Usefulness of Thrombocytopenia at Admission as a Prognostic Marker in Native Valve Left-Sided Infective Endocarditis

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In-hospital mortality of patients with infective endocarditis (IE) remains exceedingly high. Quick recognition of parameters accurately identifying high-risk patients is of paramount importance. The objective of this study was to analyze the incidence and severity of thrombocytopenia at presentation and its prognostic impact in patients with native valve left-sided IE. We studied a cohort of 533 consecutive episodes of native valve left-sided IE prospectively recruited. We distinguished 2 groups: group I (n = 175), episodes who had thrombocytopenia at admission, and group II (n = 358) gathered all the episodes who did not. Thrombocytopenia at admission was defined as a platelet count of <150,000/μl. No differences were found in the need for surgery, but in-hospital mortality was significantly higher in patients with thrombocytopenia (p <0.001). Mortality rate was associated with the degree of thrombocytopenia (p <0.001). In the multivariable analysis, thrombocytopenia at admission was an independent predictor of higher mortality (p = 0.002). A synergistic interaction between thrombocytopenia and *Staphylococcus aureus* on mortality risk was also observed (p = 0.04). In conclusion, thrombocytopenia at admission is an early risk marker of increased mortality in patients with native valve left-sided IE. Mortality rates increased with increasing severity of thrombocytopenia. Thrombocytopenia at admission should be used as an early marker for risk stratification in patients with native valve IE to identify those at risk of complicated in-hospital evolution and increased mortality. **(Am J Cardiol 2015;115:950−955)**

The objectives of this study were to analyze (1) the incidence and degree of severity of thrombocytopenia at presentation of patients with native valve left-sided infective endocarditis (IE), (2) associated risk factors for its development, and (3) the correlation of thrombocytopenia and clinical outcome in a large cohort of patients with native valve left-sided IE.

Methods

This study was conducted at 3 tertiary care university hospitals with surgical facilities. All centers are using standardized protocols, uniform data collection, and identical diagnostic and therapeutic criteria. From 1996 to 2013, data from 855 consecutive patients with left-sided IE were prospectively recorded on an on-going multipurpose database. For this study, 533 patients with native valve IE were selected. Patients with prosthetic IE were excluded to avoid potential effects of anticoagulation on platelet count. This registry was approved by the local ethical committees, and the study protocol has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). Informed consent was obtained for participation in the study. For purposes of analysis and comparison, we distinguished 2 groups: group I (n = 175), episodes who had thrombocytopenia in blood analysis at admission, and group II (n = 358), episodes who did not.

To ensure consecutive enrollment, all patients who underwent an echocardiogram to rule out IE were clinically followed until a diagnosis was established. Duke criteria were applied until 2002 and modified Duke criteria thereafter.[1] To avoid potential source of errors, only definite cases of IE were finally included in the study.

Data collection included a detailed clinical history, standard physical examination, electrocardiography, chest x-ray, blood analysis, urinalysis, a set of 3 blood cultures at admission, and 3 additional blood cultures 48 to 72 hours later, and at least 1 transthoracic and transesophageal echocardiogram. Empiric antibiotic treatment was started after blood cultures were taken, and specific antibiotic therapy was initiated once the results of blood cultures were available. If blood cultures were negative after 72 hours, specific serological tests were done for *Chlamydia*, *Brucella*, Q fever, *Legionella*, *Mycoplasma*, and *Bartonella*.

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See page 955 for disclosure information.

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0002-9149/15/$ - see front matter
http://dx.doi.org/10.1016/j.amjcard.2015.01.021

Table 1
Demographic and main clinical characteristics, electrocardiographic, radiological, and laboratory findings at admission in 533 episodes of native valve left-sided infective endocarditis

	Group I (n=175)	Group II (n=358)	p
Age (years)	60.4 (16.5)	61.7 (15.1)	0.358
Male	104 (59.4%)	253 (70.7%)	**0.010**
Community-acquired IE	120 (68.6%)	270 (75.6%)	0.106
Previous valve disease	73 (43.5%)	163 (48.7%)	0.270
Chronic anemia	38 (21.7%)	77 (21.7%)	0.995
Chronic renal failure	18 (10.3%)	35 (9.9%)	0.886
Diabetes mellitus	35 (20.0%)	69 (19.4%)	0.878
Alcoholism	23 (13.3%)	37 (10.4%)	0.329
Chronic obstructive pulmonary disease	14 (8.0%)	25 (7.1%)	0.698
Malignant neoplasia	21 (12.0%)	35 (9.8%)	0.444
Immunosuppression	28 (16.1%)	20 (5.7%)	**<0.001**
Symptoms before admission (days)	14 (6-41)	25 (8-60)	0.371
Acute onset (<15days)	99 (56.6%)	119 (31.8%)	**<0.001**
Fever at admittance	120 (70.2%)	261 (74.4%)	0.312
Heart failure	59 (33.7%)	128 (36.3%)	0.565
Acute renal failure	45 (26.0%)	63 (17.8%)	**0.029**
Septic shock	21 (12.2 %)	16 (4.5%)	**0.001**
Chest pain	15 (8.7%)	43 (12.2%)	0.231
Abdominal pain	26 (15.1%)	36 (10.2%)	0.104
Splenomegaly	26 (15.1%)	32 (9.1%)	**0.040**
Confusional syndrome	32 (18.4%)	42 (11.9%)	**0.044**
Coma	12 (6.9%)	4 (1.1%)	**<0.001**
Stroke			
Hemorrhagic	11 (6.3%)	10 (2.8%)	0.082
Ischemic	23 (13.1%)	40 (11.3%)	0.119
Systemic embolism	47 (26.9%)	71 (20.1%)	0.080
Hemorrhagic skin lesions	23 (30.7%)	17 (13.0%)	**0.002**
Hematuria	4 (2.3%)	18 (5.1%)	0.131
Arthritis/Spondylodiscitis	26 (14.9%)	57 (16.1%)	0.721
Second and third degree AV block	3 (1.7%)	7 (2.0%)	0.841
Left bundle-branch block	5 (2.9%)	13 (3.7%)	0.631
Acute myocardial infarction	1 (0.6%)	8 (2.3%)	0.283
Cardiomegaly	76 (43.7%)	182 (51.0%)	0.114
Left heart failure	59 (33.9%)	134 (37.4%)	0.428
Pleural effusion	43 (25.0%)	85 (23.7%)	0.752
C-reactive protein (mg/dl)*	15.9 (5.10-76.9)	12.5 (4.6-52.6)	**0.023**
Hemoglobin (g/L)	11.1 (2.3)	11.0 (2.0)	0.524
Leukocyte count	11.2×10^3 (6.7×10^3)	11.9×10^3(6.8×10^3)	0.546
Neutrophils (%)	80.5% (12.3)	77.8% (11.5)	**0.014**

Values are n (%) or mean (SD), except for symptoms to admission and C-reactive protein that are presented as median. Bold values are significant.
AV block = atrioventricular block.
* Upper normal limit for C-reactive protein 0.5mg/dl.

Blood results were systematically collected at presentation to the emergency department. For those patients already hospitalized at the time of infection (nosocomial IE), laboratory parameters (included platelet count) were registered on the date of the first positive blood culture.

Nosocomial and community-acquired IE were defined according to the literature.[2] Acute-onset IE was applied when the time between the appearance of symptoms and hospital admission was <15 days.[3] Under the term of immunosuppression were included patients with HIV and those who were on steroids or other immunosuppressive therapy.

Renal insufficiency was defined as the presence of a serum creatinine concentration >2 mg/dl. Heart failure was diagnosed on the basis of guidelines criteria.[4] Persistent signs of infection, septic shock, and perivalvular complications have been defined in detail elsewhere.[2,5,6]

Thrombocytopenia was defined as a platelet count of <150,000/μl.[7] The diagnosis of systemic embolism was based on clinical signs and/or data derived from imaging procedures. Vegetations were measured in various planes, and the greatest diameter was recorded for subsequent analysis. In the case of multiple vegetations, the largest was measured. Surgery was performed when any of the following occurred: heart failure refractory to medical treatment, recurrent embolism with persistent vegetations in the echocardiogram, persistent signs of infection, and fungal endocarditis. When a patient meeting surgical criteria did not undergo surgery, the reason was either because of patient rejection, unacceptably high surgical risk, or when the patient was too frail.

In the univariate analysis, we compared demographic variables, predisposing factors, co-morbidities, microbiologic