Operative risk of reoperative aortic valve replacement

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Objective: The contemporary risk of reoperative aortic valve replacement is ill-defined. We therefore compared the recent early results of reoperative and primary aortic valve replacement in our institution.

Methods: Between January 1993 and January 2001, a total of 162 patients underwent reoperative aortic valve replacement with or without coronary artery bypass grafting, and 2290 underwent primary aortic valve replacement with or without coronary artery bypass grafting. The reoperative and primary groups were similar with regard to gender (37% female in both), preoperative New York Heart Association functional class (2.8 ± 1 vs 2.8 ± 1), and ejection fraction ($58\% \pm 15\%$ vs $57\% \pm 15\%$). Patients undergoing reoperative aortic valve replacement were younger than those undergoing primary aortic valve replacement (64 ± 15 years vs 70 ± 13 years, $P < .001$). Previous prostheses were xenografts in 77 patients (48%), homografts and autografts in 25 (15%), and mechanical prostheses in 60 (37%). Mean time to reoperation was 9.7 ± 6.8 years.

Results: Early mortality for reoperative aortic valve replacement (8/162, 5%) was not statistically different from that for primary aortic valve replacement (71/2290, 3%, $P = .20$). Endocarditis was more common in the reoperative group (22% vs 3%, $P < .001$); when endocarditis was excluded from the analysis, early mortality was 3% in both groups. Multivariate predictors for early mortality were prosthetic valve endocarditis ($P < .001$, odds ratio 9.8), advanced preoperative functional class ($P < .001$, odds ratio 2.0), peripheral vascular disease ($P = .008$, odds ratio 2.0), preserved left ventricular ejection fraction ($P = .004$, odds ratio 0.98), and male gender ($P = .009$, odds ratio 0.49). After adjustment for these factors, there was no difference in early mortality between the groups ($P = .095$).

Conclusion: The risk of reoperative aortic valve replacement is similar to that for primary aortic valve replacement. These data support the expanded use of bioprosthetic valves in younger patients.

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Aortic valve replacement (AVR) is a frequently performed operation, with more than 11,000 isolated procedures and almost 12,000 combined with coronary artery bypass grafting (CABG) reported to The Society of Thoracic Surgeons (STS) database in 2003 (<http://www.ctsnet.org/file/STSNationalDatabaseSpring2004AdultCardiacExecutiveSummary.pdf>). The operative risk for isolated AVR according to the database has fallen below 5%, and that for AVR with CABG below 5%, at the most recent report. The contemporary risk of reoperative AVR, however, remains ill defined. This risk has implications not only for the assessment of an individual patient's candidacy for reparative surgery but also for the selection of prosthesis type—mechanical or biologic—among younger patients and those with longer life expectancies. We therefore examined our recent institutional experience with primary and reoperative AVR.

Patients and Methods

Patients

This study was reviewed and approved by the institutional review board at the Mayo Clinic Rochester (Rochester, Minn). We selected all patients undergoing primary or reoperative AVR at the Mayo Clinic Rochester between January 1993 and January 2001 from a computer registry maintained prospectively and in accordance with the STS guidelines for valve replacements.¹ Suture repair of perivalvular leaks was not considered reoperative AVR, and patients undergoing AVR beyond a second procedure were excluded. Patients undergoing concomitant mitral valve replacements or repairs, aortic aneurysm repair, or composite aortic root reconstruction were excluded on the grounds that the concomitant procedures might add significantly to the observed operative risk, making the results more difficult to interpret. Those undergoing concomitant CABG were included because they constituted such a large fraction of those undergoing reoperative AVR. Patients undergoing tricuspid valve repair or replacement were not excluded, because this additional procedure was judged unlikely to affect operative risk significantly.

Patients undergoing either biologic or mechanical valve implantation were included in both study groups because the type of prosthesis was thought unlikely to affect early outcomes. Similarly, those with both mechanical and biologic valves in place were included in the reoperative group. A subset analysis compared those with previous xenograft valves and mechanical prostheses. According to these criteria, we selected 2290 patients who had undergone primary AVR and 162 patients who had undergone reoperative AVR.

Definitions

In accordance with STS guidelines,¹ early operative mortality was defined as death occurring within 30 days of operation or before discharge from the hospital. Any abnormality resulting in stenosis or regurgitation of the aortic valve that was not intrinsic to the valve itself, such as pannus ingrowth, trauma, or surgical error, was considered nonstructural dysfunction. In contrast, structural

dysfunction was a change in valve function related to an intrinsic abnormality causing stenosis or regurgitation, such as calcification and leaflet tears. Any abnormality that caused malfunction of the prosthetic valve that was deemed significant by the referring physician and operating surgeon and that was not caused by structural or nonstructural dysfunction was classified as clinical dysfunction.

Patients with preoperative serum creatinine level of 2.0 mg/dL or greater were considered to have renal insufficiency, whereas postoperative renal insufficiency was defined by a creatinine level of 2.0 mg/dL or greater or by a doubling of the preoperative creatinine level. Requirement for dialysis was considered a complication of surgery only if preoperative renal function was normal. Patients who required intravenous nitrate therapy in the absence of myocardial infarction were considered to have unstable angina. Myocardial infarction was defined by the presence of two of the following four criteria: (1) prolonged (>20 minutes) typical chest pain not relieved by rest or nitrates, (2) enzyme (creatinine kinase MB fraction, lactate dehydrogenase subtype 1, and troponin T) level elevation, (3) any wall motion abnormality according to echocardiography, ventriculography, or multiple gated acquisition scanning, and (4) serial electrocardiogram with ST-T segment changes or pathologic Q waves. Operations were considered emergency if performed for cardiovascular instability necessitating a procedure outside the normal operative schedule or if another patient was displaced from a scheduled operation. Operations were considered urgent if patients had symptoms necessitating hospitalization for evaluation and were in too unstable a condition for discharge before an operative procedure. Neurologic symptoms lasting less than 1 hour and neurologic deficits that resolved within 72 hours were considered transient neurologic deficits, whereas stroke was a central neurologic deficit persisting longer than 72 hours. Gastrointestinal complications included gastrointestinal bleeding necessitating transfusion or a change in anticoagulation protocol, cholecystitis necessitating cholecystotomy drainage or surgical intervention, pancreatitis according to elevated pancreatic enzymes, or ischemic or gangrenous bowel requiring surgical resection. Sternal wound infection was marked by antibiotic use, incision and drainage, or a positive wound culture.

Statistical Analysis

Categorical factors were compared between groups with Fisher exact tests. In groups with severity classifications, such as aortic valve regurgitation, the *P* value was based on an absent versus present response. Logistic regression models were used to construct a multivariate model to predict operative mortality. A stepwise selection technique was used to identify factors for the final multivariate model.

Results

Primary Versus Secondary AVR

The mean age of patients in the reoperative group was significantly less than that of those in the primary AVR group (Table 1). Those undergoing reoperative AVR more often had a history of previous stroke, despite less commonly having a diagnosis of peripheral vascular disease, perhaps because of the previous valvular prostheses. Al-

TABLE 1. Demographic and clinical characteristics of population

	Reoperative (n = 162)	Primary (n = 2290)	P value
Age (y, mean)	63.5	69.8	<.001
Female (No.)	60 (37.0%)	845 (36.9%)	>.999
Renal insufficiency (No.)	10 (6.2%)	112 (4.9%)	.453
Stroke (No.)			<.001
Any	29 (17.9%)	131 (5.7%)	
Remote (>2 wk)	29 (17.9%)	128 (5.6%)	
Peripheral vascular disease (No.)	12 (7.5%)	401 (17.5%)	.001
Diabetes mellitus (No.)	18 (11.3%)	402 (17.6%)	.039
Chronic lung disease (No.)	18 (14.9%)	253 (14.7%)	.895
New York Heart Association functional class (No.)			.319
I	14 (8.7%)	130 (5.7%)	
II	27 (16.8%)	489 (21.4%)	
III	90 (55.9%)	1350 (59.2%)	
IV	30 (18.6%)	312 (13.7%)	
Angina (No.)			<.001
Any	40 (24.7%)	950 (41.5%)	
Unstable	0 (0.0%)	25 (1.1%)	
Myocardial infarction (No.)	16 (9.9%)	297 (13.0%)	.583
Hypertension (No.)	82 (50.9%)	1333 (58.2%)	.083
Bacterial endocarditis (No.)			<.001
Any	36 (22.2%)	59 (2.6%)	
Active	13 (8.0%)	26 (1.1%)	
Coronary artery disease			
Any disease	62 (38.3%)	1350 (59%)	.342
Three-vessel disease (No.)	20 (32.3%)	487 (36.1%)	
Ejection fraction <30% (No.)	5 (3.1%)	130 (9.9%)	.483
Aortic valve disorder (No.)			
Stenosis	23 (14.2%)	436 (19.0%)	.144
Regurgitation	85 (52.5%)	202 (8.8%)	<.001
Mixed	49 (30.3%)	1651 (72.1%)	<.001
Mitral valve disorder (No.)			
Stenosis	8 (5.0%)	120 (5.2%)	>.999
Regurgitation	117 (72.2%)	1674 (73.1%)	.316
Severe regurgitation	3 (1.9%)	38 (1.7%)	

though the overall incidences of coronary artery disease were similar in the two groups, angina pectoris was more common at presentation among patients in the reoperative AVR group. Some element of mitral regurgitation was common in both groups, although it was noted to be severe in degree in only a handful of patients. The surgeon's reason for leaving the mitral disease uncorrected is a matter of conjecture, but presumably it was considered that the mitral dysfunction would improve after successful AVR.

Patients undergoing primary AVR more commonly had a mix of stenotic and regurgitant aortic valve disease, whereas patients in the reoperative AVR group more often had regurgitant aortic valve disease. The indications for reoperative AVR were structural dysfunction in 70 patients (43.5%), nonstructural dysfunction in 24 (14.9%), perivalvular leak in 22 (13.7%), endocarditis in 21 (13.0%), clin-

ical dysfunction in 10 (6.2%), thrombosis in 4 (2.5%), unspecified in 4 (2.5%), thromboembolism in 3 (1.9%), progression of coronary artery disease in 2 (1.2%), and progression of other valvular disease in 1 (0.6%). In the primary group, surgery was indicated for calcific disease in 1342 patients (58.6%), bicuspid aortic valve in 732 (32.0%), annular dilatation in 89 (3.9%), rheumatic disease in 39 (1.7%), endocarditis in 28 (1.2%), prolapse in 16 (0.7%), unspecified or other in 27 (1.2%), hypertrophic obstructive cardiomyopathy in 9 (0.4%), and collagen vascular disease in 8 (0.3%).

Most operations in our series were elective in nature, which probably reflects referral patterns to our institution (Table 2). As one would anticipate, when only isolated AVR was considered, bypass and crossclamp times were longer for reoperative than primary procedures. Concomi-

TABLE 2. Operative characteristics of population

	Reoperative (n = 162)	Primary (n = 2290)	P value
Operative priority (No.)			.175
Elective	149 (92.0%)	2173 (94.9%)	
Urgent	11 (6.8%)	101 (4.4%)	
Emergency	2 (1.2%)	16 (0.7%)	
CPB time (min, mean and range)*	103.9 (43-350) n = 100	73.8 (20-290) n = 1027	<.001
Aortic crossclamp time (min, mean and range)†	67.4 (26-190) n = 100	51.5 (20-155) n = 1027	<.001
Concurrent procedure (No.)	62 (38.3%)	1263 (55.2%)	<.001
CABG	41 (25.3%)	1113 (48.6%)	<.001
Tricuspid valve annuloplasty	6 (3.7%)	13 (0.6%)	.001
Tricuspid valve replacement	0 (0.0%)	2 (0.1%)	>.999
Intraoperative intra-aortic balloon pump (No.)	15 (9.3%)	47 (2.1%)	<.001
Prosthesis explanted (No.)			
Mechanical	60 (37.1%)	—	
Xenograft	77 (47.5%)	—	
Homograft	23 (14.2%)	—	
Autograft	2 (1.2%)	—	
Prosthesis inserted (No.)			<.001
Mechanical	97 (59.9%)	825 (36.0%)	
Xenograft	54 (33.3%)	1415 (61.8%)	
Homograft	11 (6.8%)	41 (1.8%)	
Autograft	0 (0.0%)	9 (0.4%)	

*CPB time reported for isolated AVR only.

†Aortic crossclamp time reported for isolated AVR only.

tant CABG was performed more often in the primary group, whereas the opposite held for interventions on the tricuspid valve. Although the valve explanted at reoperation was twice as often biologic as mechanical, mechanical valves were more often inserted at the time of reoperative AVR.

There were 8 operative deaths (4.9%) in the reoperative group and 71 operative deaths (3.1%) in the primary group (Table 3, $P = .243$). The mortalities among patients undergoing an elective procedure in the absence of bacterial endocarditis were 4 of 127 (3.2%) in the reoperative group and 70 of 2231 (3.1%) in the primary group. When patients who had undergone placement of a stentless xenograft, homograft, or autograft at the initial or reoperative procedure were excluded from the analysis, the early operative risks were 4% (5/125 patients) for the reoperative AVR group and 3.1% (68/2220 patients) for the primary group ($P = .591$). When patients who required concomitant procedures were excluded, postoperative mortalities were 1 of 84 (1.2%) in the reoperative group and 24 of 1090 (2.2%) in the primary group.

Multivariate analysis of risk factors for early operative mortality was performed on the combined group of primary and reoperative AVRs considering age, sex, preoperative New York Heart Association functional class, preoperative left ventricular ejection fraction, nonelective surgical status, reoperative AVR, active endocarditis, prosthetic valve endocarditis, preoperative renal failure, previous myocardial infarction, previous CABG, mechanical or bioprosthetic

TABLE 3. Operative results for population

	Reoperative (n = 162)	Primary (n = 2290)	P value
Death (No.)	8 (4.9%)	71 (3.1%)	.243
Neurologic insult (No.)			
Stroke	2 (1.2%)	34 (1.5%)	>.999
Transient deficit	2 (1.2%)	36 (1.6%)	>.999
Myocardial infarction (No.)	0 (0.0%)	15 (0.7%)	.618
Postoperative intra-aortic balloon pump (No.)	2 (1.2%)	16 (0.7%)	.336
Intubation >48 h (No.)	27 (16.7%)	257 (11.2%)	.042
Reexploration for bleeding (No.)	9 (5.6%)	105 (4.6%)	.561
Pneumonia (No.)	5 (3.1%)	51 (2.2%)	.415
Pacemaker (No.)	18 (11.1%)	76 (3.3%)	<.001
Gastrointestinal complications (No.)	6 (3.7%)	67 (2.9%)	.479
Renal failure (No.)	9 (5.6%)	123 (5.4%)	.857
Dialysis requirement (No.)	2 (1.2%)	25 (1.1%)	.698
Sternal wound infection (No.)	1 (0.6%)	42 (1.8%)	.362
Postoperative stay (d, mean and range)	10.3 (0-71)	9.4 (0-141)	.063
Prolonged (>14 d) stay (No.)	23 (14.2%)	232 (10.1%)	.109

All values represent numbers and percentages of patients in group.

implant type, and peripheral vascular disease. Multivariate predictors for early mortality were prosthetic valve endocarditis ($P < .001$, odds ratio 9.8), advanced preoperative

TABLE 4. Demographic and preoperative clinical characteristics of reoperative group

	Mechanical (n = 60)	Xenograft (n = 77)	P value
Age (y, mean)	59.5	70.6	<.001
Female (No.)	26 (43.3%)	22 (28.6%)	.104
Renal insufficiency (No.)	5 (8.3%)	5 (6.5%)	.748
Stroke (No.)			<.001
Any	19 (31.7%)	5 (6.5%)	
Remote (>2 wk)	19 (31.7%)	5 (6.5%)	
Peripheral vascular disease (No.)	1 (1.7%)	7 (9.1%)	.137
Diabetes mellitus (No.)	7 (11.9%)	10 (13.0%)	>.999
Chronic lung disease (No.)	6 (12.8%)	10 (17.5%)	.591
New York Heart Association functional class (No.)			.771
I	6 (10.0%)	5 (6.5%)	
II	4 (6.7%)	12 (15.6%)	
III	38 (63.3%)	44 (57.1%)	
IV	12 (20.0%)	16 (20.8%)	
Angina (No.)			>.999
Any	16 (26.7%)	20 (26.0%)	
Stable	16 (26.7%)	20 (26.0%)	
Myocardial infarction (No.)	8 (13.3%)	7 (9.2%)	.583
Hypertension (No.)	27 (45.8%)	47 (61.0%)	.085
Bacterial endocarditis (No.)			.067
Any	18 (30.5%)	13 (16.9%)	
Active	6 (10.0%)	6 (7.8%)	
Sinus rhythm (No.)	49 (81.7%)	62 (80.5%)	>.999
Preoperative warfarin sodium (No.)	58 (96.7%)	29 (37.7%)	<0.001
Coronary artery disease			
Any disease	25 (41.7%)	31 (40.3%)	.493
Three-vessel disease (No.)	7 (28.0%)	11 (35.5%)	
Ejection fraction <30% (No.)	1 (1.7%)	3 (3.9%)	
Aortic valve (No.)			
Stenosis	14 (23.3%)	8 (10.4%)	.059
Regurgitation	32 (53.3%)	38 (49.4%)	.731
Mixed	13 (21.7%)	27 (35.1%)	.093
Mitral valve (No.)			
Stenosis	1 (1.7%)	6 (7.9%)	.134
Regurgitation	34 (57.6%)	65 (85.5%)	<.001
Severe regurgitation	0 (0.0%)	3 (4.0%)	
Interval from primary AVR (y, median and range)	12.1 (0-30)	8.6 (0-21)	.028

functional class ($P < .001$, odds ratio 2.0), and peripheral vascular disease ($P = .008$, odds ratio 2.0). Preserved left ventricular ejection fraction ($P = .004$, odds ratio 0.98), and male sex ($P = .009$, odds ratio 0.49) were protective. After adjustment for significant predictors identified by the multivariate model, there was no difference in early mortality between the groups ($P = .095$).

Intra-aortic balloon pumps were inserted significantly more frequently in the reoperative group, and patients undergoing reoperative AVR were more likely to require prolonged intubation. Postoperative permanent pacemakers were required three times as often in the reoperative group as in the primary group. Preoperative predictors of need for permanent pacemakers included prolonged cardiopulmonary bypass (CPB) and aortic crossclamp times, prior AVR,

preoperative endocarditis, advanced age, and the degree of hypothermia during CPB.

Subset Analysis of Reoperative Group

The results obtained among patients undergoing reoperation after previous mechanical or xenograft valve were then compared. As shown in Table 4, patients undergoing explantation of aortic xenografts were significantly older than those having mechanical prostheses replaced, although preoperative stroke was more common among patients with previous mechanical prostheses. This may in part reflect the indications for the procedure. Only 2 patients in the previous mechanical group did not have anticoagulation with warfarin sodium; the first was receiving heparin during a pregnancy and the second was

noncompliant. Of note, approximately a third of the patients in the failed xenograft group were receiving warfarin sodium before reoperation.

Among those with previous xenografts, the indications for reoperation were structural dysfunction in 59 patients (76.6%), endocarditis in 7 (9.1%), perivalvular leak in 4 (5.2%), thrombosis or thromboembolism in 3 (3.9%), non-structural dysfunction from pannus formation in 2 (2.6%), and progression of coronary artery disease in 2 (2.6%). Reoperative AVR was indicated among those with previous mechanical valves for nonstructural dysfunction from pannus formation in 22 (36.7%), perivalvular leak in 19 (31.7%), endocarditis in 11 (18.3%), patient-prosthesis mismatch in 3 (5.0%), thrombosis or thromboembolism in 3 (5.0%), and structural dysfunction in 2 (3.3%). Both instances of structural dysfunction of mechanical valves were related to cloth wear of Starr-Edwards valves.

At reoperation, mechanical prostheses were preferentially implanted in patients with previous mechanical valves. Among those with previous xenografts, however, biologic and mechanical valves were implanted at nearly equal rates (Table 5). Because of the relatively young age of the reoperative surgical group, this may have been related to reluctance of the surgeon to subject the patient to the risk of a third AVR. There was no difference in early postoperative mortality between those who underwent reoperation after mechanical and xenograft valves, as shown in Table 6. Postoperative morbidities were also similar. There were no deaths among patients undergoing reoperation for failed homografts or autografts.

Discussion

This study demonstrated similar early operative mortalities for primary and reoperative AVR at our institution. These data should encourage an aggressive attitude toward elective reoperative AVR among patients with acceptable risk profiles. The observation that advanced functional class and reduced ejection fraction were predictors of operative risk reinforces the importance of early referral of patients for surgery once prosthetic dysfunction has been identified. It also highlights the importance of serial observation of patients, whether by the responsible cardiologist or by a cardiac surgeon, on an ongoing basis after valve replacement.

These results also have implications for the use of bioprotheses among younger patients, as is being encouraged by many in the cardiac surgical community, because these are the individuals for whom the likelihood of reoperative AVR is greatest. The data are reassuring that such procedures under elective circumstances carry low risk. This is particularly true after exclusion of cases of endocarditis, a complication equally likely to occur with biologic and mechanical prostheses.^{2,3}

The operative mortality observed in this study was slightly less than the 7.8% to 11.5% previously reported.²⁻¹²

TABLE 5. Operative characteristics of reoperative group

	Mechanical (n = 60)	Xenograft (n = 77)	P value
Operative priority (No.)			.249
Elective	54 (90.0%)	73 (94.8%)	
Urgent	4 (6.7%)	4 (5.2%)	
Emergency	2 (3.3%)	0 (0.0%)	
Concurrent procedure (No.)	27 (45.0%)	28 (36.4%)	.38
CABG	17 (28.3%)	20 (26.0%)	>.999
Tricuspid valve annuloplasty	4 (6.7%)	2 (2.6%)	.404
Intraoperative intra-aortic balloon pump (No.)	10 (16.7%)	5 (6.5%)	.096
Prosthesis inserted (No.)			<.001
Mechanical	49 (81.7%)	30 (39.0%)	
Xenograft	7 (11.7%)	40 (52.0%)	
Homograft	4 (6.7%)	7 (9.1%)	

TABLE 6. Operative results of reoperative group

	Mechanical (n = 60)	Xenograft (n = 77)	P value
Death (No.)	4 (6.7%)	4 (5.2%)	.73
Neurologic insult (No.)			
Stroke	0 (0.0%)	2 (2.6%)	.504
Transient deficit	1 (1.7%)	0 (0.0%)	.438
Myocardial infarction (No.)	0 (0.0%)	0 (0.0%)	>.999
Postoperative intra-aortic balloon pump (No.)	0 (0.0%)	1 (1.3%)	>.999
Intubation >48 h (No.)	11 (18.3%)	12 (15.6%)	.818
Reexploration for bleeding (No.)	3 (5.0%)	4 (5.2%)	>.999
Pneumonia (No.)	0 (0.0%)	4 (5.2%)	.131
Pacemaker (No.)	9 (15.0%)	8 (10.4%)	.444
Gastrointestinal complications (No.)	2 (3.3%)	4 (5.2%)	.695
Renal failure (No.)	5 (8.3%)	5 (5.2%)	.505
Dialysis requirement (No.)	1 (1.7%)	1 (1.3%)	>.999
Sternal wound infection (No.)	1 (1.7%)	0 (0.0%)	.438
Postoperative stay (d, mean and range)	9.9 (0-46)	11.4 (0-71)	.554
Prolonged (>14 d) stay (No.)	7 (11.7%)	13 (16.9%)	.469

This may be due in part to the more contemporary interval during which these procedures were performed with consequent improvements in myocardial management and postoperative care. In addition, the potential for selection bias is significant. The vast majority of patients were operated on under elective circumstances, and although we would argue that under appropriate surveillance this should be the case in all environments, clearly this is not representative of all practice settings. Still, although our institution is a tertiary referral center, we also are a significant regional health care provider, with approximately a third of the patients in this study coming from within 150 miles of our institution.

Consistent with other studies, we found advanced preoperative functional class, prosthetic valve endocarditis, reduced ejection fraction, female gender, and peripheral vascular disease to be significant predictors of operative mortality. Previous studies have also identified advanced age,^{2,4,7,9,11} gender,^{4,11,13} weight,⁷ preoperative renal dysfunction or failure,^{4,7} nonelective surgical status,^{4,6} number of previous heart operations,⁷ concomitant CABG,^{7-9,11} double- or triple-vessel bypass,¹¹ thrombosis of the prosthesis,¹⁴ type and size of bioprosthesis,¹¹ tricuspid insufficiency,⁷ poor hemodynamics,⁷ repair of ascending aortic aneurysm with a composite graft,⁷ and concomitant left ventricular aneurysmorrhaphy as significant predictors of operative risk. These factors did not achieve significance in our analysis, perhaps in part because of the small number of events.

We did not identify previous mechanical prosthesis or previous bioprosthesis as a risk factor, although other studies have suggested this to be the case.^{15,16} Indeed, a previous study from our institution reported a 10% operative mortality (1/10 patients) for patients operated on for thrombosed aortic disc valves.¹⁵ Both of these studies suffered from small sample size, however, and our current findings dispute this notion. Our data are insufficient to establish superiority of either valve type from the standpoint of risk of complications, because we have only the numerator and not the denominator of the equation. Without knowledge of the total number of valves of both types implanted among the population at risk, rates of endocarditis or pannus formation cannot be calculated. The interval to reoperation was significantly longer among patients with failed mechanical aortic valves, which may have contributed to the incidence of pannus formation as an indication for surgery, although the mechanisms of pannus formation remain unclear.¹⁷ The difference between groups in endocarditis as an indication for surgery probably reflects the infrequency of structural dysfunction as an indication for surgery in the mechanical group.

Patients undergoing reoperative surgery were more likely to have an intra-aortic balloon pump inserted than were those undergoing primary AVR. This may reflect a cautious approach to these patients among the surgeons involved, because preoperative ejection fraction and functional class were actually quite similar between groups. Aortic crossclamp times were somewhat longer in the reoperative group, although the difference does not appear clinically significant.

The increased requirement for permanent pacemaker implantation in our reoperative AVR group was similar to previous reports.^{18,19} Patients in our reoperative AVR group more often had endocarditis and had longer CPB and aortic crossclamp times than the primary group. A previous study from our institution found that complete atrioventricular

block and CPB times longer than 120 minutes predicted long-term pacemaker dependence.¹⁸

Our study suffers from a number of limitations, including heterogeneity of the study group. Under ideal circumstances, a study such as this would include only patients undergoing isolated AVR. Even in this relatively large study, however, such inclusion criteria would have resulted in a sample size of only 84 patients in the reoperative group. We therefore chose to include only the procedure most commonly performed with reoperative AVR, CABG, and procedures that had minimal impact on the operative risk, namely tricuspid valve interventions. We also combined patients with failed mechanical and failed bioprosthetic valves in the reoperative AVR group for comparison with the primary group. This approach was validated by subset analysis that demonstrated the operative risk for failed mechanical valves was not different from that for failed xenografts. Despite these measures, the relatively small sample size limited our power to detect small differences between the groups and weakens our ability to define risk factors. Indeed, power analysis of our study demonstrated a 0.18 chance to detect a difference of 0.05 between the primary and reoperative groups. Additionally, our study is limited by its retrospective nature and the selection bias inherent in any surgical series.

Treatment options for patients with aortic valve disease now include aortic valve repair, the Ross autograft procedure, stentless xenografts, and human homografts, as well as stented xenografts and mechanical valves. There were insufficient numbers of patients who had undergone these procedures as primary operations to determine differences in the risks associated with reoperation; however, the risk appears low regardless of the type of bioprosthetic valve used. This is in agreement with previous studies,²⁰ although all surgeons would argue that reoperative homograft root replacement after previous homograft root replacement is a challenging procedure.

Does the risk of reoperative AVR justify the use of tissue valves in younger patients? Although early operative risk is only one element of the equation, several large studies comparing the long-term survival of patients with mechanical versus tissue valves have suggested remarkably similar survival curves through a 20-year period for patients receiving tissue and mechanical prostheses.^{3,12} A higher rate of death from bleeding complications in the mechanical group and a higher rate of reoperation in the bioprosthetic group are expected; thus the risk of the reoperation is a critical element in determining comparative survival. Patients who desire an active lifestyle may justifiably choose a tissue valve, knowingly accepting the risk of reoperative AVR in the future. Certainly the potential number of reoperations must be considered for the very young adult, and it must be recognized that such patients will be older at the time of

their reoperation and will probably have more comorbidities. With close follow-up, however, permitting elective reoperation before significant left ventricular dysfunction occurs, our data suggest that that risk associated with this approach is acceptable.

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Discussion

Dr Robert W. Emery (St Paul, Minn). Congratulations to the Mayo group for this difficult and extensive review. The well-written article is complex, because they are comparing three groups: primary AVR and reoperative tissue and mechanical prostheses. The points raised are timely, and the recommendations carry significant implications to patients undergoing AVR. I have several points and three questions.

First, I am concerned that the time to reoperation in patients with a biologic prosthesis was short, a mean of 8.6 years. Even with a low operative risk, this seems an inordinately short time frame. Even with elective operation, the patients undergoing reoperation had a higher complexity, as evidenced by the increased need intra-aortic balloon pumps, prolonged ventilation time, and longer hospital stay.

Fifty-nine percent of the patients had structural degeneration as the etiology for valve replacement in the tissue group, versus 3% for the mechanical group. If this is factored out, then the endocarditis statistics are reversed. It is a risk factor for reoperation and would have accounted for 44% versus 19% of the reoperation indications for biologic and mechanical valves, respectively.

The risk of thromboembolism and thrombosis was noted for mechanical valves, yet the incidences in the series as indications for reoperation were equal for mechanical and biologic valves.

We were not able to duplicate such excellent results in our series of reoperative AVRs presented at the American College of Cardiology in 345 patients followed up for 25 years, with our mortality being 8%, consistent with the STS database. This study does not account for patients who might not have been referred back to this tertiary center, perhaps because of acuity or distance, which could affect operative mortality and late morbidity.

And finally, with respect the younger patient, our group presented in the July 2003 *Annals of Thoracic Surgery* an operative mortality of 1% and a reoperative incidence of 1.9% among patients with mechanical valve prostheses, with a total valve-related event occurrence of 0.3% per patient-year with a 20-year follow-up of 95.8%. These data need to be taken into account as you discuss this process with the patient.

For my first question, the incidence of nonstructural dysfunction from pannus formation was 37% among patients with mechanical valves. Could this be accounted for by the significantly longer time to reoperation in this patient group?

Dr Potter. I think that the mechanism for pannus formation is quite complex and is yet to be completely defined; however, we do believe that the time that the mechanical valve is in place is a significant factor for pannus formation.

Dr Emery. Second, why did 93% of the patients in the biologic group and 59% of the patients in the mechanical group, as noted in Table 4, have mitral valve problems yet not have these addressed at the time of surgery?

Dr Potter. That's another excellent question. Because of the retrospective nature of this study, I can't address it specifically; however, after reading through all the clinical data and the operative notes, I can speculate that the consulting surgeon believed that after AVR the mitral valve disease would improve and that a double-valve procedure wasn't in the best interest of the patient.

Dr Emery. Finally, do you know what models of valves required replacement, particularly mechanical prostheses? Contemporary models have a lower incidence of valve-related events that might lead to replacement than some of the older models that are no longer used in significant numbers.

Dr Potter. We did not look at each valve individually to determine the causes of reoperation; however, the 2 incidents of structural deterioration were both due to Starr-Edwards ball-and-cage valves that had cloth wear.

Dr John G. Byrne (*Boston, Mass*). My question relates to the age cutoff that you would recommend for primary AVR with a tissue or biologic valve, because obviously if you put a tissue valve in, say, a 40-year-old, that patient is probably going to see at least three operations if he or she wants to stay with tissue for a lifetime. So it is going to be the cumulative lifetime risk of reoperation with a biologic valve, versus the cumulative lifetime risk of bleeding with a mechanical valve. So what is the age cutoff that you would recommend for placing a tissue valve at the primary operation?

Dr Potter. That's an excellent question. Because I have only spent time in Dr Sundt's laboratory and only replaced a few valves in some pigs, I might have him answer that question for us.

Dr Sundt. Thanks very much for that question. I will note that Dr Potter is a general surgical resident, and we are very proud of the job he has done in the laboratory and proud of the job he has done with this work.

Your question is a great one, and it is difficult to make a firm recommendation for an individual patient. Ultimately, I think it has to be the patient who decides on the prosthesis. My job is to advise about the risks.

Now, the issue about the number of reoperations a 40-year-old can expect with the tissue option depends on whose statistics you believe. If you talk to the manufacturers of the current generation tissue valves, they will tell you their prostheses will last for 20 years or more. If you accept this, that 40-year-old may be facing only one reoperation in a lifetime.

It is important to recognize that this study cannot answer the question of mechanical versus tissue completely, because we don't have those two comparative groups; we do not have the denominators, only the numerators, so you can't really compare them head to head. It has got to be the patient who decides which set of risks to face. It is a qualitative issue as much as a quantitative one.

Dr R. Gates (*Orange, Calif*). It seems as though you have shown in a well-selected group of patients at a tertiary referral hospital that you can perform reoperative surgery with a comparable rate of success to that of primary surgery. However, I think we have to use some caution in extrapolating that into the recommendation to use bioprostheses in younger patients. What you are

suggesting is that if you place a tissue valve in a patient at age 65 years is that in 15 years you will be able to replace that valve with minimal risk.

But the fact is that as patients get older they acquire comorbidities, their pulmonary function decreases, they have renal failure or dysfunction, they have strokes, and many of these patients are simply not candidates for reoperative surgery regardless of current bioprosthetic function. Some (many?) of these patients may be extremely ill, in New York Heart Association class IV, and in need of reoperation because of a dysfunction bioprostheses. Now these patients are not in your study because they are too high risk to be referred back to the Mayo Clinic for surgery. They simply die with a dysfunctional prosthesis.

So with the great Mayo Clinic database, have you looked at a cohort of patients who received tissue valves and mechanical valves in their mid 60s and followed them up until 80 or 85 years of age? If so, have you seen any difference in survival between the mechanical and tissue valve groups? In this paired group, I wonder whether the risk of reoperation was the same as the risk of initial operation?

Dr Potter. That's an excellent question. We have not addressed that question in this study specifically; however, we are in the process of getting long-term follow-up on our AVR population. I think what this study can say is that patients with tissue valves who are followed up closely have routine follow-ups with their cardiologists and echocardiograms and have their aortic valves replaced when they are dysfunctional, before severe heart failure sets in. They are going to do much better with their reoperation than are patients who do not receive follow-up and show up in heart failure and cardiogenic shock.

Dr Nicholas T. Kouchoukos (*St Louis, Mo*). If I understand your data correctly, you excluded patients from this analysis who had more complex reoperations rather than a simple AVR. Are you comfortable excluding patients who might have required a root replacement or resection of an ascending aortic aneurysm as the second procedure when they had a simple AVR at the first procedure?

Dr Potter. The goal of this study wasn't to evaluate the operative mortality for all AVRs. The initial goal was to determine the risk in younger patients. We did consider looking at the risk in all patients. I think Dr Sundt may be able to address this a little better than I, but our goal was more to look at a patient who needed an AVR when young. Our question was, when that valve slowly deteriorates, assuming there are no other continued problems, what is the risk for that patient with deterioration?

Dr Sundt. I take your point, Dr Kouchoukos. At the time of the first operation, you really don't know for sure what the second operation is going to be. In the end, it is just a matter of how you want to cut the data. In fact, some of my coauthors thought that even this cut was too inclusive. We tried to make it a pure enough group to come to some meaningful conclusions looking at just the risk of the reoperative AVR. Your point is certainly valid, however. Again, this was not a comparison of initial strategies but rather a look at just one element of the equation.

Dr Michael P. Siegenthaler (*Freiburg, Germany*). In most centers it seems that one or two really experienced surgeons get referrals for those complex cases such as reoperative AVR. Did you compare the mortality of those few surgeons who probably did

those reoperative cases with their own primary mortality? In other words, maybe better surgeons did those complex cases and have a different practice pattern than the others.

Dr Potter. All the surgeons at the clinic participated and operated on at least a handful of these patients, and we did not look at each individual surgeon's mortality.

Dr Paul Kurlansky (*Miami Beach, Fla*). This is an excellent study. I just wanted to comment on the suggestion of one of the previous questioners that you follow patients from 65 to 75 years and compare mechanical with tissue valves. We actually did that in a significant cohort of patients and found, both in terms of operative mortality and long-term mortality and quality of life, that there was tremendous statistical advantage to mechanical valves.

However, if you then broke down the data by propensity scale analysis, there was absolutely no difference within quintiles between the groups.

What is the bottom line? The bottom line is that the selection of patients was different for the mechanical valve than for the tissue valve. And I think one of the things that you have to take into account that goes into the surgeon's choice is not just the age of the patient but the physiologic age of the patient and the anticipation of the surgeon of the life expectancy of the patient. The ideal is that the life expectancy of the valve would be greater than that of the patient, but if the life expectancy of the patient is not that great, then regardless of age the choice of a tissue valve would obviously be preferred.

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