

# Mid-term Follow-Up of Patients Submitted to Aortic Valve Replacement with Mechanical Prosthesis

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## ABSTRACT

### Background

Aortic valve disease is one of the most frequent causes of valve replacement in our environment. This study was performed based on the lack of information related to late outcomes in patients submitted to aortic valve replacement with mechanical prosthesis.

### Objective

To assess the mortality, morbidity (major complications) and functional outcomes (clinical improvement) during the follow-up of patients with mechanical prosthesis placed in the aortic position.

### Material and Methods

Ninety five patients submitted to aortic valve replacement with mechanical prosthesis were selected. Surgeries were performed between January 1999 and December 2006. Mean follow-up was  $4 \pm 2.3$  years; percentiles 25-75: 2.5-6.3 years. Total follow-up was 427.5 patients/year.

### Results

Mean age was  $64.5 \pm 12.3$  years, 61.1% were men.

Sixty patients (63%) were in functional class (FC) III-IV prior to surgery.

During follow-up, 67 patients (70.5%) were in FC I and 28 (29.5%) in FC II. No patients presented FC III or IV.

Mean effective valve area/body surface area was  $1.06 \text{ cm}^2/\text{m}^2$ .

Actuarial survival (Kaplan-Meier) was 95% (95% CI 88-98%) at one year and 89% at 5 years (95% CI 76-95%). Nine deaths (9.5%) were related to this condition. The incidence of complications was as follows: thromboembolism 0.2% patient/year, bleeding 2.3% patient/year, and endocarditis 0.7% patient/year. Re-operation rate was 0.4% patient/year.

### Conclusions

These results were similar to those reported in international series in terms of survival and major complications.

The number of adverse events observed at mid-term is still high, as it is all around the world.

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**Key words** > Valve Prosthesis - Survival - Aortic Valve Stenosis - Aortic Valve Regurgitation

## BACKGROUND

Aortic valve disease is one of the most frequent causes of valve replacement in our environment. This study was performed based on the lack of information related to late outcomes in patients submitted to aortic valve replacement with mechanical prosthesis.

The aims of this study were:

- To assess the incidence of major adverse outcomes (morbidity and mortality) during the follow-up of patients who had undergone an aortic valve replacement with mechanical prosthesis.
- To assess the functional outcomes of these patients (clinical improvement) during follow-up.

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## MATERIAL AND METHODS

We performed a descriptive study on 95 patients submitted to aortic valve replacement with mechanical prosthesis. Data collection was prospective.

We included patients who had undergone surgery in our center between April 1999 and December 2006.

The causes for aortic valve replacement were: aortic stenosis (63 patients, 66.3%), aortic regurgitation (16 patients, 17%) and mixed aortic valve disease.

Patients submitted to reoperations, combined surgery (whether valvular surgery, coronary bypass graft surgery of aortic surgery), aortic valve replacement with biological prosthesis or homografts and those who died during hospitalization were excluded from the study.

Data on morbidity and mortality were classified according to the definitions of the Guidelines for Reporting Morbidity and Mortality after Cardiac Valvular Operations before reporting the outcomes. (1)

Patients' follow-up was performed through personal interviews, telephone contact and/or from the information of the electronic medical records of the Hospital Italiano de Buenos Aires.

All patients completed follow-up. The outcomes are informed at 1 and 5 years.

### Statistical Methodology

Quantitative variables are expressed as means with their corresponding standard deviations or 95% confidence intervals. Categorical variables are informed with their values and/or percentages of the total value.

Survival data during follow-up were determined using the Kaplan-Meier method.

The global survival curve is informed including and excluding in-hospital mortality in order to verify if this outcome has any influence on long-term survival after valvular replacement.

The risk of thromboembolism, bleeding or endocarditis is expressed as a cumulative incidence of events (events per 100 patients-year of follow-up). We consider that the actuarial method might not be appropriate to communicate non-fatal events as, in this case, it does not discriminate patients who die and it presumes that they are at risk of non-fatal events.

## RESULTS

Between January 1999 and December 2006 we performed 647 procedures on the aortic valve in our center.

Ninety five patients were eligible to be included in our study.

Mean age was  $64.5 \pm 12.3$  years and 61.1% were men.

The percentage of patients in FC IV was 18.9%; 44.2% were in FC III, 20% in FC II and 16.8% in FC I.

Mean body surface area was  $1.89 \text{ m}^2$  (95% CI 1.83-1.94).

The prosthesis size was 25 (n = 15, 16.1%), 23 (n = 35, 37.5%), 21 (n = 32, 34.4%) and 19 (n = 11, 11.8%). Annular enlargement was performed in 5 patients.

The prosthetic devices used were Carbomedics® in 57 patients (60%), St Jude® in 16 (16.8%), Sorin Bicarbon® in 11 (11.6%), On-X® in 2 (2.2%), Edwards Mira® in 4 (4.2%), and ATS® in 5 (5.3%).

Mean effective valve area/body surface area ratio was  $1.06 \text{ cm}^2/\text{m}^2$  (95% CI 1.04-1.09), range 0.87-1.3.

No patient presented mismatch.

Mean follow-up was  $4.5 \pm 2.3$  years, percentiles 25-75: 2.5-6.3 years, range 0.07-8.58 years.

All patients were on anticoagulation therapy with coumarin drugs during follow-up.

Total follow-up was 427.5 patients/year.

One patient was hospitalized during the study and died. In-hospital mortality was 1.05%. No deaths occurred within the 30 days after discharge.

Deaths occurring thereafter are included in the total follow-up.

Fifteen patients died during follow-up; 6 deaths were related to the prostheses (2 hemorrhagic strokes, 1 digestive bleeding, 1 sepsis, 1 endocarditis, 1 sudden death) whereas it was impossible to determine the cause of death in 3 cases; the rest of the deaths were not related to the prostheses.

Actuarial survival (Kaplan-Meier) was 95% (95% CI 88-98%) at one year and 89% at 5 years (95% CI 76-95%) (Figure 1).

Actuarial survival (Kaplan-Meier) including in-hospital mortality was 94% (95% CI 87-97%) at one year and 88% at 5 years (95% CI 75-94%) (Figure 2).

During follow-up, 67 patients (70.5%) are in FC I and 28 (29.5%) in FC II. No patients presented FC III or IV (Figure 3).

The annual risk to the first non-fatal event was 3.5% patients-year.

Fifteen patients presented adverse events during follow-up.

Neither structural deterioration nor thrombotic episodes were observed.

One patient presented a brain embolism 5 years after the surgery resulting in a permanent sequela.

The incidence of thromboembolism was 0.2 events/100 patients-year.

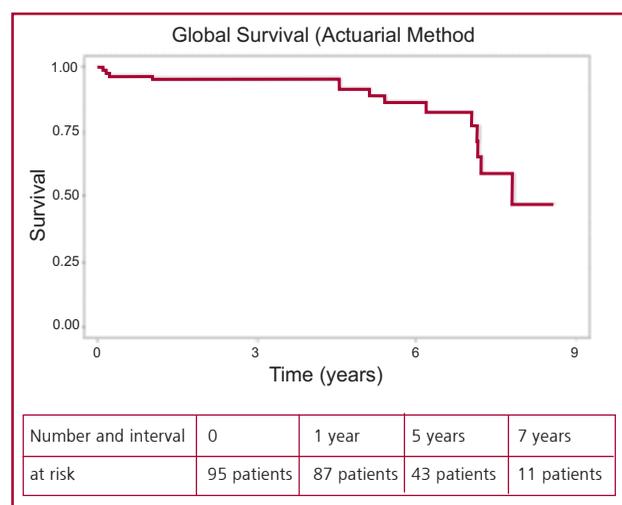
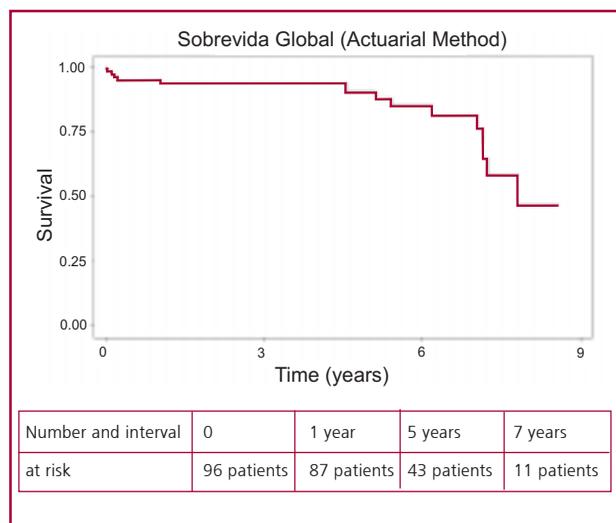
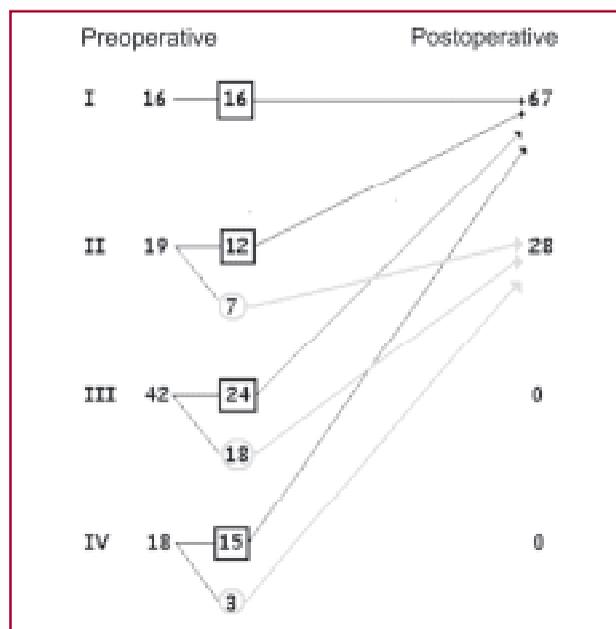


Fig. 1. Actuarial survival at mid-term follow-up of patients submitted to aortic valve replacement with mechanical prosthesis



**Fig. 2.** Actuarial survival at mid-term follow-up of patients submitted to aortic valve replacement with mechanical prosthesis including in-hospital mortality.

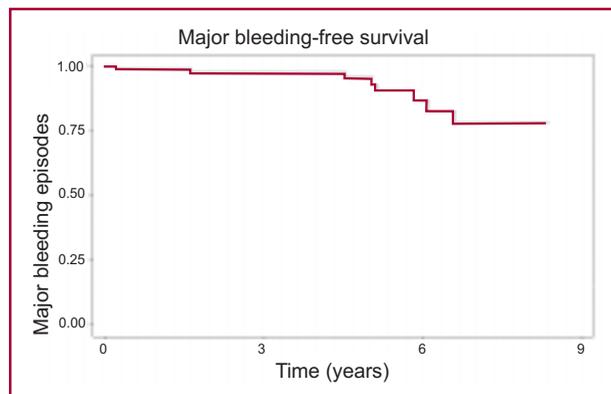


**Fig. 3.** Change in functional class after aortic valve replacement. The left column indicates preoperative functional class, and the right column shows the postoperative functional class. The numbers in the clear circles indicate the total of patients in each FC that evolved to FC II, and those in dark squares indicate the total of patients in each FC that evolved to FC I.

Ten patients presented episodes of major bleeding, especially in the digestive tract (7 patients). Two patients suffered from fatal brain bleeding, and one patient had a spontaneous retroperitoneal hematoma.

The incidence of major bleeding was 2.3 events/100 patients-year.

Figure 4 shows bleeding-free survival.



**Fig. 4.** Major bleeding-free survival (actuarial method).

Three patients presented non structural dysfunction that consisted of paravalvular leaks.

Three patients had prosthetic endocarditis. Two of them were early prosthetic endocarditis.

The annual risk for endocarditis was 0.7% patients-year.

Two patients underwent reoperation during follow-up, one for endocarditis and the other for paravalvular fistula.

The rate of reoperation was 0.4% patients-year.

**DISCUSSION**

We report the long-term outcomes in terms of morbidity, mortality and functional class in patients submitted to aortic valve replacement with mechanical prosthesis.

**Survival**

The global survival in our series was similar to that informed in international series. (2-4, 15-20). Nevertheless, when we analyzed the causes of death in this population of patients, we noticed that mortality causes were related to the prosthesis in more than half of the patients using the criteria of the American Association of Thoracic Surgery.

This is unfavorable information compared to international reports of a prosthesis-related mortality of about 37%. (2, 5, 15, 16). The small number of patients included and the observational nature of our study do not allow us to establish a relationship of causality; nevertheless, this is an important piece of information which should be exhaustively investigated with a properly designed study.

Although the aim of this study was not focused on analyzing in-hospital mortality, we feel obliged to mention this outcome as it might have an influence at late follow-up. In-hospital mortality was low (1.05%) and it did not show a significant impact in the late survival of these patients. As it can be appreciated in Figures 1 and 2, the survival curves are practically

identical irrespective of the inclusion of in-hospital mortality.

The global survival curve shows a sharp reduction at 7 years of follow-up, probably due to the small number of patients at risk in this final period of follow-up.

### **Morbidity**

No episodes of prosthetic thrombosis or structural deterioration, which are frequent with this type of prosthesis, were reported during follow-up.

These events are more frequent in those series with longer follow-up periods that included older models and brands of prosthesis (Lillehei Kaster, Bjork Shiley, etc.). We think that the absence of these events in our series might be attributed to the use of modern bileaflet prosthesis.

In fact, the structural failure of bileaflet prosthesis in the aortic position has not been informed in studies that included more than 50,000 patients/year of follow-up during long follow-up periods (2, 21, 22).

Prosthetic thrombosis is a rare event that occurs more frequently in single-leaflet mechanical valves prosthesis and in caged ball valves; in addition, this complication is more frequent in heart valve prosthesis in the mitral position than in the aortic position. (2, 24) As we only included patients submitted to aortic valve replacement with bileaflet prosthetic valves, the absence of thrombotic events is not surprising to us. One of the most important factors responsible of this complication is an inadequate anticoagulation therapy. Later we shall comment on this issue.

The reoperation rate was low and similar in number and causes to international reports. (5, -7, 15-20)

The rate of embolism was lower than expected - 0.2% patient/year. Rates of 1-2% patients/year in patients under anticoagulant drugs have been previously published. (5, 8, 15-20)

Again, we have to mention that most of the information available comes from studies with long-term follow-ups performed on prostheses with high risk of embolism.

Risk of bleeding in patients with mechanical heart prostheses varies between 0.1% and 3.5% patients/year. (9-12-20) Our results are consistent with these numbers (2.3 events/100 patients-year).

Anyway, making an analysis from another point of view, 3 of 15 deaths were due to bleeding, which means that one third of the deaths related to prosthesis (3 of 9 patients) were caused by bleeding.

It has been demonstrated that almost half of the major bleeding events related to anticoagulation therapy in patients with mechanical heart valve prosthesis occur within the first year after valve replacement (2, 12, 22); however, in our population of patients this complication took place after 5 years of follow-up, as it can be seen in Figure 4. Long follow-up

periods may mask high rates of hemorrhagic events; nevertheless, this has not happened in our study.

The exact value of the international normalized ratio (INR) in our patients is not available, thus we are not absolutely sure if the low incidence of embolism is not due to an excess of anticoagulant drugs. But, on the other hand, it seems reasonable to think that the absence of major bleeding events during the first year after the valve replacement - the period during which this complication is more frequent - (23) might be an indirect indicator that anticoagulation therapy was not excessive or incorrect.

The annual risk of prosthetic endocarditis (0.7% patients-year) is similar to most published series. (13-20)

We did not find mismatch patient/prosthesis in our patients. We always implanted as big prosthesis as we could to obtain an effective valve area/body surface area ratio greater than 0.85 cm<sup>2</sup>/m<sup>2</sup> according to our usual practice; the calculations were performed in the operating room. In 4.75% of cases we had to enlarge the aortic ring to achieve this ratio.

We think that the 100% of symptomatic improvement is related to this last issue. Nevertheless, we must clarify that the design of our research is not adequate to make such an association.

Our study constitutes one of the few reports of outcomes in local patients with aortic valve replacement with mechanical heart valve prosthesis. Morbidity and mortality rates observed within this group of patients do not seem to be trivial in a mid-term follow-up.

### **Limitations**

We have not taken into account the perioperative characteristics of our patients which might be important for long-term survival and for the incidence of certain postoperative events.

We have not registered if antithrombotic therapy was adequate during follow-up, which might explain the variations in the incidence of thromboembolism and bleeding events.

### **CONCLUSIONS**

These results were similar to those reported in international series in terms of survival and major complications.

The number of adverse events observed at mid-term is still high, as it is all around the world.

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### **RESUMEN**

#### **Introducción**

La patología de la válvula aórtica es una de las causas más frecuentes de reemplazo valvular en nuestro medio. La falta de información actualizada sobre la evolución alejada de pacientes que recibieron prótesis mecánicas en posición aórtica motivó la realización del presente estudio.

## Objetivo

Conocer la mortalidad, la morbilidad (complicaciones mayores) y los resultados funcionales (mejoría clínica) durante el seguimiento de pacientes portadores de una válvula mecánica en posición aórtica.

## Material y métodos

Se seleccionaron 95 pacientes sometidos a reemplazo valvular aórtico con prótesis mecánicas. Todos los pacientes fueron operados entre enero de 1999 y diciembre de 2006. La media de seguimiento fue de  $4,5 \pm 2,3$  años, percentiles 25-75: 2,5-6,3 años. El seguimiento total fue de 427,5 pacientes/año.

## Resultados

La media de edad fue de  $64,5 \pm 12,3$  años y el 61,1% de los pacientes eran de sexo masculino.

Sesenta pacientes (63%) estaban en clase funcional (CF) III-IV antes de la cirugía.

En el seguimiento, 67 pacientes (70,5%) se encuentran en CF I y 28 (29,5%) en CF II. No se observaron pacientes en CF III ni IV.

La media del índice área valvular efectiva / área de superficie corporal fue de  $1,06 \text{ cm}^2/\text{m}^2$ .

La supervivencia actuarial (Kaplan-Meier) fue del 95% (IC 95% 88-98%) a un año y del 89% a los 5 años (IC 95% 76-95%). La mortalidad relacionada se registró en 9 pacientes (9,5%). La incidencia de tromboembolia fue del 0,2% paciente-año, la de hemorragia del 2,3% paciente-año y la de endocarditis del 0,7% paciente-año. La tasa de reoperación fue del 0,4% paciente-año.

## Conclusiones

Los resultados obtenidos fueron similares a los comunicados en series internacionales en términos de supervivencia y complicaciones mayores.

La frecuencia de eventos adversos observados a mediano plazo, como en todo el mundo, aún permanece elevada.

**Palabras clave** > Prótesis valvular - Supervivencia - Estenosis de la válvula aórtica - Insuficiencia de la válvula aórtica

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