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Clinical and Microbiological Characteristics of Infective Endocarditis

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Abstract: Surgical treatment of active Infective Endocarditis (IE) requires not only homodynamic repair, but also, special emphasis on the eradiation of the infection to prevent recurrence. This study was undertaken to examine the outcome of surgery for active infective endocarditis in a cohort of patients. One hundred and sixty-four consecutive patients underwent valve surgery for active IE in Madani heart centre (Tabriz, Iran) from 1996-2006. The patients with diagnosis of IE (according to Duke Criteria) were eligible for the study. The mean age of patients was 36.3±16 years, with 34.6±17.5 years for native valve endocarditis and 38.6±15.2 years for prosthetic valve endocarditis (p = 0.169). Ninety-one (55.5%) of patients were males. The infected valve was native in 112 (68.3%) of patients and prosthetic in 52 (31.7%). There was no predisposing heart disease in 61 (37%) of patients. The aortic valve was infected in 78 (47.6%), the mitral valve in 69 (42.1%) and multiple valves in 17 (10.3%) of patients. Active culture-positive endocarditis was present in 81 (49.4%) whereas, 83(50.6%) patients had culture-negative endocarditis. *Staphylococcus aureus* was the most common isolated microorganism. Ninety patients (54.8%) were in NYHA classes III and IV. Mechanical valves were implanted in 69 patients (42.1%) and bioprostheses in 95 (57.9%), including homograft in 19 (11.5%) cases. There were 16 (9%) operation-related deaths, but only 1 death in patients undergoing aortic homograft replacement. Reoperation was required in 18 (10.9%) cases. Based on multivariate logistic regression analysis, *Staphylococcus aureus* infection (p = 0.008), prosthetic valve endocarditis (p = 0.01), paravalvular abscess (p = 0.001) and left ventricular ejection fraction less than 40% (p = 0.04) were independent predictors of hospital mortality. Surgery for infective endocarditis continues to be challenging and associated with high operation-related mortality and morbidity. Prosthetic valve endocarditis, impaired ventricular function, paravalvular abscess and *Staphylococcus aureus* infection associated with hospital mortality. Also we found that aortic valve replacement with an aortic homograft could be performed with acceptable hospital mortality and provided satisfactory results.

Key words: Infective endocarditis, microbiological, surgical treatment, heart disease, surgery

INTRODUCTION

Despite advances in the diagnosis and antibiotic treatment of infective endocarditis, eradication of the septic focus and abolition of the accompanying systemic manifestations frequently require surgical intervention. Despite appropriate antibiotic treatment and improved surgical techniques, hospital mortality in patients with active endocarditis is higher than expected and the incidence of recurrence is still significant (McGiffin *et al*., 1992; Dajani *et al*., 1990; Renzulli *et al*., 2001). Since, recurrent endocarditis is a dismal complication and targeted postoperative antibiotic treatment for more than 4 weeks carries a better prognosis (Dehler and Elert, 1995; Andersson *et al*., 1986), the identification of microorganisms could affect early and late post operative outcomes. Because of the heterogeneity of the clinical and pathologic make up of patients undergoing surgical treatment for active endocarditis, operation-related mortality ranges widely between 3.8 and 22% (Aranki *et al*., 1994; Dodge *et al*., 1995; Mullany *et al*., 1995; D'Udekem *et al*., 1997; Jault *et al*., 1997; Bauernschmitt *et al*., 1998; Alexiou *et al*., 2000; Renzulli *et al*., 2000; Moon *et al*., 2001; Delay *et al*., 2000; Aagaard and Anderson, 2001) and many reported risk factors for hospital mortality included the age of over 60 years, delayed diagnosis, saphylococcus infection, aortic valve endocarditis, large valvular vegetations, congestive heart failure, cerebral or coronary embolism, prosthetic valve infection, recurrent events and failed antibiotic therapy.

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In this study, we therefore, reviewed our 10-year experience in the treatment of diagnosed active endocarditis and identified factors determining operation-associated mortality, reoperation and events, particularly, focusing on culture negative endocarditis.

MATERIALS AND METHODS

One hundred and sixty-four consecutive patients underwent valve surgery for active IE in Madani Heart Centre (Tabriz, Iran) from 1996-2006. We divided the patients into 2 subgroups of Native Valve IE (NVIE) (n = 115) and Prosthetic Valve IE (PVIE) (n = 52). Patients with IE diagnosis (according to Duke Criteria) were eligible for the study. All of the patients underwent operation before completion of antibiotic treatment and all received at least 4 weeks of postoperative multidrug antibiotic treatment. Transthoracic echocardiography (WINGMED and VIVID7, GE, USA) was performed on all cases, along with routine blood cultures and valve cultures for all patients with fever or active infection.

Cases of IE were classified retrospectively according to the Duke Criteria. Endocarditis was labeled active if the patient had fever and/or leukocytosis at the time of surgery or required surgical treatment before completion of a standard course of antibiotic treatment. Prosthetic valve endocarditis was defined as infection occurring in any type of tissue or mechanical valve device. Early prosthetic valve endocarditis was present if recurrent or residual endocarditis occurred within 60 days after surgery, while, prosthetic valve endocarditis occurring after 60 days was labeled as late. Culture-negative endocarditis was present when no microorganisms could be identified either in serial blood cultures or in cultures from the explanted valvular tissue in patients presenting with a clinical picture of active endocarditis, particularly in the presence of a new regurgitant murmur, congestive heart failure and/or vegetation on echocardiogram.

The statistical analysis was performed on collected data using SPSS v.13.0 (SPSS Inc. Chicago. IL) statistical package. Continuous variables between the 2 study groups (native vs. prosthetic valve IE) compared by independent samples t-test. Categorical variables analysed by Chi-square or Fisher's exact test as appropriate. All variables that have statistically significant differences ($p<0.05$) in univariate analysis underwent multivariate logistic regression analysis to determine independent risk factor of hospital mortality.

RESULTS

The mean age of patients was 36.3±16 years with overall 34.6±17.5 years for native valve endocarditis and 38.6±15.2 years for prosthetic valve endocarditis ($p = 0.169$). Ninety-one (55.5%) of patients were men. The infected valve was native in 112 (68.3%) and prosthetic in 52 (31.7%) of patients. In 61 (37%) cases, no predisposing heart disease was found. The aortic valve was infected in 78 (47.6%), the mitral valve in 69 (42.1%) and multiple valves in 17 (10.3%) patients. Active culture-positive endocarditis was present in 81 (49.4%), whereas, 83 (50.6%) patients had culture-negative endocarditis. The results of the blood cultures and valve cultures are shown in Table 1.

Table 1: Infective microorganisms of blood or valve cultures

Microorganism	NVIE (n = 112)	PVIE (n = 52)	Total (%)
Staphylococcus aureus	13(116.1%)	24(46.15%)	37(22.6)
Staphylococcus epidermidis	2(1.8%)	1(1.9%)	3(1.8)
Streptococcus viridians	23(20.5%)	-	23(14.02)
Streptococcus other sp.	2(1.8%)	-	2(1.2)
Enterococcus	2(1.8)	-	2(1.2)
Brucellosiss	5(4.5%)	-	5(3.04)
Candida	5(4.5%)	2(3.8%)	7(4.3)
Pseudomona	-	2(3.8%)	2(1.2)
Culture-negative	60(54.4%)	23(44.2%)	83(50.6)

Staphylococcus aureus was the most commonly isolated (22.6%) microorganism (37). *Streptococcus* species were the most common infecting microorganism which was isolated from 25 (22.3%) NVIE, while, staphylococcus species were the most common infecting microorganism isolated from 25 (48.1%) of PVIE. Culture-negative endocarditis was equally distributed between NVIE 60 (54.4%) and PVIE 23 (44.2%); $p = 0.09$. New York Heart Association (NYHA) status evaluated in all patients were 62 patients (37.8%) in NYHA class III and 28 (16.6%) in NYHA class IV, while, 74 patients (55.2%) not complaining of dyspnea, were in NYHA class I or II. LVEF <40% was present in 71 patients (43.3%). Mechanical valves were implanted in 69 patients (42.1%) and bioprostheses in 95 (57.9%), including a homograft in 19 (11.5%). Eighteen patients with NVIE and 8 with PVIE had embolic events. They consisted 14 cerebral, 3 splenic, 3 peripheral and 6 renal embolisms. Typical findings of infective endocarditis were recorded at echocardiography: significant valvular regurgitation was observed in 63 cases. There were 16 cases (9%) of hospital deaths, but there was only 1 (5.3%) death in patients that underwent aortic homograft replacement. The infecting microorganisms in hospital deaths were *Staphylococcus aureus* in 6 patients, *Staphylococcus epidermidis* in 1, *Streptococcus viridians* in 2 and 7 patients with culture-negative endcarditis. Univariate analysis of variables influencing hospital mortality is shown in Table 2.

Reoperation was required in 18 (10.9%) cases. *Staphylococcus aureus* infection ($p = 0.008$) Prosthetic valve endocarditis ($p = 0.01$), paravalvular abscess

Table 2: Univariate analysis of variables influencing hospital mortality

			Univariate		
Variables	Categories	No	Hospital mortality		p-value
Sex	Male	91	9	(9/9)	0.225
	Female	73	7	(9/6)	
Age>70	Yes	8	1	(12/5)	0.793
	No	156	15	(9/6)	
NYHA III.IV	Yes	90	10	(11/11)	0.632
	No	74	6	(8/1)	
PVIE	Yes	52	10	(19/2)	0.008
	No	112	6	(5/35)	
Aortic valve	Yes	84	8	(9/52)	0.93
	No	80	8	(10)	
Mitral valve	Yes	81	7	(8/64)	0.86
	No	83	9	(10/84)	
Multiple valve	Yes	17	2	(11/8)	0.81
	No	147	14	(9/52)	
Blood culture	- ve	83	7	(8/43)	0.80
	+ ve	81	9	(11/11)	
Staphylococcus aureus	Yes	37	5	(13/51)	0.03
	No	127	11	(8/66)	
Para valvular abcess	Yes	15	4	(26/6)	0.01
	No	149	12	(8)	
LVEF ≤ 40%	Yes	71	12	(16/9)	0.003
	No	93	4	(2/3	
Reoperation	Yes	18	1	(5/5)	0.046
	No	146	15	(10/2)	

Table 3: Multivariate analysis of variables influencing hospital mortality

Variable	OR (95% CI)	p-value
PVIE	2.83(1.44-6.76)	0.0114
Staphylococcus aureus	3.19(1.09-10.6)	0.0471
Paravalvular abcess	1.93(1.14-3.98)	0.0231
LVEF≤40%	4.61(1.93-8.92)	0.0103
Reoperation	2.13(0.13-11.7)	0.0938

(p = 0.001) and left ventricular ejection fraction less than 40% (p = 0.04) determined by multivariate logistic regression analysis, were independent predictors of hospital mortality (Table 3).

DISCUSSION

Surgical treatment of active infective endocarditis by valve replacement still remains a challenge to the surgeon, because it requires not only homodynamic repair, but also, special emphasis on the eradiation of the infection to prevent early postoperative colonization of the prosthesis by remaining microorganisms. This can be addressed by the combination of aggressive debridement of infected tissue and appropriate and adequate antibiotic treatment. According to the present retrospective study, *Staphylococcus aureus* infection, prosthetic valve endocarditis, paravalvular abscess and left ventricular ejection fraction less than 40% were independent predictors for hospital mortality.

In this study, the hospital mortality was, 9%, including NVIE in 9 (8%) and PVIE in 7 (13.5%). In recent reports, the early mortality of patients with NVIE was reduced to less than 10%, although operative mortality ranged widely between 3.8 and 22% (Dodge *et al*., 1995; Mullany *et al*., 1995; D'Udekem *et al*., 1997; Jault *et al*., 1997; Bauernschmitt *et al*., 1998; Alexiou *et al*., 2000; Renzulli *et al*., 2000; Moon *et al*., 2001; Delay *et al*., 2000; Aagaard and Andersen, 2001) because of the heterogeneity of this disease. In contrast to NVIE, the early mortality from PVIE remained as high as 13-33% (Aranki *et al*., 1994; Mullany *et al*., 1995; D'Udekem *et al*., 1997; Moon *et al*., 2001; Durack *et al*., 1994; Lytle *et al*., 1996). It has been demonstrated that *Staphylococcus aureus* and annular abscess may significantly increase the risk of early mortality (Aranki *et al*., 1994; Mullany *et al*., 1995; Jault *et al*., 1997; Bauernschmitt *et al*., 1998; Moon *et al*., 2001). In fact, significant risk factors of advanced age and preoperative heart failure have been reported by many authors. Although, improvements in diagnosis, surgical techniques and postoperative care have reduced hospital mortality, the recurrence rate is still high (Mc Giffin *et al*., 1992; Dajani *et al*., 1990; Renzulli *et al*., 2001). Inevitably, reinfection or other mainly valve-related events such as periprosthetic leakage, will lead to a need for reintervention in some patients. The 10.9% reoperation rate in this series is within the reported ranges of 8.2-19.8% (Mullany *et al*., 1995; D'Udekem *et al*., 1997; Jault *et al*., 1997; Larbalestier *et al*., 1992). The use of a homograft for aortic valve or root replacement has been shown to provide good results in terms of operative

mortality and freedom from recurrence of infection (Dearani *et al*., 1997; Dossche *et al*., 1997), though with limited availability. In contrast, however, the type of prosthesis used is not considered by some investigators to be important because early and late good results can be achieved by adequate debridement of the infected tissues, reconstruction of the resulting defects and administration of appropriate postoperative antibiotics (D'Udekem *et al*., 1997; Bauernschmitt *et al*., 1998; Edwards *et al*., 1998). It has, nonetheless, a serious impact on the outcome, signified by late cardiac death. The survival after surgical treatment for active endocarditis is known to be favorable, with reported 10-year rates, ranging from 52.0-71.3% (Aranki *et al*., 1994; Mullany *et al*., 1995; D'Udekem *et al*., 1997; Jault *et al*., 1997; Alexiou *et al*., 2000).

In this study, microorganisms were not detected in 50.6% of patients in blood or tissue cultures. Prognostic impact of positive blood and tissue cultures are still controversial. Aranki *et al*. (1994), reported that long-term survival was not influenced by the activity or the type of infection (native or prosthetic endocarditis), whereas, Dehler and Elert (1995), reported a significantly worse prognosis in patients with positive intraoperative cultures than in those with negative intraoperative cultures. Renzulli *et al*. (2000), reported a higher incidence of reoperation in patients with positive intraoperative cultures although no differences were found between short and long-term survivals. The absence of microbial isolation and the results of sensitivity tests preclude specific postoperative antibiotic therapy. According to a recent report, targeted postoperative antibiotic treatment for more than 4 weeks carries a better prognosis (Dehler and Elert, 1995). This would suggest that although, surgical techniques and appropriate preoperative multidisciplinary management canavert an unfavorably early outcome, there remains a continuous risk for recurrence and mortality.

CONCLUSION

Surgery for infective endocarditis continues to be challenging and associated with high operative mortality and morbidity. Prosthetic valve endocarditis, impaired ventricular function, paravalvular abscess and *Staphylococcus aureus* infection increase hospital mortality. Also we found that aortic valve replacement with an aortic homograft can be performed with acceptable hospital mortality and provides satisfactory results.

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