

The Ross Procedure: A Fifteen-Year Experience

MARÍA C. ESCARAIN¹, GERARDO E. BOZOVICH², CAROLINA SALVATORI³, ROBERTO R. FAVALORO^{MTSAC, 4}

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Address for reprints:

Dr. Roberto René Favaloro
Av. Belgrano 1746
(C1093ASS) CABA
Tel. +54 011 4383-9081
Fax +54 011 4378-1245
Cel. +54 9 11 63 57 8300
e-mail: rfavaloro@ffavaloro.org
www.fundacionfavaloro.org

ABSTRACT

Background

The Ross procedure was introduced in 1967 as a surgical treatment for aortic valve stenosis. Since then, the procedure has been used worldwide with well-known advantages and benefits. However, concerns about the complexity of the procedure and the still uncertain durability of valve substitutes have limited its use.

Objective

To analyze the long-term outcome of the Ross procedure in the treatment of aortic valve disease performed at the Hospital Universitario Fundación Favaloro.

Methods

Between July 1995 and May 2011, 253 consecutive patients underwent the Ross procedure. Three patients were excluded: two patients reoperated on due to an indication that was not related with the Ross procedure and one patient with autograft iatrogenic injury. All patients underwent clinical and echocardiographic follow-up. Survival rates, freedom from autograft or homograft reoperation and of valve-related events (death, reoperation, thromboembolism, bleeding and endocarditis) were analyzed using Kaplan-Meier curves, and the Wilcoxon and the log rank tests.

Results

Mean age was 42 ± 14 years; 72% were men. Surgery was indicated due to aortic stenosis in 50% of the cases, aortic regurgitation in 36% and aortic valve disease in 14%. Bicuspid aortic valve was the most common etiology (77%). Isolated procedures were performed in 85% of the cases. In-hospital mortality was 3.2%. The overall survival rates at 5 and 12 years were 95% (95% CI 90-97%) and 92% (95% CI 83-96%), respectively. Autograft dysfunction occurred in 13% of patients (5%). Freedom from autograft reoperation was 100% at 5 years and 95% at 12 years (95% CI 87-98%). Homograft dysfunction occurred in 24 patients (10%). Freedom from homograft reoperation was 99% at 5 and 12 years (95% CI 95-99.9%). There was no correlation between preoperative aortic regurgitation and reoperation. Freedom from valve-related events was 89% (95% CI 82-94%) at 10 years and 85% at 12 years (95% CI 75-91%).

Conclusion

In our experience, the Ross procedure was associated with a low long-term event rate, representing a valid surgical approach for the treatment of aortic valve disease.

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Department of Cardiovascular and Thoracic Surgery, Hospital Universitario Fundación Favaloro. Buenos Aires, Argentina

^{MTSAC} Full Member of the Argentine Society of Cardiology

¹ Staff Physician of the Cardiovascular Recovery Unit

² Medical Director

³ MD, Outpatient Department

⁴ Head of the Department of Cardiovascular and Thoracic Surgery

BACKGROUND

The Ross procedure is a type of valve surgery which consists in replacing the patient's diseased aortic valve with his or her own pulmonary valve, together with the implantation of a cryopreserved pulmonary valve homograft to rebuild the right ventricular outflow tract. This procedure was introduced in 1967 by Dr. Donald Ross (1) as a surgical alternative for the treatment of aortic valve disease, and has since been practiced worldwide.

The surgical procedure provides the only living tissue valve substitute capable of reproducing most of the complex functions performed by the native aortic valve. The excellent hemodynamic profile together with the transplanted valve growth potential, are well known advantages (2). Other benefits are the low risk for endocarditis and the low thrombogenicity without anticoagulation requirements. (3, 4) However, concerns regarding the complexity of the procedure and the still uncertain durability of valve substitutes have limited the worldwide application of this surgical procedure. (5-10)

The purpose of this study is thus to evaluate the long-term outcome of the Ross procedure in the treatment of aortic valve disease performed at the Hospital Universitario Fundación Favaloro.

METHODS

Population

A cohort of 253 consecutive patients undergoing the Ross procedure at our hospital between July 1995 and May 2011 were retrospectively studied. Indication for the surgery followed international guidelines. (11) Three patients were excluded: 2 patients due to reoperation not related to the Ross procedure and 1 patient for autograft iatrogenic injury during surgery.

Echocardiographic evaluation

Prior to surgery, transthoracic color Doppler echocardiography was performed with 1500, 2500, 5500 y 7500 (Hewlett Packard), Vivid 7 (General Electric) and IE33 (Philips) ultrasound machines to assess cardiac valves, biventricular function and diagnose associated pathologies.

After the Ross procedure, a transesophageal color Doppler echocardiography was performed on all the patients in the operating room to evaluate autograft, homograft and biventricular function.

Surgical procedure

The surgical procedure was aortic root replacement, which consists in replacing the diseased aortic valve and the aortic root by the healthy pulmonary valve of the patient (autograft), with interrupted sutures around the aortic annulus reinforced with bovine pericardium, reimplant the coronary ostia and perform the distal aorto-pulmonary anastomosis with continuous suture.

During the first stage of our series no effort was performed to match the aortic annulus with autograft diameters; however, in the last years, based on the improved results reported in the international literature, (12, 13) aortic and pulmonary annuli diameters were matched when the difference between them was greater than 2-4 mm.

The right ventricular outflow tract was reconstructed

with a cryopreserved pulmonary homograft.

Surgeries were carried out using extracorporeal circulation, membrane oxygenators and moderate hypothermia. Myocardial protection was achieved with antegrade and retrograde cold blood cardioplegia. Since 2004, septal temperature was measured to assess a 10 °C reduction in order to ensure myocardial protection.

All patients, except 13, were operated on by the same surgeon, Dr. RRF.

Clinical and echocardiographic follow-up

Clinical and echocardiographic follow-up was performed by planned site or telephone visits between the third and sixth month postoperatively, and then annually.

Echocardiographic evaluation included a detailed morphological and functional analysis of valve substitutes. Regurgitation severity was classified as: 0 = none; 1 = mild; 2 = moderate; 3 = moderate-severe, 4 = severe.

Autograft and homograft dysfunction was defined as grade >2. A peak pulmonary gradient >30 mm Hg defined autograft stenosis.

Intrahospital mortality was defined as that occurring during hospitalization or within 30 days of the Ross procedure.

Statistical analysis

Continuous variables were expressed as mean $\pm$ standard deviation. Dichotomous variables were presented as whole numbers and percentages, and were analyzed with chi-square or Fischer exact tests, as applicable. Survival, freedom from autograft and homograft reoperation and freedom from associated valve events (death, reoperation, thromboembolism, bleeding, and endocarditis) were estimated with the Kaplan-Meier method, and comparison of survival curves between groups was performed with the log rank test. Strength of association between exposure and events was estimated using the relative risk (RR) and its 95% confidence interval (CI).

Ethical considerations

The study was approved by the Bioethics Committee and the Teaching and Research Department of the Hospital Universitario Fundación Favaloro. All patients signed an informed consent to perform the indicated surgical procedure with prior information on the possible inherent risks.

RESULTS

Population characteristics

Population characteristics are detailed in Table 1.

Ross procedure

Ninety four percent of the procedures were elective and in 16 patients (6%) they were urgent / emergent. The Ross procedure was an isolated procedure in 213 patients (85%), while the remaining 15% were combined procedures (Table 2). Surgical risk scores were: Parsonnet 9 ± 5 and EuroSCORE 4 ± 2 . Time of extracorporeal circulation was 187 ± 39 minutes and of aortic clamping 148 ± 24 minutes. Temperature was 27 ± 2 °C.

Intrahospital outcome

Post-operative complications were low volume syndrome requiring intraaortic balloon

Table 1. Population characteristics

Population characteristics	Nº of patients (%)
Age, mean, SD (range)	42 ± 14 (15-67)
Men, n (%)	180 (72)
Diabetes mellitus, n (%)	6 (2)
Social status, n (%)	
- Destitute	100 (40)
- Non-destitute	150 (60)
NYHA functional class, n (%)	
- I-II	183 (73)
- III-IV	67 (27)
Ejection fraction, % mean, SD (range)	55 ± 12 (30-70)
> 50%	212 (85)
50-30%	38 (15)
< 30%	-
Reoperations, n (%)	21 (8)
Surgical indication, n (%)	
- Aortic stenosis	125 (50)
- Aortic insufficiency	90 (36)
- Aortic disease	35 (14)
Etiology, n (%)	
- Bicuspid aortic valve	193 (77)
- Infectious endocarditis	21 (8)
- Active infectious endocarditis	7 (3)
- Rheumatic	14 (6)
- Prosthetic dysfunction	10 (4)
- Aortic root dilatation	9 (4)
- Subvalvular aortic stenosis	5 (2)
- Myxomatous	4 (2)

counterpulsation support in 9 patients (4%), acute renal failure requiring dialysis in 2 patients (1%), stroke in 2 patients (1%), mediastinitis in 2 patients (1%) and need for definitive pacemaker in 2 patients (1%).

Intrahospital mortality was 3.2% (8 patients): 7 patients died due to cardiogenic shock (three of whom were reoperations and one a second operation), and 1 patient due to septic shock secondary to mediastinitis with endocarditis manifestations associated to the autograft and the homograft.

Long-term follow-up

Mean follow-up was 5.88 ± 4 years. Follow-up was complete in 93% of the population.

Five-year overall survival was 95% (95% CI: 90-97%) and 92% at 12 years (95% CI: 83-96%) (Figure 1 A). Late mortality was 3.2% (8 patients). In only two patients this was due to valve-related causes: one patient coursed with premature autograft and

Table 2. Isolated and combined procedures

Type of surgery	Nº of patients (%)
Isolated Ross procedure	213 (85)
Ross + MRS	8 (3)
Ross + MVR	7 (3)
Ross + MVC	2 (1)
Ross + MVRp	2 (1)
Ross + MVR + TVR	1 (0,4)
Ross + myomectomy	5 (2)
Ross-Konno	5 (2)
Ross + AscARp	4 (2)
Ross + RAAsc + HeAAR	1 (0,4)
Ross + closure of IVC	2 (1)

MRS: Myocardial revascularization surgery. MVR: Mitral valve repair. MVC: Mitral valve commissurotomy. MVRp: Mitral valve replacement. TVR: Tricuspid valve repair. AscARp: Ascending aorta replacement. HeAAR: Hemi aortic arch replacement. Closure of IVC: Closure of interventricular communication.

homograft endocarditis 45 days after the Ross procedure, required autograft reoperation and progressed to septic shock and death. Another patient died during the autograft reoperation 13 years after the Ross procedure. The 6 remaining patients died of non cardiac causes; one patient due to aspiration pneumonia, another of pancreatitis, one patient committed suicide, one of sudden death and two of unknown causes.

During follow-up, endocarditis was diagnosed in 2 patients. One of them was diagnosed with premature autograft and homograft endocarditis that progressed to septic shock and death (previously mentioned). The other patient with late autograft endocarditis, 2 years after the Ross procedure, responded favorably to medical treatment.

No thromboembolic or hemorrhagic complications were registered at late follow-up.

Freedom from valve-related events at 5 years was 94% (95% CI: 89-96%), at 10 years 89% (95% CI: 82-94%) and at 12 years 85% (95% CI: 75-91%) (Figure 1 B).

Pulmonary autograft

Autograft dysfunction was diagnosed in 13 patients (5%), 7 of whom required reoperation. Freedom from autograft reoperation at 5 years was 100% and at 12 years 95% (95% CI: 87-98%) (Figure 2 A).

When the incidence of these events was associated with the surgical indication, patients with aortic valve insufficiency presented a significant association with the incidence of autograft dysfunction after the Ross procedure [RR: 3 (95% CI: 1.1-9.1), $p = 0.02$]; conversely, even though the incidence of reoperation was greater in patients with aortic valve insufficiency (7 reoperations: one with aortic stenosis and six with aortic insufficiency), this association did not reach

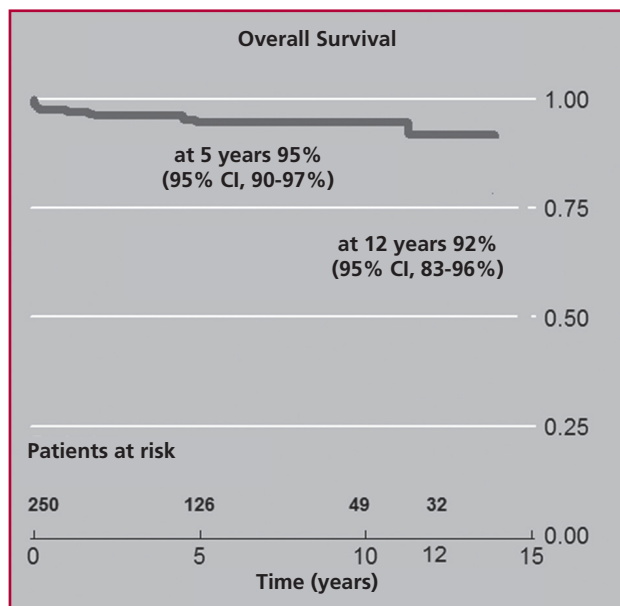


Fig. 1 A. Overall survival.

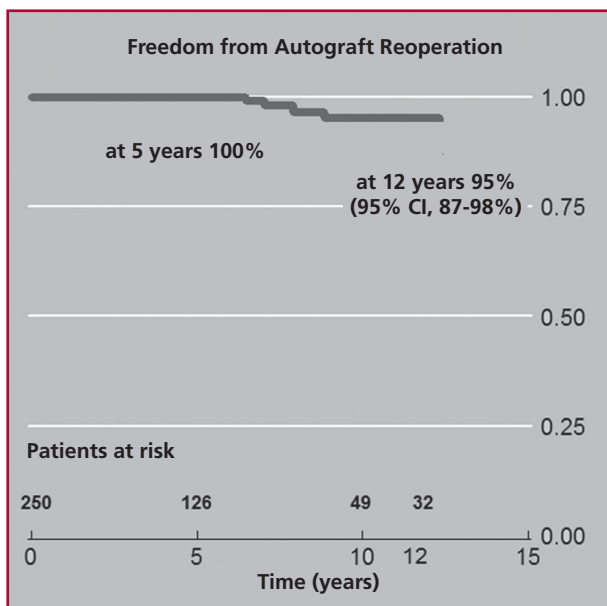


Fig. 2 A. Freedom from valve-related events.

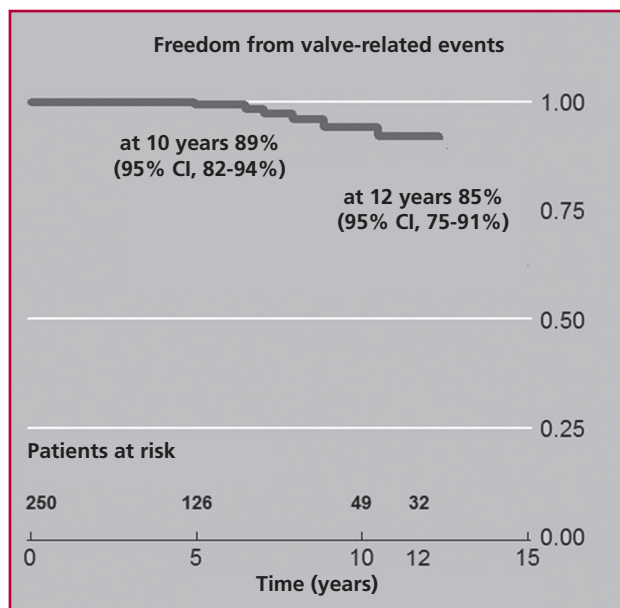


Fig. 1 B. Freedom from autograft reoperation

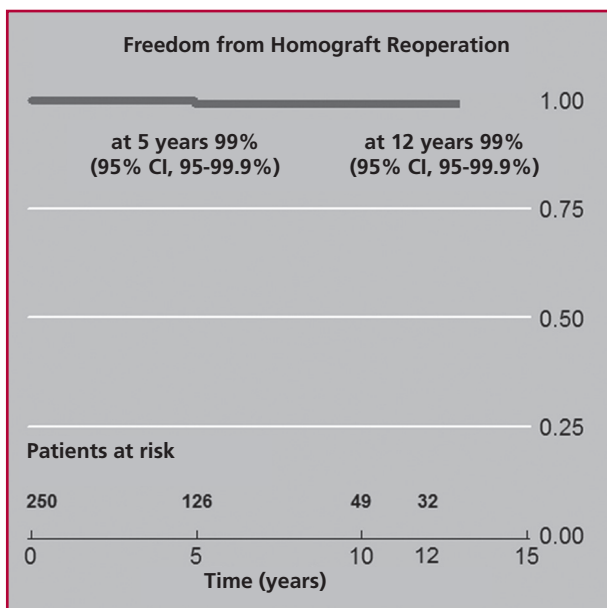


Fig. 2 B. Freedom from homograft reoperation.

statistical significance [rawRR 2.9 (95% CI: 1-12); $p = 0.11$].

Regarding the etiology of aortic valve disease, no association was observed between the presence of bicuspid aortic valve and development of autograft dysfunction in the late follow-up [raw RR 0.69 (95% CI: 0.31-1.59; $p = 0.39$)]

Pulmonary homograft

Homograft dysfunction was diagnosed in 24 patients (10%). Only one patient required reoperation 5 years after the Ross procedure, due to severe pulmonary insufficiency with moderate impairment of right ventricular function, and symptomatic dyspnea.

Freedom from homograft reoperation at 5 and 12 years was 99% (95% CI: 95-99.9%) (Figure 2 B).

During follow-up, 6 patients presented homograft stenosis. They all remain asymptomatic, without evidence of right ventricular dysfunction at control evaluation.

DISCUSSION

Aortic valve disease is still a worldwide prevalent disease in different age groups. Surgical replacement of the diseased aortic valve has improved the natural evolution of this pathology. However, valve prostheses-related events are still a matter of concern, especially thromboembolic and bleeding events, associated with

mechanical prostheses and the need of anticoagulation and eventual biograft reoperation. This is clearly seen in the lower survival curves after aortic valve replacement compared to those of the general population. (14-16) The big query is the selection of the ideal valve substitute for each patient.

An important point to be considered is life quality, with proven benefits of autograft pulmonary valve compared with mechanical heart valve prosthesis, (17, 18) such as the absence of prosthetic sound which is found disturbing according to several surveys, (19) restrictions in daily activities as a result of anticoagulation (sports, professions, food), the wish to become pregnant in women of childbearing age and its anticoagulation limitation, and finally thromboembolic complications associated more significantly with potential risk of mental or motor deficit in the case of mechanical prostheses (15, 20)

Most series on Ross procedures have revealed low intrahospital death rates, with an average of 3.2% (range: 0.3-6.8%) according to the current Takkenberg et al. meta-analysis, (21) which underlines the low mortality rates of 0.4% and 0.47% published by Sievers et al (17) and David et al (22), respectively, as well as others (10, 23, 24) comparable to the 2.5% of the International Ross Register, (25) which are similar to that of our series. Long term survival has also achieved excellent results in most series, such as 95.7% at 10 years in Chiappiani et al. (23), 95.4% at 10 years in Yacoub et al. (10), 94.7% at 10 years in Sievers et al. (17) and finally 96.6% at 15 years in David et al. Likewise, our series yields similar results.

In spite of the excellent outcomes provided by the international literature, two concerns remain regarding the Ross procedure. The first concern is that it is a technically complex surgery, thus limiting its global use. The second concern still lies in the uncertainty and dissimilar data related to the durability of valve substitutes. (5-9) Discrepant results might be explained by the different surgical techniques employed in different centers worldwide. Moreover, there are differences between the series when the procedure is performed by a single surgeon and when it is performed by a surgical team. (8-10, 17, 24-29) With reference to the durability of the pulmonary autograft, the association between preoperative aortic insufficiency and autograft dysfunction due to progressive neo-aortic root dilation in the follow-up is a matter of debate. (8-10) In a recent work published by David et al. (22) and in the last Sievers et al. report from the German-Dutch Ross Registry (30) which included 1620 patients, preoperative aortic insufficiency was an independent predictor of autograft reoperation. Likewise, in the Elkins et al. series (31) of 487 patients, preoperative aortic insufficiency was identified as an independent predictor of autograft dysfunction. However, in the recent Böhm et al. series (32) with 487 patients, no significant association was found. In our series, although a significant association

between preoperative aortic insufficiency and autograft dysfunction is observed in the follow-up, this association does not reach statistical significance relative to the need of autograft reoperation.

Much has been speculated on the feasibility of the Ross procedure in bicuspid aortic valve bearers and the long-term outcome of this group of patients. (9, 33, 35) Based upon the excellent results provided by different series and with no proved association between the presence of bicuspid aortic valve and autograft dysfunction in the long-term follow-up, (9, 33, 35) there is presently consensus on the feasibility of the surgical technique to treat this congenital disease. Thus, it validates its indication in this subgroup of young adult patients provided that the pulmonary valve is normal and the aortic root is not extremely dilated to obtain the benefits of the Ross procedure without additional risk.

The last issue to be considered is the need to use a pulmonary homograft to reconstruct the right ventricular outflow tract. Young age was the most important determinant of homograft dysfunction in most series. (22, 30, 31, 36-39) There is a variable percentage of homograft dysfunction, depending on how the complication is defined, but it has not been a relevant issue in different communications. (10, 22, 40) In our series, although homograft dysfunction is not negligible, it does not impact in a greater need of reoperation.

In conclusion, patients with aortic valve disease and planned valve replacement surgery should be informed on the different valve substitute options. No currently available prosthetic valve is free of complications. We are still far from reaching the ideal substitute. Decision making is complex and involves the clinical cardiologist, the cardiovascular surgeon and the patient with his life-style and future expectations.

Study limitations

The main limitation in our study is that since many patients live in the provinces, it was possible to contact 93% of the population in the last year; therefore, some late events may not have been considered in the final analysis.

CONCLUSIONS

The Ross procedure shows promising results for the surgical treatment of aortic valve disease. In our center this technique presents excellent short and long-term outcomes, similar to those of worldwide reference centers.

The main concern of the Ross procedure is still the uncertainty of valve substitute durability, mostly in the second postoperative decade. Series with longer follow-up are necessary to assess the need of autograft and/or homograft reoperation impact, which in our center will be known in the coming years.

In our experience, the Ross procedure was

associated with a low event rate in the long-term follow-up, representing a valid surgical approach for the treatment of aortic valve disease.

RESUMEN

Cirugía de Ross: 15 años de experiencia

Introducción

La cirugía de Ross, empleada por cirujanos de diferentes partes del mundo desde su introducción en 1967 como alternativa quirúrgica en el tratamiento de la enfermedad valvular aórtica, tiene ventajas y beneficios que son bien conocidos. No obstante ello, trae aparejadas algunas preocupaciones que han limitado su aplicación, como su complejidad técnica y la incertidumbre, que aún existe, respecto de la durabilidad de sus sustitutos valvulares.

Objetivo

Analizar los resultados a largo plazo de la cirugía de Ross en el tratamiento de la enfermedad valvular aórtica en el Hospital Universitario Fundación Favaloro.

Material y métodos

Desde julio de 1995 hasta mayo de 2011, 253 pacientes consecutivos fueron intervenidos con cirugía de Ross. Se excluyeron 3 pacientes: 2 pacientes reoperados por una indicación no relacionada con la cirugía de Ross y 1 paciente por haber sufrido una lesión iatrogénica del autoinjerto. Se realizó seguimiento clínico y ecocardiográfico. La supervivencia, la ausencia de reoperación del autoinjerto y del homoinjerto y la ausencia de eventos valvulares relacionados (muerte, reoperación, tromboembolia, sangrado, endocarditis) se analizaron mediante curvas de Kaplan-Meier, la prueba de Wilcoxon y ellog rank test.

Resultados

La edad media fue de 42 ± 14 años; el 72% de la población en estudio era de sexo masculino. La indicación quirúrgica comprendió: estenosis aórtica en el 50%, insuficiencia aórtica en el 36% y enfermedad aórtica en el 14%. La etiología más prevalente fue la válvula aórtica bicúspide (77%). El 85% de los procedimientos fueron aislados. La mortalidad hospitalaria fue del 3,2%. La supervivencia global a los 5 años fue del 95% (IC95% 90-97%) y a los 12 años, del 92% (IC95% 83-96%). Se diagnosticó disfunción del autoinjerto en 13 pacientes (5%). La ausencia de reoperación del autoinjerto a los 5 años fue del 100% y a los 12 años, del 95% (IC95% 87-98%). Se diagnosticó disfunción del homoinjerto en 24 pacientes (10%). La ausencia de reoperación del homoinjerto a los 5 y a los 12 años fue del 99% (IC95% 95-99,9%). La insuficiencia aórtica preoperatoria no se asoció con reoperación. La ausencia de eventos valvulares relacionados a los 10 años fue del 89% (IC95% 82-94%) y a los 12 años, del 85% (IC95% 75-91%).

Conclusión

En nuestra experiencia, la cirugía de Ross se asoció con una tasa baja de eventos en el seguimiento a largo plazo, por lo que representa una opción quirúrgica válida para el tratamiento de la enfermedad valvular aórtica.

Palabras clave > Estenosis de la válvula aórtica- Insuficiencia de la válvula aórtica

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Conflicts of interest

The authors declare no conflicts of interest

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