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Infective endocarditis as a morbidity predictor in patients who underwent mitral valve surgery

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ABSTRACT

Infective endocarditis (IE) often develops into rheumatic heart disease (RHD) that has many perioperative complications during the evolution of the disease. Cardiac surgery in patients with IE is often followed by post-operative morbidities that can decrease the quality of life. This study aimed to investigate the correlations between preoperative IE and the emergence of various morbidities in patients undergoing heart valve surgery. This was a cross-sectional study with secondary data analysis of the medical record in 60 patients with mitral valve surgery at Dr. Sardjito General Hospital, Yogyakarta from 2012 to 2017. As much as 30 of 60 patients were suffered IE before mitral valve surgery. The most common valve disease in the IE group was mitral stenosis (60%). IE was significantly associated with arrhythmia and cardiac event with p=0.002 (PR: 6.91), prolonged ICU stay with p=0.011 (PR: 5.68), prolonged ventilator use with p=0.015 (PR: 12.43) and severe pulmonary arterial hypertension (PAH) with p=0.033 (PR: 0.192) post mitral valve surgery. As many as 26 (87%) and 29 (96.7%) of patients with IE had a prolonged ICU stay and prolonged ventilator after mitral valve surgery respectively. The incidence of severe PAH postoperatively in the IE group was lower than in the non-IE group (10% vs 36.7%). IE was significantly associated with the increased risk of arrhythmia, prolonged ventilator use and prolonged ICU stay after mitral valve surgery.

ABSTRAK

Infective endocarditis (IE) sering berkembang menjadi penyakit jantung rematik (PJR) yang memiliki banyak komplikasi perioperatif selama evolusi penyakit. Operasi jantung pada pasien dengan IE sering diikuti oleh morbiditas pasca operasi yang dapat menurunkan kualitas hidup. Penelitian ini bertujuan untuk menyelidiki korelasi antara IE sebelum operasi dan munculnya berbagai morbiditas pada pasien yang menjalani operasi katup jantung. Penelitian ini merupakan penelitian *cross-sectional* dengan analisis data sekunder dari rekam medis pada 60 pasien dengan operasi katup mitral di Rumah Sakit Umum Dr. Sardjito, Yogyakarta tahun 2012 hingga 2017. Sebanyak 30 dari 60 pasien menderita IE sebelum operasi katup mitral. Penyakit katup yang paling umum pada kelompok IE adalah stenosis mitral (60%). IE secara bermakna dikaitkan dengan aritmia dan *cardiac event* dengan p=0,002 (PR: 6,91), lama tinggal di ICU dengan p=0,011 (PR: 5,68), penggunaan ventilator berkepanjangan dengan p=0,015 (PR: 12,43) dan *pulmonary arterial hypertension* (PAH) dengan p=0,033 (PR: 0,192) pasca operasi katup mitral. Sebanyak 26 (87%) dan 29 (96,7%) dari pasien dengan IE memiliki lama tinggal di ICU dan ventilator yang lama setelah operasi masing-masing katup mitral. Insiden PAH parah pasca operasi pada kelompok IE lebih rendah daripada kelompok non-IE (10% vs 36,7%). IE secara signifikan dikaitkan dengan peningkatan risiko aritmia, penggunaan ventilator berkepanjangan dan tinggal ICU berkepanjangan setelah operasi katup mitral.

Keywords:
endocarditis
mitral valve surgery
morbidity
infection
prognosis

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INTRODUCTION

Infective endocarditis (IE) can cause life-threatening conditions and still has a high mortality rate.[1,2] IE is often accompanied by cardiac complications, the incidence of embolism, and related to prolonged hospitalization in an intensive care unit (ICU).[2,3] Long-term IE often develops into rheumatic heart disease (RHD) which usually manifests as damage of the heart valves.[4] Clinical management of heart valve disease depends on clinical presentation and surgical treatment is an intervention that can change the progression of valve disease.[4] Surgery provides the potential for life-saving interventions to remove infected tissue and any source of embolism.[1,5] Although surgical procedures are often needed, they are associated with increased postoperative morbidity and mortality.[6]

Many complications occur during the evolution of IE,[7] and a variety of the causative microorganisms can create a wide variety of complications.[3] Patients undergoing cardiac surgery with perioperative complications require long ICU stays and this condition is usually associated with high mortality and morbidity after discharge from the hospital.[8] Most of the IE cases will require treatment in the ICU. But unfortunately, there are still few studies that focus on patients with IE and the multiple complications leading to ICU admission.[7] For this reason, this study was investigated to see any correlations between preoperative IE and the emergence of various morbidities in patients undergoing heart valve surgery.

MATERIALS AND METHODS

This study was a cross-sectional study and conducted at Dr. Sardjito General Hospital, Yogyakarta, Indonesia, on patients who underwent mitral valve surgery. Secondary data were collected from medical records from January 2012-December 2017 relating to the following inclusion criteria: all patients with primary mitral valve surgery. Informed consent was taken from all patients before the procedure was conducted.

The exclusion criteria were as follows: 1) missing data about the variables in the medical record; 2) diabetic patient with a glucose level >200mmHg; 3) patient with renal failure before surgery and 4) patient with a prior history of heart surgery. This study was approved by The Medical and Health Research Ethics Committee (MHREC) from Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia (KE/FK/0692/EC/2017).

Diagnosis of IE that was taken and made by cardiologist according to modified Duke University criteria,[9] and then pharmacologically treated by cardiologist according to service protocol of IE in Dr. Sardjito General Hospital, Yogyakarta. Surgical intervention by a cardiac surgeon was indicated when there was the condition of heart failure, uncontrolled infection or to prevent the thromboembolism event.[5,9] Mitral valve was chosen because among all heart valves, mitral valve was most frequent site of vegetation related IE, and followed by aortic valve.[10] Surgical data and the morbidities after surgery were collected from medical record.

We defined postoperative cardiac morbidities by all of the cardiac problems that appear after surgery such as pulmonary arterial hypertension, any arrhythmia, and cardiac events. We included all types of arrhythmias as one of the cardiac abnormalities which is a diagnosis from the Cardiologist. ICU admission was assessed by SOFA score[7] and prolonged stay in ICU was defined if patients stay more than 6 days in the ICU after the surgery. We defined postoperative stroke based on the Stroke Council of the American

Heart Association/American Stroke Association.[11] Acute renal failure was defined by Kidney Disease Improving Global Outcome (KDIGO) criteria.[12] Pulmonary arterial hypertension was defined by pulmonary arterial systolic pressure (PASP) above 25 mmHg, and categorized as severe pulmonary arterial hypertension when PASP >55 mmHg.[13] Mortality as major morbidity was defined as death directly related to surgery or post-surgery care, both related to cardiac and other problems.

Baseline characteristics of data between IE and non-IE groups were presented in tabular form. Comparisons to evaluate significant differences between IE and non-IE groups were conducted using chi-square or Fisher's exact test. Variables considered significantly different if the value was $p<0.05$. Statistical analysis was performed using SPSS Statistics version 23 (IBM, Chicago).

RESULTS

Characteristics data of the patients are shown in TABLE 1. A total of 60 patients who underwent mitral valve surgery were included in the study from whom 30 (50%) had IE determined by fulfilling the modified Duke criteria. Most of the subjects were female, making up 63.3% of the IE patients. The average age of the subject was 38.07±10.7 years, with the oldest age was 58 years and the youngest was 18 years. The majority of the heart valve abnormalities in IE patients were mitral stenosis 18 (60%) with mitral valve replacement as the most performed procedures in the IE group (56,7%). There were some postoperative morbidities in IE patients that were recorded, such as arrhythmia and cardiac event (63.3%), stroke (16.7%), prolonged ICU stay (86.7%), acute renal failure (30%), severe PAH (10.0%), prolonged ventilator use (96.7%) and mortality (16.7%).

TABLE 1. Baseline Characteristics of Patients

Variables	IE n (%)	Non-IE n (%)
Sex		
• Male	11 (36.7)	7 (23.3)
• Female	19 (63.3)	23 (76.7)
Age (years old)		
• ≤ 20	2 (6.7)	1 (3.3)
• 21-30	10 (33.3)	3 (10.0)
• 31-40	8 (26.7)	11 (36.7)
• 41-50	7 (23.3)	11 (36.7)
• > 51	3 (10.0)	4 (13.3)
Procedure		
• Mitral valve repair	8 (26.7)	9 (30.0)
• Double valve repair	5 (16.7)	0 (0.0)
• Mitral valve replacement	17 (56.7)	10 (33.3)
• Double valve replacement	0 (0.00)	11 (36.7)
Mitral valve disorder		
• Mitral stenosis	18 (60.0)	13 (43.3)
• Mitral regurgitation	8 (26.7)	6 (20.0)

• Mitral stenosis + regurgitation	4 (13.3)	11 (36.7)
Pulmonary hypertension		
• Severe (>55 mmHg)	3 (10.0)	11 (63.3)
• Mild to moderate (25-54 mmHg)	27 (90.0)	19 (36.7)
Postoperative morbidities		
• Arrythmia and cardiac event	19 (63.3)	6 (20.0)
• Prolonged ventilator use	29 (96.7)	21 (70.0)
• Severe PAH	3 (10.0)	11 (36.7)
• Stroke	5 (16.7)	3 (10.0)
• Prolonged ICU stay	26 (86.7)	16 (53.3)
• Acute renal failure	9 (30.0)	7 (23.3)
• Mortality	5 (16.7)	6 (20.0)

Noted: intensive care unit (ICU); pulmonary arterial hypertension (PAH)

Significant differences between IE and non-IE groups toward morbidities are shown in TABLE 2. Postoperative arrhythmia and cardiac event, prolonged ventilator use, prolonged ICU stay and severe PAH showed a significant difference with the p-value=0.002, p=0.015, p=0.011 and p=0.033, respectively. In our study, the IE group had an almost 7-fold higher risk to have any arrhythmia and cardiac event and also had risk to prolonged ventilator use up to more than 12-fold higher than the non-IE group after mitral valve surgery. Furthermore, the risk of prolonged ICU stay increased up to 5-fold higher in patients who had IE before surgery. On the other hand, the risk of severe PAH after mitral valve surgery decreased in the IE group. While the others morbidities such as stroke, acute renal failure and mortality after mitral valve surgery did not show a significant difference between IE and non-IE groups.

TABLE 2. Morbidities after mitral valve surgery

Postoperative morbidities	p	PR (95% CI)
Arrythmia and cardiac event	0.002*	6.909 (2.160 – 22.098)
Prolonged ventilator use	0.015*	12.429 (1.461-105.737)
Severe PAH	0.033*	0.192 (0.047 – 0.782)
Stroke	0.771	1.408 (0.445 – 4.453)
Prolonged ICU stay	0.011*	5.688 (1.591 – 20.330)
Acute renal failure	0.386	1.286 (0.551 – 3.003)
Mortality	1.000	0.800 (0.215 -2.972)

Noted: * significant difference; confidence interval (CI); intensive care unit (ICU); pulmonary arterial hypertension (PAH); Infective endocarditis (IE); prevalence ratio (PR)

DISCUSSION

Despite progress in the diagnosis and management of IE, the morbidity and mortality after heart valve surgery still frequently appear.[1,10,11] In our study, our patients were mostly female, and this result is the same as Rusingiza *et al.*[14] and Russell *et al.*[15] reported that IE patients who underwent mitral valve surgery was predominantly female, and composed of children and young adults.

IE often develops into RHD with the predominant site affected is the mitral valve, and followed by aortic valve.[2,10,16] Mitral stenosis is likely to reflect the more advanced IE condition related mitral valve disease.[15] Our study showed that mitral valve stenosis was most common mitral valve abnormalities in both IE and non-IE groups. The most common mitral valve surgery procedure that was performed in our study was mitral valve replacement (MVR). Russell *et al.*[15] showed mitral valve replacement procedure is mostly done in IE groups, there was no difference in adjusted short-term or long-term survival after surgery.

Our study showed that IE patients had 5-fold higher risk to experience a prolonged ICU stay more than 6 days which occurred in 86.6% of IE patients. Pato *et al.*[4] and Farag *et al.*[17] also showed that IE patients who underwent mitral valve surgery have an increased risk of prolonged stay in the ICU with an average treatment period more than 10 days. Another study with larger samples also showed similar results with an average length of stay in the ICU of almost 8 days, and it related to the advanced classifications of the New York Heart Association (NYHA III or NYHA IV) before surgery and is usually associated with poor prognosis. Additionally, another consequence of the longer stay in the ICU is the increase of the cost involved.[18] The prolonged ICU stay is also related to sepsis that can potentially appear in IE patients and usually has worse survival rates.[19] Patients who underwent heart valve surgery and prolonged ICU stay have further indicated a lower quality of life.[8]

The incidence of postoperative prolonged ventilators increased in the IE group. In our study, patients with IE were 12-fold risk to experience prolonged ventilators after mitral valve surgery. Russell et al. reported that the duration of ventilation in the IE group was longer than the non-IE group, and patients with replacement surgery had a longer period of ventilation and in ICU.[15] Both replacement and repair surgery in mitral valve are effective for MV disease.[20] Although there is superiority of MV repair over MV replacement for degenerative valve, patients with rheumatic disease because of IE may reduce the durability of MV repair.[20]

The increase of pulmonary artery pressure often occurs in both mitral stenosis and mitral regurgitation, and the presence of pulmonary arterial hypertension (PAH) in mitral valve disease is also key to determine the best treatment.[21,22] PAH can be occurred due to an increase in left atrial pressure which can be developed into pulmonary venous hypertension and subsequent pulmonary arterial hypertension. IE that has developed into mitral valve disease will increase the risk of PAH, and the risk can be reduced by eliminating the disease in the mitral valve.[21] Our study showed the same result that the increase in pulmonary arterial pressure after mitral valve surgery was lower in the IE group, because the source of the mitral valve disease has been removed by surgery procedure.

Cardiac morbidity after heart valve surgery is significantly associated with IE,[2,4] while the surgery also increases the risk of arrhythmia such as heart block, atrial and ventricular tachyarrhythmias.[1,23,24] Arrhythmias are very common complications of

open-heart surgery such as mitral valve surgery, and become the major source of other morbidity.[23] Structural damage due to heart disease such as heart valve damage increased the risk of arrhythmia, even the trauma due to the surgery itself predispose for atrial and ventricular arrhythmias.[23,24] In addition, structural damage is often accompanied by hemodynamic changes in complicated IE and this condition triggers an early atrial arrhythmia postoperatively.[24] Atrioventricular block occurred in 16.6% post-cardiac surgery patients with IE.[17] Another study found that patients with preoperative low ejection fraction are a higher risk of experiencing postoperative ventricular arrhythmia.[25] Acute coronary syndrome can also be a complication of IE due to septic embolism.[26] These findings support our study which showed that IE patients had a 7-fold higher risk of cardiac morbidity after mitral valve surgery.

Neurological complications are the most common extracardiac complications of IE patients, with incidence of embolic stroke in approximately 25% to 30% of the mitral valve IE.[27] *Staphylococcus aureus*-associated IE had a higher risk of stroke and systemic embolization.[26] Our findings show that stroke appeared in 16.7% of IE patients who underwent mitral valve surgery although considered not statistically significant. Furthermore, cardiac surgery in IE patients with stroke before surgery can potentially worsen neurological symptoms due to complications from cerebral hemorrhage related to heparinization and the expansion of ischemic stroke related to hypotension during cardiopulmonary by past.[28]

Acute renal failure can occur in about 30% of patients who underwent cardiac surgery, especially in heart failure, diabetes mellitus, and geriatric patients and associated with 30-days mortality post-cardiac surgery.[12,17] Our findings showed that acute renal failure appeared in 30% of IE patients although not considered statistically significant due to the small sample population. In a larger study, renal insufficiency increased mortality 1.6-fold higher in IE patients, although postoperative renal failure complications appeared in only 7.2% of subjects and average care in the ICU for more than 7 days.[29]

There were several limitations in this study. First, the subjects were not randomized. Second, we only took the data from the patients' medical records. This study only observed in patients who underwent mitral valve surgery without identifying the pharmacological therapies that had been given and the causative bacteria of the IE. Besides that, the determination of the relationship between preoperative IE and postoperative morbidity is difficult to determine precisely because of the wide variety of factors that affect the condition of the patients.

CONCLUSION

IE was significantly associated with the increased risk of arrhythmia, prolonged ventilator use and prolonged ICU stay after mitral valve surgery. To confirm our findings, a multicenter study with a larger sample of patients is necessary.

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REFERENCES

1. Cahill TJ, Baddour LM, Habib G, et al. Challenges in infective endocarditis. J Am Coll Cardiol 2017; 69(3): 325-44. https://doi.org/10.1016/j.jacc.2016.10.066
2. Mirabel M, Sonneville R, Hajage D, et

al. Long-term outcomes and cardiac surgery in critically ill patients with infective endocarditis. Eur Heart J 2013; 35(18): 1195-204.
https://doi.org/10.1093/eurheartj/eht303
3. Slipczuk L, Codolosa JN, Davila CD, et al. Infective endocarditis epidemiology over five decades: a systematic review. PloS One 2013; 8(12): e82665.
http://doi.org/10/1371/journal.pone.0082665
4. Pato MF, Gelape CL, Cassiano TJ, et al. Determinants of prolonged length of hospital stay after cardiac surgery: impact of rheumatic heart disease. Medical Express 2015; 2(3):M150304.
http://dx.doi.org/10.5935/MedicalExpress.2015.03.04.
5. Prendergast BD, Tornos P. Surgery for infective endocarditis: who and when?. Circulation 2010; 121(9): 1141-52.
https://doi.org/10.1161/CIRCULATIONAHA.108.773598
6. Grubitzsch H, Christ T, Melzer C, Kastrup M, Treskatsch S, Konertz W. Surgery for prosthetic valve endocarditis: associations between morbidity, mortality and costs. Interact Cardiovasc Thorac Surg 2016; 22(6): 784-91.
https://doi.org/10.1093/icvts/ivw035
7. Leroy O, Georges H, Devos P, et al. Infective endocarditis requiring ICU admission: epidemiology and prognosis. Ann Intensive Care 2015; 5(1): 45-52.
https://doi.org/10.1186/s13613-015-0091-7
8. Hellgren L, Ståhle E. Quality of life after heart valve surgery with prolonged intensive care. Ann Thorac Surg 2005; 80(5): 1693-8.
https://doi.org/10.1016/j.athoracsur.2005.04.042
9. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications: a scientific statement for healthcare professionals from the American Heart Association. Circulation 2015; 132(15): 1435-86.
https://doi.org/10.1161/CIR.0000000000000296
10. Xu H, Cai S, Dai H. Characteristics of infective endocarditis in a tertiary hospital in East China. PLoS One. 2016; 11(11): e0166764.
https://doi.org/10.1371/journal.pone.0166764
11. Sacco RL, Kasner SE, Broderick JP, et al. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/ American Stroke Association. Stroke 2013; 44(7): 2064-89.
https://doi.org/10.1161/STR.0b013e318296aeca
12. Delle Karth G, Koreny M, Binder T, et al. Complicated infective endocarditis necessitating ICU admission: clinical course and prognosis. Crit Care 2002; 6(2): 149-54.
https://doi.org/10.1186/cc1474
13. Borde DP, Asegaonkar B, Khade S, Puranik M, George A, Joshi S. Impact of preoperative pulmonary arterial hypertension on early and late outcomes in patients undergoing valve surgery for rheumatic heart disease. Indian J Anaesth 2018; 62(12): 963-71.
14. Rusingiza EK, El-Khatib Z, Hedt-Gauthier B, et al. Outcomes for patients with rheumatic heart disease after cardiac surgery followed at rural district hospitals in Rwanda. Heart 2018; 104(20): 1707-13.
https://doi.org/10.1136/heartjnl-2017-312644
15. Russell EA, Walsh WF, Reid CM, et al. Outcomes after mitral valve surgery for rheumatic heart disease. Heart Asia. 2017; 9(2): .
https://doi.org/10.1136/heartasia-2017-010916
16. Russell EA, Tran L, Baker RA, et al. A review of valve surgery for rheumatic heart disease in Australia. BMC

Cardiovasc Disord 2014; 14(1):134-45. https://doi.org/10.1186/1471-2261-14-134
17. Farag M, Borst T, Sabashnikov A, et al. Surgery for infective endocarditis: outcomes and predictors of mortality in 360 consecutive patients. Med Sci Monit 2017; 23: 3617-26. https://doi.org/10.12659/MSM.902340
18. Azarfarin R, Ashouri N, Totonchi Z, Bakhshandeh H, Yaghoubi A. Factors influencing prolonged ICU stay after open heart surgery. Res Cardiovasc Med 2014; 3(4): e20159. http://dx.doi.org/10.5812/cardiovascmed.20159.
19. Howitt SH, Herring M, Malagon I, McCollum CN, Grant SW. Incidence and outcomes of sepsis after cardiac surgery as defined by the Sepsis-3 guidelines. Br J Anaesth 2018; 120(3): 509-16. https://doi.org/10.1016/j.bja.2017.10.018
20. Fu JT, Popal MS, Zhang HB, et al. A meta-analysis of late outcomes of mitral valve repair in patients with rheumatic heart disease. J Thorac Dis 2017; 9(11): 4366-75. https://doi.org/10.21037/jtd.2017.10.97
21. Kiefer TL, Bashore TM. Pulmonary hypertension related to left-sided cardiac pathology. Pulm Med 2011; 2011: 381787. https://doi.org/10.1155/2011/381787
22. Maeder MT, Weber L, Buser M, et al. Pulmonary hypertension in aortic and mitral valve disease. Front Cardiovasc Med 2018; 5: 40. https://doi.org/10.3389/fcvm.2018.00040
23. Peretto G, Durante A, Limite LR, Cianflone D. Postoperative arrhythmias after cardiac surgery: incidence, risk factors, and therapeutic management. Cardiol Res Pract 2014; 2014: 615987. https://doi.org/10.1155/2014/615987
24. Kohári M, Pap R. Atrial tachycardias occurring late after open heart surgery. Curr Cardiol Rev 2015; 11(2): 134-40. https://doi.org/10.2174/1573403X10666141013122021
25. El-Chami MF, Sawaya FJ, Kilgo P, et al. Ventricular arrhythmia after cardiac surgery: incidence, predictors, and outcomes. J Am Coll Cardiol 2012; 60(25): 2664-71. https://doi.org/10.1016/j.jacc.2012.08.1011
26. Okai I, Inoue K, Yamaguchi N, et al. Infective endocarditis associated with acute myocardial infarction caused by septic emboli. JC Cases 2010; 1(1): 28-32. https://doi.org/10.1016/j.jccase.2009.06.003
27. Ghoreishi M, Foster N, Pasrija C, et al. Early operation in patients with mitral valve infective endocarditis and acute stroke is safe. Ann Thorac Surg 2018; 105(1): 69-75. https://doi.org/10.1016/j.athoracsur.2017.06.069
28. Murai R, Funakoshi S, Kaji S, et al. Outcomes of early surgery for infective endocarditis with moderate cerebral complications. J Thorac Cardiovasc Surg 2017; 153(4): 831-40. https://doi.org/10.1016/j.jtcvs.2016.10.074
29. Manne MB, Shrestha NK, Lytle BW, et al. Outcomes after surgical treatment of native and prosthetic valve infective endocarditis. Ann Thorac Surg 2012; 93(2): 489-93. https://doi.org/10.1016/j.athoracsur.2011.10.063