

Particularities of infective endocarditis. A retrospective study

Particularități ale endocarditei infecțioase. Studiu retrospectiv

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Abstract

Background: Despite of all progresses made in the management of infectious diseases and cardiovascular pathology, the incidence of infective endocarditis (IE) remains constant when comparing it to the pre-antibiotic era. **The aim** of the present study consists in evaluating the clinical, laboratory tests, etiological and therapeutic parameters in patients with IE. **Methods:** We conducted a retrospective study on 20 patients admitted in Third Medical Clinic – Dept. of Cardiology, First Infectious Diseases Clinic, Institute of Cardiovascular Disease and Transplantation of Targu Mures, Romania, over a period of 2 years, which were diagnosed with IE according to the Duke criteria. We studied socio-demographic parameters, co-morbidities, predisposing factors, the nature and the site of affected valves, clinical, bacteriological and therapeutic characteristics of the patients. **Results:** The patients' age varied between 26 and 65 years; 12 (60%) of them were men and 8 (40%) women. 14 patients were diagnosed with IE and 6 with possible IE, localized on native valves – aortic valve (50%), mitral valve (40%), prosthetic valves (10%). The etiology was established in 14 patients and was confirmed by positive blood cultures as follows: coagulase-positive *Staphylococcus aureus* (8), *Streptococcus pyogenes* (1), *Enterococcus* spp. (1), coagulase-negative *Staphylococcus* (1), *streptococi viridans* (1), Gram negativ bacilli (1), fungi (1). Antibacterial therapy was applied according to the results of antibiotic susceptibility tests in 70% and empirically in 30% of the patients. **Conclusion:** In our study, *Staphylococcus aureus* held the first place in IE etiology on native and prosthetic valves. We have also noticed an increased incidence of community-associated methicillin-resistant *Staphylococcus aureus* (MRSA).

Keywords: infective endocarditis, etiological, clinical, therapeutic aspects.

Rezumat

Introducere: În ciuda progreselor efectuate în ultima perioadă, atât în ceea ce privește managementul bolilor infecțioase cât și a patologiei cardiovasculare, incidența endocarditei infecțioase (EI) rămâne constantă cu cea din era pre-antibiotică. **Scopul studiului** de față a fost de a evalua etiologia, aspectele clinice, de labora-

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tor și terapeutice în cazul pacienților cu endocardită infecțioasă. **Material și metode:** S-a efectuat un studiu retrospectiv, pe un număr de 20 de pacienți internați în cadrul Clinicii Medicale III – Departamentul de Cardiologie și a Clinicii de Boli Infecțioase I, Institutul de Urgență pentru Boli Cardiovasculare și Transplant Tîrgu Mureș, România, pe o perioadă de 2 ani, diagnosticați cu endocardită infecțioasă conform criteriilor Duke. S-au studiat o serie de parametri legați de factori de risc, comorbidități, parametri socio-demografici, natura și locul afectării valvulare, parametri clinici, bacteriologici și terapeutici. **Rezultate:** Vârsta pacienților a fost între 26 – 65 de ani; 12 (60%) au fost de sex masculin și 8 (40%) au fost de sex feminin. Dintre aceștia 14 pacienți (70%) au fost diagnosticați cu EI certă și 6 cu EI posibilă, localizată fie pe valve native: valvă aortică 10 pacienți (50%) respectiv valvă mitrală 8 (40%), fie pe valve prostetice 2 pacienți (10%). Etiologia a fost stabilită în 14 (70%) cazuri, fiind confirmată prin hemoculturi pozitive după cum urmează: *Staphylococcus aureus* (8 pacienți), bacili gram negativi (1 pacient), stafilococi coagulază negativi (1 pacient), *Streptococcus viridans* (1 pacient), *Streptococcus pyogenes* (1 pacient), *Enterococcus* (1 pacient) și fungi (1 pacient). Terapia antibiotică s-a administrat conform antibiogramei la cei 14 pacienți și în mod empiric la ceilalți 6 pacienți. **Concluzii:** În cadrul studiului de față *Staphylococcus aureus* a reprezentat cea mai frecventă etiologie a EI atât pe valve native cât și pe valve prostetice. Am remarcat de asemenea și o incidență crescută a *Staphylococcus aureus* comunitar meticulo-rezistent.

Cuvinte cheie: endocardită infecțioasă, aspecte clinice, etiologice, terapeutice

Introduction

Infective endocarditis represents the infection of the valvular tissue or vascular endothelium by a variety of agents. While its characteristics have been known for centuries, this unpredictable disease remains a diagnostic and therapeutic challenge. Infective endocarditis affects mostly the cardiac valves and leads to local destruction followed by regurgitation. Embolism, mainly cerebral, is the most feared extra cardiac complication.

The diagnosis of IE relies on the presence of positive hemocultures and the echocardiographic proof of vegetations. Aggressive etiological agents and unfavourable clinical circumstances such as prosthetic valves or immunodepressed patients have often implied surgical treatment [1-4].

Infective endocarditis, known in the past as a disease that affects young adults with rheumatic valvular disease, is presently affecting older patients, probably due to the increased number of invasive diagnostic procedures (prosthetic valves, pacemakers, etc.) [5, 6].

Objectives

The aim of the present study is to evaluate the etiological, clinical and therapeutic parameters of patients with infective endocarditis.

Material and methods

We conducted a retrospective study on 20 patients diagnosed with IE according to the modified Duke criteria, admitted in Third Medical Clinic – Dept. of Cardiology, First Infectious Diseases Clinic, Institute of Cardiovascular Disease and Transplantation of Targu Mures, Romania, over a period of 2 years (January, 31, 2006 – January, 31, 2008). The following were taken into consideration: aspects regarding the socio-demographic parameters, the presence of co-morbidities, predisposing factors, the nature and the site of affected valves, clinical, trans-esophageal echocardiography, bacteriological, therapeutic characteristics and the patient's evolution. Blood cultures were processed with a Bact/Alert Automatic System in aerobic and anaerobic bottles

(BioMérieux). Blood samples were cultured on routine media: 5% Columbia sheep blood agar, chocolate agar (without antibiotics), Agar Bile Esculine and incubated at 37°C in aerobic atmosphere, 5% CO₂ and anaerobic condition; for identification of isolates a Vitek 2 Compact System (BioMérieux) was used.

Results

The study included 20 patients with ages between 26 and 65 years; 11 were aged between 26 and 46 years, 5 between 47 and 57 years, and 4 between 58 and 68 years. There were 12 (60%) male and 8 (40%) female patients. 11 patients came from urban and 9 from rural areas.

The following suggestive clinical and biological manifestations were present:

- infectious syndrome in 18 patients
- cutaneous manifestations in 8 patients, mainly Osler nodules, hemorrhages, Janeway lesions, septic cutaneous metastases (Figures 1 - 4).

Dynamic cardiac auscultation modifications were present in 10 patients:

- holosystolic regurgitation murmur at the apex associated with dyspnoea and other signs of retrograde left ventricular failure in mitral IE
- left parasternal diastolic murmur associated with dyspnoea in aortic IE.

Hepatosplenomegaly was present in 15 patients. Acute phase reagents (ESR, leukocytosis, elevated levels of fibrinogen, C reactive protein) were positive in 100% of patients, with a left deviation of the leukocyte formula and intra-infective anaemia.

Most patients presented associated diseases, such as mitral valve prolapse and aortic degenerative disease (8 patients), congenital or surgical shunt lesions (2 patients), prosthetic valves (2 patients), type 2 diabetes (4 patients).



Figure 1. Osler nodules



Figure 2. Janeway lesions

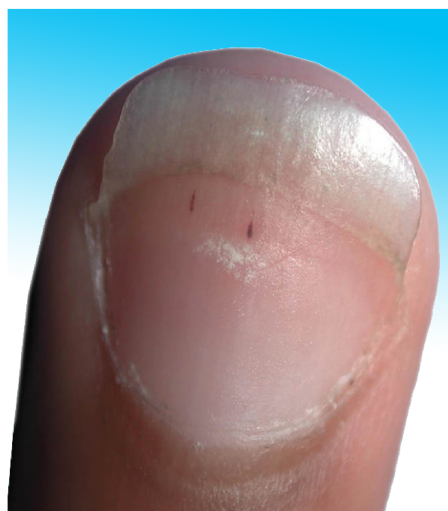


Figure 3. Spike hemorrhages

The diagnosis of IE was established according to the modified Duke criteria [7], 70% of the patients being diagnosed with definite IE, and 30% with possible IE.

The etiology was established in 14 patients (70%) and was confirmed by positive blood cultures as follows: coagulase-positive *Staphylococcus aureus* (8), coagulase-negative staphylococci (1), *Streptococcus viridans* (1), *Streptococcus pyogenes* (1), *Enterococcus* (1), Gram negative bacilli (1), yeasts (*C. albicans*) (1). The blood cultures were negative in 6 patients (Figure 5).

Several predisposing conditions of bacteraemia were identified (in 70% of patients):

- invasive procedures (central venous and urinary catheters, colectectomy): in these patients the onset of disease was less than 60 days after the procedure; the following agents were involved: methicillin-resistant *Staphylococcus aureus* (MRSA), *Enterococcus* spp., *E. coli* (3 patients)
- dental procedures, with an onset after more

than 60 days, with *Streptococcus viridans* being the involved agent (1 patient)

- respiratory and cutaneous infections, with isolated gram positive cocci (5 patients), MRSA (4 patients), *Streptococcus pyogenes* (1 patient)
- pneumonia (4 patients): *Staphylococcus aureus* and coagulase negative staphylococci (CNS) were identified
- prolonged antibiotic treatment in immunodepressed patients with type 2 diabetes, where the involved agent was *Candida albicans* (1 patient) (Table I).

Localization of endocarditis

From the total of 20 patients, the localization of vegetations was found on the native valves (NV) in 90% of patients, as opposed to the localization on prosthetic valves in 2 patients. The vegetations affected the aortic valve in 12 patients, and the mitral valve in 8 patients.

The **antibacterial treatment** of IE was started empirically, and then adjusted according to the antibiotic susceptibility results. Patients with IE caused by MSSA (3) and CNS (1) were treated with Oxacillin + Gentamicin for 4-6 weeks;



Figure 4. Septic cutaneous metastases

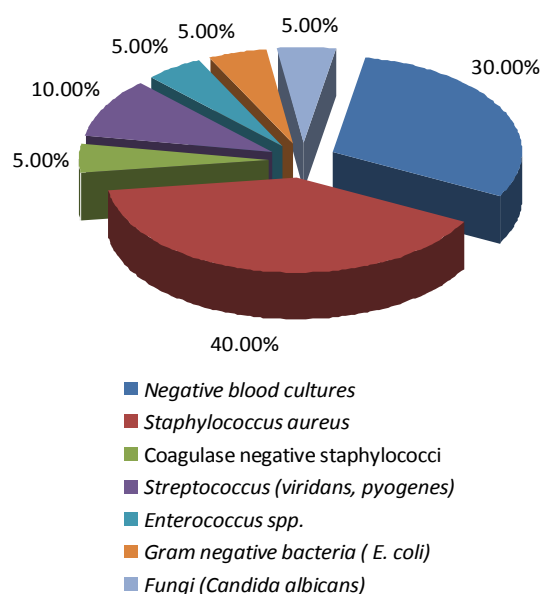


Figure 5. Distribution of etiological agents

Table I. Conditions that predispose to bacteraemia

Condition	Pathogen	Period		TOTAL n=20
		<60 days	> 60 days	
Invasive interventions:				
• Central venous catheter	• MRSA	+		1
• Urinary catheter	• Enterococcus spp.	+		1
• Colectectomy	• <i>Escherichia coli</i>	+		1
Dental procedures	<i>Streptococcus viridians</i>		+	1
Respiratory infections	MRSA	+		2
Cutaneous infections	MRSA, <i>Streptococcus pyogenes</i>	+	+	2 1
Pneumonia	MSSA CNS	+		4
Prolonged antibiotic treatment	<i>Candida albicans</i>	+		1

Table II. Treatment of infectious endocarditis

MSSA – Methicillin sensitive <i>Staphylococcus aureus</i>	Oxacillin + Gentamicin (2) Oxacillin + Netromycin (1)
MRSA – Methicillin resistant <i>Staphylococcus aureus</i>	Vancomycin + Gentamicin (5)
CNS – coagulase negative staphylococcus	Oxacillin + Gentamicin (1)
<i>Streptococcus viridans</i>	Penicillin G + Gentamicin (1)
<i>Streptococcus pyogenes</i>	Penicillin G + Gentamicin (1)
Enterococcus spp.	Vancomycin + Gentamicin (1)
<i>Escherichia coli</i>	Ceftriaxone + Gentamicin (1)
<i>Candida albicans</i>	Amfotericin B + Fluconazol (1)
Negative blood cultures	Penicillin G + Ceftriaxone + Gentamicin (6)

MRSA (25%) was treated with Vancomycin + Gentamicin for 4 weeks.

Streptococcal infections (10%) were treated with Penicillin G + Gentamicin for 6 weeks; infections caused by gram negative bacilli were treated with 3rd generation cephalosporins (Ceftriaxone) + Gentamicin for 6 weeks.

IE caused by *Candida albicans* (1) was treated with i.v. Amphotericin B for 4 weeks, then i.v. Fluconazol for 4 weeks, which was continued p.o. for another 4 weeks. Patients with IE and negative blood cultures (6) were treated with a triple combination: Penicillin G + Ceftriaxone + Gentamicin (Table II).

Complications

Structural complications were present in 7 patients: cerebral embolism, valvular ruptures, pulmonary vein abscesses and ruptures, aortic ring abscess (Figure 6).

Hemodynamic complications were present in 6 patients: aortic valve regurgitation, heart failure, paravalvular regurgitations.

Discussions

Despite of all the progress made in the field of cardiovascular pathology and infectious diseases, the incidence of IE is comparable to that of the pre-antibiotic era, at 15-30 patients/1

million inhabitants/year [7]. The incidence of IE on prosthetic valves is increasing, reaching 30% [2]. The risk of IE developing on prosthetic valves is 1% in the first 12 months and 20-30% in the first 60 months. The aortic valve is most frequently affected. In the case of IE on native valves, the most affected are the mitral valve (45-55%), followed by the aortic valve (35-40%) and the tricuspid valve (18-20%).

In our study preexisting valvular heart disease was observed in 80% of patients using echocardiography. Generally, sensitivity of transthoracic echocardiography is around 60%, and its specificity for vegetations is around 90% [6, 7]. Also transesophageal echocardiography is essential in the diagnosis of IE and its complications; a negative result does not exclude the diagnosis of endocarditis [1, 2, 7].

In the studied group *Staphylococcus aureus* was the most frequent pathogen (9 patients); other studies [5, 6] show a lower frequency (22%).

A particular characteristic of the study group is the high number of patients (12) in whom the aortic valve was involved, when IE is present on native valves.

Blood cultures were positive in 70% of patients, compared with other studies [4, 6]

which report percentages of up to 90%. This was probably due to prior antibiotic treatment. MRSA was involved in 5 patients, 4 of which were community acquired and 5% hospital acquired infections, following invasive procedures. MRSA was present mainly in immunodepressed patients (chronic renal disease, diabetes, chronic hepatopathy).

Compared with other etiologies, in the course of sepsis, staphylococci were responsible for most secondary sepsis-related respiratory and cutaneous complications.

Systemic embolism (pulmonary, splenic, limb, central nervous system) generally occurs in 25-50% of IE patients. In our study it was present in 1 patient, affecting the CNS. The evolution of patients under empirical and targeted antibiotic treatment was slowly favorable. Mortality in the studied group was 15%, comparable with literature data reporting mortality rates of 18-20% for community IE and 25-50% for nosocomial IE [1, 2, 6, 7].

Conclusions

The symptoms of IE were polymorphic and not always specific, but echocardiography led to a correct diagnosis in 70% of patients, allowing an early and proper antibiotic treatment. Infective endocarditis affected 11 patients younger than 50 years in the studied group.

Staphylococcus aureus was the most frequently involved pathological agent (9 patients). We noticed MRSA was present in 4 patients with community acquired infections.

The aortic valve was the most frequently affected (12 patients). The incidence of IE on prosthetic valves was low (2), compared with its incidence on native valves (18).

Surgical intervention was necessary in 7 patients. Mortality rates were low.

Abbreviations

AoV - Aortic valve

CNS - Coagulase negative staphylococci

IAS - Inter atrial septum

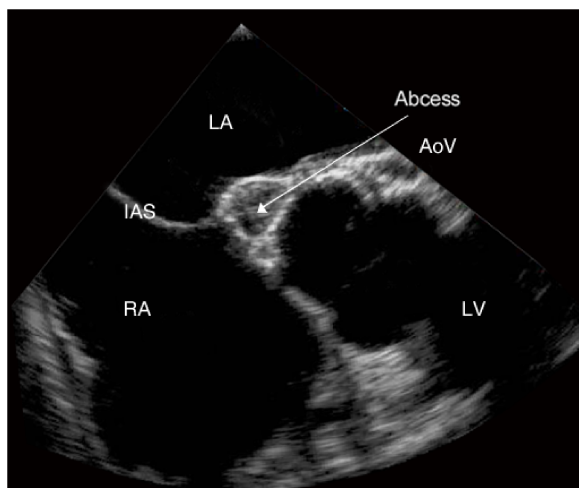


Figure 6. Aortic ring abscess, transesophageal examination

IE - Infective endocarditis

LA - Left atrium

LV - Left ventricle

MRSA - Methicillin resistant *Staphylococcus aureus*

MSSA - Methicillin sensitive *Staphylococcus aureus*

RA - Right atrium

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