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Original Article

Predictors of In-Hospital Mortality in Infective Endocarditis: A Retrospective Cohort Analysis

Enfektif Endokarditte Hastane İçi Ölüm Oranını Belirleyen Faktörler: Retrospektif Kohort Analizi

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Abstract

Background: Infective endocarditis (IE) remains a disease of high morbidity and mortality. The epidemiological profile has shifted, with fewer rheumatic cases but more healthcare-associated and prosthetic valve infections. Management remains complex, particularly regarding the role of antithrombotic therapies. We evaluated clinical features, microbiology, and predictors of in-hospital mortality among adult IE patients, focusing on anti-platelet therapy.

Materials and Methods We retrospectively reviewed 122 adult patients diagnosed with definite or possible IE at a tertiary University Hospital between 2000-2013 according to modified Duke criteria. Data on demographics, comorbidities, predisposing factors, clinical presentation, laboratory and echocardiographic findings, microbiology, antithrombotic use, surgical management, and outcomes were extracted. Univariable and multivariable analyses were performed to identify predictors of in-hospital mortality. **Results**: Results: The mean age was 52.5 ± 14.2 years; 63.1% were male. Rheumatic fever was present in 35.2%, prosthetic valves in 34.4%, and intracardiac devices in 7.4%. The most frequent pathogen was *Staphylococcus aureus* (25.5%), followed by *streptococc*i (16.3%). Culture-negative endocarditis accounted for 33.3% of cases. The overall in-hospital mortality was 26.2%. Non-survivors were significantly older (57.4 vs. 50.8 years) and had shorter duration of symptoms before admission (<15 days). Multivariable regression showed worsening echocardiographic findings (OR 5.44, p=0.026) and pre-existing antiplatelet therapy (aspirin OR 2.64, p=0.021; other antiplatelets OR 3.95, p=0.015) as the strongest independent predictors of death. **Conclusions:** This study highlights shifting epidemiology in Turkey with increasing age, prosthetic/device-associated cases, and a rising burden of *S. aureus.* Antiplatelet use was independently associated with increased mortality.

Keywords: Anti-platelet treatment, Infective Endocarditis, Mortality, Türkiye

ÖZ

Amaç: İnfektif endokardit (İE) halen yüksek morbidite ve mortaliteye sahip bir hastalıktır. Epidemiyolojik profil değişmiş, romatizmal hastalığa bağlı olgular azalırken sağlık hizmeti ile ilişkili ve protez kapak enfeksiyonları artmıştır. Yönetim hala karmaşık olup özellikle anti-trombotik tedavilerin rolü tartışmalıdır. Bu çalışmada erişkin İE hastalarında klinik özellikler, mikrobiyoloji ve hastane içi mortalite ile ilişkili prediktörler değerlendirildi, özellikle anti-trombosit tedaviye odaklanıldı.

Gereç ve Yöntem: Üçüncü basamak üniversite hastanesinde 2000–2013 yılları arasında modifiye Duke kriterlerine göre kesin veya olası İE tanısı alan 122 erişkin hasta kayıtları retrospektif olarak incelendi. Demografik veriler, eşlik eden hastalıklar, predispozan faktörler, klinik ve laboratuvar bulguları ve ekokardiyografi sonuçları, mikrobiyoloji, antitrombotik tedavi kullanımı, cerrahi tedavi ve sonlanım değerlendirildi. Hastane içi mortalitenin prediktörlerini belirlemek için tek değişkenli ve çok değişkenli analizler yapıldı.

Bulgular: Ortalama yaş 52,5 ± 14,2 yıl olup hastaların %63,1'i erkekti. Romatizmal ateş öyküsü %35,2, protez kapak varlığı %34,4, intrakardiyak cihaz varlığı %7,4 oranında saptandı. En sık izole edilen patojen *Staphylococcus aureus* (%25,5) idi; bunu *streptokoklar* (%16,3) izledi. Kültür negatif endokardit oranı %33,3 olarak bulundu. Genel hastane içi mortalite %26,2 idi. Kaybedilen hastalar daha yaşlıydı (57,4'e karşı 50,8 yıl) ve başvuru öncesi semptom süresi daha kısaydı (<15 gün). Çok değişkenli analizde ekokardiyografide kötüleşme (OR 5,44; p=0,026) ve önceden anti-trombosit tedavi kullanımı (aspirin OR 2,64; p=0,021; diğer anti-trombositler OR 3,95; p=0,015) bağımsız mortalite prediktörleri olarak saptandı.

Sonuç: Bu çalışma, Türkiye'de İE epidemiyolojisindeki değişimi; ileri yaşı, protez/cihaz ilişkili olguların artışını ve dolayısıyla *S. aureus* sıklığının yükselmesini gözler önüne sermektedir. Anti-trombosit tedavi kullanımı bağımsız olarak artmış mortalite ile ilişkili bulunmuştur.

Anahtar Kelimeler: Anti-trombosit tedavi, İnfektif Endokardit, Mortalite, Türkiye

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Highlights

- IE mortality remained high (26.2%), driven by adverse echocardiographic findings.
- *Staphylococcus aureus* was the leading pathogen in an older, prosthetic/device-heavy cohort.
- Pre-existing antiplatelet therapy independently predicted higher mortality.

Introduction

Infective endocarditis (IE) remains one of the most challenging cardiovascular infections due to its protean manifestations, diagnostic complexity, and persistently high mortality. A detailed analysis of global trends, largely informed by the Global Burden of Disease (GBD) study, reveals a significant and sustained increase in both the incidence and absolute number of cases and deaths over the past three decades. The global annual incidence of IE is estimated to be approximately 3-10 per 100,000 people, although study-specific ranges can be wider, from 1 to 15 cases per 100,000 per year, which is likely due to methodological differences (1,2). The epidemiology of IE has evolved considerably: while rheumatic heart disease-related IE has declined in many regions, healthcare-associated IE and prosthetic valve or intra-cardiac device infections have become increasingly prevalent (3). Consequently, the causative microbiology has shifted from oral streptococci toward Staphylococcus aureus, a pathogen linked with more aggressive disease and worse outcomes. Despite advances in diagnosis and treatment, the overall mortality rate remains persistently high, at approximately 25% (1,3).

A further clinical dilemma is the role of antithrombotic therapy during active IE. Thromboembolic events, especially ischemic stroke, are among the most feared complications, occurring in 20–40 % of patients (4). However, anticoagulation and antiplatelet use are controversial and carry a significant risk of hemorrhagic complications, particularly intracranial hemorrhage (ICH), which is strongly associated with poor prognosis (4-8). Observational studies and guideline committees agree that IE itself is not an indication for routine antithrombotic therapy; rather, management should be individualized based on comorbidities such as atrial fibrillation or mechanical prosthetic valves (9). This study aimed to analyze the clinical and epidemiologic features of adult IE patients at a tertiary referral center over a 14-year period, identify predictors of in-hospital mortality, and particularly assess the impact of antithrombotic exposure. Findings are contextualized within contemporary international literature and guideline recommendations.

Material and Methods

Study Population

The study was approved by the institutional Ethics Committee on June 4, 2014 (Approval No: GO 14/330-33). This retrospective cohort study included adult patients (≥18 years) admitted to our University Hospital between January 2000 and December 2013 with a diagnosis of definite or possible IE according to modified Duke criteria (10).

Diagnoses were determined according to the International Classification of Diseases-10 classification. Patients hospitalized within the study period with the codes I33 (acute and subacute endocarditis), I38 (endocarditis, valve unspecified), and I39 (endocarditis and heart valve disorders in diseases classified elsewhere) were identified. Of 171 patient files evaluated, 49 were excluded because infective endocarditis (IE) could not be confirmed or was unrelated (e.g., prophylaxis only, fever of unknown origin, fever due to other infections in patients with structural heart disease, or absence of echocardiography). Finally, 122 patients were included in the analysis. Patient charts and hospital databases were reviewed to collect demographic data, comorbidities, clinical presentation, laboratory parameters, echocardiographic findings, microbiology, and treatment modalities including antibiotic therapy, surgical interventions, and antithrombotic therapy. The endpoint (discharge, discharge with a sequel, transfer to another hospital, discharge by patient's own request, death) was recorded in detail, but analysed within two groups: survival or death. The primary endpoint of this study was to evaluate the rate of in-hospital mortality in patients with infective endocarditis. The secondary endpoints were designed to identify factors that may influence this primary outcome. These factors included the use of antithrombotic therapy, the distribution of causative microorganisms, the frequency of culture-negative cases, and the occurrence of major complications during hospitalization.

Statistical analysis

Statistical analyses were performed using PASW Statistics 18 (SPSS Inc., Chicago, IL). The distribution of numerical data was analyzed with the Kolmogorov-Smirnov test. Mean ± standard deviation (SD) was used for normally distributed data, while the median (range) values were specified for non-normally distributed data. The endpoint was grouped as survival or death. For categorical variables, Chi-square and Fisher's exact test were used. Categorical data were presented as number and/or percentage. Continuous variables were tested for normality using the Kolmogorov–Smirnov test. Normally distributed variables were compared using the Student's t-test, whereas non-normally distributed variables were analyzed using the Mann–Whitney U test. Categorical variables were compared using the chi-square test or Fisher's exact test where appropriate. Variables with a p value < 0.20 in univariate analyses were entered into the multivariate logistic regression model. A binary logistic regression analysis using a backward stepwise (likelihood ratio) method was then performed to identify independent predictors associated with mortality. Model calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test. The results of the regression analysis are presented as odds ratios (ORs) with 95% confidence intervals (CIs). Statistical significance was defined as $p < 0.05$.

Ethical approval This study was conducted in accordance with the Declaration of Helsinki and institutional ethical guidelines. The study was approved by the Hacettepe University Non-Interventional Clinical Research Ethics Committee (Number: GO 14/330-33, Date: 04.06.2014). Since this study was retrospective, informed patient consent statement was not obtained.

Results

Out of 171 patient records identified, 49 were excluded due to non-infective endocarditis (IE) diagnoses (patients receiving IE prophylaxis only, fever of unknown origin with structural heart disease, or lacking echocardiography). Thus, 122 patient records were included for analysis. The mean age was 52.5 ± 14.2 years, and 63.1% were male. Approximately 86 (70.5%) had at least one chronic comorbidity, most commonly hypertension. **Table 1** summarizes demographic and clinical characteristics. Patients who died were significantly older (57.4 ± 12.8 versus 50.8 ± 14.3 years, $p = 0.023$) and more frequently hypertensive (59.4 % vs 36.7 %, $p = 0.026$) or diabetic (28.1 % vs 12.2 %, $p = 0.037$). History of rheumatic fever (35.2%), pre-existing valvular damage (51.6 %), prosthetic valves/devices (34.4 %), and prior infective endocarditis (10.7 %) were common but not significantly associated with mortality. Patients with hematological malignancies or solid organ tumors involving the bone marrow, those who received chemotherapy within the past 3 months, individuals who have used steroids for more than 30 days, those on immunosuppressive therapy due to solid organ transplantation, and recipients of active DMARDs (disease-modifying antirheumatic drugs) were classified as being under immunosuppression. Twenty-one (17,2%) patients were immunocompromised.

Fever was the most common presenting symptom, occurring in 82.8% of patients. Other common complaints were malaise (39.3 %), dyspnea (32 %), altered mental status (27 %), widespread body pain (24.6 %), nausea/vomiting (22.1 %) and chills (15.6 %). Dyspnea and altered mental status were significantly more common among non survivors ($p = 0.011$ and $p = 0.003$, respectively). Systolic murmur was detected in 63.9 % of patients; hepatosplenomegaly in 41 %; pneumonia in 30.3 %; cutaneous embolic lesions in 14.8 %; and acute cerebrovascular events in 17.2 %. Rash was present in 22 (18.0%) of all patients. Pneumonic infiltrates and skin rash were more frequent among those who died ($p = 0.005$ and $p = 0.024$). Presenting symptoms and physical findings are summarized in **Table 2**. Patients typically sought care a median of 14 days after symptom onset (Interquartile range 1 20). About 54.7 % sought medical care within two weeks, and 73.8 % within 30 days. Acute presentation (< 15 days) was associated with significantly higher mortality (77.4 % of deaths vs 46.5 % of survivors, $p = 0.003$). Presenting symptoms and physical findings are summarized in **Table 2**.

Table 1. Patient Characteristics and Outcomes

Variables	All Patients (n = 122)	Survived (n = 90) (73.8%)	Died (n = 32) (26.2%)	p
Age (years)*	52.5 ± 14.2	50.8 ± 14.3	57.4 ± 12.8	**0.023**
Gender				
Female	45 (36.8)	30 (33.3)	15 (46.9)	NS
Male	77 (63.1)	60 (66.7)	17 (53.1)	NS
Underlying Chronic Disease History	86 (70.5)	60 (66.7)	26 (81.3)	NS
Major Chronic Disease Categories**				
Hypertension	52 (42.6)	33 (36.7)	19 (59.4)	**0.026**
Diabetes mellitus	20 (16.4)	11 (12.2)	9 (28.1)	**0.037**
Coronary artery disease	24 (19.7)	15 (16.7)	9 (28.1)	NS
Heart failure	19 (15.6)	11 (12.2)	8 (25)	NS
Atrial fibrillation	19 (15.6)	13 (14.4)	6 (18.8)	NS
Cerebrovascular event	13 (10.7)	10 (11.1)	3 (9.4)	NS
Chronic obstructive pulmonary disease	9 (7.4)	5 (5.6)	4 (12.5)	NS
Chronic kidney disease	23 (18.9)	14 (15.6)	9 (28.1)	NS
-Hemodialysis dependent	*10 (8.2)*	*5 (5.5)*	*5 (15.6)*	NS
Rheumatological disease	12 (9.8)	9 (10)	3 (9.4)	NS
Malignancy	14 (11.5)	12 (13.3)	2 (6.3)	NS
Immunosuppression***	21 (17.2)	16 (17.8)	5 (15.6)	NS

Abbreviations: *Age is presented as mean ± standard deviation, ** Some patients had more than one chronic disease,
*** Immunosuppression was defined as cases with hematological malignancies or solid organ tumors with bone marrow involvement, chemotherapy use within the last 3 months, steroid use for more than 30 days, immunosuppressive therapy due to solid organ transplantation, and active DMARD (disease-modifying antirheumatic drugs) treatment. NS: Not statistically significant

Table 2. Distribution of Presenting Symptoms and Findings

Symptom	All Patients (n = 122)	Survived (n = 90)	Died (n = 32)	p
Fever	101 (82.8)	77 (85.6)	24 (75.0)	NS
Weakness/ Poor condition	48 (39.3)	34 (37.8)	14 (43.8)	NS
Dyspnea	39 (32.0)	23 (25.6)	16 (50.0)	**0.011**
Altered mental status	33 (27.0)	18 (20)	15 (46.9)	**0.003**
Widespread body pain	30 (24.6)	21 (23.3)	9 (28.1)	NS
Nausea/Vomiting	27 (22.1)	19 (21.1)	8 (25)	NS
Chills/Tremors	19 (15.6)	18 (20)	1 (3.1)	**0.024**
Chest pain	17 (13.9)	11 (12.2)	6 (18.8)	NS
Cough/Sputum	17 (13.9)	11 (12.2)	6 (18.8)	NS
Weight loss	16 (13.1)	14 (15.6)	2 (6.3)	NS
Palpitation	10 (8.2)	8 (8.9)	2 (6.3)	NS
Lateralized weakness/numbness	8 (6.6)	7 (7.8)	1 (3.1)	NS
Finding				
Cardiac Murmur	78 (63.9)	53 (58.9)	25 (78.1)	NS
Hepatomegaly/Splenomegaly	50 (41.0)	36 (40)	14 (43.8)	NS
Pneumonic infiltration	37 (30.3)	21 (23.3)	16 (50)	**0.005**
Rash	22 (18.0)	12 (13.3)	10 (31.3)	**0.024**
Acute cerebrovascular event	21 (17.2)	14 (15.6)	7 (21.9)	NS
Embolic skin finding	18 (14.8)	10 (11.1)	8 (25)	NS

Abbreviations: NS: Not statistically significant

At admission, 59 patients (48.3%) were taking antiplatelet agents, and 43 (35.2%) were taking anticoagulants, most commonly aspirin and warfarin. Digoxin (29.5 %), non-Digoxin antiarrhythmics (31,1%), ACE inhibitors/angiotensin receptor blockers (27 %), diuretics (14.8 %), and proton pump inhibitors (15.6 %) were also used. Aspirin (36.1 % overall) and other antiplatelet agents, clopidogrel, ticlopidine or dipyridamole (12.3 %) were significantly more common in non-survivors ($p = 0.019$ and $p = 0.011$). Warfarin use did not differ between groups. **Table 3** displays the data distribution on medications.

Table 3. Distribution of data on medication use

Medication/Drug Group	All Patients (%)	Survived (%)	Died (%)	p
Digoxin	36 (29.5)	25 (27.8)	11 (34.4)	NS
Acetylsalicylic acid	44 (36.1)	27 (30)	17 (53.1)	**0.019**
Clopidogrel/ Ticlopidine/ Dipyridamole	15 (12.3)	7 (7.8)	8 (25)	**0.011**
Warfarin	43 (35.2)	29 (32.2)	14 (43.8)	NS
Antiarrhythmics (non-digoxin)	38 (31.1)	28 (31.19)	10 (31.3)	NS
ACE inhibitor/ARB*	33 (27.0)	21 (23.3)	12 (37.5)	NS
Diuretics	18 (14.8)	10 (11.1)	8 (25)	NS
Penicillin G	5 (4.1)	3 (3.3)	2 (6.3)	NS
Insulin	11 (9.0)	7 (7.8)	4 (12.5)	NS
Chemotherapeutic agents	8 (6.6)	6 (6.7)	2 (6.3)	NS
DMARD**	10 (8.2)	7 (7.8)	3 (9.4)	NS
Steroid	13 (10.7)	9 (10)	4 (12.5)	NS
Proton pump inhibitor	19 (15.6)	12 (13.3)	7 (21.9)	NS

Abbreviations: *: Angiotensin-converting enzyme inhibitor / Angiotensin receptor blocker, **: Disease-modifying antirheumatic drugs NS: Not statistically significant

Laboratory and interventional technique results among groups are shown in **Table 4**.

Among predisposing conditions to IE, cardiac factors included rheumatic fever–related valve damage (68.3 % of those with valve disease), prosthetic valves/devices (34.4 %), and previous IE (10.7 %). Non-cardiac factors included surgery or invasive procedures within the previous six months (25.5 % of patients), central venous catheterization (14.8 %), immunosuppression (17.2 %), and recent hospitalization (38.5 %). None of these factors showed a significant association with survival. Due to the relatively small sample size, subgroup analyses stratified by valve type (native versus prosthetic) were not performed, which may limit the precision of statistical associations.

Anemia was prevalent (82.8 %), and nearly half of the patients had leukocytosis (median leukocyte count $9.8 \times 10^3/\mu L$; $p = 0.002$ for higher counts in non-survivors). Elevated neutrophil counts and high C-reactive protein and creatinine were more common among those who died, as expected. Median creatinine was 1.0 mg/dL but significantly higher in non-survivors ($p = 0.046$). Hypoalbuminemia (≤ 3.5 g/dL) was present in 61.5 % of patients. Echocardiography revealed a median ejection fraction of 62 %, with 34.9 % having < 60 %. Pulmonary artery pressure averaged 50 ± 19 mmHg and was higher in non-survivors ($p = 0.005$).

Since cases with no echocardiography results in their files were excluded, echocardiographic evaluation was performed on all patients. Both transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) were available for 89 patients (73%), while 26 patients (21.3%) had only TTE, and 7 patients (5.7%) had only TEE.

Echocardiography detected vegetations predominantly on native valves (63.2 % of cases) and prosthetic valves (30.3 %). Among prosthetic valve IE, 71 % involved mitral valve replacements (MVR), 19 % aortic valve replacements (AVR), and 5 % both valves. Native valve IE involved the mitral valve in 42 % of cases, the aortic valve in 38 %, both aortic and mitral valves in 6 %, the tricuspid valve in 5 %, and septal sites in 5 %. Device-related IE included pacemaker leads (4.1 %) and patent foramen ovale closure devices (1.6 %). Only 1 (1%) patient had both prosthetic and native valve endocarditis. In 4% of cases, the location was not specified. Vegetation site (native vs prosthetic or specific valve) was not associated with mortality.

Table 4. Distribution of Laboratory Findings

Test/Unit (NR)	Patient (n)	Mean ± SD* Median (Range)**	Survived	Died	p***
Hgb*/gr/dL (13.6 - 17.2)	122	11.1 ± 2.3	11.0 ± 2.3	11.2 ± 2.3	NS
MCV*/fL (80.7 - 95.5)	122	84.5 ± 7.4	84.7 ± 7.7	84.1 ± 6.7	NS
Leu **/x10³µL (4.3 - 10.3)	122	9.8 (39.8)	9.4 (39.8)	12.4 (31.2)	**0.002**
Hleu: **/x10³µL (4.3 - 10.3)	122	16.3 (142.1)	13.5 (142.1)	22.5 (82.5)	**<0.001**
Neu **/x10³µL (2.1 - 6.1)	122	7.9 (29)	8.3 (28.5)	9.9 (25.8)	**0.002**
NR */% (41 - 73)	122	77.1 ± 12.1	75.4 ± 12.5	81.8 ± 9.2	**0.003**
Thr*/x10³µL (156 - 373)	122	253.2 ± 149.5	253.4 ± 161.3	252.7 ± 112.1	NS
MPV*/fL (6.9 - 10.8)	122	8.2 ± 1.3	8.3 ± 1.3	8.1 ± 1.5	NS
ESR*/mm/sa (0 - 20)	113	55.8 ± 32.1	55.5 ± 32.5	51.6 ± 28.3	NS
CRP **/mg/dL (0 - 0.8)	102	9.1 (40.4)	8.5 (32.4)	10.2 (37.7)	**0.028**
Procal**/ng/mL (0 - 0.05)	38	1.67 (115.96)	0.8 (115.96)	5.9 (27.13)	NS
RF**/IU/mL (0 - 20)	24	22.3 (3850)	22 (3850)	20.7 (33.3)	NS
Cr **/mg/dL (0.67 - 1.17)	122	1.00 (13.2)	1.1 (13.2)	1.4 (7.6)	**0.046**
Albumin*/g/dL (3.5 - 5.2)	122	3.4 ± 0.7	3.4 ± 0.7	3.4 ± 0.7	NS
EF**/% (≥60)	106	62 (74)	60 (64)	74.5 (7)	NS
PAP*/mmHg (≤25)	66	50 ± 19	37.5 ± 14	52.5 ± 10.6	**0.005**

Abbreviations: MCV: Mean Corpuscular Volume, MPV: Mean Platelet Volume, *: Normally distributed values are expressed as mean ± standard deviation (SD).**: Non-normally distributed values are expressed as median (range),***The difference between the two groups was analyzed using the "T-test" for normally distributed values and the "Mann-Whitney U test" for non-normally distributed values. PAP: Pulmonary artery pressure, EF: Ejection fraction, RF: Rheumatoid factor, Procal: Procalcitonin, CRP: C-reactive protein, ESR: Hleu: Highest Leukocyte, Leu: Leukocyte, NR: Neutrophil ratio, Thr: Thrombocyte, Hgb: Hemoglobin, Neu: Neutrophil, Cr: Creatinine, NR: Normal Range

Among patients with prosthetic valve endocarditis, the mitral valve prosthesis was most commonly affected (71%). Aortic valve prosthesis was involved in 19% of cases, and combined aortic and mitral prostheses were seen in 5%. The type of prosthesis was not described in the medical reports for 5% of patients. **Figure 1** illustrates the distribution of valves and/or prosthetic devices involved. Follow-up echocardiograms were also evaluated and analyzed to reveal the relationship between deteriorating echocardiographic findings and adverse outcomes. The criteria for this deterioration were set as the occurrence of at least one of the following findings: An increase in the size of the vegetation, progression towards abscess formation, an increase in the degree of valve regurgitation, or development of a new chordae or valve rupture. Worsening echocardiographic findings were significantly associated with mortality in our study. Patients who showed deterioration on their control echocardiogram had a much higher death rate (60%) compared to those who did not (21.6%). This difference was found to be statistically significant (p=0.046). Blood cultures showed Staphylococcus aureus in 25.5% of cases, followed by other staphylococcal species (14.8%), streptococci (16.3%), enterococci (6.1%), gram-negative bacilli (4.0%), and fungi (0.8%). Culture-negative endocarditis accounted for 33.3% of patients, which is significantly higher than the recommended rate of less than 5%. The causative microorganism has not been linked to differences in mortality. Surgical treatment was performed in 29.5% of patients; the in-hospital mortality in the surgical group was 22%. The overall in-hospital mortality for the cohort was 26.2%. Bleeding events and disseminated intravascular coagulation were more frequent among non-survivors, which are among the well-known mortal outcomes of IE. Variables significantly linked to mortality (outcome: survival versus death) in univariate analyses were included in a multivariate logistic regression model with a backward stepwise (likelihood ratio) approach. These variables encompassed age; presence of hypertension; presence of diabetes mellitus; dyspnea at presentation; altered mental status at presentation; chills and rigors at admission; pneumonic infiltration; skin rash; acute presentation (symptom duration less than 14 days at admission); use of acetylsalicylic acid; use of clopidogrel/ticlopidine/dipyridamole; and worsening on follow-up echocardiography. Independent predictors of mortality were identified through the backward elimination process. Worsening on follow-up echocardiography and antiplatelet therapy (either acetylsalicylic acid or non-aspirin antiplatelet agents) showed the strongest independent association with mortality.

Additionally, variables that were significant at the time of hospital admission in categorical analyses—such as age, presence of diabetes mellitus, acetylsalicylic acid use, C-reactive protein level, serum creatinine level, and duration of symptoms—were entered into a separate logistic regression model using the backward stepwise (likelihood ratio) method. In this adjusted model, the presence of diabetes mellitus (odds ratio 4.7; p = 0.021; 95% CI) and C-reactive protein level (odds ratio 1.06; p = 0.041; 95% CI) remained independently associated with mortality. Model calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test. Multivariable logistic regression identified worsening echocardiographic findings during follow-up (OR = 5.44, p=0.026) and pre-existing antiplatelet therapy (aspirin OR = 2.64, p=0.021; clopidogrel, ticlopidine, or dipyridamole OR = 3.95, p=0.015) as independent predictors of in-hospital mortality. Use of antiplatelet therapy was associated with increased mortality, independent of embolic events.

Table 5. Multivariable Logistic Regression Analysis Identifying Independent Predictors of Mortality

Variable	Wald χ^2	Odds Ratio (95% CI)	p value
Age	4.937	1.037 (1.004–1.070)	0.026
Admission date (≤2006 vs ≥2007)	5.148	2.619 (1.140–6.017)	0.023
Hypertension	4.834	2.524 (1.106–5.764)	0.028
Diabetes mellitus	4.136	2.810 (1.038–7.607)	0.042
Duration of symptoms (days)	4.927	1.030 (0.956–0.997)	0.026
Time to surgery (days)	2.661	1.047 (0.904–1.009)	0.103
Acetylsalicylic acid use	5.301	2.644 (1.156–6.051)	0.021
Clopidogrel, ticlopidine, or dipyridamole use	5.873	3.952 (1.301–12.010)	0.015
C-reactive protein level	5.963	1.058 (1.011–1.107)	0.015
Pulmonary artery pressure (mmHg)	6.399	1.041 (1.009–1.074)	0.011
Worsening on follow-up echocardiography	4.977	5.437 (1.228–24.071)	0.026
Newly developed heart failure	4.310	2.427 (0.178–0.952)	0.038

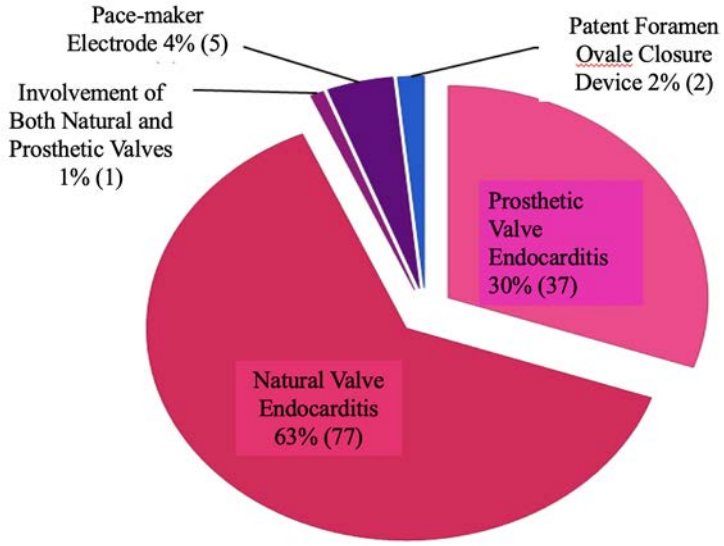

Figure 1. Distribution of data regarding the structure where vegetation was observed

Discussion

Our cohort's finding that antiplatelet therapy independently predicted in hospital mortality aligns with contemporary evidence discouraging routine antithrombotic use in active IE (4-9,12). Recent systematic reviews highlight that bleeding, including intracranial hemorrhage, complicates up to 5 % of cases and that no adequately powered trials demonstrate a protective effect of antiplatelet therapy (4,6,12). The 2023 ESC guidelines therefore

advise against routine antithrombotic therapy and emphasise individualised risk assessment (9). In our regression model, worsening echocardiographic findings and prior antiplatelet therapy were independently associated with in-hospital mortality. These findings highlight the prognostic importance of cardiac imaging during follow-up and the potential clinical implications of pre-existing antiplatelet use. We did not apply more complex multivariable or subgroup analyses because the number of mortality events in our cohort was limited, and additional modeling could lead to unstable statistical estimates. Therefore, we preferred a regression model appropriate for our sample size, which we believe provides reliable and interpretable results. Our observation of high mortality in patients with worsening echocardiographic findings and those on antiplatelet agents is consistent with these recommendations.
However, antiplatelet agents' impact on mortality should be interpreted with caution. Antiplatelet agents were not administered as part of IE treatment but were used before admission for underlying cardiovascular disease. Therefore, antiplatelet therapy likely reflects a higher baseline comorbidity burden rather than exerting a direct harmful effect. The association may thus represent an indirect relationship, where patients requiring antiplatelet therapy inherently have more severe systemic disease, contributing to worse outcomes.
The global burden of IE continues to climb; age-standardised incidence rose from 9.9 to 13.8 per 100 000 person years between 1990 and 2019 (1,10). Despite advances in diagnosis and therapy, in hospital mortality remains around 25 % worldwide (1,10). Demographically, the disease has shifted toward older patients with more comorbidities and greater exposure to prosthetic valves and implantable devices. Staphylococcus aureus has supplanted streptococci as the leading pathogen, and this shift to a more virulent organism contributes to the persistently high mortality (13). The Turkish epidemiological landscape mirrors these global changes yet shows unique features (14,15). Historically, Turkish cohorts described younger patients (mean age; 47 years) (14) and a dominance of rheumatic valve disease (14,15). Our cohort and recent national series show a transition to older patients with prosthetic valves and cardiac devices and a rise in healthcare-associated IE.
The 2025 multicentre study by Sarıcaoglu and colleagues (the Türkiye Endocarditis Group) provides the largest national dataset to date and further clarifies trends observed in our cohort and other Turkish series (16). This retrospective cohort included 1,044 patients with infective endocarditis diagnosed between 2013 and 2023 The median age of patients was 57 years (Interquartile range 44–68) and increased significantly over time. The prevalence of rheumatic and congenital heart disease declined, whereas the prevalence of intracardiac devices (prosthetic valves, cardiac implants) rose. They described a mortality rate of 22.5 %, and a predominance of staphylococci—particularly S. aureus—with decreasing degenerative and congenital heart disease as predisposing factors (16). These findings are partially consistent with our results and other recent worldwide data (17) since both studies identified independent risk factors for death. The Turkish study cited age ≥ 65, chronic kidney disease, nosocomial acquisition, Candida infection, prosthetic-valve IE, vegetations larger than 15 mm, and central nervous system emboli as risk factors. While our results support the significance of age and neurological deterioration, we did not find a significant association with vegetation size, the type of valve involved, or the causative agent.
Recent studies confirm the shift towards device-related and healthcare-associated infections and support our observation. Notably, Brucella species remain a notable cause of IE in Türkiye, but our data confirmed only 1 (1%) patient cultured positive for the regional pathogen.

Study limitations

Our study has some limitations. The retrospective design which is inherent in a review of past records. The analysis of data spanning a period from 2000 to 2013 also means that the findings may not fully reflect current trends in the epidemiology and management of infective endocarditis. The study period (2000–2013) represents a timeframe during which complete institutional records—mostly in physical form but fully accessible—enabled a reliable longitudinal analysis. Although more recent cases could provide additional insights, this period remains valuable for documenting the historical evolution of infective endocarditis in Türkiye. Additionally, the study's focus on a single institution may limit the generalizability of its findings to other centers with different patient populations and healthcare practices. The relatively small sample size of 122 patients, while robust for a single-center study, may affect the statistical power to detect associations between certain variables and clinical outcomes. Despite these limitations, the study provides valuable insights into the evolution of infective endocarditis in a major tertiary care center in Türkiye.

Conclusion

This study, conducted at a tertiary care center in Türkiye, reveals significant shifts in the epidemiology of IE that align with global trends. The patient population is aging, and while rheumatic fever remains a notable predisposing factor, the incidence of prosthetic valve and device-related infections is on the rise.

Logistic regression analysis indicated that the variables most strongly associated with mortality were worsening follow-up echocardiographic results and antiplatelet therapy. Specifically, use of acetylsalicylic acid and non-aspirin antiplatelets were independently associated with a higher risk of death. Therefore, managing these patients should include a careful reassessment of the need for anti-platelet therapy. Additionally, worsening findings on follow-up echocardiograms serve as an important alarm sign and warrant prompt attention. We also found that an acute duration of symptoms (less than 15 days) before admission was a significant predictor of death. Early identification of high-risk patients is critical. Timely and coordinated care is essential to improving patient outcomes and reducing the unacceptably high morbidity and mortality rates.

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Author Contributions: *Concept: SA, MDT. Literature Review: SA, MDT. Design: SA, MDT. Data acquisition: SA, MDT. Analysis and interpretation: SA, MDT. Writing manuscript: SA; MDT. Critical revision of manuscript: SA, MDT.*

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Data Availability: *The data used to support the findings of this study are available from the corresponding author upon request.*

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