▮ MYOCARDIUM/ENDOCARDIUM/PERICARDIUM

Predictors of Hospital Mortality in 186 Cases of Active Infective Endocarditis Treated in a Tertiary Medical Center (1992-2001)

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Introduction and objectives. The aim of this study was to describe the predictors of hospital mortality found in patients admitted for infective endocarditis (IE) to a cardiovascular surgery ward.

Patients and method. Prospective study of 186 patients with IE treated in our hospital between 1992 and 2001.

Results. One hundred fourteen patients (61.3%) had native valve endocarditis and 72 (38.7%) had prosthetic valve endocarditis (early in 28 patients [up to 12 months after surgery] and late in 44 [later than 12 months]). Blood cultures were positive in 82%. The predominant organism was *Streptococcus viridans* (36%) in native valve endocarditis and *Staphylococcus aureus* (33%) in prosthetic valve endocarditis. The hospital mortality was 22.6%. Severe sepsis (4.8%) produced a high mortality rate (88%) and was caused by *Staphylococcus aureus* in 60%. One hundred nineteen patients (64%) required surgery, 79 (66.4%) of them urgently. Negative blood cultures predicted need for surgery in native valve endocarditis ($p < 0.05$). The surgical mortality was 21.8% and was related to NYHA III-IV class ($p = 0.014$) and emergency surgery ($p = 0.009$) in patients with native valve endocarditis. This last factor also predicted higher surgical mortality in patients with early prosthetic valve endocarditis ($p < 0.001$).

Conclusions. The hospital mortality of this group of patients with infective endocarditis treated in a tertiary medical center was high. The presence of severe sepsis, although infrequent, had a somber prognosis. Severe heart failure in native valve endocarditis and urgent surgery in native and prosthetic valve endocarditis increased surgical mortality.

Key words: *Endocarditis. Hospital mortality.*

Full English text available at: www.revespcardiol.org

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Predictores de mortalidad hospitalaria en 186 episodiosde endocarditis infecciosa activa en un centro de tercer nivel(1992-2001)

Introducción y objetivos. El objetivo de este estudio es intentar reconocer los predictores de mortalidad hospitalaria de los enfermos con endocarditis infecciosa ingresados en un servicio de cirugía cardiovascular.

Pacientes y método. Estudio prospectivo de 186 casos de endocarditis infecciosa en pacientes tratados desde 1992 hasta 2001.

Resultados. Se trataron 114 casos de endocarditis infecciosa sobre la válvula nativa y 72 casos (38,7%) sobre la válvula protésica (28 tempranas [hasta 12 meses poscirugía] y 44 tardías [posteriores a este período]). Los hemocultivos fueron positivos en el 82%, predominando *Streptococcus viridans* (36%) en las válvulas nativas y *Staphylococcus aureus* (33%) entre las protésicas. La mortalidad hospitalaria global fue del 22,6%. En los pacientes no operados, la sepsis grave (4,8%, un 60% por *Staphylococcus aureus*) fue la causa del 88% de mortalidad ($p < 0,001$). En total, 119 pa-cientes (64%) requirieron cirugía (urgente en el 66,4%). En la endocarditis nativa, la presencia de hemocultivos negativos resultó predictora de necesidad quirúrgica ($p < 0,05$). La mortalidad quirúrgica fue del 21,8% y se relacionó, en las válvulas nativas, con la clase funcional III-IV de la New York Heart Association (NYHA) ($p = 0,014$) y la urgencia ($p = 0,009$). Este último factor predijo también mayor mortalidad entre las protésicas tempranas ($p < 0,001$).

Conclusiones. La mortalidad hospitalaria de los pacientes con endocarditis infecciosa tratados en un centro de derivación terciaria es elevada. La sepsis grave, aunque poco frecuente, tiene un pésimo pronóstico. En las endocarditis nativas y protésicas tempranas, la urgencia en la indicación aumenta la mortalidad quirúrgica. Esta última se encuentra incrementada en las endocarditis nativas en presencia de insuficiencia cardíaca grave.

Palabras clave: Endocarditis. Mortalidad intrahospitalaria

INTRODUCTION AND OBJECTIVES

Despite advances in diagnosis and treatment, mortality due to infective endocarditis is still high.[1] The probable causes include changes in the clinical characteristics of the disease and the absence of appropriate treatment.[2,3] Identifying predictors of poor prognosis could facilitate the choice of the most appropriate therapeutic strategy. In order to analyze predictors of mortality, we assessed the hospital course of patients diagnosed as having active infective endocarditis admitted between June 1992 and December 2001 to a center mainly specializing in cardiovascular surgery.

PATIENTS AND METHODS

The Instituto de Cardiología y Cirugía Cardiovascular (ICYCC) of the Fundación Favaloro is a 186-bed tertiary teaching hospital that serves as a reference center for cardiac surgery and heart, lung, kidney, liver and bone marrow transplantations.

Diagnosis of infective endocarditis

We used the Duke criteria for diagnosis,[4] and included only definitive or probable cases. For the analysis, infective endocarditis cases were divided into native or prosthetic valve (early, up to 12 months after surgery, and late defined as later than 12 months).

Bacteriology

At least 2 blood samples for culture were obtained within a 24-h period. Antibiograms were obtained using the disc-diffusion method to determine the minimum inhibitory concentration (E-test). Cultures and histological study were performed on the valves and on all tissues removed during surgery.

Echocardiography

Transthoracic echocardiograms (TTE) were recorded for all patients using Sonos 2500 and Sonos 5500 ultrasound scanners with 2-2.5 and 1.8-4.2 MHz transducers, respectively, and the usual methods in our laboratory. Transesophageal echocardiograms (TEE) were recorded using the same equipment, with 3.7-5.5 MHz omniplane transducers. This type of examination was indicated in patients with native infective endocarditis when the diagnosis was questionable or an abscess was suspected, as well as in all patients with prosthetic valve infective endocarditis.

Medical treatment

All patients were given antibiotic or antifungal therapy in accordance with the latest American Heart Association/American College of Cardiology (AHA/ACC) guidelines.[5]

Surgical treatment

Surgery for active endocarditis was indicated for patients who presented one or more of the following:[1,6-8] *a)* refractory heart failure; *b)* persistent fever (or sepsis) after 14 days of antibiotic therapy and no extracardiac foci; *c)* annular abscess and/or suture dehiscence with severe prosthetic valve failure, with or without heart failure; *d)* fungal infection of the valve, and *e)* two major strokes.

Inclusion criteria

Patients over 16 years of age diagnosed with definite or probable active infective endocarditis and admitted to the ICCYC between June 1992 and December 2001 were studied prospectively.

A complete medical history was obtained for each patient. Surgical, hospital and early mortality were defined as any death for any reason occurring during surgery, up to 30 days post-surgery if the patient had been discharged, or within any time if the patient had remained hospitalized due to the surgery and/or the septic process.[9] Non-surgical hospital mortality was defined as death occurring in a hospitalized patient before surgery. Renal insufficiency was defined as creatinine concentrations above 2 mg%, persistent fever as hyperthermia after 14 days of antibiotic therapy,[1] and severe sepsis with organ dysfunction, as hypotension or hypoperfusion manifesting as lactic acidosis and/or oliguria despite proper fluid replacement, and/or acute sensory alteration.[10] Emergency surgery was defined as any operation that could not be delayed more than 24 h and elective surgery was defined as any operation that could be delayed additional time without risk for the patient.

Statistical method

The EPI and SPSS 7.5 software packages were used for statistical analysis. Categorical variables were reported as percentages and continuous variables as the

mean ± standard error. Differences between continuous variables were analyzed using the Student's *t*-test and differences between non-continuous variables by the χ^2 test. Significance was set at a *P*<.05. Logistic regression analysis was applied to variables that yielded significant results in the univariate analysis to identify independent risk factors for hospital mortality.

RESULTS

A total of 186 episodes of active infective endocarditis were recorded in 184 patients: 114 in native valves and 72 in prosthetic valves (28 early and 44 late).

Native valve endocarditis

A total of 114 episodes in 114 patients were included (Table 1). Endocarditis was considered definite in 97 (85%) cases and probable in 17 (15%). Only 4 patients had a history of intravenous drug abuse.

Blood cultures were positive in 85.1% of the episodes (97 of 114). Prior use of antibiotics was recorded in 10 of 17 episodes with negative blood cultures (Table 2).

All patients underwent at least one TTE, and TEE was also performed in 80 patients. Vegetations (82.3%) were detected in 93 episodes, and images consistent with annular abscess were observed in 19 cases, all confirmed during surgery.

Complications were observed in 92 patients (81%) (Tables 3 and 4).

The percentage of patients who underwent surgery in the active phase, the reason for surgery, the need for urgent surgery and the mortality rate are shown in Table 5.

Patients with infectious endocarditis and negative blood cultures had a significantly higher probability of requiring surgery than patients with positive blood cultures (15 of 17 vs 62 of 97; *P*<.05). There were no statistically significant differences in the microorganisms in the latter group.

Surgery for native infective endocarditis was indicated in 41 of 57 aortic valves, 16 of 28 mitral valves and 14 of 20 mitral and aortic valves (*P*=NS). The others were 3 tricuspid, 2 aortic and tricuspid and 1 pulmonary valve. No differences in hospital mortality or surgical technique were observed. In order of frequency, the most important postoperative complications were: repeat surgery for bleeding in 10 patients (13.2%), complete atrioventricular block in 10 patients (13.2%), severe sepsis in 5 patients (6.6%), placement of permanent pacemaker in 5 patients (6.6%), acute renal insufficiency requiring hemodialysis in 3 patients (4%), stroke in 2 patients (2.6%) and mediastinitis in 2 patients (2.6%).

Surgical mortality

Fifteen (19.5%) patients died. Mortality tended to increase with age, with a mean age of 47.6 years (range 16-78) in survivors versus 56.47 years (range 22-72

TABLE 1. **Characteristics of 186 episodes of infective endocarditis treated at the ICYCC (1992-2001)**

| | Native valve | Prosthetic valves | | Total |
		Early	Late	
Number of patients	114	27	43	184
Number of episodes	114	28	44	186
Men:women	78:36	23:5	33:11	134:52
Age, years, mean ± SD (range)	48.9 ± 17.7 (16-83)	60.8 ± 13.9 (20-79)	56 ± 14.5 (17-80)	55 ± 16.9 (16-83)
Underlying heart disease				
Birth defect	27 (23%)[a]	-	-	-
Aortic sclerosis	15 (13%)	-	-	-
Rheumatic mitral valve disease	14 (12.3%)	-	-	-
Mitral valve prolapse	8(7%)	-	-	-
Other	3 (2.6%)[b]	-	-	-
Prosthesis	-	28 (100%)	44 (100%)	72 (38.7%)
Unknown	47 (41.2%)	-	-	-
History of endocarditis	6 (5.3%)	9 (32%)	10 (22.7%)	25 (13.4%)
Infectious foci, n (%)				
Aortic valve	57 (50%)	20 (71%)	23 (52.3%)	100 (53.7%)
Mitral valve	28 (24.5%)	5 (18%)	17 (38.8%)	50 (26.8%)
Mitral and aortic valves	20 (17.5%)	3 (11%)	3 (6.8%)	26 (14%)
Tricuspid valve	6 (5.3%)	-	1 (2.3%)	7 (3.8%)
Pulmonary valve	2 (1.8%)	-	-	2 (1%)
Aortic and tricuspid valve	1 (0.9%)	-	-	1 (0.5%)

[a]Bicuspid aortic valve in 18 patients, interventricular septal defect in 6, pulmonary stenosis in 2, persistent ductus arteriosus in 1. [b]Obstructive cardiomyopathy in patient, traumatic aortic regurgitation in 1 and history of endocarditis in 1.

TABLE 2. **Microorganisms isolated in 186 episodes of infective endocarditis treated at the ICYCC (1992-2001)**

Microorganisms	Native valve endocarditis, n (%)	Prosthetic valve endocarditis	
		Early, n (%)	Late, n(%)
Streptococcus viridans	41 (36)	3 (10.7)	10 (22.7)
Other *Streptococcus*	13[a] (11.4)	1[b] (3.6)	3[c] (6.8)
Staphylococcus aureus	19 (16.7)	11 (39.3)	12 (27.3)
Staphylococcus epidermidis	3 (2.6)	0	1 (2.3)
Enterococcus	10 (8.8)	2 (7.1)	3 (6.8)
Gram-negative bacilli	6 (5.3)	3 (10.7)	1 (2.3)
Diphtheroids	0	2 (7.1)	3 (6.8)
Molds	0	1 (3.6)	1 (2.3)
Polymicrobial	5 (4.4)	0	0
Negative blood cultures	17 (14.9)	5 (17.8)	10 (22.7)
Total	114	28	44

[a]*Streptococcus bovis* in 1 patient, beta-hemolytic *Streptococcus* in 3, *Streptococcus agalactiae* in 1, *Streptococcus* spp. in 7 and *Streptococcus pneumoniae* in 1 [b]*Streptococcus* spp. [c]Beta-hemolytic *Streptococcus* in 2 patients, *Streptococcus bovis* in 1.

TABLE 3. **Cardiac complications of 186 episodes of infective endocarditis treated at the ICYCC (1992-2001)**

	Congestive heart failure	Chordal rupture	Pericarditis	abscesses Annular	Total
Native	66	4	3	29[a]	102
Early prosthetic	7			11[b]	18
Late prosthetic	14			13[c]	27

[a]Aortic involvement in 28 of 57 and mitral in 1 of 28 patients (*P*<.01). Causative microorganism: *Staphylococcus aureus* in 7 of 19 and *Streptococcus viridans* in 3 of 41 patients (*P*<.05).
[b]9 aortic and 2 mitral (*P*<.01) Causative agent: *Staphylococcus aureus* in 6 cases
[c]Aortic in 11 of 13 and mitral in 2 of 11 patients (*P*<.001).

years) in non-survivors (*P*=.091). NYHA Class III-IV dyspnea was observed in 29 of 61 survivors (47.5%) and 11 of 15 (73.3%) non-survivors and urgent surgery was required in 40 of 62 (64.5%) survivors and 14 of 15 (93.3%) non-survivors, making these the only statistically significant predictors of hospital mortality (*P*=.014 and .009, respectively).

Ten of the 37 patients who did not undergo surgery during the active phase died. Seven of these patients died within 48 h after admission: 4 due to severe sepsis (in 2 cases due to *Staphylococcus aureus*) and 3 due to heart failure with cardiogenic shock. The remaining deaths were: 1 due to massive cerebral hemorrhage, 1 to massive pulmonary thromboembolism and 1 to sudden death, presumed to be arrhythmic.

Early prosthetic valve endocarditis

A total of 28 episodes of infective endocarditis in 27 patients were included (Table 1); 22 (78%) of these were definitive and 6 were possible infective endocarditis. Blood cultures were positive in 82% of cases (23 of 28) (Table 2). Three of the 5 cases with negative blood cultures had already received antibiotic therapy.

TEE was performed in all patients. Vegetations were visualized in 19 patients (67.9%) and annular abscess in 12 (11 confirmed; 1 false positive).

A total of 25 patients (89.3%) experienced one or more complications (Tables 3 and 4).

The percentage of patients undergoing surgery during the active phase, the main reason, the urgency of surgery and the mortality are shown in Table 5. No differences were found in the microorganisms with respect to the need for urgent surgery or the endocarditis site. In addition, there was no difference in hospital mortality with respect to the surgical technique.

The most frequent postoperative complications were: acute renal insufficiency in 3 patients (16.7%, one of them required temporary hemodialysis), complete atrioventricular block with placement of a permanent pacemaker in 2 patients (11%), repeat surgery for bleeding in 2 patients (11%) and stroke and mediastinitis in 1 patient.

Surgical mortality was 22.2% (4 patients). Urgent surgery (4 of 4 patients died) was the only predictor of mortality (*P*<.001).

Five of the 10 patients who were not operated on improved with antibiotic therapy alone and did not require surgery in the active phase. The 5 remaining patients were admitted to the ICYCC in extremely critical condition and died within 48 hours after hospital admission, before surgery was attempted. Four of

TABLE 4. **Extracardiac complications of 186 episodes of infective endocarditis treated at the ICYCC (1992-2001)**

	Strokes in the CNS	Mycotic aneurysm	Pulmonary embolisms	Splenic embolisms	Persistent fever	Severe sepsis[b]	Renal insufficiency	Total
Native	15 (20.3%)	3 (0.74%)	8 (10.8%)	4 (5.4%)	23 (31%)[a]	4 (5.4%)	17 (23%)	74
Early prosthetic	3 (17.6%)				4 (23.5%)[c]	4 (23.5%)	6 (35.3%)	17
Late prosthetic	8 (36.7)		1 (4.5%)	1 (4.5%)	6d (27.3%)[d]	1 (4.5%)	5 (22.7%)	22

[a]Due to annular abscess in 6 patients, phlebitis in 6, inadequate antibiotic therapy in 5, other infections in 4 and fever due to medications in 2.
[b]Causative microorganism: *Staphylococcus aureus* in 5 patients, *Enterococcus* in 2, *Streptoccus viridans* in 1, negative in 1 patient. Mortality 8 of 9 (*P*<.00001)
[c]Due to annular abscess in 3 patients and phlebitis in 1
[d]Due to annular abscess in 2 patients, phlebitis in 2 and inadequate antibiotic therapy in 2.

TABLE 5. **Main reason for surgical indication, urgency and mortality in 186 patients with active infective endocarditis (1992-2001)**

	Native valve endocarditis	Prosthetic endocarditis valve		Total
		Early	Late	
Total number of episodes	114	28	44	186
Surgical treatment	77 (67.5%)	18 (64.3%)	24 (54.5%)	119 (64%)
Emergency	54 (70%)	13 (72%)	12 (50%)	79 (66.4%)
Surgical mortality	15 (19.5%)	4 (22.2%)	7 (29.2%)	26 (21.8%)
Congestive heart failure	54 (70%)	1 (5.5%)	10 (42%)	65 (54.6%)
Abscess	8 (10.4%)	8 (44.4%)	8 (33%)	24 (20.2%)
Persistent fever	7 (9.1%)	-	-	7 (5.9%)
Sepsis	3 (3.9%)	5 (27.7%)	1 (4.1%)	9 (7.6%)
Recurrent strokes	3 (3.9%)	-	-	3 (2.5%)
Fungal infection	2 (2.6%)	-	-	2 (1.7%)
Periprosthetic dehiscence	-	4 (22.2%)	5 (21%)	9 (7.6%)

them had severe sepsis (3 due to *Staphylococcus aureus* and 1 with negative blood culture), and the fifth had cardiogenic shock.

Late prosthetic valve endocarditis

There were 44 episodes in 43 patients (Table 1); 31 (70.5%) were definite and 13 were possible cases (29.5%).

Blood cultures were positive in 77.2% of cases (34 of 44) (Table 2). Six of the 10 episodes with negative blood cultures had already received antibiotics.

TEE was performed in all 44 patients. Vegetations alone were observed in 17 patients and annular abscess in 8. Five patients had both. Lastly, 5 patients presented a new paraprosthetic leak as the only finding. The leaks and the abscesses were confirmed during the operation.

A total of 36 patients (81%) experienced one or more complications (Tables 3 and 4).

The percentage of patients who underwent surgery in the active phase, the main reason, the need for urgent surgery and the mortality are shown in Table 5.

There were no statistically significant differences between patients with negative (6 of 10) versus positive (18 of 34) blood cultures, nor between the microorganisms themselves or the infection site with respect to the need for surgery. The most frequent postoperative complications were: acute renal insufficiency in 9 patients (37.5%), with temporary hemodialysis indicated in 3; complete atrioventricular block which required a permanent pacemaker in 3 patients (12.5%); repeat surgery for bleeding in 4 patients (16.7%) and stroke and mediastinitis in 1 patient (4.2%).

Seven patients (29.2%) died in the postoperative period. The gender, various complications, type of microorganism, technique or urgency of surgery were not statistically significant predictors of mortality.

Twenty patients did not undergo surgery; only one died due to severe sepsis within 48 h after admission *(Streptococcus viridans).* The remaining 19 patients presented 4 negative blood cultures, 6 methicillin-resistant *S. aureus*, 6 highly penicillin-resistant *Streptococci* (minimum inhibitory concentration [MIC]<0.1 μg/mL) (4 *S. viridans*, 1 *S. bovis*, 1 beta-hemolytic *Streptococci*), 2 *Enterococcus* without high-level resistance to aminoglycosides and 1 *Propionibacterium.*

DISCUSSION

Current approaches to endocarditis should consider the differences in clinical presentation, prognosis and treatment of native and prosthetic valve endocarditis. In the latter group, cases of endocarditis which are directly related to the surgical procedure should be distinguished from those that are unrelated.[8] In this study we grouped early (first 2 months after surgery) and intermediate (2 to 6 months after surgery) prosthetic valve infective endocarditis under the term early infective endocarditis, because of the similarities in microbial resistance, which indicate the nosocomial origin of these infections. Cases that appeared after this period were considered late infective endocarditis.[8]

We found a high prevalence of prosthetic valve infective endocarditis in our series (38.7%) in comparison to epidemiological studies (10%-25%).[11] This was probably because of a bias in incoming referrals due to the availability at our center of surgery and homografts, which some consider the prosthesis of choice in surgical treatment of prosthetic aortic valve infective endocarditis.[12-14] Similar percentages of prosthetic valve infective endocarditis were observed at other hospitals.[15]

The high percentage of negative blood cultures in this series (17.2%) was mainly due to the administration of antibiotics prior to culturing, and is in agree-

ment with other series.[1,16] Although *Streptococcus viridans* was the microorganism isolated most frequently, *Staphylococci* and particularly *S. aureus* were also found, the second being most common microorganism in native infective endocarditis (16.7 vs 36% of *S. viridans*) and the most common among prosthetic valve infective endocarditis (39.3% in early and 27.3% in late). In recent large series, *S. aureus* was the microorganism found most frequently in both native and prosthetic valve infective endocarditis.[1,17,18]

Staphylococcus epidermidis frequently causes prosthetic valve infective endocarditis, and on occasion can be very aggressive;[19] in our series, however, it was not isolated in any episode of early infective endocarditis and in only one late endocarditis. It has been reported as an occasional agent in native infective endocarditis[1] and was involved in 3 cases. The percentage of infective endocarditis caused by *Enterococcus*, Gram-negative bacilli and fungi is similar to that described in large series reported in the literature.[1,17] Polymicrobial flora was found in 5 patients (2.7%). In contrast with other reports, only one of these cases was associated with intravenous drug abuse.[1]

Transthoracic echocardiography was performed in 100% and omniplane TEE in 86% of the patients with native valve endocarditis. Vegetations were detected in 82.3% of the cases. This percentage was higher than reported in other series (60%-70%),[20,21] probably because our incoming patients were seriously ill, often with extremely late diagnoses when they were referred for surgery. These patients have readily detectable vegetations,[22] and omniplane TEE has significantly better sensitivity and specificity.[20] Transesophageal echocardiographic diagnosis of annular abscess was accurate in all cases (19 of 19), as reported in an earlier article.[23] All patients with prosthetic valve infective endocarditis underwent TEE and, as expected, there were fewer vegetations than in native valve endocarditis (68% in early and 44% in late cases). Annular abscesses were detected in 25 patients (including one false positive and one false negative); sensitivity was 96% and specificity, 97%, figures similar to those in another series.[23]

In large series from the 1970s and 1980s, mitral valve involvement was more prevalent than aortic valve problems. In more recent series, aortic valve compromise[24,25] predominated, as in our study. Aortic endocarditis normally involves greater hemodynamic compromise than mitral valve endocarditis;[1] this could explain the larger number of patients with aortic involvement referred for surgery. At least one complication was recorded in 83.6% of the patients in our series, confirming the high rate of complications during the course of the disease.[1,15]

Congestive heart failure was the most frequent complication (46.8%), as reported in other studies. Its presence influenced the prognosis and was the main reason for surgery.[1] Infective endocarditis in the aortic valve was somewhat more prevalent, although this difference was not statistically significant. Neurological complications were present in 20% to 40% of the cases, which also led to a worse prognosis.[1] Of these, embolisms to the central nervous system were the most frequent, occurring in 26 patients (14%) in our series. In 3 patients cerebral mycotic aneurysm was visualized by conventional cerebral angiography, which continues to be the most sensitive method.[1] The spread of infective endocarditis beyond the valve ring is normally predictive of higher mortality and the need for surgery.[1] As in our series, this was seen more frequently in the aortic than the mitral valve, in the presence of aggressive microorganisms (*S. aureus* and Gram-negative organisms) and in prosthetic valve infective endocarditis.[1,8,26] The high prevalence of abscesses (25% native infective endocarditis, and 39% and 29.5% for early and late prosthetic valve infective endocarditis) is another finding that confirms the seriousness of the clinical situation in the population we studied. Persistent fever was observed in 33 patients (17.7%). The main cause was perivalvular abscesses (11 patients), followed by inflammations and/or infections at the site of intravenous catheter placement, as described earlier.[1] Renal insufficiency was observed in 15% of the population, although it was not predictive of hospital mortality.

Moderate-to-severe heart failure is the most frequent, most widely reported indication for surgery in active endocarditis.[1,6-9,15] Mortality in these patients decreases from 56%-86% with medical treatment to 11%-35% with combined medical and surgical treatment,[1] and early surgery is presently advocated to improve the results.[14] This indication was frequent in our series (54.6%) and most certainly due to the bias inherent in patient referral to a hospital specializing in heart surgery.[27] The second most frequent indication was annular abscess. There have been reports of exceptional cases that resolved with antibiotic therapy alone. However, drainage and surgical replacement is usually indicated.[6,7,12,13,26] The other reasons (uncontrolled infection, severe prosthetic valve dehiscence, recurrent embolisms and fungal infection) were observed less frequently and in proportions similar to those reported in other series.[1,8,15,17]

In native infective endocarditis, failure to identify the causative microorganism was a statistically significant predictor of surgery in active endocarditis; this was observed in other series and is a contributing factor to the poor prognosis of infective endocarditis with negative blood cultures.[16,28] Compromise of the aortic or the mitral and aortic valves and/or infection by *S. aureus* are generally predictive of greater hemodynamic compromise, with a greater need for surgery and higher mortality;[7,9] this trend was observed in this series, but was not statistically significant. Lastly, most

of the operations were performed for left-sided infective endocarditis, with right-sided operations being much rarer.[8]

The surgical mortality in active infective endocarditis is reportedly 5% to 30%, depending on the series.[6-9,12,13,15,26,28,29] In the present study, total mortality was 21.8%. According to various publications, the most important predictors of mortality in native infective endocarditis were NYHA Class III-IV and emergency surgery (also associated with high mortality in early prosthetic valve infective endocarditis). In addition, the surgical mortality of prosthetic valve versus native infective endocarditis was higher (25.7% vs 19.5%)[30,31] although this trend was not statistically significant, probably because of the lack of statistical power in the sample. In other series, annular abscess, number of valves infected and type of surgical technique were also associated with higher mortality.[6-9,26,31]

A total of 16 (23.8%) of the 67 non-surgical patients died: 8 from severe sepsis, 5 from cardiogenic shock at the time of admission and 3 from cerebral hemorrhage, massive pulmonary thromboembolism and sudden death. Severe sepsis was observed in 9 (13.4%) of the 67 patients who did not undergo surgery. The association of severe sepsis with high hospital mortality was statistically significant (8 of 9; 88%). The most frequent causative microorganism was *S. aureus* (5 of 9; 61% of cases). The low non-surgical hospital mortality in late prosthetic valve endocarditis is probably due to the culprit microorganisms´ low resistance to antibiotics.

Limitations of this study

The ICYCC is a referral center for cardiovascular surgery which often receives patients in extremely serious condition, hence the more frequent use of surgical treatment and higher non-surgical hospital mortality. Therefore, the results and conclusions are not applicable to general hospitals where this factor does not operate. Other series have also reported bias resulting from the type of healthcare center.[15,27] The significant number of incoming referral patients with unresolved sepsis may have affected the actual course of the condition; in fact, this influence was clearly reflected in the clinical course of most patients.

CONCLUSIONS

Patients with infective endocarditis admitted to a center providing cardiovascular surgery frequently have severe hemodynamic compromise or widespread infection. In some cases death occurs because of cardiogenic shock or severe sepsis before surgery can be performed. In native infective endocarditis, surgical mortality is higher in emergency surgery and in severe heart failure. Urgent surgery is also predictive of higher mortality in early prosthetic valve endocarditis.

ACKNOWLEDGEMENTS

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