Infective Endocarditis after Transcatheter Aortic Valve Implantation

Endocarditis infecciosa luego del implante de válvula aórtica por cateterismo

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ABSTRACT

Background: Infective endocarditis (IE) after transcatheter aortic valve implantation (TAVI) is a rare complication with high morbidity and mortality.
Methods: Of 630 consecutive patients undergoing TAVI, 6 (0.95%) presented IE.
Results: Four patients were men, mean age was 81.3 ± 2.2 years and all the patients were symptomatic. Left ventricular ejection fraction (LVEF) was $56.8 \pm 5.3\%$. The procedure was successful in all the patients and one presented moderate regurgitation. Two patients required definitive pacemaker and the lead had to be reimplanted 24 hours later in 1 patient. Time to IE was 63.5 ± 73.3 days (median 35 days). A Gram-positive coccus was isolated in four cases. One patient presented a vegetation on transesophageal echocardiography . One patient died within 30 days. During follow-up of 23 ± 22 months none of the patients presented new events or hospitalizations. On Doppler echocardiography, LVEF was $55.9 \pm 4.6\%$, mean trans-aortic gradient was 8.2 ± 1.8 mm Hg and peak systolic velocity was 1.8 ± 0.2 m/s. One patient had moderate regurgitation.
Conclusions: In this series of patients, IE after TAVI was uncommon and had a favorable course with antibiotic treatment.

Key words: Endocarditis – Heart Valve Prosthesis Implantation /Adverse Effects - Transcatheter Aortic Valve Replacement - Prosthesis-Related Infections

RESUMEN

Introducción: La endocarditis infecciosa (EI) post implante percutáneo de válvula aórtica (TAVI) es poco frecuente, con una alta tasa de morbimortalidad.
Métodos: Se analizaron 630 pacientes consecutivos con TAVI, de los cuales 6 (0,95%) presentaron EI.
Resultados: Cuatro eran hombres, edad $81,3 \pm 2,2$ años, y todos sintomáticos. La fracción de eyección ventricular izquierda (FEVI) fue $56,8 \pm 5,3\%$. Todos recibieron un implante exitoso y uno presentó regurgitación moderada. Dos requirieron marcapaso definitivo, a uno de ellos se le debió recolocar el cable a las 24 h.
La EI se presentó a los $63,5 \pm 73,3$ días (mediana de 35 días). El germen aislado fue un coco (+) en cuatro casos. En uno se observó una vegetación en el ecocardiograma transesofágico.
Un paciente falleció dentro de los 30 días. El seguimiento fue a 23 ± 22 meses, ningún paciente presentó nuevos eventos o internaciones. En el eco Doppler la FEVI fue de $55,9 \pm 4.6\%$, el gradiente medio $8,2 \pm 1,8$ mmHg y la velocidad pico de $1,8 \pm 0,2$ m/seg. Un paciente presentó una regurgitación moderada.
Conclusiones: En esta serie de pacientes, la EI post TAVI fue poco frecuente y presentó una evolución favorable con el tratamiento antibiótico.

Palabras clave: Endocarditis - Implantación de Prótesis de Válvulas Cardíacas/efectos adversos - Reemplazo de la Válvula Aórtica Transcatéter - Infecciones Relacionadas con Prótesis

Abbreviations

DLP	dyslipidemia		**PPM**	permanent pacemaker
TEE	transesophageal echocardiography		**TAVI**	transcatheter aortic valve implantation
IE	infective endocarditis		**PSV**	peak systolic velocity
LVEF	keft ventricular ejection fraction			

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INTRODUCTION

Transcatheter aortic valve implantation (TAVI) has proved to be safe and effective in symptomatic severe aortic valve stenosis in patients at extreme risk for surgery, (1-2) or with high, (3) intermediate, 4) or low (5) operative risk according to recent publications. The results may be even better in some groups using the transfermoral approach. For these reasons, TAVI is the strategy recommended in patients aged 75-80 years or greater. (4-6) Infective endocarditis (IE) is a complication after conventional aortic valve replacement with biologic prosthesis, with a reported incidence between 1-6%, (7) a torpid progression and high morbidity and mortality. Although it has been suggested that, compared with surgical valves, the presence of more prosthetic material and stent struts supporting percutaneous valves may be associated with the occurrence of IE, this has not been demonstrated yet. (6)

Despite some series have reported an incidence of IE after TAVI of 0.5-3.1%, (8-9) there is no solid evidence in the literature about its incidence and outcome.

The aim of this study was to analyze the incidence and outcome of IE after TAVI in a consecutive series of patients in two high-complexity centers with intermediate volume of TAVI procedures per year.

METHODS

Between March 26, 2009, and May 30, 2021, 630 consecutive patients underwent TAVI at Instituto de Cardiología y Cirugía Cardiovascular, Hospital Universitario Fundación Favaloro in Buenos Aires and International Heart Center Medicor in Izola, Slovenia. Six of these patients (0.95%) presented IE and were included in this analysis.

The diagnosis or aortic stenosis was made by Doppler-echocardiography before the procedure. Severe aortic stenosis was defined by the following criteria: aortic valve area < 1 cm2 or < 0.6 cm2/m2, mean gradient > 40 mm Hg or peak systolic velocity > 4.0 m/s at rest. (10) Before TAVI, all the patients underwent conventional coronary angiography to determine the presence of associated coronary artery disease and contrast-enhanced computed tomography angiography with 3-D reconstruction to analyze the aortic valve (to determine whether the valve was bicuspid or tricuspid, measure the aortic annulus, and determine the extent of calcification of the cusps, aortic annulus, left ventricular outflow tract, aorta and iliac vessels, and other potential vascular accesses).

The decision to perform TAVI versus conventional surgery was made based on the recommendations of the institutional heart team considering the patient's risk and preferences. Due to the lack of reimbursement for low-risk cases in our environment, most patients had high surgical risk.

All implants were performed according to a minimally invasive strategy, including conscious sedation for anesthesia, transthoracic echocardiogram and percutaneous closure of the vascular access. In all the procedures, 100U/kg of sodium heparin was used for anticoagulation to maintain an ACT > 240 seconds; in cases without recent coronary angioplasty, protamine was administered at the end of the procedure to reverse the effect of heparin. If transient pacing was required during or after implantation, the venous femoral access with an 8F introducer was used in most cases, contralateral to the main access. The jugular vein access was used in some

cases and in other cases no access was necessary according to the operator's criterion. In addition, the main access was protected by introducing a 0.018" guidewire in the therapeutic femoral artery from the contralateral femoral artery. The main access was closed with a PROSTAR® or PROGLIDE® percutaneous closure device using the "pre-close" technique (the suture is inserted first and then the sheath which has a greater diameter than the closure system).

In patients with clinical suspicion of IE the diagnosis was made using Duke's criteria. (11) After discharge, all the patients received double antiplatelet therapy for at least 3 months, except for those with indication of prolonged antiplatelet therapy or anticoagulation due to other causes.

Patients were followed-up at 30 days 6 and 12 months and then every 12 months through medical visits, electrocardiogram and Doppler-echocardiography.

Statistical analysis

This is a prospective and observational study performed in two high-volume centers. The results are expressed in absolute numbers, mean and standard deviation for variables with normal distribution despite the small number of patients or as expressed as median and interquartile range.

Ethical considerations

The procedure was performed following the international standards according to the protocol indicated. In all the cases, the procedure and the expected risks and benefits were explained to the patients who signed a specific informed consent after all their questions were responded

RESULTS

Mean age was 81.3 ± 2.2 years and 4 patients were men. Five patients presented hypertension, 1 diabetes and 5 dyslipidemia. Four patients had a history of myocardial infarction, 4 had previous percutaneous coronary intervention (PCI) and 1 patient underwent PCI within 3 months before TAVI. All the patients were in sinus rhythm and 1 had a previous trifascicular block. None of the patients presented renal failure; the estimated glomerular filtration rate was 77.3 ± 10.5 mL/min/1.73m². Mean STS score was 5.75 ± 2.4% and none of the patients presented atrial fibrillation or previous cardiac surgery.

Before valve implantation all the patients were symptomatic for dyspnea FC II-III. Mean LVEF was 56.8 ± 5.3%, mean aortic valve area was 0.68 ± 0.19 cm2 and mean trans-aortic gradient was 41.3 ± 4 mm Hg. (Table 1).

All the procedures were performed via the femoral access and two cases required pre-dilatation. Three patients required overlapping the right coronary cusp and left coronary cusp (cusp overlap technique) for valve implantation. The valves used were Core Valve Evolut in 2 patients, Portico in 2, Sapiens XT in 1 and Lotus in 1. Three patient required valve recapture, and post-dilatation was necessary in only 1 patient. Trans-aortic gradient after implantation was 6. 5 ± 1.04 mm Hg; only 1 patient presented moderate aortic regurgitation after implantation and there were no cases of severe aortic regurgitation.

A minimally invasive strategy was used in all the

Table 1. Characteristics of the procedure

STS Score	5.75 ± 2.4 (2.5-11.7)
LV ejection fraction	56.8 ± 5.3
Aortic valve area	0.68 ± 0.19
Mean trans-aortic gradient	41.2
Femoral access	6
Percutaneous closure	6
Pre-dilatation	2
Post-dilatation	1

Table 2. 30-day outcome and follow-up

Results at 30 days	n = 6
Mortality (IE - sepsis)	1
Stroke, myocardial infarction, urgent surgery	0
Moderate/severe leak, vascular complication, major bleeding	0
Permanent pacemaker	2
Outcome during follow-up	**n = 5**
Time (months)	23 ± 22.1 (1-48)
Mortality or major complications	0
Structural prosthesis deterioration	0
LV ejection fraction (%)	55.9 ± 4.6
Mean gradient (mm Hg)	8.2 ± 1.8
Velocity (m/s)	1.8 ± 0.2

procedures and included the percutaneous closure of the vascular access, without complications.

Mean stay in the catheterization laboratory was 158 ± 28.5 minutes and 195 ± 30.1 mL of contrast agent were used.

Two patients required definitive pacemaker before discharge due to high-degree AV block; one of them had a previous trifascicular block and the lead had to be reimplanted 24 hours later due to high threshold. There were no cases of acute myocardial infarction, stroke, reintervention, urgent surgery, major bleeding or vascular complications during hospital stay. Mean length of hospital stay was 2.3 ± 0.8 days (1-3).

Mean time to presentation of IE was 63.5 ± 73.3 days after TAVI with a median of 35 days; 3 cases occurred within 30 days and the other 3 at 45, 60 and 210 days, respectively.

The germs isolated from blood cultures were 1 Stafilococcus aureus, 1 Streptococcus bovis, 1 Enterococcus faecalis, and 1 Streptococus mitis; in 2 cases no germs could be typified.

Antibiotic treatment lasted 6 weeks in all patients and the regimen depended on the germ isolated.

In only one case, transesophageal echocardiography showed a vegetation on the ventricular side of the non-coronary cusp.

One patient died after 30 days due to septic shock and refractory heart failure.

Clinical and echocardiographic follow-up was performed in all patients at 23 ± 22.1 (1-48) months; there were no deaths, myocardial infarctions, stroke, valve replacement surgery or other reinterventions. On Doppler echocardiography performed during follow-up, LVEF was 55.9 ± 4.6%, mean trans-aortic gradient was 8.2 ± 1.8mm Hg and peak systolic velocity was 1.8 ± 0.2 m/s, with no structural impairment. None of the patients required hospitalization during follow-up and all remained in functional class I (Table 2).

DISCUSSION

In this analysis of 2 intermediate volume centers, the incidence of IE after TAVI was similar to the one reported in other published series. The clinical course was relatively favorable with the antibiotic treatment received with no additional complications, except in one of the 6 cases. In all the cases the diagnosis was

made within the first year, as it usually occurs, especially within the first 100 days after implantation, as was the case in our patients. (12)

The need for definitive pacing when self-expandable valves are used is about 17% in the modern randomized studies (13) and has been related with re-interventions and mortality (14-15). In our series, two patients required definitive pacemaker which had to be repositioned in one of them due to a high pacing threshold, but no conclusions can be drawn due to the small number of patients. We currently use the cusp overlap technique (overlapping the right coronary cusp and left coronary cusp) and we have demonstrated a significant reduction in the need for pacemaker implantation, with figures similar to those of balloon-expandable aortic valves (16-17) and surgical series. This technique could provide a significant additional benefit by reducing endovascular maneuvers and thus potentially reducing the risk of endocarditis. However, this hypothesis will require larger number of patients to be demonstrated.

One patient of our series died of early endocarditis with refractory heart failure and subsequent renal failure, with no structural valve deterioration according to the European and Valve Academic Research Consortium. (18)

It has been demonstrated that the association of heart failure and renal failure associate with high mortality, particularly in patients with high surgical risk score. (19)

The risk factors for IE that have been reported are age, particularly < 80 years, male sex, diabetes, COPD, impaired renal function, presence of perivalvular regurgitation, higher valve calcification, gastrointestinal bleeding and orotracheal intubation during the procedure. (20-21)

Prosthetic valve endocarditis is the most aggressive form, occurring in 1% to 6% of cases according to published series and accounting for 10% to 30% of all IE. (22) It is associated with high morbidity and a high mortality rate which is about 23% when it occurs after

conventional surgery and 36% after TAVI. (23-24)

The incidence of surgical explantation after TAVI is 0.2% (0.28% for first generation valves and 0.14% for new generation valves) and 20% in cases of IE. The most common indication for valve explantation is bioprosthetic valve failure. The 30-day and 1-year mortality rate of surgical explantation of thranscatheter aortic valves is 13.2% and 22.9%, respectively. Renal failure and IE are predictors of unfavorable outcome. (25)

The indication for surgical explantation has many limitations in this population of patients with high surgical risk or previous contraindications for surgery particularly in our environment.

Study limitations

The retrospective nature of our observational study performed in only 2 centers and the lack of randomization are the main limitations. In addition, as the complication is rare, the number of patients included is too small to draw definitive conclusions about this series. Although mean follow-up of the overall series is 23 ± 22.1 months (1-48), we cannot draw a definitive conclusion about the incidence of late IE (5-10 years).

CONCLUSION

In this series of patients, infective endocarditis after TAVI was very rare and had a favorable course with antibiotic treatment.

Conflicts of interest

None declared.

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

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