Impact of antimicrobial therapy on prognosis of patients requiring valve surgery during active infective endocarditis

Georges Fayad, MD,[a] Andre Vincentelli, MD, PhD,[a] Guillaume Leroy, MD,[b] Patrick Devos, MD,[c] Gilles Amr, MD,[a] Alain Prat, MD,[a] Mohammad Koussa, MD,[a] and Olivier Leroy, MD[b]

Objectives: We examined the characteristics and outcomes of patients requiring valve surgery during active infective endocarditis (IE), focusing on the impact of antimicrobial therapy.

Methods: In this retrospective study, medical charts of all consecutive patients admitted to our cardiovascular surgery department from January 1998 to December 2010, with a diagnosis of IE requiring surgical management, were reviewed. Adult patients were enrolled in the study if they had definite or possible active IE and if the antimicrobial treatment was evaluable.

Results: After initial screening of medical records, we selected 173 surgically treated patients (135 men; mean age, 55.8 years). Native valves were involved in 150 (87%) patients. IE mainly involved the aortic valve (n = 113) and then mitral (n = 83), tricuspid (n = 13), and pulmonary (n = 3) valves. The most common causative pathogens were streptococci (n = 70), staphylococci (n = 60), and enterococci (n = 29). Operative mortality was 15%. Multivariate logistic regression analysis demonstrated that adequacy of the overall antimicrobial treatment (adjusted odds ratio, 0.292; 95% confidence interval, 0.117-0.726; $P = .008$) and temperature greater than 38°C at the time of diagnosis (adjusted odds ratio, 0.288; 95% confidence interval, 0.115-0.724; $P = .008$) were independently associated with a lower risk of mortality. Conversely, age greater than 60 years (adjusted odds ratio, 4.42; 95% confidence interval, 1.57-12.4; $P = .005$) was associated with a greater risk of operative mortality.

Conclusions: Surgery for active IE is still associated with a high mortality rate, but its prognosis is significantly improved by adequate antimicrobial therapy. (J Thorac Cardiovasc Surg 2014;147:254-8)

The optimal management of infective endocarditis (IE) requires a collaborative approach, notably involving specialists in microbiology, infectious diseases, cardiology, cardiac surgery, and anaesthesiology.

Even if antimicrobial treatment represents the cornerstone of management, recent data from the International Collaboration on Endocarditis—Prospective Cohort Study[1] have shown that 1 (48%) of 2 patients required valve surgery. Perioperative mortality varies between 5% and 36%.[2-10] Prognosis depends on the causative organism, the extent of destruction of cardiac structures, the presence of complications of IE such as heart failure, and the timing of surgery.[11]

Several studies have demonstrated that adequate antibiotic therapy improves the outcome of patients with severe bacterial or fungal infection and that the involvement of an infectious disease specialist could potentially increase adequate antibiotic use.[12-15]

The goal of the present study was to identify predictive factors of mortality while focusing on the impact of antimicrobial therapy in a cohort of consecutive patients operated on through a 13-year experience for active IE.

PATIENTS AND METHODS

Study Design and Patients

A systematic retrospective review was carried out of all consecutive patients admitted to the 2 units of the Cardiovascular Surgery Department of Hôpital Cardiologique de Lille, France, from January 1998 to December 2010, with a diagnosis of IE requiring surgical management. All medical charts were analyzed by an independent group (Centre d'Investigation Clinique, CHRU, Lille, France). In accordance with French law, no ethics committee approval was required to conduct the study.

Adult patients were enrolled in the study if they had definite or possible active IE and if the antimicrobial treatment of the episode of IE was evaluable. Definite or possible IE was defined according to modified Duke criteria.[16] Endocarditis was defined as active if the patient required surgery before completion of a standard course of antibiotic treatment, irrespective of whether there were ongoing signs of sepsis or whether blood and valve cultures were positive for the infecting microorganism.[2] Antimicrobial treatment of the episode of IE was considered evaluable when the causative organism(s), antibiotics used, and duration of postoperative antimicrobial treatment were clearly identified. Patients with IE associated with pacemaker implantation were excluded.

Data Collection and Definitions

Data were recorded on a standardized report form designed by 2 of the authors (G.F., O.L.). Information about patient demographics, preexisting conditions, focus of infection, initial valve status, clinical course, echocardiographic data, microbiologic data, complications, cardiac surgery

From Centre Hospitalier Régional Universitaire de Lille,[a] Pôle de Chirurgie Cardiovasculaire, Hôpital Cardiologique, Lille; Service de Réanimation et Maladies Infectieuses,[b] Centre Hospitalier Chatiliez, Tourcoing; and Département de Bio-Statistiques,[c] CHRU, Lille, France.

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Address for reprints: Georges Fayad, MD, Pôle de Chirurgie Cardiovasculaire, Hôpital Cardiologique, CHRU de Lille, France (E-mail: g.fayad@sfr.fr).

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Abbreviations and Acronyms
ICU = intensive care unit
IE = infective endocarditis

interventions, antimicrobial therapy during the preoperative and the postoperative periods, and outcome were collected.

Prosthetic valve IE was defined as infection occurring on any type of tissue or mechanical device. *Hospital-acquired IE* was defined as infection occurring more than 72 hours after admission to the hospital or acquired in association with a significant invasive procedure performed during a recent hospitalization within 8 weeks of this hospitalization.[17] Antimicrobial therapy was considered as bacteriologically effective if it included antibiotic(s) usually proposed by current guidelines (ie, amoxicillin or a third-generation cephalosporin or a glycopeptide in the case of IE owing to *Streptococcus* spp; amoxicillin or a glycopeptide for IE owing to *Enterococcus* spp; oxacillin for IE owing to methicillin-susceptible *Staphylococcus* spp; a glycopeptide for IE owing to methicillin-resistant *Staphylococcus* spp; and a third-generation cephalosporin or fluoroquinolone for IE owing to gram-negative bacilli) and if the causative organism was in vitro susceptible to at least 1 of the antibiotics of the regimen.[18] The duration of postoperative antimicrobial treatment was considered correct when it was 2 weeks or more when the leaflet culture was negative and 6 weeks when leaflet culture was positive. The antimicrobial treatment was considered adequate when it was bacteriologically effective in both the preoperative and postoperative periods and had a correct postoperative duration. Operative mortality was defined as death occurring within the same hospitalization as surgery, regardless of its cause.[2,3]

Statistical Analysis

Descriptive analyses were performed to check and summarize the data. Quantitative variables are reported as means ± standard deviation. Qualitative variables are reported as number and percentage. Continuous variables were compared using the Student *t* test. Categorical variables were compared using the χ^2 test or Fisher's exact test when χ^2 was not appropriate.

A stepwise logistic regression analysis was performed including variables with a *P* value $\leq .10$ in univariate analysis. Adjusted odds ratios were computed using logistic regression analysis including the independent predictors of mortality.

All statistical analyses were performed using SAS software, version 9.1 (SAS Institute, Inc, Cary, NC).

RESULTS

After initial screening of 371 medical records, we excluded 140 patients who either had not had active IE or did not meet modified Duke criteria for diagnosis, and we retained 231 patients exhibiting definite or possible active IE. Among them, the antimicrobial treatment of the episode of IE was evaluable in 173 patients who met the eligibility criteria for inclusion in this study.

Most patients had definite active IE (n = 169; 98%). Blood and leaflet cultures were positive in 168 (97%) and 23 (13%) cases, respectively. Echocardiography demonstrated endocardial involvement in 163 (94%) cases. Duke minor criteria observed were predisposition (n = 57), fever (n = 127), and vascular (n = 18) and immunologic phenomena (n = 7). IE was hospital acquired in 16 (9%) cases. Demographics characteristics, underlying valve diseases, and portal of entry are reported in Table 1. Most patients (n = 130; 75%) were referred from another hospital.

Native and prosthetic valves were involved in 150 (87%) and 23 (13%) patients, respectively. IE mainly involved the aortic valve (n = 113) and then mitral (n = 83), tricuspid (n = 13), and pulmonary (n = 3) valves. Multiple valve involvement was observed in 38 (22%) patients. Valves involved were aortic plus mitral valves (n = 26), aortic plus tricuspid valves (n = 3), aortic plus pulmonary valves (n = 3), mitral plus tricuspid valves (n = 5), and aortic plus mitral plus tricuspid valves (n = 1).

One hundred eighty-eight causative pathogens were identified. IE was polymicrobial in 13 patients. The most common were streptococci (n = 70; 37%), staphylococci (n = 60; 31.5%), and enterococci (n = 29; 15.5%) (Table 2).

During the course of IE and before the surgical procedure, 84 (49%) patients exhibited extracardiac involvement. Main organs involved were central nervous system (n = 49), spleen (n = 3 4), lung (n = 13), bone and joints (n = 13), kidneys (n = 10), and liver (n = 3).

Surgery was performed in the acute phase of IE with a mean delay from diagnosis to surgery of 22.9 ± 17.5 days. Main indications for surgery were 1 or more of the following reasons: persistent infection despite 7 to 10 days of bacteriologically effective antibiotic treatment (n = 100), vegetation size (n = 50), congestive heart failure (n = 60), recurrent embolization (n = 22), annular abscess (n = 21), and conduction abnormalities (n = 5). A total of 86 bioprostheses, 63 mechanical prostheses, and 9 aortic homografts were implanted. After excision of the vegetations, valve repair was performed alone (n = 15) or in association with prosthesis implantation (n = 7) in 22 cases.

After the surgical procedure, all patients were admitted to the surgical intensive care unit (ICU). Vasopressors and/or inotropes were required in 99 (57%) cases. Renal replacement therapy was required in 19 cases. The mean duration of postoperative mechanical ventilation was 55.8 ± 96.4 hours. The mean duration of ICU stay was 150 ± 152 hours.

All patients received a preoperative antimicrobial treatment. Its mean duration before surgery was 21.4 ± 14.5 days. This antimicrobial treatment was bacteriologically effective in 159 (92%) patients. In 7 patients, antibiotics used were not usually proposed by current guidelines. In the remaining 7 patients, at least 1 causative pathogen was resistant to all antibiotics of the regimen. In 1 case, this point was explained by a late postoperative identification of causative pathogen. Blood cultures were negative whereas leaflet culture identified a pathogen resistant to the preoperative antibiotic regimen. Postoperative antimicrobial treatment was bacteriologically effective in 163 (94%) cases. In 10 patients, either antibiotics used were not usually proposed by current guidelines (n = 5) or at least 1 causative pathogen was resistant to all antibiotics of the regimen (n = 5).