Aortic root replacement with either a biological or a composite mechanically valved aortic graft is still the gold standard for various aortic root/valve pathologies. 1,2 Hugh Bentall and Antony De Bono originally described the first complete replacement of the aortic valve and ascending aorta in a 33-year-old man with a large globular dilatation of the ascending aorta and aortic valve ectasia in 1968. For the next 20 years thereafter, mechanical composite grafts were uniformly used for patients with aortic root disease, and lifelong anticoagulation was inevitable.3,4

In the early 1960s, Ross5 and Barratt-Boyes6 had introduced the aortic homograft as an alternative for such patients, but limited availability was always an important issue. Xenograft aortic roots were, therefore, an appealing alternative because they would be potentially widely available. In 1965, Binet et al7 introduced the first stentless porcine xenoroot, but it was not further pursued because of difficulties with implantation. In the late 1980s, the glutaraldehyde-preserved porcine valve was introduced with the hope that it may share many of the advantages of the homograft (ie, providing physiological flow in the aortic root, sinuses, and coronary orifices and a low risk of thromboembolism).

Longevity After Aortic Root Replacement
Is the Mechanically Valved Conduit Really the Gold Standard for Quinquagenarians?

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Background—The choice of the best conduit for root/ascending disease and its impact on longevity remain controversial in quinquagenarians.

Methods and Results—A total of 205 patients (men=155) between 50 and 60 years (mean, 55.7±2.9 years) received either a stentless porcine xenoroot (n=78) or a mechanically valved composite prosthesis (n=127) between February 1998 and July 2011. Of these, 166 patients underwent root replacement for aneurysmal disease (porcine: 39% [n=65]; mechanical: 61% [n=101]; P=0.5), 25 for acute type A aortic dissection (porcine: 32% [n=8]; mechanical: 68% [n=17]; P=0.51), and 14 for endocarditis/iatrogenic injury involving the aortic root (6.4% [n=5] versus 7.1% [n=9]; P=1.0). The predominant aortic valve pathology was stenosis in 19% (n=38), regurgitation in 50% (n=102), combined valvular dysfunction in 26% (n=54), and normal aortic valve function in 5% (n=11). Concomitant procedures included coronary artery bypass grafting (13%), mitral valve repair (7%), and partial/complete arch replacement (12%/4%), with no significant differences between porcine and mechanical root replacement. Overall hospital mortality was 7.3%, with no difference between the 2 types of valve prostheses (porcine: 7.7% for porcine and 7.1% for mechanical root replacement; P=1.0). Follow-up averaged 5.4±3.7 years (1096 patient-years) and was 100% complete. Freedom from aorta-related reoperation at 12 years was not statistically different between the groups (porcine: 94.9% versus mechanical: 96.1%; P=0.73). Survival was equivalent between both groups, with a 5-year survival of 86±3% (porcine: 88±4%; mechanical: 85±3%; P=0.96) and a 10-year survival of 76% (porcine: 80±7%; mechanical: 75±5%; P=0.84). The linearized mortality rate was 3.1%/patient-year (porcine: 2.9%/patient-year; mechanical: 3.2%/patient-year).

Conclusions—In quinquagenarians, long-term survival after stentless porcine xenograft aortic root replacement is equivalent to that after a mechanical Bentall procedure. These results bring into question the predominance of mechanical composite conduits for root replacement in quinquagenarians, particularly in the current era of transcatheter valve-in-valve procedures for structural valve deterioration. (Circulation. 2013;128[suppl 1]:S253-S262.)

Key Words: aneurysm ■ aorta ■ aortic valve ■ surgical procedures

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In the early 1990s, Dr Griepp and colleagues introduced the biological Bentall, a homemade bioprosthetic composite graft formed by sewing readily available stented bioprostheses to collagen-coated vascular grafts. This technique enabled technically uncomplicated and durable aortic root reconstruction in patients who were unable or reluctant to take anticoagulants. The BioBentall offered excellent long-term survival and low rates of thrombembolic and bleeding complications, with only 1 late reoperation for structural failure in a series of 275 consecutive patients.

More recently, aortic valve-sparing operations have become a viable alternative in the setting of aortic root dilatation associated with pure aortic regurgitation. These techniques, however, are limited to patients with pliable valve cusps, thereby precluding the vast majority of patients with bicuspid aortic valve disease, and should probably be limited to reference centers because of the relative rarity of such patients and complexity of the operations.

According to the current American Heart Association guidelines, aortic valve replacement with a mechanical valve is the first-line therapy for patients aged <65 years in the absence of contraindications for chronic anticoagulation, whereas a biological prosthesis is recommended beyond the age of 65 years. The more recently published European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines recommend mechanical valve replacement for aortic valve disease in patients aged ≤60 years. Part of the reason why the European Society of Cardiology/European Association for Cardio-Thoracic Surgery lowered the age cutoff is improved durability of contemporarily available new-generation tissue valves. Several studies have recently compared contemporary tissue valves versus mechanical prostheses in young patients.

In the setting of combined aortic valve/root disease, the impact of 2 of the most popular conduits, that is, new-generation xenografts and mechanical composite grafts, remains controversial, particularly in young patients. The objective of the current study was to compare the results of mechanical composite aortic root replacement withporcine root xenograft replacement in a cohort of patients between the age of 50 and 60 years. We chose to focus on this group because the choice of the conduit is traditionally controversial and may be particularly crucial for long-term survival.

**Methods**

A review of our institutional database revealed a total of 824 patients who underwent aortic root replacement either with a mechanical Advancing the Standards Medical, Inc. composite graft (Medtronic; n=476) or with a stentless porcine aortic root xenograft (n=348, see below for type of prostheses) from 1998 through 2011. Of these, 205 patients were between the age of 50 and 60 years and form the basis of this study. Xenograft patients who received a root inclusion or miniroot implantation were excluded. Clinical data were retrospectively analyzed from our institutional database and individual patient records. The local ethics committee did not require additional patient consent.

**Patient Demographics**

A total of 205 quinquagenarians (155 men; mean age, 55.7±2.9 years; median, 56 years) who underwent aortic root replacement at our institution between February 1998 and July 2011 were included. A mechanical composite aortic root replacement was performed in 127 patients (62.0%), and 78 patients (38.0%) received a stentless porcine root xenograft (Figure 1). The mean EuroSCORE was 11.4±8.8 for elective patients, 13.1±8.7 among patients with an urgent indication for surgery, and 29±24.5 among emergency cases.

A total of 128 (62.4%) patients were regarded as low risk (ie, primary elective cases excepting infective endocarditis and complete arch replacement surgery). High surgical risk was present in 41 (20%) patients (ie, acute type A aortic dissection or acute infective endocarditis, patients receiving complex concomitant arch reconstructions, and emergency procedures). The remaining 36 patients were classified as intermediate risk, and the clinical characteristics of all patient groups are summarized in Table 1.

The maximum root/ascending aorta diameters at the time of surgery did not differ between the 2 valve prosthesis groups (xenooort: 53±12 mm versus mechanical composite: 54±9 mm; P=0.31). Patients receiving a xenograft were slightly older than patients receiving a mechanical conduit (56.3±2.8 versus 55.3±2.9 years; P=0.01), but cardiovascular risk factors (ie, chronic obstructive pulmonary disease, history of smoking, diabetes mellitus, hyperlipidemia) were evenly distributed between both groups (Table 1).

The majority of patients had a tricuspid aortic valve (n=124), whereas 59 patients had a bicuspid aortic valve. Aortic valve morphology was evenly distributed between the 2 valve groups: 60% of the patients with a bicuspid aortic valve (n=35) versus 62% of the patients with a tricuspid valve (n=77) received a mechanical conduit (P=0.74). In 22 patients, the aortic valve morphology was not clearly specified. Of these, 14 had received an aortic valve prosthesis previously and underwent redo aortic valve surgery because of valve degeneration, infective endocarditis, or paravalvular leak. An additional 23 patients (11%) had prior cardiac surgery other than aortic valve surgery.

**Indication for Surgery**

The indication for aortic root replacement was valve disease with an aneurysmal root/ascending aorta in 81.5% (n=167), aortic dissection in 12.2% (n=25), infective endocarditis in 3.4% (n=7), and other indications in the remaining patients: 1.5% (n=3) had a small aortic root not amenable to patch enlargement, that is, a Manougian-Rastan or a Nick procedure, 1% (n=2) had failure of aortic valve replacement/repair requiring emergency root replacement, and 0.5% (n=1) had fragile wall tissue of the native root. Half of the patient population (n=102/205) presented with severe aortic regurgitation and received either a stentless porcine xenograft (n=38/78 xenografts, 49%) or a mechanical composite prosthesis (n=64/127 composite grafts, 50%). Severe aortic stenosis was present in 19% of all patients (n=38/205), and combined valve dysfunction was present in 54 patients (26%). In 10 patients (5%), there was no significant aortic valve dysfunction, but mechanical root replacement was performed because of root aneurysm after previous aortic valve replacement in 6 patients (including 2 patients with a Bjork-Shiley prosthesis), prosthetic valve endocarditis with root abscess in 2 patients, acute type A aortic dissection in 2 patients, and infected aortic root prosthesis in 1 patient.

**Figure 1.** Graft types used for aortic root replacement. SJM indicates St. Jude Medical.
involving the aortic root after previous aortic valve replacement in 1 patient, and perforated sinus aneurysm in 1 patient.

Concomitant Procedures
Concomitant procedures consisted of subvalvular myectomy (Morrow’s, 3% of total), coronary artery bypass grafting (13%), and mitral valve replacement or repair (7%). In addition, concomitant partial (n=25; 12%) or complete (n=8; 4%) arch replacement was required in 23 patients (Table 2).

Surgical Technique
Cannulation and Myocardial Protection
Our standard surgical approach was via a midline sternotomy, although some patients underwent surgery via an upper hemisternotomy. If the aortic pathology was limited to the proximal part of the ascending aorta, arterial cannulation was performed via the distal ascending aorta (n=101; 49%). Alternatively, cardiopulmonary bypass (CPB) was established via the aortic arch (n=49; 24%), the right axillary artery (n=32; 16%), or the femoral artery (n=23; 11%). Femoral cannulation was principally used for patients requiring redo surgery with an aneurysm that was located in close proximity to the sternum or when severe adhesions were anticipated (n=20). Emergency femoral cannulation was used for acute type A aortic dissection in 1 patient.

Venous drainage was established by direct cannulation of the right atrium via a 2-stage catheter (n=181; 88%) or via a wire-directed drainage cannula in the left or right femoral vein (n=24; 12%). A vent was placed in the left ventricle by cannulation of the upper right pulmonary vein to allow for decompression of the heart.

Average minimum core temperature was 30.0±5°C (30.3±4.7°C versus 29.7±4.8°C; P=0.15). Mean CPB time was 154±92 (median, 132) minutes and did not differ significantly between the 2 groups. Mean aortic cross-clamp time was longer in patients receiving a biological valved conduit (103±29 versus 100±50 minutes; P=0.02; Table 2).

Surgery was performed with mild-to-moderate hypothermia at 30°C to 34°C in the majority of cases. Myocardial protection was performed with antegrade cold crystalloid cardioplegia (Bretschneider HTK solution, Köhler Chemie, Alsbach-Hähnlein, Germany) in 82% of patients (n=169; xeno: n=60 [77%], mech: n=109 [86%]), intermittent blood cardioplegia in 17% (n=35; xeno: n=18 [24%], mech: n=17 [13%]), and St. Thomas cardioplegic solution in 1% (mech: n=1).

In the majority of patients, a clamped distal anastomosis was performed during antegrade body perfusion (n=151), whereas in 8%, selective antegrade cerebral perfusion was established for brain protection during hypothermic circulatory arrest (n=19). Isolated retrograde cerebral perfusion was used in 2.4% of cases (n=5), a technique which was abandoned in 2005. A short period of deep hypothermic circulatory arrest was used in 15% of patients (n=30) for an open distal anastomosis.

Aortic Root Replacement and Choice of Conduit
Patients opted for either a biological or a mechanical conduit after in-depth discussion with the operating surgeon. A mechanical valve was usually routinely recommended for patients aged <65 years if there were no significant contraindications to oral anticoagulation.
and the patient was not eligible for valve repair. One third (n=78) of patients might have potentially been eligible for valve repair (ie, presenting with a tricuspid aortic valve without calcifications/no stenotic disease); however, the surgeon (eg, because of technical new intraoperative findings) made the decision to replace the valve in these cases. In patients who could not be consented (ie, intubated patients requiring emergency surgery), the operating surgeon made the choice of conduit after considering the patient’s comorbidities on an individual basis.

Mechanical root replacement was exclusively performed with a mechanical aortic valve graft prosthesis (ATS Medical, Minneapolis, MN). Two different types of stentless porcine root xenografts were implanted: 49 patients received a Freestyle graft (Medtronic Inc, Minneapolis, MN) and 29 patients a St. Jude Medical Toronto root prosthesis (St. Jude Medical Inc, St. Paul, MN). Mean prosthesis size was 25±2 mm in the mechanical group versus 26±2 mm in the biological group (P=0.04).

Early postoperative anticoagulation was performed according to current recommendations. After mechanical root replacement, intravenous heparin was administered with a target partial thromboplastin time of 60 to 80 seconds, along with oral coumadin until a target international normalized ratio of 2.0 to 3.0 was attained. After aortic root replacement with a xenograft, intravenous heparin was replaced by subcutaneous low-molecular heparin in therapeutic dose when the patient was transferred to the general ward. Oral coumadin was routinely administered for 2 to 3 months postoperatively in xenograft patients.

**Management of Aneurysms Involving the Aortic Arch**

Partial (hemi-) arch replacement was performed whenever the underlying aortic disease did not extend into the distal arch or affect the supra-aortic vessels. For full arch replacement, a small island of supra-aortic branches was sewn to a Hemashield graft during antegrade selective cerebral perfusion (SCP) or, in rare cases, during a short period of hypothermic circulatory arrest. The elephant trunk technique was used when subsequent replacement of the descending part of the aorta was anticipated.

**Selective Cerebral Perfusion**

Antegrade SCP was used in 9% (n=19), and our institutional technique has been described elsewhere. Cannulation for SCP was via the right axillary artery, achieving bilateral antegrade SCP after cross-clamping of the innominate artery and insertion of a balloon perfusion catheter in the left carotid artery (and balloon occlusion of the left subclavian artery): 13 patients received bilateral SCP, whereas in 6 patients unilateral SCP via the right axillary artery was performed.

**Follow-Up**

The data of our prospectively and continuously maintained institutional database were collected and supplemented by additional data from individual patient records. Follow-up data were obtained by our research personnel either by direct telephone interview with the patient or the next of kin or by contact with the referring cardiologist or general practitioner.

Overall follow-up was 100% complete at a mean follow-up period of 5.4±3.7 years (range, 0–13 years; median, 5.2 years; 1096 cumulative patient-years; median follow-up time of survivors was 5.2 years) postoperatively. Follow-up was closed on July 18, 2011.

**Statistical Methods**

Patient and disease characteristics are described as percentages or means±SDs. Continuous variables were analyzed using the Wilcoxon log-rank test. Categorical data were analyzed using the χ², Armitage trend, or Fisher exact test, where appropriate. Long-term survival was depicted by Kaplan–Meier curves and compared between the 2 groups using the log-rank test. The linearized mortality rate (LMR) was calculated as 100× the total number of observed deaths during the entire follow-up period divided by the total person-years of follow-up. All tests were performed as 2-sided at a significance level of 5%.
Factors influencing survival were initially explored by separate univariable analyses for patients with biological and mechanical valves, each considering factors related to operative or long-term death. Operative death was defined as death within 30 days after the procedure or death before discharge if beyond 30 days. The Cox proportional hazards model was used to identify significant risk factors associated with long-term death. After univariable analysis, factors that showed a significant influence on survival ($P<0.1$) were analyzed by multivariable Cox proportional hazards model using stepwise regression. To adjust for the potential influence of variables that might be associated with the choice of conduit, we calculated an individual propensity score for each patient from the following variables: age at surgery, infective endocarditis, sex, and prior cardiac surgery. The propensity scores were subsequently included in the final Cox regression model as an additional risk factor. Prosthesis-related complications were recorded according to the Guidelines for Reporting Morbidity and Mortality After Cardiac Valvular Interventions. \cite{19}

Results

Operative Mortality and Causes of Death

Overall hospital mortality, defined as death in hospital or within 30 days after surgery, was 7.3\% ($n=15$) and equivalent for both groups: stentless porcine xenograft recipients had a hospital mortality of 7.7\% ($n=6/78$) and mechanical composite recipients 7.1\% ($n=9/127$; $P=1.0$; Figure 2).

Hospital mortality was 1.6\% in low-risk cases ($n=2/128$; 2.0\% versus 1.3\%; $P=1.0$), 5.6\% in patients in intermediate-risk cases ($n=2/36$; 7.2\% versus 4.5\%; $P=1.0$), and 26.8\% in high-risk cases ($n=11/41$; 30.8\% versus 25.0\%; $P=0.72$; see Methods for definition of risk classification).

From the 6 patients who experienced early mortality after stentless porcine xenoroot replacement, 2 died—on day 2 and day 10 after surgery—of intractable low cardiac output syndrome. One patient experienced sudden cardiac death on postoperative day 9 (cause of death: electromechanical dissociation). Two patients died from stroke/cerebral ischemia, 1 on day 3 and 1 on day 17 postoperatively: one had undergone emergency surgery for acute type A aortic dissection and the other required prolonged cardiopulmonary resuscitation (CPR) postoperatively. One patient with a significant history of smoking died from ischemic bowel disease 40 days after surgery.

In the mechanical root replacement group, 4 patients experienced fatal cerebral ischemia on postoperative days 1 ($n=2$), 7, and 14. Three of these patients underwent emergency surgery for type A dissection, 1 of whom was taken to the operating room as a last resort during prolonged CPR for $>60$ minutes. One patient, who presented with impending mesenteric ischemia because of visceral malperfusion (caused by the obstructive dissection membrane), died from multiorgan failure a few hours after surgical repair of his aorta, whereas 1 patient died from refractory septic shock on postoperative day 20. Three patients died of low cardiac output syndrome on postoperative days 3, 13, and 15, with 2 of them undergoing postoperative extracorporeal membrane oxygenation therapy as a last resort.

Postoperative Assessment of Valve Function

Postoperative echocardiographic studies before hospital discharge were available in 77\% ($n=157$) of patients. Mean postoperative left ventricular ejection fraction was 57±11\% in the porcine root group versus 58±12\% in the mechanical root group ($P=0.98$). Mean transvalvular gradients in the porcine roots were 11±5 (maximum gradient, 19±8) mm Hg compared with 13±5 (maximum gradient, 24±10) mm Hg in the composite roots and not statistically different ($P_{\text{max}}=0.11/P_{\text{mean}}=0.12$). No significant aortic insufficiency (I+ or more) was detected in any mechanical valve patient. However, 4 patients in the porcine root group had aortic insufficiency grade I (3 patients after implantation of the Freestyle prosthesis and 1 patient after root replacement with the Toronto prosthesis).

Early Postoperative Complications

During the early postoperative period, rethoracotomy for severe bleeding or pericardial effusion was required in 9.3\% of all patients ($n=19$; stentless porcine xenoroots: 11.5\%...
versus mechanical composite grafts: 7.9%; \( P=0.46 \). Twelve patients (6%) required pacemaker implantation for complete heart block.

**Long-Term Survival and Risk Factors for Long-Term Mortality**

Overall 1-year mortality was 7.8% (n=16): 7 patients with a biological valve (9%) versus 9 patients with a mechanical valve (7%) died during the first year (\( P=0.6 \)). One-year mortality was 4.4% in elective patients (n=7/159), 5.0% (n=1/20) in urgent cases, and 31% (n=8/18) in emergency patients. One-year mortality was 3.8% in low-risk patients (n=3; 3.9% versus 1.3%; \( P=0.56 \)), 5.6% in intermediate-risk patients (n=2; 7.1% versus 4.5%; \( P=1.0 \)), and 26.8% in high-risk patients (n=11; 30.8% versus 25.0%; \( P=0.72 \)).

Longevity was equivalent between both groups, with a 5-year-survival of 86±5% in all patients: 88±4% versus 85±3% for xenoroot versus mechanical composite graft recipients (\( P=0.96 \)). Overall 10-year survival was 76±4%, 80±7% among patients who received a porcine xenoroot versus 75±5% among mechanical composite graft recipients (\( P=0.84 \)). We observed a total of n=35 long-term deaths (n=11 after biological root replacement versus n=24 after mechanical root replacement). Excluding patients who experienced in-hospital death, long-term survival was still equivalent in xenoroot recipients and composite root recipients (92±4% versus 91±3% after 5 years, \( P=0.79 \), and 87±6% versus 74±8% after 12 years, \( P=0.61 \), xenoroot versus composite root, respectively).

One year after surgery, the LMR declined to 1.7%/y and was significantly lower in the xenoroot group (1.2%/y in the porcine xenoroot group versus 2.0%/y in the mechanical composite graft group; Figure 3A).

Overall long-term survival did not significantly differ with regard to sex (men: 76±5% versus women: 63±11% after 12 years; \( P=0.24 \)). Sex-specific analysis did not reveal any but a statistically significant differences after stentless porcine versus mechanical composite root replacement (women: 92±4% versus 71±6% after 12 years; \( P=0.12 \)), men: 58±15% versus 69±14% after 12 years; \( P=0.26 \)). Long-term survival of bicuspid aortic valve patients (mean age, 55.6±2.9 years) was higher compared with that of tricuspid aortic valve patients (mean age, 55.9±2.9), but this difference did not reach statistical significance (90±4% versus 67±7% after 12 years; \( P=0.13 \)).

Comparing the different porcine xenografts used in the study, long-term survival was 78±9% in patients who received a Medtronic Freestyle valve versus 84±8% in patients who received a St. Jude Medical Toronto root after 8 years (\( P=0.49 \); Figure 3C).

Risk factors included in the univariable analyses of mortality were age at surgery, CPB time, sex, diabetes mellitus, chronic obstructive pulmonary disease, hyperlipidemia, history of smoking, hypertension, type A dissection, prior cardiac surgery, cross-clamp time, concomitant procedures, concomitant coronary artery bypass grafting, concomitant mitral valve surgery, partial arch replacement, total arch replacement, and emergency operation. Multiple Cox regression revealed CPB time (\( P=0.01 \)), concomitant mitral valve replacement/repair (\( P=0.02 \)), concomitant full arch replacement (\( P=0.03 \)), and emergent timing (\( P=0.01 \)) as independent predictors of long-term mortality. Adjustment by propensity score did not influence these risk factors (Figure 4). The proportional hazards assumption of the Cox model was tested by calculating a Cox model with a time-dependent covariable, which resulted in a nonsignificant effect for this covariable (hazard ratio, 1.05 [0.83–1.33]; \( P=0.69 \)).

Risk factor analysis for long-term mortality after composite mechanical root replacement revealed CPB time (hazard ratio, 1.003; 95% confidence interval, 1.001–1.005; \( P<0.01 \)) and concomitant full arch replacement (hazard ratio, 6.15; 95% confidence interval, 1.79–21.1; \( P<0.01 \)) as significant risk factors. CPB time was the only statistically significant risk factor for long-term mortality among porcine xenoroot recipients (hazard ratio, 1.02; 95% confidence interval, 1.01–1.04; \( P<0.01 \)).

**Long-Term Survival in Patients After Primary Elective Root Replacement**

In patients undergoing primary elective operations only (Figure 3B), hospital mortality did not statistically differ between groups (xenoroots: 5.1% versus mechanical composite: 2.4%; \( P=0.65 \)). Survival was also equal after 5 (91.1±3.8 versus 93.0±3.1%; \( P=0.46 \)) and 10 years (84.6±7.2 versus 76.2±6.4; \( P=0.9 \)).

Long-term survival after 12 years was statistically not different between the groups, being 84.6±7.2% in the porcine group versus 75.9±6.4% in the mechanical group (\( P=0.84 \)). The LMR was 1.7%/patient-year versus 1.5%/patient-year after the first postoperative year.

**Long-Term Adverse Events**

Adverse events, such as aorta/valve-related reoperation, stroke, or bleeding, were recorded during long-term follow-up. Cerebrovascular events (stroke or hemorrhage) occurred in 3 porcine xenoroot recipients at 6 months, 1.3 years, and 3.2 years postoperatively (affecting 1.5% of the entire cohort and 3.8% of the xenoroot recipients). No recipient of a composite mechanical compound had a late stroke (\( P=0.05 \)). Severe gastrointestinal bleeding did not occur during the follow-up period. Event-free survival was statistically significantly inferior after porcine xenoroot replacement (95±3% versus 100±0%) after 12 years (\( P=0.02 \); Figure 5), with a total number of n=3 events (n=0 for composite root recipients, n=3 for xenoroot recipients). During follow-up, 3 patients in the porcine group (all endocarditis) versus 1 patient in the mechanical group (as a result of thrombotic appositions) required a valve-related reoperation (\( P=0.11 \)).

Freedom from aorta and valve-related reoperation after 12 years was also equivalent between groups (porcine xenoroots: 94.9% versus composite mechanical graft: 96.1%; \( P=0.73 \)).

**Discussion**

Improved durability of new-generation stented bioprostheses for aortic valve replacement has triggered discussions about the appropriate age threshold in the setting of combined aortic valve/root disease when root replacement is required.11,20 The advantages of contemporary stentless porcine xenoroots versus mechanical composite valved conduits are a subject of debate.
Limitations of the 2 main graft types (ie, thromboembolic and bleeding complications of obligatory oral anticoagulation after mechanical composite root replacement and early valve deterioration with biological grafts) have led to an ongoing quest for the optimal prosthesis, particularly in quinquagenarians. Such patients are on the verge of various physiological changes (ie, less aggressive immune response toward biological implants, imminent menopause potentially affecting anticoagulation in women) that may influence prosthesis choice in patients.

The results from previous trials comparing different aortic valve prostheses are not completely applicable to patients requiring aortic root replacement for various reasons: (1) artificial conduits may influence blood flow characteristics in the aortic root and thereby influence valve longevity; (2) some valve prostheses are not available as conduits and can only be used as homemade composite grafts; (3) first-generation stentless porcine root xenografts have been reported to have limited long-term durability compared with their stented analogs.

Our goal was to compare early and long-term outcomes in patients who underwent aortic root replacement surgery with either a mechanical valved conduit or a contemporary porcine stentless xenoroot. To obtain suitable groups for comparison, we selected the cohort for this retrospective analysis from one of the largest contemporary single-center experiences with root replacement presently available, adding a propensity score into the risk factor analysis for long-term outcome.

**New-Generation Stentless Porcine Xenografts Versus Mechanical Composite Conduits**

Overall, our findings suggest no significant difference in long-term survival between the new-generation xenografts and modern mechanical composite prostheses after root replacement surgery in quinquagenarians. Both groups displayed equivalent long-term outcomes, including the need for reoperations, ≤10 years postoperatively. The Toronto root bioprosthesis with BiLinx anticalcification treatment (St. Jude Medical) was introduced into clinical practice in 2001. Although this prosthesis is no longer available, we decided to include it in our analysis for reference purposes.22 The widely available Medtronic Freestyle aortic root model 995 was used in the majority (72%)

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**Figure 3.** Long-term survival after porcine vs mechanical composite root replacement. Long-term survival after a follow-up of 12 years is equal after biological vs mechanical root replacement (P=0.68; A). In a subgroup including primary elective operations only, survival also equals in both groups (P=0.84; B). Survival did not depend on the choice of the porcine xenoroot: 78±9% (Medtronic Freestyle, red line) vs 84±8% (St. Jude Medical [SJM] Toronto root, blue line) after 8 years (P=0.49; C).
of xenograft recipients in our series. The prosthesis offers good tissue handling and implantability, with excellent hemodynamics compared with stented or mechanical valves.\textsuperscript{23,24}

Mechanical composite prostheses used in this series were exclusively equipped with ATS aortic valves, which are designed to achieve optimal leaflet opening in a straight conduit with in vitro mean and maximum pressure gradients of 2.1 and 4.6 mm Hg, respectively. The gradients of the ATS valve observed in our study were clearly higher than in vitro values, but in vivo gradients are known to be higher, particularly in smaller prostheses, because of the fact that echocardiographically measured velocities in the central orifice of a bileaflet valve may be significantly higher than simultaneously obtained catheter gradients.\textsuperscript{25,26}

Advantages of Stentless Xenograft Roots
Early regression of left ventricular hypertrophy after stentless valve implantation has been demonstrated in longitudinal studies. However, modern mechanical valve prostheses are also associated with low gradients, and therefore the effect of this advantage on long-term survival is likely negligible. Hospital mortality for low-risk patients is low for aortic root replacement surgery, regardless of the conduit used, approaching that observed for patients undergoing isolated aortic valve replacement surgery.

We failed to find a significant difference in hospital and 1-year mortality for recipients of stentless porcine xenoroots and mechanical composite valve grafts. In addition, no differences were observed between groups according to operation timing (elective, urgent, or emergent) or risk stratification. Although long-term survival was not statistically different between the 2 groups, the LMR was significantly lower in the porcine xenoroot group 1 year after surgery (1.2%/y in the porcine xenoroot group versus 2.0%/y in the mechanical composite graft group; Figure 3A).

Embolic cerebrovascular accidents occurred in 3 xenograft recipients within the first 3 years postoperatively, whereas none of the mechanical composite recipients experienced a stroke during follow-up—a finding that might be confounded by underlying medical conditions requiring oral anticoagulation (ie, with atrial fibrillation) and linked to the inability to undergo warfarin therapy. From the 3 xenoroot patients who experienced a stroke, 1 had multiple cardiovascular risk factors (including hyperlipidemia, hypertension, insulin-dependent diabetes mellitus) and 1 patient had paroxysmal atrial fibrillation, whereas the third patient did not have any significant risk factors. On the contrary, severe bleeding complications or an increased rate of valve thrombosis in patients with a mechanical valve replacement have been reported and are potentially life limiting.\textsuperscript{27–30} Interestingly, we did not observe severe bleeding complications or valve thrombosis during our follow-up period, a finding that is in concordance with previous studies.\textsuperscript{15,16} Only 1 patient in the mechanical valve group needed a reoperation because of a valve-related complication. These results correspond to the findings of Emery et al\textsuperscript{31} who also described a low complication rate in the long-term follow-up of the St. Jude Medical prosthesis in young patients.
patients. One may speculate that anticoagulation-related complications mainly affect elderly patients. Excessive bleeding complications or valve thromboses are mainly reported in the follow-up of patients with a Bjork-Shiley prosthesis, whereas modern bileaflet prostheses have been shown to have a lower incidence of these life-threatening complications.30,31

A mechanically valved conduit remains the prosthesis of choice in young patients with aortic root disease and an aortic valve that is not amenable for repair. However, our data would suggest that the age threshold for the use of new-generation xenoroots may need to be lowered.

The ease with which a previously implanted biological valve in a homemade BioBentall conduit can be replaced during reoperative surgery does not necessarily apply for the porcine xenoroot prosthesis.32 Indeed, some investigators have observed increased technical difficulty and worse outcomes for reoperative procedures after stentless aortic valve replacement surgery.33,34

Mechanical composite prostheses are undoubtedly superior regarding long-term durability, but lifelong anticoagulation may limit patient quality of life.35 However, although an accumulated risk of bleeding has been described and certainly is not to be underestimated, particularly with increasing age of the recipient when bleeding complications may become more threatening, we failed to note any episodes of severe bleeding in the entire cohort during a 12-year follow-up period.

Clinical Implications

Overall, our findings suggest no significant difference in long-term survival and other major adverse events between the new-generation xenografts and modern mechanical composite prostheses after root replacement in quinquagenarians. Considering the significantly lower LMR after the first year postoperatively among porcine xenograft recipients (and the future option of reoperative minimally invasive transcatheter valve replacement in case of valve deterioration), our data support the notion that mechanically valved composite grafts should no longer be considered the gold standard in this age group.

Study Limitations

Because of its retrospective character, the present study is subject to selection biases. As mentioned above, selection of the valve (tissue versus mechanical) was not randomized. However, we attempted to limit the effects of selection bias with the use of a propensity score included as a variable in the risk factor analysis. The risk factors for long-term mortality were not influenced after including the propensity score as an additional variable in the analysis. Therefore, we concluded that the parameters included in the propensity score (age at surgery, infective endocarditis, sex, prior cardiac surgery) did not significantly influence long-term survival in our study group. We did not provide a propensity-matched analysis because the groups would have become too small to provide reliable outcome data.

Rationale for the Choice of Conduit and Linked Outcome

The current American Heart Association guidelines clearly recommend the implantation of a mechanical valve in the young patient. However, there are mainly 3 reasons to opt for a biological conduit in patients aged <60 years: (1) contraindications to chronic anticoagulation (such as protein C deficiency, coagulation disorders, severe liver disease), (2) patient’s refusal (eg, planned pregnancy)/foreseen lack of compliance to reliably take anticoagulants (eg, psychological disorders or chronic drug abuse), and (3) general (patient’s) preference for a biological conduit. This alone has a potential impact on outcome and may explain the higher stroke rate among recipients of porcine xenoroots, because the reluctance concerning anticoagulants may also apply in case of atrial fibrillation—the major risk factor for cerebrovascular embolism. The findings by Weber et al36 also support this assumption because they found chronic anticoagulation to be a protective factor for long-term survival after biological aortic valve replacement with pericardial valves in patients aged <60 years.

Another limitation is the fact that our follow-up was limited to a maximum of 13.3 years, which may be important given that structural valve degeneration occurs much more frequently for biological valves after a period of 12 to 15 years. Similarly, in a patient cohort of 275 biologically valved conduits, reoperation for xenograft failure at 12 years was only necessary in a single patient.13 However, the negative effects of structural valve deterioration in this patient age group may be mitigated by the performance of transcatheter valve-in-valve implantation in the coming years.37,38 As our institutional database is continuously maintained, further follow-up data will be available to clarify these concerns in the next few years.

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Disclosures

None.

References


Longevity After Aortic Root Replacement: Is the Mechanically Valved Conduit Really the Gold Standard for Quinquagenarians?
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