ORIGINAL ARTICLE

Benefits and Complications of Direct Implantation of Self-Expandable Aortic Valve Prosthesis for Severe Aortic Stenosis

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ABSTRACT

Objective

To describe the initial experience with direct implantation of a CoreValve™ self-expanding aortic valve prosthesis in a tertiary cardiovascular care center from Argentina.

Methods

From May to December 2010, 21 consecutive patients with severe aortic stenosis (SAS) and high surgical risk were included to undergo percutaneous aortic valve replacement with a CoreValve™ prosthesis. The inclusion criteria were the following: aortic valve area <1 cm2 (<0.6 cm2/m2); aortic annulus diameter of 20-27 mm; ascending aorta diameter at the level of the sinotubular junction ≤ 40 (small prosthesis) or ≤ 43 mm (large prosthesis), and femoral artery diameter >6 mm.

Results

Mean age was 79±8 years, mean aortic valve area was 0.7±0.2 cm2 and mean logistic EuroSCORE was 26±15% (50% of patients with logistic EuroSCORE ≥ 20%). After valve implantation, peak transaortic pressure gradient measured by echocardiography decreased from 80±22 to 14±5 mm Hg. Two patients developed severe aortic regurgitation which improved with post-dilation. The success rate of the procedure was of 95% as a patient died immediately after valve implantation. A definitive pacemaker was implanted in six patients due to atrioventricular block. Cumulative survival was 75% after a mean follow-up of 5±2.8 months.

Conclusion

Our initial experience suggests that direct implantation of a CoreValve™prosthesis is a safe and feasible therapeutic option for patients with SAS and high surgical risk.

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Key words > Aortic valve stenosis - Catheterization - Endovascular procedures

Abbreviations >

SAS	Severe aortic stenosis	**BAV**	Balloon aortic valvuloplasty

BACKGROUND

Percutaneous aortic valve replacement is an innovative technique for the treatment of severe aortic stenosis (SAS) that is being incorporated to clinical practice with on-growing enthusiasm, particularly in patients with high surgical risk. (1-6) The self-expanding CoreValve™ prosthesis (Medtronic, Minneapolis, Minnesota) is one of the aortic valve prosthesis most commonly used and the only one currently available in Argentina. Conventionally, balloon pre-dilation (balloon aortic valvuloplasty (BAV) is required before prosthesis implantation. However, the outcome of bal-

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loon pre-dilation is frequently unsatisfactory, with a poor reduction in the pressure gradient across the aortic valve and scarce increase in aortic valve area. Moreover, BAV is associated with complications (as acute aortic regurgitation, aortic dissection, rupture of the aortic valve annulus, tears at the level of the sinotubular junction and stroke due to calcium embolism) which could be prevented by direct implantation of the valve prosthesis. (6, 7) The purpose of our study is to report the feasibility and safety of direct implantation of the CoreValve™ prosthesis in patients with SAS.

METHODS

Study design and patient selection

We conducted a prospective registry including all the consecutive patients undergoing percutaneous aortic valve replacement in a single center since May 2010.Patients were selected by a multidisciplinary team (clinical cardiologists, interventional cardiologists, cardiovascular surgeons and specialists in diagnostic imaging). A total of 29 patients with symptomatic SAS and high surgical risk were recruited for percutaneous aortic valve replacement in a tertiary cardiovascular care center from Argentina. For the present analysis we only included patients undergoing direct aortic valve implantation (i.e. without pre-dilation). (n = 21).

All patients were evaluated with transthoracic echocardiography as a first approach for the diagnosis and assessment of the severity of the disease. To be eligible for percutaneous aortic valve replacement, and after estimating clinical risk, all the patients underwent coronary angiography with ventriculography, aortography and right and left heart catheterization to measure pressure gradients, cardiac output and aortic valve area. If the patients were selected according to the diameter of the aortic annulus, sinus of Valsalva height and anatomy of the ascending aorta and iliac or subclavian arteries, routine evaluation continued with multislice computed tomography and transesophageal echocardiography which were used to perform similar measurements.

The operative risk was estimated by the logistic EuroSCORE. (8) The inclusion criteria were the following: patients with symptomatic SAS by echocardiographic severity criteria (aortic valve area < 1 cm2, < 0.6 cm2/m2, peak velocity > 4.0 m/s or mean gradient >40 mmHg). The aortic annulus diameter measured by transthoracic and/or transesophageal echocardiography had to be ≥20 mm and ≤ 27 mm, and the diameter of the ascending aorta at the level of the sinotubular junction ≤ 45 mm. The following were considered exclusion criteria: bicuspid aortic valve, presence of thrombi in the left heart chambers, ejection fraction < 20%, ilio- femoral arteries with diameter <6 mm or significant tortuosity not allowing catheter progression, no possibility of subclavian access, and sinus of Valsalva height <15 mm.The procedure was considered successful when the prosthesis was correctly implanted (evaluated angiographically and echocardiographically) in the absence of mortality or need of emergency surgery within the first 30 postoperative days.

Procedure description

The procedure was performed under angiographic, hemodynamic and transesophageal echocardiographic guidance. A transient pacemaker was implanted (via the jugular or femoral vein) during 48 hours in those patients who did not have a definitive pacemaker. Arterial access was through the femoral artery. A 6 F introducer was inserted via the left femoral artery and a 6 F pigtail catheter was advanced and positioned at the level of the coronary sinus in order to measure pressure gradients and, simultaneously, for angiographic control. Moreover, its position in the coronary sinus was used as guidance during positioning of the CoreValve™ prosthesis. After surgical dissection of the right femoral artery, a 6 F introducer was inserted and a 0.035-inch guidewire was introduced. Then an Amplatz-like shape catheter (ALI or ALII) was advanced over the guidewire across the aortic valve.The catheter was then exchanged by an extra-stiff 0.035-inch Amplatz guidewire (William Cook Europe, Bjaeverskov, Denmark) with a flexible tip and modified curvature to reduce risk of perforation which was placed in the left ventricular apex following the curvature of the chamber. Then, the introducer was exchanged by an 18 F introducer.

After measuring the gradient across the aortic valve, the prosthesis was advanced over the Amplatz guidewire and positioned at the level of the aortic annulus. Release was attempted using high-implantation position to prevent periprosthetic leaks or development of permanent conduction disturbances requiring definitive pacemaker implantation.The prosthesis was gradually released retracting the sheath (Figure 1 A-F, Graphs I-II). One patient presented asymmetrical deployment of the device and significant valve regurgitation requiring catheter balloon dilation under rapid ventricular pacing.

Antiplatelet and antithrombotic medication

All patients received 100 mg of aspirin before the procedure and daily thereafter. In addition, a loading dose of clopidogrel was administered to all patients, followed by 75 mg/day for at least 3 months. Heparin sodium was administered during the procedure (80-100 U/kg).

Patient care after the procedure

After the procedure, all patients were admitted to the coronary care unit for continuous monitoring for at least 48 hours. The transient pacemaker was removed in the absence of rhythm disturbances. In all cases, the need for definitive pacemaker implantation was discussed between the operator, clinical cardiologists and/or electrophysiologists from the institution.

Follow-up

All patients were followed-up for 30 days and every 6 months thereafter. Median follow-up was 5 ± 2.8 years.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation and categorical variables as numbers and percentages. The Kaplan-Meier method was used to analyze cumulative survival. Statistical analysis was performed using SPSS 10 statistical package (Chicago, IL, USA).

RESULTS

Characteristics of the population

From October 2009 to June 2011, 29 CoreValve™ prostheses were consecutively implanted. The direct approach without pre-dilation was performed since May 2010 in 21 consecutive cases (72.4%). The baseline characteristics of the population who underwent direct implantation are: mean age was 79 ± 8 (range, 35 - 78) years and 33% were women. All patients presented symptomatic SAS with peak echocardio-

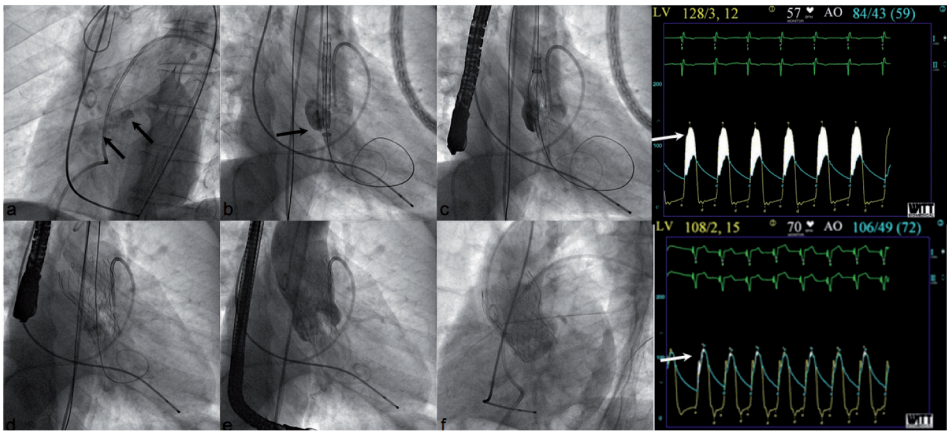

Fig. 1. A. Aortic valve with severe calcification (arrows). **B.** Undeployed valve prosthesis crossing the aortic valve plane. **C.** Partially deployed prosthesis (possibility of repositioning). **D.** Deployed and released prosthesis from the delivery system (no possibility of repositioning). **E.** Aortography in right anterior oblique view. **F.** Aortography in left anterior oblique view (symmetrical expansion, absence of significant transvalvular gradient or valve regurgitation). *Graph I.* Simultaneous pressures in the left ventricle (LV) and aorta (Ao) with significant gradient before implantation (arrows). *Graph II.* Absence of significant gradient after implantation (arrows).

graphic transvalvular aortic gradient of 80 ± 22 mm Hg (range, 50-144 mm Hg). Mean aortic valve area, estimated by echocardiography before the procedure, was 0.7 ± 0.2 cm2 and valvular annulus was 22 ± 2 mm (range, 19.5 - 26). Mean logistic EuroSCORE was 26 ± 15.4%, and 50% had logistic EuroSCORE ≥ 20%. The percentage of patients in functional class III and IV was 62% and 10%, respectively.

Procedure data

The procedure was completed successfully in 20 patients. One patient died after the prosthesis was implanted. A 26-mm prosthesis was implanted in six cases (for aortic annulus diameters between 20 and 23 mm), and the remaining patients received a 29-mm prosthesis (for aortic annulus diameters between 23 and 27 mm). Six cases required post-dilation with 23 to 28 mm valvuloplasty balloons. After valve implantation, peak instantaneous pressure gradient across the aortic valve measured by echocardiography was 14 ± 5 mmHg (Figure 2). Only two patients developed residual moderate to severe aortic regurgitation which improved to moderate regurgitation after post-dilation (Figure 3). In both cases asymmetrical expansion of the valve was observed after implantation which was corrected with post-dilation.

Complications of the procedure

In one patient the prosthesis presented displacement during implantation while the device was still attached to the delivery system. The prosthesis was successfully repositioned without complications. Six patients required implantation of a definitive pacemaker due to atrioventricular block. There were no conversions to open aortic valve replacement surgery. Mortality rate (including procedure-related mortality, in-hospital mortality and mortality at 30 days) was 5% (n = 1). Mean hospital stay was 10 days (range, 4 - 52). An elderly female who had been admitted with a

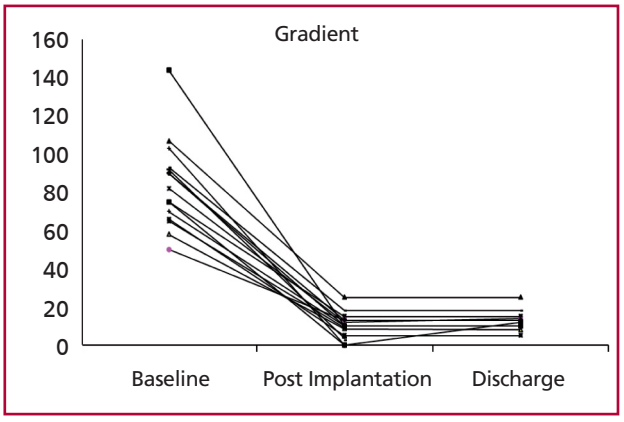

Fig. 2. Peak gradient across the aortic valve (measured by Doppler echocardiography) before and after valve implantation and at discharge.

critical medical condition two months before the procedure remained hospitalized for 52 days due to respiratory insufficiency and recurrent pleural effusions.

Follow-up

Mean follow-up was 5 ± 2.8 months. After the first month, only one patient died at 7 months due to non-cardiac causes (malignant brain tumor). Three, two and five patients completed 8 months, 6 months and 3 months of follow-up, respectively. Overall survival estimated by the Kaplan-Meier method was 75% (Figure 4).

DISCUSSION

BAV has evolved as a palliative method for patients with SAS in whom surgery is contraindicated or for patient stabilization before aortic valve replacement. (9) The procedure offers short-term symptomatic relief before percutaneous or aortic valve replacement but does not increase survival and is associated with

a restenosis rate of almost 100% within the first year. (7) The complications of BAV are aortic regurgitation, aortic lesion or rupture and calcium embolism originating from leaflet deposits. (6) For these reasons, the indication of BAV has become less common during the last two decades. However, the recent introduction of direct aortic valve implantation has renewed interest in BAV. As a rule, pre-dilation is performed in all cases before CoreValve™ implantation to aid positioning and implant of the prosthesis and improve the final outcome.

Recently, several registries from Europe have reported the experience of implanting the European CoreValve™ prosthesis. Although the results of these registries are promising (mortality rate at 30 days between 8% and 12%), uncommon catastrophic complications have been reported and include acute and severe aortic regurgitation with hemodynamic impairment, aortic dissection or rupture and ischemic stroke. (3, 10) Probably most of these severe complications occur during pre-dilation. Our hypothesis is that such complications should be reduced or even prevented by direct implantation of the prosthesis. Moreover, this approach does not require transient ventricular pacing (which will only be necessary if post-dilation is needed), aiding and shortening the procedure. In our preliminary experience, direct implantation was a feasible, safe and efficient approach. In all cases the prosthesis was correctly positioned despite the presence of critical aortic valve areas with severe calcification. Six cases required post-dilation and only two presented

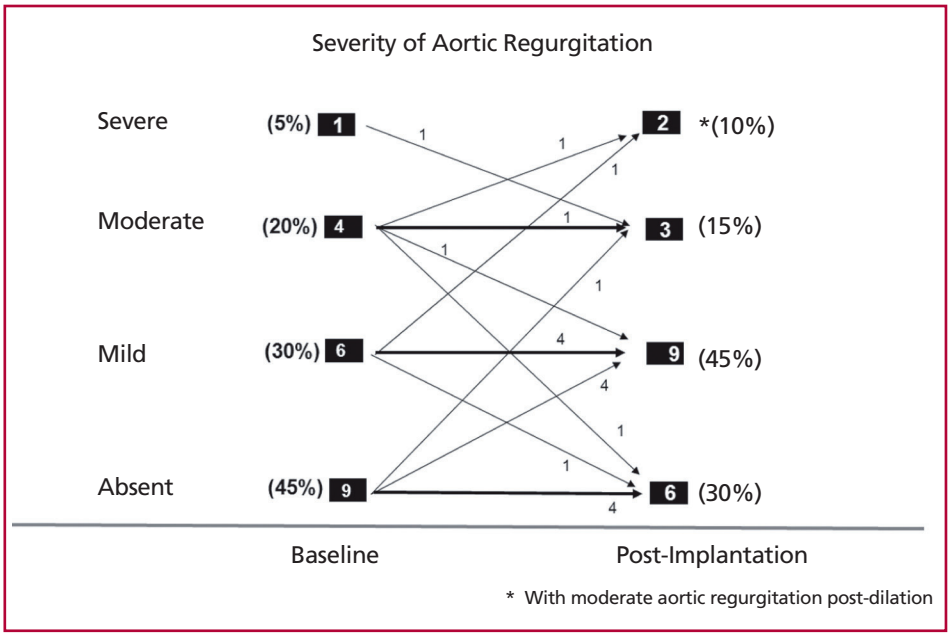

Fig. 3. Aortic regurgitation before and after implantation, and at discharge.

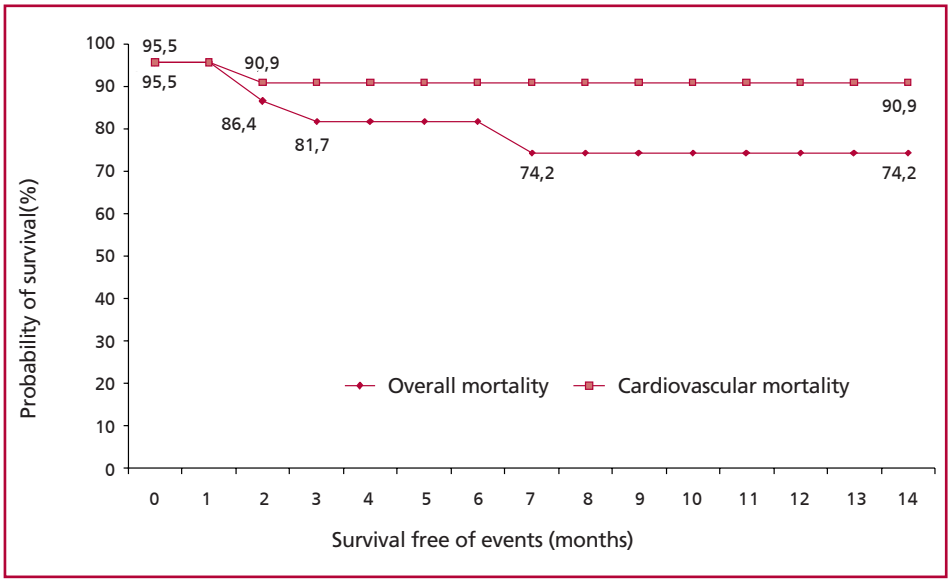

Fig. 4. Kaplan-Meier curves of cumulative survival without adverse events.

severe aortic regurgitation due to periprosthetic leak (asymmetrical deployment of the prosthesis) which improved significantly with post-dilation. The rate of definitive pacemaker implantation was 28.5%, a favorable result compared to those reported by the German (42.5%) and French (27.2%) registries. (3, 11) The absence of cerebrovascular events was a promising outcome, as previous reports have demonstrated stroke rates of 3%-10% at 30 days. However, this difference might be due to sample size and the absence of an independent committee.

The main limitations of the study are sample size, the fact that it was conducted in a single center and the short follow-up period. However, the 95% survival rate at 30 days suggests that direct implantation is a safe and efficient technique. There are two potential limitations to direct implantation: 1) the presence of critical aortic stenosis impairing prosthesis progression across the stenosed aortic valve, and 2) the presence of severe valve calcification not allowing adequate device deployment. So far, we have not experienced any difficulty in positioning the prosthesis,though we detected a case of reduced deployment that was corrected with post-dilation without complications. Probably, dilation of an already implanted prosthesis is less likely to produce embolic events compared to pre-dilation of a calcified native valve, as part of the calcium deposits are trapped within the stent and the biological tissue of the valve skirt.

CONCLUSIONS

In our preliminary report, direct implantation of the aortic CoreValve™ prosthesis is a safe and feasible approach for patients with SAS and high surgical risk. Further studies, including more patients and with longer follow-up are necessary to assess the efficacy of this technique.

RESUMEN

Beneficios y Complicaciones del Implante Directo de Prótesis Aórtica Autoexpandible para el Tratamiento de la Estenosis Valvular AórticaGrave

Objetivo

Describir la experiencia inicial con el implante directo de la prótesis aórtica autoexpandible CoreValve® en un centro argentino de alta complejidad cardiovascular.

Material y métodos

Desde mayo a diciembre de 2010 se incluyeron en forma consecutiva pacientes con estenosis aórtica grave (EAG) de alto riesgo sometidos a implante directo de prótesis CoreValve® (n=21). Los criterios de inclusión fueron: área de la válvula aórtica < 1 cm2 (< 0,6 cm2/m2), anillo valvular aórtico de entre 20 y 27 mm, diámetro de la aorta ascendente a nivel de la unión sinotubular ≤40 (prótesis pequeña) o ≤43 mm (prótesis grande) y diámetro de la arteria femoral > 6 mm.

Resultados

La edad fue de 79±8 años, el área valvular aórtica fue de 0,7±0,2 cm2 y el EuroSCORE logístico fue del 26% ±15% (50% con EuroSCORE logístico ≥20%). Tras el implante, el gradiente transaórtico máximo por ecocardiograma descendió de 80±22 mmHg a 14±5 mmHg. Dos pacientes presentaron insuficiencia aórtica de grado grave, que mejoraron luego de la posdilatación. La tasa de éxito del procedimiento fue del 95%, ya que un paciente falleció luego del implante valvular. Se implantó un marcapasos definitivo por bloqueo auriculoventricular en 6 pacientes. La sobrevida acumulada (media de seguimiento 5±2,8 meses) fue del 75%.

Conclusión

Nuestra experiencia inicial sugiere que el implante directo de la prótesis CoreValve® es una opción terapéutica segura y factible para los pacientes con EAG de alto riesgo quirúrgico.

Palabras clave > Estenosis de la válvula aórtica- Cateterismo - Procedimientos endovasculares

Conflicts of interest

Dr. Oscar Mendiz is proctor for CoreValve / Medtronic. The other authors declare no conflict of interest.

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