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

Pichoy Danial, Asma Neily, Margaux Pontailler, Régis Gaudin, Diala Khraiche, Mary Osborne-Pellegrin, Pascal Vouhe, Olivier Raisky

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24 **GLOSSARY OF ABBREVIATIONS**

25 AI: Aortic Insufficiency

26 AS: Aortic Stenosis

27 AVR: Aortic Valve Replacement

28 IE: Infective Endocarditis

29 LCOS: Low Cardiac Output Syndrome

30 LVOT: Left Ventricle Outflow Tract

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42 **CENTRAL PICTURE**

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

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46 **CENTRAL MESSAGE**

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

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51 **PERSPECTIVE STATEMENT**

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

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67 **ABSTRACT** (number of words = 250)

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

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

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

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

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

91 **INTRODUCTION**

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

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

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114 MATERIALS AND METHODS

115 Study population

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

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

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

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137 **Surgical techniques**

138 The operative technique of aortic valve repair with a pericardial patch has been
139 previously described ¹². Briefly, cardiopulmonary bypass with a venous cannula in the right
140 atrium and ascending aorta cannulation was established. The aorta was clamped and a
141 hyperkalemic warm blood cardioplegia was delivered every 10 to 15 minutes in the ascending
142 aorta or within the coronary ostia. In cases of AI with cusp retraction, a cusp-free margin
143 extension with a pericardial patch was used to repair the valve ¹³⁻¹⁵. The second method using
144 pericardial patch was extension at the cusp nadir in order to maintain a surface of coaptation
145 made by the native tissue ¹⁶. The last situation where a patch has been used was unicuspid
146 aortic valve repair by a symmetric bicuspidization technique ¹⁷. In patients with only one
147 physiological commissure, the two other rudimentary commissures and the adjacent calcified
148 areas of the valve were excised, and the normal commissure was preserved. Initially, patients
149 were treated with a single folded triangular patch. Later, the technique evolved with the use of
150 two triangular, treated, autologous pericardial patches to create a new commissure opposite
151 (180 degrees orientation) to the preserved native commissure (video 1). The surgical result
152 was then checked intraoperatively by trans-esophageal ultrasound. The repair was considered
153 satisfactory if a residual AI < moderate (if central and not eccentric) and a residual mean
154 aortic gradient < 15 mmHg was achieved.

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

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

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169 **Outcome variables**

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

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

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183 **Statistical analysis**

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

189 A propensity score (PS) framework was generated in order to balance baseline
190 characteristics of patients allowing us to compare clinical endpoints between aortic
191 valvuloplasty and Ross groups. First, a multivariable logistic regression was performed
192 controlling for all pre-specified covariates (age, size, redo surgery and excluding patients with
193 prior aortic valve surgery and not eligible for another attempt at valve repair, chronic heart
194 failure) with the type of surgery as the dependant variable. Aortic valvuloplasty and Ross group
195 patients were matched using a 1:1 nearest neighbor matching algorithm without replacement,
196 with a fixed caliper width of 0.1. Covariate balance between the two groups was assessed after
197 matching, and we considered an absolute standardized difference less than 0.2 as evidence of
198 balance. Then, clinical endpoints were compared between the two groups. Comparison
199 between the Ross procedure and aortic valvuloplasty, regarding 90-day survival, 8-year
200 survival, 8-year freedom from reoperation, 8-year freedom from reoperation in the LVOT and
201 8-year freedom from IE was performed using the Kaplan-Meier method (log-rank test was used
202 for comparison between groups). Association between baseline variables and main clinical
203 outcomes was assessed by Cox regression analyses, using a backward likelihood-ratio method.
204 Relevant variables, significant at the 15% level on univariate analysis, were included. Odds
205 ratios were then provided with 95% confidence intervals. A p-value < 0.05 was considered
206 statistically significant. All calculations were conducted using SPSS v24.0 and R v3.5.1.

207

208 **RESULTS**

209 **Population and operative data**

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

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

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229 **Early postoperative outcomes**

230 Unadjusted 90-day survival was 95% in the aortic valvuloplasty group and 91.6% in
231 the Ross procedure group ($p=0.83$) (Table 3). After controlling for confounders, 90-day

232 survival was 97% in both groups of patients ($p=1.00$). During early follow-up, 5 patients died
233 in the Ross group and 2 patients in the Aortic valvuloplasty group. All these patients were
234 under 1 year of age or suffered from Shone's syndrome with concomitant mitral anomaly.
235 Details and causes of early death are shown in the Table S1.

236 General sepsis was significantly less frequent in the aortic valvuloplasty group
237 compared with the Ross procedure group (9% vs 27%, $p=0.05$) in the propensity-matched
238 populations. There was a trend toward significance of the Ross procedure group for
239 atrioventricular block requiring pacemaker implantation (6% versus 0%, $p=0.15$) and
240 ischemic stroke (6% versus 0%, $p=0.15$). After matching, 6 patients in the aortic
241 valvuloplasty group suffered from LCOS or respiratory failure. Among them, 4 were less than
242 1 year old. Finally, there was no significant difference regarding other early surgery-related
243 outcomes in the propensity-matched population. One patient required a veno-arterial ECMO
244 in the Ross procedure group.

245 In the entire cohort, among the 5 patients in the Ross group who suffered from
246 atrioventricular block requiring a pacemaker, only 1 had a concomitant ventricular septal
247 defect closure, but the others had a concomitant Konno enlargement of the left outflow tract.
248 In the whole cohort, seven patients underwent emergency surgery for ventricular dysfunction
249 (6 in the Ross group and 1 in the aortic valvuloplasty group). Two emergency Ross
250 procedures were performed for early balloon valvuloplasty failure. No aortic valvuloplasty
251 with the use of a pericardial patch was performed for balloon valvuloplasty failure.

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257 **Midterm outcomes**

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

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

267 Adjusted freedom from reintervention at 8 years was not significantly different: 50.1%
268 in the aortic valvuloplasty group and 69% in the Ross procedure group (p=0.32) (Figure 2).

269 However, adjusted freedom from reintervention in the left ventricle outflow tract (LVOT) at 8
270 years was lower after aortic valvuloplasty than after the Ross procedure (50.1% versus 100%
271 respectively, p=0.001) (Figures 3 and S2). In the entire cohort of Ross procedures, 23 patients
272 were reoperated. Among them, 3 patients underwent AVR for deterioration of the pulmonary
273 autograft and 20 patients underwent right ventricular outflow tract reintervention (7
274 percutaneous pulmonary valve implantations, 13 surgical pulmonary valve replacements).

275 Eight patients were reoperated in the aortic valvuloplasty group (4 Ross procedures, 3 AVRs
276 and 1 percutaneous aortic valvuloplasty) (Figure S3 and see Table S2 for more details about
277 patients who were reoperated during follow-up). Predictors of reinterventions are presented in
278 Table 5. The postoperative mean aortic valve gradient (per 1 mmHg increase, adjusted
279 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
280 independently associated with reintervention. None of the patients who had a mean gradient

281 below 10 mmHg and an aortic insufficiency less (or equal) than mild were reoperated (Figure
282 S4).

283 Adjusted freedom from IE at 8 years was 100% in the aortic valvuloplasty group and
284 85.9% in the Ross procedure group with no significant difference ($p=0.21$) (Figure S5).

285 During follow-up, 7 patients developed late IE of the pulmonary heterologous graft and none
286 in the pulmonary autograft (see Table S3 for more details about patients who suffered from
287 IE). Among them, 4 patients were less than 1 year old at the time of the first surgery. Five
288 patients required redo surgery and 2 patients were successfully treated with antibiotics. Lastly,
289 no single variable was predictive of IE. Antibiotic prophylaxis protocol of our institute was
290 not changed during the study period.

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303 **DISCUSSION**

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

318

319 **Mortality and morbidity**

320 In this study, adjusted 8-year survival in the Ross group was 91%, which is
321 comparable to previously reported publications in children ^{6,23}, and 94.1% in the complex
322 aortic valve repair group. Although there was only a tendency but no statistically significant
323 difference, complex aortic valve repair could be associated with a lower operative risk than a
324 Ross procedure, mainly because the coronary ostia and their proximal segments are not
325 mobilized/reimplanted and thus cannot be injured. The cross-clamp time is also shorter and
326 might be considered as a protective effect especially for patients with borderline LV function.
327 The early post-operative outcome was in favor of aortic valve repair (Table 3) with less

328 cardiac, renal or respiratory failure, need for ECMO or pacemaker implantation and finally,
329 local or general infection. This also suggests a lower risk of valve repair compared to the Ross
330 procedure. For the most fragile patients (left ventricular dysfunction, dilated left ventricle,
331 very important hypertrophy ...) ²⁴, aortic valvuloplasty might be an option with, if necessary,
332 the use of a pericardial patch rather than a Ross procedure, expecting a better short-term
333 outcome, as we report here.

334

335 **Anatomic prerequisite for a complex repair**

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

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353 **Reoperation**

354 In this study, adjusted freedom from reintervention was 69% in the Ross procedure,
355 and 50.1% for complex aortic valve repair at 8 years, which is equivalent to previous studies
356 focusing on repair with the use of a pericardial patch¹³. However, indication for
357 reintervention was different between the two techniques. The Ross procedure group had a
358 lower incidence of reoperation on the LVOT as compared to the aortic valvuloplasty group
359 (Figure S2)^{27,28}. The Ross procedure is clearly superior in terms of limiting the number of
360 operations on the aortic valve, but the trade-off is the increased need for reoperation on the
361 pulmonary conduit. The use of percutaneous pulmonary valve implantation techniques might
362 likely prevent surgical reintervention in some cases and may improve long-term outcomes of
363 the Ross procedure^{29,30}. Our current philosophy is to initially propose aortic valvuloplasty,
364 when it is feasible, even if we consider that a repair with a patch is a palliative procedure. The
365 idea is to delay the Ross procedure and to allow, at a later age, the use of a cryopreserved
366 homograft rather than a heterologous conduit that is clearly expected to fail earlier⁶. The
367 strategy might be different if small diameter homografts could be available without
368 restriction. Moreover, we found that age under 1 year was an independent risk factor of death
369 (OR=6.1 CI [1.6-28.66] (Table 4). Of the 7 early deaths in our cohort, 5 were children
370 younger than 1 year of age (3 in the aortic valvuloplasty group and 2 in the Ross group, Table
371 S1). Donald JS and al. also found that age under 1 year was associated with higher operative
372 mortality in the Ross procedure³¹, and it appears to be similar with complex aortic
373 valvuloplasty. This might be related to technical issues but more likely to the severity of the
374 disease, usually when there is concomitant mitral valve or LV dysfunction.

375 Redo surgery after valve repair was exclusively linked to the failure of the valve,
376 mainly AS. Residual mean aortic valve gradient after repair was found as an independent
377 predictor of reintervention. None of the patients who had a post-operative mean aortic

378 gradient below 10 mmHg and an aortic insufficiency less (or equal) than mild were reoperated
379 at last follow-up. These findings represent a useful landmark in the operating room to judge
380 the quality of the repair by trans-esophageal echography. Other studies found that post-
381 operative AI up to mild and prior balloon aortic valvuloplasty were also associated with
382 reoperation^{32,33}. Thus, the goal of valvuloplasty is to obtain a mean aortic valve gradient and
383 a residual AI as low as possible; for this it may be necessary to use highly aggressive
384 valvuloplasty techniques, even for aortic valve lesions that seem to be initially simple to treat
385^{34,35}. Furthermore, neither the type of patch (autologous or heterologous) nor the technique
386 used had an impact on reoperation. The main point of the technique is to achieve a sufficient
387 free margin length (at least the perimeter of the aorta) to allow a satisfactory systolic opening
388 of the valve.

389

390 **Infective endocarditis**

391 Another advantage of aortic valvuloplasty over the Ross procedure in this study was
392 the absence of long-term IE. Indeed, no patient in the valvuloplasty group developed IE while
393 the freedom from IE was 85.9% in the Ross procedure group at 8 years. Freedom from IE in
394 the report of David and al. was 99% at 10 years³ but this study concerned only adults, which
395 may explain the difference due to the use of a homograft. Thus, younger age appears to be
396 associated with IE and the later use of percutaneous pulmonary valve implantation might even
397 increase that risk in this population.

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399 **Limitations**

400 This study has limitations. First, it was conducted in a single high-volume centre. Our
401 results require external validation even if they are similar to those reported in previous
402 studies. Furthermore, the proportion of Ross procedures remained stable over many years,

403 until complex aortic valvuloplasty increased after 2011 (see Figure S1). Selection and
404 learning curve bias can significantly influence results.

405

406 **Conclusion**

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

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427 **FIGURE LEGEND**

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

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

433

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

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

440

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

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

450 *LVOT*: Left Ventricle Outflow Tract

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

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

454

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

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

461 *LVOT*: Left Ventricle Outflow Tract

462

463 Figure S3. Type of reintervention according to initial approach

464 *RVOT*: Right Ventricle Outflow Tract

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

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

470 *AI*: Aortic Insufficiency

471

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

474 Adjusted freedom from IE at 8 years was 100% in the aortic valvuloplasty group and
475 85.9% in the Ross procedure group with no significant difference ($p=0.21$). During follow-up,
476 five patients developed IE of the pulmonary homograft and none in the pulmonary autograft.
477 Three patients required surgery and 2 patients were successfully treated with antibiotics.

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495 TABLES

496 **Table 1. Baseline characteristics of entire study cohort and after propensity score**
 497 **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	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

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

500 **Table 2. Intraoperative data of entire study cohort and after propensity score matching**
 501 **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	

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

505 *AI*: Aortic insufficiency

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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 arrhythmia	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).

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525 **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

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

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543 **Table 5. Univariable and multivariable Cox model analyses of factors associated with**
 544 **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	-	-

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

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548 **VIDEO LEGEND**

549 **Video 1.** Unicuspid aortic valve repair using glutaraldehyde-treated autologous pericardium.
550 The dilated ascending aorta is divided a few millimeters above the sino-tubular junction and
551 then excised (for younger patients, the diameter can be reduced by a triangular resection).
552 Three 5/0 polypropylene commissural stay sutures are placed to expose the valve. Tissue
553 quality, mobility and degree of calcification of each cusp, and number of functional
554 commissures are evaluated. In this patient, one physiological commissure was present. The
555 two other rudimentary commissures and the adjacent calcified areas of the valve were
556 excised, and the normal commissure was preserved. Aggressive shaving of the leaflets is
557 performed in order to obtain pliable tissue. Then, two triangular glutaraldehyde-treated (6
558 minutes for redo surgery or 8 minutes for a previously non-operated patient) autologous
559 pericardial patches were used to create a new commissure at 180° degrees, opposite to the
560 well-functioning native commissure. The free margin of the leaflet should be mobile and long
561 enough to avoid the risk of patches being too tight. This means that in the opening position,
562 the free margin should almost reach the wall of the aorta. At the same time, realignment of a
563 free margin needs to be achieved to avoid prolapse. The effective height of both cusps has to
564 be optimal and must adapt to the aortic root size to avoid prolapse. Finally, the ascending
565 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

Pichoy Danial^{1, 2}, M.D; Asma Nailly¹, M.D; Margaux Pontailier¹, M.D, Ph.D; Régis Gaudin¹, M.D; Diala Kraiche¹, M.D; Mary Osborn-Pellegrin², Ph.D ; Pascal Vouhe¹, M.D; Olivier Raisky¹, M.D, Ph.D

¹Pediatric Cardiac Surgery, Necker Sick Children's Hospital and Paris University, Paris, France

²Department of Cardiovascular and Thoracic Surgery, Institute of Cardiology, Pitié-Salpêtrière Hospital, Assistance Publique-Hôpitaux de Paris (AP-HP), Sorbonne University, 47-83, Boulevard de l'Hôpital, Paris, 75013, France.

Address for correspondence:

Prof Olivier RAISKY

Pediatric Cardiac Surgery, Necker Sick Children's Hospital

149 Rue de Sèvres, 75015 Paris, France

Tel: +33686869142

Mail: oraisky@yahoo.com

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 valvuloplasty + 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 valvuloplasty	60	Septic shock, Acute respiratory distress syndrome, cardiac arrest
Patient 7	13/05/2017	1 month	Congenial	No	Aortic valvuloplasty	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

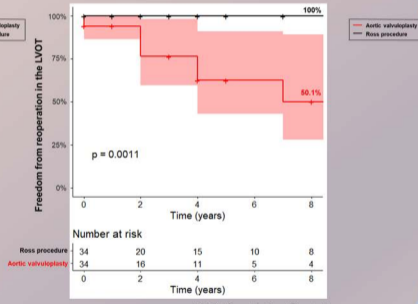
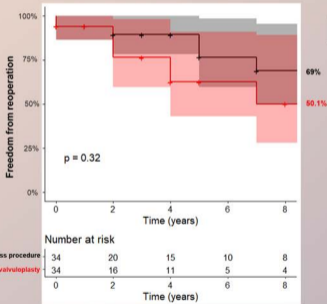
IE: Infective endocarditis

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

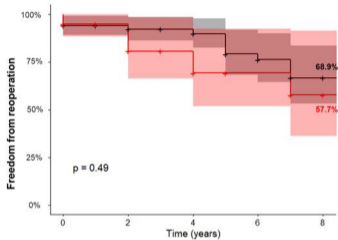


LVOT: Left ventricle outflow tract

Similar hospital and 8-year survival

IMPLICATIONS

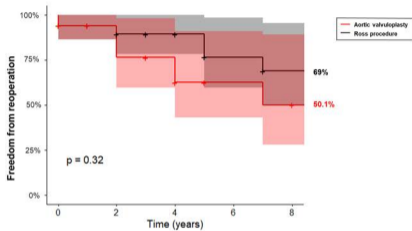
Aortic valvuloplasty using a pericardial patch can be chosen as first-line strategy for treating complex aortic valve lesions and might offer the possibility of a later Ross procedure.



Number at risk

	0	2	4	6	8
Ross procedure	86	50	38	26	19
Aortic valvuloplasty	40	20	14	6	4

Time (years)

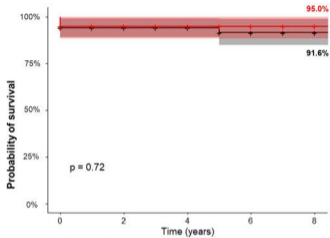


Number at risk

	0	2	4	6	8
Ross procedure	34	20	15	10	8
Aortic valvuloplasty	34	16	11	5	4

Time (years)

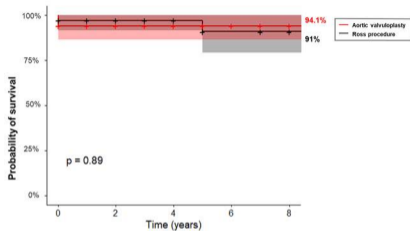
B



Number at risk

	0	2	4	6	8
Ross procedure	86	51	40	28	23
Aortic valvuloplasty	40	22	16	9	5

Time (years)

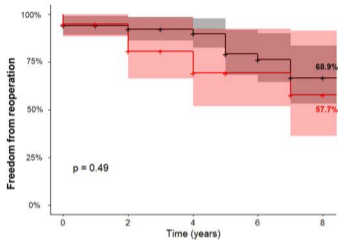


Number at risk

	0	2	4	6	8
Ross procedure	34	21	17	12	9
Aortic valvuloplasty	34	18	13	8	5

Time (years)

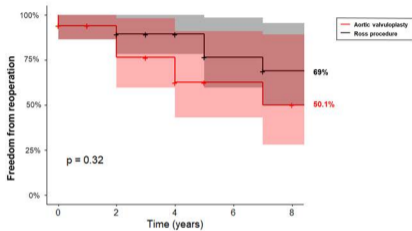
B



Number at risk

	0	2	4	6	8
Ross procedure	86	50	38	26	19
Aortic valvuloplasty	40	20	14	6	4

Time (years)



Number at risk

	0	2	4	6	8
Ross procedure	34	20	15	10	8
Aortic valvuloplasty	34	16	11	5	4

Time (years)

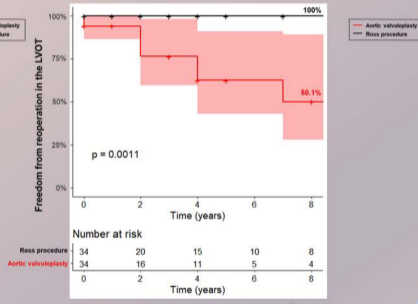
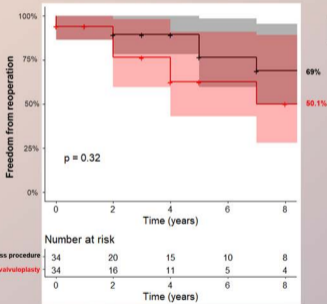
B

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

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126 patients aged under 18 operated between 2006 and 2017 for complex aortic valve lesion (single center)
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RESULTS



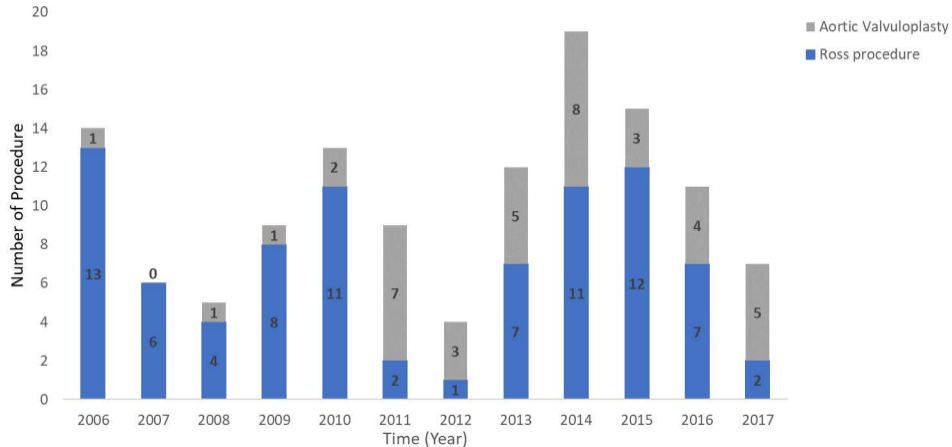
LVOT: Left ventricle outflow tract

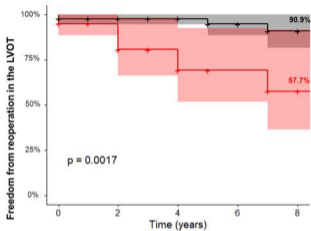
Similar hospital and 8-year survival

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.

Evolution of the number of each procedure per year

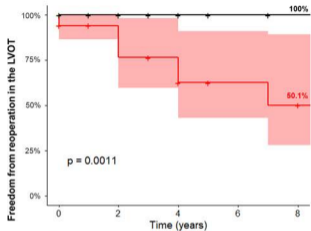




Number at risk

	0	2	4	6	8
Ross procedure	86	50	38	26	19
Aortic valvuloplasty	40	20	14	6	4

Time (years)



— Aortic valvuloplasty
— Ross procedure

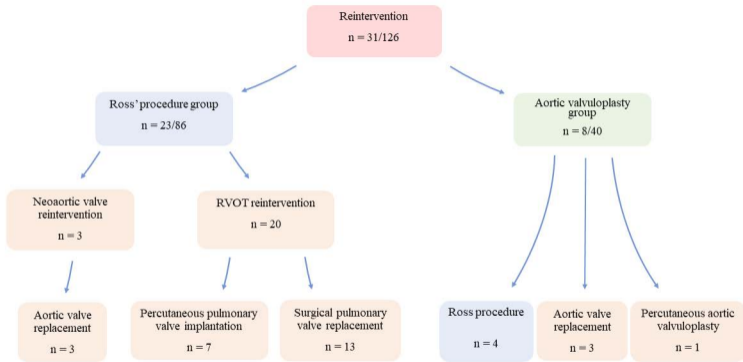
Number at risk

	0	2	4	6	8
Ross procedure	34	20	15	10	8
Aortic valvuloplasty	34	16	11	5	4

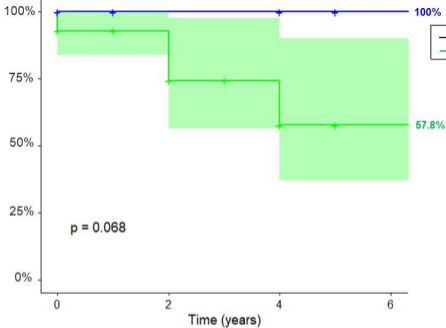
Time (years)

A

B



Freedom from reoperation split by post operative mean aortic gradient and aortic insufficiency



Number at risk

AI < I and mean aortic gradient < 10mmHg

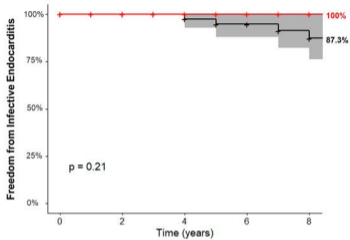
11	4	4	2
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AI > I and mean aortic gradient > 10mmHg

28	15	9	3
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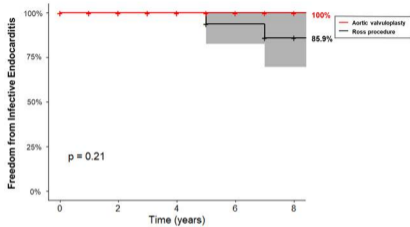
0	2	4	6
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Time (years)



Number at risk

Ross procedure	86	51	40	28	23
Aortic valvuloplasty	40	22	16	9	5
	0	2	4	6	8
	Time (years)				



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