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Risk Factors Predicting the Postoperative Outcome in 134 Patients with Active Endocarditis

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ABSTRACT

Background: Surgery remains the cornerstone in management of endocarditis.

Methods: In this retrospective cohort we evaluated the operative outcome of patients with infective endocarditis. The SPSS program was used to analyze the data.

Results: A total of 134 predominantly male patients (60%) with a mean age of 55 ± 12.4 years were examined. The procedures included single valve (n = 88; 66%), double/multiple valves (n = 29; 22%), and valve–coronary artery bypass graft (CABG) (n = 16; 12%). Perioperative mortality was 11.9% (n = 16). In the multivariate analysis, dialysis (odds ratio [OR] = 7.88; 95% confidence interval [CI] [1.78-34.77]; *P* = .006), sepsis (OR = 19.5; 95% CI [2.76-137.9]; *P* = .002), and perfusion time (95% CI [1.00-1.02]; *P* = .003) were independent predictors of perioperative mortality. The overall long-term survival at 28 months was 69.2% ± 4%. Dialysis (*P* = .0001) was a predictor of mortality, whereas elevated creatinine in nondialysis patients (*P* = .0002) was not. In the multivariate analysis, dialysis (hazard ratio [HR] 4.06%; 95% CI [0.936-8.526]; *P* = .0002), CABG (HR 2.32; 95% CI [1.086-4.978]; *P* = .0299), chronic obstructive pulmonary disease (HR 2.20; 95% CI [1.027-4.739]; *P* = .0426), and double/multiple valve procedure (HR 3.0; 95% CI [1.467-6.206]; *P* = .0027) were risk factors for long-term mortality.

Conclusion: Renal failure but not renal insufficiency is a risk factor for short and long-term mortality.

INTRODUCTION

Despite advances in diagnosis and treatment, infective endocarditis (IE) remains a serious condition and is associated with significant morbidity and mortality [Gutierrez-Martin 2010; Leone 2012]. The clinical and epidemiologic characteristics of IE are in transition; incidence is increasing among octogenarians and multimorbid patients. Earlier diagnosis and surgery may reduce mortality and morbidity [Gutierrez-Martin 2010; Leone 2012; Leone 2012]. The main indications for surgery are heart failure secondary to valvular regurgitation, uncontrolled infection, large mobile vegetations, intracardiac abscess or fistula, prosthetic endocarditis or difficult-to-treat microorganisms, and failure of medical management [Yamaguchi 2007; Gutierrez-Martin 2010; Kiefer 2011; Wang 2011].

METHODS

A retrospective cohort analysis was conducted to evaluate preoperative risk factors and operative outcomes in a contemporary cohort including 134 patients with IE who underwent open heart surgery between January 2006 and May 2011. All operations were performed using a standard approach with a median sternotomy and extracorporeal circulation. This retrospective study was approved by the Institutional Review Board at our institution.

Patients' demographic data (e.g., preoperative risk factors and postoperative outcomes) were collected. Hospital mortality was defined as death for any reason occurring within 30 days after the operation or any time during the same hospitalization, regardless of the length. Neurologic adverse events were defined as stroke, a new neurologic dysfunction that persisted for 72 hours, or a transient neurologic dysfunction. The Kaplan-Meier test was used to estimate the survival and the log-rank test was used to compare the differences between the groups. Univariate analysis was used to determine predictors of mortality and morbidity. Multivariable logistic and Cox regression methods were used to identify the independent risk factors. Adjusted odds ratios (ORs) were calculated for in-hospital outcomes and the hazard ratio (HR) for long-term outcome. Ninety-five percent confidence intervals (CIs) were calculated for each risk interval. For continuous variables, correlations were calculated with the Student t-test. A *P* value < .05 was considered statistically significant. Data analysis was performed with the SPSS program.

RESULTS

In total, 134 patients with a mean age of 55 ± 12.4 years were examined. Most patients were males (60%) with a mean ejection fraction (EF) of 52.8% ± 11.3%. The median

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Table 1. Patient Characteristics

Parameter	n	%
Preoperative		
CHF	59	44.0
COPD	33	25.0
Diabetes mellitus	55	41.0
Peripheral vascular disease	23	17.0
Immunosupression	11	8.2
Operative		
Emergency	17	13.0
Elective	17	13.0
Urgent	98	74.0
Shock	4	3.0
Unstable	5	4.5
Root abscess	8	6.0
Prosthetic valve endocarditis	5	4.5
Single valve	88	66.0
Double/multiple valves	29	22.0
Valve + CABG	16	12.0
Stroke	3	2.26
Postoperative		
Postoperative sepsis	8	6.0
Blood products	101	75.0

Table 2. Univariate Analysis of Risk Factors

Significant Parameters		Insignificant Parameters	
Parameter	*P*	Parameter	*P*
Cross-clamp time	.0008	Age	.1
Perfusion time	.0006	Gender	.17
Preoperative creatinine >1.5 mg/dl	.018	Preoperative creatinine > 1.5 (excluding dialysis patients)	.66
Preoperative dialysis	.002	COPD	.24
Concomitant CABG	.025	EF	.57
Emergency status	.01	Perioperative transfusion	.73
Hemodynamic instability	.01	Diabetes mellitus	.22
Postoperative sepsis	.0004	Immunosuppression	.37
Preoperative dialysis	.024	Prosthetic valve endocarditis	.45

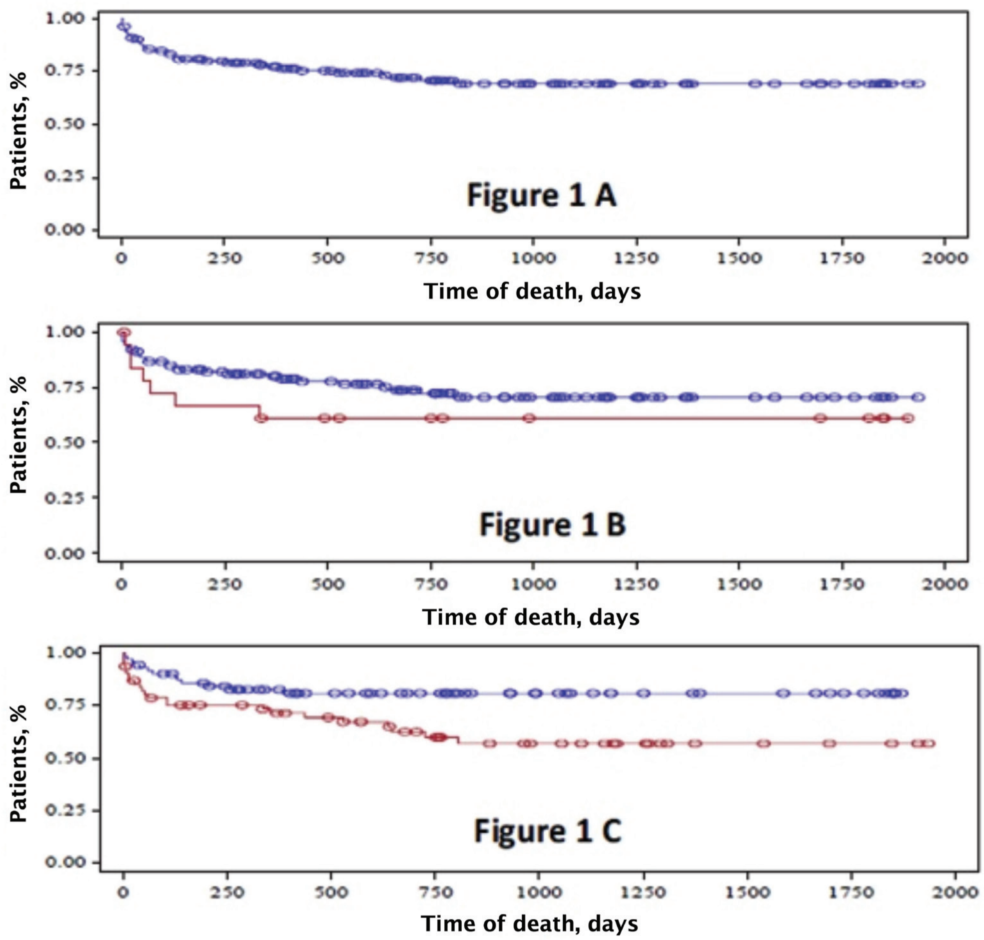

Figure 1. A. Overall survival at 6 months, 80% ± 3.5%; 1 year, 77.3% ± 3.7%; 2 years, 70.8% ± 4%; and 28 months, 69.2% ± 4%. B. Comparison of the survival in patients >70 years old (red line, n = 19) to that of patients <70 (blue line, n = 115). There was not a statistically significant difference in survival in younger and older patients below an age cutoff of 70 years (*P* = .26). C. Creatinine >1.5 mg/dl (red line, including dialysis patients, n = 62), versus creatinine <1.5 (blue line). The patients with elevated creatinine had an inferior survival rate; however, in this Figure, dialysis patients are included with patients who had elevated creatinine but were not necessarily on dialysis (*P* = .008).

cross-clamp time was 98 min (range 21-366 min) and the median perfusion time was 137 min (53-676 min). Preoperative median creatinine was 1.4 mg/dl (range 0.4-17.7 mg/dl). Preoperative creatinine >1.5 (not including the dialysis patients) (*P* = .66) were not found to be a risk factor for perioperative mortality (statistically not significant). Among the 8 patients with a root abscess, 5 patients had prosthetic valve endocarditis. Five of the 8 patients with root abscess died in the hospital (62.5%). Prosthetic valve endocarditis (PVE) (*P* = .05) and root abscess (*P* = .02) were significant risk factors for perioperative mortality. The preoperative patient characteristics are shown in Table 1.

The perioperative mortality was 11.9% (n = 16); 14 patients died on the cardiac care unit, 1 in the operating room, and 1 on the surgical floor. The univariate analysis of risk factors for perioperative mortality is illustrated in Table 2. All risk factors with *P* values < .05 were included in multivariate model. In multivariate analysis, preoperative dialysis (OR = 7.88; 95% CI [1.78-34.77]; *P* = .006), postoperative sepsis (OR = 19.5; 95% CI [2.76-137.9]; *P* = .002), and perfusion time (95% CI [1.00-1.02]; *P* = .003) (for every 30 min over a baseline of 150 min the OR increased by 1.48) were independent predictors of perioperative mortality.

The overall survival rates at 6 months, 1 year, and 28 months were 80% ± 3.5%, 77.3% ± 3.7%, 69.2% ± 4%, respectively (Figure 1A). Although advanced age has been reported to be a significant risk factor for mortality, it was not a statistically significant risk factor in our series, which may be because of the small number of patients who were older than 70 years (n = 19) compared with patients who were younger than 70 years (n = 115), *P* = .26, (Figure 1B). Elevated preoperative creatinine (>1.5, including the dialysis patients, *P* = .0002) (Figure1C) was a predictor of mortality; however, a subgroup analysis demonstrated that a creatinine

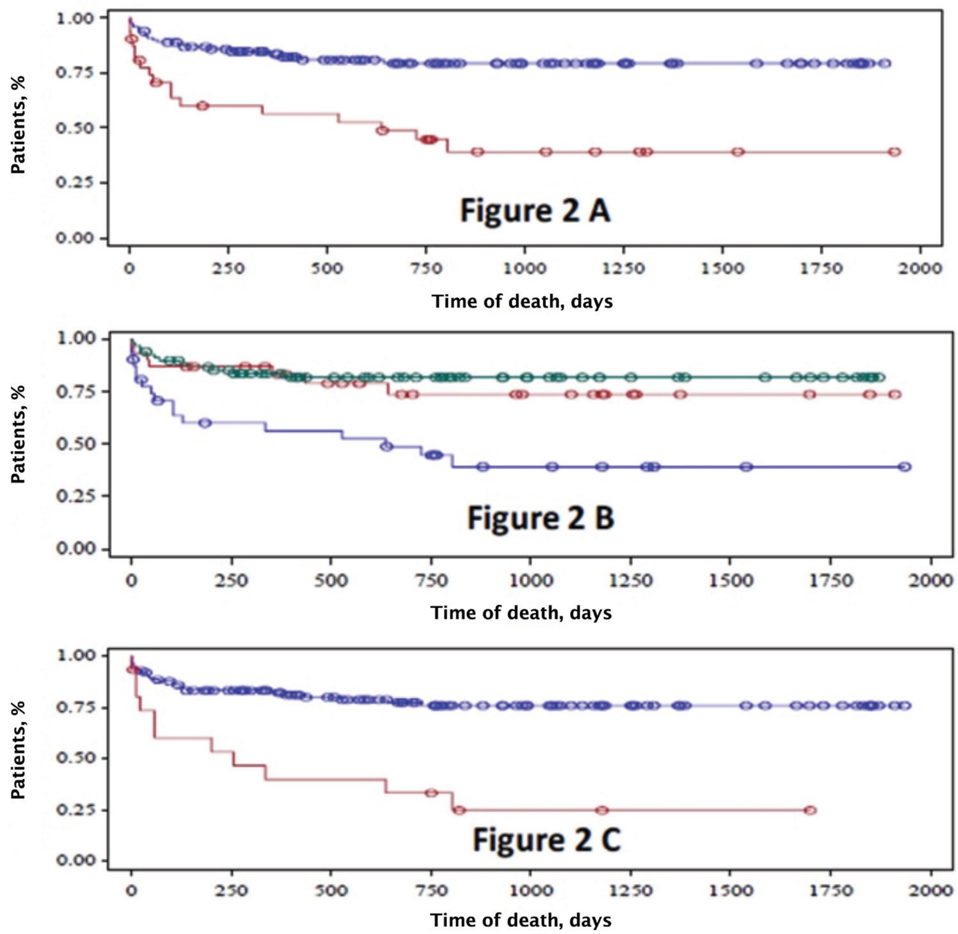

Figure 2. A. Here we compared only patients who were on dialysis (red line) to patients who were not on dialysis (blue line). The nondialysis group also includes the patients who had elevated creatinine but were not on dialysis. The 1- and 2-year survival rates of dialysis patients were 56% ± 9% and 45% ± 9%, respectively, compared to the 1- and 2-year rates of nondialysis patients at 83% ± 3% and 79% ± 4%, respectively (*P* = .0001). B. Three groups of patients: (1) dialysis patients (blue line), (2) patients with renal insufficiency (creatinine >1.5 mg/dl, but not on dialysis) (green line), and (3) patients with normal kidney function, creatinine <1.5 mg/dl (red line) (*P* = .0002). C. Patients who had only valve replacement (blue line) had better 1- and 2 year survival rates (82 ± 3% and 76% ± 4%, respectively) than did patients who required CABG at the time of surgery (40% ± 13% and 25% ± 12%, respectively) (*P* = .0001).

level above 1.5 was not a risk factor for mortality if the patients were not on dialysis. Patients with creatinine ≥1.5 mg/dl (including the patients on dialysis) had 1- and 2-year survival rates of 71% and 60%, respectively, compared to patients with creatinine <1.5 who had 1- and 2-year survival rates of 83 ± 3%, and 79 ± 4% (*P* = .008) (Figure 2A), respectively, whereas patients with end-stage renal failure requiring hemodialysis preoperatively had a 1- and 2-year survival rates of 56% ± 9% and 45% ± 9%, respectively (*P* = .0001). There was no significant difference in survival between patients with creatinine below 1.5 mg/dL compared with patients who had elevated creatinine but were not on hemodialysis (Figure 2B).

A single-valve (SV) procedure was performed in 88 patients (66%), a double/multiple-valve (DV) procedure in 29 patients (22%), and a concomitant valve-coronary artery bypass graft (CABG) procedure in 16 patients (12%). Patients who had concurrent CABG had 1- and 2-year survival rates of 40% ± 13% and 25% ± 12%, respectively, compared to 82% ± 3% and 76% ± 4% in valve-only patients (*P* = .0001) (Figure 2C). Furthermore, Kaplan-Meier survival curves showed a 1-year survival rate of 56% ± 9% for the DV compared to 83% ± 3% for the SV group (*P* = .04) (Figure 3A).

Chronic obstructive pulmonary disease (COPD) was found to be a significant predictor of long-term mortality in our series (*P* = .009); patients with COPD had 1- and 2-year survival rates

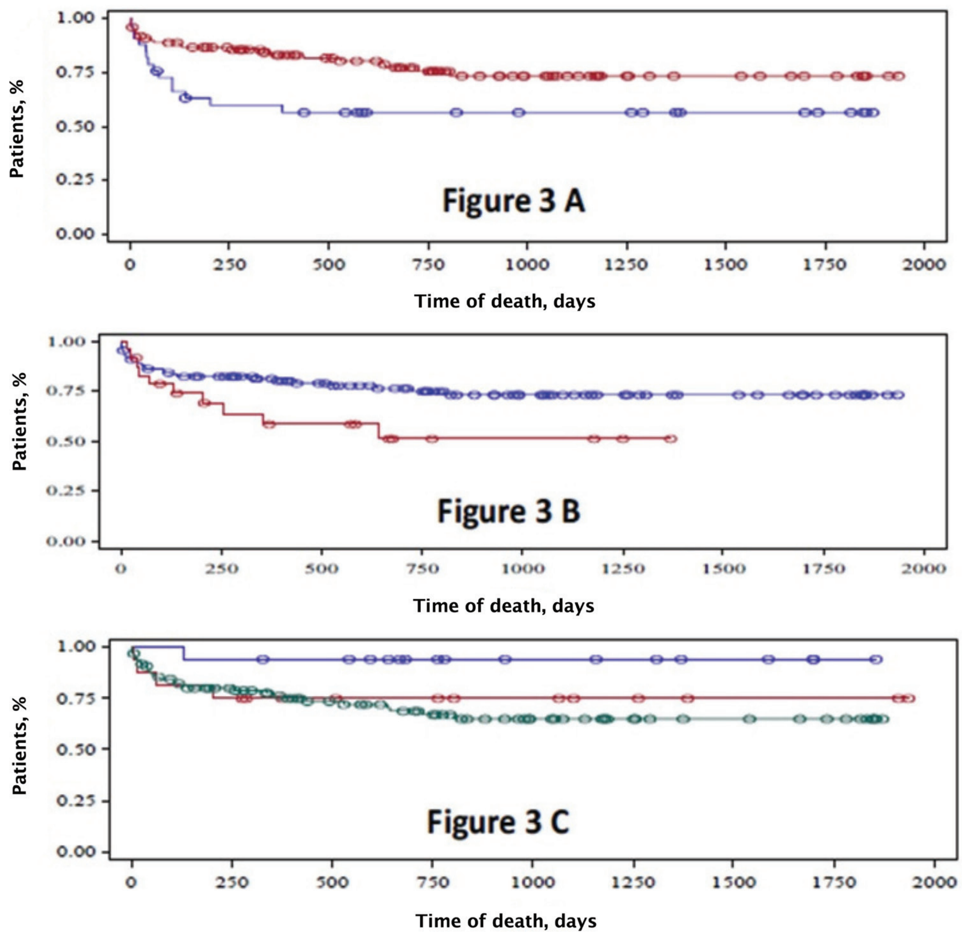

Figure 3. A. Patients with SV endocarditis had better long-term survival (red line) than did patients with double- or multiple-valve endocarditis (blue line) at 83% ± 3% versus 56% ± 9%, respectively (*P* = .04). B. patients with COPD (red line) did not have an increased perioperative mortality; however, they had a poor long-term 1- and 2-year survival compared to patients who did not have COPD preoperatively (blue line); 58% ± 10% and 51% ± 11% versus 81% ± 4% and 74% ± 4%, respectively; *P* = .009. C. The timing of surgery was a predictor of long-term mortality. Patients who underwent surgery on an emergent (red line) or urgent basis (red line) had poor long-term survival compared to patients who had an elective surgery (blue line), *P* = .017.

of 58% ± 10% and 51% ± 11%, respectively, compared to 81% ± 4% and 74% ± 4% for patients without COPD (Figure 3B).

The timing of surgery had a significant impact on survival. Emergency and urgent status at the time of surgery were associated with inferior long-term survival (*P* = .017) (Figure 3C). Multivariate analysis of long-term survival revealed that preoperative dialysis (HR 4.06%; 95% CI [.936-8.526]; *P* = .0002), concomitant CABG (HR 2.32; 95% CI [1.086-4.978]; *P* = .0299), COPD (HR 2.20; 95% CI [1.027- 4.739]; *P* = .0426), and multiple valve replacement (HR 3.0; 95% CI [1.467-6.206]; *P* = .0027) were independent risk factors for mortality.

Root abscess was a risk factor for perioperative mortality; 50% of patients with root abscess (4/8) died in the hospital; however, root abscess did not impact long-term survival, which might be due to the small number of patients who had a root abscess in our series. Considering the small number of patients with root abscess in our series (n = 8), we cannot make a statement on root abscess and its significance as a risk factor for long-term mortality. Table 2 shows the results of univariate analysis of risk factors. Thirty percent of patients (n = 40) were discharged home; the remaining (surviving) patients were discharged to rehabilitation centers or skilled nursing facilities.

DISCUSSION

Surgery remains the gold standard for the management of IE; it is more likely to be performed when the patient develops signs of heart failure in the context of uncontrolled IE [Kiefer 2011; Leone 2012]. In this cohort, we had a perioperative mortality of 11.9%, which compares favorably with the current data on mortality rates in the literature. In the International Collaboration on Endocarditis-Prospective Cohort Study including 4,166 patients with native or prosthetic-valve IE, surgery was associated with lower perioperative mortality than medical therapy alone (20.6% versus. 44.8%, respectively) [Kiefer 2011]. In a recent series of 82 patients with aortic valve IE, the perioperative mortality was 17% (n = 14) [Polat 2012]. The overall mean survival at 28 months in our series was 69.2% ± 4% (Figure 1A). In a series of 90 patients, Sheikh et al. [Sheikh 2009] reported overall survival rates of 68% and 49% at 5 and 10 years, respectively; similar survival rates have been reported in other studies. For example, Meszaros et al found a perioperative mortality of 11% and 1-year and 5-year survival rates of 77% and 69%, respectively [Meszaros 2012]. Despite high early mortality during the first year, the long-term survival of patients who underwent surgery remained favorable [Meszaros 2012]. In a series of 191 patients with IE (72% had surgery), Mokhles et al [Mokhles 2012] reported a 10-year survival rate of 59%. The authors believed that the survival of patients, even with cured IE, is lower than that of the general population [Mokhles 2012], yet in a study of 134 patients conducted in the prior year, the same authors found that mortality of IE patients following surgery is comparable to the general population if they survive the perioperative period [Mokhles 2011]. Using Society of Thoracic Surgeons data, evaluation of 1862 dialysis patients with IE revealed that cardiogenic shock, double valve, age ≥60 years, body surface area, and arrhythmia are associated with high mortality [Rankin 2007]. Patients who required concomitant CABG had an inferior survival rate of 25% ± 12% at 2 years (compared to 82% ± 3% in patients who did not require CABG).

Having DV endocarditis was associated with an inferior survival rate in our cohort; patients with SV endocarditis had a 2-year survival rate of 82%, whereas patients with DV endocarditis had a 2-year survival rate of 58%. This observation has been confirmed by other authors [Shang 2009; Meszaros 2012]. In another study, multiple-valve IE was associated more frequently with heart failure (65% versus 50%), perivalvular complications (41% versus 21%), and prior heart surgery (70% versus 54%) [Lopez 2011]. The other aspect of our study is that we found out that renal insufficiency (creatinine >1.5) was not a significant risk factor for mortality if the patients didn't require dialysis preoperatively; contrastingly, preoperative renal failure that required dialysis was an independent predictor of perioperative and long-term mortality. Other authors have reported that renal insufficiency as a risk factor for long-term mortality and morbidity in the presence of IE [Sheikh 2009; Kiefer 2011; Tamura 2012]. However, the terminology "renal insufficiency" might be deceptive, because the group includes patients with elevated creatinine who do not require dialysis."Renal failure" should be reserved for patients with end-stage renal disease who require renal replacement therapy, which should clarify the issue. We differentiated between these 2 conditions; renal insufficiency was defined as compromised kidney function (creatinine >1.5 mg/dl, but not on dialysis), and renal failure was defined as decompensated renal function requiring dialysis. Renal failure was a strong predictor of mortality in our study, whereas renal insufficiency (creatinine >1.5 mg/dl but not on dialysis) did not have a statistically significant impact on survival compared with patients who did not have renal insufficiency (creatinine <1.5 mg/dL) preoperatively.

High perioperative mortality in emergency situations and unstable patients combined with poor long-term survival following emergency/urgent surgery suggest that early surgical intervention may reduce mortality and improve patient outcomes [Kang 2012]. Emergency or urgent status at the time of surgery was associated with high perioperative mortality and inferior long-term survival in our cohort. Funakoshi et al. [Funakoshi 2011] reported favorable outcomes with early surgery in a series of 212 patients. Early surgery was performed in the active phase within 2 weeks after the initial diagnosis (n = 73), whereas the rest of the patients underwent surgery once the signs of heart failure during medical management became visible (n = 130). Perioperative mortality was significantly lower following early operation compared to the delayed approach (5% versus 13%) in their series [Funakoshi 2011].

PVE has been reported to be a significant risk factor for mortality [Shang 2009; Sheikh 2009; Manne 2012; Ohara 2012]. In our series, PVE was not a significant risk factor for long-term mortality (P = .45), which could be a bias due to small sample size. The other explanation for a low mortality rate in our patients with PVE might be the aggressive antibiotic therapy, which we used to sterilize the infected prosthetic valve prior to replacement. Some authors of studies with larger samples reported congestive heart failure (CHF) as a risk factor for perioperative mortality [Lopez 2011]. CHF was not a statistically significant (P = .9) risk factor for mortality in our cohort. This observation might be due to the small sample size. The other factor might be that in the majority of our patients CHF was acute and secondary to valve dysfunction. The myocardial contractility may have returned postoperatively before the chronic structural remodeling had taken place in the myocardium. Furthermore, our results demonstrated poor perioperative outcomes for sepsis, renal failure, DVE, concomitant CABG, and root abscess, which are in agreement with the current reports in the literature [Sheikh 2009; Kiefer 2011; Lopez 2011; Thuny 2012]. In our series, age, sex, immunosuppression, diabetes mellitus, preoperative creatinine (>1.5, but not on dialysis), and perioperative transfusion were not risk factors for perioperative or for long-term mortality (i.e., not statistically significant). Advanced age, diabetes mellitus, and stroke have been reported to be risk factors for high mortality in some other studies [Forrest 2011; Kiefer 2011].

CONCLUSIONS

Early surgical intervention provides a more favorable outcome. Perioperative mortality correlates with sepsis, dialysis, and prolonged cardiopulmonary bypass time. Prolonged perfusion is a predictor of mortality and may increase the risk of mortality. Multivalve endocarditis and concomitant CABG/ presence of significant coronary artery disease increases the risk of mortality. Dialysis patients have a high postoperative mortality; however, creatinine above 1.5 mg/dl is not a major risk factor if the patient is not on dialysis preoperatively.

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