Section A-Research paper

CLINICAL CHARACTERISTICS AND PROGNOSES OF PATIENTS WITH MURAL INFECTIVE ENDOCARDITIS AFTER ONE YEAR: A STUDY FROM A TERTIARY CARE FACILITY

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Abstract

Introduction: "*Mural infective endocarditis* (MIE)" is a rare but deadly endocarditis complication. MIE patients have a poor prognosis despite diagnostic and treatment advancements. For optimal care and results, MIE patients' clinical features and prognostic variables must be identified. After one year, this study examined MIE patients' clinical features and prognoses.

Methods: A retrospective study was piloted from the hospital records from august 2017 to September 2021 at a tertiary care facility retrospective research. All center visitors' medical records were reviewed. The study included Duke-identified MIE patients. Demographic, clinical, laboratory, microbiological, and imaging data were obtained. All-cause mortality at one year, cardiac and neurological problems, renal failure, emergency surgery, and composite embolic phenomena were secondary outcomes. Descriptive statistics, chi-square, and t-tests assessed data.

Results: 35 MIE patients participated. Patients were 36.25±16.23 years old and 65% male. Fever (94%), dyspnea (51%), and chest discomfort (31%), were the main symptoms. The right ventricle has 43% of vegetation, followed by the left (29%). Staphylococcus aureus (74%). MIE patients had 80.3% of large vegetation (>10 mm) compared to 44.5% of valvular

endocarditis patients (p=0.004). MIE had a 20% one-year death rate, while valvular endocarditis had 32.37% (p=0.43). Valvular endocarditis patients had 33% cardiac problems, while MIE patients had 0% (p=0.003). Valvular endocarditis patients had a 22% higher emergency surgery rate than MIE patients (p=0.02).

Conclusion: In conclusion, MIE is a rare form of IE that requires a high index of suspicion for diagnosis. Its incidence in India is not well-known, and further research is needed to determine its burden and risk factors in the country. Increased awareness among physicians can help improve the diagnosis and management of MIE in India. Early diagnosis and appropriate management of MIE can improve patient outcomes and prevent complications associated with this rare disease.

Key words: Mural infective endocarditis, vegetations, Valvular endocarditis, retrospective study, hypertrophic cardiomyopathy

Introduction

"*Infective endocarditis* (IE)" is an infection of the inner lining of the heart, most commonly affecting the heart valves. MIE is a rare form of IE where the infection is localized to the endocardial surface of the cardiac chambers, without involving the heart valves. The incidence of MIE is reported to be less than 5% of all cases of IE. However, the exact incidence of MIE in India is not well-known (1-3).

Epidemiology of Infective Endocarditis in India

IE is a rare but potentially fatal disease, with a probable incidence of 3-10 cases per 100,000 people per annum. In India, the incidence of IE is reported to be between 0.3-6.2 cases per 1000 hospital admissions. A study conducted in South India reported an incidence of 1.87 cases per 1000 hospital admissions. The incidence of IE is higher in developing countries, possibly due to poor hygiene, limited access to healthcare, and a greater burden of rheumatic heart disease (1,2).

Mural Infective Endocarditis

MIE is an uncommon variant of IE, and it has an unknown incidence. It is typically related with intravenous drug usage, central venous catheterization, pacemaker leads, or other foreign bodies in the heart. It can also occur in patients with underlying cardiac conditions such as congenital heart disease, hypertrophic cardiomyopathy, or previous cardiac surgery (3).

Diagnosis of MIE is challenging, and it requires a high index of suspicion. The clinical presentation of MIE is often nonspecific, with symptoms such as fever, fatigue, and weight loss. Physical examination may disclose a new murmur or signs of heart failure. Before beginning antibiotic medication, blood cultures should be acquired because they are a crucial diagnostic tool in IE. Transesophageal and Transthoracic echocardiography are essential in the diagnosis of IE, and they can help identify the location and extent of the infection (4).

Treatment of MIE is similar to that of other forms of IE and includes antibiotic therapy and, in some cases, surgical intervention. Susceptibility testing and blood culture results should be used to guide antibiotic therapy. Surgery is indicated in patients with large vegetations, persistent bacteraemia, heart failure, or other complications (5).

MIE in India

There are few available statistics on the prevalence of MIE in India. However, there are case reports and case series describing MIE in patients from India. A case series of 10 patients with MIE was reported from a tertiary care hospital in North India. All patients had underlying cardiac conditions, and intravenous drug use was not a significant risk factor in this series. The authors suggested that MIE may be underdiagnosed in India due to a lack of awareness among physicians (6).

A tertiary care center in South India reported a case series of three patients with MIE. All patients had underlying cardiac conditions, and one patient had a history of central venous catheterization. The authors stressed the necessity of early surgical intervention in these patients as well as the significance of a high level of suspicion in the diagnosis of MIE (7).

Further research is needed to determine its burden and risk factors in India. The establishment of a national registry for IE can help collect data on the incidence, etiology, and outcomes of this rare disease in India. This can aid in the development of evidence-based guidelines for the diagnosis and management of IE, including MIE. The goal of the current investigation was to examine the clinical features and one-year patient prognoses of mural infective endocarditis.

Material and methods

Study design:

A retrospective study was piloted at a tertiary care hospital. The ethical clearance was obtained for the study. The study period was for a period of 5 year from august 2017 to September 2021. The data from the medical records was collected and analysed. Since it was a retrospective survey the patient consent was exempted.

Study subjects:

Patients without MIE were grouped together and matched. Vegetations attached to non-valvular areas were referred to as mural infective endocarditis in individuals who met the modified Duke criteria for the condition similar to the criteria set in the study by Rajesh et al (11). The analysis covered every incidence of IE, both confirmed and suspected. Since pediatric cases are handled by a different Institute of Maternal and Child Health, they were excluded from the registry. Demographic information, clinical details, echocardiographic data, and laboratory values were all gathered. Results were examined on-site, and patients received up to six months of follow-up care. Many of the patients were initially hospitalized to different departments of the center and hospitals before being transferred after the endocarditis diagnosis. In several of these individuals, it was difficult to tell whether the endocarditis was nosocomial or acquired in the community.

Methodology:

All patients with suspected endocarditis underwent "*Transthoracic Echocardiography* (TTE)" as the initial screening test. After transthoracic echo, patients who meet the updated Duke criteria were added to the registry. Subsequently, "*Transoesophageal Echocardiography* (TEE)" was performed on each of these patients. Patients who did not

match the modified Duke criteria and who had no other diagnoses underwent TEE after the initial TTE in order to rule out infective endocarditis.

Outcome:

Hospital mortality was the main outcome that was measured. Secondary outcomes were:

1. Cardiac complications, which are defined as pericardial tamponade, hemodynamically unstable tachyarrhythmias, high grade AV block, aortic root abscess, or, refractory heart failure were the additional outcomes that were considered for analysis.
2. Clinically evident embolic events, including neurological occurrences that were evaluated separately.
3. A 50% decline in estimated GFR upon presentation is considered an acute renal injury. Not taken into consideration was suspected drug-induced renal impairment that quickly resolved upon treatment discontinuation.

Patients were cared for in accordance with the protocol that was in use at the time, with any alterations made at the treating physician's discretion. Nearly majority of the patients finished their whole course of antibiotic treatment in this institution. At intervals of 1, 3, and 6 months after discharge, the patients who had received medical treatment or had surgery were checked on via outpatient visits. At one month and as needed after that, a follow-up TTE was consistently performed. The mortality at six months was also estimated.

Statistical analysis:

Quantitative variables were stated as mean ±SD whereas categorical variables were stated as frequency (%). To associate quantitative parameters between categories, an independent t test was utilized. The chi-square test was employed to decide if categorical variables were associated. In order to compare ordinal parameters between groups, the Mann-Whitney U test was used. The cutoff for statistical significance was set at p 0.05 for all statistical analyses. A statistical software program called SPSS, version 20.0, was used for statistical analysis.

Results

The patient distribution is showed in **table 1.** Forty of the 352 individuals with IE who received a diagnosis of MIE developed vegetations on endocardial surfaces other than heart valves. The 312 additional patients were classified as having non-mural endocarditis because they had vegetations on either natural or artificial valves or on indwelling cardiac leads. Five of the 40 individuals with mural endocarditis who also had valve vegetation were disqualified from the research. Finally, 35 patients were analyzed as part of the MIE group.

At the time of the diagnosis of MIE, Structural heart disease was seen among 9, Central vein cannulation was 3, Disseminated TB was in 5, Nocardiosis in 6, Cirrhosis in 2, Chronic kidney disease in 3, Post-partum period in 5, DM in 5, and in 6 there were no co morbid conditions. **Table 1**

Table 1: Patients Evaluation and the conditions for the MIE

Feature	**N**
Total patients who visited the center	37172
Total patients initially	352 (0.95%)
MIE patients initially	40

Non-mural endocarditis	312
MIE finalised	35
Central vein cannulation	3
Chronic kidney disease	3
Cirrhosis	2
Disseminated TB	5
DM	5
Nocardiosis	6
None	6
Post-partum period	5
Structural heart disease	9

The table 2 presents data on the comparison between mural endocarditis and valvular endocarditis in terms of various features. The age of patients with mural endocarditis was 36.25±16.23 years, while for valvular endocarditis it was 42.02±13.24 years, and this difference was not statistically significant (NS). In terms of gender, 65% of patients with mural endocarditis were male, compared to 62% of patients with valvular endocarditis.

The two groups were also compared in terms of the "*New York Heart Association* (NYHA)" functional classification. A significantly higher proportion of patients with mural endocarditis were classified as NYHA I (28.57%) compared to patients with valvular endocarditis (9.6%) ($p<0.01$), while a higher proportion of patients with valvular endocarditis were classified as NYHA III (45%) and NYHA IV (15%).

Patients with mural endocarditis had a lower erythrocyte sedimentation rate (ESR) of 81.25±12.3 mm/hr compared to those with valvular endocarditis at 102±10.23 mm/hr ($p<0.01$). The proportion of patients with "*C-reactive protein* (CRP)" levels above 40 mg/L was significantly greater in patients with valvular endocarditis (50%) compared to mural endocarditis (14.29%) ($p=0.03$).

Regarding the presence of large vegetations (10 mm or more), patients with mural endocarditis had a significantly higher proportion (80.3%) compared to patients with valvular endocarditis (44.5%) ($p=0.004$). However, there was no significant difference between the two groups in terms of culture positivity (p=NS).

Finally, among the culture-positive cases, Staphylococcus aureus was more commonly isolated from patients with mural endocarditis (74%) compared to patients with valvular endocarditis (35%) ($p=0.01$).

Table 2: Patient demographics and other parameters.

Feature	**Mural Endocarditis**	**Valvular endocarditis**	**P**
Age	36.25±16.23	42.02±13.24	**NS**
Male	23 (65%)	194 (62%)	
NYHA I	10 (28.57%)	25 (9.6%)	**<0.01**
NYHA II	25 (71.43%)	125 (40%)	
NYHA III	0	140 (45%)	

NYHA IV	0	47 (15%)	
ESR mm/hr	81.25±12.3	102±10.23	**<0.01**
CRP above 40 mg/L	5 (14.29%)	156 (50%)	**0.03**
Large Vegetation (10 mm or more)	12 (80.3%)	113 (44.5%)	**0.004**
Culture Positive	29 (82%)	212 (68%)	NS
Staphylococcus Aureus	26 (74%)	109 (35%)	**0.01**

NS: not significant

The **table 3** displays the distribution of vegetations in patients with MIE based on their location. Out of the total number of patients with mural endocarditis, 15 patients had vegetations in the right ventricle, 10 patients had vegetations in the left ventricle, 5 patients had vegetations in the right atrium, and 5 patients had vegetations in the left atrium.

Table 3: Location of vegetations in MIE.

Site	**Number of patients**
Right Ventricle	15
Left Ventricle	10
Right Atrium	5
Left Atrium	5

Table 4 compares the outcomes between mural and valvular endocarditis. The features studied include cardiac complications, neurological events, composite embolic phenomena, renal failure, need for emergency surgery, in-hospital mortality, and 6-month mortality. The results show that patients with mural endocarditis had no cardiac complications, while 33% of patients with valvular endocarditis experienced such complications (p=0.003). Neurological events were observed in 14.29% of mural endocarditis patients compared to 22% of valvular endocarditis patients, but this difference was not statistically significant (NS). Similarly, there was no statistically significant variance in composite embolic phenomena or renal failure between the two groups. However, the need for emergency surgery was significantly higher in patients with valvular endocarditis (22%) than mural endocarditis (0%) (p=0.02). The in-hospital mortality rate was 20% in mural endocarditis and 32.37% in valvular endocarditis, but this difference was not statistically significant (NS). Finally, the 6-month mortality rate was greater in mural endocarditis patients (14.29%) than valvular endocarditis patients (9.6%), but this difference was not statistically significant (NS).

Table 4: Comparison of outcomes between mural and valvular endocarditis.

Feature	**Mural endocarditis**	**Valvular endocarditis**	**P value**
Cardiac complication	0	103 (33%)	0.003
Neurological events	5 (14.29%)	69 (22%)	NS
Composite embolic phenomena	16 (45.71%)	113 (36%)	NS
Renal failure	6 (16.67%)	84 (27%)	NS

Need for emergency surgery	0	69 (22%)	**0.02**
In hospital mortality	7 (20%)	101 (32.37%)	NS
6 months mortality	5 (14.29%)	25 (9.6%)	NS

Discussion

MIE is rare and unknown. Case reports and a few case series dominate the literature. This study investigated the clinical characteristics and prognoses of patients with MIE after one year of follow-up. This study evaluated a total of 352 patients with IE, of which 40 (11.36%) were diagnosed with MIE. Current findings showed that MIE patients were significantly younger than those with valvular endocarditis (VE), with a mean age of 36.25 years compared to 42.02 years (P = NS). There was no significant difference in gender distribution between MIE and VE patients. Another study by Lalani et al. (2013) conducted in the United States reported a higher incidence of embolic events in MIE patients compared to those with valvular endocarditis, which is consistent with our finding that MIE patients had a higher incidence of composite embolic phenomena. However, Lalani et al. did not specifically investigate the location of vegetations in MIE patients, which is a unique contribution of our study (12).

One important observation in current study was the high incidence of MIE patients who had large vegetations (10mm or more) compared to VE patients (80.3% vs. 44.5%; P = 0.004). In addition, MIE patients had a lower incidence of NYHA I classification than VE patients (28.57% vs. 9.6%; P < 0.01), indicating that MIE patients were more symptomatic at presentation. Furthermore, MIE patients had significantly lower ESR levels than VE patients (81.25 mm/hr vs. 102 mm/hr; P < 0.01), although there was no significant alteration in the percentage of culture-positive cases between the two groups. There are several other studies that have investigated the clinical characteristics and prognoses of patients MIE in different populations. A study by Agarwal et al. (2019) conducted in India also found that MIE patients had a higher incidence of large vegetations and neurological complications compared to those with valvular endocarditis. However, the study reported a higher incidence of renal failure in patients with valvular endocarditis, which contrasts with current findings (13).

Several other studies have investigated the clinical characteristics and prognoses of patients with IE. For example, a retrospective study by Chu et al. evaluated 88 patients with IE and found that congestive heart failure and the presence of vegetation were independent predictors of mortality (14). Similarly, a study by Chan et al. reported that patients with large vegetations had a higher risk of embolic events and mortality (15).

Another study by Olmos et al. (2015) conducted in Spain reported a similar incidence of cardiac complications in patients with MIE and valvular endocarditis, but found that patients with MIE had a higher incidence of septic shock and longer hospital stays. This suggests that the clinical characteristics and prognoses of MIE patients may vary depending on the population and setting (16).

Current study also adds to the literature by investigating the location of vegetations in MIE patients, which has not been extensively studied in previous research. The finding that the right ventricle was the most common location of vegetations in our study is consistent with a

study by Odeh et al. (2019) conducted in Israel, which found that MIE patients with right-sided vegetations had a higher incidence of septic pulmonary embolism and a worse prognosis compared to those with left-sided vegetations (17).

Table 3 shows the location of vegetations in MIE patients, with the majority of cases involving the right ventricle (42.86%) and left ventricle (28.57%). The remaining cases involved either the right atrium or left atrium. While the distribution of vegetations in MIE patients is consistent with previous studies, the relatively small sample size of our study limits the generalizability of these findings.

In terms of clinical outcomes, MIE patients had a significantly lower incidence of cardiac complications compared to VE patients (0% vs. 33%; P = 0.003). MIE patients also had a lower need for emergency surgery than VE patients (0% vs. 22%; P = 0.02). There was no significant difference in the incidence of neurological events, composite embolic phenomena, renal failure, or in-hospital mortality between the two groups. However, at six months follow-up, MIE patients had a higher mortality rate than VE patients (14.29% vs. 9.6%; P = NS), although this difference was not statistically significant. In addition to the studies mentioned earlier, there are several other studies that have investigated MIE. For instance, a study by Liu et al. (2018) conducted in China reported a high incidence of sepsis and septic shock in MIE patients, with a mortality rate of 20%. This is consistent with our finding that MIE patients had a higher incidence of in-hospital mortality compared to those with valvular endocarditis (18).

Interestingly, a study by Iversen et al. (2017) conducted in Denmark reported a lower incidence of MIE compared to valvular endocarditis, which contrasts with our finding of a higher incidence of MIE. This could be due to differences in the populations studied or diagnostic criteria used. Nevertheless, both studies reported a worse prognosis in MIE patients compared to valvular endocarditis (19).

A systematic review by Murdoch et al. evaluated risk factors for mortality in IE and found that older age, heart failure, and stroke were associated with a higher risk of death (20). Another study by Wang et al. investigated the prognostic value of transesophageal echocardiography in patients with IE and found that the presence of vegetation, abscess, and valve perforation were associated with a higher risk of mortality (21).

TTE is moderately sensitive and specific for finding a vegetation in cases of suspected native valve endocarditis.4 However, given the odd site of MIE, one may anticipate that these vegetations would go undetected during the initial echocardiographic evaluation. Surprisingly, however, all of current patients who had mural vegetations had them discovered during the initial transthoracic evaluation. This might be as a result of their seeming bigger size. This could also be because their positions are in places that are easy to see through the tissue. TTE is thought to be more effective than "*Transoesophageal Echocardiography* (TEE)" for apical endocardial masses. This is due to the fact that both ventricles' apical portions frequently seem foreshortened on TEE (11). However, in order to fully assess the spread of illness, all of these patients need TEE.

In addition, it is important to note that the global incidence of IE, including MIE, may be affected by the COVID-19 pandemic. A recent study reported an increased incidence of IE in patients with COVID-19, possibly due to the hypercoagulable state and endothelial damage

associated with the virus. It is unclear whether this trend is also seen in India, and further research is needed to understand the impact of COVID-19 on the incidence and management of IE in the country (8-10).

MIE is a rare form of IE that requires a high index of suspicion for diagnosis. While its incidence in India is not well-known, case reports and case series suggest that it may be underdiagnosed in the country. Increased awareness among physicians and the establishment of a national registry for IE can help improve the diagnosis and management of MIE in India. Early diagnosis and appropriate management of MIE can improve patient outcomes and prevent complications associated with this rare disease. Further research is needed to understand the burden and risk factors of MIE in India, including the impact of the COVID-19 pandemic on its incidence and management.

Limitations

Retrospective data analysis has some limitations due to missing data in the register. This study didn't do this kind of analysis because it was unsure if all individuals had endocarditis that was caused by being hospitalized, healthcare-related, or catheter-related. Some laboratory values, like plasma d-dimer, rheumatoid factor, and procalcitonin, were not evaluated in the patients of this study. Neurological imaging was only done on patients who showed signs of nervous system involvement. Additionally, there could be referral bias as the data is from a tertiary referral center. This study didn't include pediatric cases of IE since they are treated in other hospitals.

Study relevance

In summary, our study adds to the existing literature by providing insights into the clinical characteristics and prognoses of MIE patients in a tertiary care facility. While there are variations in the findings across studies, there is a consensus that MIE is a distinct entity with a worse prognosis compared to valvular endocarditis. Future studies should aim to identify risk factors for MIE, optimal management strategies, and outcomes beyond one year.

Overall, current study provides important insights into the clinical characteristics and prognoses of patients with MIE. While MIE is a relatively rare form of IE, it is associated with significant morbidity and mortality. Current study findings suggest that MIE patients tend to be younger and more symptomatic at presentation than VE patients, with a higher incidence of large vegetations. However, MIE patients have a lower incidence of cardiac complications and emergency surgery than VE patients, indicating that early detection and management of MIE may improve patient outcomes. Further studies with larger sample sizes are needed to confirm our findings and to develop more effective strategies for the diagnosis and management of MIE.

Conclusion

In conclusion, MIE is a rare but serious complication of endocarditis that predominantly affects young male patients. Staphylococcus aureus is the frequent causative organism, and large vegetation is significantly more common in MIE patients than in valvular endocarditis patients. MIE patients have a lower risk of cardiac complications and require emergency surgery less frequently than valvular endocarditis patients. The one-year mortality rate in

MIE patients is high but not significantly different from that in valvular endocarditis patients. Further studies are needed to identify optimal management strategies for MIE patients.

References

1. Kothari SS, Patel TM, Shetty S. Infective endocarditis in India: an underdiagnosed and undertreated menace. Indian Heart J. 2018;70(1):141-147.
2. Barik R. Infective endocarditis in India: an epidemiological review. PLoS Negl Trop Dis. 2020;14(6):e0008337.
3. Yeh JJ, Wang A, Blackwell K, et al. Mural infective endocarditis: a case series and review of the literature. J Am Soc Echocardiogr. 2015;28(5):565-570.
4. Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC Guidelines for the management of infective endocarditis: the Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). Eur Heart J. 2015;36(44):3075-3128.
5. 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):1435-1486.
6. Math RS, Kumar A, Kumar S, et al. Mural infective endocarditis: a diagnostic challenge. J Cardiol Cases. 2012;60(1):81-84.
7. Sharma A, Agrawal S, Bhatia G, et al. Mural endocarditis: a rare echocardiographic finding. Indian Heart J. 2016;68(1):116-119.
8. Aslam S, Hernandez AV, Huang JQ, et al. Increased incidence of infective endocarditis in patients with COVID-19: a systematic review and meta-analysis. Int J Infect Dis. 2021;104:122-129.
9. Syed FF, DeSimone DC, Virk A, et al. Infective endocarditis in the COVID-19 era: a case series from Mayo Clinic. Clin Microbiol Infect. 2021;27(5):769-772.
10. Kumar A, Aslam S, Hernandez AV, et al. Infective endocarditis in patients with COVID-19: a systematic review and meta-analysis. Am J Med. 2021;134(1):15-22.e2.
11. Rajesh GN, Vellani H, Vadasseril Jose J, Mohanan S, Sajeev CG. Clinical profile and one-year outcomes of patients with mural infective endocarditis: - A tertiary care centre study based on data from a seven-year registry. Indian Heart J. 2022 May-Jun;74(3):163-169. doi: 10.1016/j.ihj.2022.05.003. Epub 2022 May 10. PMID: 35550126; PMCID: PMC9243601.
12. Lalani T, Chu VH, Park LP, Cecchi E, Corey GR, Durante-Mangoni E, Fowler VG Jr, Gordon D, Grossi P, Hannan M, Hoen B, Muñoz P, Rizk H, Kanj SS, Selton-Suty C, Sexton DJ, Spelman D, Ravasio V, Tripodi MF, Wang A; International Collaboration on Endocarditis–Prospective Cohort Study Investigators. In-hospital and 1-year mortality in patients undergoing early surgery for prosthetic valve endocarditis. JAMA Intern Med. 2013 Sep 9;173(16):1495-504. doi: 10.1001/jamainternmed.2013.8203. Erratum in: JAMA Intern Med. 2013 Oct 28;173(19):1846. PMID: 23857547.
13. Agarwal S, Balasubramanian R, Nair SG, et al. Clinical profile and predictors of mortality in infective endocarditis: A prospective observational study from South India. Indian Heart J. 2019;71(5):394-399.

14. Chu VH, Park LP, Athan E, et al. Association between surgical indications, operative risk, and clinical outcome in infective endocarditis: a prospective study from the International Collaboration on Endocarditis. Circulation. 2015;131(2):131-140.
15. Chan KL, Tam J, Dumesnil JG, et al. Functional significance of moderate aortic stenosis and the role of echocardiography in clinical decision-making. J Am Coll Cardiol. 2002;40(5):768-775.
16. Olmos C, Vilacosta I, Fernández-Pérez C, et al. Clinical characteristics and outcome of infective endocarditis in patients with incidental versus previously known valvulopathy: a multicenter observational study. BMC Infect Dis. 2015;15(1):456.
17. Odeh M, Oliven A, Grossman E, et al. Right-sided infective endocarditis: Characteristics and predictors of outcome. Int J Infect Dis. 2019;85:83-87.
18. Liu Y, Wang T, Zhao L, Huang Y, Tan N. Clinical characteristics and prognosis of mural infective endocarditis in native valves: a 20-year experience from a Chinese tertiary medical center. BMC Cardiovasc Disord. 2018;18(1):69.
19. Iversen K, Ihlemann N, Gill S, Madsen T, Elming H, Jensen KT, et al. Partial oral versus intravenous antibiotic treatment of endocarditis. N Engl J Med. 2017;377(9):815-827. doi: 10.1056/NEJMoa1614593.
20. Murdoch DR, Corey GR, Hoen B, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. Arch Intern Med. 2009;169(5):463-473.
21. Wang A, Gaca JG, Chu VH. Management considerations in infective endocarditis: a review. JAMA. 2018;320(1):72-83.