ORIGINAL ARTICLE

Clinical Characteristics and Outcome of Infective Endocarditis in Individuals of the General Population Managed at a Teaching Hospital Without Cardiac Surgery Facilities. Study of 120 Cases

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Introduction and objectives. To assess the clinical characteristics and management of infective endocarditis at a teaching hospital without cardiac surgery facilities.

Methods. Descriptive case-control study looking at trends. Risk factors, the occurrence of complications, the rate of referral for cardiac surgery, and the mortality rate were assessed.

Results. The study included 120 patients referred between 1990 and 2004, with a mean age of 50.8 (17.8) years (67.6% men). Disease incidence did not change throughout the study. Some 55% of infective endocarditis cases were from the ordinary general population, 25% were intravenous drug users, and 20% were of nosocomial origin. The number in the last category had increased over time. The most commonly isolated microorganism was *Staphylococcus aureus*. Around 83% of patients presented with a severe complication, with cardiac failure and septic metastasis being the most common. The in-hospital mortality rate was 19.2%. Acute renal failure (odds ratio 6.7, 95% confidence interval, 1.9-24) and perivalvular abscess (odds ratio 9.2, 95% confidence interval, 1.6-54) were independent predictors of death. The introduction in 2002 of a multidisciplinary infective endocarditis team, which included a consultant cardiac surgeon, was associated with a significant increase in referrals for surgery, from 14.5% to 34.5% (*P*=.03), though in-hospital mortality was not significantly altered, decreasing from 20.9% to 13.8% (*P*=.4).

Conclusions. The occurrence of acute renal failure and perivalvular abscess worsen the prognosis of infective endocarditis. The introduction of a multidisciplinary infective endocarditis team altered management of the disease and increased referrals for cardiac surgery.

Key words: *Infective endocarditis. Intravenous drug users. Nosocomial. Cardiac surgery. Mortality.*

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Received March 17, 2006.
Accepted for publication August 3, 2006

Características clínicas y evolución de la endocarditis infecciosa en una población general no seleccionada, atendida en un hospital docente que no dispone de cirugía cardiaca. Estudio de 120 casos

Introducción y objetivos. Analizar las características clínicas y el tratamiento de la endocarditis infecciosa (EI) en un hospital docente que no dispone de cirugía cardiaca.

Métodos. Estudio descriptivo, de tendencias, y de casos y controles. Se analizaron los factores de riesgo, las complicaciones, la indicación de cirugía cardiaca y la mortalidad.

Resultados. Se recogieron 120 casos entre 1990 y 2004 con una edad de 50,8 ± 17,8 años (67,6%, varones). La incidencia se mantuvo estable a lo largo del estudio. La distribución por categorías de EI fue: población general no seleccionada, 55%; asociada a drogadicción parenteral, 25%, y nosocomial, 20%, y se observó un incremento de esta última en el tiempo. *Staphylococcus aureus* fue el aislamiento más frecuente. Un 83% de pacientes presentó alguna complicación grave, y las más frecuentes fueron la insuficiencia cardiaca y las metástasis sépticas. La mortalidad intrahospitalaria fue del

ABBREVIATIONS

IE: infective endocarditis.
IVDU: intravenous drug use.

19,2%. La insuficiencia renal aguda (*odds ratio* [OR] = 6,7; intervalo de confianza [IC] del 95%, 1,9-24) y el absceso perivalvular (OR = 9,2; IC del 95%, 1,6-54) fueron predictores independientes de muerte. La disponibilidad desde 2002 de un grupo de trabajo multidisciplinario sobre EI y de una consultoría de cirugía cardiaca se asoció con un aumento significativo de la indicación de tratamiento quirúrgico (el 14,5 frente al 34,5%; p = 0,03) y no se observaron cambios en la mortalidad intrahospitalaria (el 20,9 frente al 13,8%; p = 0,4).

Conclusiones. La insuficiencia renal aguda y el absceso perivalvular en el curso de una EI son factores de mal pronóstico. Un enfoque multidisciplinario de la EI ha comportado cambios en su tratamiento y ha incrementado la indicación de cirugía cardiaca.

Palabras clave: *Endocarditis infecciosa. Drogadicción. Nosocomial. Cirugía cardiaca. Mortalidad.*

INTRODUCTION

Infective endocarditis (IE) treatment has undergone marked changes in the last decade.[1-3] The introduction of transesophageal echocardiography and improvements in microbiological, serological and molecular biology techniques have led to earlier and more accurate diagnoses, while individualization of the different clinical forms has improved patient categorization. Furthermore, the establishment of some clear indications for cardiac surgery[4] has prevented delaying this type of treatment when indicated.[5,6] Such progress has helped to decrease mortality[7-9] which, however, continues to be high.[10,11] Nevertheless, it is striking that despite all this progress and the widespread implementation of prophylactic programs, incidence remains stable.[12-15] The impact of these changes on treating IE has been reported in several studies, most of which have been done in large tertiary university hospitals where heart surgery is easily available.[9-14,16-22] This means that patient selection is necessarily biased, since such centers receive patients referred to basic general hospitals and patients with highly complex conditions referred from other less technically equipped centers who may require heart surgery. This implies an artificial increase in the complexity of the patients affected with IE in these series, which may not necessarily reflect the more typical scenario of a large number of patients finally diagnosed with IE in a local or regional hospital. This work reviews the cases of IE in a regional university hospital without heart surgery facilities, describes their epidemiological, clinical, microbiological, and prognostic characteristics, and compares these data to those reported in the medical literature from high-technology hospitals. We also analyze the impact of the introduction of a multidisciplinary IE team and, especially, the role of a consultant cardiac surgeon in the clinical treatment of this disease.

METHODS

Design

Descriptive study looking at trends in a series of patients consecutively included according to a predefined protocol. Case-control study of the effect of a multidisciplinary IE team on surgical indications and mortality.

Place

The patients were diagnosed and treated in the Hospital Universitari Joan XXIII, the referral teaching hospital in Tarragona, Spain. The public hospital network in Catalonia, Spain consists of three types of acute-care hospitals. The basic general hospital is a first-level center covering the region. The next level is formed by referral hospitals. These are more technically equipped university hospitals with a greater range of services which act as first-line hospitals locally, but also as referral hospitals for given specialties for a greater regional area. Finally, there are the high-technology tertiary hospitals that act as referral centers for different areas of Catalonia for highly technical specialties, among which is heart surgery. There are five public centers offering this specialty in Catalonia. The Hospital Universitari Joan XXIII is a 350-bed center that serves a population of 140 000 as the basic general hospital and acts as a referral hospital for some diseases and specialties for an area embracing around 700 000 inhabitants. It has an average of 14 614(1284) admissions/year (period 1993-2004). The center has most medical and surgical specialties available, including nephrology, with an active program of hemodialysis and intensive care medicine, with a 14-bed multidisciplinary unit. Burn and cardiac surgery units are not available. Since 2002, a multidisciplinary infective endocarditis team has been in operation made up of internal medicine, cardiology, infective diseases and microbiology specialists assisted by a consultant cardiac surgeon from a high-technology tertiary hospital who has been attending our center on a monthly basis. The availability of this consultant has facilitated virtual communication with the heart surgery service of the consultant's hospital and has increased transfers of our patients with IE needing surgical treatment to the referral center.

Patients

Patients over 14 years old diagnosed with IE between 1990 and 2004. Episodes associated with a pacemaker were excluded.

Microbiology

At least two blood cultures were taken from each patient. A result was considered positive when bacteria were isolated in at least one blood culture not belonging to the cutaneous saprophytic flora. In case of negative *Staphylococcus coagulase*, streptococci from the viridans group, Propionibacterium acnes, and *Corynebacterium spp*. required at least two positive blood cultures with identical antibiograms. Serological tests for *Brucella, Mycoplasma, Legionella*, and *Coxiella burnetii* were done at the discretion of the acting physicians when the blood cultures were negative.

Echocardiographic Study

Echocardiography was done using a VINGMED 800 system by experienced cardiologists who assessed the presence of vegetations, abscesses and pseudoaneurysms, prosthetic valve dehiscence or new valvular regurgitation, and other possible intracardiac complications. Transesophageal echocardiography was also done when IE was firmly suspected and conventional transthoracic echo-carduigraphic examination offered negative results, especially in patients fitted with prosthetic valves or in those with a poor acoustic window. Transesophageal recording was done directly in six patients.

Definitions

Until 1994, infective endocarditis was diagnosed based on the criteria of von Reyn et al,[23] then on those of Durack et al,[1] and, finally, on Durack's modified criteria.[2] Patients diagnosed with IE using von Reyn's and Durack's criteria were reassessed retrospectively and re-categorized according to Durack's modified criteria. Cases of both identified and possible endocarditis were included in the study. The following IE categories were established: those associated with intravenous drug use (IVDU), nosocomial IE, and IE in the unselected general population. Infectious endocarditis was considered nosocomial based on the criteria of Watanakunakorn et al.[13] The following risk factors for acquiring endocarditis were studied: dental procedures, invasive procedures,[24] carrying a central venous catheter, hemodialysis, IVDU, prosthetic valve implantation, and concomitant staphylococcal cutaneous infection. The presence and type of previous heart disease was assessed as well as a previous history of endocarditis in the different IE categories. Alcoholism, chronic liver disease, chronic renal failure, diabetes mellitus, neoplasm, and human immunodeficiency virus infection were recorded as comorbidity. Furthermore, severe IE-associated complications occurring during treatment were assessed, such as heart failure (New York Heart Association [NYHA] grade III and IV]), perivalvular abscess, peripheral arterial embolisms, septic metastases including septic lung embolisms, valvular dehiscence, and perforation, acute renal failure unrelated to the treatment, acute myocardial infarction, pharmacological toxicity, complete heart block, reactive arthritis, ruptured mycotic aneurysm, relapsing fever (reappearance of fever after 3 days of apyrexia without other evident febrile focus), prolonged fever (fever persisting for more than 10 days not caused by another infective focus and despite antibiotic treatment),[15] pulmonary thromboembolism, and septic shock. The presence of acute renal failure was established when creatinine reached values >1.5 mg/dL, and septic shock when hypotension or tissue hypoperfusion was indicated by lactic acidosis and/or oliguria despite fluid replacement therapy. Indications for surgical cardiac intervention and mortality were assessed until discharge.

Statistical Analysis

Comparisons of continuous variables were done using Student *t* test and one-way analysis of variance. Qualitative variables were analyzed with χ^2 test or Fisher exact test when required. Independent risk factors for mortality were studied via logistic regression on the variables which were significant in the univariate analysis. Values of $P<.05$ were considered significant. The variables and data were analyzed using SPSSPC 11.5 statistical software.

Review of the Medical Literature

MEDLINE was searched using the key words 'infective endocarditis' plus 'epidemiology', 'prognosis', 'mortality', 'nosocomial' and 'microbiology'. Studies were selected which analyzed IE series in third-level hospitals with heart surgery available based in developed countries.

RESULTS

Epidemiological and Clinical Data

One hundred and twenty episodes of IE were studied: there were 92 cases of definite endocarditis and 28 possible cases. Table 1 shows the main demographic features and epidemiological, clinical and evolutionary data of the patients. Some 39.2% of the patients were over 60 years old. This percentage grew from 30.6% in the period 1990-1994 to 46.5% in the period 2000-2004. Beginning in 1993, total incidence was 0.55 cases per 1000 hospital admissions and has remained stable until the present. However, analysis by category indicated different trends: nosocomial IE increased, IE remained stable in the

TABLE 1. **Characteristics of the Different Infective Endocarditis Categories**

	IVDU, n (%)	Nosocomial, n (%)	General Population, n (%)	Total, n (%)
Number of patients	30 (25%)	24 (20%)	66 (55%)	120
Age, mean(SD)*	28.9 (6.3)	60.6 (12.6)	57.2 (14.5)	50.8 (17.8)
Sex (M/F)	25/5	18/6	38/28	81/39
Risk factors	30 (100%)	21 (87.5%)	17 (25.8%)	68 (56.7%)
IVDU	30 (100%)	0	0	30 (25%)
Dental procedures	0	0	12 (18.2%)	12 (10%)
Invasive procedures	0	15 (62.5%)	4 (6.1%)	19 (15.8%)
Hemodialysis	0	6 (25%)	0	6 (5%)
CVC	0	12 (50%)	1 (1.5%)	13 (10.8%)
Cellulitis due to *Staphylococcus* sp.	(3.3%)	1 (4.2%)	1 (1.5%)	3 (2.5%)
Previous heart disease	2 (6.7%)	10 (41.7%)	31 (47%)	43 (35.8%)
Previous endocarditis	1 (3.3%)	0	4 (6.1%)	5 (4.2%)
Rheumatic valve disease	0	1 (4.2%)	9 (13.6%)	10 (8.3%)
Degenerative valve disease	0	9 (37.5%)	10 (15.2%)	19 (15.8%)
Mitral valve prolapse	0	0	2 (3%)	2 (1.7%)
OHC	0	0	4 (6.1%)	4 (3.3%)
Congenital valve disease	1 (3.3%)	0	3 (4.5%)	4 (3.3%)
Prosthetic valve	0	1 (4.2%)	6 (9.1%)	7 (5.8%)
Valve				
Mitral	4	8 [1]†	42 [3]†	30 [2]†
Aortic	4	7	22 [4]†	33 [4]†
Aortic and mitral	0	2	10	12
Tricuspid	22	4	1	27
Pulmonary	0	0	0	0
Aortic and pulmonary	0	0	3	3
Mitral and tricuspid	0	1	0	1
Not determined	0	2	0	2
Location				
Right valves	22(73.3%)	4 (16.7%)	1 (1.5%)	27 (22.5%)
Left valves	8 (26.7%)	17 (70.8%)	62 (93.9%)	87 (72.5%)
Bilateral disease	0	1 (4.2%)	3 (4.5%)	4 (3.3%)
Not determined	0	2 (8.3%)	0	2 (1.6%)
Valve type				
Native	30 (100%)	23 (95.8%)	60 (90.9%)	113 (94.2%)
Prosthetic	0	1 (4.2%)	6 (9.1%)	7 (5.8%)
Surgical treatment	4 (13.3%)	3 (12.5%)	17 (25.8%)	24 (20%)
Over 60 years old	0	14 (58.3%)	33 (50%)	47 (39.2%)
Mortality	4 (13.3%)	6 (25%)	13 (19.7%)	23 (19.2%)

CVC: central venous catheter; SD: standard deviation; HOCM: hypertrophic obstructive cardiomyopathy; IVDU: intravenous drug use.
* *P*=.002.
†Patients with prosthetic valves.
Invasive procedures: fiberoptic bronchoscopy, 2 cases; gastroscopy, 3 cases; colonoscopy, 2 cases; orotracheal intubation, 6 cases; liver biopsy, 1 case; urinary catheterization, 10 cases; cardiac catheterization, 1 case. Data are expressed as total numbers and percentages in parentheses. Cases of prosthetic endocarditis shown in square brackets.

unselected general population and IE in IVDU decreased during the study period (Figure 1). Overall, endocarditis was nosocomial in 24/120 cases (20%), IVDU-associated in 30/120 (25%) and 66/120 cases (55%) occurred in the normal general population. Transthoracic echocardiography was done in 114/120 patients and vegetations were observed in 82 patients (71.8%). Transesophageal echocardiography was done in 50/120 patients, including the six patients who had not undergone transthoracic echocardiography, and was diagnostic in 94% of cases. Only two patients presented a normal echocardiographic study under both techniques. They were diagnosed with IE on the basis of clinical and microbiological criteria. There was no predisposing heart disease or previous risk factor in only 28 patients, 26 of whom belonged to IE cases in the general population, and who did not differ regarding age, location, surgical indication, mortality or frequency of complications from the patients who had some risk factor for endocarditis and/or predisposing heart disease. Septic metastases (38/120; 31.7%), heart failure (34/120; 28.3%) and acute renal failure (31/120; 25.8%) were the most frequent complications. Pyrogenic complications, mainly pleuropulmonary, were significantly more frequent in

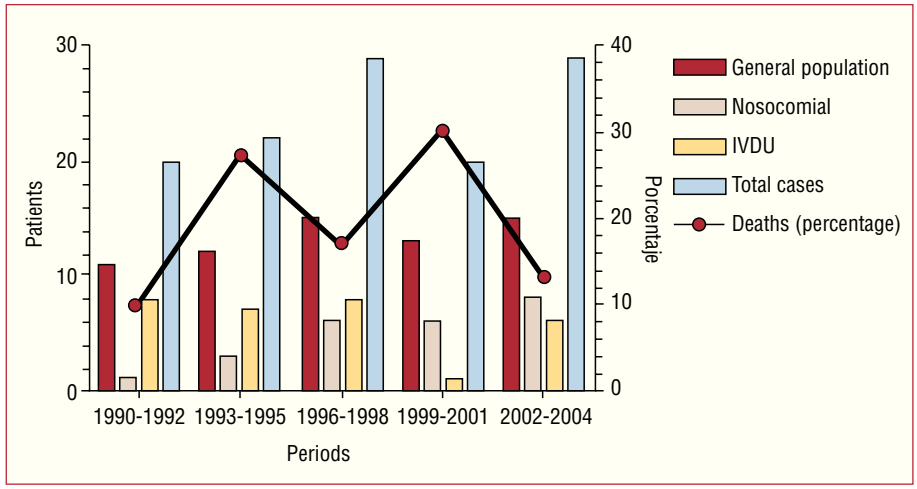

Figure 1. Number of cases of infective endocarditis and mortality in percentages over 3-year periods. Distribution of the cases by category. IVDU: intravenous drug use.

IVDU-associated endocarditis (*P*<.001) and septic shock than in nosocomial IE (*P*=.001). However, heart failure was more common in endocarditis in the general population (*P*=.045).

Microbiological Data

Microbiological results are presented in Table 2. Staphylococcus aureus (44/120; 36.7%) was the most frequently isolated microorganism in the total series, followed by *S. viridans* (29/120; 24.2%) and coagulase-negative *Staphylococcus* (12/120; 10%). The blood cultures were negative in 12.5% (15/120) of the cases. There was one case of IE due to a mixed infection by *P. aeruginosa* and methicillin-resistant *S. aureus*. There were four isolations of methicillin-resistant S. aureus, all in the nosocomial endocarditis group.

Treatment and Prognosis

Some 80% (96/120) of the endocarditis patients received medical treatment only and the remainder required additional heart surgery. Heart failure was the indication for surgery in half the cases. Age did not differ between those who underwent surgery and those who did not. Total mortality, which was 19.2% (23/120), fluctuated over 3-year periods (Figure 1). The presence of perivalvular abscess, heart failure, acute renal failure, bilateral valvular disease, septic shock, and a history of previous endocarditis were associated with greater mortality in the univariate analysis (Table 3). The appearance of antibiotic treatment-associated toxicity was associated with a trend toward greater mortality (*P*=.09) whereas S. viridans-related endocarditis was associated with lower mortality. There were no significant differences in mortality between native- and prosthetic-valve endocarditis or between the patients who received medical treatment versus those who needed heart surgery (19.8 vs 20%; *P*=.8). Neither was comorbidity associated with greater mortality. On the other hand, only acute kidney failure and the presence of perivalvular abscess behaved as independent predictors of mortality (Table 4). Twenty-nine patients have been included since 2002, when the IE team was introduced with a consultant cardiac

TABLE 2. **Isolated Microorganisms According to Infective Endocarditis Category**

	IVDU, n (%)	Nosocomial, n (%)	General Population, n (%)	Total, n (%)
S. aureus	24 (80)	9 (37.5)	7 (10.6)	40 (33.3)
MRSA	0	4 (16.7)	0	4 (3.3)
Coagulase-negative *Staphylococcus*	0	5 (20.8)	7 (10.6)	12 (10)
S. viridans	4 (13.3)	1 (4.2)	24 (36.4)	29 (24.2)
S. pneumoniae	0	0	1 (1.5)	1 (0.8)
Enterococcus spp.	0	2 (8.3)	5 (7.6)	7 (5.8)
Other *Streptococcus*	0	0	3 (4.5)	3 (2.5)
E. coli	0	0	4 (6.1)	4 (3.3)
P. aeruginosa	0	0	1 (1.5)	1 (0.8)
Anaerobic organisms	0	0	2 (3)	2 (1.6)
Other bacteria	0	1 (4.2)	1 (1.5)	2 (1.7)
Culture negative	2 (6.7)	2 (8.3)	11 (16.7)	15 (12.5)

MRSA: methicillin-resistant Staphylococcus aureus; IVDU: intravenous drug use.

TABLE 3. **Different Factors Influencing Mortality**

	Deceased (n=23)	Not Deceased (n=97)	*P*
Isolated			
S. aureus	9 (39.1%)	31 (32%)	.5
MRSA	2 (8.7%)	2 (2.1%)	.17
Staphylococcus coagulase-negative	2 (8.7%)	10 (10.3%)	1
S. viridans	2 (8.7%)	27 (27.8%)	.05
Enterococcus spp.	2 (8.7)	5 (5.2%)	.62
Streptococcus pneumoniae	0	1 (1%)	1
Other *Streptococcus*	1 (4.3%)	2 (2.1%)	.48
E. coli	1 (4.3%)	3 (3.1%)	.58
P. aeruginosa	0	1 (1%)	1
Propionibacterium spp.	0	1 (1%)	1
Other anaerobic organisms	0	1 (1%)	1
Not isolated	4 (17.4%)	11 (11.3%)	.48
Risk factor for endocarditis*	11 (47.8%)	57 (58.8%)	.34
Predisposing heart disease	10 (43.5%)	33 (34%)	.39
No risk factor or heart disease	5 (21.7%)	23 (23.7%)	.8
HIV infection	4 (17.4%)	16 (16.5%)	1
Hemodialysis	2 (8.7%)	4 (4.1%)	.32
Valve type			.13
Native	20 (87%)	93 (95.9%)	
Prosthetic	3 (13%)	4 (4.1%)	
Location			.02
Right	4 (17.4%)	23 (23.4%)	
Left	16 (69.9%)	70 (72.2%)	
Bilateral	3 (13%)	1 (1%)	
Complications			
HF	13 (56.5%)	21 (21.6%)	.001
Valvular dehiscence	1 (4.3%)	14 (14.4%)	.3
Perivalvular abscess	4 (17.4%)	4 (4.1%)	.04
AMI	1 (4.3%)	1 (1%)	.35
Complete heart block	2 (8.7%)	1 (1%)	.09
Arterial embolism	7 (30.4%)	22 (22.7%)	.44
Septic complications	6 (26.1%)	32 (33%)	.52
AKF	14 (60.9%)	17 (17.5%)	<.0001
Pharmacological toxicity	6 (26.1%)	11 (11.3%)	.09
Endocarditis category			.55
Nosocomial	6 (26.1%)	18 (18.6%)	
Associated with IVDU	4 (17.4%)	26 (26.8%)	
General population	13 (56.5%)	53 (54.6%)	
Previous endocarditis	3 (13%)	2 (2.1%)	.05
Mean age (SD)	55.6 (19.4)	49.7 (17.4)	.2
Surgical treatment	5 (21.7%)	19 (19.6%)	.79
Septic shock	8 (34.8%)	6 (6.2%)	.001
Comorbidity†	12 (52.2%)	49 (50.5%)	.9

SD: standard deviation; AMI: acute myocardial infarction; HF: heart failure; ARF: acute renal failure; MRSA: methicillin-resistant *Staphylococcus aureus*; IVDU: intravenous drug use; HIV: human immunodeficiency virus.
*Risk factors for endocarditis: IVDU, dental procedure, invasive procedure, hemodialysis, carrying a central venous catheter, cellulitis due to *Staphylococcus* spp.
†Comorbidity: HIV infection, chronic liver disease, chronic renal failure, alcohol abuse, COPD, neoplasm, diabetes mellitus. Values expressed in total numbers and percentages in parentheses.

TABLE 4. **Independent Predictors of Mortality**

	OR (95% CI; *P*<.05)	*P*
HF	2.3 (0.7-7.9)	.16
Perivalvular abscess	9.2 (1.6-54)	.01
ARF	6.7 (1.9-24)	.003
Bilateral location	9.35 (0.7-120)	.08
Septic shock	3 (0.7-13.8)	.16
Previous endocarditis	9.8 (0.9-110)	.06
S. viridans	0.4 (0.06-2.2)	.26

CI: confidence interval; HF: heart failure; AKF: acute renal failure; OR: odds ratio.

surgeon available. There were no differences between these patients and the 91 enrolled previously (1990-2001) regarding distribution by IE category, sex, age, presence of complications, risk factors for IE, and incidence of previous heart disease. However, a significant increase was found in indications for heart surgery in the former (14.5 vs 34.5%; *P*=.03) and a non-significant decrease in hospital mortality (20.9 vs 13.8%; *P*=.4).

DISCUSSION

The present IE study took place in a university hospital without heart surgery available, unlike most other studies published. From the epidemiological viewpoint, the relatively high incidence of IVDU-associated IE, the increase in nosocomial IE incidence during the study period, the limited number of cases of prosthetic-valve IE, and the high frequency of cases without risk factors or previous heart disease are noteworthy. On the other hand, total mortality, comparable to that of series in larger hospitals, presented serious oscillations over time and it decreased, although not significantly, in tandem with the changes that began with the introduction of the multidisciplinary IE team. Finally, renal failure and the presence of perivalvular abscess were the only factors which were independent predictors of death.

Comparing IE series is difficult, basically due to the varying geographical origin of the population, the study period, the changes in diagnostic criteria over time and the category of the hospital regarding the availability of heart surgery. These considerations aside, we attempted to establish whether there were any differences compared to a series from a university center without heart surgery available.

The incidence of IE in our series, and its stabilization over time, matched that of most contemporary series in tertiary hospitals, where it fluctuates between 1 and 10 cases per 100 000 population/year[12,17] and, by hospital admission, which is around 0.3-1 per 1000 hospital admissions annually.[12-15,18]

The observed relative increase in nosocomial IE probably compensated for the decrease in IVDU-associated IE and contributed to maintaining the total incidence, a situation encountered in other series in ttertiary centers.[3]

The presence of previous heart disease ranged between

TABLE 5. **Other Series of Infective Endocarditis Compared With the Present Series**

Author and Reference	Years	Mean Age, Years	IVDU, %	Nosocomial, %	Prosthetic, %	Without Heart Disease, %	Most Frequent Isolation	Total Complication Rate, %	Peripheral Embolism, %	HF, %	Heart Surgery, %	Total Mortality, %
Watanakunakorn et al[13]	1980-1990	60-70	15.7	14.7	14.2	43.6	*S. aureus*	-	-	47	14.2	21.4
Hogevik et al[20]	1984-1988	69	7	15.3	15	44	*S. aureus*	-	43	-	15	13
Castle et al[16]	1987-1999	47	0	-	32.6	25	*S. aureus*	76.5	-	-	50	18.9
Siddiq et al[19]	1990-1993	46	67	6	-	75	*S. aureus*	-	30	30	13	9
Bouza et al[17]	1994-1996	50	35.8	22	16.5	54.2	*S. aureus*	-	46	32	42	26
		38%>60										
Fefer et al[14]	1990-1999	57	-	-	31	10*	*Streptococcus* spp.	-	28	-	-	11
Horacio Casabé et al[11]	1992-2001	55	3.5	-	38.7	-	*Streptococcus* spp.	81	-	46.8	64	22.6
Loupa et al[10]	1997-2000	54.4	3	-	32	46*	*S. aureus*	-	27	-	51.5	16
Hoen et al[9]	1999	59.5	5.6	-	16	47	*Streptococcus* spp.	-	44	34	49.7	16.6
Lathes et al[22]	2001	57	5	-	26	-	*S. aureus*	-	27	58	52	12.6
		26%>70										
López-Dupla et al (PW)	1990-2004	50.8	25	20	5.8	64.2 (20%)*	*S. aureus*	83.3	24.2†	28.3	20	19.2
		39%>60										

PR: present work; IVDU: intravenous drug use.
*No heart disease or risk factor for IE.
†Peripheral embolism only (septic pulmonary embolisms are not included).

50% and 75% in most series in large hospitals, whereas in contrast, ours only involved 35.8%. The low rate of prosthetic IE (5.8%) also stands out compared with series in centers with heart surgery available (14.2%-38%). However, not only was the number of patients without heart disease relevant, but so was the number of patients with no risk factor for IE, reaching 20%. Only Fefer et al[14] refer to this finding, with half of the cases in their work belonging to the latter category. Surprisingly, these patients, and those without previous heart disease only, presented no differences compared to the others regarding epidemiology, microbiology, comorbidity, and prognosis. On the other hand, other series[16,25] reported that patients without heart disease presented lower mortality and a greater association with diabetes mellitus, inflammatory intestinal disease and chronic renal failure. Thus, what initially seems to be a less severe datum in our series was not associated with a better prognosis in that group.

However, most patients with nosocomial IE presented previous heart disease and/or risk factors, the most frequent examples being degenerative valve disease and invasive procedures. This is probably due to the higher average age of this category, where up to 50% of the patients over 60 years old in some series have degenerative valve disease[26] and undergo more frequent exposure to invasive procedures.

The high frequency of IVDU in our series probably has no relationship to the type of hospital, but to the incidence of this risk factor in our referral population, as happens in different tertiary hospitals.[13,15,17,19,21] Similarly, the predominance of *S. aureus* in our series is the same as in most third-level hospitals, where endocarditis associated with intravenous drug use or with a prosthetic valve is high.[13,15,17,19,26,27]

Nosocomial endocarditis in our series was higher than in the third-level centers and increased over time (Table 5). The most frequent risk factors were endoscopic procedures and carrying a central venous catheter, similar to other series.[28,29] In this category, 37.5% of the isolations involved coagulase-negative *Staphylococcus* and methicillin-resistant *S. aureus,* a similar figure to other series,[13] and half the patients carried a central venous catheter and/or received hemodialysis (not shown in the results).

Septic metastases, heart failure, arterial embolism, and septic shock were the most frequent serious complications in our series. Taken together (83%) and individually, they were as frequent as in the third-level centers (Table 5), except for heart failure. As expected, septic complications, basically emboligenic lung abscesses, were more frequent in IVDU-associated endocarditis.

Indications for heart surgery during the active phase of IE reached 20%, a considerably lower figure than that in comparative series (Table 5). This is especially true if the comparison is limited to the most recent series of the last decade, reaching around 50% of the patients.[9-11,16,19,22] However, our figures are similar to those reported in other

series from hospitals without cardiac surgery available.[15]

Developed countries have succeeded in reducing early mortality in IE in recent years, ranging between 9% and 26%, due to diagnostic and therapeutic progress. Mortality was 19.2% in our series, within the abovementioned range, and presented wide annual oscillations, probably due to the instability of the data in small-sized samples. Nevertheless, this decreased in the last 3 years, although not significantly, coinciding with the introduction of the multidisciplinary IE team. We cannot discard the possibility that other factors, unassessed in this work, may have played a role in the reduction in mortality during the multidisciplinary IE team's active period, such as changes in strategy and diagnostic techniques (basically the availability of transesophageal echocardiography) and in the treatment of IE over the study period. Heart failure and sepsis have been associated with greater mortality in univariate[11,18,20] and multivariate studies[15,17,19] in different works, unlike ours, where neither were independent predictors of mortality. However, the presence of perivalvular abscess, previously reported,[30] and acute renal failure were predictors in our study, as in other works.[17,18] None of the endocarditis-causing microorganisms, endocarditis category, or location were associated with worse prognosis. Finally, the information provided by our work forces us to reconsider the following question: in what kind of hospital should a patient affected with IE be looked after?[31] Since the IE team was introduced, our figures on morbidity, type of treatment and early mortality in this disease are similar to those of tertiary hospitals. This fact shows that IE treatment can be suitably done in a center without heart surgery available, providing that an experienced multidisciplinary IE team which includes a consultant cardiac surgeon attends the patients and current clinical practice guidelines are followed.[32]

CONCLUSIONS

The incidence of IE is stable in our geographical area. Nevertheless, there has been an increase in cases of nosocomial IE. The main differences compared to series of cases from tertiary hospitals are lower rates of prosthetic valve IE and previous heart disease, as well as less use of heart surgery. The patients present similar severity and mortality. The availability of a multidisciplinary team caring for the IE patient and a consultant cardiac surgeon has modified the treatment of our patients and has made the heart surgery figures similar to those of the third-level centers. The effect of the multidisciplinary IE team in the long-term needs to be studied to confirm these data and their influence on early mortality.

ACKNOWLEDGMENT

The authors would like to express their thanks to the anonymous referees whose comments and observations have contributed to significantly improving this work.

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