

Kardiyak cihazlara bağlı olarak gelişen enfektif endokardit; 15 olgunun analizi

Cardiac device- related infective endocarditis; analysis of 15 cases

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ÖZET

Amaç: Bu çalışmada, kalıcı pacemaker (PM) ve implante edilebilir kardiyoversiyon defibrilatörleri (ICD) ile ilişkili endokarditin demografik, klinik ekokardiyografik ve mikrobiyolojik özellikleri ve sonuçlarının araştırılması amaçlandı.

Çalışma planı: Kalıcı PM ve ICD endokarditi tanısı olan 15 hasta çalışmaya alındı. Hastaların demografik özellikleri, kullandıkları ilaçlar, klinik ve mikrobiyolojik özellikleri, ekokardiyografi sonuçları, cerrahi tedavi ve sonuçları kaydedildi.

ABSTRACT

Objectives: We aimed to investigate the demographic and clinical characteristics, echocardiographic and microbiologic features, and outcomes of patients with permanent pacemaker (PM), and implantable cardioverter-defibrillator (ICD) –related endocarditis in this study.

Study design: The study population consisted of 15 patients with permanent PM and ICD-related endocarditis. Data on patients' demographic characteristics,

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Bulgular: Hastaların ortalama yaşı 57 ± 16 ve 7'si (%47) kadındı. Kalıcı PM ve ICD'si olan 15 hastadan 5'i takip sırasında kaybedildi (%33). Dört hastada pulmoner emboli gelişti (%27). Kan kültürü 5 hastada (%33) negatif bulundu. Hastaların %60'ında üretilen stafilokoklar en sık saptanan mikrobiyolojik ajanlardı. Üç hastaya (%20) cerrahi tedavi uygulandı.

Sonuç: Kardiyak cihazlarla ilişkili endokardit, kardiyak cihaz implantasyonun nadir bir komplikasyonu olmasına rağmen mortalitesi halen yüksek olan bir hastalıktır.

medications used, clinical, and microbiological data, echocardiographic findings, types, and outcomes of surgical treatments were recorded.

Results: The mean age of the patients was 57 ± 16 . Seven patients (47%) were female. Of the 15 patients with permanent PM and ICD-related endocarditis, 5 died during in-hospital follow-up (33%). In four patients (27%) pulmonary embolism developed. Culture-negative endocarditis was detected in 5 cases (33%). Staphylococci were the most common causative organisms in 60% of the patients. Three (20%) patients underwent surgical treatment

Conclusion: Cardiac device-related endocarditis remains a rare complication of intracardiac device implantation still with higher mortality rates.

Abbreviations:

CRP	C-reactive protein
IE	Infective endocarditis
ICD	Implantable cardioverter - defibrillator
CD	Cardiac device
PM	Pacemaker
TEE	Transesophageal echocardiography
TTE	Transthoracic echocardiography

Infections related to cardiac devices as permanent pacemakers (PM), implantable cardioverter –defibrillators are serious diseases accompanied by higher rates of mortality.^[1] In the whole world, increasing number of patients have been undergoing permanent PM, and ICD implantation. ^[2,3] Indications, and rates of usage of these

devices gradually increase with aging of the population in general.^[4] In parallel with the increasing rates of permanent PM, and ICD use, incidence of device-related infections also rises.^[5] Increase in the incidence of mortality, morbidity, hospital stays, and economic losses related to the development of endocarditis is seen.^[6] In ICD endocarditis, mortality rates have been reported as 31, and 66 % in cases where the device is removed, and 18 % in the setting of aggressive medical therapy. ^[7,8] Scarce number of investigations related to endocarditis developed secondary to permanent PM, and

intracardiac devices have been conducted in our country.^[9-14]

Our aim is to investigate epidemiological, clinical, and microbiological characteristics of infective endocarditis (IE) developed related to permanent PM, and ICD devices used in tertiary-care university/training, and research hospitals.

PATIENTS AND METHOD

Two hundred and forty eight patients treated in tertiary-care university/training and research hospitals between 2005, and 2012 with the diagnosis of IE were investigated retrospectively. Among these patients clinical, and microbiological features of 15 patients who were diagnosed as permanent PM, and ICD-lead endocarditis were analyzed.

Table 1. Demographic features, symptoms, signs, and laboratory results of the patients at admission

	Frequency (n=15)		Mean \pm SD
	n	%	
Gender (Male)	8	53	
Admission symptoms			
Fever	11	73	
Dyspnea	10	67	
Lassitude	5	33	
Loss of appetite	2	13	
Chills	2	13	
Loss of weight	1	7	
Systolic blood pressure (mm Hg)			105 \pm 10
Diastolic blood pressure (mm Hg)			70 \pm 8
Mean heart rate (min)			87 \pm 12
Hemoglobin (g/dl)			12 \pm 2
WBC (n/ml)			18758 \pm 8300
Sedimentation rate (mm/h)			61 \pm 27
C-reactive protein (mg/dl)			67 \pm 66
Creatinine (mg/dl)			1.25 \pm 0.9
Mean age (year)			57 \pm 16

SD: standard deviation.

As is the case with other forms of infective endocarditis, in ICD endocarditis, blood cultures, and echocardiographic examinations constitute the cornerstone of the diagnostic process. However in ICD-related endocarditis, normal echocardiographic evaluation does not rule out the diagnosis of IE. Both transthoracic echocardiography (TTE), and transesophageal echocardiography (TEE)

can yield false-negative results..^[15]

Diagnosis of IE was made based on modified Duke's criteria.^[16] PM or ICD-related IE was considered when vegetation on lead or valve is detected by echocardiographic examination or Duke's criteria were met. ICD endocarditis was confirmed by detection of positive blood cultures. Cases who couldn't meet modified Duke criteria, and those with

generator pocket infection were not included in the study. From file records of the centers participated in the study, data related to clinical features, concomitant diseases, morbidities predisposing to IE, culture results, echocardiographic findings, laboratory results, in-hospital complications, and mortality were retrieved. Pretreatment C-reactive protein (CRP), erythrocyte sedimentation rate, white blood cell counts, hemoglobin values, and renal functions were recorded. All patients had been investigated as for diagnosis, and potential complications using TTE, and TEE was performed for cases with inadequate imaging quality obtained by TTE. For the conduction of our study approval of the Institutional Ethics Committee of our hospital has been obtained.

Statistical method

For statistical analysis, data were evaluated using statistical program "SPSS for Windows v. 16.0" Data were given as numbers, percentages, means (\pm SD).

RESULTS

Mean age of the patient population which consisted of 8 (53 %) men, and 7 (47 %) women was 57 ± 16 (24-80 yrs) years. The most frequent complaints observed in patients with IE were fever, and lassitude. Fever was the most frequently seen physical finding in 11 (73 %) cases, while lassitude was noted in 5

(33 %) cases. Among laboratory findings, increased levels of CRP, sedimentation rate, and WBC counts were remarkable. Demographic data, and symptoms, and laboratory findings at admission are seen in Table 1.

The patients had diabetes mellitus (n=4; 27 %), and chronic renal failure (n=3; 20 %). Three patients had to be operated, and in 2 cases leads had to be removed. Seven patients were monitored with only medical therapy. Clinical characteristics of 15 patients with ICD-related endocarditis are summarized in Table 2.

Mean left ventricular ejection fraction of the patients was estimated as 40 \pm 14 percent. The most important echocardiographic finding was vegetation found in 93 % (n=14) of the patients. Multiple vegetations (n=4; 27 %), vegetations larger than 10 mm (n=7; 47 %) were also seen. TTE, and TEE detected vegetations in a total of 14 patients (n=7) for both imaging modalities. Echocardiographic findings in IE patients are seen in Table 3.

The patients were examined as for the causative microorganisms (Table 4), and the most frequently detected microorganism was *S. aureus* in 8 (53%) cases. In the cultures obtained, growth of *S.epidermidis* (n=1), and *Pseudomonas aeruginosa* (n=1) was seen, while any microorganism was not isolated in 5 (33%) cases.

Table 2. Clinical characteristics of the patients

	PM endocarditis (n=10)	ICD endocarditis (n=5)
CRF	1	2
Diabetes mellitus	3	1
Death	3	2
Surgical intervention	3	0
Only medical therapy	7	5
Removal of the lead	2	0
Septic shock	1	2
Pulmonary embolism	3	1
Stroke	1	0
Atrial fibrillation	1	0
NYHA-III/IV	7	2

PM: Pacemaker; ICD: Implantable cardioverter-defibrillator;
CRF: Chronic renal failure; NYHA: New York Heart Association.

Table 3. Echocardiographic features of the patients

	Frequency (n=15)	%
Vegetation		
Multiple vegetation	4	27
Mobile vegetation	10	67
> 10 mm vegetation	7	47
Vegetation on the tricuspid valve	3	20
Vegetation detected on TEE	14	47
Vegetation detected on TTE	7	47
Tricuspid regurgitation	13	87
Mitral regurgitation	7	47
Ejection fraction (%)	40 ± 14	
Hospital stay (day)	26 ± 17	

TTE: Transthoracic echocardiography; TEE: Transesophageal echocardiography

Table 4. Causative microorganisms of infective endocarditis

Microorganism	n	%
Staphylococci	9	60
<i>Staphylococcus aureus</i>	8	53
<i>Staphylococcus epidermidis</i>	1	7
Gram-negative microorganisms		
<i>Pseudomonas aeruginosa</i>	1	7
Culture-negative strains	5	33
Total	15	

DISCUSSION

Despite developments in the design of the devices, and implantation techniques, ICD infections remain to be serious issues. In this study, 10 patients with PM, and 5 with ICD endocarditis

treated with the diagnosis of IE based on modified Duke's criteria in tertiary care university/training and research hospitals were retrospectively analyzed. Our study is the first multi-centered retrospective study performed in Turkey.

Fever is the most important symptom and sign in patients with infective endocarditis. In cases with unexplained fever in a patient with a cardiac device should arise the suspicion of IE related to CD. However especially in elder patients, fever is usually suppressed. CD-related IE is one the most challenging diagnosis among other forms of IE. Its clinical picture with predominant rheumatologic, and respiratory symptoms is often misleading.^[15,17] In our study fever was the most frequently (73 %) seen symptom. Shortness of breath, lassitude, and loss of appetite were other important complaints.

The role played by echocardiography in the diagnostic work-up of IE developed secondary to cardiac devices is very important. Echocardiography is helpful in the detection of lead vegetation, and involvement of tricuspid valves, and determination of tricuspid regurgitation.^[15]

Though sensitivity, and specificity of TEE are higher than TTE, in cases with suspect CD-related endocarditis, application of both methods have been recommended.^[7] In cases where TTE remains inadequate, TEE aids in the diagnosis. In our case, vegetations unrevealed by TTE in 7 patients, were demonstrated by TEE. Besides, in 14 (93 %) patients, vegetations were detected by combined use of TTE, and TEE.

Knowledge of etiology, and microbiological agent is quite important with respect to effective treatment. CD-related blood cultures is positive in 77 % of the cases.^[18] Staphylococci are the most prevalent pathogens.^[12,19,20] Gram-negative bacilli rank second among pathogenic agents.^[19] Although, differences between studies have been demonstrated, blood culture-negativity has been reported in 28-60 % of the cases.^[21,22] In our study staphylococci were the most frequently (60 %) detected microorganisms. Our blood culture-negativity was found to be in compliance with (33 %) the literature findings.

In the monitorization of the patients with infective endocarditis, many laboratory tests can be helpful. Anemia, and leukocytosis can be observed in 50-70 % of the patients.^[23] Sedimentation, and elevated CRP levels are found in most of the patients with IE. Laboratory tests revealed the presence of leukocytosis in 11 (73 %), increased CRP levels in 10 (66 %), and higher erythrocyte sedimentation rates in 12 (80 %) patients, respectively.

In most of the patients with cardiac device-related IE, removal of the device, together with long-term antibiotherapy is required.^[18,24] In most of the patients, lead can be removed percutaneously, without the need for a surgical intervention. However if the ICD was implanted few years ago, then percutaneous withdrawal of the lead creates difficulties.^[25] Surgical

intervention is recommended in the presence of severe endocarditis involving tricuspid valve or in patients with large vegetations.^[18,26] In our study, 3 patients underwent surgical intervention, 2 patients regained their health, and one patient died from postoperative septic shock. One of the two patients who had their leads removed percutaneously was lost because of pulmonary embolism. Septic pulmonary embolism is a very widespread complication of CD-related IE.^[15] In this study, septic embolism developed in 4 patients, and 2 of them died from this complication.

In conclusion, CD-related endocarditis is a rare complication of CD implantation. Despite developments in the diagnostic procedure, medical, surgical treatment, and CD designs, IE is still a serious disease with higher mortality.

Limitations of the study

Duke's criteria has a higher sensitivity in the detection of endocarditis involving the left heart, however its sensitivity is relatively lower in CD-related endocarditis. Therefore, employment of Duke's criteria in the diagnosis of IE, is one of the limitations of the present study. Besides, scarce number of our cases is another limitation of our study.

Conflict of Interest: None declared.

REFERENCES

1. Rundström H, Kennergren C, Andersson R, Alestig K, Høgevik H. Pacemaker endocarditis during 18 years in Göteborg. *Scand J Infect Dis* 2004;36:674-9.
2. Goldberger Z, Lampert R. Implantable cardioverter-defibrillators: expanding indications and technologies. *JAMA* 2006;295:809-18.
3. Birnie D, Williams K, Guo A, Mielniczuk L, Davis D, Lemery R, et al. Reasons for escalating pacemaker implants. *Am J Cardiol* 2006;98:93-7.
4. Margey R, McCann H, Blake G, Keelan E, Galvin J, Lynch M, et al. Contemporary management of and outcomes from cardiac device related infections. *Europace* 2010;12:64-70.
5. Voigt A, Shalaby A, Saba S. Rising rates of cardiac rhythm management device infections in the United States: 1996 through 2003. *J Am Coll Cardiol* 2006;48:590-1.
6. Chu VH, Crosslin DR, Friedman JY, Reed SD, Cabell CH, Griffiths RI, et al. *Staphylococcus aureus* bacteremia in patients with prosthetic devices: costs and outcomes. *Am J Med* 2005;118:1416.
7. Cacoub P, Leprince P, Nataf P, Hausfater P, Dorent R, Wechsler B, et al. Pacemaker infective endocarditis. *Am J Cardiol* 1998;82:480-4.
8. Klug D, Lacroix D, Savoye C, Goullard L, Grandmougin D, Hennequin JL, et al. Systemic infection related to endocarditis on pacemaker leads: clinical presentation and management. *Circulation* 1997;95:2098-107.
9. Cetinkaya Y, Akova M, Akalin HE, Aşçıoğlu 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.
10. Leblebicioglu H, Yilmaz H, Tasova Y, Alp E, Saba R, Caylan R, et al. Characteristics and analysis of risk factors for mortality in infective endocarditis. *Eur J Epidemiol* 2006;21:25-31.
11. 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.
12. Tuğcu A, Yildirimtürk O, Baytaroglu 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.

13. Erbay AR, Erbay A, Canga A, Keskin G, Sen N, Atak R, et al. Risk factors for in-hospital mortality in infective endocarditis: five years' experience at a tertiary care hospital in Turkey. *J Heart Valve Dis* 2010;19:216-24.
14. İnanç T, Kaya MG, Kaya EG, Doğan A, Ardiç İ, Doğu O, ark. İnfektif endokardit: Retrospektif olarak 27 hastanın değerlendirilmesi. *Tıp Araştırmaları Dergisi* 2007;5:91-9.
15. 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.
16. Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis* 2000;30:633-8.
17. Klug D, Lacroix D, Savoye C, Goullard L, Grandmougin D, Hennequin JL, et al. Systemic infection related to endocarditis on pacemaker leads: clinical presentation and management. *Circulation* 1997;95:2098-107.
18. Sohail MR, Uslan DZ, Khan AH, Friedman PA, Hayes DL, Wilson WR, et al. Infective endocarditis complicating permanent pacemaker and implantable cardioverter-defibrillator infection. *Mayo Clin Proc* 2008;83:46-53.
19. Erdinler İ, Karahan A, Zor U, Ökmen E. Kalp pili ile ilişkili endokarditler ve tedavi yaklaşımları. *Türk Kardiyol Dern Ars* 2001;29:577-83.
20. Cay S, Gürel OM, Korkmaz S. Clinical and epidemiological characteristics of infective endocarditis. [Article in Turkish] *Türk Kardiyol Dern Ars* 2009;37:182-6.
21. Sohail MR, Uslan DZ, Khan AH, Friedman PA, Hayes DL, Wilson WR, et al. Management and outcome of permanent pacemaker and implantable cardioverter-defibrillator infections. *J Am Coll Cardiol* 2007;49:1851-9.
22. Greenspon AJ, Prutkin JM, Sohail MR, Vikram HR, Baddour LM, Danik SB, et al. Timing of the most recent device procedure influences the clinical outcome of lead-associated endocarditis results of the MEDIC (Multicenter Electrophysiologic Device Infection Cohort). *J Am Coll Cardiol* 2012;59:681-7.
23. 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.
24. Rundström H, Kennergren C, Andersson R, Alestig K, Hogeveik H. Pacemaker endocarditis during 18 years in Göteborg. *Scand J Infect Dis* 2004;36:674-9.
25. Meier-Ewert HK, Gray ME, John RM. Endocardial pacemaker or defibrillator leads with infected vegetations: a single-center experience and consequences of transvenous extraction. *Am Heart J* 2003;146:339-44.
26. Ruttman E, Hangler HB, Kilo J, Höfer D, Müller LC, Hintringer F, et al. Transvenous pacemaker lead removal is safe and effective even in large vegetations: an analysis of 53 cases of pacemaker lead endocarditis. *Pacing Clin Electrophysiol* 2006;29:231-6.

Anahtar sözcükler: Defibrilatör, takılabilir/yan etki; endokardit/tanı/önleme ve kontrol /tedavi; kalp pili; kardioloji.

Key words: Defibrillators, implantable/adverse effects; endocarditis/diagnosis/prevention & control /therapy; pacemaker, artificial; cardiology.