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Original Article

Surgical and medical management of infective endocarditis in a large tertiary referral center: Clinical characteristics, microbiological profile, and predictors of in-hospital mortality

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Abstract

Aim: Real-world data from large tertiary referral centers reflecting the full spectrum of disease complexity remain limited. We aimed to characterize the clinical profile, microbiological landscape, and independent predictors of in-hospital mortality in a consecutive cohort of infective endocarditis (IE) patients managed under a guideline-directed multidisciplinary framework.

Materials and Methods: We retrospectively analyzed 156 patients diagnosed with IE at a tertiary referral center in Türkiye between March 2019 and March 2024. Patients were managed according to the European Society of Cardiology (ESC) guidelines in effect at the time of treatment, with adherence retrospectively assessed against the 2023 ESC criteria by a multidisciplinary endocarditis team. Independent predictors of in-hospital mortality were identified using multivariate logistic regression.

Results: Median age was 61 years (IQR 49 – 67); 71.8% were male and 76.3% had native valve IE. Surgery was performed in 58 patients (37.2%) and medical treatment alone in 98 (62.8%). Blood cultures were negative in 38.5%, and MRSA was the most common organism (21.2%). In-hospital mortality was 15.4%, comparable between surgical (15.5%) and medical (15.3%) groups (p = 1.000). Six variables independently predicted mortality: vasopressor/inotrope requirement (OR 35.87; 95% CI 7.18 – 179), perivalvular abscess (OR 16.79; 1.39 – 202), enterococcal infection (OR 11.43; 1.31 – 99.6), elevated lactate (OR 4.74; 1.87 – 12.0), previous cardiac surgery (OR 5.55; 1.09 – 28.2), and low albumin (OR 0.27 per 10 g/L; 0.08 – 0.95). Apparent discrimination was excellent (AUC = 0.957).

Conclusion: In this real-world IE cohort, hemodynamic instability at presentation was the dominant mortality predictor, while the high culture-negativity rate and MRSA prevalence reflect our transferred-patient profile. Among patients with a surgical indication, surgery was associated with lower mortality, though this is subject to selection bias and confounding by indication. Albumin and lactate are readily available biomarkers warranting prospective evaluation in IE risk stratification.

Keywords: Infective endocarditis, cardiac surgery, mortality predictors, multidisciplinary team, risk stratification

INTRODUCTION

Infective endocarditis (IE) is a life-threatening infection of the endocardial surface of the heart, predominantly affecting native or prosthetic cardiac valves and implanted cardiac devices. Despite significant advances in diagnostic imaging, microbiological techniques, and surgical expertise, IE continues to carry a substantial burden of morbidity and in-hospital mortality ranging from 15% to 30% in contemporary series (1,2). The condition demands urgent, coordinated, and experienced multidisciplinary management to optimize outcomes.

The clinical landscape of IE has evolved considerably. The epidemiological shift from rheumatic heart disease-related streptococcal endocarditis toward healthcare-associated staphylococcal infections, an ageing population with a higher prevalence of prosthetic valves and cardiac implantable electronic devices (CIEDs), and the increasing complexity of affected patients have collectively rendered IE management more challenging (3,4). The 2023 European Society of Cardiology (ESC) guidelines represent the most current evidence-based framework, emphasizing multidisciplinary endocarditis team (MET) decision-making, multimodal imaging including ^{18}5F-FDG PET/CT, and timely surgical intervention.

Tertiary referral centers accepting patients transferred from regional hospitals face a distinct set of challenges: delayed diagnosis compounded by prior antibiotic exposure, a disproportionately high burden of complicated disease, and a microbiological profile that may differ substantially from community-acquired IE series (3,5). This patient population has been underrepresented in the existing literature.

We report a comprehensive analysis of 156 consecutive IE patients managed at a large tertiary referral center between March 2019 and March 2024. The primary objective was to identify independent predictors of in-hospital mortality. Secondary objectives included characterization of the microbiological profile, assessment of adherence to the 2023 ESC guidelines, and comparison of clinical outcomes between surgical and medical management strategies.

MATERIALS AND METHODS

Study design and population

This was a single-center, retrospective cohort study. We included all consecutive adult patients (≥ 18 years) diagnosed with definite or possible IE according to the modified Duke-ISCVID criteria between March 2019 and March 2024 (6). Patients with incomplete clinical, microbiological, or echocardiographic records were excluded (n = 25), resulting in a final cohort of 156 patients. The study was approved by the Ankara Bilkent City Hospital Ethics Committee (TABED 1-25-1225; approval date: 9 April 2025). Informed consent was waived due to the retrospective design.

Data collection

Clinical, microbiological, echocardiographic, and outcome data were extracted from electronic medical records. Approximately one-third of patients were transferred from regional hospitals where antibiotic therapy had been initiated prior to admission; symptom onset and pre-transfer antibiotic duration were therefore not consistently available and were not included in the analysis.

Diagnostic criteria and imaging

Transthoracic echocardiography (TTE) was performed in 155 patients (99.4%) and transesophageal echocardiography (TEE) in 154 (98.7%), in accordance with ESC Class I recommendations; the small number of patients without TEE reflected clinical instability precluding the procedure or an unequivocal diagnosis on TTE. ^{18}F-FDG PET/CT was performed at the discretion of the multidisciplinary endocarditis team in cases of prosthetic valve IE, CIED infection, or inconclusive echocardiographic findings (ESC 2023 Class IIa) (7).

Microbiology

At least three blood culture sets were obtained prior to antibiotic initiation where possible. Causative organisms were classified as: S. aureus (MRSA/MSSA), coagulase-negative staphylococci (CoNS), streptococci, enterococci, Gram-negative bacilli, Brucella spp., and other/rare organisms. Culture-negative IE was defined as absence of microbial growth in all culture sets. In polymicrobial infections, each patient was assigned to a single category based on the highest-virulence organism (hierarchy: Fungal > Gram-negative > S. aureus > Enterococci > CoNS > Streptococci > Brucella spp.).

Treatment

All patients were managed by a multidisciplinary endocarditis team comprising cardiovascular surgery, infectious diseases, cardiology, and neurology specialists. Antibiotic therapy followed the ESC guidelines in effect at the time of treatment; a minimum 4-week intravenous course was planned unless limited by in-hospital death. Surgical indications included heart failure (severe valvular regurgitation or hemodynamic compromise), uncontrolled infection (perivalvular abscess, persistent sepsis), and prevention of systemic embolism (vegetation ≥ 10 mm or prior embolic event), per ESC 2023 Class I criteria. Surgical timing was categorized as early (< 2 weeks) or late (≥ 2 weeks from admission).

Outcome measures

The primary outcome was in-hospital mortality. Secondary outcomes included major complications (stroke, peripheral embolism, cardiopulmonary arrest, ventricular arrhythmia, complete AV block), ICU admission, and reoperation. Surviving patients were followed for a median of 7 months (IQR 6–9).

Statistical analysis

Continuous variables are presented as median (IQR); comparisons used non-parametric tests based on normality testing. Categorical variables are presented as frequency and percentage. Comparisons used Mann–Whitney U,

independent t-test, chi-square, or Fisher's exact test as appropriate. Variables with $p < 0.20$ on univariate analysis entered a multivariate logistic regression model with backward stepwise elimination (removal threshold $p > 0.10$). Cardiopulmonary arrest and VT/VF were excluded due to complete separation. Lactate was natural log-transformed prior to inclusion. Model performance was assessed by the apparent AUC and Nagelkerke R^2, with internal validation by bootstrapping (1000 resamples) to estimate optimism-corrected discrimination. A Firth penalised logistic regression was performed as a sensitivity analysis to address the limited number of events. Analyses were performed using Python 3.12 (SciPy, statsmodels). A two-tailed $p < 0.05$ was considered statistically significant.

RESULTS

Patient characteristics

Between March 2019 and March 2024, 181 patients were diagnosed with IE. After excluding 25 with incomplete data, 156 were included (Figure 1). Median age was 61 years (IQR 49–67) and 71.8% were male. Native valve IE was most common (76.3%), followed by mechanical prosthetic valve IE (11.5%) and bioprosthetic IE (9.0%). Baseline characteristics are detailed in Table 1. Common comorbidities included hypertension (49.4%), chronic kidney disease (31.4%), and diabetes mellitus (33.3%). Vasopressor or inotrope support was required in 24.4% at presentation. Cardiopulmonary arrest occurred in 14.7%, with 22 of 23 affected patients succumbing in hospital.

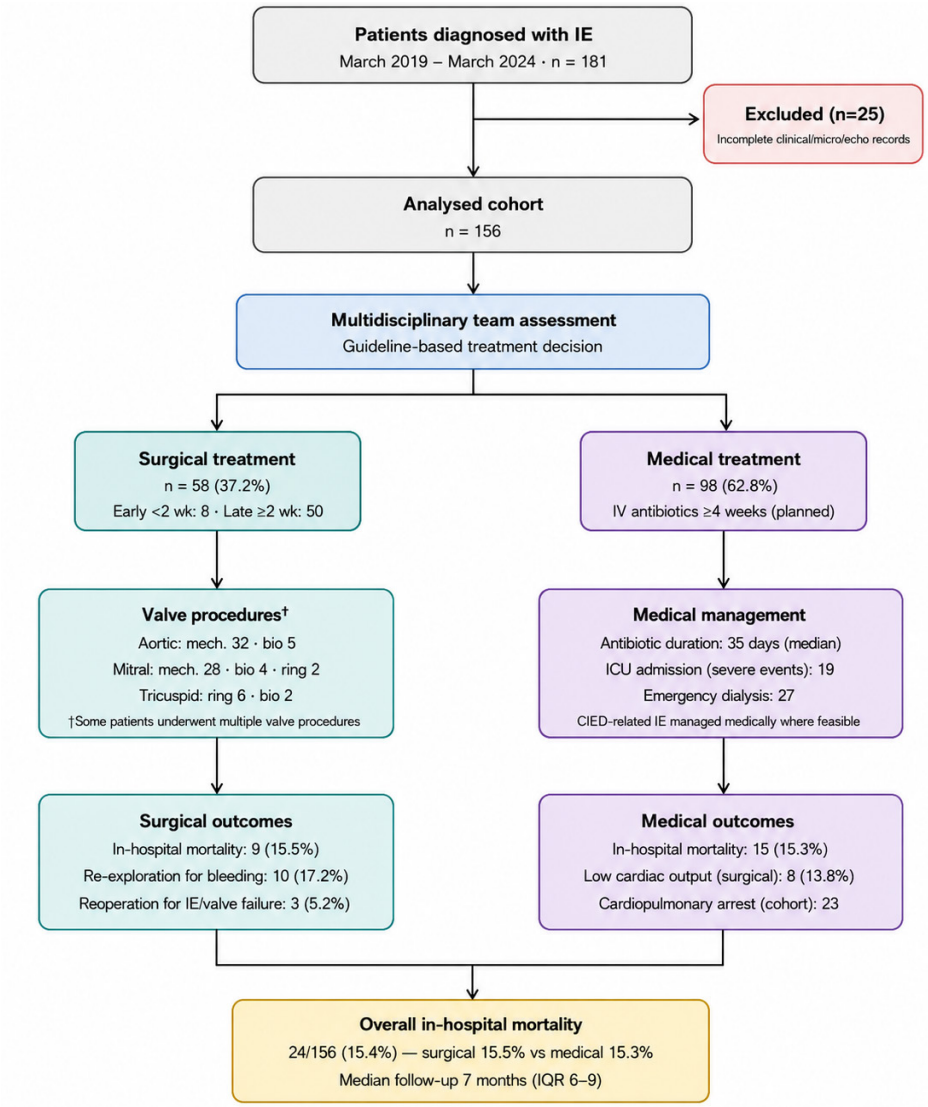

Figure 1. Patient flow diagram. Stroke (n = 3) and peripheral embolism (n = 6) occurred across the whole cohort and are shown under the branch where they were predominantly recorded: they are not exclusive to medically managed patients; A total of 181 patients were diagnosed with infective endocarditis between March 2019 and March 2024; After exclusion of 25 patients with incomplete data, 156 patients were included in the final analysis; IE: infective endocarditis, ICU: intensive care unit, CIED: cardiac implantable electronic device, IV: intravenous, MDT: multidisciplinary team

Table 1. Baseline demographic, clinical, and microbiological characteristics (n = 156)		
Variable		**n (%) or Median (IQR)**
Age, years		61.0 (48.8 – 67.0)
Male sex		112 (71.8)%
Comorbidities	**Hypertension**	77 (49.4)%
	Diabetes mellitus	52 (33.3)%
	Active smoking	18 (11.5)%
	COPD	18 (11.5)%
	Chronic kidney disease	49 (31.4)%
	Previous MI	13 (8.3)%
	Previous cardiac surgery	28 (17.9)%
	Previous IE	7 (4.5)%
	Previous stroke/TIA	18 (11.5)%
	Active malignancy	8 (5.1)%
	Pulmonary arterial hypertension	2 (1.3)%
	Permanent pacemaker	13 (8.3)%
	ICD	18 (11.5)%
	CRT	3 (1.9)%
Clinical presentation	**Fever**	75 (48.1)%
	Dyspnea	77 (49.4)%
	General deterioration	30 (19.2)%
	Syncope	2 (1.3)%
	LVEF, %	55.0 (50.0 – 60.0)
	Vasopressor/inotrope	38 (24.4)%
	Emergency dialysis	34 (21.8)%
	VT/VF	6 (3.8)%
	Complete AV block	4 (2.6)%
	Cardiopulmonary arrest	23 (14.7)%
Affected valve	**Native valve**	119 (76.3)
	Mechanical prosthesis	18 (11.5)
	Bioprosthesis	14 (9.0)
	Native+Mechanical	3 (1.9)
	Native+Bioprosthetic	2 (1.3)
Echocardiography & imaging	**TTE performed**	155 (99.4)%
	TEE performed	154 (98.7)%
	^{18}F-FDG PET/CT	43 (27.6)%
	Vegetation < 10 mm	84 (53.8)%
	Vegetation ≥ 10 mm	67 (42.9)%
	Perivalvular abscess	9 (5.8)%
	Paravalvular leak	9 (5.8)%
	Prosthetic dehiscence	8 (5.1)%
	Device lead involvement	17 (10.9)%

Data are n (%) or median (IQR); † Reoperation rate within the surgical group (n = 58); ‡ PM (n = 13), ICD (n = 18), CRT (n = 3) include patients with multiple devices; unique CIED patients = 27 (17.3%); lead involvement in IE = 17 (10.9%); CoNS: coagulase-negative staphylococci, CIED: cardiac implantable electronic device, IQR: interquartile range, LVEF: left ventricular ejection fraction

Table 1. Baseline demographic, clinical, and microbiological characteristics (n = 156)

Variable		n (%) or Median (IQR)
Microbiology	Blood culture positive	96 (61.5)%
	Blood culture negative	60 (38.5)%
	S. aureus (MRSA)	33 (21.2)
	S. aureus (MSSA)	11 (7.1)
	CoNS	10 (6.4)
	Streptococci	15 (9.6)
	Enterococci	13 (8.3)
	Gram-negative bacilli	7 (4.5)
	Brucella spp.	4 (2.6)
	Other/Rare	2 (1.3)
	Fungal	1 (0.6)
	Culture-negative	60 (38.5)
	Polymicrobial	9 (5.8)
Laboratory values at admission	WBC, $\times 10^3/\mu L$	8.4 (6.1 – 10.5)
	Hemoglobin, g/dL	10.0 (8.8 – 12.0)
	Platelets, $\times 10^3/\mu L$	245.5 (178.2 – 321.2)
	Creatinine, mg/dL	1.1 (0.8 – 1.8)
	eGFR, mL/min/1.73m²	62.0 (35.0 – 98.2)
	CRP, mg/L	56.0 (22.0 – 119.7)
	Procalcitonin, ng/mL	0.3 (0.1 – 1.3)
	Albumin, g/L	34.0 (29.0 – 39.0)
	BNP, pg/mL	1182.5 (371.8 – 5505.0)
	Lactate, mmol/L	2.0 (1.2 – 3.0)
	Troponin, ng/L	21.0 (7.0 – 58.2)
Treatment	Surgical treatment	58 (37.2)
	Early surgery (< 2 weeks)	8 (13.8 of surgical)
	Late surgery (≥ 2 weeks)	50 (86.2 of surgical)
	Medical treatment	98 (62.8)
In-hospital outcomes	In-hospital mortality	24 (15.4)
	Stroke	3 (1.9)%
	Peripheral embolism	6 (3.8)%
	Reoperation	3 (5.2†)
	Total hospital stay, days	40.0 (30.0 – 60.0)
	Follow-up duration, months	7.0 (6.0 – 9.0)

Data are n (%) or median (IQR); † Reoperation rate within the surgical group (n = 58); ‡ PM (n = 13), ICD (n = 18), CRT (n = 3) include patients with multiple devices; unique CIED patients = 27 (17.3%); lead involvement in IE = 17 (10.9%); CoNS: coagulase-negative staphylococci, CIED: cardiac implantable electronic device, IQR: interquartile range, LVEF: left ventricular ejection fraction

Echocardiographic findings

TTE was performed in 155 patients (99.4%) and TEE in 154 (98.7%). Vegetation size was ≥ 10 mm in 42.9% of patients with measurable vegetation (67/151; five patients had no measurable vegetation). Perivalvular abscess was identified in 9 (5.8%), paravalvular leak in 9 (5.8%), and prosthetic dehiscence in 8 (5.1%). Cardiac device lead involvement was present in 17 (10.9%). ^{18}F-FDG PET/CT was performed in 43 patients (27.6%), with comparable utilization in culture-negative (31.7%) and culture-positive (25.0%) patients (p = 0.470; Figure 2).

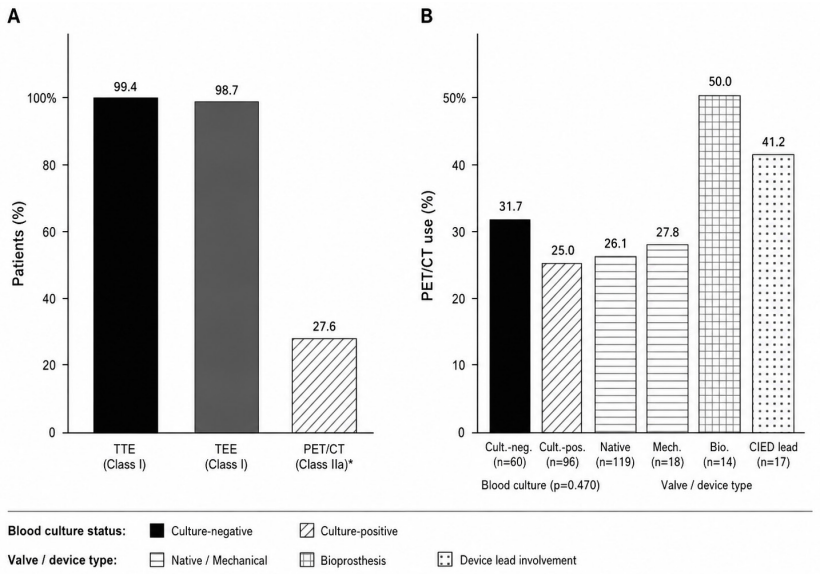

Figure 2. ^{18}F-FDG PET/CT utilization; Panel A: imaging modality rates; Panel B: PET/CT utilization by blood culture status and, separately, by valve/device type, which are distinct variables shown with separate visual codes; "Device lead involvement" denotes CIED-related IE; The Class IIa recommendation for PET/CT applies to prosthetic-valve or CIED IE and inconclusive echocardiography, not the whole cohort; PET/CT: positron emission tomography/CT, TEE: transesophageal echocardiography, TTE: transthoracic echocardiography

Microbiology

Blood cultures were positive in 96 patients (61.5%) and negative in 60 (38.5%). MRSA was most frequently identified (33, 21.2%), followed by Streptococcus spp. (15, 9.6%), Enterococcus spp. (13, 8.3%), MSSA (11, 7.1%), and CoNS (10, 6.4%). Brucella spp. was identified in 4 (2.6%), reflecting regional endemicity. Polymicrobial infection occurred in 9 (5.8%). Microbiological profile and mortality is illustrated in Figure 3 .

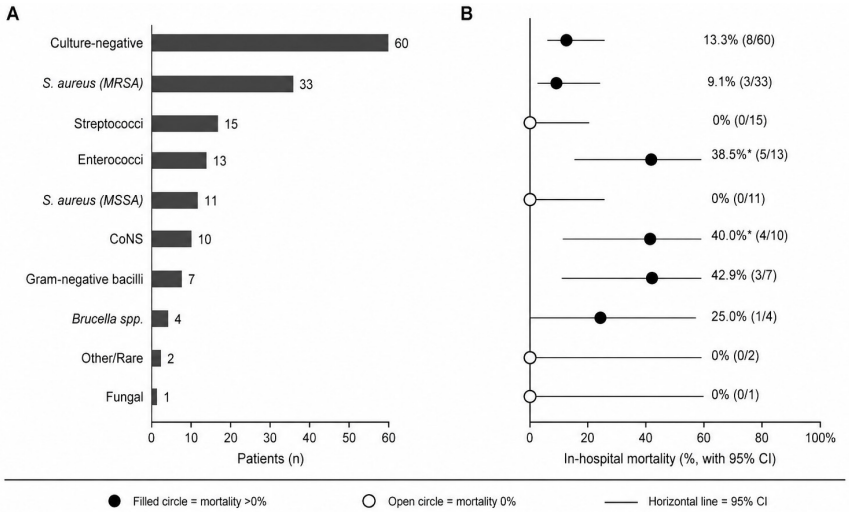

Figure 3. Causative microorganism distribution (Panel A) and in-hospital mortality rates (Panel B); Panel B shows mortality with numerators/denominators and binomial 95% confidence intervals; Filled circles: mortality > 0%; open circles: 0%; *p < 0.05 vs all other groups (Fisher's exact test); p values are exploratory and unadjusted for multiple comparisons; In polymicrobial infections, each patient was assigned to the highest-virulence organism category; CoNS: coagulase-negative staphylococci

Surgical versus medical treatment

Fifty-eight patients (37.2%) underwent surgery and 98 (62.8%) received medical treatment. Surgical patients were younger (median 52 vs. 63 years; p < 0.001) with higher rates of large vegetations, perivalvular abscess, and paravalvular complications (Table 2).

Eight patients (13.8%) underwent early surgery (< 2 weeks) and 50 (86.2%) underwent late surgery. Postoperative complications included reoperation for bleeding in 10 (17.2%), low cardiac output syndrome in 8 (13.8%), and acute kidney injury in 5 (8.6%). Three patients (5.2%) required reoperation for IE recurrence or valve failure (Table 3).

Table 2. Comparison of surgical and medical treatment groups			
Variable	**Surgical (n = 58)**	**Medical (n = 98)**	**p value**
Age, years	52.0 (39.2 – 64.0)	63.0 (53.0 – 70.0)	< 0.001*
Male sex	46 (79.3)	66 (67.3)	0.155
Comorbidities			
Hypertension	25 (43.1)	52 (53.1)	0.300
Diabetes mellitus	14 (24.1)	38 (38.8)	0.089
Chronic kidney disease	13 (22.4)	36 (36.7)	0.092
Previous cardiac surgery	18 (31.0)	10 (10.2)	0.002*
Previous IE	3 (5.2)	4 (4.1)	0.712
Previous stroke/TIA	10 (17.2)	8 (8.2)	0.145
Permanent pacemaker	0 (0.0)	13 (13.3)	0.002*
ICD	0 (0.0)	18 (18.4)	< 0.001*
Clinical Presentation			
Fever	36 (62.1)	39 (39.8)	0.012*
Dyspnea	41 (70.7)	36 (36.7)	< 0.001*
Vasopressor/inotrope	20 (34.5)	18 (18.4)	0.038*
Emergency dialysis	7 (12.1)	27 (27.6)	0.039*
Cardiopulmonary arrest	9 (15.5)	14 (14.3)	1.000
LVEF, %	56.0 (55.0 – 60.0)	55.0 (40.0 – 60.0)	0.041*
Echocardiography			
Vegetation ≥ 10 mm	42 (72.4)	25 (25.5)	< 0.001*
Perivalvular abscess	9 (15.5)	0 (0.0)	< 0.001*
Paravalvular leak	9 (15.5)	0 (0.0)	< 0.001*
Prosthetic dehiscence	8 (13.8)	0 (0.0)	< 0.001*
Device lead involvement	1 (1.7)	16 (16.3)	0.003*
PET/CT performed	11 (19.0)	32 (32.7)	0.096
Microbiology			
Blood culture positive	44 (75.9)	52 (53.1)	0.008*
S. aureus (MRSA)	13 (22.4)	20 (20.4)	0.925
Streptococci	12 (20.7)	3 (3.1)	< 0.001*
Enterococci	5 (8.6)	8 (8.2)	1.000
Culture-negative	14 (24.1)	46 (46.9)	0.008*
Laboratory Values			
WBC, ×10³/μL	9.3 (7.0 – 11.7)	7.6 (6.0 – 9.4)	0.043*
Hemoglobin, g/dL	9.8 (8.9 – 12.2)	10.0 (8.8 – 11.7)	0.853
Creatinine, mg/dL	1.0 (0.8 – 1.5)	1.3 (0.8 – 2.2)	0.038*
CRP, mg/L	69.0 (26.5 – 124.0)	52.3 (17.9 – 103.8)	0.175
Procalcitonin, ng/mL	0.3 (0.1 – 1.0)	0.3 (0.1 – 1.7)	0.902
Albumin, g/L	33.0 (29.2 – 39.0)	35.0 (29.0 – 38.0)	0.660
BNP, pg/mL	2274.5 (524.0 – 6158.8)	990.5 (312.8 – 5355.0)	0.221
Lactate, mmol/L	1.4 (1.1 – 2.3)	2.2 (1.5 – 3.5)	< 0.001*
Outcomes			
In-hospital mortality	9 (15.5)	15 (15.3)	1.000
Total hospital stay, days	45.0 (30.0 – 55.5)	35.0 (30.0 – 60.0)	0.193

Data are n (%) or median (IQR); * p < 0.05; IQR: interquartile range, LVEF: left ventricular ejection fraction, PET/CT: positron emission tomography/CT

Table 3. Clinical details of patients requiring reoperation (n = 3)

	Case 1	Case 2	Case 3
Age / Sex	66 / Male	51 / Male	48 / Male
Causative organism	MRSA	Acinetobacter baumannii	Brucella spp.
Affected valve	Mechanical aortic	Mechanical aortic	Mechanical aortic
Index operation	Bentall procedure	Mechanical AVR	Mechanical AVR
Reoperation indication	Perigraft abscess + vegetation	Aortic root abscess recurrence	Aortic root abscess + dehiscence
Reoperation procedure	Redo Bentall	Cabrol procedure	Redo Bentall
Timing	Index hospitalization	1 year post-discharge	Index hospitalization
ICU stay, days	7	7	4
In-hospital outcome	Survived	Survived	Deceased
Follow-up	7 months	12 months	--

AVR: aortic valve replacement, ICU: intensive care unit, MRSA: methicillin-resistant Staphylococcus aureus

In-hospital outcomes

Overall in-hospital mortality was 15.4% (24/156). Mortality was comparable between surgical (15.5%) and medical (15.3%) groups (p = 1.000). Kaplan–Meier analysis showed no significant survival difference over median 7-month follow-up (log-rank p = 0.98; Figure 4).

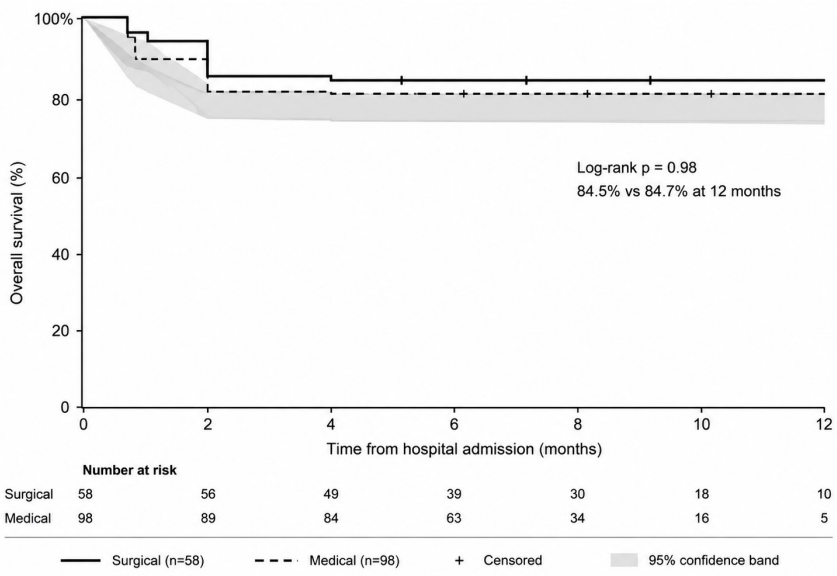

Figure 4. Kaplan–Meier overall survival curves: surgical (solid, n = 58) vs medical (dashed, n = 98); 95% confidence bands are shown, and time zero is defined as hospital admission; The curves are unadjusted and descriptive; as some patients underwent surgery ≥ 2 weeks after admission, immortal time bias cannot be excluded and the curves should not be interpreted as demonstrating therapeutic equivalence; Only 10 surgical and 5 medical patients remained at risk at 12 months; Log-rank p = 0.98; 12-month survival 84.5% vs 84.7%

ESC guideline adherence

TTE and TEE were performed in 99.4% and 98.7% respectively (ESC Class I). A minimum 4-week intravenous antibiotic course was planned for all patients unless limited by in-hospital death. Of 95 patients with at least one surgical indication, surgery was performed in 55 (57.9%); the remaining 40 (42.1%) were managed medically due to prohibitive operative risk, multiorgan dysfunction, patient or family refusal, or multidisciplinary team consensus, as documented in clinical records (formal systematic categorization was not feasible given the retrospective design). In-hospital mortality was significantly higher in patients with a surgical indication who did not undergo surgery compared with those who did (37.5% vs. 16.4%; p = 0.030; Table 4, Figure 5).

Table 4. Guideline adherence assessment for infective endocarditis

Parameter	n (%)	Recommendation class	Status
1. Diagnostic workup			
Transthoracic echocardiography (TTE)	155 (99.4)	Class I, LoE B	✓
Transesophageal echocardiography (TEE)	154 (98.7)	Class I, LoE B	✓
^{18}F-FDG PET/CT	43 (27.6)	Class IIa, LoE B	Partial
2. Antibiotic therapy & MDT			
IV antibiotics ≥ 4 weeks (planned)*	156 (100.0)	Class I, LoE B	✓
Multidisciplinary endocarditis team	156 (100.0)	Class I, LoE B	✓
3. Surgical decision — surgical indication present (n = 95)			
Surgery performed	55 (57.9)	--	✓
Surgery not performed	40 (42.1)	--	✗
Mortality — surgery performed	9 (16.4)	--	
Mortality — surgery not performed	15 (37.5)	--	
p value (Fisher's exact)	0.030*	--	
4. Surgical timing (n = 58 operated)			
Early surgery (< 2 weeks)	8 (13.8)	ESC preferred	Partial
Late surgery (≥ 2 weeks)	50 (86.2)	Acceptable	✓

* p < 0.05; Patients were managed according to the ESC guidelines in effect at the time of treatment; adherence was retrospectively assessed against the 2023 ESC criteria; Recommendation class and LoE refer to the 2023 ESC guidelines; * A minimum 4-week intravenous course was planned for all patients unless limited by in-hospital death; ESC: European Society of Cardiology, IV: intravenous, LoE: level of evidence, MDT: multidisciplinary team

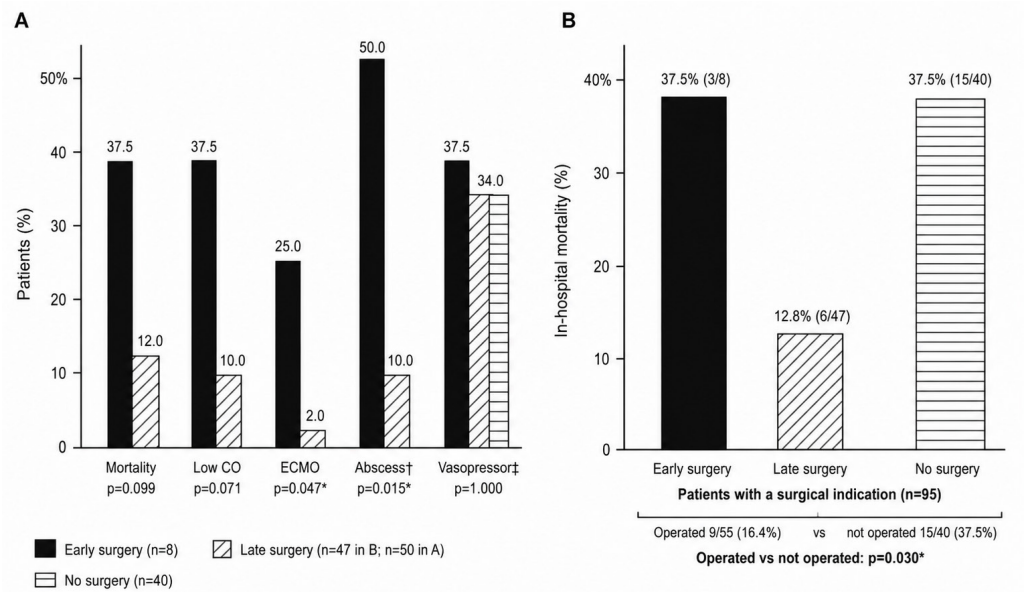

Figure 5. Surgical timing and outcomes; Panel A: postoperative outcomes and baseline severity markers in early (< 2 weeks, n = 8) vs late (≥ 2 weeks, n = 50) surgical patients (abscess and vasopressor requirement are baseline severity characteristics rather than outcomes); Panel B: in-hospital mortality among patients with a surgical indication (n = 95), shown by early surgery (3/8), late surgery (6/47), and no surgery (15/40); the p = 0.030 comparison is between all operated (9/55, 16.4%) and non-operated (15/40, 37.5%) patients; These associations are subject to selection bias and should not be interpreted causally; *p < 0.05; CO: cardiac output, ECMO: extracorporeal membrane oxygenation

Predictors of in-hospital mortality

On multivariate logistic regression (Table 5), six variables independently predicted mortality: vasopressor/inotrope requirement (OR 35.87; 95% CI 7.18 – 179; p < 0.001), perivalvular abscess (OR 16.79; 95% CI 1.39 – 202; p = 0.026), enterococcal infection (OR 11.43; 95% CI 1.31 – 99.6; p = 0.027), natural log-lactate (OR 4.74; 95% CI 1.87 – 12.0; p = 0.001), previous cardiac surgery (OR 5.55; 95% CI 1.09 – 28.2; p = 0.039), and albumin per 10 g/L (OR 0.27; 95% CI 0.08 – 0.95; p = 0.042). Apparent AUC = 0.957; Nagelkerke R^2 = 0.549 (Figure 6).

Table 5. Multivariate logistic regression — independent predictors of in-hospital mortality

Variable	Adjusted OR	95% CI	p value
Vasopressor/inotrope requirement	35.87	7.18 – 179	< 0.001
Perivalvular abscess	16.79	1.39 – 202	0.026
Enterococcal infection	11.43	1.31 – 99.6	0.027
Previous cardiac surgery	5.55	1.09 – 28.2	0.039
Lactate, mmol/L (natural log)	4.74	1.87 – 12.0	0.001
Albumin, per 10 g/L	0.27	0.08 – 0.95	0.042

Apparent AUC = 0.957; Nagelkerke R^2 = 0.549; n = 156 (24 deaths; 4 events per variable); Wide CIs reflect limited event count; Lactate natural log-transformed; albumin OR per 10 g/L; Bootstrap-corrected AUC 0.929; Firth penalised sensitivity analysis concordant; OR: odds ratio, CI: confidence interval, AUC: area under ROC curve

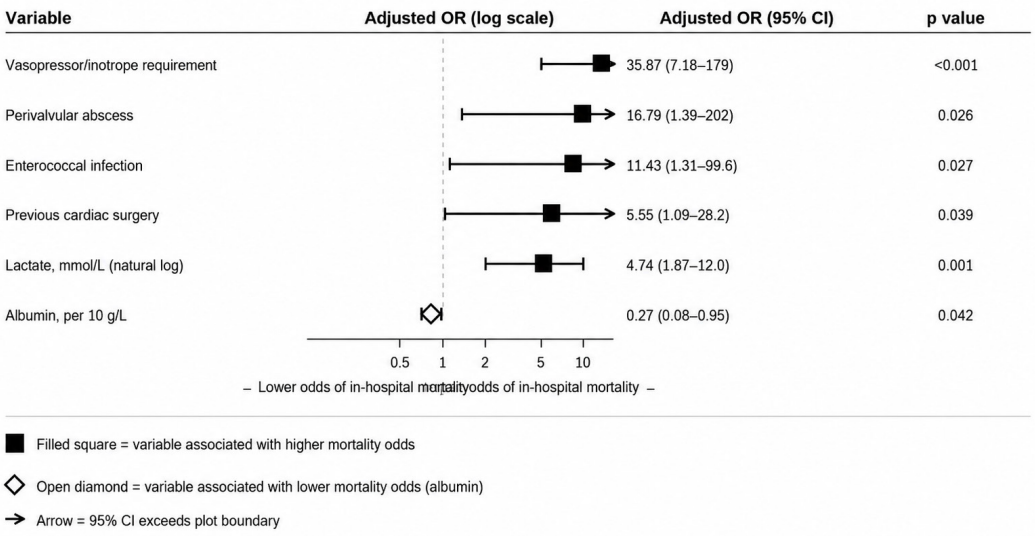

Figure 6. Forest plot of independent predictors of in-hospital mortality (multivariate logistic regression); Filled squares: variables associated with higher mortality odds; open diamond: variable associated with lower mortality odds (albumin, per 10 g/L); Arrows: 95% CIs exceeding plot boundary; Lactate was natural log-transformed; The apparent AUC of 0.957 was calculated in the development cohort without internal validation; Adjusted OR: adjusted odds ratio; CI: confidence interval; *p < 0.05

DISCUSSION

This retrospective single-center study provides a comprehensive analysis of 156 consecutive IE patients managed under a structured multidisciplinary framework at a tertiary referral center over a five-year period spanning March 2019 to March 2024. Our findings both corroborate established international evidence and depart from it in clinically meaningful ways, offering a real-world perspective from a high-complexity transferred-patient population that has been underrepresented in Western-centric IE registries.

Hemodynamic instability: The dominant mortality predictor

Vasopressor or inotrope requirement was the strongest independent predictor of in-hospital mortality (OR 35.87; 95% CI 7.18 – 179), an effect size consistent with contemporary international series reporting odds ratios of 10–40 for septic and cardiogenic shock in IE(8). This finding conveys a clear clinical message: hemodynamic status at presentation is the most powerful determinant of survival, irrespective of treatment modality chosen. Cardiopulmonary arrest, occurring in 14.7%

of patients with a 95.7% in-hospital fatality rate, was excluded from the multivariate model due to near-perfect separation but represents the endpoint of unrecognized or undertreated hemodynamic deterioration. These data argue for earlier identification of hemodynamic compromise and more proactive intervention thresholds in IE patients presenting to or being transferred to tertiary centers (9).

Perivalvular abscess: An anatomical harbinger of poor prognosis

Perivalvular abscess was the second strongest independent mortality predictor (OR 16.79; 95% CI 1.39 – 202), within the OR 5–20 range reported internationally for paravalvular extension. In our cohort, abscess formation triggered surgery in all 9 affected patients. Despite operative management, the strong independent mortality signal persisted after adjustment, underscoring that abscess-related IE represents a phenotype defined not merely by local anatomical destruction but by systemic uncontrolled infection with inherently poor outcomes (10,11). Our data support urgent rather than elective operative decision-making when abscess is identified, and underscore that outcomes depend substantially on the degree of perivalvular tissue involvement at the time of surgery.

Enterococcal endocarditis: An underestimated threat in the prosthetic valve era

Enterococcal IE independently predicted more than 11-fold higher in-hospital mortality (OR 11.43; p = 0.027), directly challenging the prevailing perception of Enterococcus spp. as a relatively low-virulence organism associated with subacute, indolent disease. In our referred population, enterococcal IE disproportionately affected patients with prosthetic valves, CIED, advanced age, and chronic kidney disease. The combination of limited antibiotic bactericidal activity, biofilm formation on prosthetic surfaces, and high comorbidity burden converged to produce a high and independently significant mortality signal (7,12). These data constitute a compelling real-world argument against the "Enterococci are less virulent" assumption and reinforce the need for heightened clinical vigilance, early surgical evaluation, and organism-specific management pathways in this patient subgroup.

MRSA: High prevalence, yet not an independent mortality predictor

MRSA was identified in 21.2% of the total cohort, making it the most common causative organism among culture-positive patients and substantially exceeding the 5–12% MRSA prevalence typically reported in Western European registries. This epidemiological divergence reflects the referral profile of our center: transferred patients carry a disproportionate burden of nosocomial MRSA strains. Importantly, MRSA was not an independent predictor of mortality in our multivariate model (univariate p = 0.414), suggesting that its adverse outcomes can be effectively mitigated through rapid targeted anti-MRSA therapy within a dedicated MDT framework. The clinical implication is that vancomycin or daptomycin should be considered as empirical first-line agents pending culture results in transferred patients at high-MRSA-prevalence centers, though limited statistical power and confounding cannot be excluded as alternative explanations (13).

Blood culture negativity and PET/CT: Navigating diagnostic uncertainty in a referral setting

The blood culture negativity rate of 38.5% substantially exceeds the 10–20% range in most international series and represents one of the most epidemiologically distinctive features of our dataset. We attribute this primarily to pre-referral broad-spectrum antibiotic exposure, a structural feature of the Turkish healthcare system's referral dynamics not readily quantifiable retrospectively. This diagnostic context amplifies the role of multimodal imaging. Our ^{18}F-FDG PET/CT utilization rate of 27.6%—comparable between culture-negative (31.7%) and culture-positive (25.0%) patients (p = 0.470)—reflects consistent clinical indication-based use, with highest utilization in bioprosthetic valve (50.0%) and CIED (41.2%) IE, consistent with ESC 2023 Class IIa guidance. These findings support systematic PET/CT integration into the diagnostic algorithm for referred IE patients and underscore the need for prospective evaluation of molecular diagnostic techniques in high culture-negativity settings (7,14).

Equivalent mortality between surgical and medical groups: Appropriate case selection, not therapeutic equivalence

The statistically identical in-hospital mortality between surgical (15.5%) and medical (15.3%) groups (p = 1.000), mirroring the pattern observed in large international observational IE series, requires careful interpretation. This finding does not imply clinical equivalence for the same patient; rather, it reflects profound opposing selection pressures. Surgical patients were significantly younger but harbored more severe anatomical disease, while medically managed patients were older with higher CIED burdens and more frequent emergency dialysis. The comparable mortality across these fundamentally different phenotypes is evidence of appropriate MDT-guided case selection (confounding by indication) rather than an argument for withholding surgery in guideline-indicated patients. This is consistent with the broader international experience in which observational equivalence between treatment groups reflects successful risk stratification by an experienced endocarditis team.

Guideline adherence and its association with clinical outcomes

The significantly higher mortality in patients with a surgical indication who did not undergo surgery (37.5% vs. 16.4%; p = 0.030) is the most clinically actionable finding of our study. Of 95 patients meeting at least one surgical indication, 40 (42.1%) did not receive operative treatment. While withholding surgery in fragile, multimorbid patients is often clinically justified, the higher mortality in patients who did not undergo surgery

highlights the potential survival benefit of operative management in appropriately selected patients. This comparison is, however, subject to treatment-selection bias and confounding by indication, and should be interpreted as an association rather than a causal effect; some non-operated patients had valid clinical or patient-centered contraindications to surgery. These findings reinforce the ESC recommendation that all IE patients with a surgical indication be evaluated by a dedicated endocarditis team, with decisions to withhold surgery remaining individualized, carefully documented, and regularly reassessed (7,15).

Albumin and lactate: Accessible biomarkers for bedside risk stratification

Low serum albumin (OR 0.27 per 10 g/L; p = 0.042) and elevated admission lactate (OR 4.74 per natural log unit; p = 0.001) independently predicted mortality, contributing prognostic information beyond clinical presentation. Hypoalbuminemia reflects chronic inflammation-driven catabolism, malnutrition, and impaired hepatic synthetic function—frequently seen in patients with prolonged IE transferred after extended illness. Elevated lactate signals acute end-organ hypoperfusion and anaerobic metabolism. The independent predictive value of both markers, even after adjustment for vasopressor requirement, suggests they capture prognostic information not fully represented by clinical status alone. We propose that systematic measurement of albumin and lactate at admission should be incorporated into IE risk stratification pathways and prospectively validated as components of a composite bedside prognostic score (16,17).

A regional perspective: Brucella endocarditis in an endemic setting

Brucella spp. was identified in 4 patients (2.6%), virtually absent from Western guidelines and registries yet well-recognized in endemic regions including the Mediterranean basin and neighboring regions. All four patients underwent surgical intervention, consistent with the consensus that medical therapy alone is inadequate for established Brucella endocarditis due to insufficient intracardiac antibiotic penetration and bactericidal activity against biofilm-embedded organisms. The 25.0% in-hospital mortality in this subgroup reflects diagnostic delays inherent to this rare presentation. Our data serve as a regional reminder that Brucella should be actively considered in the differential diagnosis of culture-negative IE in patients with relevant epidemiological exposures, and that early surgical consultation is essential once the diagnosis is established (7,18).

Contextualizing our findings within the international IE landscape

Viewed in aggregate, our results occupy a distinct and informative position within the international IE literature. Our overall in-hospital mortality of 15.4% falls at the favorable end of the 15–25% range reported across large contemporary registries including the International Collaboration on Endocarditis (ICE), EURO-ENDO, and the Society of Thoracic Surgeons (STS) National Database—a performance particularly notable given our high-complexity, heavily transferred patient population (19,20).

Several features, however, diverge substantially from Western registry benchmarks. The blood culture negativity rate of 38.5% is nearly twice the upper boundary of the 10–20% range in ICE and EURO-ENDO, reflecting structural pre-referral antibiotic exposure rather than diagnostic failure. MRSA prevalence of 21.2%, more than double most Western series, reflects the nosocomial patient profile of a tertiary referral center. Conversely, streptococcal IE—the dominant etiology in community-acquired Western series—constituted only 9.6% of our cohort, reflecting the community-to-hospital epidemiological gradient in our referral population (14,19).

Most strikingly, the enterococcal mortality signal (OR 11.43), the mortality difference between operated and non-operated patients with a surgical indication (16.4% vs. 37.5%; p = 0.030), and the independent prognostic value of albumin and lactate carry implications extending beyond regional description. Unlike studies from homogeneous, predominantly community-acquired IE populations, our data provide one of the first real-world validations of the 2023 ESC guideline framework in a high-complexity, transferred-patient setting demonstrating that guideline-adherent MDT management achieves internationally benchmarked mortality outcomes even in the most challenging referral populations (7).

Limitations

Several limitations warrant acknowledgment. The retrospective single-center design limits generalizability and introduces selection bias. The high proportion of transferred patients precluded systematic documentation of pre-hospital antibiotic duration. The absence of a prospectively calculated validated IE risk score precludes direct comparison with established prognostic tools. The median follow-up of 7 months does not allow assessment of long-term survival or IE recurrence. With only 24 events and six variables retained (approximately four events per variable), the model carries a risk of overfitting and sparse-data bias; the identified variables should be regarded as associated with mortality rather than definitively independent predictors. Wide confidence intervals for vasopressor/inotrope requirement (95% CI 7.18 – 179) and perivalvular abscess (95% CI 1.39 – 202) reflect the limited event count. The reported AUC of 0.957 is an apparent value not internally validated; optimism-corrected discrimination is likely lower. The Kaplan–Meier analysis is unadjusted and descriptive; as some patients underwent surgery ≥ 2 weeks after admission, immortal time bias cannot be excluded, and the curves should not be interpreted as demonstrating therapeutic equivalence.

CONCLUSION

In this large real-world IE cohort managed over a five-year period at a tertiary referral center, in-hospital mortality was 15.4% with comparable rates between surgical and medical

groups, reflecting appropriate multidisciplinary case selection. Hemodynamic instability at presentation is the dominant mortality predictor, while perivalvular abscess and enterococcal etiology identify high-risk anatomical and microbiological subgroups. The high blood culture negativity rate and MRSA prevalence define the epidemiological profile of a transferred-patient population and should inform empirical antibiotic and diagnostic imaging strategies. Patients who underwent surgery when guideline-indicated had significantly lower in-hospital mortality, highlighting the value of individualized multidisciplinary evaluation in determining operative candidacy. Albumin and lactate are clinically actionable, universally available biomarkers that merit prospective validation in IE risk stratification frameworks.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that there is no financial support.

Ethical Approval
The study was approved by the Ankara Bilkent City Hospital Ethics Committee (TABED 1-25-1225; approval date: 9 April 2025).

Informed Consent
Informed consent was waived due to the retrospective design.

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