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Original Article

Outcomes of Early Surgery for Infective Endocarditis

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Abstract

Background: **There is no evidence regarding the optimal timing for surgery for infective endocarditis. The decision to perform surgery mostly depends on the surgeon's opinion. The authors conducted this study to compare the outcomes of patients who underwent surgery within 14 days after established diagnosis and those who underwent surgery later than 14 days.**

Methods: **The authors retrospectively collected the data of patients who were diagnosed with definitive and possible infective endocarditis from 31 January 2008 to 1 May 2015. There were 170 patients. Surgery was performed in 110 patients. The outcomes of surgery between the patient groups whose surgery was performed within 14 days (early surgery group) and later (late surgery group) were compared.**

Results: **There were 110 patients who underwent surgery. There were 16 deaths in this group (14.5%). There were 60 patients who underwent medical treatment alone. In this group, there were 18 deaths (30%). The mortality rates in the early surgery group and the late surgery group were 17.4% and 10%, respectively, so the mortality in the early surgery group was higher with the odds ratio of 3.85. Nevertheless, the difference was not statistically significant (OR = 3.85, 95% CI: 0.58 - 25.6). The complications after surgery, length of ICU stay, and length of hospital stay were similar. However, the authors found that EuroSCORE and size of vegetation were statistically higher in the early surgery group.**

Conclusion: **Comparing the mortality rate of infective endocarditis, the authors found that the mortality rate in the early surgery group was higher than the late surgery group. However, the difference was not statistically significant.**

Keywords: **Infective endocarditis, surgical outcome**

Introduction

During the last 30 years, the incidence and mortality of infective endocarditis (IE) remains the same despite advancement in medical knowledge[1]. The incidence of native valve endocarditis is 1.7-6.2 per 100,000 population[2], whereas the incidence of prosthetic valve endocarditis is 0.94 per 100,000 population[1]. The average in-hospital mortality rate was 9.6-45%[1,3,4]. The treatment of IE requires a multi-disciplinary approach of the medical and surgical teams. Medical treatment alone results in a high mortality rate of 56-85%, yet, this rate can be lowered to 11-35% if combined medical and surgical treatment are utilized[2]. Although there is no clear evidence of the optimal timing for surgery[5], the European Society of Cardiology Guidelines 2009 recommended emergency surgery in patients who develop severe valvular regurgitation with cardiogenic shock. With

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some patients who have stable hemodynamics, the surgery can be delayed. In this group of the patients, the decision to perform surgery remains controversy, and usually depends on the surgeon's opinion. Early surgery in patients with uncontrolled sepsis, cardiogenic shock, and organ failure may increase mortality and risk of recurrence. However, delaying the surgery until the antibiotic course is completed may increase the risk of emboli, greater cardiac tissue damage rendering more difficult to repair, and also the deterioration in the course of disease resulting in cardiogenic shock, organ failure and eventual mortality.

The incidence of emboli in IE is 20-50%. The embolization usuallyoccurred within two weeks after administration of antibiotics[5,6], so the authors hypothesized that the optimal timing of surgery should remain within 14 days after establishing the diagnosis. This study was conducted to compare mortality within 30 days after surgery between the early surgery group and the late surgery group.

Materials and Methods

Study population

The authors collected the data of patients who were admitted due to IE from 31 January 2008 to 31 May 2015. All the patients were diagnosed with definite or possible IE as described in Modified Duke criteria. There were 170 patients, including native and prosthetic valve endocarditis.

Clinical data

The medical records were retrospectively reviewed. The data included co-morbidities, EuroSCORE, echocardiographic findings, laboratory test and outcomes. The end point of this study is 30-day mortality after surgery and post-operative complications.

Statistical analysis

The demographic data of this population was expressed as numbers, percentage, mean, and median. Standard deviation (SD) and interquartile range (IQR) were used for measurement of variation in continuous data. We compared the data between the patients who underwent surgery within 14 days (early surgery group) and after 14 days of established diagnosis (late surgery group). Differences between the two groups were evaluated using Chi-square test, t-test, and Mann-Whitney U test. The *p*-value of less than 0.05 is considered statistically significant.

Results

Patient characteristics

There were 170 patients who were diagnosed with IE. One hundred and fourteen patients were male. Fifty six patients were female. The average age was 44.6 years. One hundred and ten patients underwent surgery. Seventy patients received surgery within 14 days after established diagnosis (early surgery group), whereas 40 patients received surgery after 14 days (late surgery group). Three patients had prosthetic valve endocarditis (2.7%) and 3 patients had right-sided endocarditis (2.7%). The baseline characteristics between the two groups were shown in Table 1. The average age in the early surgery group was slightly higher but was not statistically significant. There were more male patients in both groups. Ejection fraction was similar in both groups. Regarding co-morbidities, the late surgery group had higher rates of previous endocarditis and congenital heart disease, whereas the early surgery group had higher EuroSCORE and larger size of vegetation significantly. Blood cultures from the patients showed that the most common causative organism was streptococcus group in 29 patients (35.7%) and the second most common organism was staphylococcus group in 20 patients (29%).

Surgical intervention

The average timing of surgical intervention was 6 days in the early surgery group and 21 days in the late surgery group. The duration of the established diagnosis after admission was similar. In the early surgery group, 49 patients had aortic valve replacement (AVR), 33 patients had mitral valve replacement (MVR), 14 patients had mitral valve repair (MV repair), 17 patients had MVR and AVR, 11 patients had tricuspid repair (TV repair), and 4 patients had MVR+AVR+ TV repair. In the late surgery group, only the number in the subgroup of patients who had AVR was significantly higher (Table 2). The total number of death was 16. There were 12 deaths (17.4%) in the early surgery group and 4 deaths (10%) in the late surgery group, which were not statistically different. There was no difference in postoperative complication, length of

Table 1 Baseline characteristics of patients who underwent early surgery (≤14 days) and who underwent late surgery (>14 days)

	Early surgery (n=70)	Late surgery (n=40)	*p*-value
Background			
Age: years, mean ± SD	42.62 ± 15.13	40.9 ± 17.87	0.591
Male, n(%)	49 (70)	24(60)	0.286
Ejection fraction, mean ± SD	59.62 ± 11.86	61.2 ± 15.43	0.544
*Vegetation size: mm, median (IQR)	12 (10,20)	10 (5,16.5)	0.048
*Euroscore(%), median (IQR)	8.13 (3.59,17.8)	3.08 (1.67,8.44)	0.002
Time to diagnosis, median (IQR)	2 (1,3)	2 (1,5)	0.260
*Time to surgery, median(IQR)	6 (3,10)	31 (19,52)	<0.001
Pathogens			
Blood culture positive, n (%)	35 (50)	17 (42.5)	0.797
Streptococcus sp, n (%)	19 (18.5)	10 (10.5)	0.806
Staphylococcus sp, n (%)	11 (15.7)	8 (20)	0.567
Comorbid			
DM, n (%)	6 (8.57)	2 (5)	0.708
HT, n (%)	2 (2.86)	5 (12.5)	0.097
Renal failure, n (%)	0 (0)	1 (2.5)	0.364
Coronary artery disease, n (%)	2 (2.86)	3 (7.5)	0.351
Dental carries, n (%)	4 (5.71)	3 (7.5)	0.703
Rheumatic, n (%)	8 (11.43)	3 (7.5)	0.743
*Previous endocarditis, n (%)	1 (1.43)	8 (20)	0.001
Previous surgery, n (%)	3 (4.29)	2 (5)	1.000
*Congenital heart disease, n (%)	1 (1.4)	7 (17.5)	0.003
Pacemaker device, n (%)	0 (0)	1 (2.5)	0.367

Table 2 Comparison of the surgical procedures between early surgery and late surgery

	Early surgery (n=70)	Late surgery (n=40)	*p*-value
AVR, n (%)	49 (70)	20 (50)	0.037
MVR, n (%)	33 (47.14)	24 (60)	0.194
MV repair, n (%)	14 (20)	6 (15)	0.513
AVR and MVR, n (%)	17 (24.31)	12 (30)	0.513
TV repair, n (%)	11 (15.7)	10 (25)	0.233
AVR-MVR+TV repair, n (%)	4 (5.7)	5 (12.5)	0.281

Table 3 Comparison of clinical outcomes between early surgery and late surgery

	Early surgery (n=70)	Late surgery (n=40)	*p*-value
CCU stay, median (IQR)	2 (1,8)	2 (1,5)	0.274
Hospital stay, median (IQR)	24 (15,39)	19 (11,32.5)	0.550
30 day mortality, n (%)	12 (17.4)	4 (10)	0.307
Complication			
Stroke, n (%)	4 (5.7)	6 (15)	0.17
Acute renal failure, n (%)	20 (28.6)	6 (15)	0.17
Limb ischemia, n (%)	2 (2.9)	3 (7.5)	0.35
Bleeding, n (%)	4 (5.7)	0 (0)	0.65
Arrhythmia, n (%)	13 (18.6)	4 (10)	0.20
Pleural effusion, n (%)	5 (7.1)	4 (10)	0.72
Pneumonia, n (%)	11 (15.7)	2 (5)	0.13

ICU stay, or length of hospital stay (Table 3). On multivariate analysis, the mortality rate was higher in the early surgery group with odds ratio of 3.85, however, the difference was not statistically significant (95% CI: 0.58-25.60).

Discussion

IE is a dreadful disease for the confronting doctor, especially for cardiac surgeons. If one could have a choice, then no one would like to perform surgery in this instance. From the past till present, the mortality rate and complications remain high despite the advancement in medical knowledge. Some cardiac surgeons prefer deferring surgery until the antibiotic course is completed, but this approach may lead to deterioration of the patient due to further damage of the cardiac tissue. This eventually leads to organ failure and cardiogenic shock, rendering a dire situation

Table 4 Outcome between early surgery and late surgery

Surgery	Death (n = 16), n (%)	Survival (n = 94), n (%)	Unadjusted OR (95%CI)	Adjusted OR (95%CI)
Late Surgery	4 (10)	36 (90)	1.00 (reference)	1.00 (reference)
Early Surgery	12 (17.1)	58 (82.9)	1.86 (0.56 - 6.22)	3.85 (0.58 - 25.60)

too difficult to save the patient's life.

The important complications of IE are mycotic aneurysm, acute renal failure, emboli, splenic abscess and myocarditis[1]. The probability of embolization in IE may be as high as 15-20%[7]. This can cause a neurologic event for 20-40%[2,8-10]. Embolization often occurs after a 2-week course of antibiotics, usually appearing at the central nervous system (65%) at the middle cerebral artery (90%)[2,8-10]. The pathologic findings could be hemorrhage (12%), cerebrovascular accident (60%), transient ischemic attack (6%), ruptured mycotic aneurysm (6%) and meningitis (6%)[11]. These events necessitate delaying surgery; three weeks for cerebral infarction and more than four weeks for cerebral hemorrhage[11,12]. The decision to perform surgery before these periods may be harmful to the patient due to hypoperfusion and hypotension during cardiopulmonary bypass resulting in cerebral edema and disruption of blood-brain barrier causing deterioration in neurologic condition and increasing mortality[11]. On the other hand, during the waiting period, the cardiac tissue is further damaged by the organism which increases the chances of complications and mortality.

There are several reports supporting the rationale to perform early surgery in patients with IE. The duration of antibiotics before surgery and the positive yield of intra-operative tissue culture do not correlate to postoperative mortality[13]. Performing surgery in the acute phase results in mortality only 6-25%, does not increase the recurrence of infection and reoperation, but could decrease mortality rate[14,15].

Funakoshi et al. found that the patients who had surgery performed within two weeks after established diagnosis had lower in-hospital mortality and better long term outcome than the conventional group[5]. Kang et al. found that in the patients who had surgery performed within 48 hours, there was no difference in mortality, but lower recurrence of infection and emboli[16]. Kim et al. found that that in the patients who had surgery performed within seven days after established diagnosis, the rate of systemic embolization was substantially lower[17]. Olaison et al. followed the patients for five years and found that the survival rate of the early surgery group was higher than medical treatment alone.

The present data showed that most of the demographic data of both groups was similar, but the early surgery group had larger vegetation and higher EuroSCORE which means that the early surgery group has greater severity. This may be the reason why this group of patients necessitated earlier surgery. When the authors compared the data of surgical procedures, mostly there was no difference, only the number of AVR was higher in the early surgery group. The clinical outcomes including postoperative complication, length of ICU stay, length of hospital stay and mortality were not statistically different. After controlling the confounding factors which affect mortality rates, the early surgery group had higher mortality but there was no statistical significance.

The data of this study also included patients with native valve, prosthetic valve and right-sided endocarditis, which differs from earlier studies that included only the patients with left-sided native valve endocarditis. This information should encourage cardiac surgeons to make the decision to perform early surgery rather than deferring it, especially in patients with refractory heart failure after the diagnosis was established.

Limitations

This is a retrospective study that did not control several confounding factors which may affect the outcome. These factors include a delay in diagnosis and consultation, and that the decision to perform surgery ultimately relies upon the opinion of the surgeons. There is no consensus about the guidelines for the management of IE. The population of this study were from only a single center, which could not

represent the whole population of IE.

Conclusions

Comparing the early surgery group and late surgery group, after an established diagnosis, the mortality rate of the early surgery group was higher, but not statistically significant, even though the early surgery group had greater severity. Multi-center prospective randomized control trial should be conducted in the future.

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บทคัดย่อ **ผลลัพธ์ของการผ่าตัดผู้ป่วย Infective endocarditis ตั้งแต่ระยะแรกของโรค**

คมกฤษณ์ โกมุทรินทร์

กลุ่มงานศัลยกรรม โรงพยาบาลมหาราชนครราชสีมา

บทนำ: ยังไม่มีข้อมูลเชิงประจักษ์ในเรื่องระยะเวลาและข้อบ่งชี้ในการผ่าตัดผู้ป่วย infective endocarditis ที่ชัดเจน การตัดสินใจผ่าตัดส่วนใหญ่ขึ้นกับความเห็นของแพทย์ผู้รักษา ผู้วิจัยจึงได้ทำการศึกษาเปรียบเทียบอัตราการตายระหว่างผู้ป่วยที่ได้รับการผ่าตัด ภายใน 14 วัน กับ หลังวินิจฉัยเกินกว่า 14 วัน

วิธีการศึกษา: งานวิจัยนี้ใช้วิธีศึกษาข้อมูลย้อนหลัง (Retrospective) ระหว่างมกราคม 2551 ถึง พฤษภาคม 2558 ในผู้ป่วยที่ได้รับการวินิจฉัยเป็น definite และ possible infective endocarditis ทั้งในกลุ่ม native และ prosthetic valve endocarditis จำนวน 170 ราย ทำการศึกษาเฉพาะในกลุ่มที่ได้รับการผ่าตัดจำนวน 110 ราย เปรียบเทียบอัตราการตายที่ 30 วัน หลังผ่าตัด ระหว่างกลุ่มที่ได้รับการผ่าตัดภายใน 14 วัน กับได้รับการผ่าตัดเกิน 14 วันหลังได้รับการวินิจฉัย

ผลการศึกษา: ผู้ป่วยที่ได้รับการผ่าตัด 110 ราย เสียชีวิต 16 ราย (14.6%) ผู้ป่วยที่ไม่ได้รับการผ่าตัด 60 ราย เสียชีวิต 18 ราย (30%) ผู้ป่วยที่ได้รับการผ่าตัดภายใน 14 วัน 70 ราย เสียชีวิต 12 ราย (17.4%) ผู้ป่วยที่ผ่าตัดหลัง 14 วัน จำนวน 40 ราย (10%) เสียชีวิต 4 ราย พบว่าอัตราการตายที่ 30 วัน ของทั้ง 2 กลุ่ม ไม่มีความแตกต่างกันอย่างมีนัยสำคัญ ($P = 0.307$) เมื่อเปรียบเทียบภาวะแทรกซ้อนหลังการผ่าตัด ระยะเวลาการนอนใน CCU และระยะเวลาการนอนโรงพยาบาลไม่มีความแตกต่างกัน แต่ในกลุ่มที่ผ่าตัดภายใน 14 วัน มีค่า Euroscore และขนาด Vegetation ที่มากกว่าอย่างมีนัยสำคัญ

สรุป: เมื่อเปรียบเทียบอัตราการตายของผู้ป่วย infective endocarditis พบว่ากลุ่มที่ได้รับการผ่าตัดภายใน 14 วัน มีอัตราการตายที่สูงกว่ากลุ่มที่ได้รับการผ่าตัดหลัง 14 วัน แต่ไม่มีความแตกต่างอย่างมีนัยสำคัญ

คำสำคัญ: Infective endocarditis, surgical outcome