TABLE 2. Risk factors for early mortality determined by univariate and multivariate analyses

Variable	Univariate *P*	Univariate OR (95% CI)	Multivariate *P*	Multivariate OR (95% CI)
Age (y)	.090	1.05 (0.99–1.11)	.096	1.06 (0.99–1.13)
Male gender	.434	1.50 (0.54–4.17)		
Dissecting aneurysm	.476	0.69 (0.25–1.92)		
Emergency surgery	.767	1.16 (0.44–3.05)		
Acute dissection	.881	0.92 (0.30–2.79)		
Ruptured nondissecting aneurysm	.023	4.56 (1.23–16.89)	.049	4.70 (1.00–22.03)
Acute dissection with critical malperfusion	.052	4.78 (0.99–23.07)		
Reoperation	.065	2.92 (0.94–9.12)		
Marfan syndrome	.393	2.50 (0.31–20.49)		
Chronic renal failure	.001	5.04 (1.94–13.13)	.007	4.82 (1.54–15.05)
Chronic obstructive pulmonary disease	.085	2.27 (0.89–5.79)		
Coronary artery disease	.001	4.65 (1.89–11.48)	.170	2.16 (0.72–6.46)
Diabetes mellitus	.010	3.48 (1.36–8.96)	.314	1.77 (0.58–5.41)
Concomitant surgery	.009	3.26 (1.35–7.90)	.843	1.12 (0.36–3.49)
Surgery (h)	<.0001	1.24 (1.14–1.36)	<.0001	1.31 (1.16–1.48)
Deep hypothermia (20°C–22°C)	.013	3.38 (1.29–8.84)	.228	1.93 (0.66–5.65)

OR, Odds ratio; *CI*, confidence interval.

malperfusion caused by acute dissection, chronic renal failure, and female gender (Table 3).

After surgery, various complications developed: bleeding in 7.5% (n = 40), low cardiac output in 6.2% (33), respiratory failure requiring tracheotomy or prolonged ventilation for 3 days in 14.1% (75), acute renal failure requiring hemodialysis in 2.3% (12), hepatic failure in 0.8% (4), gastrointestinal events in 3.0% (16), sepsis in 1.3% (7), mediastinitis in 1.3% (7), and disseminated intravascular coagulation in 0.9% (5). The median intensive care unit and hospital stays were 3 and 27 days, respectively. There were some complications related to the use of RAxA; motor palsy in 2 patients, muscle weakness in 8 patients, and numbness in 12 patients. Another 5 patients required repair of the RAxA for stenosis or thrombosed occlusion. However, except for 2 patients, most of these problems resolved. The midterm survival was 87.2% ± 1.7% at 3 years and 80.5% ± 2.6% at 5 years.

Discussion

Despite advances in brain protection, arch surgery continues to be a challenge because of the high mortality and morbidity, including neurologic sequelae.[1-5] To improve the outcome, we established the current SCP technique in 1999, which is physiologic and has a longer cerebral safety margin. This allows unhurried and secure arch surgery compared with the earlier retrograde cerebral perfusion.[6-8] Subsequently, the outcome was satisfactory with a low early mortality of 4.0% and low incidence of permanent or temporary neurologic dysfunction of 2.9% or 9.9%, even though high-risk emergency surgeries were involved.

However, during SCP, the risk of cerebral embolism associated with arch-vessel cannulation remains and may even increase the incidence of stroke.[4,5] In arch surgery, other embolic phenomena may occur as the result of 1) cannulation or clamping of the diseased aorta and arteries, 2) a high-velocity jet caused by CPB via the ascending aorta across the aneurysm, 3) retrograde femoral perfusion through the diseased aorta, 4) external manipulation of the aorta and arch vessels, or 5) dislodgement of atheroma or clot inside the aorta.[9] To overcome these problems, we used an alternative perfusion pathway using the distal segment of RAxA for both CPB and SCP.[6-8] This part of the RAxA, which has less atherosclerosis or extension of aortic dissection, can easily be exposed and cannulated. In regard to AxA perfusion, there have been numerous reports on its routine or alternative use for CPB in cardiac surgery or for CPB and SCP in aortic surgery.[9-20] These reports also advocated some advantages: less likelihood of stroke from embolic material, less likelihood of malperfusion with aortic dissection, less disruption of atheroma or calcified plaques, and the ability of administration of SCP.[20] However, the cannulation site and techniques differ from ours, and the number of patients evaluated was smaller. In all, a proximal segment of the AxA below the clavicle (infraclavicular segment) is used, where larger-sized cannulae of 20F to 26F in size are accepted. However, the exposure was more time-consuming.[9,11,13-15,18,20] For an emergency operation, our technique is more advantageous. For example, in acute dissection, 3 surgeons can start 3 different procedures without any interruptions, namely, RAxA exposure in the axilla, median sternotomy, and femoral artery exposure. In some, aortic dissection may extend down to the infraclavicular AxA,[20] although it is rarely encountered on the distal segment. Furthermore, there is a potential risk of the right common carotid artery occlusion by an overly deep

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TABLE 3. Risk factors for permanent neurologic dysfunction determined by univariate analysis

Variable	P	OR	95% CI
Age (y)	.082	1.06	0.99–1.14
Female gender	.007	4.51	1.52–13.42
Nondissecting aneurysm	.854	0.90	0.30–2.69
Emergency surgery	.070	2.60	0.92–7.31
Acute dissection	.507	1.48	0.46–4.76
Ruptured nondissecting aneurysm	.062	4.43	0.93–21.3
Arch-vessel malperfusion caused by acute dissection	.003	12.87	2.37–69.94
Atheromatous ascending aortic arch	<.0001	104.72	29.40–372.90
Chronic renal failure	.039	3.49	1.07–11.37
History of cerebrovascular event	.436	0.55	0.12–2.48
Carotid artery disease	.678	1.38	0.30–6.28
Intracranial artery disease	.188	2.40	0.65–8.79
Total arch replacement	.241	3.39	0.44–26.1
SCP (h)	.144	1.46	0.88–2.43
Open distal anastomosis with HCA (h)	.261	2.23	0.55–9.08
Deep hypothermia (20°C–22°C)	.191	2.01	0.71–5.74

OR, Odds ratio; *CI*, confidence interval; *SCP*, selective cerebral perfusion; *HCA*, hypothermic circulatory arrest.

cannula insertion.[13] In regard to the AxA perfusion technique, some authors performed direct cannulation of a straight[9,11,14,15,18,20] or right-angle cannula[13] for easy and quick CPB establishment, whereas others preferred a side-graft anastomotic technique to obtain sufficient CPB flow.[10,12,14-16,20] For small patients, the side-graft technique is more advantageous, and it has been widely used because of less neurovascular complications.[9,10,14,16] However, the side-graft procedure is more time-consuming and technically demanding. Bleeding from the anastomosis during the perfusion can become a nuisance. We therefore prefer simple and easy direct cannulation into the distal RAxA. It is the shortcomings of our technique that the distal RAxA is too small to accept larger-size cannulae. Therefore, additional (double) cannulation via the femoral artery or the ascending aorta is necessary for CPB. In the early series, femoral perfusion was routinely used.[6] In this combination, the downstream flow via the RAxA can compete with the retrograde femoral perfusion flow in the descending aorta, which may prevent the potential risk of cerebral emboli.[9,10,20] In acute dissection, this RAxA perfusion can prevent the collapse of the true channel in the proximal site.[17] On the other hand, retrograde femoral perfusion not only allows the flushing out of debris in the descending aorta but also serves to check for bleeding from the key distal anastomosis. Moreover, perfusion of the spinal cord and visceral organs is possible through balloon occlusion of the descending aorta.

In the later series, in the absence of atherosclerotic change, ascending aorta cannulation yielding antegrade systemic CPB flow became our first choice.[7,8] The proximal to mid-ascending aorta, away from the aneurysm, is generally safe. This strategy allowed us to avoid some drawbacks of femoral perfusion, including proximal emboli or retrograde dissection. Even in addition to the ascending perfusion, we still use the RAxA perfusion, because the switch from CPB perfusion to SCP is easy with no discontinuity by clamping the innominate artery, although in the standard SCP there remains by necessity a short period of circulatory arrest during insertion of the cannulae. With our technique, cannulation-induced emboli of the innominate artery or its new dissection can be avoided. Malposition of the SCP catheter in the innominate artery is not a rare event.[21] With the innominate artery cannulated, the presence of dissection or severe atherosclerotic changes would make the anastomosis more difficult. Under the reliable SCP with RAxA perfusion, we have therefore been able to increase the bladder and nasopharyngeal temperature to 28°C. If the ascending aorta is atherosclerotic, however, the femoral artery is still chosen for CPB. Femoral perfusion is added for patients presenting some difficulties with the distal anastomosis for severe atheromatous changes: to the combination of the RAxA and ascending perfusion, to perfuse the spinal cord and the visceral organs, or to flush out atheromatous debris.

In another setting, 5 patients required re-sternotomy surgery after the previous ascending aorta or arch surgery. There was a risk of aneurysmal rupture or graft injury at the re-sternotomy, even under femoro-femoral partial CPB, because the graft or enlarged aneurysm was attached to the sternum. We initiated CPB under RAxA and femoral perfusion and cooled them down. The sternum was reopened, immediately after the induction of deep hypothermia circulatory arrest, and brain protection was smoothly attained through SCP, which was easily established by just clamping the arch vessels under the RAxA perfusion.

The multivariate analysis demonstrated that chronic renal failure, ruptured nondissecting aneurysm, and prolonged surgery were the independent determinants for early mortality. All of these have been pointed out as risk factors. Svensson and colleagues[20] and Kazui and colleagues[22] also reported chronic renal failure as a risk factor for mortality. In general, patients with chronic renal failure tend to have severe atherosclerosis or calcification of the aorta and arteries.[23] Some of these patients also have diabetic nephropathy. Sepsis or mediastinitis tends to develop in patients during postoperative hemodialysis. Surgery then involves a potentially higher risk. In regard to permanent neurologic dysfunction, arch-vessel malperfusion with acute dissection and rich atheroma in the ascending aorta and arch were significant independent predictors, associated with female gender and chronic renal failure. Statistically, a history of cerebrovascular event and carotid/intracranial artery disease were not risk factors. This

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finding was expected. The majority of permanent neurologic dysfunctions are considered to be caused by an embolism resulting from atheroma or clot,[24] not cerebral hypoperfusion. Furthermore, in the cases with preoperative cerebral hypoperfusion caused by carotid or intracranial artery lesions, we modified our strategy to include a higher CPB perfusion pressure (>60 mm Hg), deeper hypothermia (20°C–22°C), and higher SCP flow rates by 20%. These refinements seemed to yield good outcomes empirically, avoiding critical cerebral hypoperfusion. On the other hand, adequate brain protection is still controversial for patients with severe atheromatous lesions in the arch and arch vessels. In our practice, 11 high-risk patients with an atheromatous aorta had permanent neurologic dysfunction, despite the SCP with RAxA perfusion aiming at avoiding stroke. SCP requiring arch-vessel cannulation may result in cerebral embolism.[4,5] Our strategy based on RAxA perfusion allows us to avoid cannulation, at least, of the innominate artery, which sometimes exhibits atheromatous changes or dissection. The left common carotid artery is less atheromatous in most, making its cannulation safe. The left subclavian artery often presents the most severe atheromatous changes, and cannulation is sometimes dangerous. Its cannulation must be carefully performed, removing some atheromatous parts, or patients should be cooled down to less than 22°C leaving the left subclavian artery uncannulated. In any case, even under RAxA perfusion, it is difficult to completely avoid cerebral emboli, particularly for high-risk patients with rich atheroma in the ascending aorta and arch, including the arch vessels. It is speculated that under RAxA perfusion, its high-velocity jet streaming retrogradely into the innominate artery might cause dislodgement of atheroma in the minor curvature of the arch, resulting in distal embolism. With a single inflow site via the AxA for CPB, as described in the other reports,[9-19] a higher-velocity jet is produced, which might adversely increase the risk of distal emboli. There is no way to completely avoid such cerebral emboli in patients with rich atheroma in the aorta, although its incidence would be reduced by our techniques. Our recommendation is to assess the ascending aorta and arch for atherosclerotic changes by epiaortic ultrasound imaging. In addition, arterial cannulation should be carefully performed with minimum manipulation of the aorta and arch vessels.

Cannulation into the distal RAxA was achieved in the overwhelming majority of patients (97.4%). However, during the same interval, attempted RAxA cannulation was abandoned in 14 patients (2.6%), who were excluded from this study. The cannulation was difficult because of the small size of the artery or the presence of stenosis. Thus, in these patients, the inflow site for CPB was shifted to the ascending aorta or femoral artery. For SCP, the innominate artery was also cannulated.[4,5] In this subset, 1 patient (7.1%) with an arch rupture associated with acute dissection died of low cardiac output, and 2 patients (14.3%) had permanent neurologic dysfunction. There were some local complications related to the RAxA perfusion, such as vascular and nerve injuries in 5.6% of patients. Two patients also had left hand weakness. We think that some nerve injuries might be due to nerve compression caused by wide opening of the sternum for the distal anastomosis. At any rate, the incidence of complications was higher than in other reports describing the use of an infraclavicular AxA.[9-20] The key to avoid these complications is gentle dissection and manipulation, while avoiding unnecessary traction of the brachial plexus. The RAxA is sometimes fragile and traumatized in younger patients and patients with aortic dissection or Marfan syndrome. For these patients, exposure and cannulation should be done carefully.

There are some limitations in this study. The logistic regression analyses were limited by the small number of events. This is a retrospective study in a single patient group who underwent aortic arch surgery with SCP through RAxA perfusion. To demonstrate the absolute (not theoretic) value of the RAxA perfusion, a multicenter prospective study is necessary.

Conclusions

RAxA perfusion in the axilla is an advantageous adjunct for CPB and SCP in arch surgery.

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Discussion

Dr Joseph Coselli *(Houston, Tex)*. Congratulations on an excellent presentation. You report to us an incremental study regarding the Osaka experience with selective cerebral perfusion using axillary artery cannulation. Your approach is unusual in that you cannulate the distal axillary artery using an axillary artery incision and a small cannula, usually 10F to 16F. Because of this, you also cannulate either the ascending aorta or the femoral artery to achieve adequate inflow. Your results are outstanding, with an operation mortality of 4% and a permanent neurologic deficit of 3% and no significant difference between elective and emergency operations, albeit with less than 8% of patients undergoing reoperation.

As your title suggests, you've evolved your strategy over a number of years with variations in such things as temperature and cannulation techniques. Because your results have been excellent apparently all along, it is not exactly clear to me as to what the motivation for the incremental alteration in your techniques has been.

Were there any differences in the outcomes from a neurologic, renal bleeding standpoint from the 4 different groups with regard to target temperatures that you have alluded to? For which patients, if any, do you continue to use deep hypothermic circulatory arrest?

You focus on bladder temperature. Knowing the limitations of bladder temperature monitoring, why do you not also monitor temperature in an area more accurately reflecting brain temperature, for example, the nasopharyngeal?

You recommend routine evaluation of cerebral circulation to help guide your perfusion strategy. One fourth of your patients had emergency procedures. What proportion of these patients had the benefit of preoperative imaging and how did this, if any, alter your technique? And if you do not have this preoperative imaging, exactly what perfusion techniques do you suggest?

Finally, rewarming strategy is also an important aspect of neuroprotection. What is your current rewarming approach? Do you use bladder temperature for this as well? What ultimate temperature do you target in your rewarming process? If you could, just mention to us your pH strategy.

Dr Ogino. As you know, in the past, we used retrograde cerebral perfusion with profound hypothermia in arch surgery. However, because the cerebral safety margin was limited and the incidence of postoperative temporary neurologic dysfunction was higher, our brain protection technique was shifted to selective antegrade cerebral perfusion in 2000.

At the moment, as I mentioned, the routine temperature is 28°C, regardless of aortic pathology. However, for high-risk patients with cerebral ischemia or renal dysfunction, we still use deep hypothermia at approximately 20°C to 22°C for cerebral or renal safety. In terms of bleeding or hemostasis, we are currently looking at the difference by a randomized control study between deep and moderate hypothermia in arch surgery. Our impression is that the amount of bleeding is less in the patient group with moderate hypothermia.

In regard to the temperature, we monitored the nasopharyngeal and bladder temperatures. In this study, we focused more on the bladder temperature as the core temperature, because we had to pay attention to the safety of spinal cord and visceral organs under moderate hypothermia. Selective antegrade cerebral perfusion is physiologic and has been well established. Under these circumstances, we focused more on the bladder temperature than the nasopharyngeal temperature.

In regard to the next question about the preoperative examination of cerebral circulation, routinely, brain computed tomography scans or carotid ultrasound was performed to evaluate the cerebral circulation. With a positive sign of ischemia in these examinations, magnetic resonance imaging or single photon emission computed tomography followed with the consultation of neurophysicians or neurosurgeon. With remarkable cerebral ischemia, we chose deep hypothermia and maintained the higher blood pressure during CPB and selective antegrade cerebral perfusion to avoid cerebral hypoperfusion. As you pointed out, one fourth of our patients were on emergency bases, such as acute dissection or ruptured nondissecting aneurysm. In this setting, preoperative evaluation was incomplete.

So for those cases, we tended to choose a lower temperature because of less information on cerebral circulation. Exceptionally, for relatively young patients with acute dissection without cerebral malperfusion, moderate hypothermic surgery at 25°C to 28°C was performed because these patients unlikely had any atherosclerotic cerebrovascular diseases.

As you mentioned, the rewarming process is also important for brain protection. Slow rewarming to the nasopharyngeal temperature of approximately 30°C to 32°C was started after reconstruction of the left subclavian artery. Full rewarming was commenced after complete reconstruction of the arch vessels. In terms of pH strategy, we used alpha-stat strategy for cooling and rewarming.

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THE ANNALS OF THORACIC SURGERY

Composite Valve Graft Replacement of the Aortic Root: Twenty-Seven Years of Experience at One Japanese Center

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Composite Valve Graft Replacement of the Aortic Root: Twenty-Seven Years of Experience at One Japanese Center

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Background. The aim of this study was to evaluate the early and long-term results of a composite valve graft root replacement for various aortic root diseases.

Methods. Between 1978 and 2005, 273 patients with various disorders of the aortic root underwent a composite valve graft root replacement. The mean age of the patients was 47.5 ± 13.2 years. There were 93 patients with Marfan syndrome, 56 aortitis, and 63 type A aortic dissections. Thirty-nine emergency operations and 55 redo operations were included. For the proximal anastomosis, a skirted technique was used in 157 patients. For the coronary reconstruction, Bentall's original inclusion technique was utilized in 36 patients, a direct button technique in 159, and a graft interposition technique in 63. The mean follow-up was 106 months.

Results. The in-hospital mortality was 9.5%. An emergency operation emerged as a significant predictor of early death. The actuarial survival rate was 87.0% and 72.9% at 5 and 15 years, respectively. The age at the operation, aortitis, Marfan syndrome, and use of a standard proximal anastomosis emerged as independent determinants of late death. The actuarial reoperation free rate was 96.3% and 89.7% at 5 and 15 years, respectively. In the patients who underwent the skirted technique the incidence of late graft detachment was less frequent than that of the standard technique.

Conclusions. A composite valve graft root replacement is a safe and reliable procedure for various aortic root diseases with stable early- and long-term results. The skirted technique seems to be attractive to avoid late graft detachment even in cases with a fragile inflammatory pathology.

(Ann Thorac Surg 2008;86:1510–7)

A composite valve graft root replacement (CGR), first reported by Bentall and DeBono in 1968 [1], has been applied to a variety of aortic root diseases. During the last two decades, CGR, with various technical modifications [2–5], has become a standard procedure for aortic root disorders. This report reviews the experience of CGR over the past 27 years in this center to overview the broad profiles of this procedure, including risk factor analyses and an evaluation of the long-term results.

Patients and Methods

This study included 273 patients who underwent a CGR at the National Cardiovascular Center, Osaka, Japan, between October 1978 and October 2005. Patients who required preoperative cardiopulmonary resuscitation were excluded. Patients who underwent an aortic root replacement using an aortic homograft, pulmonary autograft, or a stentless bioprosthesis were also excluded. All of the surgeries were identified from the Registry of Cardiovascular Surgery in the National Cardiovascular Center. The data in the registry were approved for use by the Institutional Ethical Committee. Follow-up data were obtained using a postal questionnaire or telephone interview with patients and their physicians. The preoperative patients' characteristics are summarized in Table 1. There were 93 patients with Marfan syndrome, 56 with aortitis, and 63 with an acute or chronic type A aortic dissection. Thirty-nine emergency operations and 55 redo operations were included. The patients in this study had various aortic root diseases. The indications that prompted the CGR are listed in Table 2. The majority of the patients in this series had an annuloaortic ectasia as the primary pathologic lesion (200 of 273; 73.3%). Thirty-nine patients with annuloaortic ectasia were accompanied by an acute or a chronic type A aortic dissection. The second most frequent indication was an acute type A aortic dissection (25 of 273; 9.2%), which was defined as an aortic dissection which showed apparent symptoms and was treated surgically within seven days after the onset of the symptoms. Of the 16 patients with a prosthetic valve dysfunction, 12 had aortitis, one had Marfan syndrome, and one had a chronic type A aortic dissection.

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Table 1. Patients' Profiles

Profiles	No. of Patients	%
Gender (men)	181	66.3
Age (years)	47.5 ± 13.2	
Emergent operation	39	14.3
Marfan syndrome	93	34.1
Aortitis	56	20.5
Acute type A aortic dissection	25	9.2
Chronic type A aortic dissection	38	13.9
Endocarditis	6	2.2
Redo operation	55	20.1
Hypertension	91	33.3
Diabetes mellitus	7	2.6
Cerebrovascular disease	27	9.9
Coronary artery disease	16	5.9
Chronic renal failure	7	2.6
Chronic obstructive pulmonary disease	30	11

Surgical Technique

Through a median sternotomy, a cardiopulmonary bypass was established by ascending aortic and bicaval cannulation, which was performed in a routine manner. If the ascending aortic cannulation was considered difficult, such as in an aortic dissection, axillar or femoral arterial cannulations were utilized. Myocardial protection was maintained with antegrade and retrograde cardioplegia. When replacing the aortic arch simultaneously, either profound or moderate hypothermic circulatory arrest between 18°C and 28°C and selective or retrograde cerebral perfusion were utilized according to surgeons' preferences. The details of surgical procedures are summarized in Table 3. For the coronary reconstruction and proximal aortic root anastomosis, various different surgical techniques were utilized. The method of coronary reconstruction was Bentall and De Bono's original inclusion technique in the initial 36 patients, a direct button technique in 159, a graft interposition technique of the bilateral (45) or unilateral (18) coronary arteries in 63 [4], the technique of Cabrol and colleagues [5] in 9, coronary artery bypass grafting in 5, and unknown in 1. Bentall and De Bono's original inclusion technique, in conjunction with wrapping the aortic aneurysm wall around the composite graft, was utilized until 1987. This technique was abandoned after a report in 1986 by Kouchoukos and colleagues [6] of late complications associated with this technique. The technique of Cabrol and colleagues was utilized between 1984 and 1989. This technique was discontinued because one early coronary graft obstruction and two perioperative coronary-related deaths were observed. A direct button technique has been utilized since 1985, which has been adopted as the first line technique for the coronary reconstruction. A graft interposition technique has also been utilized since 1985 and is still one of the choices when the button technique is considered difficult to perform without tension on the suture line, especially in redo cases.

For the proximal anastomosis, two different techniques were utilized. In 116 patients (42.5%), the composite valve graft was made by attaching a prosthetic valve to the edge of the graft with a continuous 3-0 polyester suture. The sewing ring of the prosthetic valve was attached to the aortic annulus with 2-0 polyester interrupted everting mattress sutures ("standard technique"). In the other 157 patients (57.5%), a prosthetic valve was anastomosed to the graft at 5 to 10 mm above the edge of the graft with continuous 3-0 polyester sutures. The segment of the proximal end of the vascular graft was referred to as the "vascular skirt." Only this soft skirt was attached to the aortic

Table 2. Indications for Operation

Indications for Operation	No. of Patients	%
Annuloaortic ectasia	200	73.3
Acute type A aortic dissection	25	9.2
Prosthetic valve dysfunction	16	5.9
Pseudoaneurysm of ascending aorta or aortic root	9	3.3
Aortic valve regurgitation and ascending aorta aneurysm	6	2.2
Chronic type A aortic dissection and aortic regurgitation	5	1.5
Aortic valve stenosis and ascending aorta aneurysm	4	1.5
Aortic regurgitation and aortitis	3	1.1
Rupture of Valsalva sinus aneurysm	2	0.7
Coronary ostial aneurysm	2	0.7
Prosthetic valve endocarditis	1	0.4

Table 3. Details of the Operation

Details	No. of Patients	%
Pump time (minutes)	243 ± 129	
Aortic clamp time (minutes)	154 ± 47	
Mechanical valve	240	87.9
Bioprosthetic valve	33	12.1
Proximal anastomosis:		
Skirted	157	57.5
Standard	116	42.5
Coronary arterial reconstruction:		
Direct button technique	159	58.2
Graft interposing technique	63	23.1
Original inclusion technique	36	13.2
Cabrol technique	9	3.3
Others	6	2.2
Concomitant procedure:		
Aortic	58	21.2
Hemi arch replacement	26	9.5
Total arch replacement	32	11.7
Cardiac	40	14.7
Mitral	22	8.1
Aortocoronary bypass	15	5.5
Others	5	1.8

Table 4. Univariate Analyses of Early and Late Results

	Hospital Mortality			Late Mortality			Reoperation		
Variables	*p*	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI
Age at operation	0.514	0.990	0.960–1.012	0.130	1.018	0.595–1.043	0.964	0.999	0.962–1.037
Male gender	0.590	0.795	0.346–1.830	0.274	1.434	0.752–2.735	0.138	2.006	0164–0.960
Emergent operation	0.000	6.984	2.930–16.65	0.552	1.299	0.549–3.076	0.268	2.038	0.579–7.182
Type A dissection	0.055	2.288	0.981–5.334	0.229	1.486	0.779–2.831	0.601	1.314	0.473–3.653
Malfan syndrome	0.709	0.847	0.354–2.028	0.722	1.114	0.614–2.021	0.968	1.019	0.407–2.548
Aortitis	0.734	1.182	0.451–3.098	0.023	2.062	1.107–3.839	0.955	0.965	0.280–3.329
Redo operation	0.161	1.891	0.776–4.612	0.034	2.097	1.059–4.149	0.467	1.586	0.458–5.490
Hypertension	0.561	1.281	0.557–2.948	0.542	0.803	0.396–1.627			
Diabetes mellitus	0.667	1.607	0.186–13.89	0.888	0.867	0.119–6.304			
Cerebrovascular disease	0.024	3.229	1.169–8.918	0.356	1.626	0.579–4.572			
Coronary artery disease	0.207	2.348	0.623–8.846	0.527	1.585	0.381–6.591			
Chronic renal failure	0.106	4.033	0.742–21.92	0.000	9.534	2.844–31.96			
Chronic obstructive pulmonary disease	0.925	1.063	0.299–3.776	0.289	1.593	0.673–3.773			
Pump time (minutes)	0.002	1.004	1.002–1.007	0.032	1.002	1.000–1.003	0.632	1.001	0.997–1.005
Aorta clamp time (minutes)	0.940	1.000	0.991–1.009	0.136	1.005	0.998–1.011	0.348	1.006	0.994–1.017
Use of bioprosthesis	0.205	0.269	0.035–2.052	0.737	0.861	0.359–2.063	0.000	8.577	3.398–21.65
Skirted proximal anastomosis technique	0.222	0.603	0.268–1.358	0.092	0.592	0.321–1.090	0.056	0.332	0.108–1.027
Direct button technique	0.001	0.230	0.093–0.568	0.605	0.854	0.470–1.552	0.004	0.160	0.046–0.559
Concomitant aortic surgery	0.792	0.872	0.314–2.421	0.705	1.152	0.553–2.404	0.247	0.037	0.000–9.755
Concomitant cardiac surgery	0.081	2.308	0.902–5.903	0.936	0.965	0.409–2.281	0.298	0.343	0.046–2.572
Era of operation (after 1995)	0.376	0.692	0.307–1.561	0.775	0.912	0.485–1.716	0.023	0.172	0.037–0.788

95% CI = 95% confidential interval; OR = odds ratio.

annulus with everting mattress sutures using 2-0 polyester sutures ("skirted technique"). The primary purpose of the modification of the proximal anastomosis with skirted technique was to secure the intraoperative hemostasis at the proximal anastomosis and to reduce the incidence of late graft detachment.

Bioprosthetic valves were utilized in 33 patients; the Ionescu-Shiley valve (Shiley Laboratory, Irvine, CA) was implanted in 19 patients until 1984 and the Carpentier-Edwards bovine pericardial valve (Edwards Lifescience, Irvine, CA) in 14 since 1987. A mechanical valve was implanted in 240 patients, the St Jude Medical bileaflet prosthesis (St. Jude Medical, St. Paul, MN) in 149 patients, the CarboMedics bileaflet prosthesis (CarboMedics Inc., Austin, TX) in 54, the Björk-Shiley tilting disc prosthesis (Shiley Laboratory) in 22, and the ATS Medical bileaflet prosthesis (ATS Medical Inc., Minneapolis, MN) in 15.

Statistical Analysis

Data analyses were performed using SPSS 15.0 for Windows (SPSS, Chicago, IL). Data are expressed as the mean ± standard deviation, with the statistical significance determined at the 95% confidence level. The variables associated with an increased risk of early death were assessed using univariate and multivariate logistic regression analyses. Long-term survival and event-free rates were calculated using the Kaplan-Meier method. The endpoints were late death, reoperation, prosthesis dysfunction, thromboembolism, bleeding requiring in-hospital treatment or blood transfusion, coronary complications, graft infection, and graft detachment. Only the first occurrence of any specified complications was considered in the analyses. The variables associated with increased risk of late death and reoperation were assessed by the univariate and multivariate Cox proportional regression analyses.

Results

Early Mortality

Overall, the in-hospital mortality rate, defined as death prior to discharge or within 30 days of the operation in discharged patients, was 9.5% (26 patients). Eighteen of those patients died from postoperative heart failure. The other causes were refractory ventricular fibrillation in 3 patients, pulmonary hemorrhage in 2, prosthetic valve endocarditis in 2 and ischemic colitis in 1. A multivariate analysis showed that an emergency operation, the presence of preoperative cerebrovascular disease, and no use of a direct button technique were statistically significant predictors for in-hospital death (Tables 4 and 5).

Table 5. Multivariate Analyses of Early and Late Results

	Hospital Mortality			Late Mortality			Reoperation		
Variables	*p*	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI
Age at operation	0.642	0.987	0.934–1.047	0.018	1.035	1.006–1.065			
Male gender									
Emergent operation	0.000	6.984	2.930–16.65	0.990	1.006	0.370–2.740			
Type A dissection	0.786	1.228	0.279–5.411	0.469	1.351	0.599–3.048	0.912	1.073	0.311–3.702
Marfan syndrome	0.506	0.594	0.128–2.759	0.015	2.912	1.229–6.897	0.525	0.687	0.216–2.184
Aortitis	0.651	0.716	0.169–3.037	0.009	3.086	1.325–7.187	0.850	1.153	0.263–5.065
Redo operation	0.752	1.199	0.331–4.350	0.023	2.556	1.138–5.740	0.144	2.881	0.097–11.90
Hypertension	0.364	1.829	0.497–6.733						
Diabetes mellitus	0.534	2.433	0.148–40.02	0.869	0.843	0.111–6.389			
Cerebrovascular disease	0.033	5.101	1.144–23.77	0.774	0.846	0.270–2.652			
Coronary artery disease	0.737	0.922	0.125–6.801	0.146	3.175	0.670–15.05			
Chronic renal failure	0.092	7.808	0.714–85.35	0.006	6.575	1.716–23.20			
Chronic obstructive pulmonary disease	0.553	1.634	0.323–8.264						
Pump time (minutes)	0.297	1.002	0.998–1.006	0.298	1.001	0.999–1.004			
Aorta clamp time (minutes)									
Use of bioprosthesis	0.353	0.325	0.030–3.474	0.597	0.749	0.257–2.186	0.002	5.346	1.838–15.55
Skirted proximal anastomosis technique	0.677	1.302	0.376–4.513	0.015	0.417	0.207–0.842	0.437	0.571	0.139–2.343
Direct button technique	0.027	0.270	0.085–0.860	0.602	0.826	0.403–1.693	0.239	0.431	0.106–1.750
Concomitant aortic surgery	0.178	0.311	0.057–1.697	0.936	1.035	0.452–2.367	0.237	0.291	0.038–2.250
Concomitant cardiac surgery	0.319	1.941	0.527–7.143	0.479	0.723	0.295–1.774			
Era of operation (after 1995)	0.341	0.524	0.138–1.982	0.969	1.014	0.490–2.100	0.442	0.501	0.086–2.916

95% CI = 95% confidential interval; OR = odds ratio.

Long-Term Survival

The mean follow-up duration was 106.1 ± 80.4 (2 to 306) months. The follow-up data were lost in 17 patients during the study period and the complete follow-up data were collected in 93.8%. A total of 45 late deaths (18.2%) were observed. Fourteen of those deaths were related to the composite valve prosthesis; graft infection in 7, cerebral hemorrhage under anticoagulation therapy in 4, gastrointestinal ischemia in 2, and acute myocardial infarction in one. Seven patients died from the rupture of a residual aortic aneurysm or aortic dissection. The cause of the late death was unknown in 5 patients. The actuarial survival rate was 87.0%, 79.9%, and 72.9% at 5, 10, and 15 years respectively (Fig 1). A multivariate analysis showed that the age at operation, Marfan syndrome, aortitis, the presence of preoperative renal failure, the use of a standard proximal anastomosis and a redo operation were all significant independent predictors of late death (Tables 4; 5).

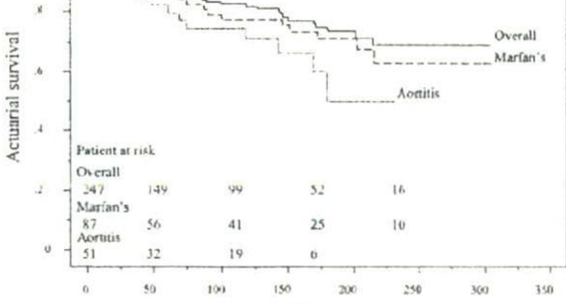

Fig 1. Overall survival curve and the influence of Marfan syndrome and aortitis on the actuarial survival.

Reoperation

Twenty-four patients (9.5%) presented for reoperation of the ascending aorta and the aortic root. Some of the 24 patients had multiple indications for the reoperation. Of these patients, a prosthetic valve dysfunction was observed in 11 patients, graft detachment in 10 patients, and graft infection in 5 patients. Of the 11 patients with a

Table 6. Procedures for Reoperation

Procedures Performed at Reoperation	No. of Patients
Aortic valve replacement	10
Recomposite graft replacement	8
Repair of graft detachment with/without coronary reconstruction	4
Homograft replacement	2
Total	24

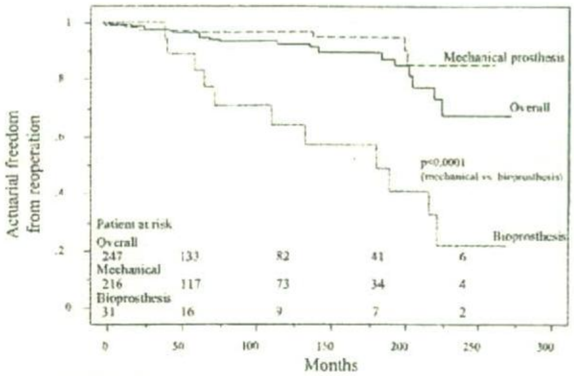

Fig 2. Actuarial freedom from reoperation of the ascending aorta and the aortic root in overall patients, patients with mechanical prosthesis, and patients with bioprosthesis.

prosthetic valve dysfunction, 9 of them underwent a secondary aortic valve replacement. The other 2 patients had a redo CGR for a coexisting graft detachment or a coronary ostial true aneurysm. Four patients with a graft detachment underwent a direct repair of the detachment with or without coronary reconstruction, and the other 6 patients with a graft detachment received a redo CGR. All the patients who were treated for a graft infection underwent a redo CGR. An aortic homograft was utilized in 2 patients. One patient underwent an aortic homograft root replacement due to methicillin-resistant staphylococcal prosthetic endocarditis 10 months after the initial CGR and concomitant total aortic arch replacement. He required a re-total arch replacement to treat the residual infection and a graft detachment 4 months later and died from an uncontrollable infection. Another patient who required an aortic homograft root replacement had giant-cell aortitis and repeated graft detachment. An aortic homograft was utilized for his third root replacement. He died 9 years after the aortic homograft root replacement. The procedures for reoperation are summarized in Table 6. Three patients (12.5%) died after the reoperation for graft infection. The reoperation free rates of the total patient population were 96.3%, 92.2%, and 89.7% at 5, 10, and 15 years, respectively (Fig 2). The multivariate analysis showed that the use of a bioprosthesis was the only significant independent predictor for reoperation (Tables 4; 5). In the patients who underwent a CGR with a mechanical valve, no prosthetic valve dysfunction was observed and the reoperation free rates were 96.5%, 96.5% and 95.0% at 5, 10, and 15 years, respectively (Fig 2). Univariate and multivariate analyses did not identify any variables as a significant predictor for reoperation in the patients who utilized mechanical valves.

Graft Infection

Ten patients (4.0%) developed a graft infection. Three of them experienced an accompanied graft detachment. Five patients underwent reoperation; a redo CGR in four patients and an aortic homograft root replacement in one. Three of them (60%) died after the reoperation. Five patients were observed without reoperation, and four of them (80%) eventually died. The actuarial probability of remaining free of a graft infection was 95.5% at 15 years.

Detachment of the Graft Anastomosis

Fourteen graft detachments were observed in 12 patients (4.8%) including 6 patients with Marfan syndrome and 5 with aortitis. Seven detachments occurred at the proximal anastomosis. Of the 7 patients who developed a proximal graft detachment, the standard proximal anastomosis technique was utilized in 5 patients (5 of 105; 4.8%) and the skirted proximal anastomotic technique in 2 patients (2 of 147; 1.4%). The other 6 detachments developed at the coronary anastomosis. Of these 6 patients, Bentall and De Bono's original inclusion technique [1] was utilized in 2 patients, the graft interposition technique in 3, and the direct button technique in 1. One patient presented with multiple detachments at both the proximal and coronary anastomoses due to a graft infection. Ten of 12 patients with graft detachment underwent reoperation. One patient with a detachment of the proximal anastomosis accompanied by coronary true aneurysms has been followed up medically, and another patient with a detachment of the coronary anastomosis died from chronic renal failure before a reoperation was considered. The actuarial probability of remaining free of detachment of the graft anastomosis was 96.9% at 10 years and 95.5% at 15 years.

Thromboembolisms

Thromboembolic events occurred in 8 patients (3.2%); cerebral infarction in 7 and thromboembolism of the superior mesenteric artery in one. Seven patients had received anticoagulation therapy for the use of a mechanical valve. The actuarial probability of remaining free of thromboembolic events was 96.5% at 15 years.

Anticoagulant-Related Complications

Fourteen patients (5.6%) had complications related to anticoagulant therapy which required blood transfusion or in-hospital treatment; an intracranial hemorrhage in 7 patients, gastrointestinal bleeding in 5, and genital bleeding in 2. Four of the intracranial hemorrhages were fatal. In all, the actuarial probability of remaining free of these complications was 93.6% at 15 years.

Coronary Artery Complications

Coronary ostial aneurysms developed at 6 coronary anastomoses in 4 Marfan patients (1.6%). Of the 6 coronary ostial aneurysms, Bentall and De Bono's original inclusion technique was utilized in 3 of the anastomoses and the graft interposition technique was utilized in 3 anastomoses. A coronary obstruction was observed in 3 patients. Of the 3 patients, the Cabrol technique was utilized in 1 and the direct button technique in 2. Two of the 3 patients with a coronary obstruction had aortitis.

Event-Free Survival Rate

The actuarial probability of being alive and free from a prosthesis-related complication was 79.4%, 67.8%, and

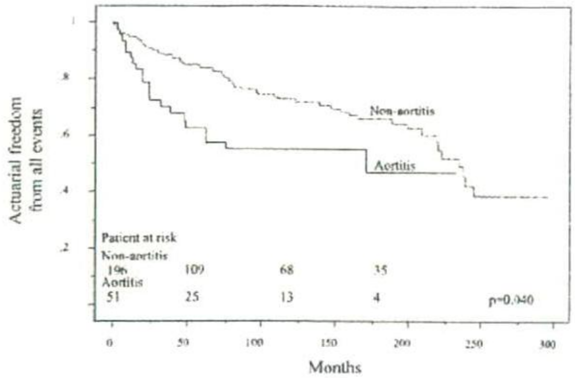

Fig 3. Actuarial freedom from all events including late deaths in aortitis and nonaortitis patients.

60.7% at 5, 10, and 15 years, respectively. The incidence of prosthesis-related complication was significantly high in aortitis patients (Fig 3).

Comment

Several large studies have demonstrated excellent outcomes associated with a CGR with low 30-day mortality rates ranging from 4.3 to 9.0% [2, 3, 7]. The current study documented a comparable result of 9.5% of the in-hospital mortality, even including that of the emergency surgeries. The mortality of elective surgery was 4.3%. Since 1995, no in-hospital death has occurred in 95 elective patients. The increased experience, as well as other factors, such as the development of a refined pump oxygenator system and the myocardial protection technique, the availability of "zero porosity" vascular grafts, and improved perioperative management, has contributed to the improvement of the outcome.

The actuarial survival rate was also comparable with the range of 62% to 93% at 10 years, which were previously published [7–9]. The present results suggest that one of the significant independent risk factors of late death is aortitis, which is predominant in Asian countries. The prevalence of aortitis leading to surgery is high in the current series. Takayasu arteritis was dominant among the 56 patients with the pathology of aortitis. The main pathologic findings associated with Takayasu arteritis are severe destruction of the medial elastic fibers and thickening of intima, media, and adventitia. The pathologic fragility causes frequent detachment of the prosthesis after an aortic valve replacement or CGR [10, 11]. Indeed, in the current study, late graft detachment was observed in 5 of 56 aortitis patients (8.9%). Although the appropriate approach to the aortic valve diseases associated with aortitis is unclear, we prefer a CGR, especially in the active stage, because the graft detachment was less frequent when treated with a CGR than with an isolated aortic valve replacement [10]. Ishikawa and colleagues [12] reported the long-term mortality of the patients having Takayasu arteritis with major complications who require surgical treatment was considerably poor, with only 43% at 15 years [12]. In the present study, the 10-year and 15-year survival rates of aortitis patients were 69% and 58%, respectively. In addition, the incidence of prosthesis-related complications was significantly high in aortitis patients; 5 graft infections (8.9%), 4 cerebral infarctions (7.1%), and 2 coronary arterial obstructions (3.4%). Not only the poor natural history of this subset, but also the frequent need for a reoperation for graft detachment, the life-long steroid therapy, and the high incidence of graft infection can thus influence the poor long-term survival.

Although controversy remains in regard to whether Marfan syndrome decreases the late survival rate [2, 7, 13, 14], the current results suggested that Marfan syndrome was one of the significant predictors of late deaths. The high incidence of an aortic dissection and an aneurysm of the residual aorta, or subsequent operations can potentially increase the late mortality in Marfan patients. In fact, in the current series, the incidence of a reoperation on the residual aorta was significantly higher in Marfan patients (27 patients; 29%) than in non-Marfan patients (5%). In addition, 16 of 27 Marfan patients who required an operation on the residual aorta required a third or fourth operation. The incidence of graft detachment and coronary ostial true aneurysm were significantly high in Marfan patients. To reduce these complications, a direct button technique can be the most favorable technique, especially in Marfan patients. The size of the side hole made in the graft must be reduced to fit the diameter of the coronary artery, and a suture should be placed inside the origin of the coronary artery so that a residual aortic wall can be eliminated [15].

A composite valve graft root is one of the best treatment strategies for an acute type A aortic dissection and aortic regurgitation [16, 17]. In the current study only 25 patients had acute type A aortic dissection. The low prevalence of acute aortic dissection in this study can be explained by the fact that most of patients with acute type A aortic dissection and aortic regurgitation were effectively treated by an aortic valve resuspension and ascending aortic replacement, unless aortic root was pathologically dilated or destroyed by the dissection process. In addition, recently, an aortic valve-sparing operation has been used as an alternative strategy for this condition.

Although recent studies report an excellent early survival rate for a proximal reoperation after a CGR, ranging between 70% and 86% [15, 18, 19], a redo CGR remains a challenging procedure with a high morbidity and mortality, especially in the setting of graft infection. Graft detachment is one of the predominant indications for late reoperation [3, 8, 15, 20–23]. In the present study, graft detachment occurred in 11 patients with Marfan syndrome or aortitis. Extreme caution is necessary for the anastomosis in these patient subsets. The direct button technique is widely utilized and has reduced the rate of reoperation on the ascending aorta or aortic valve after a CGR (0% to 19% at 3 to 10 years) [2, 3, 8, 9, 14, 20]. Since 1985, we have utilized the direct button technique for coronary artery reconstruction and that technique has contributed to reducing the incidence of graft detachment and coronary complications. At present, the direct button technique is our first-line technique. However, if there is anatomic difficulty or dense adhesion precluding the direct button anastomosis, especially in a redo root surgery, the alternative is a short-length graft interposition technique [4]. The current data support the efficacy of the graft interposition technique with nearly the same long-term reliability as the direct button technique. With regard to the proximal anastomosis, the skirted technique has been the current preference. The concept of translocating the prosthetic valve, initially described by Cabrol and colleagues in 1981 [5], was adopted in 1989 to secure the anastomosis without bleeding and to reduce the risk of late graft detachment. In the skirted technique, the prosthetic valve does not apply direct stress on the aortic annulus by separating the suture-line of the prosthetic valve from that of the aortic annulus [24]. Although the current study was not designed to compare the two proximal anastomosis techniques and it was not assumed that the skirted technique would completely surpass the standard technique, the current results demonstrate some advantages of the skirted technique by improving the frequency of late proximal graft detachment and the long-term survival. The results encourage the continued utilization of the skirted technique, especially in patients with a fragile aortic annulus, such as those with aortitis and Marfan syndrome. However, 2 patients experienced proximal graft detachment after a CGR using the skirted technique. One patient had giant cell aortitis and another had Behçet disease. The former underwent a second skirted CGR and repeated graft detachment of the right coronary ostium and was eventually treated with an aortic homograft root replacement. The latter underwent 3 CGR procedures for repeated graft detachment. In patients with a fragile inflammatory aortic pathology, further refinement of the anastomotic technique, such as buttress sutures from the lateral side of the aortic wall for reinforcement of the prosthesis at the aortic annulus, placement of thick belt-like Teflon felt on the lateral side of the aortic wall, is required to reduce late graft detachment [24].

The use of a bioprosthesis is an independent risk factor for a late reoperation. It is obvious that the prosthetic valve dysfunction is an inherent late complication of a bioprosthesis. However, all of the valve failures occurred in use of the Ionescu-Shiley (Shiley Laboratory) bioprosthesis implanted early in the study period. Since 1987, the Carpentier-Edwards bovine pericardial prosthesis has been used and there have been no valve failures. The durability of the manufactured bioprosthesis, especially the pericardial valve, is well-documented [25]. Galla and colleagues [26] also reported excellent long-term performance of bioprosthetic CGR with no instances of valve failure during a 5-year follow-up. A CGR using a bioprosthesis is a useful option for some subsets such as elderly patients, or those who are contraindicated for anticoagulation therapy. Currently, a "Valsalva graft" has been used with a bioprosthetic aortic valve for the long-term valve durability.

The current study has inherent biases. The series of patients examined were derived from a retrospective review covering a long time interval and the patients included in this study had various different surgical indications and were treated by different surgeons.

This report presented the 27-year experience in performing a CGR and concluded that a CGR is a safe and reliable procedure for various aortic root diseases, thus resulting in sufficient early and long-term results. Aortitis is the significant predictor of late death after CGR, with a high incidence of late graft detachment and other complications. The skirted proximal anastomotic technique can help surgeons to avoid late proximal graft detachment and the need to perform a reoperation.

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Composite Valve Graft Replacement of the Aortic Root: Twenty-Seven Years of Experience at One Japanese Center

Tomohiro Tsunekawa, Hitoshi Ogino, Hitoshi Matsuda, Kenji Minatoya, Hiroaki Sasaki, Junjiro Kobayashi, Toshikatsu Yagihara and Soichiro Kitamura

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Dilatation of the Aneurysmal Sac After Total Arch Replacement

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In our institution, total arch replacement for distal arch aneurysms is performed through a median sternotomy with antegrade selective cerebral perfusion. The distal anastomosis to the completely transected descending aorta is made through the aneurysmal sac. We report on three interesting cases presenting late dilatation of the aneurysmal sac due to collateral flow after total arch replacement.

(Ann Thorac Surg 2008;85:639–41)

In general, prosthetic graft replacement of aortic aneurysm is carried out without complete resection of the aneurysmal sac. In particular, total arch replacement for distal or proximal descending aortic aneurysm is performed through the aneurysm sac without resection of the aneurysmal wall to prevent injury to the phrenic and vagus nerves and to the lung. In this report, we present three interesting cases that developed late dilatation of the aneurysmal sac after total arch replacement for a distal arch aneurysm through a median sternotomy.

Case Reports

Patient 1

An 82-year-old man underwent total arch replacement for a huge saccular-type distal arch aneurysm of 94 mm in 2002. The postoperative course was uneventful. One year later, the follow-up enhanced computed tomographic scans revealed a small leakage of the contrast medium around the prosthetic graft (Fig 1). The leak was considered from the distal anastomosis site. Therefore, stent graft insertion was performed to cover the leak; however, even after this was performed the leak did not disappear. Angiography was then performed to identify some collateral vessels opening into the aneurysmal sac. A collateral vessel originating from the right internal thoracic artery (ITA) to the aneurysm sac was opacified. Coil embolization of the right ITA was then performed. Thereafter, the leak decreased, although it did not vanish completely. The aneurysm sac had not dilated 36 months after coil embolization.

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Patient 2

An 82-year-old woman underwent total arch replacement for a saccular-type distal arch aneurysm of 60 mm in 2002. The postoperative course was uneventful. One year later, the follow-up enhanced computed tomographic scans revealed some leak of contrast medium into the aneurysmal sac (Fig 1). Although angiography did not reveal any leakage from the distal anastomosis site, a collateral vessel originating from the left ITA to the aneurysmal sac was opacified. Coil embolization of the left ITA was performed. The leak of contrast medium to the aneurysmal sac did not completely vanish. However, the aneurysmal sac was not dilated 41 months after coil embolization.

Patient 3

A 75-year-old man underwent total arch replacement for a huge fusiform type distal arch aneurysm of 100 mm in 2001. The postoperative course was uneventful. Five years later, hemoptysis developed in the patient. Computed tomographic scans revealed a small dilatation of the aneurysmal sac (Fig 1). Although angiography did not reveal leakage from the distal anastomosis site, a collateral vessel originating from the left ITA to the aneurysmal sac was revealed (Fig 2). After coil embolization of the left ITA was performed (Fig 2), hemoptysis disappeared. The patient continues to be carefully followed.

FEATURE ARTICLES

Comment

Pseudoaneurysm formation after thoracic aortic replacement develops in the late stage. Although it can be secondary to trauma or infection, previous cardiac surgery is the most frequent cause [1]. It occurs in less than 0.5% of all cardiac surgical cases [2]. Pseudoaneurysms are located at previous anastomotic sites, aortotomy sites, cannulation and venting sites, and proximal vein graft anastomotic sites. Anastomotic pseudoaneurysm after ascending or aortic arch replacement for aortic dissection has been reported at various rates ranging from 2% [3] to 38% [4]. It is usually caused by anastomotic leak or cutting of the aortic tissue. In the presented series, the residual aneurysmal sacs dilated after total arch replacement, although in most cases they shrink after surgery. Several causes were considered for these phenomena. Obviously they might be caused by anastomotic leak or cutting of the aortic tissue. However, angiography did not reveal any leak from the anastomotic sites. Even after stent grafting that covering the anastomotic sites, some leakage remained.

In our surgical techniques of total arch replacement for distal arch aneurysm, distal anastomosis is made by division of the descending aorta at the distal site of the aneurysm. The aneurysm is not resected. Some arteries opening into the aneurysm are closed by suturing. However, some of them might be disguised with mural thrombi or atheroma in the aneurysmal sac, because all mural thrombi or atheroma were not always removed in our routine techniques. Thus, the aneurysm sac might be

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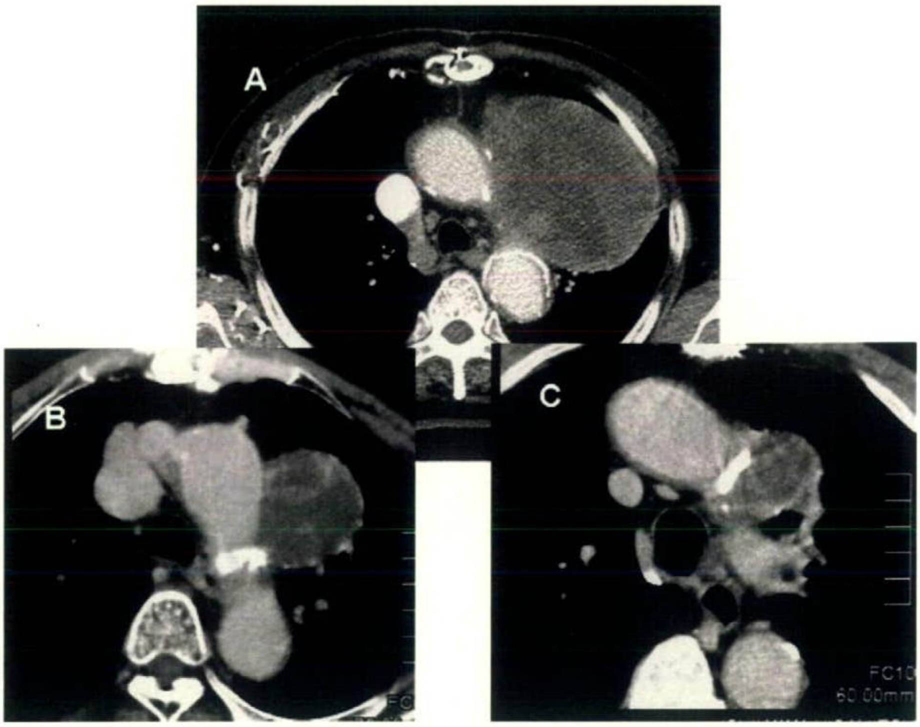
Fig 1. Enhanced computed tomographic scans for (A) patient 1, (B) patient 2, and (C) patient 3 showing leakage of contrast medium around the artificial graft and inflow of contrast medium to the aneurysm wall.



enhanced and dilated. It might have a similar mechanism to that of type II endoleak after endovascular aortic repair. Gould and colleagues [5] reported there were 20% type II endoleaks with preoperative coil embolization for aortic side branches and 23.3% type II endoleaks without preoperative coil embolization during the follow-up period. Therefore, coil embolization was performed to occlude the collateral vessels. There are two similar reports on coil embolization of an aortic arch false aneurysm [6, 7]. Miguel and colleagues [6] succeeded in coil embolization of a pseudoaneurysm over the distal suture line of an ascending aortic graft replacement. Chapot and colleagues [7] succeeded in coil embolization of a pseudoaneurysm at the level of the aortic arch after surgical replacement of the aortic root and arch for aortic dissection. However, in our cases, coil embolization was successful in only 1 patient, presumably because there might be many collateral sources opening into the aneurysmal sac.

Otherwise, systemic pressure has recently been revealed within the aneurysm sacs of patients with collateral endoleak. This discovery suggests that these patients could remain unprotected and at risk for aneurysm rupture [8]. Consequently, close observation for a long period is mandatory even after successful total arch replacement.

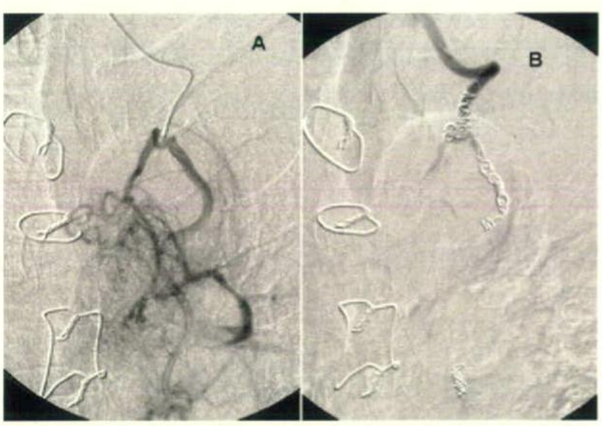


Fig 2. Angiography of patient 3. (A) Inflow of contrast medium from the left internal thoracic artery (ITA) to the aneurysm wall (B) after coil embolization for the left ITA branch.

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Aneurysm of a Right-Sided Descending Aorta With a Normal Left-Sided Aortic Arch

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We encountered an extremely rare case of a saccular aneurysm of the descending aorta developing to the right of the spinal column with a normal left-sided aortic arch. An 80-year-old man was admitted to our hospital because of a saccular aneurysm of the right-sided descending aorta that had increased in diameter. Resection of the aneurysm and prosthetic graft replacement of the right-sided descending thoracic aorta were successfully performed under deep hypothermia through a right thoracotomy.

(Ann Thorac Surg 2008;85:641–3)

Because aneurysms of the right-sided descending aorta with the left-sided aortic arch are quite uncommon, few opinions on surgical treatment exist. We report our surgical strategy for this unusual entity and present a review of the literature.

An 80-year-old man was admitted to our hospital because of a saccular aneurysm of the descending aorta, which was detected on computed tomography several years previously, but it had increased in size from a diameter of 50 mm to 70 mm within 1 year. Hypertension had been present for more than 18 years. However, no symptoms had been noted. A chest x-ray film showed the dilatation of the mediastinum toward the right hemithorax (Fig 1). A computed tomographic scan (Fig 2) and angiographic examinations (Fig 3) revealed that the tortuous descending aorta was on the spinal column at the sixth thoracic vertebra just behind the esophagus, which ran along the right side of the spinal column to the first lumbar vertebra, and then returned to the usual position. The dilatation of the aorta was seen from the seventh thoracic to the first lumbar vertebra. The patient had a past history of tuberculous pleuritis of the left hemithorax, partial gastrectomy for a gastric ulcer, and cholecystectomy for cholecystitis. Serological tests for syphilis were negative. No congenital anomalies were found on examination.

The right fifth intercostal space was opened, and a seventh intercostal pleurotomy was added to access the distal part of the descending aorta. Dense adhesions were seen in the pleural cavity. Cardiopulmonary bypass through ascending aortic perfusion and right atrial drainage was established, and perfusion cooling was initiated. A venting catheter was inserted into the left atrium through the right upper pulmonary vein. When the rectal temperature dropped below 18°C, the descending aorta just proximal to the diseased segment was clamped. Partial extracorporeal circulation was continued to maintain the cerebral and coronary circulation under ventricular fibrillation. The partial circulatory flow was 1,000 mL/min and the mean aortic pressure was maintained around 40 mm Hg. The proximal aorta was transected at the appropriate level. The aneurysm was then incised longitudinally just above the diaphragm. The aneurysm was extensively atherosclerotic with dense calcification, and all intercostal arteries were occluded. The anastomosis to the proximal aorta using a woven polyester, gelatin coated, 22 mm-prosthetic branched graft (Gelweave Ante-Flo; Sulzer Vascutek Ltd, Renfrewshire, Scotland) was completed using 3-0 polypropylene sutures, reinforced with polyester felt. Distal anastomosis was performed by an open aortic technique. Extracorporeal circulation lasted 160 minutes. The duration of the ventricular fibrillation was 106 minutes and the circulatory arrest of the lower body was 49 minutes. No neurocognitive dysfunction was found during the postoperative period. The postoperative chest computed tomographic scan showed no abnormal findings. Respirator management was required for 12 hours. However, he took time for rehabilitation for respiratory functional disorder. The patient was discharged on postoperative day 40.

Comment

Although there are some reports of right-sided descending aortas with a right-sided aortic arch [1, 2], atherosclerotic aneurysm of the descending aorta developing to the right of the spinal column with a normal left-sided aortic arch is extremely rare. Because Epstein and Friedman [3] reported the first case of the aneurysm of the descending aorta protruding to the right of the spine in 1949, several case reports have been subsequently made [4–6]. These reports usually focused on the difficulty of the diagnosis, because chest x-ray films were the major diagnostic method in those days.

The first successful surgical case was reported by Claxton and Dillon in 1969 [5]. The patient underwent closure of the neck of the saccular aneurysm and resection of the aneurysmal wall through a right thoracotomy. In 1970, Engelman and Clauss [6] reported another case of an aneurysm presenting in the right thorax. They performed resection of the aneurysm and an end-to-end

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超高圧処理技術を応用した人工角膜の作製と評価

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第15回生物関連高圧研究会20周年記念シンポジウム抄録集

2008年1月24日受付／2008年1月31日受理

要旨

人工角膜として、これまでに多くの材料研究が行われているが、移植後の感染や脱落により、長期間有用である人工角膜開発には至っていない。一方、異種組織から細胞を除去し、残存する基材を移植組織として用いる方法として、組織の脱細胞化が検討されている。これまで我々は、脱細胞化法として、超高圧印加により組織内の細胞を破壊し、洗浄により細胞残渣を除去する超高圧脱細胞化法を考案した。本手法で、細胞の除去による免疫反応の抑制と生体の微小構造の保持による適合性の向上が期待できる。本研究では、超高圧脱細胞化法による人工角膜の作製とその物性解析を行ない、角膜移植片としての可能性を検討した。超高圧処理で得られた脱細胞角膜は、生体角膜に比べ白濁はしていたが組織内部から細胞は完全に除去されていた。また、移植結果により白濁していた角膜は透明となり移植後の拒絶も観察されなかった。このことから、超高圧印加法は、組織構造を維持しつつ、組織内からの細胞除去が行え、組織適合性が高い組織の作製ができるものと考えられ、かつ眼科領域における移植組織不足を解消できるものと考えられる。

キーワード：人工角膜、脱細胞化、超高圧処理技術

1. はじめに

現在、角膜移植術を要する患者は、全世界で１００万人以上と見積もられている。しかしながら、角膜移植を受けている患者数は年間約６万人足らずであり、多くの国で提供眼球不足が大きな問題となっている。我が国においても、日本アイバンク協会に登録されている待機患者数が約５０００人であるに対し、献眼者数が約１０００人、利用眼球は約１５００個に留まっており移植用角膜は不足している状況である。このような問題の抜本的な解決として、人工角膜の開発が待望されている。人工角膜としては、合成高分子であるポリメチル

メタクリレート（PMMA）、ポリテトラフルオロエチレン（PTFE）やポリビニルアルコール（PVA）などが試みられている[1-4]。我が国においても人工角膜の開発は、長い歴史を持っている[5]。それにもかかわらず、高い信頼性・機能を有する人工角膜は開発されていない。最近では、AlphaCore（PMMA製）が米国FDAにて承認され、臨床治験の集積段階にある。しかしながら、これらの材料と角膜組織との適合性は十分とは言えず、その結果、レシピエント細胞の基材上への接着が十分になされず、人工角膜接合部での融解に伴う脱落や感染症などが重要課題となっている。この要因の一つとして、生体角膜と人工角膜との物性の相違が挙げられる。

一方、最近では、再生医療や組織工学の側面から角膜再生の研究が行われている。再生医療技術によって、角膜上皮および角膜内皮が臨床応用されており、再生医療技術の角膜再生への有効性から、角膜全層の再生が期待されている。しかし、角膜上皮および角膜内皮の再生は、細胞のみを用いた細胞シートや羊膜を用いた基本的には細胞層のみの再生であり、角膜のほぼ９０％を占める実質部分の再生に関しては、未だ臨床応用にいたる再生技術は開発されていない。このため、角膜実質部の再生については、コラーゲンゲル・スポンジを用いた研究が大半を占めている。そこで我々は、生体組織の物性に類似する人工角膜として、脱細胞化角膜の調製について検討している。脱細胞化組織とは、異種組織から細胞を除去し、残存する生体支持組織を指す。脱細胞化組織の調製法としては、界面活性剤やタンパク質分解酵素などの薬液による化学的手法と、最近我々が開発した物理的手法である超高圧処理法がある。後者は、超高圧印加により細胞を破壊し、細胞残渣を洗浄により除去する手法である（Fig.1）。これまで、血管、心臓弁、靭帯、骨などの種々の組織における脱細胞化に成功している[6-7]。本研究では、界面活性剤法、超高圧処理法による角膜の脱細胞化処理により得られた脱細胞化角膜の物性と *in vivo* での異種移植実験を行い、脱細胞化角膜の人工角膜としての有効性について検討した。

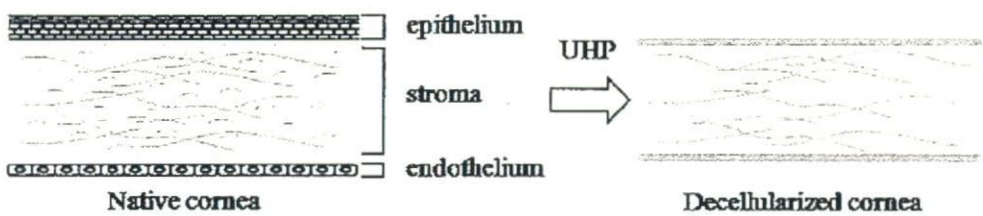

Fig.1. Structure of native cornea (left) and scheme of decellularized porcine corneas(right).

2. 材料と方法

2.1. 界面活性剤による角膜の脱細胞化

食用成体ブタ眼球から角膜を摘出し、各種処理溶液（1 w/v% SDS, 1 w/v% TritonX-100）に浸漬し、37℃で24時間の条件で連続振盪した。得られた脱細胞化組織は、HE染色により評価した。

2.2. 超高圧処理技術を用いた角膜の脱細胞化

食用成体ブタ眼球から角膜を摘出し、PBS （Dextran70 35mg/ml, penicillin streptomycin 10ul/ml)中において、超高圧処理装置（Dr.CHEF、㈱神戸製鋼所）を用い、処理圧力10000気圧で処理時間10分（圧力印加速度666気圧／分、処理温度10℃）で超高静水圧印加した。処理後に組織を洗浄液に浸漬し、37℃のインキュベーター内で連続振盪し、細胞残渣を除去し