Original Article

Outcomes of Tissue versus Mechanical Valve Replacement for Infective Endocarditis

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Abstract

Objective: There is no consensus regarding the best prosthetic valve for patients with infective endocarditis (IE). The aim of the present study was to compare short and long-term outcomes of tissue versus mechanical valve replacement in patients with left-sided severe IE.

Methods: A retrospective medical chart review of IE patients treated between January 1st, 2008 and September 30th, 2020 was performed. Patients were categorized into two groups according to the type of prosthetic valve used (tissue or mechanical). Outcomes included in-hospital mortality, recurrent infection, reoperation and long-term survival.

Results: There were 147 patients. The overall in-hospital mortality was 17%. The in-hospital mortality rate was 27% and 14% for patients undergoing tissue and mechanical valve replacement, respectively. The recurrent infection rate was 3% and reoperation rate was 1%. The 5-year survival for patients in the tissue valve group was 71.4% (95% CI: 53.4% to 83.5%) and for the mechanical valve group, 81.5% (95% CI: 72.4% to 87.8%).

Conclusion: Mechanical prosthetic valve replacement in left-sided active endocarditis had better in-hospital mortality and long-term survival than tissue valve replacement, although the preoperative status of patients in the tissue valve group was worse. However, the recurrence rate was low and long-term survival was good for both groups.

Keywords: Infective endocarditis, Prosthetic valve, Tissue valve, Mechanical valve

INTRODUCTION

The choice of prosthetic valve for patients with active infective endocarditis (IE) is controversial. Long-term results are unknown. In Thailand, the incidence of IE is 5.7 per 1,000 admissions.[1] The incidence is 4 per 1000 admissions in the Northeastern region of Thailand.[2] In hospital mortality for active IE is 15% to 20%, and can be as high as 40%.[3] Modern management focuses on early surgery without 4 to 6 weeks of antibiotics. Although preoperative antibiotics did not affect in-hospital mortality and recurrence,[4] the placement of foreign body in patients who have active infection,[5] which may prevent further infection, can also increase the risk of reinfection and mortality.[6-8] Early mortality of surgery in active IE is 5% to 26%.[9-14]

The principle of surgery is radical debridement,

which decreases the possibility of valve repair, and most patients end up with valve replacement. Guidelines from the American Association for Thoracic Surgery (AATS), the American College of Cardiology/American Heart Association (ACC/AHA) and the European Society of Cardiology (ESC) recommend mechanical valves in patients younger than 60 to 65 years and tissue valves in those 60 to 65 years or older. There is a gray zone between 50 to 70 years where there is no conclusion regarding the most suitable choice of prosthetic valve.[3,15-17] Theoretically, tissue valve is more likely to be infected whereas the mechanical valve is more resistant to infection. Tissue valves also has a tendency towards early degeneration.[18,19]

Most studies of active IE are observational and conducted at single centers in European countries and North America, and are less likely to involve Asian populations.[20] Different regions of the world have different patient characteristics and risk factors. Many reports were from over 10 years ago. Several of these included both active IE and healed IE. The aim of the present study was to determine more recent short and long-term outcomes of mechanical and tissue valve replacement in patients with left-sided active infective endocarditis of the native valve.

PATIENTS AND METHODS

Patients over 18 years who were diagnosed with left-sided native valve active infective endocarditis according to the modified Duke's criteria who underwent valve replacement at Maharat Nakhon Ratchasima hospital between Jan 1st, 2008 and Sep 30th, 2020 were included in the study. The definition of active endocarditis included the presence of wet vegetation, presence of valvular abscesses seen on echocardiogram or during surgery, presence of fever, leukocytosis, positive blood culture or tissue culture, valvular inflammation with PMN predominance and duration of antibiotics use of less than 4 to 6 weeks.[21-24] Patients with prosthetic valve infection or those who had both tissue and mechanical valve replacement were excluded.

This study was approved by the Maharat Nakhon Ratchasima Institutional Review Board (MNRH IRB). Patients were categorized into two groups according to the type of prosthetic valve received (mechanical or tissue). Early outcomes included in-hospital mortality, ICU stay, postoperative stay and complications. Long term outcomes included 5-year survival, the reinfection rate

and reoperation rate. All survivors were followed from hospital discharge after surgery till Oct 31th, 2020. The cause of mortality was determined from medical records or from the civil registration.

All patients were managed by an IE Multidisciplinary Team. Preoperative echocardiography (transthoracic or transesophageal, TTE or TEE, respectively) was performed on every patient. Preoperative coronary angiography was performed in patients who were 40 years or older. We performed surgery via full sternotomy with standard cardio-pulmonary bypass under mild to moderate hypothermia. Cold blood cardioplegia was used for myocardial protection. The prosthetic valves used were selected according to patient preference or the decision of the surgeon. Patients were transferred to the ICU for postoperative care. Antibiotics was used under supervision of infectious disease specialists.

Quantitative variables were summarized as mean and standard deviation (SD), or median and interquartile range (IQR) as appropriate. Categorical data were summarized as frequency and percentage. Average survival was estimated using the Kaplan-Meier method, along with 95% confidence intervals. Stata statistical software (Stata Corp, College Station, TX, USA) was used for data analysis.

RESULTS

There were 147 patients in the study, with 37 patients in the tissue valve group and 110 patients in mechanical valve group. Table 1 shows the characteristics of patients in the study. Most patients had definite IE (99%) and received TTE (88%). The average age was 45.4 years, and was higher in the tissue valve group than the mechanical valve group. Most patients in both groups were male. Associated diseases included: hypertension (HT; 13%), rheumatic heart disease (10%), and diabetes mellitus (DM; 6%). The prevalence of HT, coronary artery disease, renal failure, and stroke was higher in the tissue valve group, whereas the prevalence of DM, rheumatic heart disease, previous cardiac surgery and congenital heart disease was higher in mechanical valve group.

Two patients in mechanical valve group had end-stage renal disease (ESRD) requiring long-term hemodialysis before surgery. Two patients in the mechanical valve group had previous cardiac surgery (PBMV and MVR), and 4 had associated congenital heart disease (mostly VSD).

Table 1 Patient and disease characteristics, operations and complications

Characteristics / Operations	Total (n = 147)	Mechanical (n = 110)	Tissue (n = 37)
Age (years): mean (SD)	45.4 (13.6)	41.9 (12.2)	55.9 (12.4)
Men: number (%)	103 (70)	76 (69)	27 (73)
Comorbid: number (%)			
DM	9 (6)	7 (6)	2 (5)
HT	19 (13)	10 (9)	9 (24)
Serum Cr > 2 mg/dL	3 (2)	2 (2)	1 (3)
Coronary artery disease	5 (3)	1 (1)	4 (11)
Stroke	5 (3)	3 (3)	2 (5)
COPD	4 (3)	2 (2)	2 (5)
Rheumatic	15 (10)	14 (13)	1 (3)
Previous cardiac surgery	2 (1)	2 (2)	0
Congenital heart disease	6 (4)	5 (5)	1 (3)
Laboratory finding: number (%)			
WBC > 15,000	5 (3)	4 (4)	1 (3)
Albumin < 3 gm/d	75 (52)	56 (51)	19 (53)
Hct < 30%	68 (47)	47 (43)	21 (57)
Cr clearance < 50%	48 (33)	26 (24)	22 (60)
EF < 40%	5 (3)	3 (3)	2 (5)
Euroscore II: median (IQR)	6.9 (3.6-16)	5.8 (2.9-12)	13.5 (5.1-25)
Echocardiography: number (%)			
TEE	18 (12)	14 (13)	4 (11)
TTE	129 (88)	107 (87)	33 (89)
Vegetation size (mm): mean (SD)	13.7 (7.1)	14.3 (7.6)	12.2 (5.6)
< 10	26 (20)	19 (20)	7 (22)
10 - 15	63 (50)	46 (48)	17 (53)
> 15	38 (30)	30 (32)	8 (25)
Microorganisms: number (%)	86 (63)	68 (67)	18 (50)
Staphylococcus aureus	10 (7)	9 (8)	1 (3)
Staphylococcus epidermidis	2 (1)	2 (2)	0
Coagulase-neg staphylococci	5 (3)	4 (4)	1 (3)
Streptococcal group	58 (40)	45 (41)	13 (35)
Enterococcus species	3 (2)	2 (2)	1 (3)
Positive tissue culture: number (%)	13/77 (17)	11/60 (18)	2/17 (12)
Diagnosis of IE: number (%)			
Definite IE	145 (99)	108 (98)	37 (100)
Possible IE	2 (1)	2 (2)	0
Site of infection: number (%)			
AV	74 (50)	54 (49)	20 (54)
MV	40 (27)	32 (29)	8 (22)
AV+MV	28 (19)	20 (18)	8 (22)
MV+TV	3 (2)	3 (3)	0
AV+TV	1 (1)	1 (1)	0
AV+MV+TV	1 (1)	0	1 (3)

Table 1 (cont.) Patient and disease characteristics, operations and complications

Characteristics / Operations	Total (n = 147)	Mechanical (n = 110)	Tissue (n = 37)
Operation procedure: number (%)			
AVR	49 (33)	38 (35)	11 (30)
MVR	38 (26)	31 (28)	7 (19)
AVR+MVR	29 (20)	21 (19)	8 (22)
AVR+TV repair	2 (1)	2 (2)	0
MVR+TV repair	14 (10)	11 (10)	3 (8)
AVR+MV repair	10 (7)	3 (3)	7 (19)
AVR+MVR+TV repair	3 (2)	3 (3)	0
AVR+MVR+TVR	2 (1)	1 (1)	1 (3)
Complication: number (%)			
Stroke	15 (10)	12 (11)	3 (8)
Transient ischemic attack	3 (2)	2 (2)	1 (3)
Prolong fever	10 (7)	7 (6)	3 (8)
Acute renal failure	35 (24)	24 (22)	11 (30)
Splenic abscess	1 (1)	1 (1)	0
Pericardial effusion	1 (1)	0	1 (3)
Limb ischemia	7 (5)	5 (5)	2 (5)
Post-op bleeding	5 (3)	4 (4)	1 (3)
Arrhythmia	38 (26)	29 (26)	9 (24)
Pleural effusion	16 (11)	10 (9)	6 (16)
Pneumonia	18 (12)	11 (10)	7 (19)

SD: standard deviation; DM: diabetic mellitus; HT: hypertension; EF: ejection fraction; WBC: white blood cell count; Cr: creatinine; TEE: transesophageal echocardiography; TTE: transthoracic echocardiography; IQR: interquartile range; Hct: hematocrit; AV: aortic valve; MV: mitral valve; TV: tricuspid valve

In the tissue valve group, hypoalbuminemia, anemia and severe renal impairment was more frequent and the median Euroscore II was higher. Most vegetation size was 10 mm or larger. In the mechanical valve group, vegetation size was larger than in the tissue valve group.

Positive blood culture was present preoperatively in 86 patients (63%). There was no record of preoperative blood cultures in 10 patients. Streptococcus group is the most common pathogen in both groups. Intraoperative tissue culture was performed on 77 patients, of which 13 were positive (17%). In the mechanical valve group, 11 (18%) cultures were positive, which was more than in the tissue valve group (2 patients, 12%). The infection mostly involved a single valve. The most common site of infection was the aortic valve. There were multivalvular involvement in 33 cases (22%). There was trivalvular involvement in one patient in the tissue valve group.

The most common operation was a single valve operation (59%). The most common was aortic valve replacement (AVR; 33%), followed by mitral valve replacement (MVR; 26%). AVR and MVR were more common in the mechanical valve group. In the tissue valve group, multiple valve operations were necessary in 51%, which included AVR and MVR, AVR plus mitral valve repair (MV repair), and combined AVR, MVR plus tricuspid valve surgery (TV surgery). TV surgery was required in 15% of patients in the mechanical valve group, and in 11% in the tissue valve group.

The most common arrhythmia was atrial fibrillation. Twenty-two patients required postoperative dialysis, most of which was peritoneal dialysis. Five patients had postoperative bleeding requiring reoperation. The incidence of postoperative transient ischemic attack, prolonged fever, acute renal failure, pericardial effusion, limb ischemia, pleural effusion and pneumonia was higher in the tissue valve group, whereas the incidence of stroke, splenic abscess, postoperative bleeding, and arrhythmia was higher in mechanical valve group.

Table 2 compares the early outcomes between the two groups. In the mechanical valve group, cross clamp time and bypass time were slightly longer, as well as the length of hospital stay. However the length of ICU stay was shorter. There were 25 in-hospital deaths (17%). Intraoperative mortality occurred in 5 patients. The tissue valve group had higher in-hospital mortality (27%) than the mechanical valve group (14%).

Table 3 shows the long-term outcomes. In tissue valve group, there was no recurrent infection or reoperation. In the mechanical valve group, there was 3% recurrent infection and 1% reoperation. Overall, 122 patients survived until hospital discharge (95 patients in mechanical valve group and 27 patients in tissue valve group). At the last follow up, 113 of 122 patients survived (93%), including 88 in the mechanical valve group (93%) and 25 in the tissue valve group (93%). The average 5-year survival was 81.5% (95% CI: 72.4 to 87.8) in mechanical valve group, which was better than the 71.4% (95% CI: 53.4 to 83.5) in the tissue valve group (see Figure 1).

Table 2 Early outcomes

Outcome	Total (n = 147)	Mechanical (n = 110)	Tissue (n = 37)
CCU stay (day): median (IQR)	4 (2 to 7.5)	4 (2 to 8)	5 (1 to 7)
Hospital stay (day): median (IQR)	14 (8 to 27)	15 (9 to 27)	11 (7 to 20)
Clamp time (min): median (IQR)	77 (54 to 108)	79 (52 to 107)	75 (60 to 108)
Bypass time (min) median (IQR)	98 (73 to 133)	99 (73 to 129)	98 (71 to 146)
In-hospital mortality: number (%)	25 (17)	15 (14)	10 (27)

CCU: cardiac care unit; min: minutes; IQR: interquartile range

Table 3 Long term outcomes

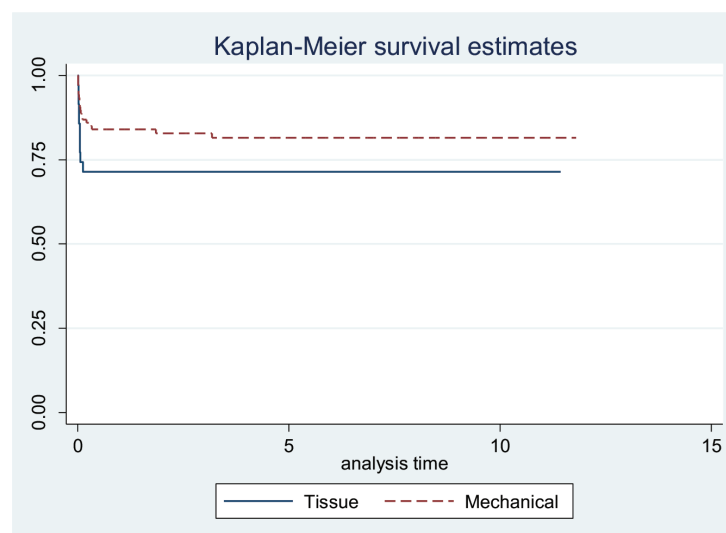| Outcome	Mechanical (n = 110)	Tissue (n = 37)
Reinfection: number (%)	3 (3)	0
Reoperation: number (%)	1 (1)	0
5-year survival, % (95% CI)	81.5 (72.4 to 87.8)	71.4 (53.4 to 83.5)

Figure 1 Survival estimates of tissue vs mechanical valve replacement

DISCUSSION

In the present study of patients with left-sided native valve, active IE, we found that patients who had tissue valve replacement had higher in-hospital mortality than those who had mechanical valve replacement. Even though the mortality rate was high in the early postoperative period, long term outcomes, which included reinfection, reoperation and long-term survival, were good.

Baseline characteristics of patients in the present study were similar to those of previous studies, in which the average age was 36 to 60 years,[25-28] male patients were twice as many as female patients,[29] and common associated medical conditions included renal impairment (28%), anemia (38%), heart block (12%), hematuria (25%), and splenomegaly (11%).[9-11,29,30] In developing countries, active IE is commonly associated with rheumatic heart disease and poor dental hygiene. Common sites of involvement included the aortic valve (42%), mitral valve (34%), or multiple valves (24%). Common pathogens included streptococcus group (34%), staphylococcus aureus (27%), and staphylococcus coagulase negative (21%).[9,33-35]

In the present study, the prevalence of positive blood culture and tissue culture was low. The percentage of positive blood culture is usually from 83% to 92%, but positive tissue culture could be much lower, from 25% to 34%.[22,24,36] The reason for this might be due to antibiotic treatment before taking culture. Also, a negative blood culture is associated with low positive tissue culture, in the range of 5% to 15%.[22,25,29,30] In the present study, 5 patients developed stroke, which might be related to large mobile valvular vegetation, with higher chance of systemic embolization and cerebral complication in 15% to 20% of patients prior to operation, especially at 1 to 2 weeks after antibiotics administration.[3,4,20,29]

In the present study, patients who underwent tissue or mechanical valve replacement had similar operative time and length of hospital stay, which were similar to those of previous studies. For example, cross-clamp time was 78.8 ± 41.5 minutes, cardio-pulmonary bypass (CPB) time was 117.8 ± 58.3 minutes, ICU stay was 4.6 ± 5.3 days and length of hospital stay was 15.3 ± 14.7 days.[24,25]

From previous studies, postoperative complications included reoperation (15%) due to postoperative bleeding (6%) and deep sternal wound infection (1%), atrial fibrillation (AF; 20%), prolonged ventilation (28%), new stroke (3%), transient ischemic attack (1%) and coma (1%). Other complications included acute renal failure (ARF), cardiac tamponade, heart block, sepsis, cholecystitis, mesenteric ischemia, recurrent IE and low cardiac output.[5,20] In the present study, common complications were ARF requiring dialysis and cardiac arrhythmia.

Moon *et al.* found that in left-sided, active or healed IE, mechanical valve replacement had an operative mortality of 19% and tissue valve replacement 17%, which were not significantly different.[19] Nguyen *et al.* found that aortic valve replacement in active IE had an early mortality of 10% in the mechanical valve group, and 19% in the tissue valve group.[27] Bauernschmitt *et al.* found that early mortality of mechanical valve replacement in active IE was 12%.[5] Musci *et al.* found that 30-day overall survival of tissue valve replacement in active IE was 77%.[21] in the present study, the in-hospital mortality in the tissue valve group was 27%, which was higher than the 14% in the mechanical valve group.

Risk factors of postoperative mortality include advanced age, pulmonary embolism, large valvular vegetation, DM, critical status, prolonged ICU stay, previous cardiopulmonary bypass graft (CABG), emergency operation, active IE, previous valve surgery, renal dialysis, drug abuse, fungal infection, moderate to severe ischemic stroke, cerebral hemorrhage, double valve endocarditis, myocardial infarction, valvular abscess formation, CPB time longer than 120 minutes, massive blood transfusion, aortic valve involvement, Left ventricular ejection fraction less than 35%, WBC greater than 15,000 mm^3, creatinine level greater than 2 mg/dL, body temperature greater than 38 $^\circ$C, hemoglobin level less than 10 g/dL, low serum albumin and high EuroSCORE.[7,19,20, 25, 32-34, 35-41]

Delahaye *et al.* found that tissue valve replacement had higher 1-year in hospital mortality than that of mechanical valve replacement.[42] This result is similar to that of the present study, but we also found that patients in the tissue valve group had higher EuroSCORE, older age, and required multiple valve operations. The reinfection and reoperation rate was low, especially in the mechanical valve group which is reported to be 3% to 9%, and in the tissue valve group, 7% to 29%.[43] In another study, in the first 5 years, the recurrence rate of native valve IE in the mechanical valve group was 2% and in the tissue-valve group was 1%; both rates were not significantly different.[19]

In another study of active IE, tissue valve replace-

ment has a reoperation rate of 7% and a reinfection rate of 9%.[21] Toyoda et al. found that recurrence rates of IE in mechanical and tissue valve groups were not statistically different. In aortic valve replacement, the rate of recurrent IE in the mechanical valve group was 10% and in the tissue valve group, 9%, whereas in mitral valve replacement, the rates of recurrent IE were 9% and 10% respectively.[33] At 1 to 2 years after surgery, reinfection, reoperation, and mortality rates gradually decrease.[18,22] In the present study the rate of recurrent IE was 3%, and the reoperation rate was 1%, all found in the mechanical valve group. These rates were lower than those of previous studies.

Factors influencing long-term survival include presence of coronary artery disease, renal disease, DM, and ejection fraction less than 40%.[44] Reul and Sweeny reported a 85% survival rate at 4 years in the mechanical valve group, which was higher than the 79% rate of the tissue valve group.[18] Delay et al. found a 71% 5-year survival rate in the mechanical valve group and 61% in the tissue valve group, and these rates were not significantly different.[45] This result was similar to that of a study by Saide et al., with 5-year survival rates of 75% and 62% in the mechanical and tissue valve groups, respectively.[46] Musci et al., in patients with active IE, found that by using tissue valves the survival rates at 1, 3 and 5 years were 60%, 53%, and 47%, respectively.[21] Flynn et al. conducted a meta-analysis comparing the results of tissue and mechanical valves, and found that the survival rates at 1, 3 and 5 years in the mechanical valve group was 73%, 57% and 49% and in the tissue valve group, 72%, 57% and 49%, respectively.[47]

In the present study, long-term survival rates of the two groups were similar and better than those of previous studies. Survival in the mechanical valve group was better than that in the tissue valve group, at 81.5% (95% CI: 72.4% to 87.8%) and 71.4% (95% CI: 53.4% to 83.5%), respectively. Flynn et al. found similar results and proposed that the choice of prosthetic valve replacement in IE should be based on age, co-morbidity and preference of patients and surgeons.[47]

The present study has many limitations. The design was retrospective and observational, conducted at a single center. The criteria for prosthetic valve selection were unclear. However, long-term follow-up was reasonably complete because all data were collected from medical records and civil registration, though there was some discrepancy in the cause of death.

CONCLUSION

In patients with left-sided native valve active endocarditis, tissue valve replacement was associated with higher in-hospital mortality than mechanical valve replacement. However, the preoperative status of patients undergoing tissue valve replacement was worse. Long-term recurrence and survival rates were good in both groups.

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บทคัดย่อ   **ผลลัพธ์ในระยะยาวของลิ้นหัวใจแบบเนื้อเยื่อและโลหะในผู้ป่วยลิ้นหัวใจติดเชื้อในระยะรุนแรง**

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หน่วยศัลยกรรมทรวงอก กลุ่มงานศัลยกรรม โรงพยาบาลมหาราชนครราชสีมา

     ความเป็นมา: ยังไม่มีข้อสรุปว่าลิ้นหัวใจชนิดใดเหมาะสมที่สุดสำหรับผู้ป่วยลิ้นหัวใจติดเชื้อ ซึ่งเป็นโรคที่มีความรุนแรง และโอกาสเสียชีวิตสูง ปัจจุบันการรักษามุ่งเน้นในการทำ early surgery โดยไม่รอให้ยาฆ่าเชื้อจนครบกำหนด ทำให้มีโอกาส ติดเชื้อซ้ำส่งผลต่อการรอดชีวิตในระยะยาว ผู้วิจัยจึงทำการศึกษาผลลัพธ์ในระยะสั้นและระยะยาวของลิ้นหัวใจแบบเนื้อเยื่อ และโลหะในผู้ป่วยลิ้นหัวใจติดเชื้อด้านซ้ายในระยะรุนแรง

     วิธีการศึกษา: เป็นการศึกษาแบบย้อนหลัง ระหว่าง 1 มกราคม 2551 ถึง 30 กันยายน 2563 มีผู้ป่วย 147 ราย แบ่งเป็น 2 กลุ่ม คือ กลุ่มได้รับการใส่ลิ้นแบบเนื้อเยื่อและแบบโลหะ เก็บข้อมูลอัตราการเสียชีวิตในโรงพยาบาล การติดเชื้อซ้ำ การผ่าตัด ซ้ำ และการรอดชีวิตในระยะยาวของผู้ป่วย ทั้ง 2 กลุ่ม

     ผลการศึกษา: อัตราการเสียชีวิตในโรงพยาบาลอยู่ที่ร้อยละ 17 กลุ่มลิ้นแบบเนื้อเยื่อมีอัตราการเสียชีวิตร้อยละ 27 กลุ่ม ลิ้นแบบโลหะมีอัตราการเสียชีวิตร้อยละ 14 พบมีการติดเชื้อซ้ำร้อยละ 3 และผ่าตัดซ้ำร้อยละ 1 เฉพาะในกลุ่มลิ้นแบบโลหะ อัตราการอยู่รอดที่เวลา 5 ปี (5-yer Survival) ของลิ้นแบบเนื้อเยื่ออยู่ที่ร้อยละ 71.4 (95% CI : 53.4 – 83.5) และลิ้นแบบโลหะ อยู่ที่ร้อยละ 81.5 (95%CI : 72.4 – 87.8)

     สรุปผลการศึกษา: การทำผ่าตัดเปลี่ยนลิ้นหัวใจในผู้ป่วย Lt. side native valve active endocarditis พบว่ากลุ่ม mechanical valve จะมี in-hospital mortality และ long term survival ที่ดีกว่ากลุ่ม tissue valve โดยทั้ง 2 กลุ่ม มีอัตราการเสียชีวิตใน โรงพยาบาลค่อนข้างสูง ทั้งนี้ผู้ป่วยในกลุ่ม tissue valve มีสภาพก่อนผ่าตัดที่แย่กว่าแต่เมื่อติดตามในระยะยาวพบว่ามีอัตรา การติดเชื้อและการผ่าตัดซ้ำต่ำ รวมถึงมีอัตราการรอดชีวิตที่ยืนยาว