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ORIGINAL ARTICLE
Cardiovascular Surgery

Surgical Management of Infective Endocarditis Complicated With Acute Cerebral Infarction

— Preoperative Management Using Modified Rankin Scale and Sequential Organ Failure Assessment (SOFA) Score —

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Background: The optimal timing of surgery for infective endocarditis (IE) with acute cerebral infarction (CI) remains controversial. We examined the surgery policy at Ise Red Cross Hospital after negative blood cultures and antibiotic administration for at least 2 weeks.

Methods and Results: Thirty-nine IE patients who underwent surgery between 2012 and 2020 were divided into Groups S (n=13; with acute CI) and N (n=26; without acute CI). Patients with IE who underwent conservative treatment were classified as group C (n=16). At the time of IE diagnosis, the modified Rankin Scale (mRS) score was significantly higher in Group S than Group N (mean [±SD] 3.9±0.6 vs. 2.8±1.3; P=0.009). However, there was no significant difference between Groups S and N moments before surgery (3.0±1.5 vs. 2.1±1.5, respectively; P=0.10) or at discharge (2.7±0.8 vs. 2.6±0.9, respectively; P=0.89). There were no significant differences in the Sequential Organ Failure Assessment (SOFA) score between groups. There were no differences in intra- and postoperative outcomes between Groups S and N. In Group C, the mRS score was significantly higher at discharge than in Group S (2.7±0.8 vs. 4.4±0.8, respectively; P<0.001), and long-term results were poor (P=0.004).

Conclusions: Preoperative management and the timing of surgery for IE patients using the mRS and SOFA scores at our institution were reasonable.

Key Words: Cerebral infarction; Infective endocarditis; Modified Rankin Scale; Sequential Organ Failure Assessment (SOFA) score

Infective endocarditis (IE) is often complicated by acute cerebral infarction (CI),[1–3] which increases mortality.[2] The optimal timing of surgery is essential in improving the surgical outcomes of IE patients with acute CI. The 2015 European Society of Cardiology (ESC) guidelines for the management of infective endocarditis states that: "evidence regarding the optimal time interval between stroke and cardiac surgery is conflicting",[4] but recent data favor early surgery.[1,5] In cases with intracranial hemorrhage, the neurological prognosis is worse and surgery should generally be postponed for at least 1 month.[6,7] Therefore, the optimal timing of surgery in IE patients with acute CI remains controversial.

At Ise Red Cross Hospital, IE patients with acute CI in whom infection and heart failure can be controlled and who are not at high risk of embolism due to vegetation are treated with sufficient antibacterial drugs before surgery. In addition, the modified Rankin Scale (mRS)[8] and Sequential Organ Failure Assessment (SOFA)[9] scores are used as indicators of a patient's general condition during preoperative management. In this study we examined the adequacy of the strategy used at Ise Red Cross Hospital.

Methods

All surgical and clinical data were collected at Ise Red Cross Hospital, Ise, Japan. Clinical outcome data were obtained from the hospital's patient records.

This study was approved by the Institutional Review Board of Ise Red Cross Hospital (10/1/2021; Approval no. ER2021-35). Because of the retrospective nature of the study, the need for informed consent was waived. All methods were performed in line with the relevant guidelines and regulations.

Study Design and Patients

Between January 2012 and December 2020, 39 patients underwent valve surgery for IE at Ise Red Cross Hospital.

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Table 1. Preoperative Characteristics 1

	Group S (n=13)	Group N (n=26)	P value
Age (years)	57.8±16.6	69.0±10.8	0.02
Female sex	6 (46.1)	9 (34.6)	0.50
Hemodialysis	0	2 (7.6)	0.54
Preoperative laboratory valuables at time of IE diagnosis			
Hematocrit (%)	30.8±4.3	32.1±6.9	0.53
WBC (×1,000/mm^3)	10.5±7.2	10.5±4.7	0.97
C-reactive protein (mg/dL)	9.42±6.81	7.80±6.46	0.47
Creatinine (mg/dL)	0.78±0.22	1.09±0.85	0.21
eGFR (mL/min/1.73 m^2)	74.3±18.4	64.8±26.3	0.24
Albumin (g/dL)	2.6±0.4	3.0±0.7	0.07
Total bilirubin (mg/dL)	0.8±0.5	0.8±0.5	0.93
AST (IU/L)	49.6±46.0	31.6±21.0	0.10
ALT (IU/L)	43.3±43.9	30.2±23.5	0.22
Preoperative echocardiography			
LVDd (mm)	51.8±7.2	53.9±6.8	0.38
LVDs (mm)	31.6±5.4	33.1±7.5	0.54
LVEF (%)	68.5±5.2	67.6±11.1	0.79
Aortic valve regurgitation			
Severe	2 (15.3)	1 (3.8)	0.25
Moderate	3 (23.0)	1 (3.8)	0.09
Mild	2 (15.3)	8 (30.7)	0.44
Trivial	4 (30.7)	5 (19.2)	0.44
None	2 (15.3)	11 (42.3)	0.15
Mitral valve regurgitation			
Severe	1 (7.6)	5 (19.2)	0.64
Moderate	3 (23.0)	10 (38.4)	0.47
Mild	7 (53.8)	8 (30.7)	0.18
Trivial	1 (7.6)	1 (3.8)	1.0
None	1 (7.6)	2 (7.6)	1.0
Size of vegetation (mm)	11.7±5.3	12.2±5.8	0.83

Unless indicated otherwise, data are given as the mean±SD or n (%). ALT, alanine aminotransferase; AST, aspartate aminotransferase; eGFR, estimated glomerular filtration rate; Group N, patients without acute cerebral infarction (CI); Group S, patients with acute CI; IE, infective endocarditis; LVDd, left ventricular end-diastolic dimension; LVDs, left ventricular end-systolic dimension; LVEF, left ventricular ejection fraction; WBC, white blood cells.

Endocarditis was defined based on the Duke criteria.[10] Patients were divided into Group S (n=13; with preoperative acute CI) and Group N (n=26; without acute CI). Preoperative characteristics, operative data, and postoperative outcomes were compared between these 2 groups. Over the same period, IE patients with acute CI who completed conservative treatment without surgery for some reason were included in the study as Group C (n=16). Patient characteristics and outcomes were compared between Groups S and C. We also compared the long-term survival rates of Groups S, N, and C.

Definition of CI

Preoperative acute CI was detected by brain computed tomography (CT) or magnetic resonance imaging (MRI) of all IE patients, regardless of the presence or absence of related neurological symptoms. All MRI and CT scans were reviewed by a radiologist or a neurologist at Ise Red Cross Hospital.

Preoperative Management

First, each patient was managed by a general physician or cardiologist, consulted an infectious disease specialist, and received intravenous antibiotics for at least 2 weeks after diagnosis. After a negative blood culture result and 2 weeks administration of antibiotics, surgery was performed. However, if infection/heart failure could not be controlled or a high risk of embolism due to vegetation was suspected during this regimen, urgent surgery was performed.

Operative Technique

All patients underwent surgery with a median sternotomy using moderately hypothermic cardiopulmonary bypass. Myocardial protection was performed with cold and warm blood cardioplegia, a combination of antegrade and retrograde methods. Radical debridement of the infected tissues was performed. The defective area was reconstructed using autologous or bovine pericardium. Valve repair was performed as much as possible, but valve replacement with a prosthetic valve was performed if this was not possible.

Statistical Analysis

All statistical analyses were performed using the statistical software EZR (Easy R) on R Commander.[11] Continuous

Table 2. Preoperative Characteristics 2

	Group S (n=13)	Group N (n=26)	P value
Affected valve			
Aortic valve	3 (23.0)	6 (23.0)	1.0
Mitral valve	6 (46.1)	14 (53.8)	0.74
Multivalve endocarditis	3 (23.0)	2 (7.6)	0.31
Prosthetic valve endocarditis	1 (7.6)	4 (15.3)	0.64
Species			
Staphylococcus aureus	6 (46.1)	7 (26.9)	0.29
Staphylococcus spp.	0	3 (11.5)	0.53
Streptococcus spp.	5 (38.4)	9 (34.6)	1.0
Enterococcus spp.	1 (7.6)	2 (7.6)	1.0
Others	1 (7.6)	5 (19.2)	0.64
Septic shock	3 (23.0)	1 (3.8)	0.09
Renal emboli/splenic emboli	7 (53.8)	2 (7.6)	0.002
Pyogenic spondylitis	3 (23.0)	0	0.03
Cerebral aneurysm embolization	1		
SMA aneurysm resection	1		
Neurological symptoms	6 (46.1)	0	<0.001
At the time of IE diagnosis			
mRS score	3.9±0.6	2.8±1.3	0.009
SOFA score	3.3±2.1	2.6±3.0	0.52
Moments before the operation			
mRS score	3.0±1.5	2.1±1.5	0.10
SOFA score	2.2±2.2	2.0±2.4	0.77
Time between IE diagnosis and CI diagnosis (days)	5.0±7.6		
Time between CI diagnosis and operation (days)	14.0±11.2		
Time between IE diagnosis and operation (days)	17.6±15.1	92.6±174.4	0.13
Duration of preoperative antibiotic administration (days)	18.1±14.8	29.1±15.3	0.03
JAPAN score (median)	2.7±1.2 (2.7)	9.2±12.5 (3.7)	0.07
EuroSCORE (median)	4.9±4.0 (3.9)	9.8±11.2 (4.5)	0.14
Preoperative intubation	1 (7.6)	1 (3.8)	1.0

Unless indicated otherwise, data are given as the mean±SD or n (%). Group N, patients without acute cerebral infarction (CI); Group S, patients with acute CI; IE, infective endocarditis; mRS, modified Rankin Scale; SMA, superior mesenteric artery; SOFA, Sequential Organ Failure Assessment.

variables are expressed as the mean±SD and were compared using Student's t-test; categorical variables are expressed as counts and percentages and were compared using the χ^2 test. Kaplan-Meier survival curves were created to assess differences in survival between Groups S, N, and C. Survival distributions were compared using the log-rank test. For all analyses, statistical significance was set at P<0.05.

Results

Preoperative Characteristics

The preoperative characteristics of patients in Groups S and N are summarized in **Tables 1**,**2**. As indicated in **Table 1**, mean age was significantly lower in Group S than Group N (57.8±16.6 vs. 69.0±10.8 years, respectively; P=0.02). However, there were no significant differences in renal, liver and cardiac function, or in the degree of aortic valve and mitral valve regurgitation between the 2 groups. Vegetation size did not differ significantly between Groups S and N (11.7±5.3 vs. 12.2±5.8 mm, respectively; P=0.83; **Table 1**). There were no differences in the affected valves and species between the 2 groups (**Table 2**). However, the number of renal and splenic emboli was significantly higher in Group S (P=0.002), as was the incidence of pyogenic spondylitis (P=0.03; **Table 2**). Cerebral aneurysm embolization and superior mesenteric artery (SMA) aneurysm resection with laparotomy were observed in Group S, but not in Group N (**Table 2**). The number of neurological symptoms was significantly higher in Group S than in Group N (P<0.001; **Table 2**). Although the mRS score at the time of IE diagnosis was considerably higher in Group S than Group N (3.9±0.6 vs. 2.8±1.3, respectively; P=0.009), moments before the operation, there was no significant difference in the mRS score between the 2 groups (3.0±1.5 vs. 2.1±1.5, respectively; P=0.10; **Table 2**). The SOFA score was numerically higher in Group S than Group N at the time of IE diagnosis, but the difference was not statistically significant (3.3±2.1 vs. 2.6±3.0, respectively; P=0.52); moments before the operation, the difference in SOFA score between the 2 groups was small (2.2±2.2 vs. 2.0±2.4; P=0.77; **Table 2**). The mean duration between IE diagnosis and operation in Group S was 17.6±15.1 days (median 11.0 days). The duration of administration of preoperative antibiotics was significantly shorter in Group S than in Group N (18.1±14.8 days vs. 29.1±15.3 days, respectively; P=0.03; **Table 2**).

Table 3. Intraoperative Outcomes

	Group S (n=13)	Group N (n=26)	P value
Emergency/urgent patient	4 (30.7)	3 (11.5)	0.70
Redo	1 (7.6)	8 (30.7)	0.22
Procedure			
Aortic valve			
Aortic valve repair	1	0	
Bioprosthetic valve	5	8	
Mechanical valve	1	0	
Mitral valve			
Mitral valve repair	6	15	
Bioprosthetic valve	2	6	
Operation time (min)	425.5±126.7	429.7±113.6	0.91
Cardiopulmonary bypass time (min)	277.3±91.9	262.1±81.1	0.60
Aortic cross-clamp time (min)	206.6±67.1	190.5±66.5	0.48

Unless indicated otherwise, data are given as the mean±SD or n (%). Group N, patients without acute cerebral infarction (CI); Group S, patients with acute CI.

Table 4. Postoperative Outcomes

	Group S (n=13)	Group N (n=26)	P value
ECMO/IABP support	3 (23.0)	3 (11.5)	0.38
Required CHF	2 (15.3)	5 (19.2)	1.0
Tracheostomy	0	2 (7.6)	0.54
Intracranial hemorrhage	0	0	
Permanent pacemaker	0	4 (15.3)	0.28
ICU stay (days)	4.2±2.9	5.8±6.0	0.41
Hospital stay (days)	29.1±15.4	25.5±21.2	0.59
Hospital death	3 (23.0)	3 (11.5)	0.38
LOS	2	1	
Pneumonia		2	
Aortic dissection	1		
mRS at discharge	2.7±0.8	2.6±0.9	0.89
Discharge to home	7 (53.8)	18 (69.2)	0.48

Unless indicated otherwise, data are given as the mean±SD or n (%). CHF, continuous hemofiltration; ECMO, extracorporeal membrane oxygenation; Group N, patients without acute cerebral infarction (CI); Group S, patients with acute CI; IABP, intra-aortic balloon pumping; ICU, intensive care unit; LOS, low output syndrome; mRS, modified Rankin Scale.

Intraoperative Outcomes

Intraoperative outcomes for patients in Groups S and N are summarized in **Table 3**. Emergency or urgent cases were more frequent in Group S than in Group N, but the difference was not statistically significant (30.7% vs. 11.5%, respectively; P=0.70). Redo cases were more frequent in Group N than in Group S, but the difference was not statistically significant (7.6% vs. 30.7%, respectively; P=0.22). There were no differences between the 2 groups in the surgical procedure, operation time, cardiopulmonary bypass (CPB) time, and aortic clamp time.

Postoperative Outcomes

Postoperative outcomes for patients in Groups S and N are summarized in **Table 4**. No postoperative intracranial hemorrhage was observed in either group. There were no differences between Groups S and N in intensive care unit or hospital stay or in the mRS score at discharge (2.7±0.8 vs. 2.6±0.9, respectively; P=0.89; **Table 4**). The discharge rate to home was similar in both groups.

Characteristics and Outcomes of Groups S and C

The characteristics and outcomes of Groups S and C are summarized in **Table 5**. Mean age was significantly higher in Group C than in Group S (72.4±13.2 vs. 57.8±16.6 years, respectively; P=0.01). The causes of conservative treatment in Group C were coma/severe decline in activities of daily living in 5 cases, intracranial hemorrhage in 4 cases, family intentions in 4 cases and "other" in 3 cases. The mRS score at the time of IE diagnosis was similar in Groups S and C (3.9±0.6 vs. 4.2±1.0, respectively; P=0.31; **Table 5**). However, the mRS score at discharge was significantly lower in Group S than in Group C (2.7±0.8 vs. 4.4±0.8, respectively; P<0.001; **Table 5**). The discharge rate to home was did not differ significantly, but was numerically lower in Group C than in Group S (18.7% vs. 53.8%, respectively; P=0.06; **Table 5**).

Table 5. Characteristics and Outcomes

	Group S (n=13)	Group C (n=16)	P value
Age (years)	57.8±16.6	72.4±13.2	0.01
Neurological symptoms	6 (46.1)	12 (75.0)	0.14
Cause of conservative treatment			
Coma, severe decline in ADL		5	
Intracranial hemorrhage		4	
Family intentions		4	
Others		3	
At the time of IE diagnosis			
mRS score	3.9±0.6	4.2±1.0	0.31
SOFA score	3.3±2.1	6.0±4.8	0.06
Hospital death	3 (23.0)	7 (43.7)	0.43
Hospital stay (days)	29.1±15.4	32.3±22.7	0.67
mRS at discharge	2.7±0.8	4.4±0.8	<0.001
Discharge to home	7 (53.8)	3 (18.7)	0.06

Unless indicated otherwise, data are given as the mean±SD or n (%). ADL, activities of daily living; Group C, patients with infective endocarditis (IE) who underwent conservative treatment; Group S, patients with acute cerebral infarction; mRS, modified Rankin Scale; SOFA, Sequential Organ Failure Assessment.

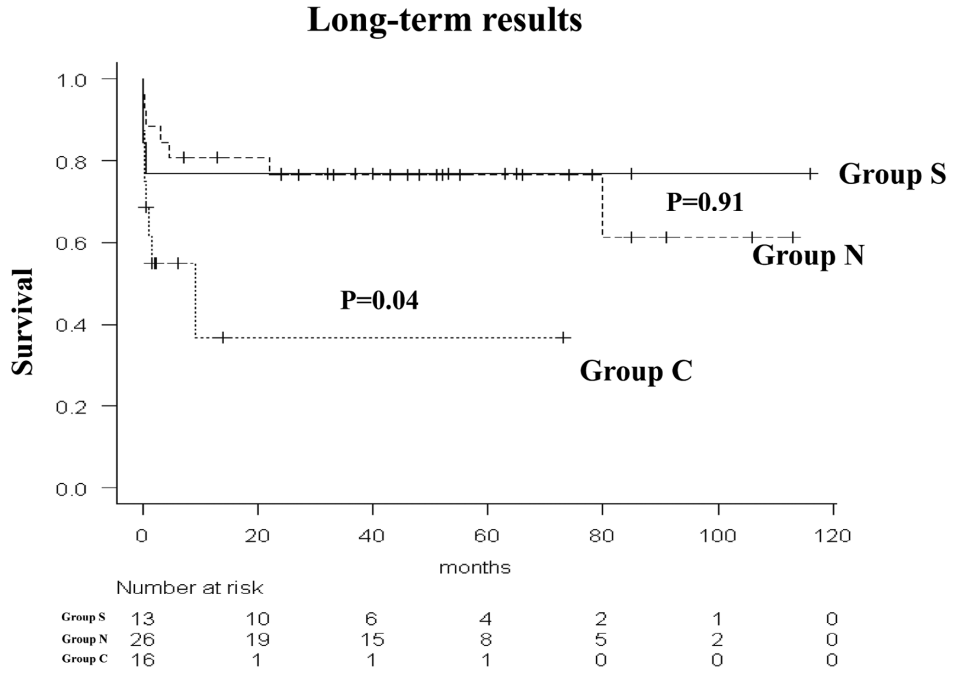

Figure. Comparison of long-term results among Groups S (with acute cerebral infarction [CI]), N (without acute CI), and C (patients with infective endocarditis who underwent conservative treatment).

Long-Term Results

Long-term results were significantly worse for patients in Group C (P=0.04; **Figure**). There was no significant difference in long-term results between Groups S and N (P=0.91; **Figure**).

Discussion

The optimal timing of surgery in IE patients with neurological complications remains controversial. The following, from the ESC 2015 guidelines,[4] constitute the basic policy: after a stroke, surgery is indicated for heart failure, uncontrolled infection, abscess, or persistent high embolic risk and should be considered without any delay as long as coma is absent and the presence of cerebral hemorrhage has been excluded by cranial CT or MRI.

Previously, surgery was performed safely 4 weeks after CI.[6,7,12,13] Therefore, delayed surgery was recommended.

Recently, many reports have suggested that early surgery (within 2 weeks after CI) does not worsen outcomes.[14,15] Samura et al reported that early surgery for IE within 3 days after CI improved clinical results without significant neurological deterioration.[16] Yoshioka et al reported that the risk of postoperative neurological damage resulting from the exacerbation of hemorrhage lesions seemed relatively low, even in IE patients who underwent valve surgery within 2 weeks of intracranial hemorrhage onset.[17]

As mentioned above, early surgery is recommended even for IE patients with intracranial hemorrhage. Therefore, IE patients with acute CI are strongly advised to undergo early surgery. However, the policy at Ise Red Cross Hospital has been that surgical intervention is considered after negative blood culture and the administration of antibiotics for at least 2 weeks. In contrast, IE patients with acute CI have mainly selected delayed surgery at Ise Red Cross Hospital.

In this study, the mRS was used as an indicator to evaluate a patient's neurological status. The mean mRS score at the time of IE diagnosis in Group S was 3.9±0.6 (median 3; interquartile range [IQR] 3.5–4.0), which was significantly higher than that in Group N. However, moments before surgery, the difference in mRS score between the 2 groups had disappeared.

Conversely, in reports recommending early surgery, median preoperative mRS scores were reported as being 1.5 by Yoshioka et al[17] and 0 (IQR 0–3) by Samura et al.[16] Therefore, the reported cases for which early surgery was recommended may have been milder than those in the present study. In the present study, an mRS score of 3–4 indicates that a patient requires some assistance with walking and other physical demands. The mRS score in Group S at IE diagnosis was comparable to that in Group C, considered off-label for surgical intervention (3.9±0.6 vs. 4.2±1.0, respectively; P=0.31). It may be reasonable for such patients to undergo rigorous medical treatment, improve their general condition, and then undergo surgery. The policy of performing surgery after enhancing the state of moderate-to-severe neurological disorders is appropriate.

The SOFA score is an essential indicator of severe infectious disease[9] and is reported as a prognostic indicator after cardiac surgery.[18] In the present study, the SOFA score improved from IE diagnosis to moments before surgery. It is reasonable to perform preoperative management of IE patients using the mRS and SOFA scores as indicators to improve patients' general condition, and then perform surgery. Although the mRS and SOFA scores are not direct determinants of the optimal timing of surgery, they can be considered guides to improve the general condition of IE patients with acute CI.

Okura et al reported that consulting with the infectious disease department to manage IE patients led to better clinical outcomes.[19] We also consulted the infectious disease department for severe infectious diseases, such as IE, and performed systemic management, including appropriate antibiotic administration. In addition, close collaboration between cardiovascular surgeons, cardiologists, neurosurgeons, neurologists, and infectious disease physicians is important in determining appropriate surgical timing.

Study Limitations

The present study was limited by its retrospective, single-center design. Furthermore, the small number of cases made it difficult to draw clear conclusions.

Conclusions

Based on our findings, the strategy for the preoperative management and timing of surgery for IE patients at Ise Red Cross Hospital is appropriate. The mRS and SOFA scores can be used to guide strategies to improve the general condition of IE patients with acute cerebral complications. Close collaboration between cardiovascular surgeons, cardiologists, neurosurgeons, neurologists, and infectious disease physicians is essential for infection control, heart failure management, and appropriate surgery timing.

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This study did not receive any funding.

Disclosures

The authors have no conflicts of interest directly relevant to the contents of this study to declare.

IRB Information

This study was approved by the Institutional Review Board of Ise Red Cross Hospital (10/1/2021; Approval no. ER2021-35).

Data Availability

The deidentified participant data will not be shared.

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