

Incidence rate of long-term infective endocarditis after transcatheter aortic valve implantation

Incidencia de endocarditis infecciosa a largo plazo luego del implante percutáneo de válvula aórtica protésica

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ABSTRACT

Background. Reports on the incidence rate of infective endocarditis (IE) after transcatheter aortic valve implantation (TAVI) are scarce and limited to case reports and international registries, without information coming from our own country. The objective of this study was to know the long-term incidence rate of this entity, its microbiological profile, and the clinical results in an effort to assess strategies that may prevent and treat this disease in our region.

Methods and Results. We retrospectively analyzed the TAVI registry of all consecutive patients who received the device from 3 centers from the Centro de Estudios en Cardiología Intervencionista. Patients were included in the study from 2009 through March 2020 (n = 122). We used the Modified Duke criteria to adjudicate the occurrence of prosthetic valve infective endocarditis (PVIE). We categorized PVIE based on the time elapsed since the early procedure into early PVIE (from 0 to 60 days), intermediate PVIE (from 60 to 360 days), and late PVIE (after 1 year). Also, we assessed the baseline clinical data, as well as the follow-up results and microorganisms found on the cultures. The SPSS v. 17.1 statistical software package was used for statistical analysis. The mean age was 82.5 +/- 7.3 years, and 52.7% of the study sample were male patients. A total of 54.9% of the TAVIs performed used self-expandable valves. Femoral access was used in 83.7% of the patients, and 5.4% were already carriers of a definitive pacemaker when the procedure was performed. A total of 18.4% of the patients needed pacemaker implantation after the procedure. The average hospitalization time was 6.4 +/- 5.8 days. The complete follow-up time was 1064 +/- 488 days and the incidence rate of PVIE was 2.4%. *Staphylococcus epidermidis* was isolated in 2 cases and *Enterococcus faecalis* in 1. Conventional surgical aortic valve replacement was achieved in 1 patient with PVIE, and 1 patient was successfully treated with antibiotics. The overall mortality rate due to PVIE was 33%.

Conclusion. The incidence rate of PVIE in our population was low, which is similar to the incidence rate reported in other regions. The prophylactic strategy and treatment used must be directed to the common microorganisms reported in the medical literature available.

Key words: prosthetic valve endocarditis, TAVR, TAVI, infective endocarditis.

RESUMEN

Antecedentes. Los reportes acerca de la incidencia de endocarditis infecciosa (EI) luego del implante percutáneo (TAVI) es baja, estando limitada a reportes de casos y registros internacionales, sin existir datos de nuestro país. El objetivo de este estudio fue el de conocer la incidencia a largo plazo de esta patología, el perfil microbiológico y los resultados clínicos, a fin de mejorar estrategias de profilaxis y tratamiento en nuestro medio.

Métodos y resultados. Se analizó de forma retrospectiva el registro de todos los pacientes a los que se les implantó una TAVI por estenosis aórtica severa sintomática en los 3 laboratorios de cateterismo cardíaco pertenecientes al Centro de Estudios en Cardiología Intervencionista desde marzo de 2009 hasta diciembre de 2020 inclusive (n=122). Se utilizaron los criterios de DUKE modificados para adjudicar la ocurrencia de EI protésica, clasificándose además de acuerdo al tiempo del diagnóstico de la EI en temprana (dentro de los primeros 60 días), intermedia (60 días a un año) y tardía, luego del año. Se evaluaron los datos basales, clínicos y de seguimiento así como el microorganismo hallado. Se utilizó el paquete SPSS v. 17.1 para el análisis estadístico al evaluar los diferentes tiempos de aparición de la EI protésica. La edad promedio de los ptes fue de 82,5 +/- 7,3 años, siendo 52,7% hombres. De las 122 TAVI implantadas, 54,9% fueron autoexpandibles, 83,7% fueron por acceso femoral, el 5,4% tenían implantado un marcapaso previo al procedimiento o requirieron marcapaso definitivo en un 18,4% de los casos. El tiempo de internación fue de 6,4 +/- 5,8 días. El seguimiento de los pacientes luego del alta hospitalaria fue de 1064 +/- 488 días. A largo plazo, la incidencia global de EI protésica fue del 2,4% y el microorganismo hallado en fue el estafilococo epidermidis en dos casos y enterococo faecalis en 1. Se realizó reemplazo valvular convencional exitosamente en un caso, y tratamiento antibiótico en el 100%, con una mortalidad global de la EI del 33%.

Conclusión. La incidencia de EI protésica en nuestra población es baja, similar a los reportes presentados en otros países. La estrategia de profilaxis y tratamiento deben dirigirse a gérmenes habituales para endocarditis.

Palabras claves: endocarditis infecciosa de válvula protésica, TAVR, TAVI, endocarditis infecciosa.

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INTRODUCTION

Currently, the indications for transcatheter aortic valve implantation (TAVI) have gone from the management of inoperable or high-surgical risk patients with symptomatic, severe aortic stenosis to the management of younger low-surgical risk patients with fewer comorbidities with similar results compared surgical aortic valve replacement (SAVR) (1-2). Infective endocarditis (IE) is a rare disease that impacts patients significantly and has high short- and long-term morbidity and mortality rates (3). Patients treated with surgical aortic valve replacement have a higher risk of developing endocarditis. As a matter of fact, almost 20% of all cases of IE occur in patients with SAVR (4). When infective endocarditis takes over prosthetic valves it is considered a severe short- and long-term complication associated with high morbidity and mortality rates that go from 0.3% to 1.2% per year, and a 10-year cumulative risk of 5%. It is more common in bioprostheses compared to mechanical valves (5-9). The

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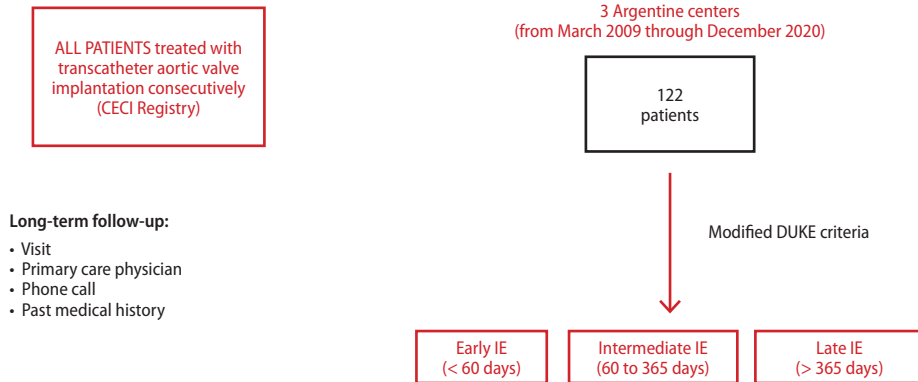


Figure 1. Design of the CECI Registry. CECI: Centro de Estudios en Cardiología Intervencionista. IE: infective endocarditis.

information available on the long-term incidence rate of PVIE in patients treated with TAVI is scarce in our region, and the international data on this regard do not included patients from our setting (10-13). The Registry of Infective Endocarditis in Argentina (EIRA 3) published back in 2018 is the largest series of IE ever reported in Latin America. Based on the EIRA, 18.3% of all endocarditis were found in prosthetic aortic valves. However, it did not specify whether the devices studied came from surgical or transcatheter procedures (14).

The objective of this consecutive registry of patients treated with TAVI is to know the long-term in-hospital incidence rate of PVIE, its microbiological profile, and the clinical results in an attempt to assess strategies that may prevent and treat this disease in our region.

MATERIAL AND METHODS

Study Design

This is a longitudinal, retrospective, and follow-up registry that evaluated all patients treated with TAVI from March 2009 through December 2020 from 3 Argentine centers. Data were collected from the *Centro de Estudios en Cardiología Intervencionista* prospective TAVI registry from a web-based database that included a standard case report form with the demographic, clinical, angiographic, and echocardiographic data of all consecutive patients treated with transcatheter aortic valve implantation (Figure 1).

Definitions

The Modified Duke criteria were used to define infective endocarditis, also at the follow-up. The cases reported were assessed together with the internal medicine and infectious disease units to study each case. IE was classified as possible or definitive based on the time elapsed until the event occurred (late, within the first 60 days; intermediate, from 61 to 1 year; and late, after 1 year).

Endpoints

The study primary endpoint was the incidence rate of prosthetic valve infective endocarditis. The study secondary endpoints included all-cause mortality and stroke after the diagnosis of endocarditis. The microorganisms found and the antibiotic prophylaxis administered were reported too.

TABLE 1. Baseline characteristics.

Total patients	122
Age	82.5±7.3 years
Male	52.7%
Arterial hypertension	85%
Dislipidemia	63.7%
Diabetes	13%
Smoking	3.3%
Chronic kidney disease	17.4%
Dialysis	4.3%
Preoperative pace maker	5.4%
Previous revascularization	37%
Previous sternotomy	13%
Previous valve replacement	7.6%
Peripheral vascular disease	9.8%
Atrial fibrillation	12%
Chronic obstructive pulmonary disease	10.9%
Complete right bundle branch block (RBBB) on the baseline ECG	3.3%
Complete left bundle branch block (LBBB) on the baseline ECG	3.3%
Left anterior fascicular block (LAFB)	5.4%
First-degree atrioventricular block	22.8%
EuroSCORE	13.5±7.3

from Statistical analysis

Regarding the statistical analysis, discrete variables were expressed as frequencies (percentage of patients). Continuous variables were expressed as mean and standard deviation. *P* values were estimated using the Student *t* test, the chi-square test or Fisher's exact test, when necessary. The statistical software package SPSS v.17.7 (IBM Corp, Armonk, NY, United States) was used.

RESULTS

A total of 122 patients treated with TAVI were studied. The median follow-up was 1064 +/- 488 days. The mean age was 82.5 +/- 7.3 years, and 52.7% of the study patients were males. The EuroSCORE was 13.5 +/- 7.3. Femoral access was used in 83.7% of the cases being 54.9% of the valves used self-expandable valves. The remaining baseline clinical characteristics are shown on Table 1. This table also includes the baseline electrocardiographic data of the study population. A total of 5.4% of these patients were already carriers of a definitive pacemaker prior to the procedure while 18.4% were implanted with a pacemaker after TAVI; none of these 2 groups had infective complications associated with the device during the procedure or in the long-term. Table 2 shows

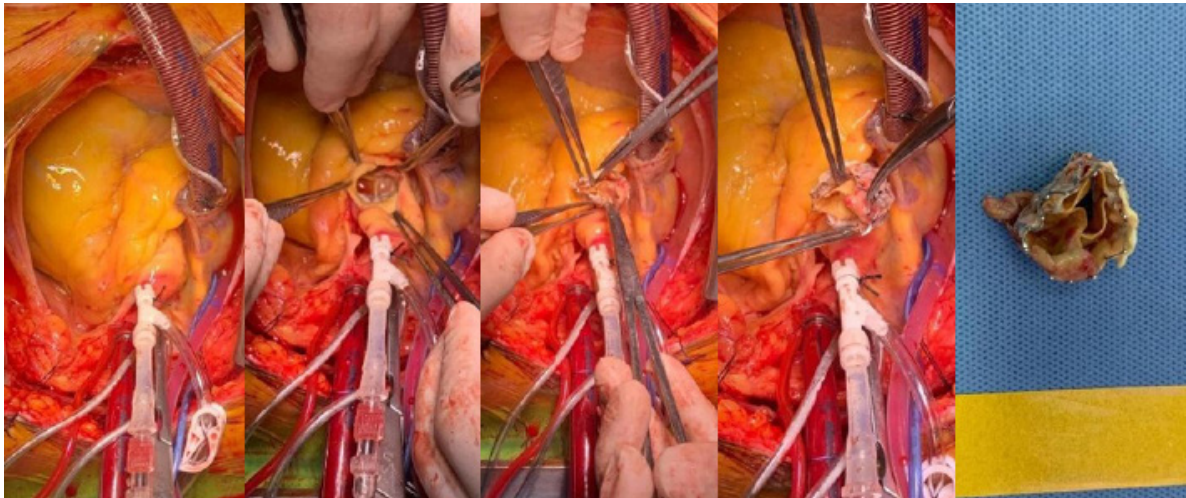


Figure 2. Conventional surgical valve aortic replacement for the management of prosthetic valve infective endocarditis. (Courtesy of Dr. Miguel Rubio).

TABLE 2. Procedural characteristics; 122 patients.

EuroSCORE	13.5±7.3
Femoral access	83.7%
Self-expanding valve	54.9%
Valve-in-valve procedures	4.3%
Amount of contrast used	208±68 ml
Fluoroscopy time	25±11.4 min
Antithrombotic/anticoagulants cheme	
Clopidogrel	13.6%
Clopidogrel + aspirin	70.4%
Clopidogrel + aspirin + vitamin K antagonists	4.5%
Clopidogrel + vitamin K antagonists	11.3%
Hospital stay	6.4±5.8 days

the procedural characteristics of transcatheter aortic valve implantation. **Table 3** shows the long-term overall results. The mean hospitalization time were 6.4 +/- 5.8 days.

One patient had an early episode of PVIE (within the first 60 days after the procedure), and 2 patients experienced late episodes of PVIE (1 patient after 13 months and the other one 19 months later). The overall rate of PVIE was 2.4%. In all the cases, diagnosis was achieved after confirmation of positive hemocultures and the presence of the lesion in the prosthetic valve as seen on the ECG (1 Jena valve, JENA, Germany, 1 Portico self-expandable valve, Abbott- Saint Jude, United States, and 1 Edwards Sapiens balloon-expandable valve, Edwards-Lifesciences valve, United States). The microorganisms isolated were *Staphylococcus epidermidis* in 2 cases and *enterococcus faecalis* in 1. Conventional surgical aortic valve replacement was successful in 1 case (**Figure 2**) while antibiotics were administered in 100% of the patients with an overall mortality rate for PVIE of 33% due to the occurrence of a stroke during the PVIE-related hospitalization. **Figure 2** shows images of valve replacement in the patient with PVIE. Antibiotics were administered to the patient who received conservative management (daptomycin and linezolid). No direct correlation was found between previous surgical procedures and the appearance of endocarditis in any of the 3 patients.

DISCUSSION

The rate of PVIE was studied from the longitudinal registry of consecutive patients from 3 TAVI-capable centers in Ar-

TABLE 3. Clinical outcomes after 1064±488 days of follow-up; 122 patients.

In-hospital mortality rate	4.4%
Acute kidney injury	10.8%
Need for red bloodcells transfusion	17.4%
Need for definitive pacemaker implantation	18.4%
Angioplasty during the procedure	3.3%
Overall mortality rate	17.4%
Prosthetic infective endocarditis	2.4 %
Mortality due to prosthetic valve infective endocarditis	0.8%

gentina and the following findings were reported: first, the 3-year cumulative incidence ratio of PVIE in high-surgical risk patients was 2.4%, which is somehow similar to the rate reported by most results from the registries and reviews published to this date (15). Although the numbers may vary, they never exceed 5% at the 5-year follow-up, which is similar to the rate reported regarding SAVR (3). Back in 2015, a multicenter study published on *Circulation* reported incidence rates of 0.3% to 1.2% per patient/year while the 2633-patient cohort registry conducted by Butt et al. reported an incidence rate of PVIE of 4.4% at the median follow-up of 3.6 years. On the other hand, the Swedish national registry reported a higher rate of PVIE within the first year of 2.3%, indicative that the higher risk was reported within the first year after implantation. Nonetheless, we did not see these results in our study (10, 15, 16).

Secondly, the microorganisms found were the same ones reported in the series of surgical prosthetic valves (3). In the EIRA-3 registry, the *Staphylococcus species* were the most common germ followed by *Streptococcus* and *Enterococcus* (14). In our registry similar results were reported and the most common germs were *Streptococcus* (66%) and *Enterococcus* (33%). In the Swedish series the results reported were similar to those obtained in our registry (18).

Although the implantation of cardiac devices is associated with higher morbidity and mortality rates, as well as with more infections, in our registry, none of the 3 patients were pacemaker carriers (17). Similarly, no direct correlation was seen between previous surgical procedures and the development of PVIE in either one of the patients.

Our registry has some limitations. First, although it is a consecutive series of patients treated by the same group of operators from 3 different centers, the size of the sample is rather small. Secondly, although the registry was prospective

in nature, it was conducted to know the procedural characteristics and the long-term results of transcatheter aortic valve implantation without specifically looking for endocarditis. That is why the retrospective search for this entity can be associated with both selection and survival biases.

Unanswered questions on transcatheter aortic valve implantation in the assessment of PVIE still remain since this procedure is not exactly the same as conventional surgical aortic valve replacement. TAVI is a hybrid procedure performed at cath labs that happen to be different from conventional operating rooms regarding asepsis. Also, the preparation, hospitalization, and follow-up of the patients is “stent-like” and, therefore, similar to angioplasty; also, care is similar regarding the previous preparation of the patient and follow-up care. At the beginning of the registry, the use of antibiotic prophylaxis was not regulated as in traditional valve replacement surgeries vs other procedures like dental or diagnostic interventions. Another limitation when it comes to drawing definitive conclusions is that patients treated with TAVI had severe comorbidities that were seen in the risk score used (EuroSCORE). This added to the frailty of this

group of patients, which also elevates the risk of infections. We should remember that, in this consecutive series, almost 20% of the patients were treated via transapical access (19), an access site that has fallen into disuse and that is associated with worse short-term results. The only death reported due to early PVIE was a patient in whom this strategy had to be used due to the impossibility of using femoral accesses and an absolute contraindication to surgical aortic valve replacement. Finally, we should not forget that TAVI does not remove the native valve and that, given the special characteristics of this procedure, a macroscopic and microscopic lesion of native endothelium occurs that is adjacent to the valve predisposed to this entity.

CONCLUSION

In our population, the rate of prosthetic valve infective endocarditis associated with TAVI is low, and similar to the rates already reported in other countries. The prophylactic strategy and treatment used should target the common germs responsible for endocarditis.

REFERENCES

- Mack MJ, Leon MB, Thourani VH, et al. PARTNER 3 Investigators. Transcatheter aortic-valve replacement with a balloon-expandable valve in low risk patients. *N Engl J Med* 2019;380:1695-705.
- Popma JJ, Deeb GM, Yakubov SJ, et al. Evolut Low Risk Trial Investigators. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med* 2019;380:1706-15.
- Murdoch DR, Corey GR, Hoen B, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. *Arch Intern Med* 2009;169:463-73.
- Ostergaard L, Valeur N, Ihlemann N, et al. Incidence of infective endocarditis among patients considered at high risk. *Eur Heart J* 2018;39:623-9.
- Habib G, Thuny F, Avierinos JF. Prosthetic valve endocarditis: current approach and therapeutic options. *Prog Cardiovasc Dis* 2008;50:274-81.
- Glaser N, Jackson V, Holzmann MJ, Franco-Cereceda A, Sartipy U. Prosthetic valve endocarditis after surgical aortic valve replacement. *Circulation* 2017;136:329-31.
- Ostergaard L, Valeur N, Ihlemann N, et al. Incidence of infective endocarditis among patients considered at high risk. *Eur Heart J* 2018;39:623-9.
- Maresh B, Angelini G, Caputo M, Jin XY, Bryan A. Prosthetic valve endocarditis. *Ann Thorac Surg* 2005;80:1151-8.
- Edlin P, Westling K, Sartipy U. Long-term survival after operations for native and prosthetic valve endocarditis. *Ann Thorac Surg* 2013;95:1551-6.
- Butt JH, Ihlemann N, De Backer O, et al. Long-Term Risk of Infective Endocarditis After Transcatheter Aortic Valve Replacement. *J Am Coll Cardiol* 2019;73:1646-55.
- Olsen NT, De Backer O, Thyregod HG, et al. Prosthetic valve endocarditis after transcatheter aortic valve implantation. *Circ Cardiovasc Interv* 2015;8:e001939.
- Amat-Santos IJ, Messika-Zeitoun D, Eltchaninoff H, et al. Infective endocarditis after transcatheter aortic valve implantation: results from a large multicenter registry. *Circulation* 2015;131:1566-74.
- Regueiro A, Linke A, Latib A, et al. Association between transcatheter aortic valve replacement and subsequent infective endocarditis and in-hospital death. *JAMA* 2016;316:1083-92.
- Avellana PM, García AM, Swieszkowski S, et al. Endocarditis infecciosa en la República Argentina. Resultados del estudio EIRA 3. *Revista Argentina de Cardiología*, vol. 86, núm. 1, pp. 20-28, 2018.
- Khan A, Aslam A, Satti KN, Ashiq S. Infective endocarditis post-transcatheter aortic valve implantation (TAVI), microbiological profile and clinical outcomes: A systematic review. *PLoS ONE* 15(1): e0225077.
- Amat-Santos IJ, Messika-Zeitoun D, Eltchaninoff H, et al. Infective endocarditis following transcatheter aortic valve implantation: results from a large multicenter registry. *Circulation* 2015;131:1566-74.
- Glaser N, Persson M, Dalén M, et al. Long-term Outcomes Associated With Permanent Pacemaker Implantation After Surgical Aortic Valve Replacement. *JAMA Netw Open* 2021;4(7):e2116564.
- Bjursten H, Rasmussen M, Nozohoor S, et al. Infective endocarditis after transcatheter aortic valve implantation: a nationwide study. *Eur Heart J* 2019;40:3263-9.
- Mieres J, Menéndez M, Fernández-Pereira C, Rubio M, Rodríguez AE. Transapical Implantation of a 2nd-Generation JenaValve Device in Patient with Extremely High Surgical Risk. *Case Rep Cardiol* 2015;2015:45815.