SURGERY FOR ACQUIRED HEART DISEASE

AORTIC ROOT REPLACEMENT

Risk factor analysis of a seventeen-year experience with 270 patients

Between September 1976 and September 1993, 270 patients underwent aortic root replacement at our institution. Two hundred fifty-two patients underwent a Bentall composite graft repair and 18 patients received a cryopreserved homograft aortic root. One hundred eighty-seven patients had a Marfan aneurysm of the ascending aorta (41 with dissection) and 53 patients had an aneurysm resulting from nonspecific medial degeneration (17 with dissection). These 240 patients were considered to have annuloaortic ectasia. Thirty patients were operated on for miscellaneous lesions of the aortic root. Thirty-day mortality for the overall series of 270 patients was 4.8% (13/270). There was no 30-day mortality among 182 patients undergoing elective root replacement for annuloaortic ectasia without dissection. Thirty-six of the 270 patients having root replacement also had mitral valve operations. There was no hospital mortality for aortic root replacement in these 36 patients, but there were seven late deaths. Twenty-two patients received a cryopreserved homograft aortic root; 18 of these were primary root replacements and four were repeat root replacements for late endocarditis. One early death and two late deaths occurred in this group. Actuarial survival for the overall group of 270 patients was 73% at 10 years. In a multivariate analysis, only poor New Year Heart Association class (III and IV), non-Marfan status, preoperative dissection, and male gender emerged as significant predictors of early or late death. Endocarditis was the most common late complication (14 of 256 hospital survivors) and was optimally treated by root replacement with a cryopreserved aortic homograft. Late problems with the part of the aorta not operated on occur with moderate frequency; careful follow-up of the distal aorta is critical to long-term survival. (J THORAC CARDIOVASC SURG 1995; 109:536-45)

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Replacement of the aortic root, first performed by Bentall and DeBono[1] in 1968, has been applied to a variety of aortic diseases. Although early results of this procedure have been described with particular focus on patient subsets, such as those with the Marfan syndrome, few broad overviews of the procedure including risk factor analysis and examination of long-term results have been published.[2-4] This report summarizes our experience with all patients (with and without the Marfan syndrome) undergoing aortic root replacement at our institution over the past 18 years.

Patients and methods

Patient selection. All patients undergoing aortic root replacement between September 1976 and September 1993 are included in this report. Patients were identified from a computerized patient registry, operative log books, and office records. Data were collected retrospectively from operative records, hospital charts, and clinic follow-up notes. Late follow-up data were obtained from clinic records and direct contact with patients and their primary physicians.

The majority of patients in this series (187/270; 69%) had the Marfan syndrome and aneurysm of the ascending aorta (Table I); this reflects a referral pattern in our institution resulting from the Center for Medical Genetics of The Johns Hopkins Hospital, which sees a large number of patients with Marfan syndrome annually.

Operative technique. Two hundred fifty-two of the 270 patients undergoing aortic root replacement had a composite graft placed by means of the Bentall technique or its modification.[1] The other 18 patients underwent root replacement with a cryopreserved aortic homograft.

Early in the series, the Bentall procedure included wrapping the aortic aneurysm wall around the composite

graft for hemostasis; the first 87 patients with Marfan syndrome in the series had aneurysm wraps. After a report in 1986 by Kouchoukos, Marshall, and Wedige-Stecher[5] on late complications of the wrap, the technique was discontinued. Also early in the series, direct anastomosis of the coronary arteries to the Dacron graft was performed without excision of the coronary arteries from the aortic wall. After description of the Cabrol interposition graft,[6] this type of graft was used with moderate frequency commencing August 1986 but was discontinued January 1989 after compression of the left coronary ostium was observed in one case.

Between 1976 and May 1986, Björk-Shiley composite grafts (Shiley, Inc., Irvine, Calif.) were used. Initially, these grafts were fabricated at the operating table from a prosthetic valve and a Dacron tube. Since May 1986, the St. Jude Medical composite graft valve (St. Jude Medical, Inc., St. Paul, Minn.) has been preferred.

Standard hypothermic (28° to 30° C) cardiopulmonary bypass techniques were used. Myocardial protection consisted of simple antegrade administration of crystalloid potassium cardioplegic solution (Stanford solution, 1 L) and maintenance of myocardial hypothermia by continuous topical 4° C saline solution given at a rate of 100 ml/min.

Our operative technique has been described in earlier publications.[7, 8] If the coronary ostia have migrated more than 2 cm from the aortic anulus, mattress sutures are placed in everting fashion; if the ostia are relatively low lying, mattress sutures are placed from below the anulus, as described by Helseth and colleagues.[9] Although we still prefer direct anastomosis of the coronary arteries to the Dacron graft without excision of the coronaries from the aortic wall, if either coronary ostium is low in the aorta, it is excised, mobilized, and anastomosed slightly higher on the composite graft. After completion of the two coronary anastomoses, the distal ascending aorta is transected and anastomosed to the composite graft with continuous 3-0 polypropylene.

Homografts were implanted in a manner similar to composite grafts, except that a thin strip of Teflon felt was occasionally used to reinforce the homograft side of the proximal anastomosis.

Of the 270 patients having root replacement, 28 (28/270; 10%) required hypothermic circulatory arrest to permit partial resection of the aortic arch or facilitate anastomosis of the composite graft to the proximal arch.

Statistical methods. Survival and event-free curves were calculated by the Kaplan-Meier method. Univariate analysis was performed by the Mantel-Cox method and the multivariate analysis by the Cox proportional hazards method. Survival data are presented with standard error of the estimate. Statistical computations were made with the use of the BMDP statistical software package (BMDP Software, Los Angeles, Calif.).

Results

Operative data were available for all patients. Follow-up data were available for 94% of 256 hospital survivors at a mean interval of 4 years after the operation.

Preoperative patient characteristics. Mean patient age was 38.3 years. Mean age of the patients with the Marfan syndrome was 32.8 years, and for those with non-Marfan medial degeneration it was 49.3 years. The 30 patients with other miscellaneous diagnoses had a mean age of 53.0 years. Two hundred three of the 270 patients were male (203/270; 75%). Eighty-eight patients were in New York Heart Association (NYHA) functional class I (33%), 75 (28%) were in class II, 54 (20%) were in class III, and 43 (16%) were in class IV. NYHA functional class information was not available in 10 patients (3%).

The various pathologic lesions for which root replacement was performed are shown in Table I. The majority of patients in this series had a Marfan aneurysm of the ascending aorta (187/270; 69%). Fifty-three patients (53/270; 20%) had aortic root replacement for aneurysm caused by nonspecific medial degeneration but not associated with the Marfan syndrome. Thus 240 patients (240/270; 89%) had annuloaortic ectasia as the primary pathologic lesion. The remaining 30 patients (30/270; 11%) had miscellaneous diagnoses: prosthetic endocarditis (n = 15), atherosclerotic aneurysm (n = 8), aortic injury from crossclamping (n = 3), arteritis (n = 2), and Ehlers-Danlos syndrome (n = 2). Of the 15 cases of prosthetic endocarditis, 11 were infections of aortic valve prostheses, 2 were sleeve graft infections, and 2 were composite graft infections. Thirty-six of the 270 patients treated by root replacement also underwent mitral valve operations and 13 underwent coronary artery bypass for obstructive disease.

Operative results. Thirty-day mortality for the series of 270 patients was 4.8% (13/270; Table II). However, no early deaths occurred among the 182 patients undergoing root replacement for annuloaortic ectasia aneurysm without dissection; this group included 146 patients with Marfan syndrome and 36 patients with other types of medial degeneration. Among the 240 patients with annuloaortic ectasia with or without dissection, there were six early deaths (2.5%). Causes of death, both early and late after operation, are detailed in Table II. Low cardiac output was the most common cause of death early after operation. In this report, the terms *30-day mortality* and *early mortality* are used interchangeably.

In 63 of the 270 patients dissection of the ascending aorta was documented during the operation (63/270; 23%). The distribution of acute versus

Table I. *Aortic root replacement in 270 patients at The Johns Hopkins Hospital*

	Annuloaortic ectasia (patients)				
	Marfan	*Other medial degeneration*	*Total*	*Miscellaneous*	*Total*
Aneurysm (nondissected)	146	36	182	10*	192
Aortic dissection	41	17	58	5	63
Acute					
DeBakey I	16	3	19		19
DeBakey II	4	2	6	1†	7
Chronic					
DeBakey I	3	5	8	2‡	10
DeBakey II	18	7	25	2§	27
Postprosthetic endocarditis				15‖	15
Total	187	53	240	30	270

*Atherosclerotic aneurysm, $n = 7$; arteritis, $n = 2$; Ehlers-Danlos, $n = 1$.

†Ehlers-Danlos.

‡Postoperative aortic clamp injury and atherosclerotic aneurysm.

§Postoperative aortic clamp injury, $n = 2$.

‖After aortic valve replacement, $n = 11$; after composite graft, $n = 2$; after sleeve graft, $n = 2$.

Table II. *Causes of death after aortic root replacement*

	Marfan (n = 187)		*Other medial degeneration (n = 53)*			*Total mortality*	
Causes of death	*Aneurysm (n = 146)*	*Dissection (n = 41)*	*Aneurysm (n = 36)*	*Dissection (n = 17)*	*Miscellaneous (n = 30)*	*30 day*	*Late*
Low output (operating room)		2*		1*	3*	6	
Multiorgan failure			1	1	4*	4	2
Hemorrhage				1*		1	
Neurologic injury, circulatory arrest				1*		1	
Gangrenous gallbladder			1				1
Arrhythmia†	6			1*		1	6
Pulmonary sepsis		1					1
Drug overdose		1					1
Composite graft endocarditis	2	1	1	1	1		6
Rupture of distal aorta	1	2					3
Coronary dehiscence	1						1
Secondary to late thoracoabdominal resection‡		1			1		2
Unknown	1	3	1				5
Total	11	11	4	6	9	13	28

*Thirty-day mortality.

†Known or presumed.

‡A patient with Marfan disease and DeBakey type I dissection died 4 years after a composite graft operation after a thoracoabdominal procedure; a patient with Ehlers-Danlos syndrome died 5 years after a composite graft operation after a thoracoabdominal procedure.

chronic dissection and the DeBakey type are presented in Table I. In the 63 patients with dissection, mean aortic diameter at the sinus level was 7.8 cm, in contrast to 6.7 cm in those without dissection. Forty-one of the 187 patients with the Marfan disease had ascending aortic dissection (41/187; 22%); mean aortic diameter in this group was 7.6 cm versus 6.7 cm for those without dissection. Of note, 10 patients with the Marfan syndrome had dissection in an aorta smaller than 6.5 cm. Two of the 41 patients who had the Marfan syndrome with ruptured aorta and pericardial tamponade died during the operation of low cardiac output; both were moribund on hospital admission.

Seventeen patients with non-Marfan medial degeneration had dissections, five acute and 12 chronic. Four early deaths occurred among these 17 patients (see Table II).

Thirty-six of the 270 patients undergoing root replacement also had mitral valve operations (Table

III). All of these patients were in the annuloaortic ectasia group. Thirty-two mitral procedures were concomitant with root replacement, and four were performed at a separate operation. There were 26 mitral repairs and 10 mitral replacements with prostheses. No hospital deaths occurred as a result of aortic root replacement in these 36 patients.

The highest operative mortality occurred in the group with miscellaneous diagnoses (see Tables I and II). Nine of these 30 patients died (9/30; 30%), typically of low cardiac output or multiple organ failure. Half of the miscellaneous group (15/30) had endocarditis; four early deaths occurred among these 15 patients (4/15; 27%), all as a result of low cardiac output or multiple organ failure and all in patients with infected aortic prostheses. Of 15 patients undergoing root replacement for prosthetic endocarditis, 11 received a cryopreserved homograft. One early death occurred in this group as a result of multiple organ failure. Seven patients with the Marfan syndrome (two adults and five children) also received homograft roots as their primary procedure, mainly to avoid anticoagulation associated with mechanical prostheses; no early deaths occurred in this group.

Late results. A total of 28 late deaths have occurred among the 256 hospital survivors (see Table II). Twenty of these late deaths fall into four major categories: arrhythmia ($n = 6$), composite graft endocarditis ($n = 6$), unknown ($n = 5$), and rupture of the unoperated aorta distal to the composite graft ($n = 3$). The remaining 11 deaths were from diverse causes. Only one death resulted from late dehiscence of a coronary artery–composite graft anastomosis.

Fig. 1 depicts actuarial survival for the overall group of 270 patients. Survival was 82% at 5 years, 73% at 10 years, and 67% at 14 years.

Risk factor analysis. Multiple patient- and procedure-related variables were screened by univariate and subsequent multivariate analysis as potential risk factors for early or late death. These variables included preoperative NYHA functional class, gender, age, presence of aortic dissection, Marfan syndrome, race, use of hypothermic circulatory arrest, type of graft used for root replacement, urgency of operation, mitral valve operation, coronary artery disease, previous root surgery, and era of operation. In a multivariate analysis, only poor NYHA class (III or IV), non-Marfan status, preoperative dissection, and male gender emerged as significant independent predictors of early or late death (Figs. 2, 3, and 4 and Table IV). The impact of type I and II dissections on survival is depicted in Fig. 4; survival at 5 years was 87% without dissection but was 79% and 55% for type II and Type I dissections, respectively. At 10 years, survivals dropped to 81%, 66%, and 45% for patients without dissection and for patients with type II and type I dissections, respectively.

Table III. *Mitral valve operations among 240 patients undergoing aortic root replacement for annuloaortic ectasia*

	No. of patients		*Late mortality*
Marfan ($n = 187$)			
Concomitant with root replacement		30	
Annular repair	24*		4§
MVR	6		
Not concomitant with root replacement		4	
Annular repair	1†		
MVR	3		2‖
Other medical degeneration ($n = 53$)			
Concomitant with root replacement		2	
Annular repair	1‡		
MVR	1		1¶
Total		36	7

*Twenty-three patients had annular ring and one patient had annuloplasty.

†Annular ring.

‡Annuloplasty.

§Two patients, presumed arrhythmia at 4 and 5 years; one patient, presumed dissection and rupture of descending thoracic aorta at 3 years; one patient, cause unknown at 10 months (preoperative ejection fraction was 10%).

‖One patient, presumed arrhythmia at 20 months; one patient, porcine mitral valve placed 2 years before composite graft and St. Jude Medical mitral valve placed 7 years after composite graft. Patient had chronic stable dissection of abdominal aorta and chronic atrial fibrillation. Died of unknown cause 9 years after composite repair.

¶Endocarditis at 2 years.

Endocarditis. Endocarditis was the most common late complication after root replacement. Fourteen of the 256 hospital survivors had late endocarditis (14/256; 5%). Seven were treated nonoperatively and two survived. Two other patients with infected prostheses underwent repeat composite graft placement; one died and the other required a third and finally successful root replacement with an aortic homograft. Three additional patients received homografts for infected composite grafts and two survived. All four homografts remained free of endocarditis and functioned satisfactorily, but one

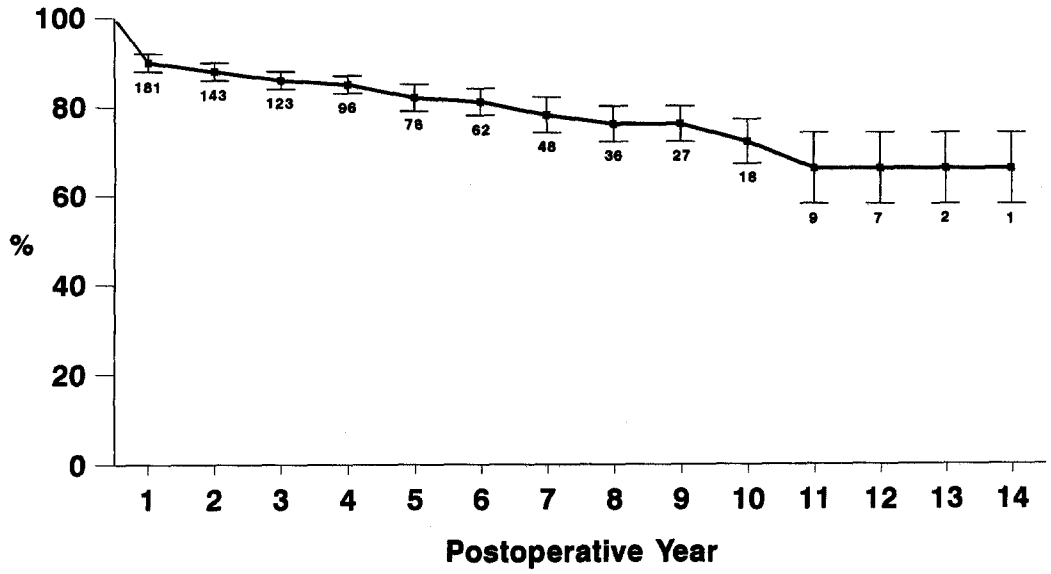

Fig. 1. Actuarial survival after aortic root replacement in 270 patients.

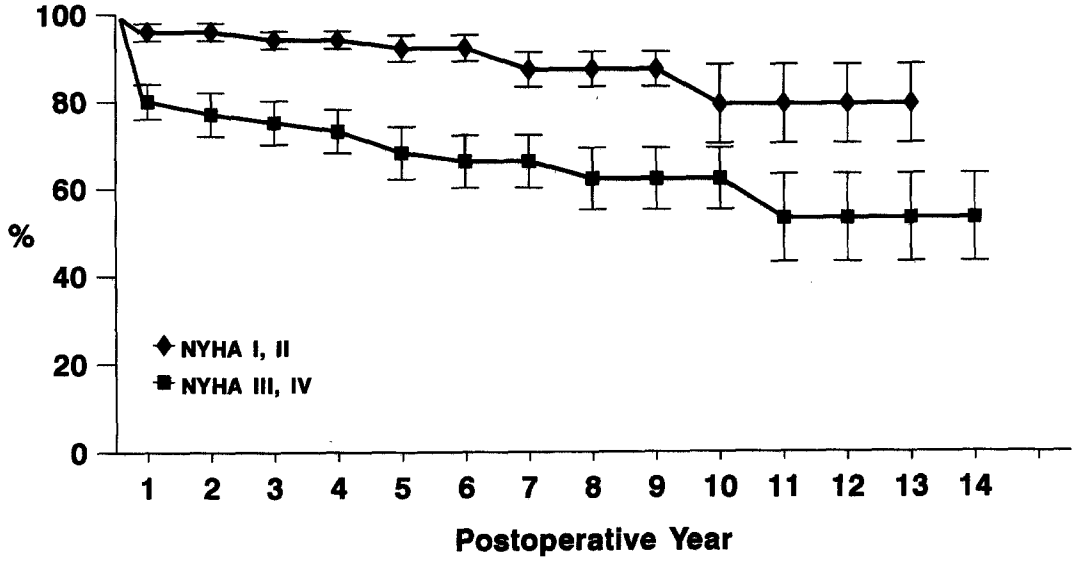

Fig. 2. Actuarial survival by preoperative NYHA classification.

patient died of a drug overdose 10 months after the operation.

Freedom from endocarditis in the overall series was 93%, 88%, and 88% at 5, 10, and 14 years, respectively (Fig. 5).

Other late complications. Despite use of the aortic wrap during the first 12 years of this operative series, only one late death resulting from coronary anastomotic dehiscence has occurred. However, five other patients had late coronary dehiscence and underwent successful repair. Actuarial freedom from coronary dehiscence was 93% at 10 years. Although the Cabrol interposition graft was discontinued in January 1989 because of intraoperative compression of the left coronary ostium in one patient, no late complications have resulted from this particular technique.

Fourteen patients required a subsequent thoracic or abdominal aortic procedure for dissection or progressive dilatation; nine of these 14 patients are long-term survivors. Thus actuarial freedom from reoperation on the residual aorta was 86% at 10

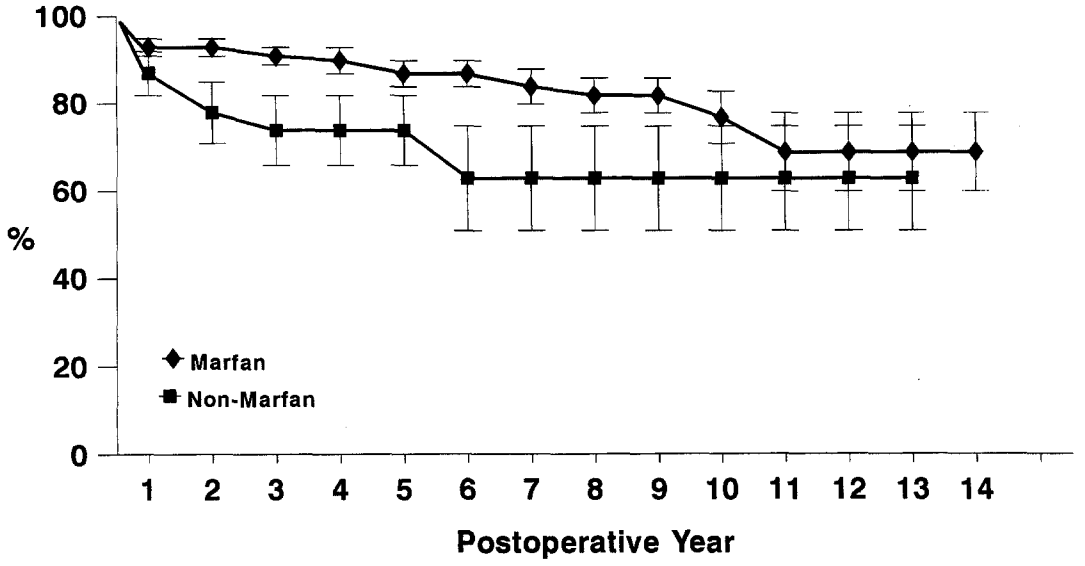

Fig. 3. Influence of Marfan disease on actuarial survival.

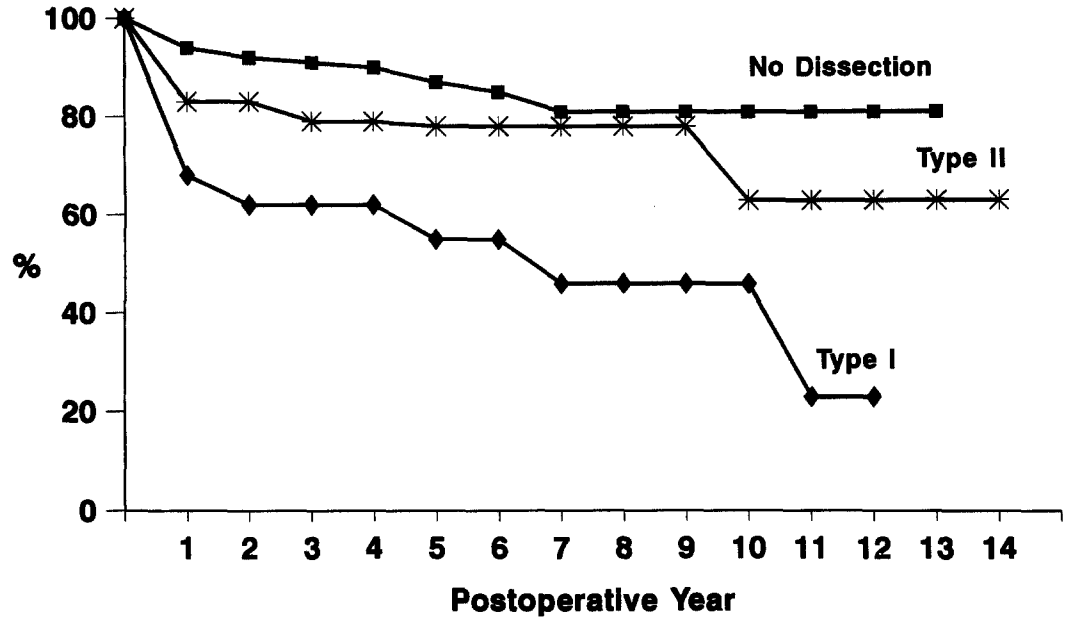

Fig. 4. Influence of preoperative dissection on actuarial survival.

years (Fig. 6). Three patients also had late aortic rupture; freedom from this complication was 97% at 10 years (Fig. 6).

Fig. 7 presents actuarial freedom from thromboembolism, a complication that occurred in four patients. In one patient thrombus developed on a Björk-Shiley valve 10 years after the operation; this patient underwent successful composite rereplacement with a St. Jude Medical prosthesis. Embolic episodes were recorded in three other patients; all three patients recovered completely. Two of the embolic events were in the setting of inadequate anticoagulation. One patient had a stroke on the third postoperative day, before therapeutic anticoagulation was achieved. The second patient had a small stroke when warfarin was interrupted for pacemaker placement. The rate of thromboembolic events was 0.42 events/100 patient-years (4 events/962 patient-years of follow-up).

Table IV. *Univariate and multivariate predictors of mortality*

	p Value	
Risk factors	*Univariate*	*Multivariate*
NYHA class	0.0001	0.0001
Preop dissection	0.0004	0.015
Non-Marfan	0.0005	0.007
Male gender	0.024	0.012
Urgent operation	0.0001	NS
Age	0.033	NS
Previous aortic root operation	0.04	NS
Mitral valve operation	0.32	NS
Circulatory arrest	0.11	NS
Era of operation	0.67	NS

NS, Not significant

Discussion

Before 1970, surgical procedures to replace the ascending aorta and aortic valve carried high operative mortality. Repair typically consisted of replacement of the aortic valve and placement of a supracoronary sleeve graft in the ascending aorta, frequently on an emergency basis, for acute dissection or rupture. In the 10 years before this series began, operative mortality for such a procedure at our institution approached 60%. After the initial use of the Bentall composite graft procedure at our institution in 1976, our operative results improved dramatically, as they did elsewhere. Thirty-day mortality for aortic root replacement has fallen below 5% in this report and others.[2-4, 10] These results are gratifying given the high mortality attending untreated ascending aortic aneurysm, dissection, and root infection. Improved results can be traced to growing surgical experience, refinement of operative technique, and advances in management of anesthesia, cardiopulmonary bypass, and myocardial protection, as well as early surgical intervention before aortic catastrophe.

Although the mortality rate for root replacement is low, risk factors for early or late death have been identified. We chose to group early and late deaths in this analysis because heterogeneity of the patient series made separate analysis of early and late mortality unnecessarily complex. In this series, poor preoperative NYHA functional class, non-Marfan status, presence of aortic dissection, and male gender were predictors of death. Surprisingly, era of operation, concomitant mitral valve operation, previous aortic root operation, and use of hypothermic circulatory arrest were not significant predictors of mortality.

Dissection at the time of root replacement, especially type I, was a strong predictor of late mortality. Indeed, survival at 10 years in patients with type I dissection was only 45%. The presence of dissection not only predicted greater risk of death, but also portended late aneurysm and possible aortic rupture. Given the high mortality and complication rate seen in patients with dissection remaining in the aorta distal to the composite graft, meticulous management of blood pressure by β-adrenergic blockade and close follow-up imaging of the distal aorta are warranted. We recommend an echocardiogram 6 months after root replacement and annual magnetic resonance imaging of the aorta thereafter.

Endocarditis remains the most common late complication after aortic root replacement. Appropriate antibiotic prophylaxis remains the mainstay preventative measure. Alternate initial surgical approaches, such as homograft root replacement and pulmonary autograft procedures, may reduce this risk further but are unlikely to eliminate it altogether. Although graft sterilization with antibiotic therapy alone was occasionally successful, rereplacement of the aortic root with a crypopreserved aortic homograft was the only reliable and consistently successful treatment.

The rate of thromboembolism in this series was strikingly low. We are aware of only four patients among 256 hospital survivors with a composite graft who had a clinically significant thromboembolism. The low thromboembolic rate (0.42 events/100 patient-years) is superior to that of isolated Björk-Shiley and St. Jude Medical aortic valves, typically reported to be 1 event/100 years.[11] Anticoagulation management has been identical to that for patients with isolated aortic valve replacement. We speculate that the lower incidence of thromboembolism may relate to the fact that the valve sutures, pledgets, knots, and much of the valve sewing ring are excluded from the bloodstream in a composite graft, but remain exposed in isolated valve replacement.

In summary, this experience has shown that aortic root replacement by means of Bentall's composite graft technique (in conjunction with selective use of cryopreserved aortic homografts) can be applied successfully to a variety of diseases affecting the aortic valve and ascending aorta. Operative and late mortality have been low. Risk factors for death have been identified and include poor preoperative func-

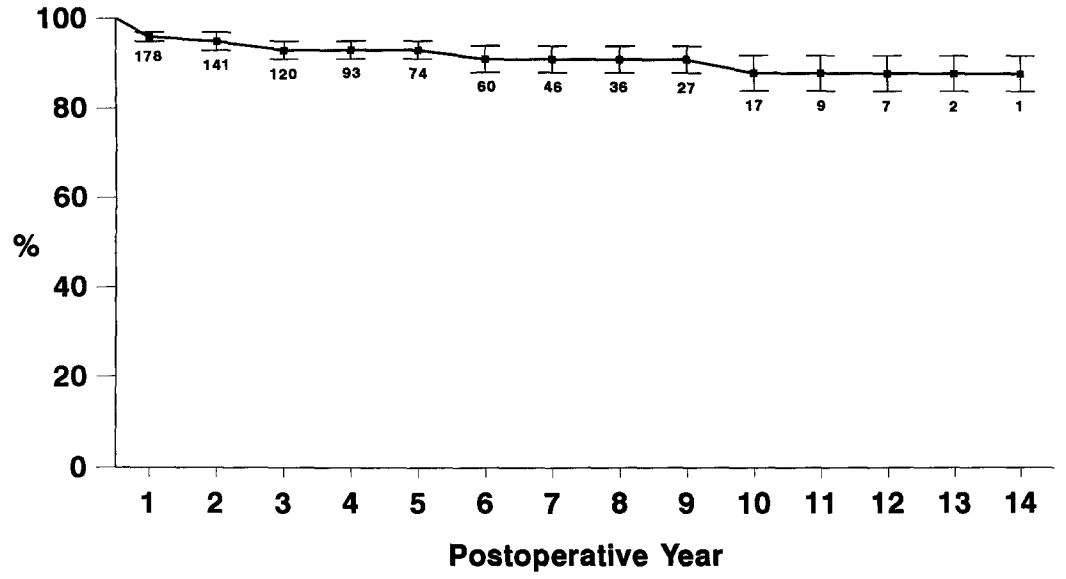

Fig. 5. Actuarial freedom from endocarditis.

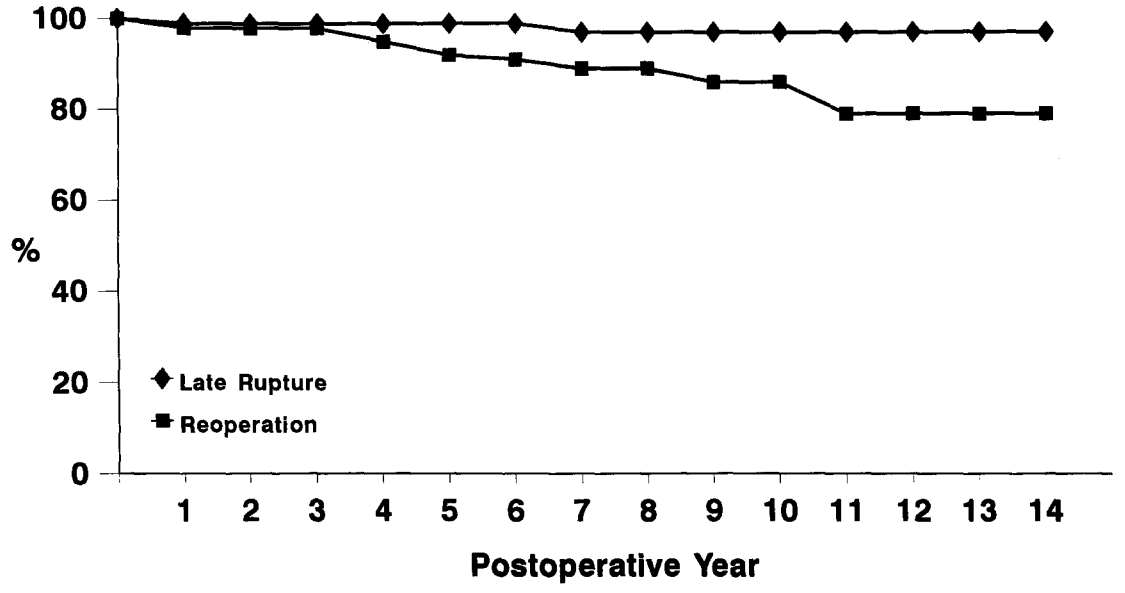

Fig. 6. Actuarial freedom from complications in the residual aorta.

tional class, non-Marfan status, presence of aortic dissection, and male gender. Concomitant mitral operations have not increased operative risk. Endocarditis remains the most common late complication and is best treated by root rereplacement with a cryopreserved aortic homograft. Late thromboembolism has been rare. When dissection is present at operation or the distal native aortic tissue is diseased, careful follow-up of the distal aorta is critical to long-term survival.

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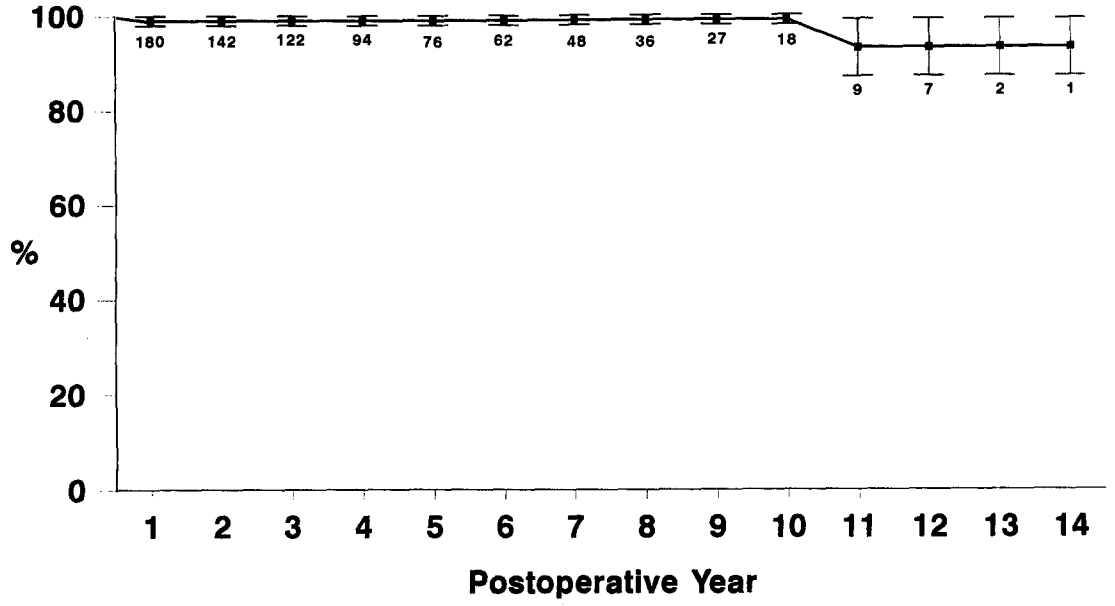

Fig. 7. Actuarial freedom from thromboembolism.

analysis of clinical data and Vera Kuda for preparation of the manuscript.

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Discussion

Dr. C. E. Anagnostopoulos *(New York, N.Y.).* On the basis of these results, do you advocate new early indications for doing the operation in the patient with Marfan syndrome with annular aortic ectasia, even though the aortic valve insufficiency may be only 1+ or 2+, particularly when there is a recent change in the size of the aorta? Would you advocate doing the operation in a patient with a 4.5 cm aorta that has changed over the past 6 months?

Dr. Gott. Ordinarily we would not operate on a 4.5 cm aorta. However, the majority of our patients who were operated on with a 6 cm root had no aortic insufficiency, so the great proportion of these patients were operated on prophylactically.

Dr. Pyeritz has pointed out to me that in patients with a family history of dissection, we need to move ahead at 5 cm. Four or five patients in the group have had dissection at 5.5 cm.

If we were operating to correct mitral regurgitation in a

patient with a 4.5 cm aorta, we would certainly perform root replacement.

Dr. Hans G. Borst *(Hannover, Germany).* We noted that the early mortality in patients with dissections was substantially greater than in patients with aneurysms. Did you include chronic dissections in your report?

Dr. Gott. About two thirds of the 41 patients with Marfan syndrome had chronic dissections and one third had acute dissections.

Dr. Borst. Why do you think that the risk in chronic dissection was substantially greater? We do not find that to be true. In our experience, there is a big difference in the operative risk of acute versus chronic cases.

Dr. Gott. I think a couple of late deaths occurred in patients with chronic dissection as a result of a problem with the part of the aorta that was not operated on. That may explain the difference, but I do not have a good explanation.

Dr. Borst. Your study gives the opportunity to assess Bentall's original method once again. Some physicians have been very worried about wrapping the ascending aorta in terms of a possible perigraft hematoma and a perfused perigraft space. Inasmuch as you have done so many of the original Bentall operations, I wonder how often you have seen these complications and whether you consider them to be a major problem.

Dr. Gott. We used the wrap until 1988, when Dr. Kouchoukos published his paper, and we stopped using the wrap after that. We have had six coronary dehiscences, with fortunately only one late death at 7 years; the other five have been successfully repaired. We no longer wrap the graft tightly. We merely lay the residual aortic wall on the graft.

Dr. Borst. I think this is a very important notion. When discussing these complications, it is always interesting to know whether the operation was performed by an experienced surgeon. In the former case, the complications might be due to the innate shortcomings of the procedure; in the latter, the operation may not have been properly performed.

Dr. Robert W. M. Frater *(New York, N.Y.).* You had had such an enormous experience of with the Marfan syndrome. I saw a case not so long ago with about a 4.5 cm aneurysm, and on the magnetic resonance imaging scan was a tiny dissection. The internist following the case said we did not have to worry about that. In his words: "Marfan's cases always have little bits of dissection here and there."

Dr. Gott. I do not agree. If we see a small dissection in a patient with Marfan syndrome, the patient is sent to the operating room right away. By contrast, in the patient with coronary disease, we can observe that type of dissection.