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GLOSSARY OF ABBREVIATIONS

AI: Aortic Insufficiency

AS: Aortic Stenosis

AVR: Aortic Valve Replacement

IE: Infective Endocarditis

LCOS: Low Cardiac Output Syndrome

LVOT: Left Ventricle Outflow Tract

CENTRAL PICTURE

Central picture legend. Survival Estimate in patients treated by aortic valvuloplasty or the Ross procedure

CENTRAL MESSAGE

Aortic valvuloplasty with the use of a pericardial patch to treat complex aortic valve lesions is associated with similar freedom from reoperation and 8-year survival compared to the Ross procedure.

PERSPECTIVE STATEMENT

In patients treated for complex aortic valve lesions (aortic stenosis and/or insufficiency), aortic valvuloplasty using a pericardial patch is a reliable method resulting in similar freedom from reintervention and 8-year survival compared to the Ross procedure. Aortic valvuloplasty tended to be associated with fewer early complications and fewer cases of infective endocarditis at 8 years.

ABSTRACT (number of words = 250)

Objective. Hard-to-repair aortic valve lesions, requiring the use of a valve substitute, remain controversial in the face of the Ross procedure, despite undeniable technical advances. This study was undertaken to compare mid-term outcomes of children treated by the Ross procedure or aortic valvuloplasty for complex aortic valve lesions.

Methods. Between January 2006 and December 2017, 126 patients aged under 18 were treated for complex aortic stenosis and/or aortic insufficiency and were included in this retrospective study. Only aortic valve lesions requiring repair with an autologous or heterologous pericardial patch were considered as complex lesions. Propensity score framework analyses were used to compare outcomes of Ross and aortic valvuloplasty groups while controlling for confounders.

Results. Among the 126 patients with complex aortic valve lesions, propensity score matching selected 34 unique pairs of patients with similar characteristics. Survival (aortic valvuloplasty, 94.1%; Ross, 91%; p=0.89), freedom from overall reintervention (aortic valvuloplasty, 50.1%; Ross, 69%; p=0.32) and freedom from infective endocarditis at 8 years (aortic valvuloplasty, 100%; Ross, 85.9%; p=0.21) were similar. However, freedom from reintervention in the left ventricle outflow tract at 8 years was lower after aortic valvuloplasty than after the Ross procedure (50.1% versus 100% respectively, p=0.001).

Conclusion. Aortic valvuloplasty and the Ross procedure yielded similar 8-year outcomes regarding death, reoperation and infective endocarditis although aortic valvuloplasty tended to be associated with fewer cases of infective endocarditis. Aortic valvuloplasty using a pericardial patch can be chosen as first-line strategy for treating complex aortic valve lesions and might offer the possibility of a later Ross procedure.

KEYWORDS: aortic valvuloplasty; Ross procedure; complex aortic valve disease

INTRODUCTION

In children, aortic valve repair is the first choice for treating simple aortic valve lesions. For more severe or hard-to-repair conditions, three main options are available: prosthetic aortic valve replacement (AVR), the Ross procedure or aortic valvuloplasty. Although few studies have compared aortic valvuloplasty with AVR, recently published data showed similar safety and durability between aortic valve repair and replacement [1,2]. On the other hand, the Ross procedure is preferred by many surgeons. In fact, several studies have demonstrated the safety and the good long-term results of this procedure in young adults and children [3–7]. Data from observational studies and one randomized clinical trial have shown better long-term survival and outcomes of the Ross procedure as compared to mechanical valve replacement in young adults and children [8–11]. However, aortic valvuloplasty is increasingly being used to repair severe aortic valve lesions. Thus, regarding durability and mortality, the difference between aortic valvuloplasty and the Ross procedure for complex lesions remains unclear.

This retrospective study was undertaken to compare short and mid-term outcomes of children treated by the Ross procedure or aortic valvuloplasty for complex aortic valve lesions.

MATERIALS AND METHODS

Study population

All children under the age of 18 years who were treated for aortic stenosis (AS) or aortic insufficiency (AI) between January 2006 and December 2017 in Necker-Enfants-Malades Hospital (Paris, France) were reviewed in a retrospective study. In cases of AS with or without AI, the indication of intervention depended on the severity of the mean aortic valve gradient (> 50 mmHg) and left ventricular hypertrophy. In cases of AI with or without AS, the indication of intervention depended on the severity of the AI (⩾ III/IV) and dilatation of the left ventricle. (z-score > 3).

All patients with simple commissurotomy, shaving, resuspension, annular reduction, subcommissural plication, commissural closure, free margin realignment were excluded from this study. Only patients with complex aortic lesions were included. A complex aortic valve lesion was defined as an AS or AI requiring a commissural or a leaflet repair with an autologous glutaraldehyde-treated patch or a heterologous pericardial patch (Matrix Patch™, Auto Tissue, Berlin GmbH; Duravess™, Edwards Lifesciences, Irvine, California, USA). Patients under 1 month of age and those undergoing single ventricle palliation were excluded from the study.

In accordance with our committee for the protection of human subjects, written informed consent for demographic and outcome data analyses was collected in compliance with French law on retrospective studies consisting of analyses of anonymous data.

Surgical techniques

The operative technique of aortic valve repair with a pericardial patch has been previously described [12]. Briefly, cardiopulmonary bypass with a venous cannula in the right atrium and ascending aorta cannulation was established. The aorta was clamped and a hyperkalemic warm blood cardioplegia was delivered every 10 to 15 minutes in the ascending aorta or within the coronary ostia. In cases of AI with cusp retraction, a cusp-free margin extension with a pericardial patch was used to repair the valve [13–15]. The second method using pericardial patch was extension at the cusp nadir in order to maintain a surface of coaptation made by the native tissue [16]. The last situation where a patch has been used was unicuspid aortic valve repair by a symmetric bicuspidization technique [17]. In patients with only one physiological commissure, the two other rudimentary commissures and the adjacent calcified areas of the valve were excised, and the normal commissure was preserved. Initially, patients were treated with a single folded triangular patch. Later, the technique evolved with the use of two triangular, treated, autologous pericardial patches to create a new commissure opposite (180 degrees orientation) to the preserved native commissure (video 1). The surgical result was then checked intraoperatively by trans-esophageal ultrasound. The repair was considered satisfactory if a residual AI < moderate (if central and not eccentric) and a residual mean aortic gradient < 15 mmHg was achieved.

For the Ross procedure, a standard technique of complete root replacement with coronary transfer was used with interrupted sutures [18]. The neoaortic root was reinforced with a circumferentially placed glutaraldehyde-tanned strip of autologous or heterologous (up to 3 years old) pericardium. A pulmonary homograft was preferentially used for pulmonary valve replacement when available in the appropriate size (> 20mm). No root inclusion technique was used in older children.

During the study period, all procedures (both aortic valvuloplasty and the Ross procedure) were performed by two senior surgeons who equally performed the same proportion of the two procedures. Only patients in whom aortic valvuloplasty might have been considered a reasonable alternative to the Ross procedure were included. Decision-making was not protocol-driven but in accordance with the medical and surgical staff. Recent practice in our department is to push for aortic repair for lesions considered repairable by cardiac ultrasound assessment.

Outcome variables

Main outcome variables were early postoperative-related outcomes, 8-year overall survival, 8-year freedom from reoperation, 8-year freedom from reoperation in the LVOT, and 8-year freedom from infective endocarditis (IE). Low cardiac output syndrome (LCOS) was defined as monitored cardiac index <2.2l/min/m^2 secondary to left and/or right ventricular failure without associated relative hypovolemia or as the need for veno-arterial extracorporeal membrane oxygenation. Acute renal failure was defined according to pRIFLE criteria [19,20]. Diagnosis of wound infection or general sepsis required positive local or blood culture. Prolonged mechanical ventilation beyond day five was considered as respiratory failure. Other early surgical adverse events were defined according to the Congenital Heart Surgery Nomenclature and Database Project [21] and such as described by Brown and al. [22].

Follow-up was performed either via a hospital visit or telephone contact. Recording of death, reoperation and IE were updated at the end of July 2019.

Statistical analysis

Continuous variables were expressed as means ± standard deviations or as medians with interquartile ranges (IQR), and were compared using the Wilcoxon rank sum test or Student's t-test as appropriate. Distribution was assessed using the Kolmogov-Smirnov test. Categorical variables were expressed as percentages and were compared using chi-squared or Fischer's exact tests, as appropriate.

A propensity score (PS) framework was generated in order to balance baseline characteristics of patients allowing us to compare clinical endpoints between aortic valvuloplasty and Ross groups. First, a multivariable logistic regression was performed controlling for all pre-specified covariates (age, size, redo surgery and excluding patients with prior aortic valve surgery and not eligible for another attempt at valve repair, chronic heart failure) with the type of surgery as the dependant variable. Aortic valvuloplasty and Ross group patients were matched using a 1:1 nearest neighbor matching algorithm without replacement, with a fixed caliper width of 0.1. Covariate balance between the two groups was assessed after matching, and we considered an absolute standardized difference less than 0.2 as evidence of balance. Then, clinical endpoints were compared between the two groups. Comparison between the Ross procedure and aortic valvuloplasty, regarding 90-day survival, 8-year survival, 8-year freedom from reoperation, 8-year freedom from reoperation in the LVOT and 8-year freedom from IE was performed using the Kaplan-Meier method (log-rank test was used for comparison between groups). Association between baseline variables and main clinical outcomes was assessed by Cox regression analyses, using a backward likelihood-ratio method. Relevant variables, significant at the 15% level on univariate analysis, were included. Odds ratios were then provided with 95% confidence intervals. A p-value < 0.05 was considered statistically significant. All calculations were conducted using SPSS v24.0 and R v3.5.1.

RESULTS

Population and operative data

During the study period, 86 patients were treated by the Ross procedure and 239 patients by aortic valvuloplasty, among which 40 were considered as complex repair. Among the 239 aortic valve repairs performed, 8 initial decisions of aortic valvuloplasty were intra-operatively switched to the Ross procedure (n=4) or mechanical AVR (n=4) because the aortic valve was too retracted, fused and/or calcified. These 8 patients were excluded from the study. No attempt of aortic valve repair was switched to Ross or AVR. No patient in the Ross procedure was switched to AVR or aortic valvuloplasty. Evolution of the number of each procedure per year in our center is presented in Figure S1. Baseline characteristics of the entire study cohort and after propensity score matching analysis are presented in the Table 1. Matching on the propensity score allowed selecting 34 unique pairs of patients with similar characteristics. In the aortic valve group, four patients underwent concomitant mitral valvuloplasty for congenital mitral regurgitation (n=1) and rheumatic mitral diseases (n=3). In the Ross group, 5 patients underwent concomitants mitral valvuloplasty for congenital mitral regurgitation (n=2) and Shone’s syndrome (n=3).

Intraoperative data before and after propensity score matching are presented in the Table 2. There was a tendency to obtain a lower mean aortic valve gradient with the use of two triangular pericardial patches as compared to the use of a single folded triangular pericardial patch (12 ± 10.4 mmHg vs 16.1 ± 9.9 mmHg, p=0.26).

Early postoperative outcomes

Unadjusted 90-day survival was 95% in the aortic valvuloplasty group and 91.6% in the Ross procedure group (p=0.83) (Table 3). After controlling for confounders, 90-day survival was 97% in both groups of patients (p=1.00). During early follow-up, 5 patients died in the Ross group and 2 patients in the Aortic valvuloplasty group. All these patients were under 1 year of age or suffered from Shone's syndrome with concomitant mitral anomaly. Details and causes of early death are shown in the Table S1.

General sepsis was significantly less frequent in the aortic valvuloplasty group compared with the Ross procedure group (9% vs 27%, p=0.05) in the propensity-matched populations. There was a trend toward significance of the Ross procedure group for atrioventricular block requiring pacemaker implantation (6% versus 0%, p=0.15) and ischemic stroke (6% versus 0%, p=0.15). After matching, 6 patients in the aortic valvuloplasty group suffered from LCOS or respiratory failure. Among them, 4 were less than 1 year old. Finally, there was no significant difference regarding other early surgery-related outcomes in the propensity-matched population. One patient required a veno-arterial ECMO in the Ross procedure group.

In the entire cohort, among the 5 patients in the Ross group who suffered from atrioventricular block requiring a pacemaker, only 1 had a concomitant ventricular septal defect closure, but the others had a concomitant Konno enlargement of the left outflow tract. In the whole cohort, seven patients underwent emergency surgery for ventricular dysfunction (6 in the Ross group and 1 in the aortic valvuloplasty group). Two emergency Ross procedures were performed for early balloon valvuloplasty failure. No aortic valvuloplasty with the use of a pericardial patch was performed for balloon valvuloplasty failure.

Midterm outcomes

In the propensity-matched population, median follow-up was 53.8 (IQR, 2-89): 61.9 (IQR, 2-106) months in the Ross procedure group and 45.6 (IQR, 2-80) months in the aortic valvuloplasty group.

Midterm survival comparison analysis showed no significant difference between the 2 groups in the matched study population (Figure 1). Adjusted 8-year survival rate was 94.1% after aortic valvuloplasty and 91% after the Ross procedure (p=0.89). Risk factors for death after aortic valvuloplasty or the Ross procedure are presented in Table 4. Variables associated with death in multivariate Cox model analyses were age < 1 year (OR=6.1 CI [1.6-28.66] and concomitant mitral valve repair or replacement (adjusted OR=10.95 ci [2.66-45.03], p<0.001).

Adjusted freedom from reintervention at 8 years was not significantly different: 50.1% in the aortic valvuloplasty group and 69% in the Ross procedure group (p=0.32) (Figure 2). However, adjusted freedom from reintervention in the left ventricle outflow tract (LVOT) at 8 years was lower after aortic valvuloplasty than after the Ross procedure (50.1% versus 100% respectively, p=0.001) (Figures 3 and S2). In the entire cohort of Ross procedures, 23 patients were reoperated. Among them, 3 patients underwent AVR for deterioration of the pulmonary autograft and 20 patients underwent right ventricular outflow tract reintervention (7 percutaneous pulmonary valve implantations, 13 surgical pulmonary valve replacements). Eight patients were reoperated in the aortic valvuloplasty group (4 Ross procedures, 3 AVRs and 1 percutaneous aortic valvuloplasty) (Figure S3 and see Table S2 for more details about patients who were reoperated during follow-up). Predictors of reinterventions are presented in Table 5. The postoperative mean aortic valve gradient (per 1 mmHg increase, adjusted OR=1.05 [1.01-1.09], p=0.01), and Shone’s syndrome (OR=4.44 [1.42-13.89], p=0.01) were independently associated with reintervention. None of the patients who had a mean gradient below 10 mmHg and an aortic insufficiency less (or equal) than mild were reoperated (Figure S4).

Adjusted freedom from IE at 8 years was 100% in the aortic valvuloplasty group and 85.9% in the Ross procedure group with no significant difference (p=0.21) (Figure S5). During follow-up, 7 patients developed late IE of the pulmonary heterologous graft and none in the pulmonary autograft (see Table S3 for more details about patients who suffered from IE). Among them, 4 patients were less than 1 year old at the time of the first surgery. Five patients required redo surgery and 2 patients were successfully treated with antibiotics. Lastly, no single variable was predictive of IE. Antibiotic prophylaxis protocol of our institute was not changed during the study period.

DISCUSSION

Based on the adult cardiac surgery progress in aortic valve repair, valvuloplasty for complex aortic valve disease in children has significantly evolved over recent years (even during the study period), especially for unicuspid valves. We decided to review our cohort of patients for whom it was mandatory to repair the valve with the use of a pericardial patch due to a lack of tissue (reduced geometric height) and/or the presence of a unicuspid valve. In our opinion, it appeared logical to compare complex patch repair with the Ross procedure due to the fact that many complex aortic valve repairs with pericardial insertion might or should benefit from a Ross procedure, the gold standard procedure to date, and the procedure of choice in many centers. This observational study showed 3 main results: (i) Aortic valvuloplasty tended to be associated with less early surgery-related morbidity; (ii) both approaches yielded significantly similar survival, freedom from reintervention and freedom from IE at 8 years but aortic valvuloplasty was associated with a trend toward significantly less IE; (iii) Reinterventions after complex aortic valve repair were independently associated with the persistence of a residual mean aortic valve gradient.

Mortality and morbidity

In this study, adjusted 8-year survival in the Ross group was 91%, which is comparable to previously reported publications in children [6,23], and 94.1% in the complex aortic valve repair group. Although there was only a tendency but no statistically significant difference, complex aortic valve repair could be associated with a lower operative risk than a Ross procedure, mainly because the coronary ostia and their proximal segments are not mobilized/reimplanted and thus cannot be injured. The cross-clamp time is also shorter and might be considered as a protective effect especially for patients with borderline LV function. The early post-operative outcome was in favor of aortic valve repair (Table 3) with less cardiac, renal or respiratory failure, need for ECMO or pacemaker implantation and finally, local or general infection. This also suggests a lower risk of valve repair compared to the Ross procedure. For the most fragile patients (left ventricular dysfunction, dilated left ventricle, very important hypertrophy …) [24], aortic valvuloplasty might be an option with, if necessary, the use of a pericardial patch rather than a Ross procedure, expecting a better short-term outcome, as we report here.

Anatomic prerequisite for a complex repair

For the last 15 years, the anatomic prerequisite for repair has evolved and will probably continue to change in the future. Our current practice is to propose repair when there is at least: one functional commissure (good height, reasonable commissure coaptation), native cusps with a good mobility after shaving and/or decalcification, and a cusp-free margin after repair which is composed of 50% of native tissue (ideally 2/3). The geometric height of the preserved part of the native cusp needs to be adequate but providing values is of limited use due to the high variability in the size of the annulus in the pediatric population. If the aortic annulus is below -2DS, the Ross procedure is probably the procedure of choice, but the annulus can be enlarged also by a modified Konno procedure associated with an aortic valve repair (by bicuspidization) with a cusp triangular extension (3 patients were operated by this technique after 2017 and were not included in this study). In contrast with the Ozaki procedure [25,26], the goal is to preserve as much native tissue as possible in order to preserve some mobility of a cusp when the pericardial zone becomes rigid at a later time.

Reoperation

In this study, adjusted freedom from reintervention was 69% in the Ross procedure, and 50.1% for complex aortic valve repair at 8 years, which is equivalent to previous studies focusing on repair with the use of a pericardial patch [13]. However, indication for reintervention was different between the two techniques. The Ross procedure group had a lower incidence of reoperation on the LVOT as compared to the aortic valvuloplasty group (Figure S2) [27,28]. The Ross procedure is clearly superior in terms of limiting the number of operations on the aortic valve, but the trade-off is the increased need for reoperation on the pulmonary conduit. The use of percutaneous pulmonary valve implantation techniques might likely prevent surgical reintervention in some cases and may improve long-term outcomes of the Ross procedure [29,30]. Our current philosophy is to initially propose aortic valvuloplasty, when it is feasible, even if we consider that a repair with a patch is a palliative procedure. The idea is to delay the Ross procedure and to allow, at a later age, the use of a cryopreserved homograft rather than a heterologous conduit that is clearly expected to fail earlier [6]. The strategy might be different if small diameter homografts could be available without restriction. Moreover, we found that age under 1 year was an independent risk factor of death (OR=6.1 CI [1.6-28.66] (Table 4). Of the 7 early deaths in our cohort, 5 were children younger than 1 year of age (3 in the aortic valvuloplasty group and 2 in the Ross group, Table S1). Donald JS and al. also found that age under 1 year was associated with higher operative mortality in the Ross procedure [31], and it appears to be similar with complex aortic valvuloplasty. This might be related to technical issues but more likely to the severity of the disease, usually when there is concomitant mitral valve or LV dysfunction.

Redo surgery after valve repair was exclusively linked to the failure of the valve, mainly AS. Residual mean aortic valve gradient after repair was found as an independent predictor of reintervention. None of the patients who had a post-operative mean aortic gradient below 10 mmHg and an aortic insufficiency less (or equal) than mild were reoperated at last follow-up. These findings represent a useful landmark in the operating room to judge the quality of the repair by trans-esophageal echography. Other studies found that post-operative AI up to mild and prior balloon aortic valvuloplasty were also associated with reoperation [32,33]. Thus, the goal of valvuloplasty is to obtain a mean aortic valve gradient and a residual AI as low as possible; for this it may be necessary to use highly aggressive valvuloplasty techniques, even for aortic valve lesions that seem to be initially simple to treat [34,35]. Furthermore, neither the type of patch (autologous or heterologous) nor the technique used had an impact on reoperation. The main point of the technique is to achieve a sufficient free margin length (at least the perimeter of the aorta) to allow a satisfactory systolic opening of the valve.

Infective endocarditis

Another advantage of aortic valvuloplasty over the Ross procedure in this study was the absence of long-term IE. Indeed, no patient in the valvuloplasty group developed IE while the freedom from IE was 85.9% in the Ross procedure group at 8 years. Freedom from IE in the report of David and al. was 99% at 10 years [3] but this study concerned only adults, which may explain the difference due to the use of a homograft. Thus, younger age appears to be associated with IE and the later use of percutaneous pulmonary valve implantation might even increase that risk in this population.

Limitations

This study has limitations. First, it was conducted in a single high-volume centre. Our results require external validation even if they are similar to those reported in previous studies. Furthermore, the proportion of Ross procedures remained stable over many years, until complex aortic valvuloplasty increased after 2011 (see Figure S1). Selection and learning curve bias can significantly influence results.

Conclusion

This observational retrospective study showed that aortic valvuloplasty and the Ross procedure yielded similar 8-year outcomes regarding death, reoperation and IE, but there was a trend for aortic valvuloplasty to be associated with better early outcome and less IE. Aortic valvuloplasty using a pericardial patch can be chosen as first-line strategy for treating complex aortic valve lesions and might offer the possibility to delay the Ross procedure.

FIGURE LEGEND

Figure 1. Kaplan–Meier Survival estimates in the unadjusted (A) and propensity-matched populations (B) receiving aortic valvuloplasty or the Ross procedure.

Midterm survival comparison analysis showed no significant difference between the 2 groups in the matched study population. Adjusted 8-year survival rate was 94.1% in the aortic valvuloplasty group and 91% in the Ross procedure (p=0.89).

Figure 2. Kaplan–Meier Freedom from reoperation estimates in the unadjusted (A) and propensity-matched populations (B) receiving aortic valvuloplasty or the Ross procedure

Adjusted freedom from reintervention at 8 years was not significantly different: 50.1% in the aortic valvuloplasty group and 69% in the Ross procedure group (p=0.32) in the matched study population.

Figure 3. Kaplan–Meier freedom from overall reoperation and freedom from reoperation in the LVOT in the propensity-matched populations receiving aortic valvuloplasty or the Ross procedure.

Adjusted freedom from reintervention was 69% in the Ross procedure, and 50.1% for complex aortic valve repair at 8 years. However, indication for reintervention was different between the two techniques. The Ross procedure group had a lower incidence of reoperation on the LVOT as compared to the aortic valvuloplasty group. The Ross procedure is clearly superior in terms of limiting the number of operations on the aortic valve, but the trade-off is the increased need for reoperation on the pulmonary conduit.

LVOT: Left Ventricle Outflow Tract

Figure S1. Evolution of the number of each procedure per year

The proportion of Ross procedures remained stable up to 2010, while complex aortic valvuloplasty increased after 2011.

Figure S2. Kaplan–Meier Freedom from reoperation in the Left ventricle outflow tract estimates in the unadjusted (A) and propensity-matched populations (B) receiving aortic valvuloplasty or the Ross procedure

At 8 years, the risk of reintervention in the left ventricle outflow tract (LVOT) was higher after aortic valvuloplasty than after the Ross procedure (50.1% versus 100% respectively, p=0.001)

LVOT: Left Ventricle Outflow Tract

Figure S3. Type of reintervention according to initial approach

RVOT: Right Ventricle Outflow Tract

Figure S4. Kaplan–Meier reoperation estimate split by post-operative mean aortic gradient and aortic insufficiency.

None of the patients who had a mean gradient below 10 mmHg and an aortic insufficiency less (or equal) than mild were reoperated.

AI: Aortic Insufficiency

Figure S5. Kaplan–Meier Freedom from infective endocarditis estimates in the unadjusted (A) and propensity-matched populations (B) receiving aortic valvuloplasty or the Ross procedure.

Adjusted freedom from IE at 8 years was 100% in the aortic valvuloplasty group and 85.9% in the Ross procedure group with no significant difference (p=0.21). During follow-up, five patients developed IE of the pulmonary homograft and none in the pulmonary autograft. Three patients required surgery and 2 patients were successfully treated with antibiotics.

TABLES

Table 1. Baseline characteristics of entire study cohort and after propensity score matching analysis

	Before matching			After matching		
	Aortic valvuloplasty n=40 (%)	Ross procedure n=86 (%)	p-value	Aortic valvuloplasty n=34 (%)	Ross procedure n=34 (%)	Standardized mean difference
Age, years	9.5 [3-14]	5 [1-10]	0.006	7.9 [2-12]	7 [1-11]	0.12
0-1 year	8 (20)	23 (27)		8 (24)	8 (24)	
2-10 years	13 (33)	44 (51)		14 (41)	17 (50)	
11-18 years	19 (57)	19 (22)		12 (35)	9 (26)	
Male	26 (65)	52 (61)	0.63	21 (62)	18 (53)	0.18
Weight, kg	30.5 [16-53.8]	17.7 [9.1-30.8]	0.009	26.8 [12-40]	24 [11-32.5]	0.15
Height, cm	fneo-137 [98-164]	109 [74-140]	0.006	116 [87-150]	111 [85-141]	0.12
Diagnosis			0.24			0.18
Aortic stenosis	18 (45)	41 (48)		16 (47)	15 (44)	
Aortic insufficiency	13 (33)	17 (20)		11 (32)	8 (24)	
Mixed aortic valve disease	9 (22)	28 (32)		7 (21)	11 (32)	
Etiology			0.06			0.05
Congenital	31 (77)	68 (79)		26 (76)	27 (79)	
Acute rheumatic fever	5 (12)	1 (1)		4 (12)	1 (3)	
Infective Endocarditis	1 (3)	4 (5)		1 (3)	1 (3)	
Laubry-Pezzi Syndrome	1 (3)	2 (2)		1 (3)	0 (0)	
Genetic syndrome (Shone, Noonan, DiGeorge, Williams Beuren or Turner)	2 (5)	11 (13)		2 (6)	5 (15)	
History of balloon aortic valvuloplasty	5 (12)	18 (21)	0.25	5 (15)	8 (24)	0.22
History of surgical aortic valvuloplasty	5 (12)	32 (37)	0.005	0 (0)	0 (0)	0

Re-do surgery	11 (28)	54 (63)	< 0.001	11 (32)	14 (41)	0.18
Chronic heart failure	3 (8)	8 (9)	1.00	3 (9)	2 (6)	0.11
History of pulmonary arterial hypertension	7 (18)	10 (12)	0.37	5 (15)	4 (12)	0.09
Emergency surgery	1 (3)	6 (7)	0.43	1 (3)	1 (3)	0
Concomitant surgery						
Valvuloplasty or Ross alone	23 (58)	63 (73)	0.08	19 (56)	25 (73)	0.37
Ventricular septal defect	0 (0)	4 (5)	0.31	0 (0)	2 (6)	0.35
Mitral valve plasty or replacement	4 (10)	5 (6)	0.46	4 (12)	2 (6)	0.2
Septal myomectomy	3 (8)	2 (2)	0.33	2 (6)	0 (0)	0.35
Coronary plasty	2 (5)	1 (1)	0.24	2 (6)	1 (3)	0.14
Aortic arch replacement	1 (3)	2 (2)	1.00	1 (3)	1 (3)	0
Coarctation	0 (0)	1 (1)	1.00	0 (0)	0 (0)	0
Pulmonary artery plasty	1 (3)	1 (1)	0.54	1 (3)	0 (0)	0.24
Aortic insufficiency			0.96			0.25
0 (none or trivial)	15 (38)	34 (39)		14 (41)	12 (35)	
I (mild)	1 (3)	4 (5)		2 (6)	3 (6)	
II (mild to moderate)	4 (10)	8 (9)		1 (3)	4 (15)	
III (moderate to severe)	9 (22)	16 (19)		8 (23)	7 (21)	
IV (severe)	11 (27)	24 (28)		9 (26)	8 (23)	
Preoperative mean aortic valve gradient, mmHg	36.7 ± 19.3	45.3 ± 17.9	0.10	35.6 ± 19.7	47.9 ± 16.2	0.67
Number of cusps						
Unicuspid	10 (25)	6 (6)	0.01	6 (18)	3 (9)	0.25
Bicuspid	16 (40)	37 (44)	0.68	15 (44)	10 (30)	0.28
Tricuspid	14 (35)	42 (49)	0.12	13 (38)	20 (60)	0.45
Quadricuspid	0 (0)	1 (1)	1.00	0 (0)	1 (1)	0.1

Continuous data are presented as means ± standard deviation or as medians [interquartile range], categorical data as numbers (percentage).

Table 2. Intraoperative data of entire study cohort and after propensity score matching analysis

	Before matching			After matching		
	Aortic valvuloplasty n=40 (%)	Ross procedure n=86 (%)	p value	Aortic valvuloplasty n=34 (%)	Ross procedure n=34 (%)	p value
Bypass time, min	107 ± 40	186 ± 45	< 0.001	102 ± 37	186 ± 48	< 0.001
Cross-clamp time, min	71 ± 31	126 ± 25	<0 .001	66 ± 27	128 ± 27	< 0.001
Valvuloplasty technique						
Leaflet repair with a pericardial patch	16 (40)	N/A		14 (41)	N/A	
Commissural repair with a pericardial patch	24 (60)	N/A		20 (59)	N/A	
Type of pericardial patch						
Autologous pericardial patch	31 (77)	N/A		25 (74)	N/A	
Heterologous pericardial patch	9 (23)	N/A		9 (26)	N/A	
Conduits used in the Ross procedure						
Pulmonary homograft	N/A	41		N/A	16	
Aortic homograft	N/A	6		N/A	3	
Heterografts	N/A	39		N/A	15	
Postoperative aortic insufficiency			0.04			0.24
0 (none or trivial)	18 (45)	56 (67)		16 (47)	23 (68)	
I (mild)	17 (42)	26 (31)		14 (41)	9 (26)	
II (mild to moderate)	5 (13)	2 (2)		4 (12)	2 (6)	
III (moderate to severe)	0 (0)	0 (0)		0 (0)	0 (0)	

IV (severe)	0 (0)	0 (0)		0 (0)	0 (0)	
Postoperative mean aortic valve gradient, mmHg	14 ± 10	4 ± 6	< 0.001	14 ± 10	3.5 ± 6	< 0.001
Aortic valve repair results						
Optimal (mean aortic valve gradient < 10mmHg and AI < I)	12 (30)	N/A		10 (29)	N/A	
Suboptimal (mean aortic valve gradient > 10mmHg and AI > I)	28 (70)	N/A		24 (71)	N/A	

Continuous data are presented as means ± standard deviation or as medians [interquartile range], categorical data as numbers (percentage).

AI: Aortic insufficiency

519 **Table 3. Early surgery-related outcomes in patients treated by the Ross procedure or**
520 **aortic valvuloplasty before and after propensity score matching.**

	Before matching			After matching		
	Aortic valvuloplasty n=40 (%)	Ross procedure n=86 (%)	p value	Aortic valvuloplasty n=34 (%)	Ross procedure n=34 (%)	p value
90-day overall survival	38 (95)	81 (94)	0.83	33 (97)	33 (97)	1.00
Wound infection or general sepsis	3 (8)	28 (33)	0.002	3 (9)	9 (27)	0.05
LCOS	6 (15)	25 (29)	0.09	6 (18)	9 (27)	0.38
Respiratory failure	3 (8)	16 (19)	0.11	3 (9)	6 (18)	0.28
LCOS or respiratory failure	6 (15)	27 (31)	0.05	6 (18)	9 (27)	0.38
Need for an ECMO	0 (0)	4 (5)	0.17	0 (0)	1 (3)	0.31
Acute renal failure	1 (3)	4 (5)	0.57	1 (3)	2 (6)	0.56
Ischemic Stroke	0 (0)	2 (2)	0.33	0 (0)	2 (6)	0.15
General or local bleeding	2 (5)	4 (5)	1.00	1 (3)	1 (3)	1.0
Atrioventricular block requiring PM	0 (0)	5 (6)	0.12	0 (0)	2 (6)	0.15
Myocardial infarction	0 (0)	3 (4)	0.23	0 (0)	1 (3)	0.31
Postoperative pulmonary arterial hypertension	1 (3)	3 (4)	0.76	1 (3)	2 (6)	0.54
Supraventricular or ventricular arrythmia	2 (5)	7 (8)	0.52	2 (6)	3 (9)	0.64

521 *LCOS:* Low cardiac output syndrome*; ECMO*: Extracorporeal membrane oxygenation; *PM:* Pacemaker
522 Continuous data are presented as means ± standard deviation, categorical data as numbers (percentage).
523
524

Table 4. Univariate and multivariate Cox model analyses of factors associated with death.

Variables	Univariable analysis		Multivariable analysis	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age < 1 year	**5.01 [1.20-20.97]**	**0.03**	**6.1 [1.6-28.66]**	**0.02**
Concomitant mitral plasty or replacement	**13.20 [3.30-52.78]**	**<0.001**	**10.95 [2.66-45.03]**	**<0.001**
Shone's syndrome	5.33 [1.27-22.44]	0.02	-	NS
Pre-operative pulmonary arterial hypertension	6.46 [1.61-25.84]	0.008	-	NS
Type of surgery				
Ross procedure	1.33 [0.27-6.61]	0.73	-	NS
Aortic valvuloplasty	0.75 [0.15-3.73]	0.73	-	NS

OR: Odds Ratio; adj: adjusted; *CI* : confidence interval;

Table 5. Univariable and multivariable Cox model analyses of factors associated with reintervention.

Variables	Univariable analysis		Multivariable analysis	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Shone's syndrome	**4.86 [1.95-12.10]**	**0.001**	**4.44 [1.42-13.89]**	**0.007**
Postoperative mean aortic valve gradient (per 1 mmHg increase)	**1.05 [1.01-1.09]**	**0.03**	**1.05 [1.01-1.09]**	**0.01**
History of balloon aortic valvuloplasty	0.29 [0.07-1.24]	0.10	-	NS
Type of surgery				
Ross procedure	0.76 [0.33-1.73]	0.51	-	NS
Aortic valvuloplasty	1.33 [0.57-3.05]	0.51	-	NS
Number of cusps				
Unicuspid	1		1	-
Bicuspid	0.56 [0.17-1.83]	0.34	-	-
Tricuspid	0.63 [0.2-1.94]	0.42	-	-
Autologous Patch	0.70 [0.08-6.29]	0.75	-	-
Heterologous Patch	1.44 [0.16-13.03]	0.75	-	-
Leaflet repair with a pericardial patch	1.27 [0.28-5.77]	0.76	-	-
Commissural repair with a pericardial	0.79 [0.73-3.57]	0.76	-	-

OR: Odds Ratio; adj: adjusted; *CI* : confidence interval; *VSD*: ventricular septal defect

VIDEO LEGEND

Video 1. Unicuspid aortic valve repair using glutaraldehyde-treated autologous pericardium. The dilated ascending aorta is divided a few millimeters above the sino-tubular junction and then excised (for younger patients, the diameter can be reduced by a triangular resection). Three 5/0 polypropylene commissural stay sutures are placed to expose the valve. Tissue quality, mobility and degree of calcification of each cusp, and number of functional commissures are evaluated. In this patient, one physiological commissure was present. The two other rudimentary commissures and the adjacent calcified areas of the valve were excised, and the normal commissure was preserved. Aggressive shaving of the leaflets is performed in order to obtain pliable tissue. Then, two triangular glutaraldehyde-treated (6 minutes for redo surgery or 8 minutes for a previously non-operated patient) autologous pericardial patches were used to create a new commissure at 180° degrees, opposite to the well-functioning native commissure. The free margin of the leaflet should be mobile and long enough to avoid the risk of patches being too tight. This means that in the opening position, the free margin should almost reach the wall of the aorta. At the same time, realignment of a free margin needs to be achieved to avoid prolapse. The effective height of both cusps has to be optimal and must adapt to the aortic root size to avoid prolapse. Finally, the ascending aorta is replaced by a vascular graft.

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Online Data Supplement

Ross procedure or complex aortic valve repair using the pericardium in children: a real dilemma

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Table S1. Details and causes of early death of patients who underwent complex aortic valve surgery or the Ross procedure

	Date of surgery	Age at surgery	Etiologies of aortic disease	Emergency	Procedure	Time between surgery and death (days)	Etiologies of death
Patient 1	04/05/2006	3 years	Shone's Syndrome	No	Ross + mitral valve replacement	16	Cardiogenic, shock, multiple organ failure
Patient 2	23/08/2007	2 months	Congenial	Yes	Ross + VSD closure	13	Septic shock, tamponade
Patient 3	14/12/2009	2 months	Congenial	No	Ross + mitral plasty	51	Sudden death
Patient 4	11/01/2010	2 months	Shone's Syndrome	No	Aortic valvuloplast y + VSD closure	4	Sudden death
Patient 5	12/02/2015	5 years	Shone's Syndrome	No	Ross + mitral plasty	32	Dress syndrome, ARDS, multiple organ failure
Patient 6	15/02/2017	5 months	Congenial	Yes	Aortic and mitral valvuloplast y	60	Septic shock, Acute respiratory distress syndrome, cardiac arrest
Patient 7	13/05/2017	1 month	Congenial	No	Aortic valvuloplast y	89	Cardiogenic shock

VSD: Ventricular Septal defect ; *ARDS*: Acute respiratory distress syndrome

Table S2. Reoperation data from patients who underwent complex aortic valve surgery

	Date of first surgery	Age at surgery (years)	Date of re-intervention	Times between surgery and reintervention (months)	Etiologies of reintervention	Mean aortic valve gradient / Aortic regurgitation severity	Type of reintervention
Patient 1	16/02/2010	8	05/12/2018	57	Aortic stenosis	60 mmHg / I	Ross procedure
Patient 2	07/07/2011	1	05/06/2019	6	Aortic stenosis	50 mmHg / 0	Ross procedure
Patient 3	08/12/2011	3	17/02/2014	25	Aortic insufficiency	5 mmHg / IV	Ross procedure
Patient 4	26/01/2012	8	30/08/2018	8	Aortic insufficiency	5 mmHg / IV	mAVR
Patient 5	14/03/2012	8	01/04/2019	85	Aortic insufficiency	15 mmHg / IV	mAVR
Patient 6	03/06/2013	6	08/03/2017	34	Aortic insufficiency	5 mmHg / IV	mAVR
Patient 7	11/08/2014	14	25/01/2019	59	Aortic stenosis	50 mmHg / 0	mAVR
Patient 8	22/08/2016	8	22/02/2019	30	Aortic stenosis	70 mmHg / 0	Balloon aortic valvuloplasty

mAVR: mechanical aortic valve replacement

Table S3. Description of patients who suffered from Infective Endocarditis

	Type of Surgery	Date of first surgery	Age at first surgery	Date of IE	Time between surgery and IE (years)	Infection site	Type of treatment
Patient 1	Ross procedure	29/06/2006	6 years	23/06/2018	12	Pulmonary heterologous conduit	Redo surgery
Patient 2	Ross procedure	30/03/2006	9 months	01/04/2019	13	Pulmonary heterologous conduit	Redo surgery
Patient 3	Ross procedure	05/03/2007	11 years	25/01/2019	12	Pulmonary heterologous conduit	Redo surgery
Patient 4	Ross procedure	04/09/2007	1 year	05/06/2019	12	Pulmonary heterologous conduit	Prolonged antibiotics
Patient 5	Ross procedure	17/01/2008	2 years	25/10/2013	5	Pulmonary heterologous conduit	Prolonged antibiotics
Patient 6	Ross procedure	24/01/2012	5 months	30/08/2018	7	Pulmonary heterologous conduit	Redo surgery
Patient 7	Ross procedure	28/06/2014	2 months	22/02/2019	4	Pulmonary heterologous conduit	Redo surgery

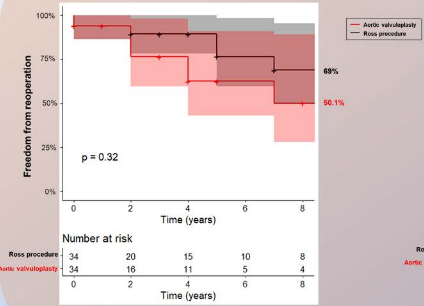
IE: Infective endocarditis

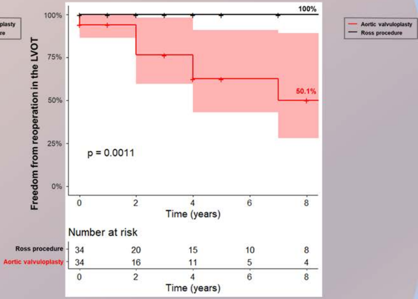
Complex aortic valve lesions in children:
Ross procedure versus aortic valve repair using pericardium

METHODS:

126 patients aged under 18 operated between 2006 and 2017 for complex aortic valve lesion (single center)
34 unique pairs of patients with similar characteristics (Propensity score framework analyses)

RESULTS



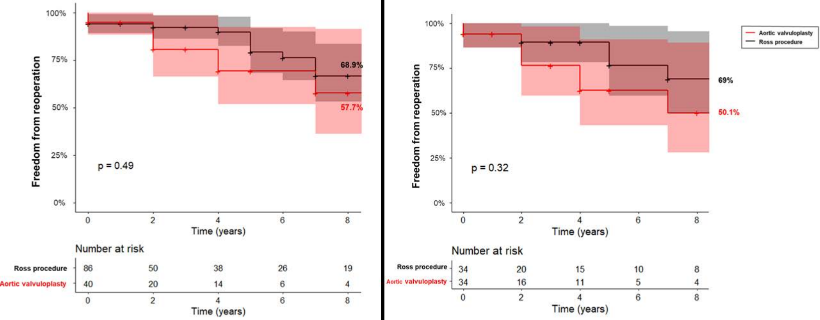


LVOT: Left ventricule outflow tract

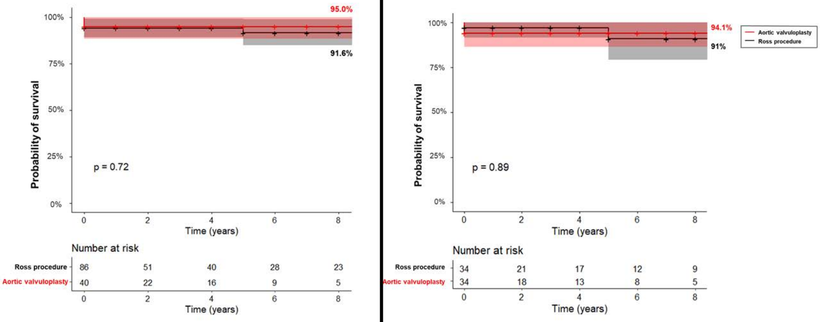
Similar hospital and 8-year survival

IMPLICATIONS

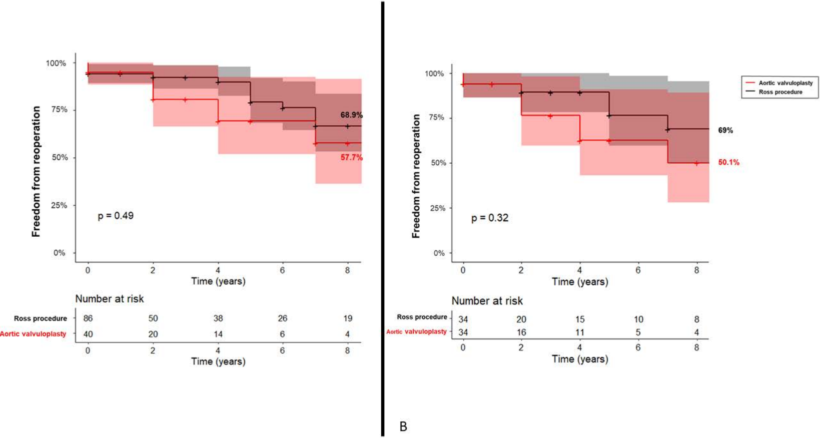
Aortic valvuloplasty using a pericardial patch can be chosen as first-line strategy for treating complex aortic valve lesions and might offer the possibility of a later Ross procedure.


100%
75%
50%
25%
0%
Freedom from reoperation
68.9%
57.7%
p = 0.49
0
2
4
6
8
Time (years)
Number at risk
Ross procedure 86 50 38 26 19
Aortic valvuloplasty 40 20 14 6 4
0
2
4
6
8
Time (years)
100%
75%
50%
25%
0%
Freedom from reoperation
Aortic valvuloplasty
Ross procedure
69%
50.1%
p = 0.32
0
2
4
6
8
Time (years)
Number at risk
Ross procedure 34 20 15 10 8
Aortic valvuloplasty 34 16 11 5 4
0
2
4
6
8
Time (years)

B


95.0%
91.6%
100%
75%
50%
25%
0%
Probability of survival
p = 0.72
0
2
4
6
8
Time (years)
Number at risk
Ross procedure 86 51 40 28 23
Aortic valvuloplasty 40 22 16 9 5
Time (years)
94.1%
91%
Aortic valvuloplasty
Ross procedure
p = 0.89
Ross procedure 34 21 17 12 9
Aortic valvuloplasty 34 18 13 8 5

B



Freedom from reoperation
100%
75%
50%
25%
0%
68.9%
57.7%
p = 0.49
Time (years)
Number at risk
Ross procedure 86 50 38 26 19
Aortic valvuloplasty 40 20 14 6 4
0 2 4 6 8
Time (years)
Aortic valvuloplasty
Ross procedure
69%
50.1%
p = 0.32
Number at risk
Ross procedure 34 20 15 10 8
Aortic valvuloplasty 34 16 11 5 4

B

Complex aortic valve lesions in children:
Ross procedure versus aortic valve repair using pericardium

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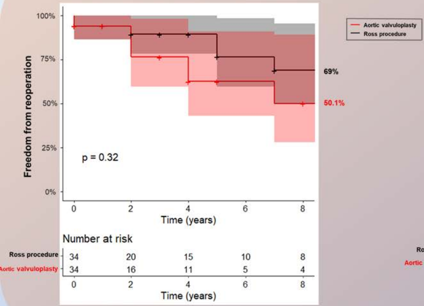

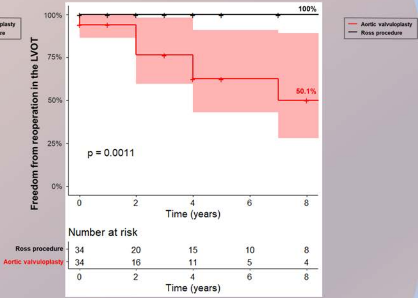

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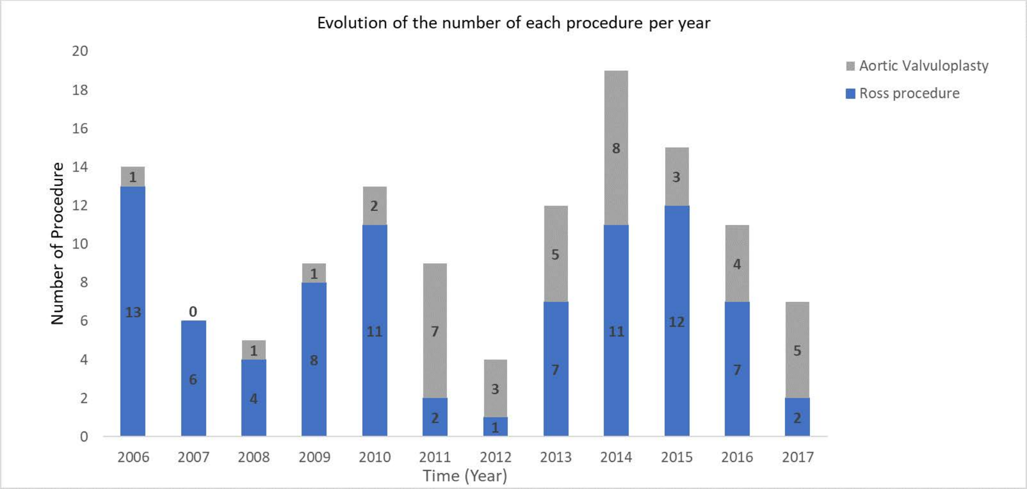
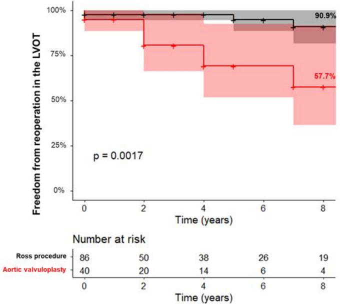
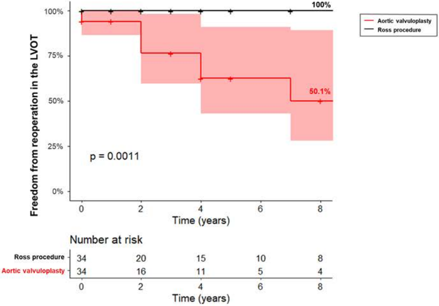
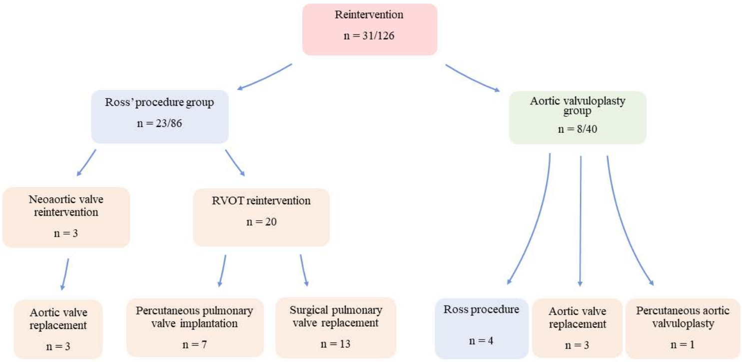

Evolution of the number of each procedure per year
Aortic Valvuloplasty
Ross procedure
Number of Procedure
Time (Year)
0
2
4
6
8
10
12
14
16
18
20
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
13
1
6
0
4
1
8
1
11
2
2
7
1
3
7
5
11
8
12
3
7
4
2
5


Freedom from reoperation in the LVOT
100%
75%
50%
25%
0%
90.9%
57.7%
p = 0.0017
0
2
4
6
8
Time (years)
Number at risk
Ross procedure 86 50 38 26 19
Aortic valvuloplasty 40 20 14 6 4
0
2
4
6
8
Time (years)

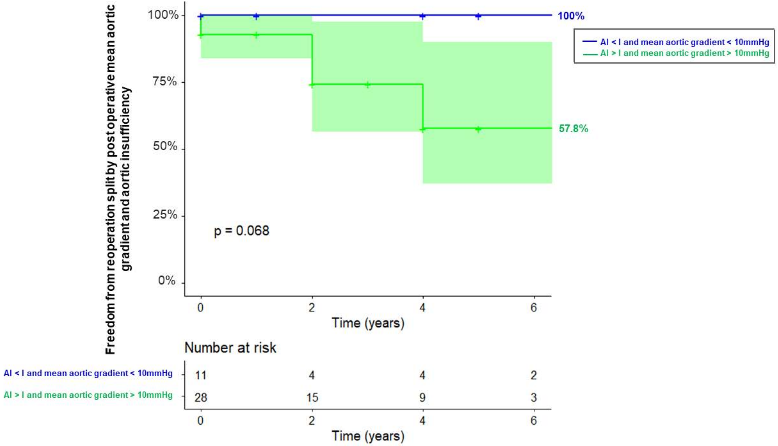
A


Freedom from reoperation in the LVOT
100%
75%
50%
25%
0%
100%
50.1%
p = 0.0011
Aortic valvuloplasty
Ross procedure
0
2
4
6
8
Time (years)
Number at risk
Ross procedure 34 20 15 10 8
Aortic valvuloplasty 34 16 11 5 4
0
2
4
6
8
Time (years)

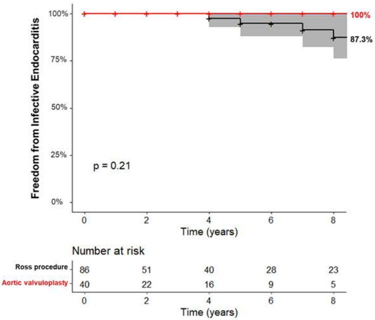
B



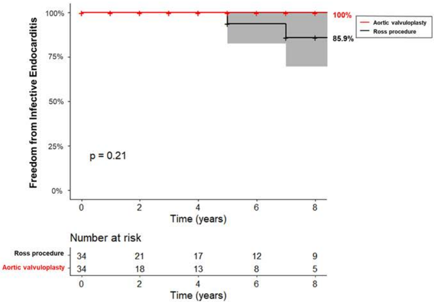
Reintervention
n = 31/126
Ross' procedure group
n = 23/86
Aortic valvuloplasty group
n = 8/40
Neoaortic valve reintervention
n = 3
RVOT reintervention
n = 20
Aortic valve replacement
n = 3
Percutaneous pulmonary valve implantation
n = 7
Surgical pulmonary valve replacement
n = 13
Ross procedure
n = 4
Aortic valve replacement
n = 3
Percutaneous aortic valvuloplasty
n = 1



Freedom from reoperation split by post operative mean aortic gradient and aortic insufficiency
100%
75%
50%
25%
0%
100%
57.8%
AI < I and mean aortic gradient < 10mmHg
AI > I and mean aortic gradient > 10mmHg
p = 0.068
0
2
4
6
Time (years)
Number at risk
AI < I and mean aortic gradient < 10mmHg
11
4
4
2
AI > I and mean aortic gradient > 10mmHg
28
15
9
3
0
2
4
6
Time (years)



100%
75%
50%
25%
0%
Freedom from Infective Endocarditis
100%
87.3%
p = 0.21
0
2
4
6
8
Time (years)
Number at risk
Ross procedure
86
51
40
28
23
Aortic valvuloplasty
40
22
16
9
5
0
2
4
6
8
Time (years)



100%
75%
50%
25%
0%
Freedom from Infective Endocarditis
100%
85.9%
Aortic valvuloplasty
Ross procedure
p = 0.21
0
2
4
6
8
Time (years)
Number at risk
Ross procedure
34
21
17
12
9
Aortic valvuloplasty
34
18
13
8
5
0
2
4
6
8
Time (years)

B