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# Epidemiological, Clinical, and Prognostic Features of Infective Endocarditis: A Retrospective Study with 90 Episodes

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## *Abstract*

**Objective:** To evaluate the epidemiological, clinical, microbiological, and echocardiographic features, as well as the prognosis and long-term outcome of patients with infective endocarditis.

**Methods:** The clinical records and follow-up data of 90 endocarditis episodes in 86 patients diagnosed with definite and possible infective endocarditis according to the modified Duke criteria in a tertiary university hospital, between 1998 and 2016, were reviewed.

**Results:** Fifty-six patients were male (65.1%), and the mean age was 49.9 ± 14.3. Native valve endocarditis constituted 62.2% of the cases, while the remaining patients had prosthetic valve endocarditis. The aortic (34.4%) and mitral (24.4%) valves were infected more frequently. Streptococci (27.7%) and staphylococci (24.4%) were the most frequently isolated microorganisms. Embolic complications (35.5%) were the leading cause of morbidity, followed by valve insufficiency (28.8%) and heart failure (21.1%). Valve replacement surgery was performed in 28 patients (31%). The in-hospital mortality rate was 15.1% ($n$ = 13). Chronic renal failure ($P$ = .042) and degenerative valves ($P$ = .036) were significantly associated with mortality. Among 43 of the 73 cases available for telephonic survey, 36 (83.7%) patients were alive and without disease, with a median follow-up of 52.9 (4-163) months. Twenty-five (69.4%) of these patients were younger than 55 years, and 24 (66.6%) had native valve endocarditis.

**Conclusion:** Underlying cardiac conditions and chronic renal failure increase mortality in infective endocarditis, regardless of the pathogen. Long-term survival seems promising in cases with native valve endocarditis and in younger patients with low rates of comorbidities.

**Keywords:** Infective endocarditis, epidemiology, prognosis, mortality, long-term outcome

## *İnfektif Endokarditin Epidemiyolojik, Klinik ve Prognostik Sonuçları: 90 Atağın Retrospektif Kohortu Öz*

**Amaç:** İnfektif endokardit tanısıyla izlenen hastaların epidemiyolojik, klinik, mikrobiyolojik, ekokardiyografik özellikleri, prognozu ve uzun dönem sonuçlarını değerlendirmek.

**Yöntemler:** 1998 ve 2016 yılları arasında bir üniversite hastanesinde modifiye Duke kriterlerine göre kesin ve olası infektif endokardit tanısı konan 86 hastanın 90 endokardit atağının klinik kayıtları ve takip verileri retrospektif olarak incelendi.

**Bulgular:** Çalışmamızda hastaların 56'sı (%65,1) erkek ve ortalama yaş 49,9 ± 14,3 idi. Doğal kapak endokarditi olguların %62,2'sini oluştururken, diğerlerinde protez kapak mevcuttu. En sık aort (%34,4) ve mitral (% 24,4) kapak tutulumu saptandı. Etken olarak streptokoklar (%27,7) ve stafilokoklar (%24,4) en sık izole edilen mikroorganizmalardı. Tüm komplikasyonlar içinde embolik komplikasyonlar (%35,5) ilk sırada yer almış, bunu kapak yetmezlikleri (%28,8) ve kalp yetmezliği (%21,1) izlemiştir. Hastaların 28'ine (%31) kapak replasman operasyonu yapılmış ve tüm hastalar içinde 13 hasta (%15,1) hastane takibinde kaybedilmiştir. Mortalite kronik böbrek yetmezliği ($P$ = ,042) ve dejeneratif kapak hastalarında ($P$ = ,036) istatistiksel olarak daha anlamlı bulundu. Taburculuk sonrası prognoz ve uzun dönem sonuçlar değerlendirildiğinde sağ kalan 73 hastanın 43'üne ulaşılabilmiş ve bu hastalardan 36'sının (%83,7) ortalama 52,9 ay (4-163) hayatta ve genel durumlarının iyi olduğu, 25 hastanın (%69,4) <55 yaş, 24'ünün (%66,6) doğal kapak endokarditi tanısıyla izlenmiş olduğu görülmüştür.

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**Sonuç:** İnfektif endokardit hastalarında altta yatan kalp hastalıkları ve kronik böbrek yetmezliği patojenden bağımsız olarak mortaliteyi arttırmaktadır. Doğal kapak endokarditi ve komorbiditeleri daha az olan genç yaş hastalarda ise uzun dönem sağkalım umut verici görünmektedir.

**Anahtar Kelimeler:** İnfektif endokardit, epidemiyoloji, prognoz, mortalite, uzun dönem sonuç

Infective endocarditis (IE) remains a relatively common challenging clinical entity with high rates of mortality. The incidence of IE is 3-7/100 000 worldwide, varying in epidemiology.[1,2] Mortality is approximately 20%, even in high-income countries.[3,4] The cardiac risk factors for IE include rheumatic valvular disease, prosthetic or degenerative valve, and congenital heart diseases, which differ according to several socio-economic indicators.[5] In high-income countries, although the incidence of rheumatic valvular heart disease has decreased, degenerative heart valve disease has increased in parallel to the increased number of patients in the elderly population. On the contrary, the patient population with rheumatic valvular disease is dramatically younger in low-income countries, as it is an ongoing problem. Due to a low socio-economic situation, community-acquired cases are more frequent than healthcare-associated cases, and the pathogenic microorganisms vary over a broader spectrum.[6] Besides epidemiology, the diagnostic methods and treatment modalities of IE have also significantly changed during the last decade.[7,8] Streptococci and staphylococci account for 80% of the etiology.[6] In recent years, staphylococci have increased proportionally due to the increase in healthcare-associated endocarditis.

National studies have reported that acute rheumatic fever (ARF) is the leading cause of valvular disease in Turkey.[9] Although a decrease has been reported during recent years, the incidence of ARF is still as high as 20/100 000,[9-11] which may correlate to the relatively high incidence of IE in Turkey. Intracardiac foreign bodies also constitute a risk factor for IE and are considered to be responsible for 10% of all IE cases. Implant-related IE consists of approximately 6% of the cases in Turkey.[12] Intravenous drug use, which is a very rare cause in our country affecting less than 1% of the cases, is a predisposing factor in 10% of all IE cases in high-income countries.[3,12]

In this study, we aimed to evaluate the epidemiological, clinical, laboratory, echocardiographic, and microbiological characteristics, as well as the treatment outcomes of IE in a tertiary referral center.

## Methods

Retrospectively collected data of the patients diagnosed with IE in our institution between 1998 and 2016 were reviewed. Patients older than 18 years with an International Classification of Disease code of any type of IE were included in the study. The study was approved by the local ethics committee. Informed consents for all medical treatments and for collecting and using the data in clinical studies were received from all patients. Patients who did not meet the definitive diagnostic criteria and patients without complete records of clinical follow-up were excluded.

The blood cultures were performed by automated hemoculture systems. Conventional procedures were used for microbiological identification. Antimicrobial susceptibility tests were performed according to the current Clinical and Laboratory Standards Institute criteria. All the samples were examined in the institutional microbiology laboratory.

Modified Duke criteria were used for definitions. Patients with IE were classified as having "acute" endocarditis if the duration between initial symptom and diagnosis was <6 weeks, "subacute" if between 6 weeks and 3 months, and "chronic" if >3 months. An IE episode was defined as "nosocomial healthcare-associated" if positive blood cultures were obtained from a patient hospitalized for more than 48 hours without relevant symptoms and signs on admission. "Non-nosocomial healthcare-associated" IE was defined if at least one of the following criteria was present within 48 hours of the patient's admission: (1) had received intravenous therapy, wound care, specialized nursing care, hemodialysis or intravenous chemotherapy within 30 days prior to the onset of IE, (2) was hospitalized in an acute care hospital for 2 or more days within 90 days before the onset of IE, or (3) resided in a nursing home or long-term care facility before admission.[13] The infection was recorded as "community-acquired" when the symptoms and signs of IE occurred within 48 hours of admission in a patient not fulfilling the criteria for non-nosocomial healthcare-associated infection. Cases with prosthetic valve endocarditis were tiered into 2 groups, as "early" (within 1 year after operation) and "late" (endocarditis >1 year of operation).

Ethical approval was obtained from the scientific Ethics Committee of İstanbul University-Cerrahpaşa with the approval number 83045809/604.01/02-405910 dated December 23, 2015.

### Statistical analysis

The IBM Statistical Package for the Social Sciences 22.0 (IBM SPSS Corp., Armonk, NY, USA) package

**Table 1.** Epidemiological characteristics, symptoms, and clinical and laboratory findings of the patients ($n$ = 90)

| **Characteristics, *n* (%)** | **Clinical findings, *n* (%)** |
|---|---|
| **Cardiac risk factors** | Fatigue 90 (100) |
| Chronic rheumatic heart disease 29 (33.7) | Sweating 87 (96.6) |
| Prosthetic valve 32 (37.2) | Fever 85 (94.4) |
| Degenerative heart valve disease 22 (25.5) | Anorexia and weight loss 43 (47.7) |
| Congenital heart defects 13 (15.1) | Dyspnea 16 (17.7) |
| **Non-cardiac risk factors** | Lumbar and back pain 4 (4.4) |
| Dental procedure 9 (10.4) | **Laboratory findings** |
| Diabetes mellitus 8 (9.3) | Cardiac murmur 63 (70) |
| Chronic renal failure 6 (6.9) | Hepatomegaly/splenomegaly 24 (26.6) |
| Hemodialysis 3 (3.4) 3 (3.4) | Arthralgia 4 (4.4) |
| Central venous catheter 2 (2.3) | Roth spot ($n$ = 33) 2 (6)† |
| Intravenous drug use 1 (1.1) | Osler nodules 1 (1.1) |
| **Epidemiological classification** | Cerebrovascular and peripheral 32 (35.5) findings of emboli |
| Community-acquired 78 (86.6) | Hematuria ($n$ = 68) 18 (26.4)† |
| Healthcare-associated 12 (13.3) | Rheumatoid factor positivity ($n$ = 29) 9 (31)† |
| Nosocomial 2 (2.2) | Elevated C-reactive protein 87 (96.6) |
| Non-nosocomial 10 (11.1) | Elevated ESR ($n$ = 81) 74 (91.3)† |
| Native valve endocarditis 56 (62.2) | |
| Prosthetic valve endocarditis 34 (37.7) | |
| **Clinical onset and course** | |
| Acute endocarditis 50 (56) | |
| Subacute endocarditis 20 (22) | |
| Chronic endocarditis 20 (22) | |

†Roth spot was investigated in 33, Urinalysis was performed in 68, RF was investigated in 29, and ESR was detected in 81 episodes.
*Abbreviations*: PE, Physical examination; ESR, Erythrocyte sedimentation rate.

program was used for statistical analyses. Continuous variables were expressed as means and ranges, and categorical variables as frequencies and percentages. The association between categorical variables and age was determined with the chi-square test. The association between continuous variables and age was tested by the independent samples *t*-test. *P* values < .05 were defined as statistically significant.

## Results

There were 114 patients in total who were admitted with an IE diagnosis. Twenty-four patients were excluded because they did not meet the diagnostic criteria and/or were lacking follow-up data. Eighty-six patients with 90 IE episodes were included in the analysis. The mean age was 49.9 ± 14.3, 56 (65%) patients were male, and 30 (35%) were female. Definite and possible endocarditis were determined in 71 (78.8%) and 19 (21.2%) cases, respectively.

The most common predisposing condition for IE was a prosthetic valve ($n$ = 32, 37.2%), followed by chronic rheumatic heart disease ($n$ = 29, 33.7%) and degenerative valve disease ($n$ = 22, 25.5%). Out of the 29 patients with a rheumatic valve disease, 6 had a definitive history of ARF. Congenital heart disease was significantly higher in patients <50 years old ($P$ = .048), while degenerative valve disease was more common in patients ≥50 years ($P$ = .004). None of the patients

**Table 2.** The distribution of causative agents ($n = 90$)

| Microorganisms | *n* (%) |
|---|---|
| *Streptococcus* spp. | 25 (27.7) |
| Viridans group streptococci | 20 (22.2) |
| *Streptococcus bovis* | 2 (2.2) |
| *Peptostreptococcus anaerobius* | 2 (2.2) |
| *Lactococcus garvieae* | 1 (1.1) |
| *Staphylococcus* spp. | 22 (24.4) |
| Methicillin-sensitive *Staphylococcus aureus* | 10 (11.1) |
| Methicillin-resistant coagulase-negative staphylococci | 6 (6.6) |
| Methicillin-sensitive coagulase-negative staphylococci | 4 (4.4) |
| Methicillin-resistant *S. aureus* | 1 (1.1) |
| *Kocuria varians* | 1 (1.1) |
| *Enterococcus* spp. | 15 (16.6) |
| *Brucella* spp | 2 (2.2) |
| *Haemophilus parainfluenzae* | 1 (1.1) |
| *Escherichia coli* | 1 (1.1) |
| *Acinetobacter* spp. | 1 (1.1) |
| *Pseudomonas mendocina* | 1 (1.1) |
| *Corynebacterium jeikeum* | 1 (1.1) |
| MSSA + VGS + MSCoNS | 1 (1.1) |
| *Coxiella burnetii*[*] | 1 (1.1) |
| Undefined causative agents | 19 (21.1) |

*Serology (IgG phase I >1 : 800)
*Abbreviations*: MSSA, methicillin-sensitive *S. aureus*; VGS, Viridans group streptococci; MSCoNS, methicillin-sensitive coagulase-negative staphylococci.

had an implanted cardiac device. The clinical features of the cases are shown in Table 1.

Blood cultures and/or serological tests (1 case of *Coxiella burnetii* was verified only serologically) were positive in 71 (78.8%) episodes. None of the cases were histopathologically confirmed. Streptococci (27.7%), staphylococci (24.4%), and enterococci (16.6%) were the most common pathogens isolated in the whole cohort group (Table 2). Regarding community-acquired cases, streptococci accounted for 30%, staphylococci for 21.2%, and enterococci for 17.5%. Staphylococci were identified as the major pathogen among the healthcare-associated cases. The relationship between etiological agent, type of valvular diseases, and age were evaluated. Staphylococci ($P = .016$) and streptococci ($P = .035$) were found to be significantly associated with prosthetic valve endocarditis. There was no statistically significant relationship between the etiological agents (streptococci, staphylococci, and enterococci; $P = .674$, $P = .701$, $P = .129$) and age.

Echocardiography was performed in all the patients. Vegetations were detected in 79 (88%) cases, periannular abscess was detected in 5 (5.5%) cases, and chordal rupture in 4 (4.4%) cases. The aortic valve was the most frequently involved structure (34.4%), followed by the mitral (24.4%), and the mitral + aortic valve (22.2%). Among all complications, embolic complications (35.5%) were the most common. Echographically documented cardiac vegetations were complicated by peripheral emboli in 31.6%, and heart failure in 22.7% of the patients, and mortality was seen in 15%. One-third of the cases with complications underwent surgical valve replacement. In the echography-negative group, peripheral emboli, heart failure, and mortality rates were 36.3%, 19%, and 9.1%, respectively. In one echography-negative patient with *C. burnetii*, valvular involvement was detected by PET-CT. This patient died after valve replacement surgery. The distribution of cardiac and systemic complications is presented in Table 3. The overall in-hospital mortality was 15.1% ($n = 13$). Three of these patients (23%) had chronic renal failure and 7 patients (53.8%) had underlying degenerative heart disease. When the surviving and the deceased patients were compared, the presence of degenerative valve ($P = .036$) and chronic renal failure ($P = .042$) were found as the major determinants of mortality. However, the causative agent, patient age ($P = .080$), clinical course (acute, subacute, or chronic endocarditis) ($P = .093$), and the location of the vegetation ($P = .093$) were not found to be statistically associated with survival. Baseline characteristics and complications of the cases in terms of in-hospital mortality are shown in Tables 4 and 5.

Out of 73 cases, 43 (59%) were available for phone surveys during the post-discharge follow-up. The second IE episode was determined in 4 patients with prosthetic valves in the first year, and 2 patients had died due to a cardiac failure. The other 2 recurrent episodes caused by methicillin-sensitive *Staphylococcus aureus* (MSSA) were medically treated. Five patients died due to other cardiac or non-cardiac conditions. Thirty-four (79%) patients have been followed-up uneventfully, without any sign or symptom of IE or cardiac disease.

**Table 3.** Distribution of systemic and cardiac complications

| **Systemic Complications** | ***n* (%)** |
|---|---|
| Major arterial emboli | 32 (35.5) |
| Cerebral complication | 12 (13.3) |
| Cerebrovascular disease (ischemia/ hemorrhage) | 9 (10) |
| Cerebral artery mycotic aneurysm | 2 (2.2) |
| Cerebral abscess | 1 (1.1) |
| Splenic infarct | 5 (5.5) |
| Splenic infarct + superior mesenteric artery embolism | 1 (1.1) |
| Abdominal aortic mycotic aneurysm | 1 (1.1) |
| Pulmonary emboli | 3 (3.3) |
| Coronary artery emboli | 1 (1.1) |
| Janeway lesions | 3 (3.3) |
| Splinter hemorrhage | 4 (4.4) |
| Skin rashes | 1 (1.1) |
| Septic shock | 2 (2.2) |
| **Cardiac complications** | ***n* (%)** |
| New-onset valve regurgitation (± heart failure) | 26 (28.8) |
| Mitral regurgitation | 18 (20) |
| Aortic regurgitation | 4 (4.4) |
| Tricuspid regurgitation | 4 (4.4) |
| Advanced heart failure (± advanced valve regurgitation) | 19 (21.1) |
| Periannular abscess | 5 (5.5) |
| Chordal rupture | 4 (4.4) |

## Discussion

There has been a slow but prominent shift in the characteristics of IE in high-income countries; from rheumatic valve diseases towards degenerative heart diseases as a major risk factor, from community-acquired cases towards healthcare-associated cases, and from streptococci toward *S. aureus* in the etiology. Our retrospective study, consisting of 90 cases, has partly verified this epidemiologic trend for Turkey.

IE is usually a disease that affects persons over 60, in high-income countries, whereas it is more common at younger ages in low- and middle-income countries.[4] In a retrospective study from Turkey covering IE cases diagnosed between 1974 and 1999, the mean age was 36 and the rate of underlying rheumatic valve disease was 65%.[14] Recent similar studies have demonstrated an apparent decrease in the proportion of rheumatic valve diseases (46%, 36%, 28%), and an increase in the mean age (between 45 and 51).[9,12,15-17] In our study, the mean age of the patients was 49.9, and the rate of rheumatic heart diseases was 33.7%, compatible with the literature. Congenital heart diseases were found more frequently in patients under 50 years of age, and degenerative and prosthetic heart valve diseases were more common in patients over 50 years of age. Intravenous drug use was a risk factor in only 1 patient (1.1%) with tricuspid valve endocarditis. This result was compatible with the data of similar Turkish patients,[12] and considered to be lower when compared with high-income countries where the rate of IV drug use among IE cases is about 10%.[18] Of 90 cases, acute endocarditis ($n$ = 50, 56%) was the most common clinical form, comprised of 24 native valve, 22 "late" prosthetic, and 4 "early" prosthetic valve endocarditis diagnoses. Staphylococci accounted for 38% of the overall etiology of the whole cohort group, with MSSA being the most common among acute and healthcare-associated cases. These findings were compatible with the results of N'Guyen et al.,[19] reporting *S. aureus* as 32.9% in the etiology of "early diagnosed" (vs. 8.9% among late-diagnosed) cases of IE, and Fowler et al.[20] which also reported S. aureus as the most common organism in each major risk group, including cases with intracardiac devices. Among the 20 episodes of "chronic" endocarditis, the Viridans streptococci were more commonly seen in patients below age 60 (2 episodes were due to *Streptococcus bovis*) and enterococci were more common in patients above the age 60, compatible with the study of Olmos et al.[21]

Definite etiology was microbiologically demonstrated in 71 (78.8%) episodes in our study, which was similar to the rate (77.8%) reported in another cohort of 325 cases from Turkey,[12] but lower than some high-income countries reporting a rate of 90%.[18] Staphylococcal endocarditis is much more common in most high-income countries due to the proportional increase of degenerative valve diseases and healthcare-associated cases.[18,22] However, despite the similar epidemiological shift, streptococcal endocarditis remains important in Turkey because of the relatively higher prevalence of rheumatic and congenital valve diseases in the community.[9] The etiology did not statistically differ according to the age (below or above 50 years) or cardiac comorbidities (presence or

**Table 4.** Baseline characteristics of patients with infective endocarditis in terms of in-hospital mortality

| Feature | Total Cases (*n* = 86) Total Episodes (*n* = 90) | Patients Who Died (*n* = 13) | Patients Who Survived (*n* = 73) | *P* |
|---|---|---|---|---|
| **Sex** | | | | .761 |
| Male | 56 | 8 | 48 | |
| Female | 30 | 5 | 25 | |
| **Age, years** | | | | .080 |
| >50 | 47 | 11 | 36 | |
| ≤50 | 39 | 2 | 37 | |
| **Cardiac predisposing factors (*n* = 86 cases)** | | | | |
| Chronic rheumatic heart disease | 29 | 4 | 25 | 1 |
| Degenerative heart disease | 22 | 7 | 15 | .036 |
| Prosthetic heart disease | 32 | 7 | 25 | .147 |
| Congenital heart disease | 13 | 1 | 12 | .681 |
| **Non-cardiac predisposing factors (*n* = 86 cases)** | | | | |
| Chronic renal failure | 6 | 3 | 3 | .042 |
| Hemodialysis | 3 | 1 | 2 | .392 |
| History of previous endocarditis | 6 | 2 | 4 | |
| **Onset of endocarditis (*n* = 90 episodes)** | | | | .093 |
| Acute endocarditis | 50 | 8 | 42 | |
| Subacute endocarditis | 20 | 1 | 19 | |
| Chronic endocarditis | 20 | 4 | 16 | |
| **Origin of infection acquisition (*n* = 90 episodes)** | | | | .683 |
| Community-acquired | 78 | 11 | 67 | |
| Healthcare-associated | 12 | | | |
| Nosocomial | 2 | 0 | 2 | |
| Non-nosocomial | 10 | 2 | 8 | |
| **Type of valve involvement (*n* = 90 episodes)** | | | | .226 |
| Native valve endocarditis | 56 | 6 | 50 | |
| Prosthetic valve endocarditis | 34 | 7 | 27 | |
| Late | 29 | 6 | 23 | |
| Early | 5 | 1 | 4 | |
| **Localization of vegetations (*n* = 90 episodes)** | | | | .093 |
| Aortic valve | 32 | 3 | 28 | |
| Mitral valve | 22 | 4 | 18 | |
| Aortic and mitral valve | 20 | 4 | 16 | |
| Tricuspid valve | 5 | 0 | 5 | |

(*Continued*)

**Table 4.** Baseline characteristics of patients with infective endocarditis in terms of in-hospital mortality (*Continued*)

| Feature | Total Cases (*n* = 86) Total Episodes (*n* = 90) | Patients Who Died (*n* = 13) | Patients Who Survived (*n* = 73) | *P* |
|---|---|---|---|---|
| Aortic, mitral and tricuspid | 1 | 1 | 0 | |
| No defined vegetation | 11 | 1 | 10 | |
| **Surgical intervention (*n* = 90 episodes)** | | | | .533 |
| Surgery applied | 28 | 3 | 25 | .728 |
| No surgery | 62 | 10 | 52 | |
| ***Staphylococcus* spp.** | 22 | 4 | 18 | |
| MSSA | 10 | 2 | 8 | |
| MRSA | 1 | 1 | 0 | |
| MRCoNS | 6 | 1 | 5 | |
| ***Streptococcus* spp.** | 25 | 2 | 23 | .503 |
| *Viridans streptococcus* | 20 | 1 | 19 | |
| *Streptococcus bovis* | 2 | 1 | 1 | |
| ***Enterococcus* spp.** | 15 | 2 | 13 | 1 |
| *Coxiella burnetii* | 1 | 1 | 0 | |
| Undefined causative agents | 19 | 4 | 15 | |

*Abbreviations*: MSSA, methicillin-sensitive *Staphylococcus aureus*; MRSA, methicillin-resistant *S. aureus*; MRCoNS, methicillin-resistant coagulase-negative staphylococci.

**Table 5.** Distribution of complications in cases of death and survival

| Complications | Total Episodes (*n* = 90) | Patients Who Died (*n* = 13) | Patients Who Survived (*n* = 73) |
|---|---|---|---|
| Peripheral embolism | 17 | 1 | 16 |
| Splenic infarct | 5 | 1 | 4 |
| Cerebrovascular complications | 12 | 3 | 9 |
| Ischemia/hemorrhage | 9 | 3 | 6 |
| Congestive heart failure | 19 | 11 | 8 |
| No complication | 71 | 1 | 70 |

absence of rheumatic and congenital heart diseases); while staphylococci ($P$ = .016) and streptococci ($P$ = .035) were significantly more common in cases with prosthetic valve endocarditis.

In our study, embolic complications were the most common (35.5%), followed by valve insufficiency (28.8%), and heart failure (21.1%). Valve replacement was performed in 31% of the cases and in-hospital mortality was 15.1%. Heart failure has been reported in 42-60% of cases with native (mostly aortic) valve endocarditis in the literature.[23,24] The corresponding statistic was 17.8% (10/56) in our native valve cases, and it was only slightly higher (23.8%) in those patients with aortic valve involvements. In a study by Elbey et al.[16] from Turkey, which included 248 patients, heart failure was the leading cause of all complications, at 35.4%, while overall mortality was 33%. Similarly, in the study by Murdoch et al.,[18] the most common complication was heart failure (32.3%), and 48.2% of the patients underwent surgery, while

17.7% mortality was reported. In one of the largest series in our country, the mortality rate was found to be 27.8%, and this situation was explained by the admissions of complicated cases because the hospital was a reference center.[12] The relatively lower rates of cardiac complications and mortality in our study might be due to the early diagnosis and prompt treatment facilities, the younger age of the patients, and lower rates of underlying comorbidities. In the prospective cohort study by Murdoch et al.[18] comprising 2781 patients, acute *S. aureus* endocarditis was associated with poor prognosis and higher mortality. Similarly, according to the prospective study by N'Guyen et al.,[19] which shared the follow-up results of 486 cases that were diagnosed within 1 month, the presence of prosthetic valve and *S. aureus* in the etiology were associated with a poor prognosis, as well as higher mortality during the hospital stay and within a 1-year follow-up. In our data, mortality was significantly associated with a chronic renal failure ($P = .042$) and the presence of underlying degenerative valve disease ($P = .036$). In the study by Netzer et al.[25] evaluating the long-term prognosis of IE, the presence of at least 6 of the symptoms and signs of endocarditis during diagnosis (early diagnosis), absence of heart failure, an age of 55 years and younger, streptococcal etiology, and early surgical intervention were found to be good prognostic indicators. The 10-year survival rate was 50% in the patients.[25] Heart failure was the most common cause of death, and even more rarely, the incidence of a new IE episode was higher than in the general community.[25] In another study conducted by Delahaye et al.[26] which evaluated the long-term prognosis of patients, all-cause mortality in the first year was found to be higher than in the general population, but gradually decreased over time. As expected, the most common cause of mortality was heart failure. Repeated episodes of IE were rare, but more frequent than in the general community.

Of the patients we were able to reach, 36 (83.7%) were alive for an average of 4.27 years (between 6 months and 14 years) and well in general, suggesting a better rate of 10-year survival (50%) in comparison to the recent literature.[25] Having community-acquired native valve endocarditis or being below 55 years of age at the time of diagnosis were the 2 common features that might explain the higher rate of survival.

In conclusion, the current epidemiology and clinical outcomes of IE have been highlighted with this study. Community-acquired native valve endocarditis in patients younger than 55 years and who had lower loads of comorbidities, particularly chronic renal failure, showed better outcomes in short-term and long-term follow-up.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Ethics Committee of İstanbul University-Cerrahpaşa (Date: December 23, 2015, Approval number 83045809/604.01/02-405910).

**Informed Consent:** Written informed consent was obtained from patientst who participated in this study.

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## References

1. Duval X, Delahaye F, Alla F, et al. Temporal trends in infective endocarditis in the context of prophylaxis guideline modifications: three successive population-based surveys. *J Am Coll Cardiol*. 2012;59(22):1968-1976. [CrossRef]

2. Federspiel JJ, Stearns SC, Peppercorn AF, Chu VH, Fowler Jr VG. Increasing US rates of endocarditis with Staphylococcus aureus: 1999-2008. *Arch Intern Med*. 2012;172(4):363-365. [CrossRef]
3. Hoen B, Duval X. Clinical practice. Infective endocarditis. *N Engl J Med*. 2013;368(15):1425-1433. [CrossRef]
4. Selton-Suty C, Célard M, Le Moing V, et al. Preeminence of *Staphylococcus aureus* in infective endocarditis: a 1-year population-based survey. *Clin Infect Dis*. 2012;54(9):1230-1239. [CrossRef]
5. Strom BL, Abrutyn E, Berlin JA, et al. Risk factors for infective endocarditis, oral hygiene and nondental exposures. *Circulation*. 2000;102(23):2842-2848. [CrossRef]
6. İnfektif Endokardit Ş.-Y.S. Güncel bilgiler. *Klimik Derg*. 2015;28(2):46-67.
7. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: diagnosis, Antimicrobial Therapy, and management of complications: A scientific statement for healthcare professionals From the American Heart Association. *Circulation*. 2015;132(15):1435-1486. [CrossRef]
8. Habib G, Lancellotti P, Antunes MJ, et al. ESC Guidelines for the management of infective endocarditis. The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). *Eur Heart J*. 2015;17(4):277-319.
9. Demirbağ R, Sade LE, Aydın M, Bozkurt A, Acartürk E. The Turkish registry of heart valve disease. *Turk Kardiyol Dern Ars*. 2013;41(1):1-10. [CrossRef]
10. Tibazarwa KB, Volmink JA, Mayosi BM. Incidence of acute rheumatic fever in the world: a systematic review of population-based studies. *Heart*. 2008;94(12):1534-1540. [CrossRef]
11. Orün UA, Ceylan O, Bilici M, et al. Acute rheumatic fever in the Central Anatolia Region of Turkey: a 30-year experience in a single center. *Eur J Pediatr*. 2012;171(2):361-368. [CrossRef]
12. Şimşek-Yavuz S, Şensoy A, Kaşıkcıoğlu H, et al. Infective endocarditis in Turkey: aetiology, clinical features, and analysis of risk factors for mortality in 325 cases. *Int J Infect Dis*. 2015;30:106-114. [CrossRef]
13. Benito N, Miró JM, de Lazzari E, et al. Health care-associated native valve endocarditis: importance of non-nosocomial acquisition. *Ann Intern Med*. 2009;150(9):586-594. [CrossRef]
14. Çetinkaya Y, Akova M, Akalın HE, 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):1-7. [CrossRef]
15. 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(2):107-111.
16. Elbey MA, Akdağ S, Kalkan ME, et al. A multicenter study on experience of 13 tertiary hospitals in Turkey in patients with infective endocarditis. *Anadolu Kardiyol Derg*. 2013;13(6):523-527. [CrossRef]
17. Leblebicioğlu H, Yılmaz H, Taşova Y, et al. Characteristics and analysis of risk factors for mortality in infective endocarditis. *Eur J Epidemiol*. 2006;21(1):25-31. [CrossRef]
18. Murdoch DR, Corey GR, Hoen B, et al. Clinical Presentation, Etiology, and Outcome of Infective Endocarditis in the 21st Century: the International Collaboration on Endocarditis-Prospective Cohort Study. *Arch Intern Med*. 2009;169(5):463-473. [CrossRef]
19. N'Guyen Y, Duval X, Revest M, et al. Time interval between infective endocarditis first symptoms and diagnosis: relationship to infective endocarditis characteristics, microorganisms and prognosis. *Ann Med*. 2017; 49(2):117-125. [CrossRef]
20. Fowler VG, Miro JM, Hoen B, et al. *Staphylococcus aureus* endocarditis: a consequence of medical progress. *JAMA*. 2005;293(24):3012-3021. [CrossRef]
21. Olmos C, Vilacosta I, Sarriá C, et al. Streptococcus bovis endocarditis: update from a multicenter registry. *Am Heart J*. 2016;171(1):7-13. [CrossRef]
22. Vogkou CT, Vlachogiannis NI, Palaiodimos L, Kousoulis AA. The causative agents in infective endocarditis: a systematic review comprising 33,214 cases. *Eur J Clin Microbiol Infect Dis*. 2016;35(8):1227-1245. [CrossRef]
23. Nadji G, Rusinaru D, Rémadi JP, et al. Heart failure in left sided native valve infective endocarditis: characteristics, prognosis, and results of surgical treatment. *Eur J Heart Fail*. 2009;11(7):668-675. [CrossRef]
24. Hasbun R, Vikram HR, Barakat LA, Buenconsejo J, Quagliarello VJ. Complicated left-sided native valve endocarditis in adults: risk classification for mortality. *JAMA*. 2003;289(15):1933-1940. [CrossRef]
25. Netzer ROM, Altwegg SC, Zollinger E, et al. Infective endocarditis: determinants of long term outcome. *Heart*. 2002;88(1):61-66. [CrossRef]
26. Delahaye F, Ecochard R, de Gevigney G, et al. The long-term prognosis of infective endocarditis. *Eur Heart J*. 1995;16(supply B):48-53. [CrossRef]