Infective endocarditis and complications; a single center experience

Enfektif endokardit ve komplikasyonları; tek merkez deneyimi

Olcay Özveren, M.D., Mehmet Akif Öztürk, M.D.,# Cihan Şengül, M.D.,*
Ruken Bengi Bakal, M.D.,* Taylan Akgün, M.D.,* Cemil Izgi, M.D.,* Zekeriya Küçükdurmaz, M.D.,
Atiye Elif Eroğlu Büyüköner, M.D., Muzaffer Değertekin, M.D.

Department of Cardiology, Yeditepe University Faculty of Medicine, İstanbul;
#Department of Internal Medicine, Yeditepe University Faculty of Medicine, İstanbul;
*Department of Cardiology, Kosuyolu Training and Research Hospital, İstanbul

ABSTRACT

Objectives: The aim was to investigate the microbiological characteristics and complications of infective endocarditis (IE) in 119 patients treated in our center for IE, diagnosed by modified Duke criteria.

Study design: The archive records of 119 patients (82 [69%] males; 37 [31%] females; mean age 39±16 years) with a definite diagnosis of IE between January 1997 and November 2004 were systematically reviewed for clinical and microbiological properties and complications.

Results: The most common complaint of the patients was fever and malaise (102 patients, 85.7%, each). Culture was negative in 68 patients (57.1%), while *Staphylococcus aureus* was the most common etiological agent in culture positive cases. The aortic valve was the most common region of vegetation (43 patients, 36.1%). The frequency of surgical operation for valvular insufficiency due to IE was 75.6%, and the frequency of congestive heart failure was 53.8% (64 patients).

Conclusion: IE is still an important disease considering its high morbidity and mortality rates, increased life expectancy of the patients, and increased number of valve replacement procedures.

ÖZET

Amaç: Bu çalışmada, merkezimizde modifiye Duke kriterlerine göre tanı konarak tedavi edilen enfektif endokarditli 119 hastanın mikrobiyolojik özellikleri ve komplikasyonlar araştırıldı.

Çalışma planı: Ocak 1997 Kasım 2004 tarihleri arasında enfektif endokardit kesin tanısı konan 119 hastanın (82 [%69] erkek; 37 [%31] kadın; ortalama yaş 39±16 yıl) arşiv kayıtları klinik ve mikrobiyolojik özellikleri ve komplikasyonlar açısından incelendi.

Bulgular: Hastaların en sık şikayeti ateş ve halsizlik (her biri için, 102 hasta, %85.7) idi. *Staphylococcus aureus*, kültür pozitif olgularda en sık etiyolojik ajan iken 68 hastada (%57.1) kültür negatif idi. Aort kapak (43 hasta, %36.1) en sık tutulan bölge idi. Enfektif endokardit nedeniyle kapak yetersizliği için cerrahi işlem sıklığı %75.6 ve konjestif kalp yetersizliğinin sıklığı %53.8 (64 hasta) olarak tespit edildi.

Sonuç: Enfektif endokardit, yüksek morbidite/mortalite oranları, artan kapak replasman prosedürleri ve artan yaşam beklentisi göz önünde bulundurulduğunda halen önemini koruyan bir hastalıktır.

Infective endocarditis (IE) is the infection of the endothelial surface of the heart. It remains as a life-threatening condition despite medical progress. According to prospective studies in western societies,[1] the incidence of IE is 1.9-6.2/100,000 persons per annum Classification of the disease is based on the activation pattern of the disease, presence of recurrence, pathogenesis, anatomic localization and the causative microbiological agent. Duke criteria aid clinicians in the diagnosis.[2] Vegetation

Abbreviations:

ECG	*Electrocardiography*
IE	*Infective endocarditis*
MRSA	*Methicillin resistant S. aureus*
MSSA	*Methicillin sensitive S. aureus*
PVE	*Prosthetic valve endocarditis*
TEE	*Transesophageal echocardiography*
TTE	*Transthoracic echocardiography*

Received: January 17, 2014 *Accepted:* April 21, 2014
Correspondence: Dr. Mehmet Akif Ozturk. Yeditepe Üniversitesi Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, İstanbul.
Tel: +90 216 - 578 40 00 e-mail: akifozturk@hotmail.com

is the characteristic lesion of IE, andmight exist anywhere on the endocardium, but usually arising on the heart valves. IE is usually associated with rheumatic valvular heart disease in developing countries, but acute rheumatic fever has declined, and degenerative lesions have become the most frequent abnormalities predisposing to infection in the west;[3,4] some other risk factors such as valve prostheses, intravenous drug abuse and increased use of invasive procedures resulting in bacteremia have become more prominent.[5]

In this study, we aimed to investigate the characteristics and complications of IE in 119 patients treated in our center.

PATIENTS AND METHODS

Design

The study was designed as a retrospective observational single-center study.

Study population

119 consecutive patients treated for definite IE at our hospital were included. A diagnosis of IE was established for all patients according to modified Duke criteria. Patients with possible IE were excluded. Retrospective evaluation of the patients was performed using archive records. All patients were evaluated with routine physical examination, postero-anterior chest X-ray, electrocardiography (ECG), routine biochemistry, full blood count, blood cultures and transthoracic echocardiography (TTE), and transesophageal echocardiography (TEE) if necessary. The study was approved by the Local Medical Ethics Committee.

Microbiological evaluation

The blood cultures used to evaluate IE were obtained by the microbiology laboratory of the hospital and processed by standard methods to identify bacterial and fungal species and antimicrobial susceptibility profiles. Three sets of 10 cc blood samples were obtained on admission from each patient for blood cultures under sterile conditions. The sampling procedures were performed every 60 min/from different veins and were inoculated in blood agar, sheep blood agar and eosin methylene blue agar and evaluated 24-48 h later automatically by BACT/ALERT device (BacT/ALERT3D, BioMérieux, Durham, NC, USA). At least three aerobic and anaerobic bottles were inoculated with blood for at least 14 days. The Wright seroagglutination test was used for brucella microorganisms.

Echocardiography

All patients were evaluated with TTE and 67 (56%) of the patients underwent TEE. All procedures were performed by Vingmed CFM 800 (Horten, Norway) and Vivid 5 (GE, Horten, Norway), echocardiograhy devices using 3.25 MHz multifrequency transthoracic and 5 MHz multiplane transesophageal transducers.

Statistical analysis

The variables are expressed as frequency or mean±standard deviation. Categorical variables were compared using Chi-square or Fisher's exact test, and continuous variables were compared using the Student's t-test or Mann-Whitney U-test, whichever was appropriate.

The parameters that remained significant in the univariate analysis were included in the multivariate analysis model and evaluated by step-wise logistic regression analysis. $P<0.05$ was accepted as statistically significant in all analyses.

RESULTS

The mean age of our study patients was 39±16 years. 37 (31%) of the 119 patients were female. The most frequent symptoms of the patients on admission was fever in 102 patients (85%), malaise in 102 (85%) patients, weight loss in 42 (35%) patients, arthralgia, and myalgia in 21 (17%) patients (Table 1).

Table 1. Symptoms of infective endocarditis patients on admission

Symptoms	n	%
Fever (>38°C)	102	85.7
Malaise	102	85.7
Weight loss	42	35.3
Artralgia-myalgia	21	17.6
Headache	17	14.3
Loss of appetite	47	39.5
Cough	45	37.8
Dyspnea	66	55.5
Chest pain	19	16
Stroke	15	12.6

Table 2. Distribution of vascular and immunologic phenomena in patients with infective endocarditis

	n	%
Vascular phenomena	54	45.6
Arterial embolization	28	23.5
Petechia and splinter hemorrhage	28	23.5
Micotic aneurysm	5	4.2
Janeway lesion	9	7.6
Intracranial hemorrhage	2	1.7
Immunologic phenomena	48	40.3
Glomerulonephritis	18	15.1
Roth spot	5	4.2
Osler nodes	19	16
Elevation of rheumatoid factor	29	24.4

The functional capacities of the patients were NYHA Class I and II in 55 (46%) patients and NYHA Class III and IV in 64 (54%) patients.

The ECG investigation of the patients revealed normal sinus rhythm in 80 (67%) patients, atrial fibrillation in 28 (23.5%) patients, permanent pacemaker rhythm in 6 (5%) patients, and left a bundle brunch block in 4 (3.5%) patients.

Vascular and immunological phenomena were observed in 54 (45.6%) and 48 (40.3%) patients, respectively consecutively. Most common vascular phenomena were arterial embolization in 28 (23.5%) patients and petechias or splinter hemorrhages in 28 (23.5%) patients, while the most common immunological phenomenon was rheumatoid factor elevation in 29 (24.4%) patients (Table 2).

Blood culture was negative in 68 (57%) of the patients. Of the culture positive patients, 13 (11%) had methicillin sensitive *Staphylococcus aureus* (MSSA), 13 (11%) had methicillin resistant *Staphylococcus aureus* (MRSA), 10 (8%) had *Streptococcus viridans*, 4 (3%) had *Brucella*, 3 (2.5%) had *Enterococcus faecalis*, 2 (1.7%) had *Staphylococcus epidermidis* and 3 (3.4%) had other rare bacteria (Table 3).

Vegetation was observed most frequently on the aortic valve; 43 (36%), and mitral valve 36 (30%) (Table 4).

The most frequent complications were congestive heart failure in 64 (53.8%) patients, major arterial em-

Table 3. Blood culture results in patients with infective endocarditis

Blood culture	n	%
Culture negative	68	57.1
Streptococcus viridans	10	8.4
Meticilline sensitive *S. aureus*	13	10.9
Meticilline resistant *S. aureus*	13	10.9
Brucella	4	3.4
Staphylococcus epidermidis	2	1.7
Acinetobacter	1	0.8
Enterococcus faecalis	3	2.5
Gram-negative bacilli	1	0.8
Streptococcus bovis	1	0.8

Table 4. Localization of vegetations in patients with infective endocarditis

Localization	n	%
Aortic valve	43	36.1
Mitral valve	36	30.3
Aort + mitral valve	23	19.3
Tricuspid valve	7	5.9
Pulmonary valve	1	0.8
Endarteritis	2	1.7
Multivalvular (>2 valves)	3	2.5
Pacemaker lead	2	1.7
Heart valve + endarteritis	2	1.7

Table 5. The frequency of complications in patients with infective endocarditis

Complication	n	%
Periannuler abssess	14	11.8
Chordal rupture	13	10.9
Cusp or leaflet perforation	27	22.7
Congestive heart failure	64	53.8
Pericardial effusion	5	4.2
Shock	3	2.5
Renal complications	20	16.8
Fistula	5	4.2
Micotic aneurysm	5	4.2
Pseudoaneurysm	10	8.4
Embolization	28	23.5
AV block on electrocardiography	4	3.4
Intracranial hemorrhage	2	1.7

bolization in 28 (23.5%) patients and renal complications in 20 (16%) patients (Table 5).

DISCUSSION

Although it is expected that the frequency of IE should decrease as a result of better application of rheumatic heart disease prophylaxis in western societies, increased implantation of intracardiac devices, and prosthetic heart valves has caused an increase in the cases of IE. Intravenous drug use, nosocomial infection, and a progressively increasing elderly population have also changed admission profiles.

In European societies, cases of IE were more common in the >50-year-old population, while in our study population, the mean age of the patients was 39±16 years.

In a study by Heper et al.,[6] consisting of 74 patients, rheumatic etiology was 66%, which was only 38.7% in our population.

Fever, which used to be the most common finding in most studies, is nowadays a minor criterion compared to other signs. In the presence of a predisposing heart disease, IE should be primarily considered when a patient has a fever (>38°C) which lasts more than 1 week and does not respond to antibiotherapy. In our series, the frequency of patients presenting with fever was 85.7%, similar to other studies.[7-9]

All patients underwent TTE, while TEE was performed on only 56% of our study patients, a rate much lower than those of other studies and the guidelines.[10,11] TEE usage is lower in studies performed in developing countries, probably not as an outcome of technical insufficiency, but rather by the obvious presentation of the disease in younger rather than older persons, with valvular calcifications, devices and comorbidities.

Splenomegaly secondary to infection or secondary vasculitis was observed in 50% of the patients in several series.[4] In our study, splenomegaly was present in 40.8% patients. Osler's nodules were present in 16% of our study population, which is similar to other series.[4] Janeway lesions were present in 7% of our patients, comparable to other series.[4] Nonspecific signs such as arthralgia and myalgia result in confusion of IE patients with rheumatic patients. Presence of arthralgia and myalgia is 40% in the literature, while it was observed in 17.6% of patients in our series.[4]

Of the culture-positive patients, 11% had MSSA, 11% had MRSA, while only 8% patients had S. viridans, which reveals that *Staphylococcic* IE has increased in our country as it has worldwide.[12,13] In a series by Sucu et al.,[14] 26.4% of 72 patients had *Staphylococcus* infection, while 22.2% of them had *Streptococcus* infection. In our population, 57% of the patients did not have any growth of microorganism in the culture. This culture-negative IE ratio seems to be higher than that observed in reported series. The possible reasons for this condition might be use of antibiotics prior to sampling of blood culture or the presence of fastidious intracellular organisms.[15]

Previous studies reported that IE most commonly involve native mitral and aortic valves.[7,16,17] In a study by Chu et al.,[8] the authors investigated the echocardiographic and microbiological properties of the patients and discovered that 34% of patients had native valve endocarditis and 23% of patients had prosthetic valve endocarditis (PVE). Only 11% of patients had predisposing surgical or dental procedures. In our study, 74.8% patients had NKE while 20.2% patients had PVE. Vegetation was present in 43 (36%) patients; 36 patients had aortic valve involvement, and 23 patients had mitral valve involvement. Comparable with the literature, 14.3% of our patients had predisposing surgical or dental procedures.

Mathew et al.[18] investigated the complications of IE in 114 patients and revealed severe aortic insufficiency in 7%, and severe mitral regurgitations in 3%. In our population, severe mitral regurgitation was present in 41.4% of patients, severe aortic regurgitation in 47% of patients and severe tricuspid regurgitation in 18% of patients, including the cases with prosthetic valves. Hence, the frequency of surgical operation for valvular insufficiency due to IE was higher than the literature (75.6% of all cases). In our study, the frequency of congestive heart failure was 53.8% (64 patients), which was similar to a recent series of 68 patients by Tuğcu et al.[11]

Limitations

One of the limitations of our study is its retrospective observational design. Other limitations are the limited number of patient population, the high per-

centage of patients referred from other hospitals that had initiated antibiotherapy, and other possible infectious causes which might have led to the higher percentage of culture-negative cases. This situation might explain in part the high complication rates of our patient population.

This study revealed that IE is still an important disease with high morbidity and mortality rates. Compared to other western studies, a higher prevalence of rheumatic heart disease rate still exists, but shows a decrease when compared to previous national studies. Also, higher culture negativity reflects the under- estimation of IE by primary and secondary centers, so this is a handicap. TEE usage was found to be higher than in previous national studies, but lower than in studies in western societies, which may be a result not of any technical insufficiency, but of the obvious presentation of the disease in younger rather than older persons, with valvular calcifications, devices and co-morbidities, which decreases the necessity for the usage of TEE. Hence, this study revealed that IE management is better than in the past, but continues to be inadequate.

Conflict-of-interest issues regarding the authorship or article: None declared

REFERENCES

1. Leviner E, Tzukert AA, Benoliel R, Baram O, Sela MN. Development of resistant oral viridans streptococci after administration of prophylactic antibiotics: time management in the dental treatment of patients susceptible to infective endocarditis. Oral Surg Oral Med Oral Pathol 1987;64:417-20. CrossRef
2. Durack DT, Lukes AS, Bright DK. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Duke Endocarditis Service. Am J Med 1994;96:200-9. CrossRef
3. Elbey MA, Akdağ S, Kalkan ME, Kaya MG, Sayın MR, Karapınar H, et al. A multicenter study on experience of 13 tertiary hospitals in Turkey in patients with infective endocarditis. Anadolu Kardiyol Derg 2013;13:523-7.
4. Crawford MH, Durack DT. Clinical presentation of infective endocarditis. Cardiol Clin 2003;21:159-66. CrossRef
5. Habib G, Hoen B, Tornos P, Thuny F, Prendergast B, Vilacosta I, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for Infection and Cancer. Eur Heart J 2009;30:2369-413. CrossRef
6. Heper G, Yorukoglu Y. Clinical, bacteriologic and echocardiographic evaluation of infective endocarditis in Ankara, Turkey. Angiology 2002;53:191-7. CrossRef
7. Ferreiros E, Nacinovich F, Casabé JH, Modenesi JC, Swieszkowski S, Cortes C, et al. Epidemiologic, clinical, and microbiologic profile of infective endocarditis in Argentina: a national survey. The Endocarditis Infecciosa en la República Argentina-2 (EIRA-2) Study. Am Heart J 2006;151:545-52. CrossRef
8. Chu J, Wilkins G, Williams M. Review of 65 cases of infective endocarditis in Dunedin Public Hospital. N Z Med J 2004;117:U1021. CrossRef
9. Schulz R, Werner GS, Fuchs JB, Andreas S, Prange H, Ruschewski W, et al. Clinical outcome and echocardiographic findings of native and prosthetic valve endocarditis in the 1990's. Eur Heart J 1996;17:281-8. CrossRef
10. Bonow RO, Carabello BA, Chatterjee K, de Leon AC Jr, Faxon DP, Freed MD, et al. ACC/AHA 2006 practice guidelines for the management of patients with valvular heart disease. Executive summary: a report of the American College of Cardiology/ American Heart Association Task Force on practice guidelines (writing committee to revise the 1998 guidelines for the management of patients with valvular heart disease) developed in collaboration with the Society of Cardiovascul Anesthesiologists endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. J Am Coll Cardiol 2006;48:598-675. CrossRef
11. Tuğcu A, Yildirimtürk O, Baytaroğlu C, Kurtoğlu H, Köse O, Sener M, et al. Clinical spectrum, presentation, and risk factors for mortality in infective endocarditis: a review of 68 cases at a tertiary care center in Turkey. Turk Kardiyol Dern Ars 2009;37:9-18.
12. Cetinkaya Y, Akova M, Akalin HE, Aşçioğlu S, Hayran M, Uzuns O, et al. A retrospective review of 228 episodes of infective endocarditis where rheumatic valvular disease is still common. Int J Antimicrob Agents 2001;18:1-7. CrossRef
13. Benn M, Hagelskjaer LH, Tvede M. Infective endocarditis, 1984 through 1993: a clinical and microbiological survey. J Intern Med 1997;242:15-22. CrossRef
14. Sucu M, Davutoğlu V, Ozer O, Aksoy M. Epidemiological, clinical and microbiological profile of infective endocarditis in a tertiary hospital in the South-East Anatolia Region. Turk Kardiyol Dern Ars 2010;38:107-11.
15. Krcmery V, Hricak V, Babelova O. Culture negative endocarditis: analysis of 201 cases. Scand J Infect Dis 2007;39:384.
16. Letaief A, Boughzala E, Kaabia N, Ernez S, Abid F, Ben Chaabane T, et al. Epidemiology of infective endocarditis in Tunisia: a 10-year multicenter retrospective study. Int J Infect Dis 2007;11:430-3. CrossRef

17. Gotsman I, Meirovitz A, Meizlish N, Gotsman M, Lotan C, Gilon D. Clinical and echocardiographic predictors of morbidity and mortality in infective endocarditis: the significance of vegetation size. Isr Med Assoc J 2007;9:365-9.
18. Mathew J, Anand A, Addai T, Freels S. Value of echocardiographic findings in predicting cardiovascular complications in infective endocarditis. Angiology 2001;52:801-9. CrossRef

Key words: Diagnosis, differential; echocardiography, transesophageal; endocarditis, bacterial/diagnosis.

Anahtar sözcükler: Tanı, ayırıcı; ekokardiyografi, transözofajiyal; endokardit, bakteriyel/tanı.