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# Aortic Root Replacement after Aortic Valve or Ascending Aorta Surgery

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**Abstract:** Reoperative Aortic Root Replacement (RARR) is a complex and high-risk operation. We studied outcome of patients who underwent RARR after previous surgery on aortic valve, aortic root or ascending aorta. Between 1981 and 2006, 141 consecutive patients underwent 156 RARRs at the institution. Patient and peri-operative characteristics, short and long-term outcome were analyzed. Mean age was 37 years (0.3-76 years). RARR was performed on 56 prosthetic valves, 23 allografts, 28 pulmonary autografts and 49 native valves. RARR indications were: structural failure 47% (n = 72), neo-aortic root dilatation 18% (n = 28), aneurysm/dissection 13% (n = 21), endocarditis 15% (n = 24), non-structural failure 6% (n = 10) and valve thrombosis 1% (n = 1). About 36% (n = 56) received an allograft, 34% (n = 54) an aortic valve conduit (Bentall) and 30% (n = 46) a pulmonary autograft. Hospital mortality was 9% (n = 14): 14% (n = 8) prosthetic valve patients, 13% (n = 3) allograft patients, 6% (n = 3) native valve patients and 0% autograft patients died. Potential hospital mortality predictors were longer perfusion and cross clamp time, older patient age, female gender, unplanned CABG, concomitant mitral valve replacement and emergency surgery. During follow-up (mean 6.5 years, range 0-18 years), 13 patients died (LOR 1.3%/patient year); 8 prosthetic valves patients, 1 allograft patient, 3 native valve patients and 1 autograft patient. Overall 10 years survival was 78±4%; for prosthetic valve patients 65±8%, for allograft patients 82±8%, for native valve patients 87±5% and for autograft patients 96±4%. RARR can be safely performed. Especially, pulmonary autograft reoperation has low hospital mortality and morbidity rates with excellent survival. In this respect, these results may contribute to decision making in valve substitute selection in primary aortic valve replacement, especially in adolescents and young adults.

**Key words:** Reoperation, aortic root, heart valve (allograft), heart valve (autograft), statistics, survival analysis

## INTRODUCTION

Primary Aortic Root Replacement (ARR) is a reliable and relatively safe operation with a low mortality rate, especially in the elective setting and regardless of the type of composite graft used (Lytle *et al*., 1990; Kouchoukos *et al*., 1991; Luciani *et al*., 1998). Recent developments in aortic valve and root surgery including valve sparing procedures on the aortic root, pulmonary autograft implantation, aortic allograft implantation and aortic valve preservation in acute aortic dissection and the aging population will lead to an increasing incidence of secondary ARR after these procedures. Reoperative ARR is a complex and high risk operation.In particular reopening of the chest with possible adherence of the aorta to the sternum and the need for mobilization and reimplantation of the coronary arteries may contribute to the high risk character of the operation and therefore to a higher expected mortality risk in these patients (Schepens *et al*., 1999; Girardi *et al*., 2006; Kirsch *et al*., 2006; Szeto *et al*., 2007). In the center, a high volume of pulmonary autograft procedures and aortic allograft implantations was performed over the past two decades. The use of these operations is a matter of debate and recent reports have shown an increasing incidence of reoperations when using allografts and pulmonary autografts as valve substitutes in aortic valve or root replacement (Elkins *et al*., 1996; Luciani *et al*., 2003; Kouchoukos *et al*., 2004; Smedira *et al*., 2006; Klieverik *et al*., 2007). Furthermore, these reoperations are complex due to extensive calcification of the allograft wall and at annular level and due to dilatation of the autograft which might negatively influence reoperative and long-term outcome (Hokken *et al*., 2003; Schoof *et al*., 2006; Yacoub *et al*., 2006).

The purpose of this study was to analyze the experience in reoperative aortic root replacement after previous surgery on the aortic valve, the ascending aorta

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or both. Main focus is the type of valve *in situ* at the moment of reoperation and the influence on outcome after reoperation. This may be helpful in the choice for a valve substitute at primary operation.

## MATERIALS AND METHODS

**Patients:** Between October 1981 and December 2006, about 141 patients underwent 156 reoperative aortic root replacements. All patients underwent RARR after aortic valvulotomy, aortic valve replacement, aortic root replacement or surgery on the ascending aorta. All patients who receive an autograft or allograft in aortic position in the center are enrolled in the ongoing prospective follow-up study (Takkenberg *et al*., 2001, 2006; Willems *et al*., 2001; Yacoub *et al*., 2006).

Patients who underwent previous isolated coronary artery bypass grafting or other cardiac procedures that were not aortic valve-related were not included. In 56 patients, a Prosthetic Valve (PV) was replaced (36 mechanical prostheses and 20 bioprostheses) in 23 patients an Allograft (ALLO), in 28 patients a pulmonary Autograft (AUTO) and in 49 patients, the Native Valve (NV). In the latter group, 36 patients of which 28 patients had a bicuspid valve had previously undergone aortic valve repair or a valvulotomy. None of the repairs were either a David reconstruction or a Yacoub reconstruction. Furthermore, 7 patients (1 bicuspid valve) underwent surgery of the ascending aorta for acute aortic dissection and 6 patients (4 bicuspid valves) underwent surgery for a discrete subaortic stenosis. Approval from the Institutional Review Board was obtained for this study; the Institutional Review Board waived informed consent. For patients who received an allograft or pulmonary autograft at primary operation or reoperation, information was collected from the ongoing prospective cohort study (Willems *et al*., 2001). For all other patients, information on patient characteristics, perioperative details and follow-up was collected retrospectively from hospital records, correspondence with the treating physicians and through the civil registry.

**Surgical procedures:** All operations were performed through a median sternotomy and on cardiopulmonary bypass with moderate hypothermia. We used central canulation in the ascending aorta and right atrium or caval veins. To anticipate on possible perforation of the heart or aorta when reopening the chest, we instituted cardiopulmonary bypass with canulation of the femoral vessels and deep cooling in 9 patients before performing the sternotomy. Crystalloid, cardioplegia and topical cooling were used for myocardial protection. Total circulatory arrest with deep hypothermia was needed in 30 patients with ascending aorta or arch pathology. In patients with a native aortic valve or valve prosthesis *in situ*, root replacement followed the removal of the valve or the prosthesis. In patients with an allograft *in situ*, it was necessary to remove all calcified allograft material before root replacement. The original coronary buttons were dissected from the allograft aortic wall. In patients with a pulmonary autograft *in situ*, the neo-aortic root was in most cases dilated without any signs of root or valve calcification. After opening the autograft root, the autograft valve leaflets were excised and the coronary buttons mobilized. Excess autograft wall tissue was removed, leaving parts of the autograft at annular level *in situ*.

**Mortality and follow up:** All patients who receive an autograft or allograft at Erasmus MC are followed prospectively by annual telephone interviews and through visits to their cardiologist. For patients who underwent surgery for a dissection of the ascending aorta or those who had replacement of a prosthetic aortic valve, information on patient characteristics, perioperative details and follow-up was collected retrospectively from hospital records, correspondence with treating physicians and through the civil registry. Mortality and other valve-related events were registered according to the guidelines for reporting morbidity and valve-related events (Edmunds *et al*., 1996). Operative mortality was defined as death within 30 days or within any time interval after operation if the patient was still hospitalized.

The database was frozen on January 1st, 2007. Follow-up was 98.0% complete. Three patients were lost to follow-up due to emigration. Overall mean follow-up after RARR was 6.2 years (range 0-18.3 years) with total follow-up of 973 patient years.

**Statistical analysis:** For data analysis, SPSS 12.0.1 for Windows was used (SPPS, Chicago, Illinois). Descriptive statistical analysis was done for preoperative and perioperative data. Continuous variables are displayed as mean±1 SD and compared using the unpaired t-test or Kruskal Wallis-test.

Discrete variables are displayed as proportions and compared using the Chi-square ($\chi^2$) test. Univariable logistic regression was used to determine factors associated with different valve substitute groups and to determine potential risk factors for hospital mortality. The following factors were analyzed: age at operation (continuous variable), sex, time period of operation (before and after 1998), New York Heart association class (defined as I-IV and cardiogenic shock as NYHA V),

preoperative creatinin level (micromoles/L), preoperative ventilation support, abnormal cardiac rhythm preoperative (other rhythm preoperative than sinus rhythm), left ventricular function (defined as good when ejection fraction was >50%, impaired when ejection fraction was 40-50% and moderate/bad when ejection fraction was <40%), emergent surgery (<24 h after diagnosis), concomitant procedures, indication for reoperation, active endocarditis (operated on before completing a standard course of 6 weeks of antibiotics), cardiopulmonary bypass time (in min) and cross clamp time (min).

The variable valve prosthesis type used at reoperation was additionally analyzed to determine its possible influence on hospital mortality.

Cumulative survival, freedom from reoperation and freedom from valve-related events were analyzed with the Kaplan-Meier method. The Log-rank test was used to compare the Kaplan-Meier curves and Tarone-Ware test was used where appropriate to correct for significant differences in follow-up time between the different groups. The Cox regression proportional hazards model was used for univariable analysis for time-related events. A p = 0.05 was considered statistically significant. All testing was two-sided.

## RESULTS AND DISCUSSION

Preoperative patient characteristics are shown in Table 1. The prosthetic valves *in situ* were bioprotheses (n = 20) and mechanical prostheses (n = 36). None of the patients with a mechanical prosthesis *in situ* had structural failure in contrast to the biological prostheses. Perioperative details are shown in Table 2. In 46 patients, a pulmonary autograft was inserted, 56 patients underwent allograft root replacement and in 54 patients an aortic valved conduit (Bentall procedure) was employed. Of the patients with etiology of aneurysm ascending aorta or root dilatation 8 patients had a bicuspid valve in history (16%).

**Characteristics of different valve substitute groups:** Patients who received an allograft at RARR more often had a prosthetic valve *in situ* (OR 8.3, 95% CI 3.9-17.5;

Table 1: Patient characteristics per valve substitute *in situ* before RARR

| Characteristics | All valves (n = 156) | Prosthetic valve (n = 56) | Native valve (n = 49) | Allograft (n = 23) | Autograft (n = 28) |
|---|---|---|---|---|---|
| Mean age (years (range))[a] | 37 (0.3-76) | 51 (7-76) | 22 (0.3-61) | 38(16-65) | 34 (15-50) |
| Male gender[a] | 69% (n = 107) | 73% (n = 41) | 53% (n = 26) | 87% (n = 20) | 71% (n = 20) |
| **Systolic LVF** | | | | | |
| Good[a] | 80% (n = 125) | 71% (n = 40) | 90% (n = 44) | 78% (n = 19) | 82% (n = 23) |
| Impaired | 14% (n = 22) | 18% (n = 10) | 10% (n = 5) | 9% (n = 2) | 18% (n = 5) |
| Moderate/bad | 6% (n = 9) | 11% (n = 6) | - | 13% (n = 3) | - |
| **Cardiac rhythm** | | | | | |
| Sinus rhythm | 90% (n = 141) | 86% (n = 48) | 96% (n = 47) | 82% (n = 19) | 96% (n = 27) |
| Atrial fibrillation | 4% (n = 6) | 5% (n = 3) | - | 9% (n = 2) | 4% (n = 1) |
| Other | 6% (n = 9) | 9% (n = 5) | 4% (n = 2) | 9% (n = 2) | - |
| Creatinin (μmol $L^{-1}$) | 79 (22-305) | 95 (32-305) | 61 (22-142) | 79 (58-125) | 79 (61-110) |
| **NYHA** | | | | | |
| I | 37% (n = 57) | 32% (n = 18) | 41% (n = 20) | 26% (n = 6) | 46% (n = 13) |
| II/III | 31% (n = 49) | 43% (n = 24) | 53% (n = 26) | 65% (n = 14) | 54% (n = 15) |
| IV/V[a] | 32% (n = 19) | 25% (n = 14) | 6% (n = 3) | 9% (n = 2) | - |
| **Hemodynamic diagnosis** | | | | | |
| AR[a] | 53% (n = 83) | 53% (n = 30) | 20% (n = 10) | 61% (n = 14) | - |
| AS[a] | 20% (n = 31) | 13% (n = 7) | 47% (n = 23) | 4% (n = 1) | -- |
| AR+AS | 18% (n = 28) | 13% (n = 7) | 31% (n = 15) | 26% (n = 6) | |
| None[a] | 9% (n = 15) | 21% (n = 12) | 2% (n = 1) | 9% (n = 2) | 100% (n = 28) |
| Time interval previous-current operation (years (range)) | 8 (0-33) | 6 (0-20) | 9 (0-33) | 7 (0-14) | 10 (4-16) |
| **Indication RARR[a]** | | | | | |
| SVD | 47% (n = 72) | 18% (n = 10) | 84% (n = 41) | 92% (n = 21) | - |
| NSVD | 6% (n = 10) | 16% (n = 9) | - | 4% (n = 1) | - |
| Endocarditis | 15% (n = 24) | 41% (n = 23) | 2% (n = 1) | - | - |
| Active | 12% (n = 18) | n = 18 | - | - | - |
| Aneurysm/dissection | 13% (n = 21) | 23% (n = 13) | 14% (n = 7) | 4% (n = 1) | |
| RD and/or AR | 18% (n = 28) | - | - | - | 100% (n = 28) |
| Valve thrombosis | 1% (n = 1) | 2% (n = 1) | - | - | - |
| Preop ventilation support | 5% (n = 8) | 5% (n = 3) | 8% (n = 4) | 4% (n = 1) | |
| Type surgery[a] | | | | | |
| Emergent | 5% (n = 7) | 9% (n = 5) | 2% (n = 1) | 4% (n = 1) | - |
| Urgent | 30% (n = 47) | 57% (n = 32) | 10% (n = 5) | 26% (n = 6) | 14% (n = 4) |
| Elective | 65% (n = 102) | 34% (n = 19) | 88% (n = 43) | 70% (n = 16) | 86% (n = 24) |

[a]Significant differences between the groups with p<0.05; AR = Aortic Regurgitation, AS = Aortic Stenosis, LVF = Left Ventricular Function, NSVD = Non-Structural Valve Degeneration, NYHA = New York Heart Association, other cardiac rhythm = pacemaker rhythm and heart block, RD = autograft Root Dilatation, SVD = Structural Valve Degeneration, time interval = mean time interval between last aortic valve-related or ascending aorta-related operation and root re-replacement

Table 2: Perioperative data per valve substitute *in situ* before RARR

| Perioperative data | All valves (n = 156) | Prosthetic valve (n = 56) | Native valve (n = 49) | Allograft (n = 23) | Autograft (n = 28) |
|---|---|---|---|---|---|
| CPB time[a] (min (range)) | 236 (79-685) | 246 (79-660) | 217 (116-685) | 278 (118-542) | 214 (115-389) |
| Cross clamp[a] (min (range)) | 151 (61-331) | 158 (61-302) | 139 (70-240) | 175 (79-331) | 137 (85-271) |
| Circulatory arrest[a] (min (range)) | n = 30 27 (2-99) | n = 9 20 (10-34) | n = 5 55 (16-99) | n = 7 22 (7-48) | n = 9 22 (2-59) |
| **Valve type inserted[a]** | | | | | |
| Aortic valve conduit (Bentall) | 35% (n = 54) | 20% (n = 11) | 12% (n = 6) | 52% (n = 12) | 89% (n = 25) |
| Allograft root | 35% (n = 56) | 67% (n = 38) | 22% (n = 11) | 22% (n = 5) | 11% (n = 3) |
| Pulmonary autograft | 30% (n = 46) | 13% (n = 7) | 66% (n = 32) | 26% (n = 6) | - |
| **Concomitant procedures** | | | | | |
| Planned CABG | 3% (n = 4) | 4% (n = 2) | - | 9% (n = 2) | - |
| Unplanned CABG | 2% (n = 3) | 2% (n = 1) | 3% (n = 2) | - | - |
| MVR | 3% (n = 4) | 7% (n = 4) | - | - | - |
| MVP | 4% (n = 6) | 4% (n = 2) | - | 9% (n = 2) | 7% (n = 2) |
| PVR[a] | 3% (n = 5) | 2% (n = 1)[b] | - | - | 14% (n = 4) |
| Extended root | 17% (n = 26) | 16% (n = 9) | 12% (n = 6) | 17% (n = 4) | 25% (n = 7) |
| Other | 14% (n = 22) | 7% (n = 4) | 20% (n = 10) | 4% (n = 1) | 25% (n = 7) |
| **Complications** | | | | | |
| Rethoracotomy | 17% (n = 26) | 23% (n = 13) | 10% (n = 5) | 26% (n = 6) | 7% (n = 2) |
| Stroke | 2% (n = 3) | 4% (n = 2) | - | - | 3% (n = 1) |
| Myocardial infarction | 1% (n = 1) | - | 2% (n = 1) | - | - |
| Permanent pacemaker | 1% (n = 2) | 2% (n = 1) | 2% (n = 1) | - | - |
| Length of hospital stay (days (range)) | 15 (0-91) | 22 (0-91) | 12 (0-72) | 10 (0-31) | 10 (5-41) |
| Hospital death | 9.0% (n = 14) | 14% (n = 8) | 6% (n = 3) | 13% (n = 3) | 0% |

[a]Significant differences between the groups with $p<0.05$, [b]other than the autograft procedure; CABG = Coronary Artery Bypass Grafting, MVP = Mitral Valve repair, MVR = Mitral Valve Replacement, other including surgery for discrete subaortic stenosis, closure patent ductus arteriosus and tailoring ascending aorta

Table 3: Details on hospital deaths

| *In situ* valve | Age RARR | Time since previous operation | Indication RARR | Implanted | Cause of death | Days postop |
|---|---|---|---|---|---|---|
| Prosthetic | 65 | 0.9 years | Endocarditis | Allograft | Heart failure | Peroperative |
| Prosthetic | 69 | 19.8 years | Endocarditis | Allograft | Myocardial infarction | Peroperative |
| Prosthetic | 74 | 17 days | Endocarditis | Allograft | Myocardial infarction | 1 |
| Prosthetic | 53 | 8.1 years | NSVD | Allograft | Heart failure | 4 |
| Prosthetic | 71 | 1 day | NSVD | Allograft | Multi organ failure | 5 |
| Prosthetic | 66 | 9.7 years | NSVD | Allograft | Heart failure | 23 |
| Prosthetic | 63 | 5.8 years | Aneurysm ascending aorta | Allograft | Heart failure | 34 |
| Prosthetic | 61 | 60 days | Dissection ascending aorta | Bentall | Heart failure | 22 |
| Allograft | 49 | 14.4 years | SVD | Bentall | Heart failure | Peroperative |
| Allograft | 63 | 0 days | SVD | Allograft | Heart failure | 5 |
| Allograft | 65 | 14.0 years | SVD | Bentall | Heart failure | 16 |
| Native valve | 0.3 | 31 days | SVD | Pulmonary autograft | Heart failure | Peroperative |
| Native valve | 40 | 9.2 years | SVD | Pulmonary autograft | Heart failure | Peroperative |
| Native valve | 24 | 13.7 years | SVD | Pulmonary autograft | Mediastinitis+sepsis | 13 |

NSVD = Non Structural failure, SVD = Structural Failure

$p<0.001$), endocarditis as the indication for reoperation (OR 13.3, 95% CI 4.3-41.7; $p<0.001$) were in NYHA class IV or V (OR 6.3, 95% CI 2.1-18.7; $p = 0.001$) had an impaired left ventricular function (OR 3.8, 95%, CI 1.5-9.8; $p = 0.005$), underwent more urgent surgery (OR 3.3, 95% CI 1.6-6.6; $p = 0.001$) and had an increased preoperative creatinin level (OR 1.02, 95% CI 1.01-1.03; $p = 0.008$). Patients who received a Bentall procedure more often had a previously inserted pulmonary autograft (OR 28.4, 95% CI 8.0-101.0, $p<0.001$) and had an aortic aneurysm as the indication for reoperation (OR 5.6, 95% CI 2.0-15.6; $p = 0.001$). Finally, patients who received a pulmonary autograft were younger than the allograft and Bentall patients (OR 1.09, 95% CI 1.06-1.12; $p<0.001$) had a normal preoperative creatinin level (OR 1.04, 95% CI 1.02-1.06; $p<0.001$), a good left ventricular function (OR 3.4, 95% CI 1.1-10.4; $p = 0.03$) and underwent more elective surgery (OR 4.1, 95% CI 1.7-10.1; $p = 0.002$).

**Early morbidity and mortality:** During hospital stay, 26 patients (17%) required a rethoracotomy for persistent bleeding, 3 patients (2.0%) had a stroke of which one was lethal, one patient (1%) had a myocardial infarction and one patient (1%) required a permanent pacemaker.

A total of 14 patients died in hospital (9.0%). Details on operative deaths are shown in Table 3. Potential predictors of hospital mortality were longer perfusion time (OR 1.01, 95% CI 1.01-1.02; $p<0.001$), longer cross clamp time (OR 1.02, 95% CI 1.01-1.04; $p<0.001$), older patient age (OR 1.07, 95% CI 1.03-1.10; $p = 0.001$), female gender (OR 3.3, 95% CI 1.1-10.1; $p = 0.04$), abnormal cardiac rhythm preoperative (OR 7.3, 95% CI 2.1-26.1; $p = 0.02$), NYHA class IV or V (OR 10.8, 95% CI 3.3-36.1; $p<0.001$), concomitant mitral valve replacement (OR 11.7, 95% CI 1.5-90.3; $p = 0.02$), preoperative ventilation support (OR 14.7, 95% CI 3.1-68.5; $p = 0.006$), emergency surgery (OR 18.5, 95% CI 3.6-94.5; $p<0.001$) and unplanned CABG

Table 4: Characteristics per valve substitute implanted at RARR

| Characteristics | All valves (n = 156) | Bentall (n = 54) | Allograft (n = 57) | Autograft (n = 46) |
|---|---|---|---|---|
| Mean age (years (range)) | 37 (0.2-76) | 42 (15-73) | 45 (4-76) | 21 (0.2-57) |
| Male gender | 69% (n = 107) | 78% (n = 42) | 65% (n = 37) | 61% (n = 28) |
| **Systolic LVF** | | | | |
| Good | 81% (n = 126) | 88% (n = 47) | 65% (n = 37) | 91% (n = 42) |
| Impaired | 13% (n = 21) | 8% (n = 4) | 24% (n = 14) | 7% (n = 3) |
| Moderate/bad | 6% (n = 11) | 4% (n = 2) | 11% (n = 6) | 2% (n = 1) |
| **Cardiac rhythm** | | | | |
| Sinus rhythm | 93% (n = 143) | 88% (n = 47) | 88% (n = 51) | 98% (n = 45) |
| Atrial fibrillation | 3% (n = 6) | 6% (n = 3) | 6% (n = 3) | - |
| Other | 4% (n = 7) | 6% (n = 3) | 6% (n = 3) | 2% (n = 1) |
| Creatinin (μmol $L^{-1}$) | 79 (22-305) | 82 (55-142) | 88 (22-305) | 64(23-120) |
| **NYHA** | | | | |
| I | 37% (n = 57) | 37% (n = 20) | 30% (n = 17) | 43% (n = 20) |
| II/III | 51% (n = 80) | 59% (n = 32) | 44% (n = 25) | 50% (n = 23) |
| IV/V | 12% (n = 20) | 4% (n = 2) | 26% (n = 15) | 7% (n = 3) |
| **Hemodynamic diagnosis** | | | | |
| AR | 52% (n = 81) | 81% (n = 43) | 47% (n = 27) | 22% (n = 11) |
| AS | 21% (n = 32) | 6% (n = 3) | 19% (n = 11) | 40% (n = 18) |
| AR+AS | 18% (n = 28) | 4% (n = 2) | 16% (n = 9) | 38% (n = 17) |
| None | 11% (n = 15) | 9% (n = 5) | 18% (n = 10) | - |
| Time interval previous-current operation (years (range)) | 8.3 (0-33) | 9.7 (0.2-31) | 7.5 (0-31) | 7.6 (0.1-33) |
| **Indication RARR** | | | | |
| SVD | 60% (n = 94) | 59% (n = 32) | 37% (n = 21) | 89% (n = 41) |
| NSVD | 1% (n = 2) | - | - | 4% (n = 2) |
| Endocarditis | 14% (n = 23) | 2% (n = 1) | 33% (n = 19) | 7% (n = 3) |
| Aneurysm/dissection | 13% (n = 21) | 25% (n = 13) | 14% (n = 8) | - |
| RD and/or AR | 11% (n = 15) | 14% (n = 7) | 14% (n = 8) | - |
| Valve thrombosis | 1% (n = 1) | - | 2% (n = 1) | - |
| Preop ventilation support | 19% (n = 30) | - | 11% (n = 6) | 52% (n = 24) |
| **Type surgery** | | | | |
| Emergent | 5% (n = 8) | 4% (n = 2) | 11% (n = 6) | - |
| Urgent | 30% (n = 47) | 26% (n = 14) | 45% (n = 26) | 15% (n = 7) |
| Elective | 65% (n = 101) | 70% (n = 37) | 44% (n = 25) | 85% (n = 39) |
| CPB time (min (range)) | (79-685) | 239 (115-660) | 241 (79-485) | 224 (129-685) |
| Cross clamp[a] (min range)) | (61-331) | 146 (77-331) | 158 (61-302) | 144 (90-240) |
| Circulatory arrest (min (range)) | (2-99) n = 39 | 22 (2-71) n = 22 | 47 (15-99) n = 15 | (11, 64) n = 2 |
| **Concomitant procedures** | | | | |
| Planned CABG | 3% (n = 4) | 2% (n = 1) | 5% (n = 3) | - |
| Unplanned CABG | 2% (n = 3) | - | 2% (n = 1) | 4% (n = 2) |
| MVR | 3% (n = 4) | - | 7% (n = 4) | - |
| MVP | 4% (n = 6) | 6% (n = 3) | 5% (n = 3) | - |
| PVR | 3% (n = 5) | 7% (n = 4) | 2% (n = 1) | - |
| Extended root | 17% (n = 26) | 22% (n=12) | 19% (n = 11) | 7% (n = 3) |
| Rethoracotomy | 11% (n = 17) | 20% (n = 1) | 16% (n = 9) | 15% (n = 7) |
| Length of hospital stay (days (range)) | 15 (0-91) | 12 (0-72) | 22 (0-91) | 10 (0-42) |
| Hospital death | 9% (n = 14) | 6% (n = 3) | 14% (n = 8) | 7% (n = 3) |

(OR 23.3, 95% CI 1.9-278.3; p = 0.01). A good left ventricular function was associated with a lower hospital mortality (OR 0.2, 95% CI 0.07-0.63; p = 0.006). The type of valve prosthesis type used at RARR had no effect on hospital mortality (Table 4).

**Follow-up and survival:** For PV patients mean follow-up was 6.2 years, range 0-16.3 years with total follow-up of 347 patient years. For NV patients mean follow-up was 9.3 years, range 0-18.3 years with total follow-up of 455 patient years. For ALLO patients, mean follow-up was 4.8 years, range 0-14.4 years with total follow-up of 110 patient years. For AUTO patients, mean follow-up was 2.1 years, range 0.1-8.8 years with total follow-up of 58 patient years.

During follow-up 13 patients (LOR 1.3%/patient year) died; 8 PV patients, 3 NV patients, one ALLO patient and one AUTO patient died. Table 5 shows details on deaths during follow-up. Overall 10 years survival after RARR was 78.3±4.0%. For PV patients 10 years survival was 65.4±7.6%, for NV patients 86.6±5.2% for ALLO patients 82.4±8.0% and for AUTO patients 10 years survival was 96.3±3.6% (p = 0.06) (Fig. 1).

Potential predictors for late mortality were longer perfusion time (HR 1.01, 95% CI 1.003-1.01; p = 0.001), older patient age (HR 1.04, 95% CI 1.004-1.07; p = 0.03), preoperative increased creatinin level (HR 1.01, 95% CI 1.001-1.02; p = 0.03), active endocarditis (HR 4.1, 95% CI 1.2-13.7; p = 0.02) abnormal cardiac rhythm preoperative (HR 4.4, 95% CI 1.2-16.2; p = 0.03), the use of an allograft

Table 5: Details on deaths during follow-up

| *In situ* valves | Indication RARR | Implanted | Cause of death | Years postop |
|---|---|---|---|---|
| Prosthetic | Endocarditis | Allograft | Endocarditis | 1.5 |
| Prosthetic | SVD | Allograft | SUUD | 2.3 |
| Prosthetic | NSVD | Allograft | Heart failure | 3.8 |
| Prosthetic | Endocarditis | Allograft | Cancer | 3.8 |
| Prosthetic | Endocarditis | Allograft | Heart failure | 6.2 |
| Prosthetic | Endocarditis | Allograft | COPD | 8.2 |
| Prosthetic | Aneurysm ascending aorta | Allograft | Heart failure | 10.4 |
| Prosthetic | Aneurysm ascending aorta | Bentall | Heart failure | 0.2 |
| Allograft | SVD | Allograft | Heart failure | 0.3 |
| Pulmonary autograft | SVD | Bentall | Myocardial infarction | 0.1 |
| Native | Aortic dissection | Allograft | Myocardial infarction | 0.3 |
| Native | Aneurysm ascending aorta | Allograft | Heart failure | 4.3 |
| Native | SVD | Allograft | Traumatic intracerebral bleeding | 8.4 |

RARR = Reoperative Aortic Root Replacement, NSVD = Non-Structural Valve Degeneration, SUUD = Sudden Unexplained Unexpected Death, SVD = Structural Valve Degeneration substitute inserted at reoperation

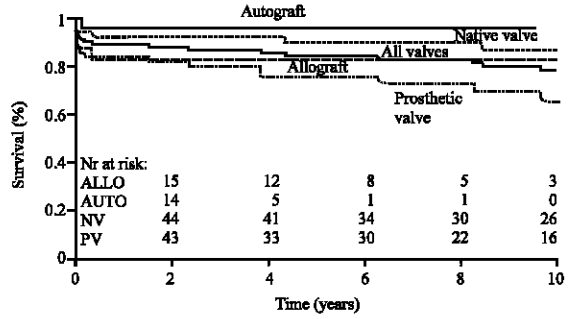


Fig. 1: Patient survival after reoperative aortic root replacement per valve substitute *in situ* before RARR

root at RARR (HR 10.0, 95% CI 2.2-45.5; p = 0.003) and concomitant mitral valve repair (HR 23.6, 95% CI 5.6-99.5; p<0.001). RARR on a prosthetic valve showed a trend to be a risk factor for late mortality (HR 2.8, 95% CI 0.9-8.6; p = 0.07).

**Valve-related events:** One PV patient who received an allograft root at RARR, underwent an aortic valve re-reoperation for structural failure. The allograft was replaced 9.7 years after RARR by a stentless bioprosthesis and the patient survived the procedure. One patient who received an allograft root at RARR had a non-fatal stroke after 14.1 years. Four patients had a TIA during follow up; one patient who underwent a Bentall procedure at RARR had a TIA after 0.1 years and 3 patients who received an allograft at RARR had a TIA, respectively after 0.3, 3.6 and 4.5 years of which 1 patient had two TIAs in the 1st year after RARR at 0.3 and 0.5 years, respectively. Linearized occurrence rates for thrombo-embolic complications were 1.2% patient year$^{-1}$ for RARR with an allograft and 0.65% patient year$^{-1}$ for RARR with a Bentall procedure. One patient who received an autograft at RARR had a late episode of recurrent endocarditis after 8.8 years (LOR 0.20% patient year$^{-1}$) and one allograft recipient at RARR had an episode of recurrent endocarditis after 1.5 years (LOR 0.30% patient year$^{-1}$). Both patients were treated medically and survived. No bleeding events, valve thrombosis, or non-structural failure were observed.

Reoperative aortic root replacement remains a high risk and demanding procedure. However, the study shows that it can be performed with satisfying results regarding operative mortality and long-term survival.

**Hospital mortality:** Overall hospital mortality after reoperative aortic root replacement is comparable to other series that report on hospital mortality after this type of surgery (Schepens *et al*., 1999; David *et al*., 2004; Kirsch *et al*., 2006). Hospital mortality for RARR after a previously inserted prosthetic valve was 14% in the study. Although this seems high compared with most of the other valve substitutes in the majority of these patients endocarditis was the indication for reoperation. Also most of these patients were severely symptomatic had an impaired left ventricular function and often underwent emergent or urgent surgery which were all potential predictors of hospital mortality. This is also described by David *et al.* (2004). Furthermore, surgery for prosthetic valve endocarditis is known to be associated with a higher urgency of surgery and a high hospital mortality rate (Lytle *et al*., 1996; Tornos *et al*., 1997). This can explain the high hospital mortality risk in these patients in the study.

Reoperative aortic root replacement after a previous allograft valve or root replacement in the study resulted in 13% hospital mortality. A possible explanation for this might be that RARR after a previous allograft implantation is a technically difficult and demanding procedure. It is complicated to make a proper proximal anastomosis due to the fact that the allograft not only calcifies in the part of the root but also at the annular level. Furthermore, the

coronary buttons need to be dissected from the calcified allograft, making it difficult to maintain a large enough button that can be properly reinserted without distortion or kinking. In some patients, unforeseen bypass grafting is necessary. These factors contribute in the study to a significantly longer CPB time and aortic cross clamp time compared with the other groups which are potentially associated with higher hospital mortality in the study.

Patients who had their native valve *in situ* and required RARR had a hospital mortality rate of 6%. All patients that died underwent a pulmonary autograft procedure. A pulmonary autograft procedure carries more risk than a conventional root replacement, especially as a reoperation but after successful operation survival of these patients is comparable to the age-matched general population (Klieverik *et al*., 2007). Patients reoperated on their native valve are the youngest of all study groups with low co-morbidity and required in most cases an elective reoperation with almost no concomitant procedures.

The pulmonary autograft procedure is the optimal solution in pediatric patients requiring aortic valve replacement (Elkins *et al*., 1994; Simon *et al*., 2001). Many studies favor the pulmonary autograft procedure also in young adult patients (Knott-Craig *et al*., 2000; Bohm *et al*., 2003; Yacoub *et al*., 2006) but enthusiasm for this operation has been tempered in recent reports due to the high incidence of reoperations (Kouchoukos *et al*., 2004; Luciani *et al*., 2005; Klieverik *et al*., 2007). However in this study, reoperation after the pulmonary autograft procedure shows a much better outcome with 0% hospital mortality so far, suggesting that reoperation after this procedure can safely be performed.

This is comparable to the findings of Brown *et al*. (2007). Yet at present in the institution, we perform the Ross operation as a secondary operation after previous aortic valve operation in young patients. For these patients, a third operation must be anticipated, probably at an age a Bentall operation will be chosen as a definitive procedure. For older adult patients requiring reoperation, we tend to perform a Bentall procedure. Main indication for reoperation after the Ross operation was an aneurysmal dilatation of the aortic root causing aortic valve regurgitation.

Although, an aneurysmal aortic root is still difficult to reoperate on, it takes less effort to explant a dilated autograft root than a calcified allograft root. The dilated aortic root allows a clear view at the insufficient autograft and its dilated annulus on which an anastomosis is easier to perform. Furthermore, the dilated pulmonary autograft wall shows no signs of calcification (Schoof *et al*., 2006). Although, a reoperation after the pulmonary autograft

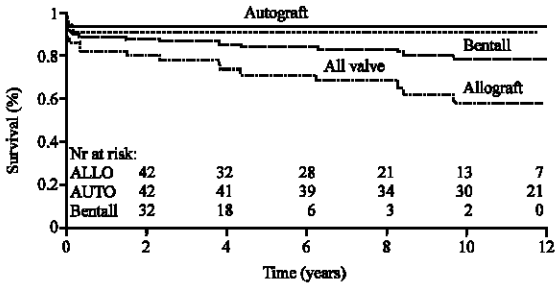


Fig. 2: Patient survival after reoperative aortic root replacement per valve substitute inserted at reoperation

procedure also requires reimplantation of the coronary arteries, the coronary buttons can be maintained to a larger size in absence of calcification which necessitates resizing. However, reimplantation of the coronaries after a pulmonary autograft is not without the risk of kinking of the coronary arteries sometimes necessitating coronary bypass grafting.

Three patients required an unplanned CABG due to distortion of the coronaries as a procedural complication; two autograft patients and one allograft patient of these patients one autograft patient and one allograft patient died. In the study, the need for an unplanned CABG is potential associated with a higher hospital mortality which is also reported in other series (Byrne *et al*., 2005; Kirsch *et al*., 2006).

**Long-term survival:** The overall 10 years survival in the study is 78% at 10 years and is satisfactory and even better compared with other reports (Schepens *et al*., 1999; David *et al*., 2004; Kirsch *et al*., 2006; Szeto *et al*., 2007). Comparing the four study groups, it shows that reoperation with a pulmonary autograft has the best long-term survival. Reoperation with an allograft root after previous surgery on the aortic valve or ascending aorta was one of the potential predictors of late mortality in the study and is also shown in Fig. 2. Most of the allograft recipients were older patients with prosthetic valve endocarditis which implies that not the inserted allograft but mostly patient and operative characteristics contributed to the increased late mortality, we observed in allograft recipients.

**Limitations:** The partially retrospective nature of study may have led to an underestimation of the valve-related events during follow-up which might have influenced the results. Furthermore, the four study groups differ in baseline characteristics which make comparisons between the groups difficult.

## CONCLUSION

The study indicates that reoperation after previous surgery on the aortic valve, ascending aorta or both can safely be performed. Although, several patient factors play a role, reoperation after a pulmonary autograft procedure has low hospital mortality and morbidity rates with long-term survival that is better compared with patients in which a reoperation is necessary after native valve repair or valvulotomy, a previous inserted allograft or prosthetic valve. In this respect, these results may contribute in the decision making in selecting the proper valve substitute in primary aortic valve replacement, especially in adolescents and young adults.

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