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Right-Sided Infective Endocarditis: A 6-Year Retrospective Cohort Study from a Tertiary Care Center in Türkiye

ABSTRACT

Background: With evolving risk factors, the frequency of right-sided infective endocarditis (RSIE) is increasing. Despite its distinct clinical features, data on RSIE remain limited, and no dedicated cohort has been reported from Türkiye. This study aimed to describe the epidemiological and clinical characteristics of RSIE and identify factors associated with mortality in a tertiary-care center.

Methods: This retrospective cohort study evaluated 65 adult patients diagnosed with definite RSIE between January 2018 and January 2024. Demographic data, risk factors, echocardiographic findings, causative microorganisms, and outcomes were analyzed. Statistical comparisons were performed between intravenous drug use (IVDU) and non-IVDU groups.

Results: The cohort was predominantly male (76.9%) with a median age of 36 years. Intravenous drug use was the primary risk factor (55.4%), followed by central venous catheters (24.6%) and hemodialysis (23.1%). Staphylococcus aureus was the leading causative agent (79%). Septic pulmonary embolism was detected in 81.6% of patients. The overall in-hospital mortality rate was 26.2%. Mortality was significantly lower in IVDU patients than in non-IVDU patients (17.4% vs. 44%; $P = .036$); however, multiple regression analysis identified hemodialysis as an independent predictor of mortality (OR = 6.72, 95% CI: 1.27-35.42; $P = .025$). Multiple Cox regression analysis further demonstrated that hemoglobin level and age were independent predictors of mortality.

Conclusion: Although IVDU patients demonstrated higher survival rates—likely attributable to a younger age profile and fewer comorbidities—RSIE remains a critical condition requiring high clinical suspicion and early intervention. RSIE in this region is strongly associated with IVDU and typically presents with respiratory symptoms due to septic pulmonary emboli.

Keywords: Hemodialysis, intravenous drug use, right-sided endocarditis

ORIGINAL INVESTIGATION

INTRODUCTION

Infective endocarditis (IE) is a rare but highly fatal infectious disease. An increase in the global incidence of IE has been reported over the past 3 decades.[1,2] The aging global population, the proliferation of invasive procedures (e.g., hemodialysis, cardiac implantable electronic devices), and rising intravenous drug use (IVDU) have increased the population at risk. Concurrently, the profile of patients at risk has shifted significantly.

Infective endocarditis typically affects the left-sided heart valves, with right-sided infective endocarditis (RSIE) accounting for 5%-10% of all IE cases.[3] However, paralleling the shift in the at-risk patient profile, an increase in the prevalence of RSIE has been reported.[3,4,5] The RSIE possesses a distinct epidemiology, clinical characteristics, and set of treatment approaches. While comprehensive data exist regarding left-sided IE, published literature concerning the characteristics and management of right-sided IE remains limited. Based on the current information, there are no cohort studies from Türkiye specifically focusing on RSIE.

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The aim of this study was to investigate the epidemiological, clinical, and microbiological characteristics of RSIE, identify risk factors, and explore factors potentially associated with mortality in patients diagnosed with definite IE at a tertiary care center.

METHODS

This retrospective descriptive study was conducted between January 2018 and January 2024 at a 1500-bed tertiary training and research hospital in Türkiye, which serves as a regional referral center for cardiology and cardiovascular surgery.

During the study period, patients diagnosed with IE according to ICD-10 codes were identified from the electronic medical record system, and their records were reviewed. Among patients diagnosed with "definite" IE according to the Modified Duke criteria, all consecutive patients with RSIE were included in the study.[6] Patients with concomitant left-sided involvement were not excluded. The study included adult patients aged 18 years and older. For cases presenting with multiple episodes, only the initial episode of IE was evaluated. Outcomes were limited to the index hospitalization, and the primary endpoint was in-hospital mortality during the index admission.

Data were recorded using a standardized data collection form. Demographic characteristics, clinical and laboratory findings, comorbidities, predisposing conditions, echocardiographic and radiological findings, blood culture results and causative microorganisms, surgical treatment interventions, and prognostic data were analyzed.

Right-sided endocarditis was defined as the presence of vegetation on the tricuspid valve, pulmonary valve, right atrial wall, or an intracardiac device lead. Echocardiographic analyses were performed using data from transthoracic and/or transesophageal echocardiography reports provided by a cardiologist. Vegetation size was recorded in millimeters based on the maximal long-axis measurement.

Hemodialysis was defined as participation in a regular hemodialysis program due to chronic kidney disease. Intravenous drug use was defined as the presence of a documented history of intravenous substance use either at the time of admission or in previous medical records.

Ethics Committee Approval: This study was approved by Ethics Committee of the regional hospital (Approval No:2897, Date October 26, 2023).

Statistical Analysis

Data obtained in this study were analyzed using SPSS 27 statistical software. For descriptive statistics, categorical variables were expressed as numbers (n) and percentages (%), while non-normally distributed continuous variables were expressed as median (minimum-maximum) values. As the assessment of continuous variables using the Shapiro–Wilk test indicated that none followed a normal distribution, the Mann–Whitney *U*-test was used for comparisons between 2 groups. The Pearson chi-square test was used to evaluate the relationships between categorical variables; however, Fisher's exact test was used in 2x2 tables when the expected count was less than 5. Multiple logistic regression analysis was performed to identify independent risk factors for in-hospital mortality and multiple Cox proportional hazards regression analysis was used to evaluate survival outcomes. Variables with clinical relevance were entered into the model simultaneously. Odds ratios (ORs) and hazard ratios (HRs) with 95% CI were calculated, and $P < .05$ was considered statistically significant.

RESULTS

A total of 65 patients diagnosed with RSIE were included in the study (Figure 1). Of the patients, 23.1% (n = 15) were female and 76.9% (n = 50) were male. The median age of the total patient population was 36 (18-85) years. Patients in the IVDU group were significantly younger than those in the non-IVDU group (median 34 vs. 54 years; $P < .001$). The comparison of demographic characteristics, clinical presentation, microbiology, treatment and outcomes between IVDU and non-IVDU patients is presented in Table 1.

When risk factors for IE at presentation were evaluated, IVDU was present in 55.4% (n = 36) of the patients, diabetes mellitus in 13.8% (n = 9), cardiac pacemakers in 15.4% (n = 10), and heart failure in 15.4% (n = 10). Central venous catheters were present in 29.2% (n = 19) of the patients; of these, 15 patients were receiving hemodialysis, while in 4 patients the catheter was used for vascular access.

Regarding presenting symptoms, fever was observed in 60% (39/65), dyspnea in 33.8% (22/65), cough in 29.2% (19/65), chest pain in 30.8% (20/65), and fatigue in 21.5% (14/65) of the patients. Additionally, 2 patients presented with pacemaker pocket infection.

At the time of presentation, 10.8% (7/65) of the patients had sepsis, and 9.3% (6/65) presented with acute cerebrovascular disease. Furthermore, pneumothorax was present in 2 patients. The baseline characteristics and laboratory findings of the patients with IE are presented in Table 2 and Table 3.

Examination of echocardiographic findings revealed vegetations located on the tricuspid valve in 78.5% (n = 51), solely

HIGHLIGHTS

- This study presents the first cohort from Türkiye exclusively examining right-sided infective endocarditis.
- Intravenous drug use (IVDU) was the leading risk factor and right-sided infective endocarditis predominantly affected younger patients.
- Septic pulmonary embolism was highly prevalent, reflecting the characteristic pulmonary-dominant presentation.
- Mortality was significantly lower in patients with IVDU compared to non-IVDU, whereas hemodialysis patients exhibited markedly higher mortality; vegetation size showed no significant association with mortality.

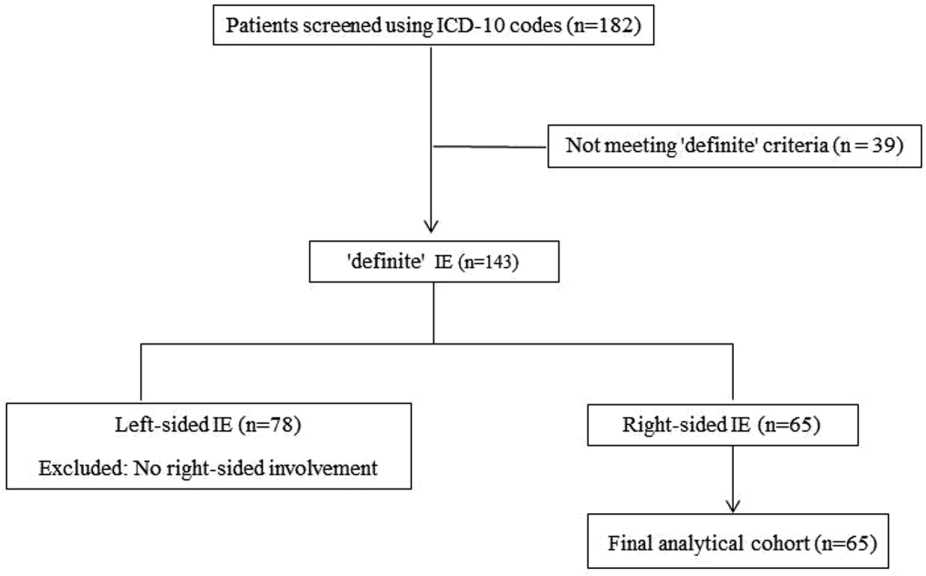


Figure 1. Flowchart of the study.

in the right atrium in 7.7% (n = 5), on an intracardiac lead in 6.2% (n = 4), and in the right atrium combined with an intracardiac lead in 1 patient. Additionally, aortic valve involvement accompanying the tricuspid valve was observed in 2 patients, and vegetation on the mitral valve accompanying the tricuspid valve was observed in another 2 patients. The median vegetation size was 16 mm (2-44 mm). Vegetation size was found to be ≥20 mm in 43.1% (n = 28) of the patients.

Analysis of blood culture results revealed no growth in 20% (13/65) of the patients. Among those with positive blood cultures, *Staphylococcus aureus* was the causative agent in 79% (41/52), coagulase-negative staphylococci in 5.8% (3/52), and *Candida* sp. in 5.8% (3/52). The distribution of causative microorganisms isolated from blood cultures is shown in Table 4.

Septic pulmonary embolism was detected in 49 (81.6%) of the 60 patients who underwent thoracic computed tomography.

Table 1. Baseline Characteristics and Outcomes of Right-Sided IE Patients According to IVDU

Characteristics	IVDU (n = 36)	Non-IVDU (n = 29)	*P*
Age (Years)	34 (18-50)	54 (19-85)	**<.001**
Gender (Male, n)	36	14	**<.001**
Concomitant left-sided EE (n)	1	3	.316
Clinical presentation			
Cough (n)	18	1	**<.001**
Sepsis (n)	4	3	.622
Chest pain (n)	16	4	**.007**
Fever (n)	25	14	.070
Microbiology			
MSSA	14	6	.094
MRSA	13	8	.323
Non-*S.aureus*	0	11	**<.001**
Surgery	19	11	.173
Inhospital mortality	4	13	**.010**

IE, infective endocarditis; IVDU, intravenous drug use, MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, Methicillin-susceptible *Staphylococcus aureus*. $P < .05$ was considered statistically significant

Table 2. Baseline Characteristics of Patients with IE

Characteristics	Patient (%)
Symptoms	
Fever	39 (60.0)
Dyspnea	22 (33.8)
Cough	19 (29.2)
Chest pain	20 (30.8)
Fatigue	14 (21.5)
Clinical presentation	
Pneumothorax	2 (3.0)
Sepsis	7 (10.8)
Pacemaker pocket infection	2 (3.0)
Stroke	6 (9.3)
Predisposing factors	
Hemodialysis	15 (23.1)
IVDU	36 (55.4)
Diabetes mellitus	9 (13.8)
Cardiac pacemaker	10 (15.4)
Central venous catheter	4 (2.8)
Heart failure	10 (15.4)
Echocardiographic findings	
Tricuspid valve involvement	51 (78.5)
Lead involvement	4 (6.2)
Right atrial involvement	5 (7.7)
Tricuspid and left-sided valve involvement	4 (6.2)

IE, infective endocarditis; IVDU, intravenous drug use.

Table 3. Baseline Laboratory Findings of Patients with IE

Laboratory Findings	Mean ± SD
C-reactive protein (mg/L)	159 ± 102
Leukocyte (10^3/μL)	14.7 ± 8.9
Hemoglobin (g/dL)	10.0 ± 8.6
Plateletes (10^3/μL)	191.6 ± 127.9

IE, infective endocarditis.

Table 4. Blood Culture Results of Patients with IE

Microorganism	n (%)
Staphylococcus aureus	
Methicillin-sensitive *Staphylococcus aureus* (MSSA)	20 (38)
Methicillin-resistant *Staphylococcus aureus* (MRSA)	21 (40)
Coagulase-negative staphylococci	3 (5.8)
Enterococcus faecalis	1 (1.9)
Brucella spp.	1 (1.9)
Candida spp.	3 (5.8)
Enterobacter sp.	1 (1.9)
Corynebacterium striatum	1(1.9)

IE, infective endocarditis; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.

Findings consistent with septic embolism were detected in 9 (23.7%) of the 38 patients who underwent cranial imaging. Of these patients, 4 had concomitant left-sided endocarditis. One patient had a concomitant small atrial septal defect and a bicuspid aortic valve; however, there was no evidence of aortic valve involvement. Medical therapy alone (antibiotics) was administered to 53.8% (n = 35) of the patients, while 46.1% (n = 30) received both antibiotic and surgical therapy. The patients received antibiotic therapy for a mean duration of 38.6 ± 21.4 days. Of the 30 patients who underwent surgery, it was determined that 12 underwent tricuspid valve replacement and 17 underwent valve repair combined with vegetation resection. Lead extraction was performed in all 7 patients with cardiac devices and lead infections; in one of these patients, the device was removed surgically.

Regarding prognosis, 63% (41/65) of the patients were discharged with recovery. The overall in-hospital mortality rate was 26.2% (17/65), while the 30-day mortality rate was 17.2% and the 90-day mortality rate was 29.3%. The mortality rate among surgically treated patients was 33.3% (10/30). Additionally, 7 patients using intravenous drugs left the hospital against medical advice before completing their treatment.

The mortality rate of patients with IVDU was found to be significantly lower compared to non-IVDU patients (17.4% vs. 44%, $P = .036$). The mortality rate in hemodialysis patients was found to be higher compared to other patients (24.3% vs. 53.3%, $P = .046$). No significant relationship was found

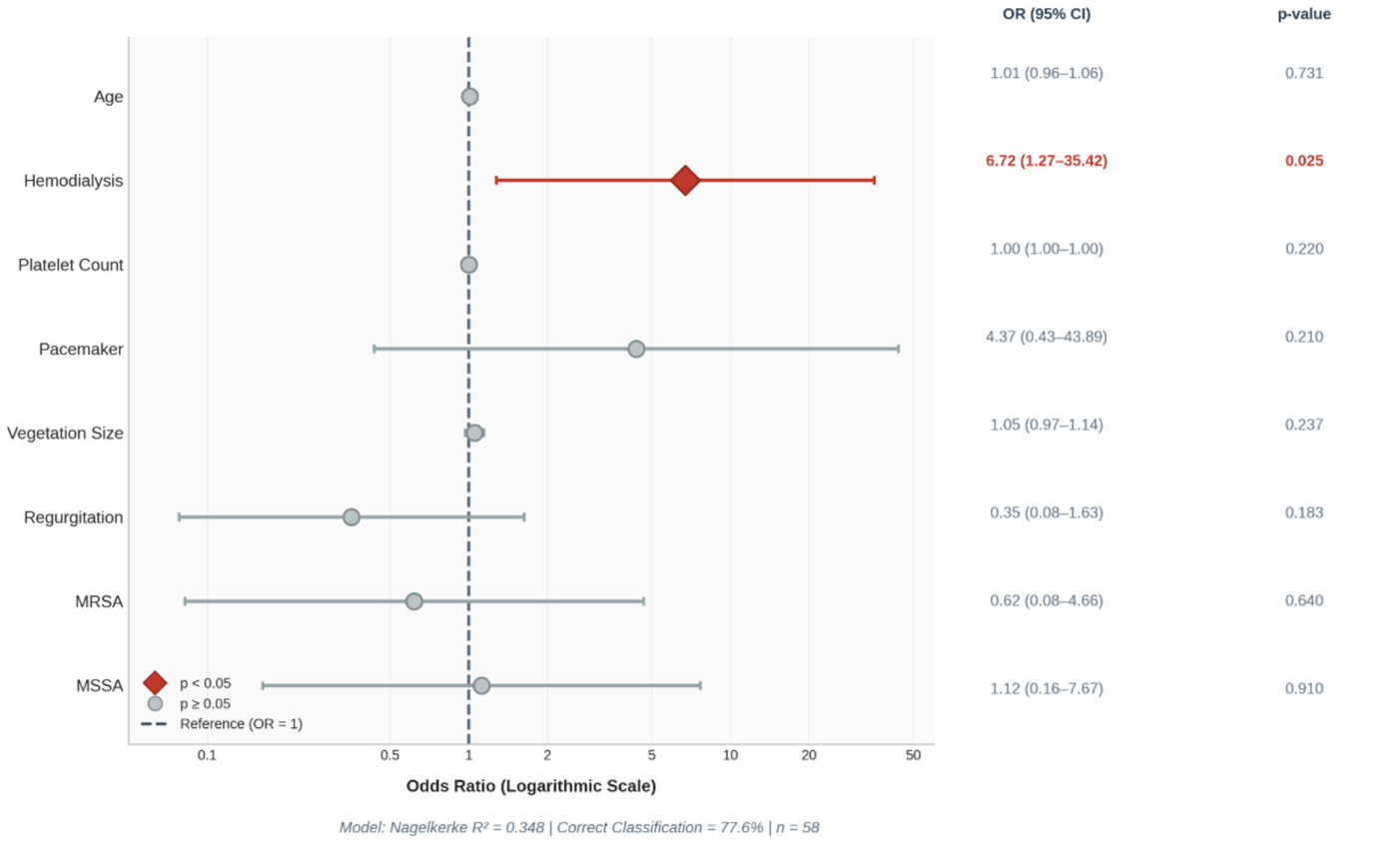


Figure 2. Factors affecting in-hospital mortality in patients with RSIE: a multiple regression analysis. RISE, right-sided infective endocarditis.

Table 5. Multiple Cox Regression Analysis

Variables	Adjusted HR (95% CI)	*P*
30-day mortality		
Hemoglobin	1.395 (1.050-1.848)	.037
90-day mortality		
Age	1.035 (1.002–1.056)	.023

HR, hazard ratio.

between mortality and heart failure, diabetes mellitus, presence of a cardiac device, age, or vegetation size.

In the multiple logistic regression analysis, among the variables entered into the model, only hemodialysis was found to be statistically significant (OR = 6.72, *P* = .025, 95% CI: 1.27-35.42). Patients receiving hemodialysis had an approximately sevenfold higher risk of in-hospital mortality compared with those not on hemodialysis (Figure 2).

Multiple Cox proportional hazards regression analysis demonstrated that hemoglobin level independently predicted 30-day mortality, with each 1-unit decrease associated with a 1.395-fold increase in hazard (HR = 1.395, *P* = .037, 95% CI: 1.050-1.848). Age was an independent predictor of 90-day mortality, with each 1-year increase associated with increased hazard (HR = 1.035, *P* = .023, 95% CI: 1.002-1.056) (Table 5).

DISCUSSION

It has been reported that the incidence of RSIE has increased as a result of the shift in the profile of patients at risk for IE.[3,4] Based on the current information, this is the first cohort study from Türkiye specifically focusing on RSIE. This study evaluated the epidemiological and clinical characteristics, risk factors, and factors potentially associated with mortality in patients diagnosed with right-sided endocarditis.

The study findings demonstrate that RSIE is more frequently observed in the young age group and in individuals with IVDU. This observation is consistent with studies reporting that 60-90% of RSIE cases occur in individuals with IVDU.[4,7,8] The incidence of IE is significantly higher in individuals with IVDU compared to the general population. It is stated that the proportion of IVDU among all IE cases is gradually rising and contributes to the increasing incidence of endocarditis, particularly in developed countries.[9]

The rate of IVDU-associated IE was reported as 6.9% in the ESC-EORP EURO-ENDO registry study, and between 4.4% and 10.1% in multicenter studies involving large patient series conducted in Türkiye.[10,11,12] Compared to prior regional studies, the IVDU-associated IE rate observed in this cohort is remarkably high. The relatively high prevalence of intravenous substance use in this region may explain this elevated rate.[13,14,15] The tricuspid valve is the most frequently affected site in IVDU-associated IE. The proposed mechanism involves mechanical valve damage caused by particulate matter in injected substances and a high bacterial load directly entering the venous circulation during non-aseptic injection.[16] Notably, in the cohort, 2 IVDU patients presented with concomitant right- and left-sided involvement, indicating that multivalvular infection can also occur in this population.[17]

In the current analysis, central venous catheter use and hemodialysis were identified as the second most common risk factors, while the presence of intracardiac devices was the third. The risk of developing IE is high in hemodialysis patients due to bacteremia episodes resulting from recurrent vascular interventions and the development of calcific valve disease.[18,19,20] Although the mitral and aortic valves are most frequently affected in these patients, right-sided endocarditis may also be observed.[21]

Among the cases reviewed, 5 of the 6 patients with right atrial wall involvement had venous catheters for hemodialysis, and one had a cardiac implantable device. Right atrial wall involvement is an atypical localization for IE. Nonvalvular IE is rare in the literature and is usually reported as case reports.[22,23] Right atrial involvement is thought to be a result of mechanical damage caused by catheters and intracardiac devices on the right atrial wall.[3,23] This damaged endocardium predisposes to the development of endocarditis on the atrial wall and the valve, particularly in hemodialysis patients with bacteremia.

Regarding clinical presentation, fever accompanied by respiratory symptoms such as chest pain, dyspnea, and cough was the most common presenting complaint. Two patients presented with pneumothorax. Infiltrations consistent with septic pulmonary emboli were detected in 82% of patients who underwent pulmonary imaging. This finding reflects the characteristic feature of right-sided IE. In RSIE, many typical clinical signs seen in left-sided endocarditis are generally absent. Pathologic murmurs and signs of peripheral embolization are usually not present at admission. Conversely, septic pulmonary embolism develops in approximately 75%-84% of tricuspid valve endocarditis cases.[24,25] The predominance of a pneumonia-like clinical picture at presentation can lead to missed or delayed diagnosis of IE. Therefore, it is stated that a high clinical suspicion for right-sided IE should be maintained in patients with risk factors for IE who present with persistent fever, respiratory symptoms such as cough, chest pain, or hemoptysis, and the presence of multiple pulmonary infiltrations on lung imaging.[25,26,27]

As a reflection of the change in risk factors, *Staphylococcus aureus* is currently reported to be the most common causative agent in both right- and left-sided IE.[3,10,11,12] Consistent with the literature, *Staphylococcus aureus* was the most frequently isolated agent in this series. However, in addition to the predominance of S. aureus, a cardiac device–associated case due to Brucella melitensis was also identified, consistent with rare reports of Brucella-related device endocarditis.[28]

Compared to left-sided IE, RSIE is generally associated with a better prognosis and lower mortality rates. Antibiotic therapy is successful in most patients.[3,25,27] Current data revealed that the mortality rate was significantly lower in patients

with IVDU compared to other patients, whereas the mortality rate was found to be higher in hemodialysis patients. In a large cohort of hemodialysis patients with IE, the in-hospital mortality rate was reported to be 43%.[29]A study conducted on a non-IVDU IE patient group reported that in-hospital mortality in RSIE was not different from that of left-sided IE.[21] In these patients, comorbidities such as concomitant heart failure and renal failure, as well as advanced age, negatively affect the prognosis. In this study, hemodialysis was associated with a sevenfold increase in mortality risk, highlighting the substantial vulnerability of this patient population.

In this study, lower hemoglobin levels independently predicted 30-day mortality. Previous studies have also demonstrated that anemia is associated with worse clinical outcomes in patients with IE.[30,31] Anemia is very common among patients with IE and its development is likely multifactorial. Chronic systemic inflammation, hemolysis, underlying renal dysfunction, and pre-existing iron deficiency have been suggested as potential contributors to anemia in this patient population.[32] Anemia may also reflect the overall severity of infection, which could partly explain its association with increased mortality in patients with IE.

Moreover, age was identified as an independent predictor of 90-day mortality. Advanced age is a well-established prognostic factor in IE and has consistently been linked to increased mortality in İE.[10,11] This association is likely related to a higher comorbidity burden and reduced tolerance to septic complications in elderly patients.

Many studies in the literature also report a better prognosis in the IVDU group.[7,8,33] This is thought to be primarily related to the predominance of right heart involvement in this group, the younger age of the patients, and the generally lower prevalence of accompanying comorbidities. However, treatment adherence is a major challenge in this demographic. In this cohort, 7 IVDU patients left against medical advice prior to treatment completion. Returning to substance use in this patient group can lead to recurrent endocarditis episodes and, unfortunately, negatively affects long-term outcomes.[33,34]

There are studies in the literature reporting both the presence and absence of a significant relationship between vegetation size and mortality.[35,36]No significant relationship was observed between vegetation size and mortality in the present dataset.

Limitations

Since the study had a retrospective design, there is a potential risk of information bias inherent to record-based data. The inclusion of only "definite" cases according to the Modified Duke criteria, while excluding "possible" cases, may have introduced selection bias. Another important limitation of this study is that in 4 patients who had acute cerebrovascular events on cranial imaging and did not have concomitant left-sided IE, a dedicated evaluation for the presence of a patent foramen ovale was not performed. Therefore, a paradoxical embolic mechanism cannot be definitively excluded in these patients. The presence of concomitant left-sided endocarditis in a small subset of patients with neurological embolic events may have influenced mortality outcomes. However, due to the limited number of such cases, subgroup analysis was not feasible and this should be considered when interpreting the results. Furthermore, long-term mortality, recurrent IE episodes, and late complications could not be evaluated. The exclusion of patients who discontinued treatment and left the hospital against medical advice from the in-hospital mortality analysis may have led to an underestimation of mortality rates.

Although hemodialysis remained the only significant predictor of in-hospital mortality in the multiple logistic regression analysis, and hemoglobin level (for 30-day mortality) and age (for 90-day mortality) were identified as significant predictors in the multiple Cox proportional hazards regression analyses, these findings should be interpreted with caution. The limited number of mortality events may have reduced the statistical power of the models and limited the generalizability of the estimates.

In addition, as right-sided endocarditis is relatively rare, the sample size was limited, which reduced statistical power in certain subgroup analyses. The results of this study may be more generalizable to patient populations presenting to tertiary referral centers in the region, where IVDU is relatively common, and may not fully reflect the demographics of the entire country.

CONCLUSION

Right-sided IE typically presents with persistent fever and respiratory symptoms, whereas signs of systemic embolization observed in left-sided endocarditis are generally absent. Therefore, a high index of suspicion is crucial for early diagnosis. Intravenous drug use is the primary predisposing factor for RSIE.

Data regarding RSIE in the literature are limited. In this study, the clinical characteristics, complications, surgical requirements, and prognostic data of RSIE cases in the region have been presented in detail for the first time. As the first detailed cohort of RSIE from Türkiye, this study fills a significant gap in the regional literature and highlights the urgent need for targeted addiction support alongside infectious disease management.

Ethics Committee Approval: This study was approved by Ethics Committee of Adana City Training and Research Hospital (Approval No:2897, Date October 26, 2023).

Informed Consent: Informed consent was not obtained because of retrospective nature of the study.

Peer-review: Externally peer-reviewed.

AI-Assisted Technologies Statement: AI-assisted language tools (ChatGPT, OpenAI) were used to improve the grammar, clarity, and readability of the manuscript. No content, data analysis, or scientific conclusions were generated by AI. The authors are fully responsible for the accuracy and integrity of the work.

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Declaration of Interests: The authors have no conflict of interest to declare.

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