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Impact of Surgical Timing on Mortality in Infective Endocarditis Patients with Neurological Complications

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This study was carried out at the Department of Cardiovascular Surgery, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, Istanbul, Turkiye.

ABSTRACT

Introduction: The optimal timing of cardiac surgery in infective endocarditis (IE) patients with neurological complications remains controversial.
Objective: To evaluate the effects of early surgical intervention compared with medical therapy on in-hospital and one-year mortality, highlighting the prognostic value of neurological severity and clinical variables.
Methods: This retrospective study included 109 patients with neurological complications out of a total of 452 patients diagnosed with infective endocarditis at our hospital between January 2013 and December 2023. The patients were divided into a surgical group (n = 48) and a medical therapy group (n = 61). Surgical cases were further classified as early (≤ 7 days) and late (> 7 days). Demographic data, echocardiographic findings, vegetation size (≥ 1 cm), mobility, causative microorganisms, and stroke severity were assessed using the National Institutes of Health Stroke Scale (NIHSS) method (mild-moderate-severe). Mortality predictors over a one-year period were evaluated using multivariate logistic regression.
Result: When comparing one-year in-hospital and post-discharge mortality between the medical and surgical patient groups, mortality was significantly higher in the medically treated group (54.1% and 46.4%, respectively) compared to the surgical group (16.7% and 0%, respectively, $P < 0.001$). No significant difference was observed between the early and late surgical subgroups. Age and NIHSS were independent predictors of in-hospital mortality, while age, treatment type, NIHSS, white blood cells, and hemoglobin were associated with one-year mortality.
Conclusion: In IE patients with neurological complications, early cardiac surgery, when carefully selected and managed using a multidisciplinary approach, does not increase mortality compared to late surgery and may improve long-term survival.
Keywords: Infective Endocarditis, Neurological Complications, Surgical Timing, One-Year Mortality

Abbreviations, Acronyms & Symbols

AF	= Atrial fibrillation	Hct	= Hematocrit
CHF	= Congestive heart failure	HT	= Hypertension
CI	= Confidence interval	IE	= Infective endocarditis
CKD	= Chronic kidney disease	MRI	= Magnetic resonance imaging
Creat	= Creatinine	NIHSS	= National Institutes of Health Stroke Scale
CRP	= C-reactive protein	OR	= Odds ratio
CT	= Computed tomography	PLT	= Platelet
CVA	= Cerebrovascular accident	SE	= Standard error
DM	= Diabetes mellitus	TEE	= Transesophageal echocardiography
EF	= Ejection fraction	TIA	= Transient ischemic attack
ESC	= European Society of Cardiology	WBC	= White blood cells
Hb	= Hemoglobin		

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INTRODUCTION

Despite all advances in treatment, infective endocarditis (IE) remains a serious, life-threatening disease with a high morbidity rate and an overall mortality rate of approximately 30%[1,2]. The necessity of a multidisciplinary approach in both the management and treatment of IE is an undeniable fact[3]. Targeted antibiotic therapy, initiated according to appropriate antibiogram results after diagnosis of IE, aims to halt the progression of the disease and reduce the development of complications. Studies show that IE, especially in advanced cases, can frequently lead to complications involving almost all systems, and neurological complications such as ischemic stroke or intracranial hemorrhage can be seen in approximately 20 - 55% of cases[4-6]. The occurrence of neurological complications is considered one of the most severe extracardiac complications of IE and is associated with poor outcomes. Neurological complications in IE may be vascular or infectious in origin. Vascular complications may ultimately manifest as ischemic and hemorrhagic events. Approximately 70% of neurological complications are ischemic events; the majority of these are cerebral infarctions, while the remainder are transient ischemic attacks (TIAs). Here, the source of ischemia is mostly emboli from infected valve tissue. Although infectious neurological complications are less common, they can have a more severe course[4]. Various studies have shown that surgical treatment in appropriately selected patients can be effective in preventing neurological sequelae and reducing mortality[5-7].

Due to the rarity of the disease, the limited number of well-conducted randomized controlled trials that have thoroughly examined IE, the difficulty of collecting prospective data, the controversial nature of current recommendations for clinical management, and the fact that surgical treatment involves risks that cannot be standardized, there is no consensus on the management of IE and the timing of surgical treatment.

Although there is no clear approach regarding the timing of surgery in IE patients with neurological complications, it seems more appropriate to evaluate each patient individually based on their current neurological clinical presentation and radiological findings. In stroke patients, it is important to evaluate many factors together, such as the clinical severity, lesion location, or lesion size, in addition to stroke subtypes (ischemic, hemorrhagic) when deciding on surgical intervention.

This article presents a retrospective analysis of 109 patients who developed neurological complications among a total of 452 patients diagnosed with IE over a 10-year period at our center, which performs high-volume and specialized cardiology and cardiac surgery procedures. Our study aims to contribute to cardiac surgery practice by evaluating the positive outcomes of early surgery and the clinical data obtained from these patients in comparison with the literature.

METHODS

This study was conducted retrospectively on patients diagnosed with IE at our hospital between January 2013 and December 2023, developed neurological complications while under follow-up and treatment, presented to the hospital with neurological stroke complaints, and subsequently received a diagnosis of IE based on clinical and radiological findings while the etiology of the stroke was being investigated.

Patients who suffered a stroke while undergoing treatment for IE underwent early cranial computed tomography (CT) scans, followed by a control cranial CT scan 24 hours later or diffusion magnetic resonance imaging (MRI) when necessary, to document neurological diagnoses. Neurological assessments, including National Institutes of Health Stroke Scale (NIHSS) scoring, were performed by the same neurology specialist using standardized clinical criteria. All patients underwent transesophageal echocardiography (TEE) upon hospital admission to determine the presence and size of vegetations, valve status, and accompanying pathologies. Subsequently, follow-up TEE examinations were performed as needed to evaluate the response to drug therapy. The growth status in blood and valve cultures was recorded, and patients were divided into subgroups according to the causative microorganism.

Patients were divided into subgroups based on their neurological complications: ischemic, hemorrhagic, hemorrhagic infarction, and encephalitis. Lesions were also classified according to vascular territory as anterior cerebral artery, middle cerebral artery, posterior cerebral artery, basilar artery, borderline, and bilateral microembolisms, while also being classified according to infarct size as microembolism, focal, or extensive infarct.

Patients' demographic data, echocardiographic findings, vegetation size (≥ 1 cm), and vegetation mobility were examined. They were subdivided into subgroups based on the causative microorganisms.

The severity of the stroke was assessed in the early stage using the NIHSS (mild-moderate-severe).

Patients were divided into two main groups: those receiving medical treatment and those receiving surgical treatment. Patients who underwent surgery were further divided into two subgroups: early surgery (≤ 1 week) and late surgery (> 1 week). In this classification, we took into account the recommendations in line with the current guideline. The clinical data, prognoses, and one-year post-discharge mortality rates of 48 patients who underwent surgery and 61 patients who were medically followed up were compared.

Patients who had previously suffered a stroke, those without cranial imaging, those with lead endocarditis, and those under the age of 18 were excluded from the study, regardless of the infectious endocarditis process.

The endpoints in this study were the rate of neurological improvement and mortality over a one-year period. The modified Rankin scale was used to assess residual neurological disability.

For the retrospective study, permission was obtained from the hospital's Local Ethics Committee (or LEC) (E-28001928-604.01-28277254), and the one-year mortality analysis was performed with legal permission obtained through the 'national identity sharing system'.

Statistical Methods

Data were analyzed using IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA). Descriptive statistics were presented as number of subjects (n), percentage (%), mean ± standard deviation, median, and interquartile range. The normal distribution of data for numerical variables was assessed using the Shapiro-Wilk normality test. The homogeneity of variance between groups was analyzed using the Levent test. Comparisons between groups for numerical variables were performed using the independent samples *t*-test if the data showed a normal dis-

tribution, and the Mann-Whitney U test if the data did not show a normal distribution. Chi-square analyses (Pearson chi-square, Yates chi-square, Fisher's exact test) were used to compare groups with categorical variables. When chi-square analysis results were found to be significant, subgroup analyses were performed using the Bonferroni-corrected two-ratio Z test. Factors affecting in-hospital and one-year mortality were evaluated using multiple binary logistic regression analysis. The backward Wald method was used as the elimination method in the binary logistic regression analysis. A $P < 0.05$ value was considered statistically significant.

RESULTS

A total of 109 patients were included in the study. The number of patients who presented to the hospital with neurological complaints and were subsequently diagnosed with IE was 74/109 (67.8%), while the number of patients who suffered an acute stroke while receiving treatment for IE was 35/109 (32%).

The basic demographic and clinical characteristics of the 48 patients who underwent surgery and the 61 patients who received medical treatment are summarized in Table 1.

The mean age of patients in the surgical group was significantly lower than that of the medical treatment group (53.6 ± 14.4 *vs.* 64.2 ± 13.9 years; $P < 0.001$). There was no statistically significant difference between the surgical and medical patient groups in terms of sex distribution.

Among comorbid conditions, hypertension and chronic renal failure were observed at higher rates in the medical treatment group ($P < 0.022$ and $P < 0.013$, respectively).

The distribution of valve involvement, valve structure status, valve insufficiency, and IE timing in artificial valves was not statistically different between treatment groups. However, the rates of mitral valve involvement and natural valve endocarditis were high in both the surgical and medical treatment groups. In the group of patients with IE who underwent surgery, the rate of severe valve insufficiency was high (50%), while in patients who did not undergo surgery, the rate of mild valve insufficiency was higher (32.8%). Of the patients who underwent surgery, 14 had prosthetic valves and developed IE (29.2%), while 34 (70.8%) had natural valves and underwent replacement due to endocarditis. Among prosthetic valve endocarditis cases, late-stage prosthetic valve endocarditis was most common in both groups.

When evaluated in terms of echocardiographic findings, the association of vegetation with valve degeneration was more common in the surgical group ($P < 0.007$) (Table 1). In those followed medically, only the incidence of vegetation was high. There was no statistically significant difference in vegetation size and mobile vegetation between the groups; however, in both groups, a large proportion of vegetations were ≥ 1 cm and mobile.

Microorganism distributions were not statistically different between groups. *Staphylococcus* was the most common causative agent of infection.

NIHSS distributions differed statistically between groups. The proportion of patients with mild NIHSS was high in the surgical group, while the proportion of patients with severe NIHSS was statistically higher in the medical group. The number of patients with severe NIHSS was three (6.3%) in the operated group and 26 (42.6%) in the medical group.

The modified Rankin score and creatinine, hemoglobin (Hb), hematocrit (Hct), and white blood cells (WBC) values at one year of follow-up were statistically higher in medically treated patients than in operated patients. The differences in platelet and C-reactive protein values were not statistically significant between the groups.

When patients who underwent surgery were examined as early (n = 14) and late (n = 34) surgical groups, no significant differences were found in terms of demographic and clinical characteristics (Table 2). The length of stay between admission and surgery was significantly longer in the late surgical group (five days *vs.* 19 days; $P < 0.001$). No statistical difference was observed in hospital and one-year mortality rates between the early and late surgical groups.

According to the comparisons of in-hospital and one-year mortality in Table 3, age was significantly higher in both the in-hospital and one-year mortality groups ($P < 0.023$ and $P < 0.003$). This indicated that advanced age was a strong risk factor for both short-term and long-term mortality. No statistically significant relationship was found between mortality and sex. Survival was significantly higher in patients who underwent surgery. Both in-hospital and one-year post-discharge mortality rates were statistically higher in the medical group ($P < 0.001$).

Of the patients who died in hospital, eight (19.5%) were surgical patients, while 33 (80.5%) were medical patients. In one-year mortality, there were zero deaths in the surgical group, while there were 13 (46.4%) deaths in the medical group.

According to in-hospital mortality, the distributions of comorbidities, valve type, valve status, and valve insufficiency status were not statistically different.

NIHSS was a statistically significant predictor of both in-hospital and one-year mortality. A high NIHSS score was strongly associated with both in-hospital and one-year mortality ($P < 0.006$ in both analyses). 80.7% of patients with a mild NIHSS score were alive, while 86.2% of those with a severe score had in-hospital mortality. Mortality distributions were not statistically different in patients with moderate NIHSS scores.

In one-year mortality comparisons, chronic kidney disease and a history of dialysis were associated with long-term mortality ($P < 0.011$ and $P < 0.006$, respectively). Their association with in-hospital mortality was weaker. This indicates that kidney dysfunction and dialysis are particularly decisive factors in long-term prognosis.

The distribution of central event times according to mortality was statistically different. A significant difference was found in terms of one-year mortality: the prognosis was worse for patients who experienced a central vascular event while undergoing treatment ($P < 0.006$). The ex rate was statistically higher in those who had a cerebrovascular accident (CVA) while undergoing treatment. This was probably because their operations were postponed due to the development of acute stroke. Mortality distributions were not statistically different in those with initial presentation of CVA and recurrent CVA. It was noteworthy that events developing during treatment were associated with higher mortality compared to those with central events at initial presentation.

In the one-year mortality group, WBC was higher ($P < 0.031$), and Hb and Hct were significantly lower ($P < 0.001$). These findings suggest that hematological parameters and renal function may be important in predicting prognosis.

According to the study data in Table 4, age, treatment groups, NIHSS, WBC, and Hb were found to be effective on one-year mortality in the final model. For each unit increase in age, the risk of one-year mortality increases by 1.063 times. The mortality risk

Table 1. Comparison of patient characteristics by treatment groups.

	Treatment Groups		*P*-value
	Operated CVA (n = 48)	Unoperated CVA (n = 61)	
Age (years)	53.6 ± 14.4	64.2 ± 13.9	**< 0.001†**
Sex, n (%)			
Male	30 (62.5)	29 (47.5)	0.173‡
Female	18 (37.5)	32 (52.4)	
Comorbidities, n (%)			
HT	28 (58.3)	49 (80.3)	**0.022‡**
DM	11 (22.9)	22 (36)	0.203‡
AF	4 (8.3)	9 (14.7)	0.466‡
CKD	3 (6.3)	16 (26.2)	**0.013‡**
CHF	2 (4.2)	5 (8.2)	0.462‡
Rheumatic disease	7 (14.6)	4 (6.6)	0.208‡
Dialysis	3 (6.3)	13 (21.3)	0.053‡
Valve involvement, n (%)			
Mitral	24 (50.0)	34 (55.7)	0.888‡
Aortic	19 (39.6)	21 (34.4)	
Aortic + mitral	3 (6.3)	4 (6.6)	
Mitral + tricuspid	1 (2.1)	2 (3.3)	
Aortic + tricuspid	1 (2.1)	0 (0.0)	
Valve condition, n (%)			
Native	34 (70.8)	43 (70.4)	> 0.999‡
Prosthetic	14 (29.1)	18 (29.5)	
IE timing on prosthetic valve, n (%)			
Early	4 (28.6)	5 (27.8)	> 0.999‡
Late	10 (71.4)	13 (72.2)	
IE location, n (%)			
Left	46 (95.8)	59 (96.7)	> 0.999‡
Bilateral	2 (4.2)	2 (3.3)	
Vegetation presence, n (%)			
Absent	1 (2.1)	3 (4.9)	0.629‡
Present	47 (97.9)	58 (95.1)	
Mobile vegetation, n (%)			
Absent	9 (19.1)	8 (13.8)	0.635‡
Present	38 (80.9)	50 (86.2)	
Echocardiographic findings, n (%)			
Vegetation only	34 (70.8)a	52 (85.2)a	**0.007‡**
Vegetation + valve degeneration	11 (22.9)a	2 (3.3)b	
Degeneration only	1 (2.1)a	2 (3.3)a	
Abscess	0 (0.0)a	1 (1.6)a	
Abscess + degeneration	1 (2.1)a	0 (0.0)a	
Abscess + vegetation	1 (2.1)a	4 (6.6)a	

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Vegetation size, n (%)			
< 1 cm	11 (23.4)	18 (31.0)	0.516‡
> 1 cm	36 (76.6)	40 (69.0)	
Mobile vegetation, n (%)			
Absent	9 (19.1)	8 (13.8)	0.635‡
Present	38 (80.9)	50 (86.2)	
Central event time, n (%)			
CVA at initial presentation	37 (77.1)	32 (52.5)	**< 0.001‡**
CVA during treatment	8 (16.7)	29 (47.5)	
Patients with recurrent CVA	3 (6.3)	0 (0.0)	
Neurological event, n (%)			
Ischemic	36 (75.0)	42 (68.9)	0.051‡
Hemorrhagic	4 (8.3)	15 (24.6)	
Ischemic + hemorrhagic	6 (12.5)	4 (6.6)	
Meningoencephalitis	1 (2.1)	0 (0.0)	
CVA + encephalitis	1 (2.1)	0 (0.0)	
Ischemia, n (%)			
Focal	25 (67.6)	18 (42.9)	0.091‡
Extensive	4 (10.8)	9 (21.4)	
Bilateral	8 (21.6)	15 (35.7)	
NIHSS, n (%)			
Mild	33 (68.8)[a]	24 (39.3)[b]	< 0.001‡
Moderate	12 (25.0)[a]	11 (18.0)[a]	
Severe	3 (6.3)[a]	26 (42.6)[b]	
Rankin, 1 year	1.00 (1.75)	4.00 (5.00)	**< 0.001&**
WBC	8.50 (7.00)	10.00 (7.00)	0.216&
Hb	10.50 (1.95)	10.00 (2.85)	0.057&
Hct	32.50 (5.60)	31.00 (7.10)	0.178&
PLT	225.0 (116.5)	196.0 (146.0)	0.643&
Creatinine	0.80 (0.30)	1.10 (1.90)	**0.032&**
CRP	8.55 (16.60)	13.20 (33.95)	0.302&
In-hospital mortality, n (%)	8 (16.7)	33 (54.1)	**< 0.001‡**

†Independent *t*-test; ‡Chi-square test; [a] and [b] indicate differences between groups; there is no statistically significant difference between groups with the same superscripts; &Mann-Whitney U test
AF=atrial fibrillation; CHF=congestive heart failure; CKD=chronic kidney disease; CRP=C-reactive protein; CVA=cerebrovascular accident; DM=diabetes mellitus; Hb=hemoglobin; Hct=hematocrit; HT=hypertension; IE=infective endocarditis; PLT=platelet; WBC=white blood cells

in patients receiving medical treatment is 6.003 times higher than in patients who underwent surgery. The mortality risk in patients with severe NIHSS scores is 41.965 times higher than in those with mild scores. Mortality risk increases as WBC values increase, while it decreases as Hb values increase. Similarly, in our multiple regression analysis, NIHSS levels emerged as determinants of in-hospital mortality in Table 5. Age and NIHSS scores were found to ultimately affect in-hospital mortality. Each unit increase in age increased the risk of in-hospital mortality by 1.042 times. Patients with severe NIHSS scores also had a 31.738 times higher mortality risk than those with mild scores.

DISCUSSION

Discussions regarding surgical intervention in IE largely focus on appropriate timing and patient selection criteria. In addition to the general assessment of the role of surgery in IE, determining the timing of surgical treatment in cases of IE with neurological complications requires the evaluation of many factors together, such as the presence and type of stroke (ischemic or hemorrhagic), the location and size of the lesion, and the clinical severity. The presence of neurological symptoms before surgery can significantly increase the mortality risk of surgery. Although there are no clear

Table 2. Comparison of patient characteristics according to surgical time.

	Surgical Time		*P*-value
	Early	Late	
	(n = 14)	(n = 34)	
Age (years)	52.2 ± 15.5	54.2 ± 14.2	0.674†
Sex, n (%)			
Male	10 (71.4)	20 (58.8)	0.521‡
Female	4 (28.6)	14 (41.2)	
Comorbid conditions, n (%)			
HT	8 (57.1)	20 (58.8)	> 0.999‡
DM	5 (35.7)	6 (17.6)	0.258‡
AF	0 (0.0)	4 (11.8)	0.307‡
CKD	1 (7.1)	2 (5.9)	> 0.999‡
CHF	0 (0.0)	2 (5.9)	0.578‡
Rheumatic disease	1 (7.1)	6 (17.6)	0.427‡
Dialysis	1 (7.1)	2 (5.9)	> 0.999‡
Valve involvement, n (%)			
Mitral	5 (35.7)	19 (55.9)	0.562‡
Aortic	8 (57.1)	11 (32.4)	
Aortic + mitral	1 (7.1)	2 (5.9)	
Mitral + tricuspid	0 (0.0)	1 (2.9)	
Aortic + tricuspid	0 (0.0)	1 (2.9)	
Valve condition, n (%)			
Native	12 (85.7)	22 (64.7)	0.181‡
Prosthetic	2 (14.3)	12 (35.3)	
Vegetation presence, n (%)			
Absent	0 (0.0)	1 (2.9)	> 0.999‡
Present	14 (100.0)	33 (97.1)	
Mobile vegetation, n (%)			
Absent	3 (21.4)	6 (18.2)	> 0.999‡
Present	11 (78.6)	27 (81.8)	
Growth, n (%)			
Absent	4 (28.6)	10 (29.4)	0.060‡
In blood	5 (35.7)	22 (64.7)	
In valve	2 (14.3)	1 (2.9)	
In both	3 (21.4)	1 (2.9)	
Microorganism, n (%)			
Streptococcus	0 (0.0)	6 (25.0)	0.238‡
Staphylococcus	7 (70.0)	14 (58.3)	
Enterococcus	2 (20.0)	3 (12.5)	
Gram-	0 (0.0)	1 (4.2)	
Rare agents	1 (10.0)	0 (0.0)	

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Central event time, n (%)			
CVA at initial presentation	13 (92.9)	24 (70.6)	0.273‡
CVA during treatment	1 (7.1)	7 (20.6)	
Patients with recurrent CVA	0 (0.0)	3 (8.8)	
Neurological event, n (%)			
Ischemic	10 (71.4)	26 (76.5)	0.201‡
Hemorrhagic	0 (0.0)	4 (11.8)	
Ischemic + hemorrhagic	3 (21.4)	3 (8.8)	
Meningoencephalitis	0 (0.0)	1 (2.9)	
CVA + encephalitis	1 (7.1)	0 (0.0)	
Ischemia, n (%)			
Focal	7 (63.6)	18 (69.2)	0.732‡
Extensive	2 (18.2)	2 (7.7)	
Bilateral	2 (18.2)	6 (23.1)	
NIHSS, n (%)			
Mild	10 (71.4)	23 (67.6)	> 0.999‡
Moderate	3 (21.4)	9 (26.5)	
Severe	1 (7.2)	2 (5.9)	
Rankin, 1 year	1.00 (2.00)	1.00 (1.00)	0.838&
WBC	7.00 (6.50)	10.00 (8.00)	0.187&
Hb	11.00 (2.50)	10.00 (1.25)	0.790&
Hct	33.00 (9.25)	32.00 (4.00)	0.531&
PLT	185.50 (163.5)	229.0 (108.00)	0.454&
Creatinine	0.85 (0.48)	0.80 (0.30)	0.731&
CRP	6.95 (39.33)	9.55 (13.05)	0.901&
Time between CVA and operation	11.50 (10.00)	37.50 (34.75)	**0.001&**
Time between hospital admission and operation	5.00 (5.00)	19.00 (22.25)	**< 0.001&**
In-hospital mortality, n (%)	2 (14.3)	6 (17.6)	> 0.999‡
Preoperative EF	57.5 (10.0)	60.0 (5)	0.252&
Postoperative EF	50.0 (7.50)	50.0 (15.0)	0.618&

†Independent samples *t*-test; ‡Chi-square test; [a] and [b] indicate differences between groups; there is no statistically significant difference between groups with the same superscripts; &Mann-Whitney U test
AF=atrial fibrillation; CHF=congestive heart failure; CKD=chronic kidney disease; CRP=C-reactive protein; CVA=cerebrovascular accident; DM=diabetes mellitus; EF=ejection fraction; Hb=hemoglobin; Hct=hematocrit; HT=hypertension; NIHSS=National Institutes of Health Stroke Scale; PLT=platelet; WBC=white blood cells

recommendations in the guidelines, a comprehensive preoperative evaluation and careful risk-benefit analysis are appropriate in these complex cases. According to the European Society of Cardiology (ESC) and American College of Cardiology/American Heart Association guidelines, early surgical intervention is generally defined as intervention performed during the initial hospital admission, before completion of antibiotic therapy[8]. Delgado et al. classify the timing of surgical intervention in the 2023 ESC guidelines as urgent (within 24 hours), early (within a few days), or elective (after at least 1 - 2 weeks of antibiotic treatment)[9].

The risk-benefit balance of early surgery has been frequently debated in the literature. Many studies have debated whether early surgery increases the risk of hemorrhagic transformation or, conversely, whether delaying surgical intervention leads to worsening outcomes due to recurrent septic embolism resulting from large and mobile vegetations blocking cerebral or meningeal arteries, causing ischemic infarction, meningitis, or abscess, thereby worsening the outcomes of recurrent septic embolism[10].

Most publications show that the risk of secondary hemorrhagic transformation in uncomplicated ischemic lesions is lower than

Table 3. Comparison of in-hospital and one-year mortality.

	In-hospital Mortality			1-year Mortality		
	Alive (n = 68)	**Exitus (n = 41)**	***P*-value**	**Alive (n = 55)**	**Exitus (n = 13)**	***P*-value**
Age (years)	57.03 ± 16.38	63.80 ± 11.72	**0.023†**	54.22 ± 15.58	68.92 ± 14.71	**0.003†**
Sex, n (%)						
Male	38 (64.4)	21 (35.6)	0.636‡	32 (84.2)	6 (15.8)	0.432‡
Female	30 (60)	20 (40)		23 (76.7)	7 (23.3)	
Treatment group, n (%)						
Operated CVA	40 (83.3)	8 (16.7)	**< 0.001‡**	40 (100)	0 (0)	**< 0.001‡**
Unoperated CVA	28 (45.9)	33 (54.1)		15 (53.6)	13 (46.4)	
Timing of surgery						
Early surgery	12 (85.7)	2 (14.3)	1.000	-	-	-
Late surgery	28 (82.4)	6 (17.6)		-	-	
Comorbid conditions, n (%)						
HT	44 (57.1)	33 (42.9)	0.080‡	33 (75)	11 (25)	0.095‡
DM	18 (54.5)	15 (45.5)	0.266‡	14 (77.8)	4 (22.2)	0.696‡
AF	7 (53.8)	6 (46.2)	0.498‡	5 (71.4)	2 (28.6)	0.531‡
CKD	9 (47.4)	10 (52.6)	0.137‡	4 (44.4)	5 (55.6)	**0.011‡**
CHF	3 (42.9)	4 (57.1)	0.422‡	4 (44.4)	5 (55.6)	1.000‡
Rheumatic disease	6 (54.5)	5 (45.5)	0.812‡	6 (100)	0 (0)	0.482‡
Dialysis	7 (43.8)	9 (56.3)	0.166‡	3 (42.9)	4 (57.1)	**0.028‡**
Valve involvement, n (%)						
Mitral	37 (63.8)	21 (36.2)	0.831‡	30 (81.1)	7 (18.9)	0.166‡
Aortic	24 (60)	16 (40)		21 (87.5)	3 (12.5)	
Aortic + mitral	5 (71.4)	2 (28.6)		3 (60)	2 (40)	
Mitral + tricuspid	1 (33.3)	2 (66.7)		0 (0)	1 (100)	
Aortic + tricuspid	1 (100)	0 (0)		1 (100)	0 (0)	
Valve status, n (%)						
Native	50 (64.9)	27 (35.1)	0.394‡	39 (78)	11 (22)	0.511‡
Prosthetic	18 (56.3)	14 (43.8)		16 (88.9)	2 (11.1)	
Valve insufficiency, n (%)						
None	7 (87.5)	1 (12.5)	0.460‡	7 (100)	0 (0)	0.281‡
Mild	17 (60.7)	11 (39.3)		13 (76.5)	4 (23.5)	
Moderate	20 (64.5)	11 (35.5)		14 (70)	6 (30)	
Severe	24 (57.1)	18 (42.9)		21 (87.5)	3 (12.5)	
New operation, n (%)						
No operation on native valve	20 (46.5)	23 (53.5)	**0.001‡**	9 (45)	11 (55)	**< 0.001‡**
No operation on prosthetic valve	8 (44.4)	10 (55.6)		6 (75)	2 (25)	
Redo	10 (71.4)	4 (28.6)		10 (100)	0 (0)	
New operation	30 (88.2)	4 (11.8)		30 (100)	0 (0)	
IE location, n (%)						

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Left	66 (62.9)	39 (37.1)	0.631‡	54 (81.8)	12 (18.2)	0.830‡
Bilateral	2 (50)	2 (50)		1 (50)	1 (50)	
Vegetation presence, n (%)						
Absent	2 (40)	3 (60)	0.362‡	2 (100)	0 (0)	1.000‡
Present	66 (63.5)	38 (36.5)		53 (80.3)	13 (19.7)	
Vegetation status, n (%)						
No vegetation only	2 (40)	3 (60)	0.300‡	2 (100)	0 (0)	1.000‡
Vegetation only	66 (63.5)	38 (36.5)		53 (80.3)	13 (19.7)	
1	53 (61.6)	33 (38.4)	0.491‡	42 (79.2)	11 (20.8)	0.124‡
2	10 (76.9)	3 (23.1)		10 (100)	0 (0)	
3	1 (33.3)	2 (66.7)		1 (100)	0 (0)	
4	0 (0)	1 (100)		-	-	
5	1 (100)	0 (0)		1 (100)	0 (0)	
6	3 (60)	2 (40)		1 (33.3)	2 (66.7)	
Vegetation size, n (%)						
< 1 cm	20 (29.4)	13 (31.7)	0. 801‡	16 (80)	4 (20)	0.905‡
> 1 cm	48 (70.6)	28 (68.3)		39 (81.3)	9 (18.8)	
Mobile vegetation, n (%)						
Absent	12 (57.1)	9 (42.9)	0.581‡	10 (83.3)	2 (16.7)	0.812‡
Present	56 (63.6)	32 (36.4)		45 (80.4)	11 (19.6)	
Growth, n (%)						
None	20 (57.1)	15 (42.9)	0.829‡	18 (90)	2 (10)	> 0.452‡
In blood	44 (65.7)	23 (34.3)		33 (75)	11 (25)	
In valve	2 (66.7)	1 (33.3)		2 (100)	0 (0)	
In both	2 (50)	2 (50)		2 (100)	0 (0)	
Central event time, n (%)						
CVA at initial presentation	46 (66.7)	23 (33.3)	0.136‡	40 (87)	6 (13)	0.063‡
CVA during treatment	19 (51.4)	18 (48.6)		12 (63.2)	7 (36.8)	
Patients with recurrent CVA	3 (100)	0 (0)		3 (100)	0 (0)	
Neurological event, n (%)						
Ischemic	52 (66.7)	26 (33.3)	0.080‡	43 (82.7)	9 (17.3)	0.755‡
Hemorrhagic	7 (36.8)	12 (63.2)		5 (71.4)	2 (28.6)	
Ischemic + hemorrhagic	7 (70)	3 (30)		5 (71.4)	2 (28.6)	
Meningoencephalitis	1 (100)	0 (0)		1 (100)	0 (0)	
CVA + encephalitis	52 (66.7)	26 (33.3)		1 (100)	0 (0)	
NIHSS, n (%)						
Mild	46 (80.7)	11 (19.3)	< 0.001‡	41 (89.1)	5 (10.9)	< 0.006‡
Moderate	18 (78.3)	5 (21.7)		13 (72.2)	5 (27.8)	
Severe	4 (13.8)	25 (86.2)		1 (25)	3 (75)	

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Growth, n (%)						
None	20 (57.1)	15 (42.9)	0.826	18 (90)	2 (10)	0.455
In blood	44 (65.7)	23 (34.3)		33 (75)	11 (25)	
In valve	2 (66.7)	1 (33.3)		2 (100)	0 (0)	
In both	2 (50)	2 (50)		2 (100)	0 (0)	
WBC	9 (7.68)	10 (7.5)	0.271[&]	8.00 (7.00)	12.00 (7.00)	**< 0.037[&]**
Hb	10 (2)	10 (2.5)	0.147[&]	11.00 (2.80)	8.00 (2.00)	**< 0.001[&]**
Hct	31.5 (6.5)	31 (6)	0.234[&]	33.00 (5.00)	26.00 (7.00)	**< 0.001[&]**
PLT	243 (153.25)	177 (148.5)	**0.007[&]**	242.0 (144.0)	244 (158)	0.901[&]
CREAT	0.9 (0.5)	1.1 (1.85)	0.155[&]	0.80 (0.40)	1.00 (2.00)	**< 0.400[&]**
CRP	9.85 (22.75)	11.45 (22.23)	0.300[&]	7.5 (17.3)	14 (109.30)	0.242[&]

[†]Independent samples *t*-test; ‡Chi-square test; [a] and [b] indicate differences between groups; there is no statistically significant difference between groups with the same superscripts; [&]Mann-Whitney U test
AF=atrial fibrillation; CHF=congestive heart failure; CKD=chronic kidney disease; Creat=creatinine; CRP=C-reactive protein; CVA=cerebrovascular accident; DM=diabetes mellitus; Hb=hemoglobin; Hct=hematocrit; HT=hypertension; IE=infective endocarditis; NIHSS=National Institutes of Health Stroke Scale; PLT=platelet; WBC=white blood cells

the risk of recurrent embolism under antibiotic treatment. This suggests that early surgery can be performed safely[11].

Our findings align with this evidence, demonstrating that early surgery can be performed safely in appropriately selected patients without increasing mortality, particularly in centers with stable neurological assessment and an experienced surgical team.

Some publications also recommend postponing endocarditis surgery for at least one month if intracranial hemorrhage is present, due to the possibility of enlargement of the bleeding area or rebleeding caused by heparin administered during intraoperative cardiopulmonary bypass[8].

However, more recent data indicate that early surgery after ischemic stroke is not significantly associated with neurological deterioration or mortality[4,11,12]. A large-scale study conducted in China reported that neurological complications developed in 24.5% of IE patients prior to surgery, with a mortality rate of 14.3% in this group compared to 4.4% in those without complications[13]. In cases of ischemic CVA, it is recommended that cardiac surgery not be delayed after silent embolism or TIA[14].

Patients who underwent surgery within 14 days of the onset of cranial infarction had a lower hospital mortality rate than those who underwent surgery two weeks after the onset of cranial infarction, although this difference was not statistically significant. Therefore, early surgery is recommended[15].

In our study, the in-hospital mortality rate was found to be 16.7% in IE patients with stroke who underwent valve surgery. This rate is similar to findings in the literature[8,16]. In the medically treated patient group, both in-hospital and one-year mortality rates were significantly higher than in the surgical group, which is consistent with previous studies[14,17]. Furthermore, the zero post-discharge mortality rate in patients with stroke who underwent surgery in our study indicates that the selection of surgical patients was appropriate. Similarly, in a study conducted by Thuny et al.[14], survival was found to be higher in the group undergoing surgery among IE patients with acute stroke; it was reported that the duration between stroke and surgery being shorter or longer than 72 hours did not make a difference in terms of mortality.

In our study, the stroke clinic was evaluated using the NIHSS, which is more specific for stroke than the Glasgow Coma Scale. According to our findings, both in-hospital and one-year mortality were significantly associated with the NIHSS. Survival was significantly higher in patients with mild neurological deficits, while mortality was significantly higher in patients with severe neurological deficits. Similarly, Murai et al. reported that early surgery was safe in patients with mild-to-moderate neurological deficits (NIHSS ≤ 10) and improved survival compared to medical treatment[18].

These results highlight NIHSS as a decisive prognostic marker and support its integration into individualized surgical decision-making for IE patients with neurological complications.

Ruttmann et al. examined 135 symptomatic stroke cases among 440 patients with left-sided IE and demonstrated that the risk of in-hospital mortality was 1.4 times higher in symptomatic strokes[19].

In our data, the multiple regression analysis showed that for each one-unit increase in age, the risk of one-year mortality increased by 1.063 times. Similarly, in our multiple regression analysis, NIHSS levels emerged as predictors of in-hospital mortality. Age, treatment type, NIHSS, WBC, and Hb were significant factors in one-year mortality.

A study by Florent Arregle et al.[20] reported significantly higher rates of death and major complications while awaiting surgery in patients whose surgery was delayed due to neurological complications. Similarly, Dashkevich et al.[16] emphasized that the timing of surgery (early, intermediate, late) did not make a significant difference in mortality in 119 IE patients with cerebral embolism, and therefore surgery should not be delayed in patients with large vegetations.

In an analysis of 135 patients with IE and neurological complications based on imaging methods (CT/MRI), mortality was 20% in patients who underwent surgery, while mortality was 68% in those who did not undergo surgery. The mortality rate among patients with neurological complications who underwent surgery was lower than that among patients who had an indication for surgery but did not undergo surgery[17].

Table 4. Evaluation of factors affecting one-year mortality using multivariable binary logistic regression analysis.

	β	SE	Wald	*P*-value	OR	95% CI	
						Lower	Upper
Constant	-0.485	2.923	0.028	0.868	0.616		
Age	0.061	0.028	4.812	0.028	1.063	1.007	1.123
Treatment group							
Medical *vs.* surgical	1.792	0.715	6.283	0.012	6.003	1.478	24.377
NIHSS							
Moderate *vs.* mild	0.588	0.787	0.559	0.455	1.801	0.385	8.427
Severe *vs.* mild	3.737	0.750	24.819	< 0.001	41.965	9.647	182.543
WBC	0.161	0.067	5.815	0.016	1.174	1.031	1.338
Hb	-0.526	0.211	6.222	0.013	0.591	0.391	0.893

Variables included in the model: age, treatment group, NIHSS, WBC and Hb
Model statistics: Hosmer-Lemeshow Test $\chi^2 = 3.362$; $P = 0.910$; Nagelkerke $R^2 = 0.744$
Elimination method: backward Wald
CI=confidence interval; Hb=hemoglobin; NIHSS=National Institutes of Health Stroke Scale; OR=odds ratio; SE=standard error; WBC=white blood cells

Table 5. Evaluation of factors affecting in-hospital mortality using multivariable binary logistic regression analysis.

	β	SE	Wald	*P*-value	OR	95% CI	
						Lower	Upper
Constant	-2.588	1.334	3.763	0.052	0.075		
Age	0.041	0.019	4.403	0.036	1.042	1.003	1.082
NIHSS							
Moderate *vs.* mild	0.069	0.653	0.011	0.916	1.071	0.298	3.852
Severe *vs.* mild	3.458	0.699	24.458	< 0.001	31.738	8.063	124.932

Variables included in the model: age and NIHSS
Model statistics: Hosmer-Lemeshow Test $\chi^2 = 8.117$; $P = 0.422$; Nagelkerke $R^2 = 0.518$
Elimination method: backward Wald
CI=confidence interval; NIHSS=National Institutes of Health Stroke Scale; OR=odds ratio; SE=standard error

The statistically higher ex rate among patients with CVA during treatment in our study supports a similar outcome, as their operations were probably postponed due to the development of acute stroke in these patients.

In a study conducted by Arregle et al.[20] on 351 patients with IE, neurological complications were observed in 94 patients. Among these patients, those with temporary surgical contraindications due to neurological complications had a higher risk of death (35%) and major complications while waiting for surgery.

In a study by Dashkevich et al.[16] involving 119 patients with IE and cerebral embolism, when patients were classified as early, intermediate, or late stage based on the timing of surgery, no statistically significant difference in mortality was observed. Therefore, surgical treatment was recommended for patients with cerebral embolism and large vegetations.

Despite the complexity, recent studies, particularly in cases where emergency surgical intervention is necessary due to serious complications, suggest that early surgical intervention may provide better long-term survival rates compared to medical treatment alone[12,20].

In our study, there was no significant difference in mortality between patients who underwent early surgery and those who underwent late surgery. This finding is consistent with recent studies showing that early surgery does not increase mortality in appropriately selected patients[10,11,13,18].

In contrast, Llah ST et al.[21] did not find a significant reduction in hospital mortality in cases undergoing early surgery, despite the low incidence of cerebral embolism. Nevertheless, the general trend in the literature is that early surgery provides an advantage in terms of long-term survival, despite neurological complications[12,15].

Our study demonstrates that the NIHSS score is a strong predictor of mortality, highlighting the decisive role of the neurological status at presentation in determining prognosis. Age was also found to be strongly associated with mortality, emphasizing the need for careful patient selection in the surgical planning process. Furthermore, the association of hematological parameters such as leukocytosis and anemia with poor prognosis supports the effect of systemic inflammatory response on mortality.

Limitations

This study's retrospective and single-center design may limit the generalizability of its findings. However, by including one of the largest and most detailed cohorts of patients with IE complicated by neurological events, it provides clinically meaningful insights into surgical timing. Despite minor limitations in neuroimaging follow-up, the results strongly reflect real-world clinical practice.

CONCLUSION

In conclusion, the findings of our study contribute to the ongoing debate in current ESC guidelines. The findings support that early surgery can be safely performed without increasing mortality in centers with stable neurological status and an appropriate surgical team. Therefore, it was concluded that in cases of IE with neurological complications, surgical timing should be planned on an individualized basis according to the clinical situation rather than a rigid, time-dependent approach.
Furthermore, the NIHSS score independently stratifies risk and should be incorporated as a core parameter in multidisciplinary surgical decision-making. Collectively, these findings support the refinement of current management algorithms toward more timely surgical strategies in specialized centers.

Data Availability

The authors declare that they cannot provide a link to the study data, as doing so would allow unauthorized access to personal data protected by applicable national laws. Since no new data were generated or analyzed beyond what is presented in this article, data sharing is not deemed necessary.

Artificial Intelligence Usage

The authors declare that no artificial intelligence tool was used in the preparation of this article.

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Potential Conflict of Interest

The authors declare that there is no conflict of interest in this study.

Authors' Roles & Responsibilities

MK	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; final approval of the version to be published
ZY	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published

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