Redo aortic valve surgery: Influence of prosthetic valve endocarditis on outcomes

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Objective: Compared with reoperative aortic valve replacement for nonendocarditis causes, the contemporary risk and long-term outcomes of reoperation for aortic prosthetic valve endocarditis are ill-defined.

Methods: Between December 1994 and April 2008, 313 patients underwent reoperative aortic valve replacement, of whom 152 (48.6%) had prosthetic valve endocarditis. Mean follow-up was 6.5 ± 0.4 years and 97.4% complete.

Results: Patients with prosthetic valve endocarditis were older with a higher risk profile. The overall hospital mortality was 15.3% ($n = 48$) (prosthetic valve endocarditis vs nonendocarditis: 24.3%, $n = 37$, vs 6.8%, $n = 11$; $P < .001$). Independent predictors of perioperative mortality for prosthetic valve endocarditis were sepsis (odds ratio [OR], 6.5; 95% confidence interval [CI], 2.0–21.0; $P < .01$), ejection fraction less than 30% (OR, 5.8; 95% CI, 1.3–25.0; $P = .02$), concomitant coronary artery bypass grafting (OR, 3.3; 95% CI, 1.1–9.8; $P = .03$), and aortic root abscess (OR, 2.7; 95% CI, 1.2–6.4; $P = .02$), and for the nonendocarditis group were concomitant coronary artery bypass grafting (OR, 8.1; 95% CI, 2.0–33.0; $P < .01$), and mitral valve surgery (OR, 4.8; 95% CI, 1.3–17.9; $P = .02$). The 1-, 3-, 5-, and 10-year survivals for patients with and without prosthetic valve endocarditis were $52\% \pm 4\%$ versus $82\% \pm 3\%$, $43\% \pm 5\%$ versus $73\% \pm 4\%$, $37\% \pm 5\%$ versus $63\% \pm 5\%$, and $31\% \pm 7\%$ versus $56\% \pm 8\%$, respectively (log rank < 0.001). Predictors of long-term mortality in prosthetic valve endocarditis were sepsis (OR, 3.1; 95% CI, 1.5–4.5; $P < .01$) and unstable preoperative status (OR, 1.8; 95% CI, 1.2–3.5; $P = .04$), whereas in nonendocarditis patients the only predictor was New York Heart Association class IV (OR, 2.5; 95% CI, 2.8–7.4; $P < .01$). Five-year actuarial freedom from endocarditis was $80\% \pm 0.3\%$ versus $95\% \pm 0.6\%$ (prosthetic valve endocarditis versus nonendocarditis; $P = .002$).

Conclusions: Despite contemporary therapy, reoperation for aortic prosthetic valve endocarditis is still associated with relatively high perioperative mortality and limited long-term survival. (J Thorac Cardiovasc Surg 2011;142:99–105)

Aortic valve replacement (AVR) is a frequently performed operation with more than 20,000 isolated procedures and 16,000 combined with coronary artery bypass grafting (CABG) reported to the Society of Thoracic Surgeons database in 2008 (http://www.sts.org/documents/pdf/ndb/2ndHarvestExecutiveSummary_2009.pdf). The operative risks for isolated AVR and AVR + CABG have now fallen below 3.2% and 5.0%, respectively, according to the database. Serious complications of prosthetic valves occur in 2% to 3% per patient-year, with prosthetic valve endocarditis (PVE) occurring in 0.98% per patient-year.¹ The

cumulative incidence at 5 years is 3% and at 10 years, 5%.² PVE now represents about one fifth of all cases of infective endocarditis, occurring for example in 26% of cases in the Euro Heart Survey and in 556 (20.1%) of 2670 patients with definite endocarditis in the International Collaboration on Endocarditis–Prospective Cohort Study.³

Reoperative surgery is needed in approximately 42% to 49% of patients with PVE, but the contemporary risk and long-term outcomes of this, particularly with periannular involvement, remain ill-defined. Much of our current understanding is based on studies limited by small sample size and retrospective design and many antedate the routine use of echocardiography and the contemporary and validated Duke diagnostic criteria.^{3,4} Reported mortalities of surgical intervention have ranged from 13% to 80%, and better identification of high-risk subgroups of patients is required. This has implications for the assessment of an individual patient's suitability for reoperative surgery and conceivably also the choice of prosthetic valve substitute. The objectives of this study were to (1) prospectively describe the clinical characteristics, outcome, and survival of patients undergoing reoperation for aortic PVE, (2) compare

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Disclosures: Authors have nothing to disclose with regard to commercial support. Received for publication March 11, 2010; revisions received July 17, 2010; accepted for publication Aug 15, 2010; available ahead of print Oct 18, 2010.

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0022-5223/\$36.00

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doi:10.1016/j.jtcvs.2010.08.042

Abbreviations and Acronyms

AVR	= aortic valve replacement
CABG	= coronary artery bypass grafting
CI	= confidence interval
NYHA	= New York Heart Association
OR	= odds ratio
PVE	= prosthetic valve endocarditis

this to a reference group of reoperative AVR for nonendocarditic causes, and (3) determine prognostic factors for both early mortality and long-term survival in both groups.

PATIENTS AND METHODS**Patients**

This study was reviewed and approved by the Institutional Review Board at Herzzentrum, Universität Leipzig (Leipzig, Germany). All patients undergoing reoperative AVR over a 14-year period between December 1994 and April 2008 were selected. Patients undergoing concomitant coronary, valvular, or aortic surgery were included. Patients were classified according to the presence of PVE diagnosed according to the modified Duke criteria.⁴ For patients with PVE, the surgical tenet of radical debridement of all infected tissue, drainage and exclusion of myocardial abscesses from the bloodstream, and repair of annular defects was adhered to. The choice of the best valvular substitute was left to the discretion of the surgeon. Data were prospectively collected from a computer registry maintained prospectively. Patients were followed up annually by postal questionnaire and, when needed, by contacting the referring cardiologist or family physician.

Definitions

In accordance with Society of Thoracic Surgeons guidelines, *early mortality* was defined as all-cause mortality at 30 days. *Nonstructural dysfunction* was defined as any abnormality not intrinsic to the valve itself that resulted in stenosis or regurgitation of the operated valve or hemolysis, such as pannus ingrowth or paravalvular leak. In contrast, *structural valve deterioration* was dysfunction or deterioration involving the operated valve related to an intrinsic abnormality, such as calcification or leaflet tears. Operations were considered *emergency* if performed within 24 hours of hospital admission for cardiovascular instability and *urgent* if performed during the index hospital admission. *Sepsis* was defined as fever, leukocytosis, positive blood culture, hemodynamic instability needing vasopressors, or organ failure. *Early endocarditis* was defined as occurring within 1 year of the operation. *Complications* from PVE were defined as perianular abscess, thromboembolic events, sepsis, or critical preoperative state.

Statistical Analysis

Continuous variables are expressed as mean $\pm$ standard deviation and compared using an unpaired Student *t* test or Kruskal–Wallis test; categorical data are presented as proportions and compared using the χ^2 or Fisher's exact test. Univariate and multivariate logistic regression modeling with backward stepwise elimination was performed separately for PVE and non-PVE inasmuch as these 2 entities displayed profound pathophysiologic and prognostic differences. The 23 factors listed in Appendix 1 were used to construct models of adverse outcomes and are expressed as odds ratios (OR) and 95% confidence intervals (CI). For multiple comparisons, analysis of variance was performed using a Bonferroni correction. Event-free survival was calculated by Kaplan–Meier methods. Independent predictors of long-term survival were determined using Cox proportional hazards

analysis. All statistical analyses were performed using SPSS 17.0 (SPSS Inc, Chicago, Ill).

RESULTS

This study included 313 patients undergoing reoperative AVR, of whom 152 (48.6%) had PVE and 161 (51.4%) did not. Patients with PVE had a higher risk profile, being older with more urgent/emergency cases and a higher incidence of preoperative neurologic dysfunction, thromboembolic events, renal failure, diabetes, and congestive cardiac failure (Table 1). Sixty-four (42.1%) patients with PVE had an aortic root abscess with the most common organism being *Staphylococcus* in 50%. Cerebral embolism occurred in 15 (9.9%) patients and renal or splenic emboli in 26 (17.1%) (indications not mutually exclusive). Endocarditis was classified as active in all patients. In patients with early PVE, the most common organisms were coagulase-negative *Staphylococcus* and *S aureus*, whereas *Streptococcus* and gram-negative infections were more common in late PVE (Table 2). Patients with PVE were more likely to have had either a xenograft or concomitant mitral valve operation and less likely to have had a mechanical prosthesis at the primary operation compared with patients without endocarditis (Table 3).

The reasons for reoperation in patients with PVE were periannular complications in 42.1% ($n = 64$), systemic embolization in 27% ($n = 41$), prosthetic dysfunction leading to cardiac failure in 19.1% ($n = 29$), persistent sepsis in 15.8% ($n = 24$), and large mobile vegetation in 13.4% ($n = 42$). The reasons for reoperation in those without endocarditis were nonstructural dysfunction ($n = 62$, 38.5%), structural dysfunction ($n = 57$, 35.4%), aortic root aneurysm or dissection ($n = 30$, 18.6%), and valve thrombosis ($n = 12$, 7.5%).

The most common procedure performed for PVE was an aortic root replacement (aortic root $\pm$ concomitant procedure vs AVR $\pm$ concomitant procedure, 55.8% vs 43%; $P < .01$). For nonendocarditic reoperations, AVR and root replacement were performed with similar frequency (46.4% vs 50.8%, respectively; $P = .1$).

Concomitant Procedures

Concomitant mitral valve surgery was needed more frequently in patients with PVE (38.8% vs 20.5%; $P < .01$; PVE vs non-PVE), most commonly owing to either mitral regurgitation (26% vs 13%; $P = .005$) or mitral endocarditis (prosthetic mitral endocarditis 8.5% [$n = 13$] and native mitral endocarditis 9.5% [$n = 14$] vs 0%; $P = .002$). Only 27% and 21% of these patients (PVE vs non-PVE) underwent mitral valve repair; the majority of valves were replaced.

CABG was required in similar proportions in each group (15.1% vs 12.3%; $P = .5$; PVE vs non-PVE). The indication for aortic surgery was either ascending aortic or arch aneurysm (8% vs 29%; $P < .01$) or aortic dissection (1.3% vs 4.3%; $P = .1$).

TABLE 1. Demographic and preoperative clinical characteristics

	PVE	Non-PVE	P
N	152	161	
Age (y)	65.8 ± 14.7	57.6 ± 16.2	<.01
Female	31 (20)	45 (28)	.1
Timing			
Elective	20 (13.2)	93 (57.8)	<.01
Urgent	65 (42.8)	50 (31.1)	.03
Emergency	67 (44)	18 (11.3)	<.01
Interval from primary operation (y)			
Mechanical	7.7 ± 5.7	10.4 ± 6.8	.01
Bioprosthetic	2.2 ± 2.5	4.9 ± 3.6	<.001
COPD	17 (11.2)	20 (12.4)	.7
PVD	7 (4.6)	9 (5.6)	.6
Neurologic dysfunction	41 (27.0)	15 (9.3)	<.001
Serum creatinine > 200 μmol/L	19 (12.5)	5 (3.1)	.002
Diabetes mellitus	42 (27.6)	31 (19.3)	.03
Ejection fraction			
30%–50%	45 (29.6)	45 (28.0)	.7
<30%	11 (7.2)	19 (11.8)	.1
Pulmonary hypertension	19 (12.5)	19 (11.8)	.8
CCF	29 (19.1)	8 (5.0)	<.01
NYHA III–IV	89 (58.5)	64 (39.7)	.001

Data shown are numbers of cases (%), unless otherwise indicated. CCF, Congestive cardiac failure; COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association; PVD, peripheral vascular disease; PVE, prosthetic valve endocarditis.

Analysis of Risk Factors for Mortality

In concordance with patients with PVE being an altogether more complex and sicker group, they had longer operative times and higher incidence of postoperative complications (Table 4). Thirty-day mortality for the entire cohort was 15.3% (n = 48) and patients with PVE had higher mortality than those without PVE (24.3%, n = 37

TABLE 2. Microbiological data for patients with PVE*

Organism	Early (n = 39)	Late (n = 67)	P
Staphylococcus species	19 (49)	23 (34)	.2
<i>S aureus</i>	7	20	
Coagulase-negative	8	3	
Other <i>Staphylococcus</i>	4	0	
Streptococcus species	3 (8)	11 (16)	.04
<i>Strep pneumonia</i>	1	0	
Other <i>Streptococcus</i>	2	11	
Enterococcus species	8 (21)	12 (18)	.6
<i>Enterococcus faecalis</i>	5	6	
Other <i>enterococcus</i>	3	6	
Gram-negative	0	5 (7)	.09
<i>E coli</i>	0	3	
<i>Pseudomonas</i>	0	1	
<i>Proteus</i>	0	1	
Candida	3 (8)	3 (4)	.4
Other	0	3 (4)	.1
Culture negative	6 (15)	10 (15)	1

Data shown are numbers of cases (%), unless otherwise indicated. PVE, Prosthetic valve endocarditis. *Data are available for 106 patients.

TABLE 3. Primary and reoperative surgical details

	Primary			Reoperation		
	PVE	Non-PVE	P	PVE	Non-PVE	P
Valve substitute						
Bioprosthesis	97 (63.8)	52 (32.3)	<.001	131 (86.2)	152 (94.4)	.07
Mechanical	51 (33.6)	83 (51.6)	<.001	8 (5.3)	9 (5.6)	.3
Homograft	3 (2.0)	7 (4.3)	.2	13 (8.5)	0	<.001
Other*	1 (0.6)	19 (11.8)	.02	0	0	1
Concomitant						
Mitral valve	26 (17.1)	14 (8.7)	.02	52 (34.2)	32 (19.9)	.01
CABG	29 (19.1)	19 (11.8)	.07	23 (15.1)	16 (9.9)	.4
Asc aorta/arch	9 (5.9)	3 (1.9)	.06	19 (12.5)	27 (16.7)	.2

Data shown are numbers of cases (%). PVE, Prosthetic valve endocarditis; CABG, coronary artery bypass grafting. *Other: Ross operation, aortic valve commissurotomy.

vs 6.8%, n = 11; $P < .001$). Patients with complicated PVE had higher mortality than those without complications (30.9%, n = 30 vs 12.7%, n = 7; $P = .01$). This difference was greater when just restricted to those with periannular abscesses (40.6%, n = 26 vs 12.5%, n = 11; $P < .001$). The mortality of patients with uncomplicated PVE was not significantly different from that of the non-PVE group although it was nearly double, suggesting that a type II error may have occurred (12.7%, n = 7 vs 6.8%, n = 11; $P = .1$; respectively). In patients with PVE, both *Staphylococcal* infection (23.8%, n = 10 vs 15.6%, n = 10, *Staph* vs non-*Staph* infection; $P = .3$) and early endocarditis (23.5%; n = 12 vs 24.8%, n = 25 early vs late endocarditis; $P = .5$) did not influence mortality.

Univariate analysis of risk factors (Appendix 1) for mortality in the PVE group identified sepsis (OR, 10.1; 95% CI, 3.6–28.0; $P < .01$), left ventricular ejection fraction less than 30% (OR, 4.6; 95% CI, 1.3–16.9; $P < .01$), concomitant procedures (CABG: OR, 3.1; 95% CI, 1.2–7.7; $P = .01$; mitral valve surgery: OR, 2.6; 95% CI, 1.2–5.4;

TABLE 4. Intraoperative and postoperative results

	PVE	Non-PVE	P
Operative time (min)	310.1 ± 121.1	254.7 ± 98.8	.009
CPB time (min)	204.4 ± 105.6	159.8 ± 81.9	.006
Crossclamp time (min)	126.9 ± 54.6	95.8 ± 41.4	<.001
Reoperation for bleeding	29 (19.1)	19 (11.8)	.7
Low cardiac output	45 (29.6)	22 (13.7)	.001
IABP	32 (21.1)	10 (6.2)	<.001
Pneumonia	28 (18.4)	23 (14.3)	.3
Stroke	10 (6.6)	5 (3.1)	.1
Renal failure	38 (25)	22 (13.7)	.01
Gastrointestinal ischemia	17 (11.2)	5 (3.1)	.005
Pacemaker implantation	39 (25.7)	38 (23.6)	.6
Early endocarditis	4 (2.6)	0 (0)	.04
Hospital stay (d)	20 ± 21	16 ± 11	.011
Thirty-day mortality	37 (24.3)	11 (6.8)	<.001

Data shown are mean ± standard deviation, or number of cases (%) where appropriate. CPB, Cardiopulmonary bypass; IABP, intra-aortic balloon pump; PVE, prosthetic valve endocarditis.

$P = .02$), aortic root abscess (OR, 2.7; 95% CI, 1.1–6.4; $P = .02$), diabetes mellitus (OR, 2.3; 95% CI, 1.0–4.8; $P = .04$), and preoperative New York Heart Association (NYHA) class IV (OR, 2.2; 95% CI, 1.1–4.7; $P = .01$). However, by multivariate analysis, only sepsis (OR, 6.5; 95% CI, 2.0–21.0; $P < .01$), left ventricular ejection fraction less than 30% (OR, 5.8; 95% CI, 1.3–25.0; $P = .02$), concomitant CABG (OR, 3.3; 95% CI, 1.1–9.8; $P = .03$), and aortic root abscess (OR, 2.7; 95% CI, 1.2–6.4; $P = .02$) were independent predictors of mortality.

Postoperative causes of death in patients with PVE were low cardiac output with multiorgan dysfunction ($n = 19$; 12.5%), sepsis ($n = 2$; 1.3%), neurologic ($n = 2$; 1.3%) and respiratory ($n = 4$; 2%) dysfunction (pneumonia and adult respiratory distress syndrome), right heart failure owing to right coronary artery occlusion ($n = 2$; 1.3%), bleeding ($n = 2$; 1.3%), mesenteric ischemia ($n = 3$; 2%), and uncertain etiology ($n = 3$; 2%). Eight patients died intraoperatively owing to cardiac failure and hemorrhage.

In the non-PVE group, univariate analysis of predictors of mortality identified preoperative unstable status (OR, 8.5; 95% CI, 1.7–41.1; $P = .01$), emergency indication for operation (OR, 4.2; 95% CI, 1.1–15.6; $P = .02$), concomitant procedures (mitral valve surgery: OR, 3.8; 95% CI, 1.1–12.3; $P = .02$; CABG: OR, 3.1; 95% CI, 1.2–7.7; $P = .01$), and NYHA class IV (OR, 2.2; 95% CI, 1.1–4.7; $P = .01$). Multivariate analysis identified only concomitant procedures (CABG: OR, 8.1; 95% CI, 2.0–33.0; $P < .01$; mitral valve surgery: OR, 4.8; 95% CI, 1.3–17.9; $P = .02$) as an independent predictor of mortality.

Patients without PVE died of low cardiac output ($n = 4$; 3%), sepsis ($n = 2$; 1.2%), neurologic ($n = 2$; 1.2%) and respiratory dysfunction ($n = 1$; 0.6%), right heart failure ($n = 2$; 1.2%), mesenteric ischemia ($n = 1$; 0.6%) and uncertain etiology ($n = 1$; 0.6%).

Analysis of Predictors of Long-Term Survival

Follow-up was 97.4% complete with a mean of 6.5 ± 0.4 years (range, 0–12 years) and a total of 620.3 patient-years. The 1, 3, 5, and 10-year survivals for patients with and without PVE were $52\% \pm 4\%$ versus $82\% \pm 3\%$, $43\% \pm 5\%$ versus $73\% \pm 4\%$, $37\% \pm 5\%$ versus $63\% \pm 5\%$, and $31\% \pm 7\%$ versus $56\% \pm 8\%$ (log rank $P < .001$) (Figure 1, A). For complicated and uncomplicated PVE, the 1, 3, 5, and 10-year survivals were $44\% \pm 5\%$ versus $64\% \pm 7\%$, $38\% \pm 5\%$ versus $53\% \pm 8\%$, $38\% \pm 5\%$ versus $41\% \pm 9\%$, and 0% versus $41\% \pm 9\%$ ($P = .028$) (Figure 1, B). Survival was worse for patients with uncomplicated PVE than for the non-PVE group ($P = .02$). There was no significant difference in survival between early and late endocarditis ($P = .68$) or between *Staph* versus non-*Staph* infection ($P = .8$). Independent predictors of long-term survival in patients with PVE were sepsis (OR, 3.1; 95% CI, 1.5–4.5; $P < .01$) and unstable preoperative status

(OR, 1.8; 95% CI, 1.2–3.5; $P = .04$), whereas in non-PVE patients the predictor was NYHA class IV (OR, 2.5; 95% CI, 2.8–7.4; $P < .01$).

Thirteen patients needed a second reoperation for PVE (PVE group, $n = 10$; non-PVE group, $n = 3$). Seven of 10 patients with PVE who subsequently had recurrent PVE had a root abscess at their first reoperation. Actuarial 5-year freedom from endocarditis was $80\% \pm 0.3\%$ (PVE) versus $95\% \pm 0.6\%$ (non-PVE) (log rank $P = .002$) (Figure 1, C).

DISCUSSION

In one of the largest published series of patients with active aortic PVE undergoing surgical intervention, this study demonstrates high mortality (24.3%) and poor mid and long-term survival (37% at 5 years, 31% at 10 years) despite contemporary medical and surgical treatment, underlining the fact that treatment of this group of patients still remains a therapeutic challenge. High-risk subgroups were those with sepsis, poor left ventricular function, periannular complications, and those requiring concomitant CABG. In fact, those with uncomplicated PVE did not have a significantly different mortality from those having nonendocarditic reoperations. Endocarditis recurred in one fifth of patients within 5 years. Reoperative AVR for nonendocarditic causes was associated with lower mortality (6.8%) and better long-term survival (63% at 5 years, 56% at 10 years), representing the very different disease processes, preoperative patient characteristics, and intraoperative challenges of these patients.

The operative mortality for both PVE and non-PVE reoperations observed in this study compares favorably with contemporary data.^{5,6} Many studies report mortality for reoperation for PVE ranging between 20% and 29%.^{7–9} The most comprehensive study to date concerning PVE (The International Collaboration on Endocarditis–Prospective Cohort Study) reported an in-hospital mortality of 22.8% among 556 PVE patients.³ This study identified older age, health care–associated infection, *Staph aureus* infection, and complicated PVE as predictors of mortality, confirming in a large number of patients the presence of high-risk subgroups. Similarly, we identified the complications of sepsis and periannular abscess as predictors of mortality.

The surgical treatment of root abscesses is a challenge, and our study confirmed the association of periannular complications with both increased early mortality and *Staphylococcus* infection. Aortic root abscesses occurred in 42%, which is higher than the 19% to 29% previously reported.^{7,10} In our data, 50% of patients with *Staphylococcus* infection and 32% with *S aureus* infection had a root abscess. Prior data have demonstrated (1) higher mortality for patients with periannular abscesses, (2) higher incidence of root

FIGURE 1. A, Kaplan–Meier survival after reoperative aortic valve surgery for patients with and without PVE. B, Kaplan–Meier survival after reoperative aortic valve surgery for patients with PVE stratified by complications. C, Freedom from endocarditis after redo aortic valve surgery for patients with and without PVE. *PVE*, Prosthetic valve endocarditis.

abscesses in both PVE (vs native valve endocarditis) and *Staphylococcus* infection (vs non-*Staph*), and (3) *S aureus* infection to be an independent prognostic factor for mortality in patients who have abscess formation.^{11,12}

Sepsis was a predictor of both mortality and long-term survival, which is concordant with data from Davierwala

and associates.⁵ *Staphylococcus* is the most frequent causative organism in early PVE, where it is considered a perioperative contaminant, has an incidence of 24% to 40%, and has been shown to be a predictor of in-hospital mortality and late death in some¹³ but not all studies.¹⁴ It is not possible to conclude from our data that high-risk subgroups

such as this should be managed more aggressively or that uncomplicated PVE can be managed with antibiotics alone inasmuch as we do not have a medically treated PVE group for comparison.

Additionally, poor left ventricular function and concomitant CABG were predictors of mortality. Increasing operative complexity by adding concomitant procedures has been previously shown to increase risk,¹⁵ and our findings concur. Kumar and associates¹⁶ found all other valvular procedures performed simultaneously with reoperative aortic valve surgery were univariate predictors of mortality, whereas several studies have documented increased risk with concomitant CABG, which is likely related to embolic coronary occlusion.¹⁷

There was no effect of the previous type of prosthesis on the early and long-term survival. However, data from Tang and coworkers¹⁵ suggest that explanting mechanical valves is associated with higher perioperative mortality than is explanting bioprosthetic valves, likely because of different modes of failure and presentation; the authors further suggest that this should be considered when patient and surgeon are discussing valve type.¹⁵ Potter and associates⁶ also recommend the expanded use of bioprosthetic valves but on the basis that the risk of reoperation is similar to that for primary surgery. Potentially, our results have implications for the use of bioprosthetic valves among younger patients needing a reoperation for PVE. In our series, 86% of patients with PVE had a biological valve substitute. However, inasmuch as less than one third of patients survived 10 years, structural valve dysfunction is unlikely to be an issue for most patients.

Patients with PVE were more likely to have had either a xenograft or concomitant mitral valve surgery, and less likely to have had a mechanical prosthesis, at the primary operation than were patients without endocarditis. It is not possible to conclude from this information that patients having xenografts at the primary operation are more likely to have PVE, or vice versa for mechanical valves; we do not know the denominator of the total number of xenografts or mechanical prostheses inserted because in many cases the primary operation had been performed in other centers.

The long-term survival of patients with PVE is significantly lower than that of patients with either native valve endocarditis or other modes of failure of prosthetic valves. The 5-year survival in our study of PVE patients was only 37% $\pm$ 5% (non-PVE 63% $\pm$ 5%), which is similar to 30% $\pm$ 6% reported by Cortina and colleagues.¹⁸ However, other studies have reported better 5-year survivals ranging from 59% to 64%, which may be related to differences in patient characteristics.^{19,20} Our 10-year survival of 31% is similar to the 37.6% reported by the UK Heart Valve Registry.²¹ The University of Toronto group reported a 15-year survival of 25% $\pm$ 7%,²² and Stanford University reported a 20-year survival of 16% $\pm$ 7%.²³ Regardless, it

is clear that long-term survival is poor, underlining the high-risk nature of these patients.

The freedom from recurrent endocarditis of 80% at 5 years in this study compares favorably with 60% reported by Akowuah and coworkers.²⁴ In a recent study, Alonso-Valle and colleagues⁷ reported 91% freedom from recurrent endocarditis at 32 months. However, d'Udeken and associates²⁵ reported a 10-year rate of 79% $\pm$ 9%, with all patients in whom this late complication developed having a paravalvular abscess at the time of the original operation. In our study, 70% of patients with PVE in whom a recurrence developed had an abscess at their first reoperation.

Study Limitations

Several limitations of our study have to be outlined. First, it is retrospective and nonrandomized, but we believe that this is a reasonable approach to assess predictors of outcome in one of the largest series of surgically treated patients with active aortic PVE and has long-term follow-up that was 97% complete. Second, such a long-term experience will inevitably be biased by a learning curve, intersurgeon variability, and improvements in perioperative medical and surgical management.

In conclusion, despite contemporary medical and surgical therapy, reoperative aortic valve surgery in the setting of PVE is still associated with high early mortality and poor long-term survival. High-risk subgroups are those with sepsis, periannular complications, poor left ventricular function, and those requiring concomitant CABG. Long-term survival is worse in those with sepsis or instability before the operation.

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APPENDIX 1. Preoperative Factors Used in Cox Multivariate Regression Analyses

Sex, age, body mass index, chronic pulmonary disease, peripheral vascular disease, previous stroke or transient ischemic attack, chronic renal insufficiency, **preoperative dialysis**, diabetes mellitus, syncope, history of myocardial infarction, unstable angina, cardiogenic shock, New York

Heart Association functional class (I–IV), left ventricle ejection fraction (%), pulmonary hypertension, surgical timing (elective, urgent, and emergent), active endocarditis, active endocarditis with vegetation, active endocarditis with perianular complication, Staphylococcus infection, biologic valve dysfunction or degeneration, paravalvular leak, mechanical valve dysfunction (thrombosis), ascending aortic aneurysm, mitral valve surgery, coronary artery bypass grafting.