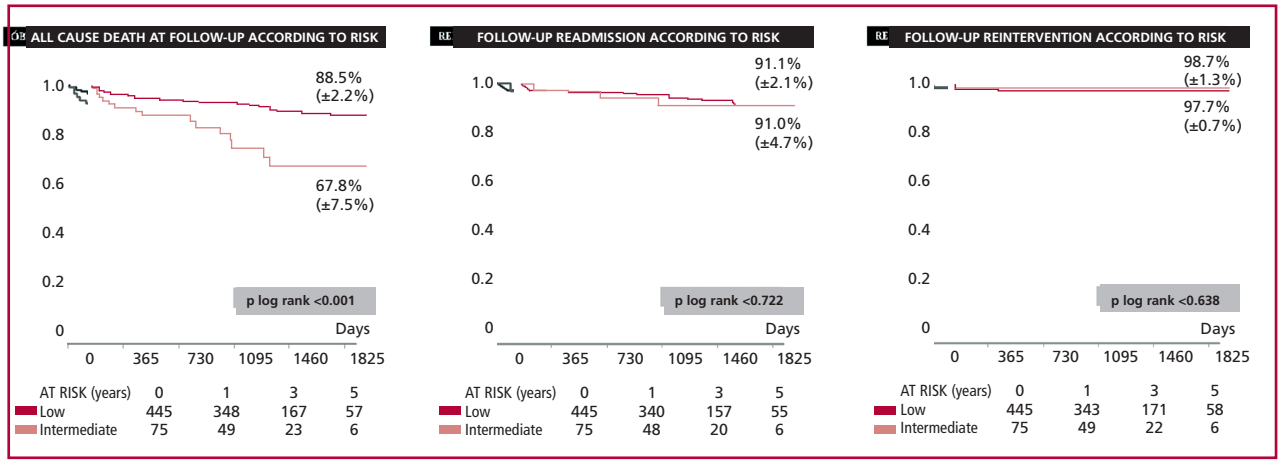

Fig. 1. A: AVR long-term survival at 5 years according to low risk or intermediate risk. **B:** Freedom from readmission in AVR patients according to low risk or intermediate risk. C: Freedom from reintervention in AVR patients according to low risk or intermediate risk

Dewey showed that STS risk calculations usually underestimate early mortality in low-risk patients; however, it has great precision to predict mortality in high-risk patients. (17) Post-operative length of stay was lower compared with AVR studies in low/intermediate risk patients; the groups of AVR patients in the PARTNER 2 study presented a mean hospital stay of 9 days.

In agreement with the experience of most groups, biological prostheses were mostly used in this series of over 70 year-old patients, supported by the greater durability of the new prostheses and the risk of anticoagulation in elderly patients. (19, 20) The elevated incidence of postoperative stroke in randomized multicenter studies is noteworthy in low/intermediate risk patients, not only in the group undergoing surgical AVR but also in TAVI patients. (5, 21, 22) In our series of patients, the incidence of postoperative stroke was <1% without a marked increase in the long-term follow-up. The need for definitive pacemaker was 3.5%, similar to those reported and very inferior to the ones recorded in TAVI patients (25%), with negative impact in the long-term outcome. (23) In our series, survival at 5 years was 88.5%, in contrast with results from the OBSERVANT registry for patients with EuroSCORE II <4, where AVR patients had a 3-year long-term survival of 83.4% and 72% for TAVI patients (p=0.001). (24)

Are TAVI and AVR "equivalent" treatments in intermediate-risk patients?

The noninferiority concept is introduced when comparing AVR and TAVI outcomes on intermediate-risk patients in multicenter randomized studies. This concept does not statistically refer to equivalent therapies, but rather that TAVI "is not inferior" to AVR, as any equivalence analysis would need another statistical approach and a greater number of patients. However, TAVI has been generalized in intermediate-risk patients. These studies present certain selection bias in the inclusion criteria and on the definition of combined endpoints, the latter being a particular limitation in the use of the noninferiority statistical method, where the analysis of combined endpoints may weaken the statistical power of the results obtained. (25) The follow-up events become very relevant when TAVI is indicated to low-risk patients and with longer life expectancy. In the SURTAVI study, 25% of patients were followed-up for less than one years and less than 50% were followed-up for two years, which can be critical in the analysis of the long-term benefit with this type of treatment. (26) A more frequently used methodol-

ogy to perform retrospective studies is to match comparable patients according to a risk propensity score. Recent studies, using this approach have given better results with TAVI in intermediate-risk patients, (27) but the method used was incorrect invalidating the results. (28) Undoubtedly, the recent PARTNER 2 study results in intermediate-risk patients have provided greater competence between TAVI vs. AVR indication. (29) As previously mentioned this study not only has the limitations inherent to any noninferiority study, but also its design reflects a certain selection bias: a) only TAVI patients who were candidates for transfemoral (TF) access were included, not considering more complex patients who were candidates for transapical (TA) access; b) patients in the AVR group had a greater number of associated procedures (23.4%) than TAVI patients (3.9%); in the AVR group, only 14% underwent CABG and 9% other procedures, the latter being reflected in the in-hospital mortality of the surgical group; c) the study was designed and monitored by the economical sponsor, which also participated in the selection of the participating sites, data collection and study monitoring. (30) Finally, we may state that: 1) percutaneous treatment of aortic stenosis is today a reality, still without a clear definition of which group of patients will be the most benefitted candidates; 2) both retrospective studies performed using risk scores as randomized multicenter studies with noninferiority methodology have limitations and selection biases that influence the final results; 3) the economic presence of the industry is strong and somehow contributes in the generalization of results in the medical community and in the choice of patients; 4) as with anything, the new developing therapies must be evaluated according to the reality of results and feasibility of each specific center considering the pros and cons of each therapeutic alternative,

Our study has several limitations, among them being a retrospective, single-center study. Long-term follow-up was only for 5 years, hampering the durability analysis of the biological prostheses used, as already reported by our group in a 7-year follow-up study, where the need for new AVR due to prosthesis dysfunction was 8%. (31)

In conclusion, AVR in low/intermediate-risk patients presented low incidence of in-hospital morbidity and mortality, with a low incidence of postoperative stroke and definitive pacemaker, and low frequency of events in the 5-year follow-up. These results are helpful in our setting as reference for the use of new therapeutic options.

REFERENCES

1. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, et al. Heart disease and stroke statistics – 2011 update: a report from the American Heart Association. Circulation 2011;123:e18-209. http://doi.org/dmkg2t

2. Ortman JMO, Guarneri CE. United States Population Projections: 2000 to 2050. Available at: http://www.census.gov/population/projections/files. [Accessed May 14, 2012]

3. Bonow RO, Carabello BA, Chatterjee K, de Leon AC Jr, Faxon DP, Freed MD, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2008 focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1998 guidelines for the management of patients with valvular heart disease). Endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol 2008;52:e1-142. http://doi.org/bw957v

4. Cribier A, Eltchaninoff H, Bash A, Borenstein N, Tron C, Bauer F, et al. Percutaneous trans-catheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. Circulation 2002;106:3006–8. http://doi.org/cv6smx

5. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, et al; PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010;363:1597-607. http://doi.org/dvzg9k

6. Makkar RR, Fontana GP, Jilaihawi H, Kapadia S, Pichard AD, Douglas PS, et al; PARTNER Trial Investigators. Transcatheter aortic-valve replacement for inoperable severe aortic stenosis. N Engl J Med 2012;366:1696-704. http://doi.org/2nd

7. Osten MD, Feindel C, Greutmann M, Chamberlain K, Meineri M, Rubin B, et al. Transcatheter aortic valve implantation for high risk patients with severe aortic stenosis using the Edwards Sapien balloon-expandable bioprosthesis: a single centre study with immediate and medium-term outcomes. Catheter Cardiovasc Interv 2010;75:475-85. http://doi.org/fcw274

8. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, et al; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011;364:2187-98. http://doi.org/c54zng

9. Kodali SK, Williams MR, Smith CR, Svensson LG, Webb JG, Makkar RR, et al; PARTNER Trial Investigators. Two-year outcomes after transcatheter or surgical aortic-valve replacement. N Engl J Med 2012;366:1686-95. http://doi.org/bff8

10. O'Brien SM, Shahian DM, Filardo G, Ferraris VA, Haan CK, Rich JB, et al; Society of Thoracic Surgeons Quality Measurement Task Force. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 2--isolated valve surgery. Ann Thorac Surg 2009;88:S23-42. http://doi.org/dxqtnq

11. Dunning J, Gao H, Chambers J, Moat N, Murphy G, Pagano D, et al. Aortic valve surgery: marked increases in volume, and significant decreases in mechanical valve use: an analysis of 41,227 patients over 5 years from the Society for Cardiothoracic Surgery in Great Britain and Ireland National Database. J Thorac Cardiovasc Surg 2011;142:776-782. e3. http://doi.org/b4w39f

12. Shekar PS. Minimal access aortic valve surgery through an upper hemisternotomy approach. Operative Techniques in Thoracic and Cardiovascular Surgery: A Comparative Atlas 2010; 15:321-35. http://doi.org/b669zf

13. Carabello BA, Paulus WJ. Aortic stenosis. Lancet 2009;373:956–66. http://doi.org/ctdcm6

14. Gaudino M, Anselmi A, Glieca F, Tsiopoulos V, Pragliola C, Morelli M, et al. Contemporary results for isolated aortic valve surgery. Thorac Cardiovasc Surg 2011;59:229–32. http://doi.org/c9s9pr

15. Brown JM, O'Brien SM, Wu C, Sikora JA, Griffith BP, Gammie JS. Isolated aortic valve replacement in North America comprising 108,687 patients in 10 years: changes in risks, valve types, and outcomes in the Society of Thoracic Surgeons National Database. J Thorac Cardiovasc Surg 2009;137:82-90. http://doi.org/bv4gj8

16. Thyregod HG, Steinbrüchel DA, Ihlemann N, Nissen H, Kjeldsen BJ, et al. Trans-catheter versus surgical aortic valve replacement in patients with severe aortic valve stenosis: one-year results from the All-comers Nordic Aortic Valve Intervention (NOTION) randomized clinical trial J Am Coll Cardiol 2015;65:2184-94. http://doi.org/f3jd34

17. Dewey TM, Brown D, Ryan WH, Herbert MA, Prince SL, Mack MJ. Reliability of risk algorithms in predicting early and late operative outcomes in high-risk patients undergoing aortic valve replacement. J Thorac Cardiovasc Surg 2008;135:180-7. http://doi.org/ddxcf8

18. Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, et al. Trans-catheter or Surgical Aortic-Valve Replacement in Interme-

diate-Risk Patients. N Engl J Med 2016;374:1609–20. http://doi.org/bff4
19. Bonow RO, Carabello BA, Chatterjee K, de Leon AC Jr, Faxon DP, Freed MD, et al. 2008 focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the ACC/AHA Task Force on Practice Guidelines (Writing Committee to revise the 1998 guidelines for the management of patients with valvular heart disease). Endorsed by the SCA, SCAI, and STS. J Am Coll Cardiol 2008;52: e1–142. http://doi.org/bw957v
20. Banbury MK, Cosgrove DM 3rd, White JA, Blackstone EH, Frater RW, Okies JE. Age and valve size effect on the long-term durability of the Carpentier-Edwards aortic pericardial bioprosthesis. Ann Thorac Surg. 2001;72:753-7. http://doi.org/c2c2mf
21. Thyregod HG, Steinbruchel DA, Ihlemann N, Nissen H, Kjeldsen BJ, Petursson P, et al. Trans-catheter Versus Surgical Aortic Valve Replacement in Patients with Severe Aortic Valve Stenosis: 1-Year Results from the All-Comers NOTION Randomized Clinical Trial. J Am Coll Cardiol 2015;65:2184–94. http://doi.org/f3jd34
22. Adams DH, Popma JJ, Reardon MJ. Transcatheter aortic-valve replacement with a self-expanding prosthesis. N Engl J Med 2014;371:967-8. http://doi.org/cqdp
23. Dizon JM, Nazif TM, Hess PL, Biviano A, Garan H, Douglas PS, et al; PARTNER Publications Office. Chronic pacing and adverse outcomes after transcatheter aortic valve implantation. Heart. 2015;101:1665-71. http://doi.org/f7sstn
24. Rosato S, Santini F, Barbanti M, Biancari F, D'Errigo P, Onorati F, et al; OBSERVANT Research Group. Trans-catheter aortic valve implantation compared with surgical aortic valve replacement in low-risk patients. Circ Cardiovasc Interv 2016;9:e003326. http://doi.org/cqdq
25. Mauri L, D'Agostino RB Sr. Challenges in the Design and Interpretation of Noninferiority Trials N Engl J Med 2017;377:1357-67. http://doi.org/gcrnqn
26. Spencer FA, Guyatt GH. In severe aortic stenosis with intermediate surgical risk, TAVR was noninferior to SAVR for death or disabling stroke. Ann Intern Med. 2017;166:JC68. http://doi.org/cqdr
27. Thourani VH, Kodali S, Makkar RR, Herrmann HC, Williams M, Babaliaros V, et al. Trans-catheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis. Lancet 2016;387:2218–25. http://doi.org/bqg9
28. Barili F, Freemantle N, Folliguet T, Muneretto C, De Bonis M, Czerny M, et al. The flaws in the detail of an observational study on transcatheter aortic valve implantation versus surgical aortic valve replacement in intermediate-risks patients. Eur J Cardiothorac Surg 2017;51:1031-5. http://doi.org/cqds
29. Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, et al. Trans-catheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med 2016;374:1609–20. http://doi.org/bff4
30. Böning A. Partner 2 Trial: comparing apples and oranges? 30th EACTS Annual Meeting Barcelona, Spain 1-5 October 2016.
31. Piccinini F, Vrancic M, Vaccarino G, Raich H, Thierer J, Navia D. Reemplazo valvular aórtico biológico. Seguimiento a largo plazo y predictores de mortalidad, reinternación y reintervención Rev Argent Cardiol 2008;76:266-71.