

Short- and Long-Term Prognosis of Infective Endocarditis in Non-Injection Drug Users: Improved Results Over 15 Years (1987–2001)

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Introduction and objectives. The treatment of infective endocarditis has undergone significant change within the last few years. The aim of this study was to evaluate the clinical features and prognosis of infective endocarditis over both the short and long term in patients who are not intravenous drug users.

Patients and method. We carried out a prospective study of 222 consecutive patients who were diagnosed with infective endocarditis between 1987 and June 2001 at two centers.

Results. Their mean age was 48 (19) years, with 145 (65%) being male. Overall, 154 (69%) had native valve endocarditis and 68 (31%) had prosthetic valve endocarditis. In 61 patients (27%), no predisposing heart disease was found. *Staphylococci* were the causal microorganisms in 37% of cases (81 patients), and *streptococci*, in 35% (78 patients). Some 48% of patients underwent surgery during the active disease phase. Overall, inpatient mortality was 17% (39 cases); a significant decrease had occurred in recent years, from 25% in 1989-1995 to 12% in 1996-2001 ($P < .01$). In addition, the percentage undergoing early elective surgery had increased between the two periods, from 22% to 32% ($P < .05$). During a follow-up of 60 (48) months, 15 patients (8%) needed late cardiac surgery and 18 (10% of the whole series) died. The 6-year survival rate was 72% overall, and 80% in those who survived the active disease phase.

Conclusions. Short- and long-term prognoses for patients with infective endocarditis appear to have improved over recent years at our hospitals.

Key words: *Infective endocarditis. Prognosis. Cardiac surgery.*

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Pronóstico a corto y largo plazo de la endocarditis infecciosa en pacientes no usuarios de drogas por vía parenteral. Resultados durante un período de 15 años (1987-2001)

Introducción y objetivos. La endocarditis infecciosa ha experimentado cambios importantes en los últimos años. El objetivo de nuestro trabajo es estudiar las características clínicas y el pronóstico a corto y largo plazo de la endocarditis infecciosa en pacientes no usuarios de drogas por vía parenteral.

Pacientes y método. Hemos analizado 222 casos diagnosticados consecutivamente en nuestros centros desde 1987 hasta junio de 2001.

Resultados. La edad media fue de 48 ± 19 años y 145 pacientes (65%) eran varones. En 154 casos se trataba de una endocarditis nativa (69%) y en 68 (31%) de una endocarditis protésica. En 61 pacientes (27%) no había cardiopatía predisponente. Los gérmenes causales más frecuentes fueron estafilococos (81 casos; 37%) y estreptococos (78 casos; 35%). Un 48% de los casos (107 pacientes) precisó cirugía durante la fase activa de la enfermedad. La mortalidad hospitalaria global fue del 17% (39 casos) y se redujo de forma significativa en los años más recientes (el 25% en 1989-1995 frente al 12% en 1996-2001; $p < 0,01$). La tasa de cirugía precoz electiva aumentó del 22% en 1989-1995 al 32% en 1996-2001 ($p < 0,05$). Tras un seguimiento de 60 ± 48 meses, 15 pacientes (8%) necesitaron cirugía tardía y 18 (10%) murieron. La supervivencia global a los 6 años fue del 72% y la de los pacientes que habían sobrevivido a la fase activa de la enfermedad del 80%.

Conclusiones. El pronóstico a corto y largo plazo de los pacientes con endocarditis infecciosa parece estar mejorando en nuestro medio en los últimos años, en comparación con el de épocas más antiguas.

Palabras clave: *Endocarditis infecciosa. Pronóstico. Cirugía cardíaca.*

ABBREVIATIONS

IE: infective endocarditis.
 PVE: prosthetic valve endocarditis.
 NVE: native valve endocarditis.
 IDU: injection drug users.

INTRODUCTION

Infective endocarditis (IE) is a serious disease with elevated short- and long-term mortality. The poor prognosis for IE is not only due to the high in-hospital mortality rate and rate of in-hospital complications, but also to late sequelae that present once the infection has been eliminated.^{1,2} Short-term prognosis for IE has improved as a result of recent progress in diagnostic techniques and antibiotic treatment and because complications can be detected earlier, although most studies still report in-hospital mortality rates above 20%.³⁻⁷ In order to assess the clinical characteristics, treatment, and prognosis of patients with IE in Spain, we have analyzed the findings from the study and follow up of all consecutive non-injection drug users (IDUs) diagnosed with IE in our 2 hospitals since 1987. The specific aims of this study were to analyze the general characteristics of the entire series, to assess short and long-term prognosis and possible predictors of prognosis, and to compare surgical treatment and mortality during the active phase of IE in 2 periods (1987-1995 vs 1996-2001).

PATIENTS AND METHOD

Between January 1987 and June 2001, 222 consecutive non-IDUs were diagnosed with IE in our 2 hospitals. Before 1994, IE was diagnosed in accordance with the criteria of von Reyn et al.⁸ Thereafter, the criteria of Durack et al were applied.⁹ According to retrospective analysis, all cases met the new criteria of the European Society of Cardiology.² Early prosthetic valve endocarditis (PVE) was defined as an IE episode that occurred within 12 months of prosthetic valve replacement, whereas episodes diagnosed more than 12 months after replacement surgery were classified as late PVE. The indications for surgery during the active phase of the disease (early surgery) are shown in Table 1. Surgery was performed in the presence of perivalvular abscesses larger than 1 cm or when the patient presented with severe complications. Even if these 2 criteria were not met, surgery was also considered when the patient

TABLE 1. Indications for Surgery During the Active Phase of Endocarditis in the Present Study

Moderate or severe heart failure
Significant valve or prosthetic regurgitation, possibly asymptomatic
Two or more major embolisms
Severe mechanical complications (septal rupture, aortocavitary fistulas, etc)
Endocarditis caused by virulent pathogens and/or those difficult to eliminate with antibiotic treatment alone (<i>Brucella</i> , <i>Coxiella</i> , fungi, etc)
Early prosthetic endocarditis
Pacemaker endocarditis
Endocarditis due to unidentified pathogen and lack of response to empirical antibiotic treatment
Persistence of infection despite appropriate antibiotic treatment (persistent fever and/or positive blood cultures for the same pathogen after 1 week of appropriate antibiotic treatment)

responded poorly to antibiotic treatment (abscess growth or persistence of sepsis). Emergency surgery was defined as an operation that could not be delayed more than 24 hours without endangering the patient's life, whereas elective surgery was considered as a procedure that could be put back a few days without increasing the risk to the patient's life.

All patients who survived the active phase of IE were included in a long-term follow up protocol in our clinics. If a patient failed to report for a scheduled visit, he or she was called at home. There were no losses to follow-up. The infection was considered eliminated when blood cultures obtained 2 months after discharge from hospital were negative. Early death was considered to have occurred if the patient died before hospital discharge. Deaths occurring after discharge were considered late deaths. A relapse of IE was defined as the reappearance of signs of infection within 2 months of discharge from hospital with positive blood cultures for the same pathogen that was responsible for the initial episode, whereas a new episode of IE caused by a pathogen other than the first one was considered as a recurrence of IE. We analyzed the variables according to 2 periods (1987-1995 vs 1996-2001) to assess possible changes in early death and in the rates and types of surgery undertaken during the study period.

Statistical Analysis

Continuous variables were expressed as mean±SD and qualitative variables as percentages. Group differences were assessed with the χ^2 test or the Fisher exact test for qualitative variables and the Student *t* test for unpaired quantitative variables. Survival estimates were calculated using the Kaplan-Meier method and survival curves were compared using the Mantel

log-rank test. Multivariate analysis of possible predictors of overall mortality was done with a Cox model. Statistical significance was set at $P < .05$.

RESULTS

General Characteristics

Our series included 222 cases of IE in 209 patients. The general characteristics of these patients are presented in Table 2. Mean age was 48 (19) years, with a range of 2 months to 81 years. Thirteen patients were children under 14 years (5% of the total) and, overall, 145 patients were male (65%) and 77 (35%) were female. Fourteen patients (6%) had a prior history of endocarditis, and 68 admissions were for PVE (31%) compared to 154 (69%) for NVE. The number of cases per year is shown in Figure 1. The 34 cases of early PVE (processes that developed within 12 months of valve replacement surgery) were evenly spread throughout the duration of the study (2-3 per year), were not related to problems of infection in the operating areas, and were not considered as outbreaks of infection. The mean number of cases of IE per year was 15.

Figure 1 also shows the incidence of endocarditis in patients with no history of predisposing heart disease; 61 cases (28% of the entire series) had no prior cardiac lesion (Table 2), but the incidence of IE increased during the course of the study as shown in Figure 1. No predisposing cardiac lesion was present when no structural heart disease was identified and echocardiography (usually transesophageal) revealed no valve defects. Thirty of the 61 patients with no history of predisposing heart disease who underwent operations for IE showed no significant valve abnormalities according to inspection of the operating field and histology of tissue samples taken from the valve.

TABLE 2. General Characteristics in 222 Cases of Infective Endocarditis in Non-Intravenous Drug Users*

	Number of Cases (%)
Age, years, mean (SD)	48 (19)
Sex	
Male	145 (65)
Female	77 (35)
Type of endocarditis	
NVE	154 (69)
PVE	68 (31)
Type of PVE	
Early PVE	34 (50)
Late PVE	34 (50)
Prior endocarditis	14 (6)
No predisposing lesion	61 (28)
Site of infection	
Mitral	99 (45)
Aortic	93 (42)
Tricuspid	17 (8)
Others	13 (5)

*NVE indicates native valve endocarditis; PVE, prosthetic valve endocarditis.

Rheumatic disease was reported in 34% of the patients and congenital disease in 16% of the patients, whereas degenerative valve disease was found in the remaining 16% of the patients (Table 2). As shown in Table 3, among the 35 patients with underlying congenital heart disease, the most frequent conditions were ventricular shunts (9 patients) and bicuspid aortic valve (6 patients). Infection affected the left side of the heart in 193 cases (89%), with no differences between the mitral and aortic valves (Table 2). The median duration from the first symptom until diagnosis was 21 days (range, 7-210 days). Echocardiography detected vegetations in 89% of the cases (in 59%

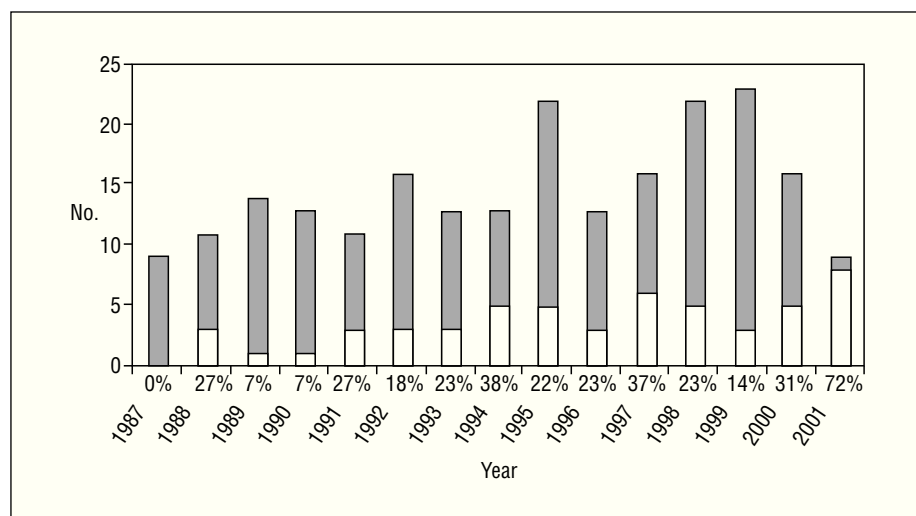


Figure 1. Absolute number of cases of infective endocarditis and absolute number of cases with no history of predisposing heart disease (unshaded bars) per year in our study. The percentages given below the bars indicate the patients with no history of predisposing heart disease in the given year.

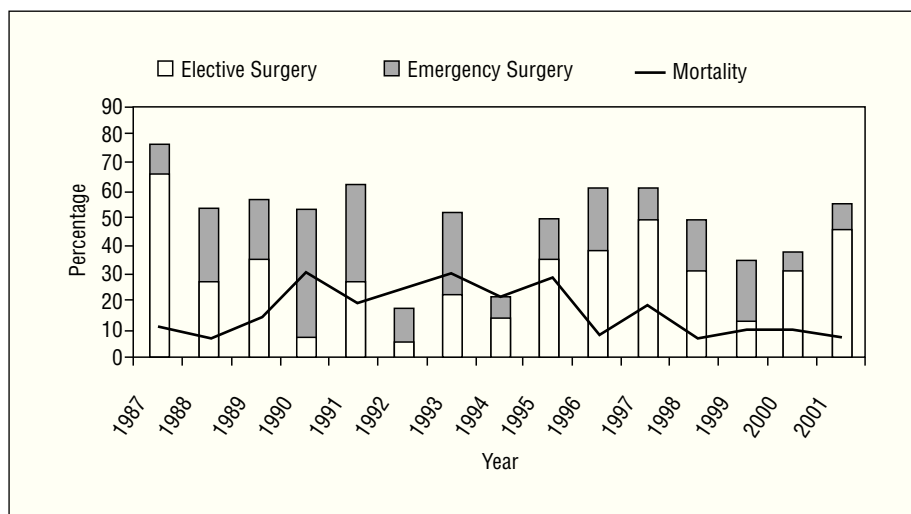


Figure 2. Early (in-hospital) mortality and proportion of patients who require surgery (emergency or elective) while in hospital per year.

of transthoracic examinations and 93% of transesophageal examinations; $P < .01$). The difference in detection rates between transthoracic and transesophageal echocardiography was greater for PVE (vegetation detected in 24% vs 82%; $P < .001$) than for NVE (75% vs 98%; $P < .05$). Rates of detection of verrucous vegetations were similar for mitral and aortic valve IE.

Causative Pathogens

Table 4 shows the microorganisms responsible for IE in our series. The causative pathogen was not identified in 22 of the 222 cases (10%), with no differences between the first and second period (11% for 1987-1995 and 8% for 1996-2001). Staphylococci and streptococci were responsible for the same proportion of cases of NVE; staphylococci were more common causative agents in early PVE and streptococci in late PVE (Table 2). *Coxiella burnetii* was the causative

agent in 4% of all cases (10)—14% of cases of late PVE (5) and 3% (5) of all cases of NVE (Table 4).

In-Hospital Complications

As shown in Table 5, cardiac and extracardiac complications in hospital were very common—73% of the cases ($n=163$) were associated with at least 1 severe complication. The most common complications were cardiac ones (almost all heart failure due to valve regurgitation or prosthetic dysfunction), followed by embolisms, persistent sepsis, and neurological disorders (Table 5). There were no differences between NVE and PVE with regard to complications.

Treatment

All patients received antibiotic treatment. In 48% of the cases ($n=107$), valve surgery was performed while the patient was in hospital and the percentage of these patients with PVE or NVE was similar (47% and 50%, respectively). Elective surgery was more common than emergency surgery (29% vs 19%, respectively). The most common indications for surgery were heart failure (53% of all indications) and persistent sepsis despite appropriate antibiotic treatment (27%). Other indications for surgery (recurrent embolism, virulent bacteria, underlying heart disease, and glomerulonephritis) accounted for the remaining 20%. Heart failure accounted for 83% of all emergency indications but just 31% of elective procedures ($P < .01$). Perioperative mortality was 20% (38% for emergency surgery and 8% for elective surgery; $P < .01$).

The proportion of patients who underwent elective surgery increased significantly from the first to second period (22% in 1987-1995 and 32% in 1996-2001), due mainly to a decrease in emergency procedures (25% vs 16%, respectively; $P < .05$). Overall, the per-

TABLE 3. Endocarditis in Congenital Heart Disease: Type and Frequency of Underlying Lesions (n=35)*

Ventricular shunt	9 cases
Bicuspid aortic valve	6 cases
Subaortic membrane	4 cases
Tetralogy of Fallot	3 cases (corrected: 1)
Complete atrioventricular canal defect	3 cases
Ductus arteriosus	2 cases
VS+AR (Laubry syndrome)	2 cases
Pulmonary stenosis	2 cases
Aortic stenosis not due to bicuspid valve	2 cases
Double outlet right ventricle, operated	1 case
Pulmonary atresia with intact septum	1 case†

*VS+AR indicates ventricular shunt with aortic regurgitation.

†Patient with infection of left ventricular thrombus.

TABLE 4. Causative Pathogens in Our Series of 222 Cases of Infective Endocarditis*

	Number of Cases, %			
	Overall	NVE	Early PVE	Late PVE
<i>Staphylococcus</i>	81 (37)	56 (36)	17 (49)	8 (24)
<i>S aureus</i>	57 (26)	45 (29)	6 (17)	6 (16)
Coagulase negative	24 (11)	11 (7)	11 (32)	2 (5)
<i>Streptococcus viridans</i>	49 (22)	34 (22)	2 (6)	13 (36)
<i>Enterococci</i>	29 (13)	23 (15)	3 (9)	3 (8)
<i>Corynebacterium</i>	11 (5)	6 (4)	3 (9)	2 (5)
<i>Brucella</i>	4 (2)	4 (3)	—	—
<i>Coxiella burnetii</i>	10 (4)	5 (3)	—	5 (14)
Fungi	4 (2)	2 (1)	1 (3)	1 (3)
Others	10 (4)	6 (4)	3 (9)	1 (3)
Not identified	24 (10)	18 (11)	5 (15)	1 (3)

*NVE indicates native valve endocarditis; PVE, prosthetic valve endocarditis.

centage of patients undergoing operations while in hospital was similar for both periods (47% and 48%). The perioperative mortality in cases of elective surgery decreased from the first period (17%) to the second one (3%) ($P<.05$), whereas mortality rates remained constant for emergency surgery (39% vs 37%). Figure 2 shows the annual change in patients requiring surgery during the study period.

Mortality

Overall early (in-hospital) mortality was 17% (39 patients). Mortality by year is shown in Figure 2. The most common cause of death was complications related to surgery (40%), followed by heart failure (25%), intracranial hemorrhage (17%), extracardiac infections (14%), and pulmonary embolism (4%). Of the 7 patients who died of intracranial hemorrhage, 4 had received prior anticoagulation because they had mechanical prosthesis implanted, and 3 received no anticoagulation treatment. In the latter 3 patients and in 2 of the patients who received anticoagulation therapy, imaging studies showed rupture of a mycotic

TABLE 5. Incidence of Severe Complications in Our Series of 222 Cases of Infective Endocarditis*

	Number of Cases (%)
Overall	163 (73)
Cardiac	95 (43)
Heart failure	90 (40)
Others	5 (3)
Embolisms	58 (26)
Persistent sepsis	49 (22)
CNS disorders	41 (18)
Renal insufficiency	19 (8)
Abscesses	25 (11)
Mycotic aneurysms	11 (5)

*CNS indicates central nervous system.

aneurysm, whereas in the other 2, initial examination revealed only ischemic infarction which later became hemorrhagic. Early mortality decreased significantly from the period 1987-1995 to the period 1996-2001 (25% vs 12%, respectively; $P<.01$). The lowest rates of early mortality occurred in patients under 65 years

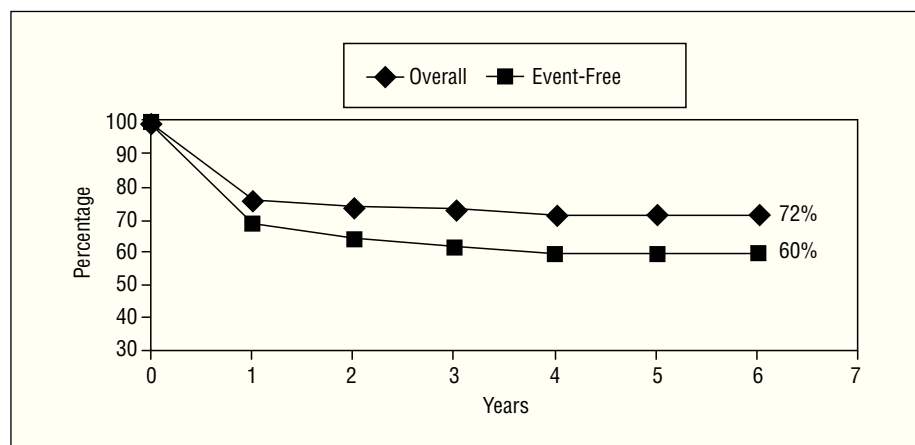


Figure 3. Kaplan-Meier survival curves. Overall survival and event-free survival for the entire series, 222 cases (including in-hospital mortality).

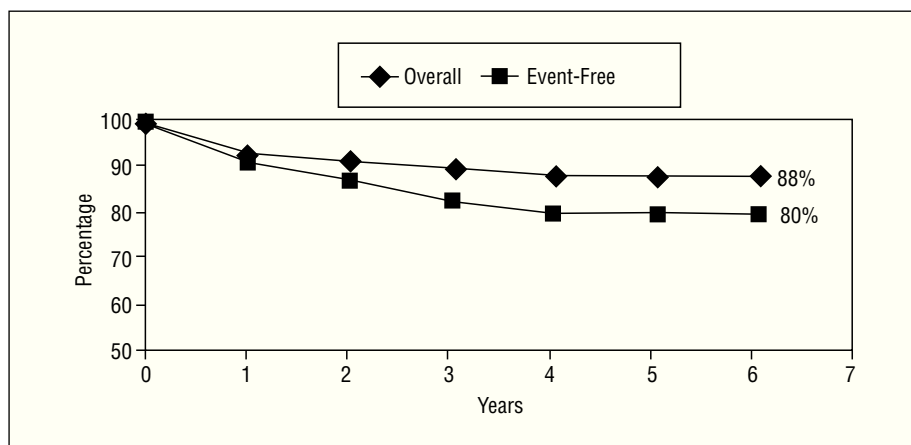


Figure 4. Kaplan-Meier survival curves. Overall survival and event-free survival in the 183 survivors of the active phase.

(12%), and in patients with late PVE (11%), no predisposing heart disease (9%), streptococcal IE (8%), elective surgery (8%), and no complications (2%). Overall survival (including in-hospital mortality) was 76% after 1 year and 72% after 6 years (Figure 3). In the multivariate analysis, age greater than 65 years (hazard ratio [HR]=3.35; 95% confidence interval [CI], 1.90-4.15), the presence of heart failure (HR=3.36; 95% CI, 1.75-3.88), and the need for emergency surgery (HR=6.80; 95% CI, 4.67-7.34) were independent predictors of higher mortality. Elective surgery was associated with lower mortality compared to emergency surgery (HR=0.14; 95% CI, 0.09-0.65), and medical treatment without surgery (HR=0.71; 95% CI, 0.66-0.93). Survival for patients discharged from the hospital, with exclusion of early deaths, was 93% at 1 year and 88% at 6 years (Figure 4).

Late Events

Mean follow-up for the 183 patients who survived until discharge from hospital lasted 60 (48) months (range, 4-204 months). Event-free survival (defined as patients who survived with no late surgery, recurrence of IE, or major complications during follow-up) was 71% at 1 year and 60% at 6 years for the overall population (including in-hospital mortality) (Figure 3) compared to 91% at 1 year and 80% at 6 years for those who survived until discharge from hospital (Figure 4). Survival at 6 years for those who survived until discharge is shown in Table 6 by subgroups. Late survival was similar for most of the subgroups, except for age (91% at 6 years for patients <65 years vs 74% for those >65 years; $P<.05$) and type of endocarditis (91% for NVE vs 78% for PVE; $P<.05$) (Table 6). Survival at 6 years for patients who survived until discharge according to whether they underwent an operation while in hospital was similar (88% for both groups; Table 6) but was 92% for patients undergoing emergency operations

and 87% for those undergoing elective surgery ($P=NS$).

Infective endocarditis recurred in 13 of the 183 survivors (6%). Two of these patients with recurrent IE died (1 due to intracerebral hemorrhage and 1 due to left ventricular dysfunction). No relapses were reported. Of the 13 patients with recurrent IE, 8 had valve prostheses implanted prior to the episode of endocarditis, 3 had prior untreated NVE, and 2 had Q fever endocarditis (both were patients with valve prostheses). One of the patients with Q fever had an aortic valve prosthesis and presented with mitral valve endocarditis with chordae rupture and acute pulmonary edema 4 days after the first episode. The patient progressed favorably after mitral valve replacement. The other patient with Q fever had a mitral valve bioprosthesis and developed another mitral valve endocarditis 5 years after the first episode. He died of intracranial hemorrhage. The 3 patients with recurrent NVE progressed favorably, 1 after valve replacement surgery and the other 2 without surgery. Two of these patients had prior aortic valve IE and the other had mitral valve IE. In all cases, the initial pathogen was *S viridans*. Recurrence was after 2, 3, and 6 years, and due to *Staphylococcus aureus* in 1 patient (who underwent surgery) and to enterococci in the other 2 patients. In the 8 remaining patients with recurrent PVE, the pathogens responsible for the initial episode were *S aureus* (3 patients), *S viridans* (2 patients) and *Corynebacterium* sp (1 patient), whereas the pathogen was not identified in the 2 remaining patients. Three of these recurrences, all caused by *S epidermidis*, presented within 12 months of surgery (early PVE) whereas the other 5 presented at 16, 23, 27, 49, and 66 months after the first episode and were caused by *S aureus*, *S viridans*, enterococci, *S viridans*, and *Corynebacterium* sp, respectively. Two of the patients with IE due to *S epidermidis* underwent successful operations and the other died of heart failure before surgery. The other 5

cases progressed favorably with antibiotic therapy alone and did not require surgery. Early mortality among patients with recurrent IE was therefore 15%, which is similar to the rate for the overall series, and 31% of these patients required surgery during the active phase of IE.

During follow-up, 15 patients required surgery (8% of the survivors of the in-hospital phase). Only 1 patient required 2 interventions. In most cases, the operation took place within 3 years of discharge from hospital after an episode of IE. None of the patients undergoing late surgery died. The indications for valve surgery during follow-up were progression of underlying heart disease in 11 patients and recurrence of IE in the 4 remaining patients. Late mortality during follow-up was 10% (18 patients). The causes of late death were heart failure secondary to progression of the underlying cardiac lesion (7 patients), sudden death (2 patients), embolic or hemorrhagic cerebrovascular accidents (4 patients), recurrence of IE (2 patients), digestive diseases (2 patients), and pneumonia (1 patient). The mean time from discharge after hospitalization for an IE episode until late death was 15 (12) months (range, 2-48 months). The mean time until late surgery was 26 (36) months (range, 1-150 months). The mean time until late death or surgery was 21 (27) months (range, 1-150 months). At the end of follow-up, 151 of the 209 patients were still alive and free of major events (67% of the population).

DISCUSSION

Our study included all non-IDUs diagnosed with IE in our hospitals over a period of 15 years. Mean follow-up for these patients was 50 (48) months. The sample size, 222 cases, is similar to or larger than that of other series described in recent years.^{7,10,11} As shown in Figure 1, the number of cases of IE seems to be increasing in Spain. Likewise, an increase is seen in the proportion of cases with no history of predisposing heart disease, which has been reported to range from 2% to 45% in other studies.^{8,10-14} In the most recent series,^{7,11} the incidence is as high as 22% to 45%. This change has a practical implication because prognosis seems to be somewhat better in patients with no predisposing heart disease.¹³ In our study, early mortality was twice as high in patients with prior cardiac lesions than in patients with no history of predisposing heart disease. The reason for this increase in the number of cases of IE in patients without heart disease could not be attributed to a decrease in the number of cases of IE associated with rheumatic valve disease. This is because the number of patients with underlying rheumatic disease remained constant throughout the study period (probably because cases of PVE in patients undergoing

TABLE 6. Survival at 6 Years by Subgroups in Patients With Endocarditis Who Survived Until Discharge*

	Survival, %	P
Age		<.05
<65 years	91	
>64 years	74	
Sex		NS
Male	87	
Female	90	
Type of IE		<.05
NVE	91	
PVE	78	
Type of PVE		NS
Early	72	
Late	81	
Predisposing heart disease		NS
Yes	86	
No	87	
Causative pathogen		NS
Unknown	93	
Identified	87	
Staphylococci	90	
Streptococci	88	
Others	80	
Severe complications		NS
Yes	87	
No	91	
Early Surgery		NS
No	84	
Yes	88	
Emergency	92	
Elective	87	

*IE indicates infective endocarditis; NVE, native valve endocarditis; PVE, prosthetic valve endocarditis; NS, not significant.

surgery for rheumatic valve diseases many years earlier were classed as rheumatic). Instead, the increase in the number of cases of IE in patients without heart disease was due to an increase in other risk factors, such as inflammatory bowel disease, liver disease, chronic renal insufficiency, hemodialysis, or sustained use of intravenous catheters, as was the case in many of our patients.¹⁵

Surgery during the active phase of IE was performed in 48% of all the cases, regardless of the type of endocarditis. This percentage is higher than that reported for other series (15%-34%).^{7,8,16} As shown in Figure 2, the percentage of patients undergoing early surgery did not change during the course of our study (47% in 1987-1995 and 48% in 1996-2001), but a significant increase in the percentage of elective interventions was reported along with a decrease in the number of emergency procedures (Figure 2). In the second period (1996-2001), 32% of the patients underwent elective surgery and only 16% had an emergency operation. Emergency operations were mainly

for severe heart failure caused by valve regurgitation or prosthesis-related disease and were associated with a high rate of perioperative mortality for the entire duration of the study (39% during the first period and 37% during the second period). This represented the strongest independent predictor of mortality (HR=6.80). In contrast, mortality during elective surgery was low and decreased during the study period to 3% between 1996 and 2001. Overall in-hospital mortality decreased significantly for this type of surgery (25% for the period 1987-1995 vs 12% for the period 1996-2001). It is important to highlight the relationship between elective surgery and prognosis. We think that, in general, it is advisable for patients with endocarditis to be attended in hospitals with heart surgery facilities or in hospitals with experience of handling this disease and with the possibility of rapid transfer to hospitals that can perform heart surgery.

Outcomes of patients who received only medical treatment during the active phase of IE without the need for surgery (52% of the 222 cases) were comparable to those of patients who underwent surgery (early mortality rate of 19% vs 16%, respectively). However, the patients who received medical treatment alone were very heterogeneous—the group comprised both those at low risk with good prognosis who progressed favorably without any complications and those indicated for surgery that could not be performed because of high surgical risk with a poor prognosis. The results for the two groups could not therefore readily be compared. Nevertheless, only 10 of these 115 patients did not undergo surgery because of high surgical risk. Six of these 10 patients died, and if these patients are excluded, the mortality in the subgroup of patients without indication for surgery was only 6% (6 out of 105 cases).

According to the findings of the limited number of studies with detailed long-term follow up of IE, a large proportion of patients, between 27% and 47%, require surgery in the long term,^{6,7,16} contrary to our findings (only 15 patients, 8%, of survivors of the active phase of IE, required surgery after a mean follow up of 50 [48] months). This low rate of late surgery is probably due to the fact that most patients with moderate to severe valve regurgitation but without heart failure had already undergone surgery during the hospital phase. Only 2 patients who underwent an operation during the hospital phase had to undergo further surgery during long-term follow up, in both cases due to a new episode of endocarditis. Late mortality was also very low, only 10%, and lower than that reported by other authors.^{3,6,7,16} At the end of follow up, 67% of all patients were alive and event-free, which contrasts with percentages that range from 22% to 38% in other series.^{9,16} The long-term prognosis was similar for both subgroups of endocarditis, as shown in

Table 6, except for age (higher mortality for patients >65 years) and early PVE. Overall survival at 6 years, including early in-hospital mortality, was 72%—much higher than that described by other authors.^{3,16}

In conclusion, the percentage of cases of IE with no history of predisposing heart disease and the age of the patients seem to be increasing in Spain. In-hospital mortality has decreased to rates of 12% in the most recent period (1996-2001). Our results suggest that a factor that might be related with this better prognosis is an appropriate selection of patients who require elective surgery while in hospital, reducing the need for late surgery in the long term and improving overall survival. However, given that medical treatment without surgery was also associated with good short- and long-term outcomes in patients without poor prognostic factors who progressed favorably, the management of patients with IE remains a challenge for the treating physicians. The results of our study seem to suggest that patients with IE should be attended in hospitals with heart surgery facilities, or in hospitals with experience at managing this disease and with rapid communication with surgical hospitals.

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