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CLINICAL RESEARCH STUDY

# Prognostic Stratification of Patients with Left-Sided Endocarditis Determined at Admission

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## ABSTRACT

**BACKGROUND:** The prognosis of patients with left-sided endocarditis remains poor despite the progress of surgical techniques. Identification of high-risk patients within the first days after admission to the hospital would permit a more aggressive therapeutic approach.

**METHODS:** We designed a prospective multicenter study to find out the clinical, microbiologic, and echocardiographic characteristics available within 72 hours of admission that might define the profile of high-risk patients. Of 444 episodes, 317 left-sided endocarditis cases were included and 76 variables were assessed. Events were surgery in the active phase of the disease and in-hospital death. A stepwise logistic regression analysis was undertaken to determine variables predictive of events.

**RESULTS:** Multivariate analysis of the clinical variables found to have statistical significance in the univariate analysis identified the following as predictive: patient referred from another hospital (odds ratio [OR]: 1.8; confidence interval [CI], 1.1-2.9), atrioventricular block (OR: 2.5; CI, 1.1-5.9), acute onset (OR: 1.7; CI, 1.1-2.9), and heart failure at admission (OR: 2.3; CI, 1.4-3.8). When the echocardiographic and microbiological variables statistically significant in the univariate analysis were introduced, the presence of heart failure at admission (OR: 2.9; CI, 1.8-4.8), periannular complications (OR: 1.8; CI, 1.1-3.1), and *Staphylococcus aureus* infection (OR: 2.0; CI, 1.1-3.8) retained prognostic power. Risk could be accurately stratified when combining the 3 variables with predictive power: 0 variables present: 25% of risk; 1 variable present: 38% to 49% of risk; 2 variables present: 56% to 66% of risk; and 3 variables present: 79% of risk.

**CONCLUSIONS:** The risk of patients with left-sided endocarditis can be accurately stratified with the assessment of variables easily available within 72 hours of admission to the hospital. © 2007 Elsevier Inc. All rights reserved.

**KEYWORDS:** Left-sided endocarditis; Prognosis; Risk stratification

Every physician accustomed to treating patients with left-sided endocarditis is aware not only of its devastating nature but also of its uncertain prognosis. Despite profound knowledge of the disease and a strictly correct management according to accepted guidelines,[1,2] a feeling of frustration predominates if rates of mortality are rigorously examined. Before the inclusion of antibiotics in the therapeutic armamentarium, left-sided endocarditis was almost always a fatal disease. With antibiotics, uncontrolled infection decreased significantly and hemodynamic deterioration emerged as the main cause of death. Two decades ago, surgery in the active phase of the disease in patients who met strict criteria was introduced in the therapeutic approach, and death again decreased.[3,4] Since then, mortality rates remain unchanged.[3-8] At this point, different therapeu-

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tic options must be tested with the aim of improving prognosis. We hypothesize that an early aggressive surgical therapeutic approach in patients with poor prognosis would be beneficial. To test this hypothesis, we first have to identify the profile of patients with poor prognosis within the initial 72 hours of admission to the hospital. Bearing the preceding considerations in mind, we have undertaken a prospective multicenter study to identify early epidemiologic, clinical, electrocardiographic, radiographic, analytic, microbiological, and echocardiographic predictors of poor prognosis.

## CLINICAL SIGNIFICANCE

- Our model can help clinicians care for patients with endocarditis and predict their risk.
- The 3 cornerstones in the diagnosis of endocarditis are pivotal regarding prognosis: clinical examination, blood cultures, and echocardiography.
- Patients with heart failure, periannular complications, and/or *Staphylococcus aureus* infection should be closely followed.
- Hospitals without surgical facilities should refer these patients to tertiary care centers without delay.
- A multidisciplinary team including cardiac surgeons should take care of these patients.

## PATIENT POPULATION

In 1996, 5 tertiary care centers with surgical facilities initiated a prospective study. For every patient, a standardized case report form with 18 epidemiologic, 8 clinical, 10 analytic, 4 radiographic, 6 electrocardiographic, 14 microbiological, and 16 echocardiographic variables was completed. Between 1996 and 2003, 441 patients who met Duke criteria[9] (406 with definite and 35 with possible criteria) were included. Of these patients, 333 had left-sided endocarditis. Sixteen patients with septic shock at admission were excluded from further analysis to avoid an obvious bias because it was an absolute indication for urgent surgery. The remaining 317 patients made up our study population. The characteristics of these patients are shown in Table 1.

To ensure consecutive enrollment, all patients who underwent echocardiography to rule out endocarditis were followed until a diagnosis was established. In patients with a final diagnosis of endocarditis, clinical data at admission were collected. Patients were interviewed regarding their past and current clinical history. All patients underwent a detailed history, standard physical examination, electrocardiogram, blood analysis, urine analysis, set of 3 blood cultures, and transthoracic and transesophageal echocardiography.[10] All were done within 24 hours of admission except echocardiography, which depends on expert availability; in any case, it was performed within 48 hours. Blood culture results were reported within 72 hours. Therefore, all variables entered in the statistical model were available within 72 hours of admission.

Patients referred from another institution were not sent straight to surgery but were evaluated and treated according to our protocol. They underwent operation only when they met any of the 3 requirements described afterward.

## ECHOCARDIOGRAPHY

All patients underwent transthoracic and transesophageal echocardiography. After introduction of the probe into the esophagus, a systematic approach to cardiac structures was used. We focused on special areas of interest, namely, native cardiac valves and their annuli, prosthesis and their annuli, and mitroaortic continuity. Doppler was used to interrogate the hemodynamic status of the valves, presence or absence of flow within the cavities, and communication between chambers. From an echocardiographic perspective, a vegetation was defined as a thrombus-like mass with shaggy echoes and erratic motion independent of that of the valve. The vegetation was measured in various planes. The maximal diameter and area were used for subsequent analysis. In case of multiple vegetations, the largest was measured. Periannular complications were defined as follows:[11-13] abscess, well-delineated perivalvular area of reduced echodensity with no flow; pseudoaneurysm, echo-free perivalvular pouch with flow in its interior; and fistula, narrow communication between 2 adjacent chambers. Once a periannular lesion was seen, it was further analyzed by subtle movements of the transducer to better determine its morphologic characteristics.

## DEFINITION OF EVENTS

Death and surgery in the active phase of the disease were regarded as events. Any death occurring during hospital stay was considered an event irrespective of the final cause. Surgery in the active phase, that is, before adequate antibiotic treatment was completed according to established guidelines,[1,2] was performed when any of the following occurred: left-sided heart failure unresponsive to maximal medical treatment; septic shock; or uncontrolled infection defined as persistent bacteriemia or fever lasting more than 7 days after starting adequate antibiotic treatment when other causes had been excluded. The isolated echocardiographic finding of a periannular complication (abscess, pseudoaneurysm, fistula) was not considered an absolute indication for surgery.

## DEFINITION OF TERMS

Acute onset was defined as the span of time between the onset of symptoms and the admission to the hospital less

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