Original article

The relationship between causative microorganisms and cardiac lesions caused by infective endocarditis: New perspectives from the contemporary cohort of patients

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ABSTRACT

Background: The etiology of infective endocarditis (IE) is changing. More aggressive forms with multiple IE cardiac lesions have become more frequent. This study sought to explore the relationship between contemporary causative microorganisms and IE cardiac lesions and to analyze the impact of multiple lesions on treatment choice.

Methods: In 246 patients hospitalized for IE between 2008 and 2015, cardiac lesions caused by IE were analyzed by echocardiography, classified according to the 2015 European Society of Cardiology guidelines and correlated with microbiological data. We defined a new parameter, the Echo IE Sum, to summarize all IE cardiac lesions in a single patient, enabling comprehensive comparisons between different etiologies and treatment strategies.

Results: Staphylococcus aureus was associated with the development of large vegetation (OR 2.442; 95% CI 1.220–4.889; $p = 0.012$), non-HACEK bacteria with large vegetation (OR 13.662; 95% CI 2.801–66.639; $p = 0.001$), perivalvular abscess or perivalvular pseudoaneurysm (OR 5.283; 95% CI 1.069–26.096; $p = 0.041$), and coagulase-negative staphylococci (CoNS) with leaflet abscess or aneurysm (OR 3.451; 95% CI 1.285–9.266, $p = 0.014$), and perivalvular abscess or perivalvular pseudoaneurysm (OR 4.290; 95% CI 1.583–11.627; $p = 0.004$). The Echo IE Sum significantly differed between different etiologies ($p < 0.001$), with the highest value in non-HACEK and the lowest in streptococcal endocarditis. Patients operated for IE had a significantly higher Echo IE Sum vs those who were medically treated ($p < 0.001$).

Conclusion: None of the IE cardiac lesions is microorganism-specific. However, more severe lesions were caused by S. aureus, CoNS, and non-HACEK bacteria. The highest propensity to develop multiple lesions was shown by the non-HACEK group. Higher Echo IE Sum in patients sent to surgery emphasized the importance of multiple IE cardiac lesions on treatment choice and potential usage of Echo IE Sum in patient management.

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Introduction

Infective endocarditis (IE) is still a disease with high morbidity and mortality [1–4]. More challenging forms, frequently with multiple cardiac lesions, are seen more often [5]. A potential reason is a change in the microbiology of IE [6]. Due to more aggressive and invasive diagnostic and therapeutic procedures, previously marginal pathogens have become more frequent [7–9]. Despite a large number of studies about demographics and clinical features of IE, the direct analyses of the relationship between causative microorganisms and IE cardiac lesions in contemporary clinical practice are scarce [10].

The first aim of this study was to explore the relationship between specific IE cardiac lesions and contemporary causative microorganisms. Since one microorganism might cause multiple heart lesions in a single patient, the second aim was to define a new parameter that will summarize all IE cardiac lesions per patient, enabling a more comprehensive comparison of IE severity between different etiologies. Finally, the third aim was to analyze the impact of multiple IE lesions on treatment strategies.

Methods

The study population

This prospective observational study included consecutive patients with IE hospitalized in a tertiary medical center – the Clinical Centre of Serbia – between 1st July 2008 and 31st December 2015. The diagnosis of IE was established according to the European Society of Cardiology (ESC) 2015 criteria [1,11]. Only those patients with a complete medical history, echocardiographic examination, and microbiological data were included in the study.

The echocardiographic evaluation of IE cardiac lesions

At least one detailed transthoracic echocardiographic examination (TTE) was done in all patients, whereas transesophageal echocardiographic examinations (TEE) were performed in 65% of all patients. Attention was focused on the presence of the main IE lesions according to the previous echocardiographic definitions [12], slightly modified for the purpose of this study. We analyzed seven types of IE cardiac lesions: (1) vegetation – defined as an intracardiac mass on a valve or another endocardial structure or an implanted intracardiac material (the presence, the size, and the number of the vegetations; the vegetation ≥15 mm is considered large); (2) leaflet perforation – defined as an interruption of the continuity of leaflet tissue, with a color-Doppler flow; (3) leaflet aneurysm – defined as the saccular bulging of the valve leaflet; the leaflet abscess – defined as a thickened non-homogenous area within the leaflet with echodense or echolucent appearance; for the purpose of this study, leaflet abscess and leaflet aneurysm were analyzed together; (4) perivalvular abscess – defined as a thickened non-homogenous perivalvular area with echodense or echolucent appearance; (5) perivalvular pseudoaneurysm – defined as a pulsatile perivalvular echo-free space, with color-Doppler flow; (6) fistula – a color-Doppler communication between the two neighboring cavities through a perforation; and (7) dehiscence of the prosthetic valve – defined as a paravalvular regurgitation, identified by TTE/TEE, with or without rocking motion of the prosthesis.

In order to summarize all IE cardiac lesions per patient, a novel parameter, the Echocardiographic Infective Endocarditis Sum (Echo IE Sum), was developed. It was defined as the sum of aforementioned lesions (one point for each lesion + one point for a vegetation ≥15 mm + one point for the presence of multiple vegetations) (Supplement).

During the study period, the echocardiographic examinations were performed on the following commercial systems: Vivid 4 [General Electric (GE) Healthcare, Boston, MA, USA], Sequoia C250 (Siemens, Munich, Germany), and iE33 (Philips, Amsterdam, the Netherlands).

Microbiology

Isolated microorganisms were obtained from blood cultures, postoperative valve material, and serological tests, when indicated. In all patients, at least three blood sets were taken at 30-min. intervals (from separate peripheral venipunctures) for analysis on aerobic and anaerobic microorganisms. The valve extracted during the surgery was bacteriologically examined. For the purpose of this study, the pathogens were sorted into nine groups: *Streptococcus*, *Staphylococcus aureus*, coagulase-negative staphylococci (CoNS), *Enterococcus*, HACEK group (*Haemophilus* spp., *Aggregatibacter*, *Cardiobacterium*, *Eikenella*, *Kingella*), non-HACEK Gram-negative bacteria, rare pathogens, blood culture-negative IE, and polymicrobial endocarditis. We applied the microbiological criteria for non-HACEK endocarditis according to the previously published data [8], as well as for polymicrobial endocarditis [9] and blood culture-negative IE [1].

In all patients, the standard hematological and biochemical analyses were done.

Clinical data and the outcome

Predisposing cardiac conditions (PCC) for IE were identified according to the ESC 2015 recommendations (PCC with high-, intermediate-, and low-risk). The complications of IE (new-onset heart failure, uncontrolled systemic infection, neurological sequels, embolic event) were analyzed. Diabetes mellitus (DM), hemodialysis, malignancy, and intravenous drug abusers were identified. In-hospital mortality was analyzed. According to the epidemiological data, IE was classified as community- or healthcare-associated IE in compliance with the previous definitions [6,7]. The time from symptom onset to hospitalization exceeding 1 month was noted and included in further analysis.

Statistical analysis

Continuous variables are presented as the mean ± the standard deviation (SD) or the median and the interquartile range (IQR; the 25th and the 75th percentiles), as appropriate. Categorical variables are expressed as the number and percentage of the specified group. Statistical significance was determined at the 0.05 level. The statistical analyses were carried out by using the SPSS software (version 20.0. IBM Corp., Armonk, NY, USA).

The primary outcome was an echocardiographic finding. Each one of the seven predefined cardiac lesions was analyzed as a dichotomous variable, as well as a large vegetation (the diameter ≥15 mm) and the presence of multiple vegetations. The comparisons between the incidences of the nine predefined groups of causative microorganisms for each one of the analyzed cardiac lesions were assessed by the Kruskal–Wallis one-way analysis of variance (ANOVA). In order to identify microorganisms significantly associated with IE cardiac lesion, a univariable logistic regression analysis was first used. The significant univariable predictors were further tested by a multivariable (backward Wald) binary logistic regression analysis for each IE cardiac lesion. The variables previously shown that might affect IE prognosis and development of certain IE cardiac lesions (age, gender, diabetes mellitus, hemodialysis, intravenous drug use, carcinoma, healthcare-associated infection, time from the symptom to a diagnosis >1 month, and PCC classified as high-, intermediate-, and low-/no-risk) [1,3], were also tested by univariable