Stentless biological valved conduit for aortic root replacement: Initial experience with the Shelhigh BioConduit model NR-2000C

Abdullah Kaya, MD,^a Robin H. Heijmen, MD, PhD,^a J. C. Kelder, MD,^b Marc A. Schepens, MD, PhD,^c and Wim J. Morshuis, MD, PhD^a

Objectives: We retrospectively evaluated our results with the Shelhigh biological conduit model NR-2000C (Shelhigh, Inc, Milburn, NJ).

Methods: From November 1998 through December 2007, 175 patients with a mean age of 71.1 ± 7.4 years underwent aortic root replacement with a Shelhigh biological conduit. Indication for surgery was aneurysmal disease of the aorta in 120 (68.6%) patients, aortic valve endocarditis in 20 (11.4%), acute type A aortic dissection in 11 (6.3%), and other in 24 (13.7%) patients.

Results: Overall hospital mortality was 13.7% ($n = 24$; 95% confidence limits, 9.0%–19.7%). Cause of death was cardiac failure in 12 patients, central neurologic damage in 5 patients, pulmonary in 3 patients, gastrointestinal ischemia in 2 patients, and aorta-related in 2 patients. Mean follow-up was 3.1 years (range 0.2–9.9 years). In total, 50 (33.1%) late deaths occurred; of these 7 were valve-related. The overall survival at 1 and 5 years is $77.6\% \pm 3.2\%$ and $54.6\% \pm 4.6\%$ respectively. Six (4.0%) patients required reoperation, either for endocarditis of the bioconduit ($n = 5$) or for false aneurysm ($n = 1$). Endocarditis of the bioconduit was reported in 11 (7.3%) patients, of whom 6 were treated nonoperatively and 5 required reoperation.

Conclusions: Midterm results of the implantation of the Shelhigh biological valved conduit are worrisome. The relatively high incidence of endocarditis of the Shelhigh BioConduit has forced us to look for other alternatives. (J Thorac Cardiovasc Surg 2011;141:1157–62)

Bentall and DeBono¹ described the first complete replacement of the aortic root with a conduit in 1968. The initial composite valved graft contained a mechanical valve, but nowadays there are also complete biological conduits as substitutes for aortic root replacement. The homograft or autograft is an alternative but has the disadvantage of limited donor availability and durability.² Aortic valve-sparing surgery may not be applicable for all pathologic situations of the aortic root and in particular the aortic valve.^{3,4} Nowadays, only a few biological valved conduits are readily available off the shelf in all sizes and without the need for lifelong oral anticoagulation. At the end of the 1990s, a new stentless biological valved conduit, the Shelhigh BioConduit model NR-2000C (Shelhigh, Inc, Milburn, NJ), was introduced. This is a bovine pericardial straight graft with an incorporated porcine stentless valve, which is glutaraldehyde cross-linked, detoxified, and heparin treated (No-React process). Since 1998 we have used this

biological valved conduit for aortic root replacement in elderly patients or for specific indication, such as infective aortic root abscesses. In this report we describe and analyze our initial results.

PATIENTS AND METHODS

Patients

From November 1998 through December 2007, 175 patients with a mean age of 71.1 years (range, 31–84 years) underwent aortic root replacement with a Shelhigh BioConduit model NR-2000C. Fifty-two (29.7%) patients were 75 years or older. There were 102 (58.3%) male and 73 (41.7%) female patients. The ethics committee approved this retrospective cohort study and waived the need for patient consent. Aortic root diseases treated with this complete biological conduit consisted of the following: aneurysm, $n = 120$ (68.6%); aortic valve endocarditis, $n = 20$ (11.4%); acute type A aortic dissection, $n = 11$ (6.3%), calcified (“porcelain”) aortic root, $n = 8$ (4.6%); and other, for example, small aortic annulus or aortic stenosis owing to pannus formation after previous aortic valve replacement, $n = 16$ (9.1%). The intervention was a reoperation after previous cardiac surgery in 45 patients (25.7%), of whom the majority (33 patients) had previous aortic valve surgery. Twenty-two (12.6%) patients were treated under emergency conditions. Four (2.3%) patients were preoperatively supported with the ventilator, mainly owing to complicated type A aortic dissection or prosthetic valve endocarditis. Comorbid medical conditions consisted of hypertension ($n = 123$, 70.3%), renal dysfunction ($n = 25$, 14.3%; serum creatinine $> 120 \mu\text{mol/L}$, among whom 2 required hemodialysis), chronic obstructive pulmonary disease ($n = 23$, 13.1%), previous cerebrovascular accident or transient ischemic attack ($n = 16$, 9.1%), diabetes ($n = 13$, 7.4%), and Marfan syndrome ($n = 3$, 1.7%). Mean aortic diameter for aneurysmal disease was 59.7 ± 10.1 mm (range, 43–108 mm). Concomitant aortic valve disease consisted of severe aortic regurgitation (grade ≥ 3) in 88 (50.3%) patients, moderate to severe aortic valve stenosis (mean gradient, 65.6 ± 25.6 mm Hg) in 54 (30.9%) patients, and mixed

From the Departments of Cardiothoracic Surgery^a and Cardiology Research and Statistical Analysis,^b St Antonius Hospital, Nieuwegein, The Netherlands; and the Department of Cardiac Surgery,^c AZ St Jan Hospital, Brugge, Belgium.

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Address for reprints: Abdullah Kaya, MD, Department of Cardiothoracic Surgery, St Antonius Hospital, Koekoekslaan 1, 3435 CM Nieuwegein, The Netherlands (E-mail: a_kaya33@hotmail.com).

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Abbreviations and Acronyms

CL	= confidence limits
OR	= odds ratio

aortic valve lesion in 26 (14.9%) patients. A bicuspid aortic valve was present in 16 (9.1%) patients. Preoperative mitral valve regurgitation (grade ≥ 3) as a comorbid cardiac lesion was present in 8 (4.6%) patients and coronary artery disease in 46 (26.3%) patients. Pertinent patient data are given in Table 1.

Procedure

Full aortic root replacement for insertion of a composite valved graft with the button technique for reattachment of the coronary ostia was used in all patients in combination with standard cardiopulmonary bypass.⁵ The aortic cannulation site was mainly the distal ascending aorta or the common femoral artery in case of a reoperation or a type A dissection. Cold crystalloid cardioplegic solution cardioplegia was administered antegradely through the aortic root or coronary ostia selectively with intermittent cardioplegic reinfusion if needed. During cardioplegic arrest, the myocardial septal temperature was measured and kept around 10°C using a Shumway cold line. Depending on the aortic disease, the location and extension of the lesion, a distal clamp could be used in 67 (38.3%) patients. If the lesion extended to the aortic arch necessitating open distal anastomosis, deep hypothermic circulatory arrest was used in 63 (36.0%) patients and antegrade selective cerebral perfusion with mild hypothermia was used in 45 (25.7%). The latter technique was used when a circulatory arrest period of more than 30 minutes was anticipated.^{6,7} The proximal suture technique was by preference of the surgeon and consisted of 3 separate, continuous 4–0 polypropylene sutures ($n = 108$, 61.7%) for the attachment of the BioConduit sewing ring to the aortic annulus or interrupted pledget-supported 2–0 braided polyester mattress sutures ($n = 67$, 38.3%). In recent years a continuous 5–0 polypropylene suture was used to reinforce the proximal annular anastomosis against anastomotic leakage.

The diameter of the implanted biological conduits ranged from 21 to 27 mm with a median of 25 mm. Aortic root replacement solely was done in only 12 (6.9%) patients. Aortic root and distal ascending aorta replacement was realized in 72 (41.1%) patients. Root replacement and ascending aorta with partial arch replacement was effected in 68 (38.9%) patients. Finally, aortic root, ascending aorta, and total arch replacement with or without elephant trunk was performed in 23 (13.1%) patients. In 99 (56.6%) patients, a woven vascular graft was used as an extension of the BioConduit and the native downstream aorta. The graft diameter ranged from 22 to 32 mm with a median of 26 mm.

Concomitant procedures included planned coronary artery bypass grafting in 41 (23.4%) patients, coronary artery bypass grafting owing to preoperative technical problems in 6 (3.4%) patients, mitral valve repair or replacement in 5 (2.9%) patients, combination of planned coronary artery bypass grafting and mitral or tricuspid valve surgery in 5 (2.9%) patients, or other procedures, such as the Morrow procedure or closure of an atrial septal defect, in 7 (4.0%) patients. Operative data are given in detail in Table 2.

Follow-up

Recent (< 6 months) information about the status of all hospital survivors was collected from the referring cardiologist, by visit at our outpatient clinic, by our cardiology department, or by the general physician. December 31, 2008, was the closing date for follow-up and included physical examination, computed tomography scan, echocardiography, and chest radiography, if available. End points of the study were death, valve-related death, reoperation for valve failure, and endocarditis of the BioConduit. These end points were defined according to the guidelines reported by Akins and associates.⁸

TABLE 1. Patient characteristics (n = 175)

	No.	%
Age (y)		
Mean (SD; range)	71.1 (7.4; 31–84)	
Gender		
Male	102	58.3
NYHA class		
I	30	17.1
II	62	35.5
III	53	30.3
IV	30	17.1
Indication		
Aneurysmatic disease	120	68.6
Degenerative	110	
False	6	
Postdissection	4	
Aortic valve endocarditis	20	11.4
Prosthetic	16	
Native	4	
Acute type A dissection	11	6.3
Calcified aortic root	8	4.6
Other	16	9.3
Valvular disease		
Aortic valve regurgitation		
Grade I	55	31.4
Grade II	32	18.3
Grade III	55	31.4
Grade IV	33	18.9
Aortic valve stenosis	54	30.9
Mean gradient, mm Hg (SD; range)	65.6 (25.6; 20–135)	
Mixed aortic valve lesion	26	14.9
Bicuspid aortic valve	16	9.1
Reoperation	45	25.7
Previous aortic valve surgery	33	
Comorbid medical conditions		
Hypertension	123	70.3
Renal insufficiency	25	14.3
COPD	23	13.1
CVA	21	12.0
Diabetes	13	7.4
Marfan	3	1.7

SD, Standard deviation; NYHA, New York Heart Association; COPD, chronic obstructive pulmonary disease; CVA, cerebral vascular accident.

Data Analysis

Retrospective review was done on the data of all consecutive patients who underwent aortic root replacement with the Shelhigh BioConduit. Quantitative data are presented as mean $\pm$ standard deviation. Odds ratios (OR) and Fisher's exact *P* value were used for comparison. Kaplan–Meier survival curves were used for analysis of survival times. Precision was indicated by 95% confidence limits (CL). All statistical analyses were done by R (version 2.9; www.r-project.org).

RESULTS**Early Results**

Overall hospital mortality was 13.7% ($n = 24$; 95% CL, 9.0%–19.7%), of which 8.5% was for elective and 50.0%

TABLE 2. Operative characteristics (n = 175)

	No.	%
Emergency		
Elective	153	87.4
Emergency	22	12.6
Cannulation site		
Ascending aorta	134	76.6
Common femoral artery	39	22.3
Axillary artery	2	1.1
Perfusion data		
CPB and distal clamp	67	38.3
DHCA	63	36.0
ASCP	45	25.7
CPB time; min, mean (SD; range)	190.4 (53.6; 117 - 376)	
Aortic crossclamp time	125.1 (30.2; 73 - 228)	
DHCA time	24.5 (5.9; 17 - 40)	
ASCP time	57.1 (14.8; 38 - 79)	
Conduit suture technique		
Continuous polypropylene sutures	108	61.7
Interrupted pledget-supported polyester sutures	67	38.3
Extent of aorta replacement		
Root only	12	6.9
+ Ascending	72	41.1
+ Ascending and partial arch	68	38.9
+ Ascending and total arch	6	3.4
+ Ascending, total arch and ET	17	9.7
Concomitant procedure		
CABG planned	41	23.4
CABG unplanned	6	3.4
Mitral valve repair or replacement	5	2.9
Combination	5	2.9
Other	7	4.0

CPB, Cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest; ASCP, antegrade selective cerebral perfusion; SD, standard deviation; ET, elephant trunk; CABG, coronary artery bypass grafting.

for emergency cases ($P < .0001$). All the patients undergoing emergency surgery who died had acute type A dissection or endocarditis, and the predominant causes of death were ischemic cardiac or severe neurologic causes. There were 3 (1.7%) intraoperative deaths. All patients who died intraoperatively had poor left ventricular function (ejection fraction $\leq 25\%$), 2 had emergency operations, and the causes of death were cardiac failure, myocardial infarction, and electromechanical dissociation after ventricular fibrillation. Causes of in-hospital death are summarized in Table 3. Univariate analysis showed acute type A dissection (OR, 9.7; 95% CL, 2.7–35.2; $P = .0005$), endocarditis (OR, 4.4; 95% CL, 2.5–7.7; $P = .0058$), and emergency operation (OR, 10.8; 95% CL, 6.4–18.1; $P < .0001$) as important variables for hospital mortality. Multivariate analysis did not produce any independent predictor. Especially, there was no independent association between indication type and emergency operation on hospital mortality. The hospital mortality for patients with an aortic aneurysm (nondissection

TABLE 3. Causes of early and late death (n = 74)

Causes of death	No.	%
Early: In hospital	24	13.7
Operative	3	1.7
Elective: arrhythmia	1	
Emergency		
Heart failure	1	
Ischemic	1	
Postoperative, hospital	21	12.0
Elective	14	
Cardiac	6	
Cerebrovascular accident	3	
Respiratory failure	3	
Bleeding (proximal anastomosis)	2	
Emergency	7	
Cardiac	2	
Cerebrovascular accident	2	
Respiratory failure	1	
Gastrointestinal ischemia	2	
Late: Follow-up	50	33.1
Prosthesis related	7	4.6
Endocarditis*	7	
Early (<1 y)	4	
Late (> 1 y)	3	
Cardiac	8	5.3
Ischemic	4	
Heart failure	2	
Arrhythmia	1	
Endocarditis MV prosthesis	1	
Neurologic	7	4.6
Cerebrovascular accident	6	
Meningitis	1	
Respiratory failure	3	2.0
Cancer	7	4.6
(Peripheral) vascular	4	2.7
Dissection	2	
Ruptured aneurysm	2	
Sudden, unexplained	14	9.3

MV, Mitral valve.

and nonendocarditis) having elective surgery was 4.2% (n = 5). In 6 (3.4%) patients, an intraoperative problems required a second cardiopulmonary bypass run and in 5 of these patients a second crossclamp of the aorta with cardioplegic arrest was necessary. Main cause was to obtain control of bleeding from the proximal suture line or left coronary ostial anastomosis.

Mean and median intensive care unit stay was 6 days and 3 days, respectively (range, 1–60 days). Thirty-one (18.0%) patients needed ventilatory support for more than 48 hours and a tracheostomy was inserted in 9 (5.2%) patients. A rethoracotomy was performed in 48 (27.9%) patients, mostly for excessive bleeding (n = 18), because of diffuse leakage (n = 8) from the coronary reattachment line (n = 4), distal BioConduit suture line (n = 2), proximal BioConduit suture line (n = 2), or other (n = 2). Signs of tamponade (n = 17)

were also a predominant reason for rethoracotomy, and only half of these patients ($n = 9$) did have a clear tamponade during the rethoracotomy. A planned rethoracotomy in the next few days for removal of gauzes ($n = 12$) was the third major cause of rethoracotomy. Perioperative myocardial damage (serum creatinine kinase level > 300 IU/L, with a creatinine kinase MB isoenzyme fraction $> 5\%$) occurred in 14 (8.1%) patients. Permanent pacemaker implantation was necessary in 17 (9.9%) patients. Postoperative temporary hemodialysis was necessary in 7 (4.1%) patients. Three of these patients died in the hospital, the others recovered without the need for long-term dialysis.

New neurologic symptoms were observed in 23 (13.1%) patients. Ischemic cerebral accidents occurred in 19 patients, critical illness polyneuropathy in 2 patients, and transient peripheral neuropathy in 2 patients. In the stroke group, 7 patients died in the hospital, 2 of nonneurologic causes, and permanent neurologic damage was manifest in 6 (3.4%) patients. The OR for ischemic stroke in the group having deep hypothermic circulatory arrest was 4.6 (95% CL, 1.7–12.8; $P = .0035$) in comparison with the group having antegrade selective cerebral perfusion and distal clamping.

Late Results

There were 151 hospital survivors and all were entered in the follow-up study (100% complete). Mean and median follow-up were 3.1 years and 2.9 years, respectively (range 0.2–9.9 years). Total follow-up was 543 patient-years. During follow-up, 50 (33.1%) patients died, and 15 of these deaths occurred in the first postoperative year. Causes of death during follow-up are summarized in Table 3. Seven of these late deaths were prosthesis related owing to endocarditis of the BioConduit. Among the other 43 patients with non-prosthesis-related late deaths, 8 patients died of cardiac causes, 1 of whom had recurrent endocarditis of the mitral valve prosthesis (Shelhigh), with vegetations on echocardiography. The overall survivals at 1 and 5 years are $77.6\% \pm 3.2\%$ and $54.6\% \pm 4.6\%$, respectively. This information is presented in Figure 1 for the total group and selectively for the patients having elective and emergency operations. For the complete follow-up period, there is a significant difference between the elective and emergency groups ($P = .003$). After exclusion of the first 30 postoperative days, this difference disappears ($P = .679$).

Six (4.0%) patients required reoperation for significant prosthesis dysfunction owing to endocarditis of the BioConduit ($n = 5$) and false aneurysm ($n = 1$). Mean length of time between the initial aortic root replacement and reoperation was $21.7 \text{ months} \pm 22.1 \text{ months}$. Three patients underwent reoperation within 1 year after the initial root replacement, and in all these cases the cause of reoperation was endocarditis. During reoperation most patients received a second Shelhigh BioConduit, except 1 patient who received a homograft. One patient, known to have a false aneurysm, is being

FIGURE 1. Survival curve after aortic root replacement with a Shelhigh BioConduit for the elective, emergency, and total group.

followed up conservatively because she underwent multiple sternal wound explorations, and a reoperation for false aneurysm correction is estimated to be too high a risk. One patient died after reoperation for endocarditis. One- and 5-year freedom from reoperation is $76.4\% \pm 3.2\%$ and $50.8 \pm 4.6\%$ as presented in Figure 2.

Endocarditis of the Shelhigh BioConduit was reported in 11 (7.3%) patients. Five of these patients were reoperated on and only 1 patient died 3 months after the reoperation, as described earlier. Six patients were not referred for surgery by their cardiologist and were treated medically, and all these patients died subsequently. Two of them had autopsy, which

FIGURE 2. Freedom from reoperation after aortic root replacement with a Shelhigh BioConduit.

confirmed endocarditis of the BioConduit. The indication for the initial aortic root replacement was prosthetic valve endocarditis for 1 patient, and the rest of the patients had new-onset endocarditis of the BioConduit with *Staphylococcus* and *Enterococcus* as predominant microorganism. The incidence of late endocarditis was lower in the rethoracotomy group (2.1%) than in the nonrethoracotomy group (7.9%; $P = 0.2297$). Nine (81.8%) of the 11 patients who had new-onset endocarditis received the implant after the year 2003. Mean interval between initial aortic root replacement and new-onset endocarditis was 18.9 months $\pm$ 20.4 months, with a median of 9.3 months.

Follow-up imaging was mostly done by computed tomography scan. This was available for 82 (81.2%) patients and showed the 2 cases of false aneurysm as described earlier. Distal native aorta diameter increased in 5 patients without indication for reoperation. Dilatation or calcification of the pericardial tube was not observed. Echocardiographic evaluation of the BioConduit function was performed by most referring cardiologists when there was a clinical indication. A recent echocardiographic assessment of the BioConduit function was available in 43 (42.6%) survivors. Apart from adequate valve function, this showed previously mentioned vegetations and false aneurysms. Besides, there were 2 patients with moderate aortic regurgitation and 3 patients with moderate aortic stenosis (mean gradient, 50.7 $\pm$ 12.9 mm Hg) during a mean follow-up of 3.1 years.

DISCUSSION

The aortic homograft was the first complete biological composite valved graft used in our center, predominantly for endocarditis and for relatively young patients. Its limited donor availability and suboptimal long-term durability has made us less enthusiastic to use this graft.² As an alternative, commercially available stentless biological valved conduits were introduced, which have the benefit of being readily available off the shelf in all sizes. The Shelhigh BioConduit is such a biological composite valved graft. We used this BioConduit predominantly in elderly patients (mean age, 71 years) with degenerative aortic root disease, but also in patients with aortic valve endocarditis (mean age, 64 years) because of its complete biological aspect.

The limited initial results with the Shelhigh BioConduit in the literature were promising, with good clinical and echocardiographic results, even in patients with active infective endocarditis.⁹⁻¹¹ Recently, the US Food and Drug Administration published a preliminary public health notification on possible contamination and malfunction of devices manufactured by Shelhigh, Inc.¹² After this, Carrel and associates^{13,14} reported several precarious cases of reoperations and unexplained deaths occurring after implantation of the Shelhigh BioConduit. In their total group of 115 patients who received a Shelhigh BioConduit, 7 (6.1%) had “sudden disastrous findings” and 4 of them

required emergency reoperation. In our series, 11 (7.3%) patients had blood culture–positive endocarditis and 5 of them required reoperation. Patients with endocarditis of the BioConduit who were not referred for surgery all died, and in 2 of these patients endocarditis was proven by autopsy. Our aggressive rethoracotomy policy did not have a significant effect on late endocarditis because the incidence of late endocarditis was lower in the rethoracotomy group than in the nonrethoracotomy group (2.1% vs 7.9%; $P = .2297$).

Beside endocarditis of the BioConduit, there were 2 instances of false aneurysm formation at the BioConduit and the number of patients with sudden, unexplained death was relatively high (9.3%). Unfortunately, we could not find detailed information about the cause of death of these patients (mean age, 75.8 $\pm$ 8.4 years). It is conceivable that there might be some sudden, unexplained deaths because of endocarditis of the BioConduit. If we look at the 7.3% incidence of endocarditis of the Shelhigh BioConduit in this study and in our previous homograft series, we note that the incidence of endocarditis of the homograft was only 3.2%, despite a higher number of patients with endocarditis as the initial indication for surgery.² A true comparison, however, is not valid, because the patient groups are not comparable. It is important to note that most of the endocarditis of the BioConduit cases (81.8%) were Shelhigh conduits implanted after 2003. In 2007 the Food and Drug Administration published its preliminary public health notification. As a consequence, we have now strictly limited the implantation of the Shelhigh BioConduit for extensive aortic valve endocarditis complicated by annular abscesses. In the elective setting, we are in search of an alternative for the Shelhigh BioConduit.

Because of the lack of published clinical experience reports specifically about the Shelhigh BioConduit, we sought literature concerning other stentless biological conduits.¹⁵⁻¹⁹ Compared with these reports, our operative mortality of 1.7% and hospital mortality of 13.7% satisfies in a group with a mean age of 71 years, extended graft repair of the ascending aorta (41%), and involved aortic arch repair (52%) with aortic valve endocarditis (11.4%) or acute type A dissection (6.3%) in 17.7% of the patients. The incidence of endocarditis of the stentless biological conduits in these reports is lower than our 7.3%. The freedom from reoperation is comparable with these reports.

In conclusion, although perioperative results are satisfactory, the follow-up results are worrisome and the relatively high incidence of endocarditis of the Shelhigh BioConduit in our retrospective single-center analysis has led us to change our policy. There is a need for other centers to report their experiences as well, to draw more solid conclusions. Patients who have received the Shelhigh BioConduit should be monitored closely and long-term results should be evaluated.

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