# **Autograft Failure During Follow-Up After the Ross Procedure: Predictive Factors in a Prospective Series**

Martín Ruiz Ortiz,ª Mónica Delgado,ª Dolores Mesa,ª Elías Romo,ª Jaime Casares,b Pedro Alados,b Ignacio Muñoz, b and José Suárez de Lezoa

<sup>a</sup>Servicio de Cardiología, Hospital Reina Sofía, Córdoba, Spain bServicio de Cirugía Cardiovascular, Hospital Reina Sofía, Córdoba, Spain

To determine the incidence of, and predictive factors for, aortic autograft failure during follow-up after the Ross procedure. Of 102 consecutive patients who underwent surgery at our centre between 1997 and 2009, we selected 83 (age 32±11 years), all of whom had been discharged without significant autograft regurgitation and for whom at least one follow-up echocardiogram was available. Autograft failure was defined as the presence of at least moderate regurgitation on echocardiography. After a median follow-up period of 4.2 years (range 0.2-10.9 years), eight patients (9.6%) developed this complication, three of whom required valve replacement. The probability of survival without autograft failure at 5 years was 90% (95% confidence interval [CI] 83%-98%). Multivariate analysis showed that undergoing surgery during the first 6 months of the learning curve (hazard ratio = 9.1; 95% CI, 1.4-59.4; P=.021) and a large pulmonary annulus size, normalized by body surface area, (hazard ratio = 1.4; 95% CI, 1.016-1.924; P=.04) were independent predictors of this complication.

Key words: Ross procedure. Echocardiography. Aortic valve disease.

# Insuficiencia del autoinierto durante el seguimiento tras la intervención de Ross: factores predictores en una serie prospectiva

Para analizar la incidencia y los factores predictores de la insuficiencia del autoinjerto aórtico durante el seguimiento tras la intervención de Ross, de 102 pacientes operados consecutivamente en nuestro centro entre 1997 y 2009, se seleccionó a 83 (media de edad,  $32 \pm 11$ años) sin regurgitación significativa del autoinjerto al alta y con al menos un ecocardiograma de seguimiento. La insuficiencia del autoinjerto se definió como aquella al menos moderada por ecocardiografía. Tras una mediana (intervalo) de 4,2 (0,2-10,9) años de seguimiento, 8 (9,6%) pacientes presentaron esta complicación (3 precisaron sustitución valvular). La probabilidad de supervivencia libre de insuficiencia del autoinjerto fue del 90% (intervalo de confianza [IC] del 95%, 83%-98%) a los 5 años. En el análisis multivariable, la intervención en los primeros 6 meses de la curva de aprendizaje (hazard ratio [HR] = 9,1; IC del 95%, 1,4-59,4; p = 0,021) y el mayor tamaño del anillo pulmonar (normalizado para la superficie corporal, HR = 1,4; IC del 95%, 1,016-1,924; p = 0,04) fueron predictores independientes de esta complicación.

Palabras clave: Intervención de Ross. Ecocardiografía. Valvulopatía aórtica.

#### INTRODUCTION

Ever since Ross proposed replacing the aortic valve with the patient's own pulmonary valve (autograft) and the pulmonary valve with a homograft, this procedure has proved to be a valuable alternative to aortic valvular replacement in children and young adults.<sup>2</sup> The pulmonary autograft can grow,<sup>3</sup> has a lower risk of infection, 4,5 does not produce haemolysis or require anticoagulation<sup>4</sup> and has an excellent haemodynamic profile that allows for the reversal of remodeling.6

Autograft valve failure (AGF) is a possible complication during follow-up. Most series report rates of autograft re-operation,5,7-11 however, echocardiographic studies on the emergence of AGF are scarce<sup>4,12,13</sup> and not all of them report rates for this complication. Our goal is to analyse the incidence of AFG during follow-up in patients who have undergone the Ross operation in our institution and to study the factors that predict AFG.

Correspondence: Dr. M. Ruiz Ortiz. San Adolfo, 18, 3.o A. 14005 Córdoba. Spain E-mail: maruor@gmail.com

Received June 29, 2009. Accepted for publication September 16, 2009.

## **METHOD**

From the 102 patients treated with the Ross technique in our hospital from November 1997 to January 2009, we selected those with no significant autograft regurgitation at discharge and with at least one follow-up echocardiogram.

All procedures were elective. The autograft was implanted as a total aortic root replacement. Prior to surgery, a complete echocardiographic evaluation (Acuson Sequoia, Siemens equipment) performed to analyse ventricular size and function, aortic and pulmonary valve anatomy and function and associated lesions. Since the series included paediatric patients, echocardiographic dimensions were normalised by dividing them by body surface area. We conducted a clinical and echocardiographic follow-up every 6 months for the first year and once a year thereafter.

AGF was defined as the moderate to severe regurgitation of the autograft according to the integrated assessment proposed by the American Society of Echocardiography guidelines,14 whose criteria for considering regurgitation as moderate or severe are, among others: a regurgitation jet width that is ≥25% or ≥65% of the left ventricular outflow tract: a vena contracta ≥0.3 cm<sup>2</sup> or >0.6 cm<sup>2</sup>; a diastolic reversal flow in the descending aorta that lasts longer than the proto-diastolic or holo-diastolic and pressure half-times <500 ms or <200 ms, respectively. The regurgitant volume and fraction and the effective regurgitant orifice area were calculated only in uncertain cases. In case of discrepancies in severity when using the different methods, the ones with the highest quality data were favoured. Endocarditis and surgical pseudoaneurysms cases were excluded.

Comparisons of baseline characteristics between groups with and without AGF were performed using the Student t or the Mann-Whitney U tests, as appropriate, for quantitative variables and the  $\gamma^2$ test for qualitative variables. AGF-free survival was analysed using a Kaplan-Meier curve. A multivariate analysis was performed using the Cox proportional hazards model and we included as covariables all those that in the univariate analysis had shown an association with AGF with P<.1. P values <.05 were considered significant. We used SPSS version 12.0 for the statistical analysis.

## **RESULTS**

From the 102 patients who underwent Ross operations at our centre between November 1997 and January 2009, 19 were excluded from the study: one for early death, 2 for autograft surgery because of pseudoaneurysms (1 for early endocarditis and 1

TABLE 1. General Characteristics of the Sample Prior to the Operation

Aetiology	
Congenital	62
Rheumatic	20
Degenerative	10
Other	8
Aortic lesion	
Stenosis	28
Failure	63
Double lesion	9
Functional level	
1	20
II	46
III	34

Figures are expressed in percentages (%).

for iatrogenic cause, both with severe regurgitation), 1 for moderate autograft regurgitation at discharge and 15 for not having a follow-up echocardiogram. In the end, 83 patients (average age, 32 [11]; range, 6-54 years; 60 males [72%]) met the inclusion criteria and constituted the study group.

Table 1 shows the baseline characteristics of the 83 patients. After a median (interval) of 4.2 (0.2-10.9) years of follow-up, 8 (9.6%) patients had AGF: 4 with severe failure (3 required valve replacement). 1 with moderate-severe failure and 3 with moderate failure. The probability of AGF-free survival was 90% (95% [CI], 83%-98%) at 5 years (Figure). The rate of autograft reoperation for AGF was 0.79/100 patients/year. In the univariate analysis (Table 2), AGF was associated with the intervention in the first 6 months after starting the implementation of the technique (learning curve), non-congenital aetiology, lower ejection fraction and larger pulmonary ring (normalised by body surface area) in the echocardiogram prior to surgery. In the multivariate analysis, only intervention in the first six months after starting the implementation of the technique (learning curve, HR=9.1; 95% CI, 1.4-59.4; P=.021) and larger normalised pulmonary ring (HR=1.4; 95% CI, 1.016-1.924; P=.04) were independent predictors of AGF, after adjusting for the rest of the variables that were associated with this complication in the univariate analysis.

## DISCUSSION

In our series, we noted an autograft reoperation rate for AGF of 0.79/100 patients/year, to the extent described in previous series,7-11 and an AGF rate of 9.6% after 4.2 years of follow-up, somewhat lower than the approximately 14% at 4.4 years reported by other authors.4 Unlike previous studies, we did not

TABLA 2. Factors Associated With the Occurrence of Autograft Failure During Follow-up in the Univariate **Analysis** 

Variable	Failure	Without Failure	P
Age, mean (SD), y	31 (10)	32 (11)	.84ª
Sex, %			.49 <sup>b</sup>
Males (n=59)	9	91	
Females (n=22)	14	86	
Aortic lesion, %			.9 <sup>b</sup>
Stenosis (n=20)	10	90	
Failure (n=45)	11	89	
Double lesion (n=6)	17	83	
Congenital aetiology, %			.024 <sup>b</sup>
Yes (n=50)	4	96	
No (n=31)	19	81	
Learning curve, (%)			<.001b
Yes (n=12)	42	58	
No (n=71)	4	96	
LV diastolic diameter, mm/m <sup>2</sup>	37 (6)	35 (8)	.66ª
LV ejection fraction, %	60 (7)	68 (8)	.018ª
Aortic ring, mm/m <sup>2</sup>	16 (1)	14 (3)	.13ª
Sinotubular junction, mm/m <sup>2</sup>	19 (1)	17 (4)	.4 <sup>a</sup>
Pulmonary ring, mm/m <sup>2</sup>	15 (1)	13 (2)	.015ª

LV indicates left ventricle.

First 6 months of implementation of the procedure in our center.

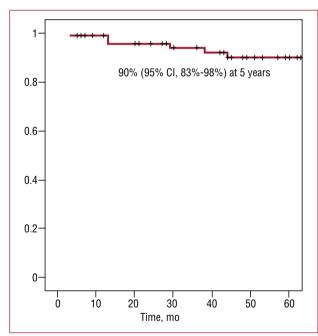


Figure Survival free of moderate or severe autograft regurgitation.

observe any influence of age,10 sex,12 aetiology,10 or type of lesion in the appearance of AGF. 10,12

One of the main contributions of our study is the impact of the learning curve in the frequency of AGF during follow-up. Beyond that period, the incidence of AGF is extremely low (4%). As expected given the complexity of the Ross operation, the learning curve influenced the results, a fact scarely mentioned in the literature and that needs to be evaluated by centres that employ this technique. Another interesting observation is that larger pulmonary ring size measured prior to surgery, is associated with AGF. This finding is consistent with earlier studies indicating that patients who underwent autograft reoperation had a larger ring initially. 12 A possible explanation for this finding, among others, could be that the parietal stress borne by the autograft will be greater the larger its radius, according to Laplace's law. Further studies are needed before recommending a pulmonary ring size beyond which intervention is not advisable.

Our findings indicate that the Ross procedure, when implemented in experienced centres, remains an excellent alternative to conventional aortic valve replacement in certain patients (paediatric, young adults, women of childbearing age). Longer followup periods and comparative studies with other alternatives are needed to definitively establish the role of this procedure in the treatment of a rtic valve disease in this population.

A limitation of this study is the exclusion of 15% of patients treated in our centre in which no followup echocardiography was performed. Other series also suffer from this weakness, 13 but despite this, we believe our results help shed light on the clinical evolution of the autograft at 5 years, the incidence of

<sup>&</sup>lt;sup>a</sup>Value of P calculated using the Student t test.

significant failure of the autograft and the value of echocardiography in patient monitoring.

#### REFERENCES

- 1. Ross DN. Replacement of aortic and mitral valve with a pulmonary autograft. Lancet. 1967;2:956-9.
- 2. Concha M, Legarra JJ, Casares J, Franco M, Mesa D, Chacón A, et al. Sustitución valvular aórtica con autoinjerto pulmonar (operación de Ross) en pacientes adultos y pediátricos. Rev Esp Cardiol. 2000;53:28-38.
- 3. Solymar L, Sudow G, Holmgren D. Increase in zise of the pulmonary autograft after the Ross operation in children: growth or dilation? J Thorac Cardiovasc Surg. 2000;119:4-9.
- 4. Kouchoukos NT, Masetti P, Nickerson NJ, Castner CF, Shannon WD, Dávila-Román VG. The Ross procedure: longterm clinical and echocardiographic follow-up. Ann Thorac Surg. 2004;78:773-81.
- 5. Chiappini B, Abril B, Rubay J, Noirhomme P, Funken JC. Verhelst R, et al. The Ross procedure: clinical and echocardiographic follow-up in 219 consecutive patients. Ann Thorac Surg. 2007;83:1285-9.
- 6. Lennart F, Duebener MD, Ulrich Stierle MD, Armin Erasmo MD, Matthias F, Bechtel MD, et al. Ross procedure and left ventricular mass regression. Circulation. 2005;112 Suppl
- 7. Laudito A, Brook MM, Suleman S, Bleiweis MS, Thompson LD, Hanley FL, et al. The Ross procedure in children and

- young adults: a word of caution. J Thorac Cardiovasc Surg 2001:122:147-53.
- 8. Takkenberg JJ, Dossche KM, Hazekamp MG, Nijveld A, Jansen EW, Waterbolk TW, et al. Report of the Dutch experience with the Ross procedure in 343 patients. Eur J Cardiothorac Surg. 2002;22:70-7.
- 9. Luciani GB, Favaro A, Casali G, Santini F, Mazzucco A. Ross operation in the young: a ten-year experience. Ann Thorac Surg. 2005;80:2271-7.
- 10. Takkenberg JJM, Klieverik LMA, Schoof PH, Van Suylen RJ, Van Herwerden LA, Zondervan PE, et al. The Ross procedure: a systematic review and meta-analysis. Circulation. 2009:119:222-8.
- 11. BöhmJO, Hemmer W, Rein JG, Horke A, Roser D, Blumenstock G et al. A single-institution experience with the Ross operation over 11 years: Ann Thorac Surg. 2009;87:51420.
- 12. Takkenberg JJ, Van Herwerden LA, Galema TW, Bekkers JA, Kleyburg-Linkers VE, Eijkemans MJ, et al. Serial echocardiographic assessment of neo-aortic regurgitation and root dimensions after the modified Ross procedure. J Heart Valve Dis. 2006;15:100-6.
- 13. Hanke T, Stierle U, Boehm JO, Botha CA, Matthias Bechtel JF, Erasmi A, et al. Autograft regurgitation and aortic root dimensions after the Ross procedure: the German Ross Registry experience. Circulation. 2007;116 Suppl:I251-8.
- 14. Zoghbi WA, Enriquez-Sarano M, Foster E, Grayburn PA, Kraft CD, Levine RA, et al. Recommendations for evaluation of the severity of native valvular regurgitation with twodimensional and Doppler echocardiography. J Am Soc Echocardiogr. 2003;16:777-802.