BRIEF RESEARCH COMMUNICATION

Infective Endocarditis as a Cause of Critical Illness, In-hospital Mortality, and Complications

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Abstract

Background: Critical illness due to infective endocarditis (IE) has high in-hospital mortality. Besides being a cause of sepsis, this disease has the potential nature to affect multiple organs.

Patients and methods: Data for 84 patients managed at the critical care medicine unit at Cairo University for 7 years were surveyed for IE using modified Dukes criteria. Among the patient group with a verified diagnosis of IE, patient characteristics (age and comorbidities), the grade of diagnosis, the blood culture result, echocardiographic findings, minor diagnostic signs (fever, presence of prosthetic valves and pacemaker, vascular phenomena, immunologic phenomena) and clinical complications (heart failure, septic shock, neurologic complications renal failure) were studied regarding their association to in-hospital mortality. Incidence of clinical complications was compared to the control group with sepsis due to other causes.

Results: The mortality rate in the IE group is 18.8%. Factors showing significant association to in-hospital mortality are; septic shock $p = 0.01$, neurological complications $p = 0.025$ (especially cerebral hemorrhage $p = 0.025$), indicated non-performed surgery $p = 0.008$, and presence of underlying heart failure with reduced ejection fraction (HFrEF), $p = 0.002$. Incidence of clinical complications showed no significant difference in IE patients and patients with other causes of sepsis except heart failure which showed significantly increased incidence in the IE group, $p = 0.004$.

Conclusion: Septic shock, neurological complications, indicated nonperformed surgery, and presence of underlying HFrEF are in-hospital mortality risk factors in critically ill patients due to IE. In-hospital mortality and clinical complication incidence (except heart failure) are similar to other causes of sepsis.

Keywords: Complications, Critical illness, Infective endocarditis, In-hospital mortality.

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Highlights

Septic shock, neurological complications (especially cerebral hemorrhage), reduced LV EF, and indicated nonperformed surgery are associated with in-hospital mortality in critical illness due to IE.

Introduction

Infective endocarditis is defined as an infection of the endocardial lining of the heart that includes heart valves, mural endocardium, and endocardial covering of the implanted material such as intracardiac devices and prosthetic valves.[1]

Clinically, the diagnosis of IE usually depends on the presence of both signs and/or symptoms of infection and evidence of endocardial involvement. The original Duke criteria were modified in 2000 for better diagnostic accuracy. The diagnostic classification (definite, possible, or rejected) is based on echocardiographic findings (vegetation, abscess, fistula, prosthetic valve dehiscence) and positive blood culture for organisms consistent with IE as major criteria. Minor criteria include many clinical findings (fever, predisposition, vascular phenomena, immunologic phenomena, and serology.[2]

Generally, transthoracic echocardiography (TTE) can detect vegetation in roughly 75% of clinically suspected endocarditis cases.[3]

Transesophageal echocardiography is superior to TTE (sensitivity 23% vs 94%) in case of endocarditis on pacemaker lead and prosthetic valves. The difficulty in diagnosis is due to reverberations produced by the metallic material.[4]

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In case of low clinical suspicion of IE diagnosis, the sensitivity and specificity of TTE and TOE are diminished when applied randomly, so the combined use of echocardiography in the appropriate time in addition to using the minor clinical criteria gives better diagnostic yield. Reevaluation by echocardiography is mandatory in many clinical circumstances.[5]

Echocardiography is also mandatory for risk stratification; the most dangerous and feared complications of IE are; heart failure due to valve structural damage, an extension of infection to the perivalvular tissue, and metastatic infection due to hematogenous seeding of infected emboli, especially to the central nervous system. Detection of any of the complications by echocardiography mandates arrangement for surgical interference at the proper time. Echocardiography also heralds the development of heart failure by providing early signs

of hemodynamic deterioration, even before evident clinical signs of congestive heart failure arise. The presence of these echocardiographic signs suggests the need for valve surgery since evolution to heart failure is inevitable.[6]

The rate of in-hospital mortality of IE is around 22% and worse long-term outcome is reported; about 45% 5 year mortality rate.[7,8]

Four main factors influence the short-term outcome in IE; patients' characteristics, the causative microorganism, the echocardiographic signs, and the presence of cardiac and/or extra-cardiac complications.[9]

The study aims to search for risk factors for in-hospital mortality in critical illness due to infective endocarditis.

Patients and Methods

We extracted patients' related data from the existing database in the Critical Care Department at Cairo University (HIS, Hospital Information system Medicaplus running at SQL database), using search terms infective endocarditis, cardiac device infection, and fever unspecified. These patients were managed at The Critical Care Medicine Department at Cairo University from January 2010 to December 2016.

Inclusion and Exclusion Criteria

We evaluated all the studied patients (84) for the modified Dukes criteria for diagnosis of infective endocarditis.

Inclusion Criteria

- Definite and possible IE cases (group I)
- Other causes of sepsis (group II)

Exclusion Criteria

Patients not fulfilling modified Dukes criteria

Statistical Analysis

Using EpiINFO 7-statcalc. Program, 2 × 2 tables were fed with numbers of patients affected with the studied factors according to their outcome. Fisher exact test and Mantel-Haenszel tests were used to assess the association between the factor and the outcome.

Results

- Thirty-two patients fulfilled modified Dukes criteria (definite or possible).
- Eighteen patients were excluded because of not fulfilling modified Dukes criteria (Table 1).
- Among group I (IE group),

  The mean age of the included group is 41 ± 17 years (range 18–81 years), with no significant difference in outcome in relation to age less or more than 50 years, $p = 0.9$.

- In-hospital mortality: six patients (18.8%), died during their hospital stay, while 26 patients (81.2%) survived to hospital discharge.

Nonsurvivors:

- Four left-sided IE.
- Two had right-sided IE.

The following factors revealed a significant association with in-hospital mortality:

Table 1: Patients with primary diagnosis IE in the department (50 patients)

Excluded cases (n = 18)	*Left-sided IE cases (n = 17)*	*Right-sided IE cases (n = 15)*
Rejected by criteria 14	Prosthetic valve $n = 8$	Permanent pacemaker $n = 7$
Battery end of life $n = 2$	Rheumatic heart disease $n = 4$	Intravenous drug abuser (IVDU) $n = 7$
Pocket infection $n = 2$	No documented predisposition $n = 5$	No concomitant Left-sided IE, not IV drug abuser and had no implanted device $n = 1$

- **Septic shock:** Five patients (16%) had septic shock, two of them survived to hospital discharge (40%) and three patients died (60%), showing a significant association with mortality $p = 0.01$.
- **Neurologic complications:** Six patients out of 32 (19%) had neurologic complications, 50% survived to hospital discharge ($n = 3$) and in-hospital mortality was 50% ($n = 3$), showing a significant association with mortality, $p = 0.029$. Among these six patients, three patients (9%) had cerebral hemorrhage with a mortality of 67% (2/3) showing a significant association with in-hospital mortality, $p = 0.025$
- **Low LV EF:** Two patients (6%) had low LV EF (both had underlying cardiomyopathy) and both died in hospital (100%), $p = 0.002$
- **Indicated nonperformed surgery:**
  - Eight out of 32 (25%) patients had indicated nonperformed surgery,
  - Four of them died (50% of patients who had indicated nonperformed surgery representing 36% of patients who indicated surgery), $p = 0.008$
- Among the IE group, the following factors are not risk factors for in-hospital mortality,
- **The grade of diagnosis:** Fifty-six percent had a possible diagnosis, $n = 18$ patients and 44% had a definite diagnosis, $n = 14$ patients. No significant association between the grade of diagnosis (possible/ definite) and in-hospital mortality ($p = 0.13$).
- **Presence of other comorbidities:** Sixteen patients (50%) had one or more other comorbidities; 13 patients survived to hospital discharge (82%) and 3 patients died in hospital (18%), The presence of diabetes mellitus or other comorbidities also showed no significant association to mortality $p = 1.0$
- **The blood culture result:** Fifty-three percent had blood culture-negative IE ($n = 17$), 6.3% had *Staphylococcus aureus* infection ($n = 2$), and 9% ($n = 3$) had blood culture positive for other bacteria. In 10 patients (32%), culture result was not available. No significant relation between blood culture-negative IE and in-hospital mortality, $p = 0.86$

The echocardiographic data:

- **Severe prosthetic valve dysfunction:** One patient (3%) had moderate to severe paravalvular MR
- **Large vegetation (>10 mm):** Eleven (34%) patients had large vegetation, in-hospital mortality was 18%, ($n = 2$), $p = 0.95$
- **Perivalvular complications:** None had perivalvular complications (abscess, fistula, pseudoaneurysm, or valve dehiscence)

Minor criteria related to the outcome:

- **Predisposition:** Twenty-six patients (81%) had predisposing condition; 19% mortality (5/26); no significant association between the presence of the predisposing condition and the outcome, $p = 0.19$

Table 2: Vascular phenomena

	Outcome		
Vascular phenomena	*Survivors*	*Deaths*	*Total*
Vascular			
Absent	19	2	21
Cerebral hemorrhage	1	1	2
Ischemic stroke	1	1	2
Pulmonary emboli	3	1	4
Peripheral emboli	1	0	1
Central + peripheral emboli	1	1	2
Total	26	6	32

  - Eight of 26 (30.5%) patients had prosthetic valves.
  - Four (50%) had a mitral prosthesis.
  - One (12%) had a double valve replacement.
  - Three (38%) had an aortic prosthesis.
  - Seven (27%) patients had a permanent pacemaker.
  - Eight (30.5%) patients were IV drug abusers (IVDU).
  - Three (12%) patients had rheumatic heart disease.
- **Prosthetic valves and pacemaker:**
  - Fifteen patients (47%) had either a prosthetic valve ($n = 8$) or pacemaker ($n = 7$).
  - Three patients (20%) patients died, with no significant relation to mortality, $p = 0.86$.
- **Fever:**
  - Thirty-one (97%) patients had a fever ≥38°C. Among them, six patients died, $p = 0.65$
- **Vascular phenomena:**
  - Eleven patients (34%) had vascular phenomena (Table 2), and four of them died (36%), $p = 0.06$
- **Immunologic phenomena:**
  - Two patients (6%) had immunologic phenomena.
  - Fifty percent mortality.
    - One patient had Roth's spot (died).
    - The other had rheumatoid factor (survived to hospital discharge).

Clinical Complications

- **Heart failure:**
  - Fourteen of 32 patients (44%) developed heart failure, and four patients died (29%), $p = 0.2$
- **Renal failure:**
  - Two (6%) patients had renal failure.
  - One of them died and one survived.
- **Ischemic stroke:** Three patients presented with ischemic stroke, and one case died (33%) with no significant association to mortality, $p = 0.49$.

Indication of Surgery

Eleven patients (34%) had indications of surgery (according to ESC guidelines), 36% died in hospital ($n = 4$) with no significant association to mortality, $p = 0.06$.

Discussion

In our observational study, for patients in group I (IE diagnosis is verified), the mean age is 41 years (range 18–81 years), the in-hospital mortality is 18.8% and the recurrence rate is 6.3% with no significant difference in outcome relates to be definite (7%) or possible case (27%) ($p = 0.13$).

Vivian et al.[10] evaluated 267 consecutive patients matching the modified Duke criteria. They found 19% in-hospital mortality rate, with no difference in the outcome according to the grade of diagnosis; definite or possible IE (20% vs 16%, respectively; $p = 0.464$).

Regarding Neurological Complications

Nine percent (6/32) had neurologic complications; in-hospital mortality was 50% ($n = 3$), showing a statistically significant association with mortality, $p = 0.029$.

- Three (50%) patients had an ischemic stroke.
- Three (50%) had a cerebral hemorrhage, two died showing a statistically significant association with mortality ($p = 0.03$).
- Fifty percent developed neurologic complications after antibiotic therapy initiation.
- None had *S. aureus*.
- Aortic to mitral endocarditis is 3:1.
- Two of six (33%) had a supratherapeutic dose of warfarin, and both developed cerebral hemorrhage.
- Three of six (50%) patients developed encephalopathy; all of them died.

García-Cabrera et al.[11] used prospectively collected data to do a retrospective analysis of 1,345 episodes of left-sided infective endocarditis from multicenter. Three-hundred and forty patients (25%) experienced neurological complications. Fourteen percent had ischemic events and (4%) had hemorrhages. Among the independent risk factors of neurological complications development were large vegetation; ≥3 cm, *S. aureus*, and mitral valve endocarditis. Treatment with anticoagulant therapy was particularly associated with a greater incidence of hemorrhagic complications. Mortality was 30%. Ischemic stroke (At least moderate) and cerebral hemorrhage were significantly associated with a poorer outcome. Antimicrobial treatment reduced the incidence of neurological complications (by 33–75%).

Heiro et al.[12] found that of 218 episodes of IE, 55 episodes of neurologic complications were identified (in 25%), and mortality during the acute phase of IE was about 2.5-fold in patients affected by neurologic complications compared to patients who did not suffer neurologic complications 24% vs 10% ($p < 0.03$).

Indication of Surgery

According to ESC guidelines, 34% (11/32) had indications and had an in-hospital mortality rate of 36% (4/11), and 73% (8/11) had indicated nonperformed surgery with an in-hospital mortality rate of 50% (4/8), showing statistically significant association to mortality, $p = 0.008$.

Nonperforming surgery in all deaths was due to associated other complications (two cases with septic shock and two cases with cerebral hemorrhage).

- Seven patients with left-sided IE had indications of surgery; three of them died. Two had indicated nonperformed surgery and both died.
- Four patients with right-sided IE had surgical indications; one of them died.
- Most of the indication was due to secondary or primary prevention of embolization ($n = 5$), followed by uncontrolled infection ($n = 4$), only two patients had urgent indication due to uncontrolled heart failure.

- Heart failure due to other causes other than severe valve regurgitation or underlying cardiomyopathy is not associated with mortality.

Revilla et al.[13] evaluated 508 attacks of IE, 391 patients had left-sided IE, and 89 required urgent surgery. The main reasons for urgent surgery were refractory heart failure (72%) and infection by an organism resistant to the appropriate antibiotic therapy (31%). Thirty-two patients (36%) died during their hospital stay. They noticed complicated and bad clinical courses in patients who needed urgent surgery. Despite being the main cause of urgent surgery, heart failure was not associated with significantly higher in-hospital mortality.

Rita et al.[14] in 2018 found that in 36.9% of IE patients who had surgical indication ($n = 133$), surgery was done. The prominent features of that group were the predominance of aortic valve IE, the presence of large vegetations, an extension of infection to the perivalvular area, severe valvular regurgitation, and consequent heart failure. Higher in-hospital mortality was evident in those who were not submitted for surgical treatment despite the indication compared to those who underwent surgery (32.6% vs 15.5%, $p = 0.028$).

Regarding the left ventricular function in our study, the two patients who had reduced LV EF died (100% mortality).

Krecki et al.[15] studied the clinical characteristics and prognosis of patients with infective endocarditis and concluded that impaired ejection fraction of the left ventricle is one of the prognostic factors.

Septic Shock

Sixteen percent of patients had septic shock, and three patients died (60%), showing a statistically significant association with mortality $p = 0.01$. None of them was immune-compromised.

Cresti et al.[16] performed a prospective study of the epidemiology of infective endocarditis (17 year population-based study). In-hospital mortality was 24%. They showed that among the independent predictors of mortality was septic shock.

Al-Mogheer et al.[17] evaluated 155 Egyptian patients with Duke definite/possible IE, among predictors of mortality on univariate analysis were CHF and fulminant sepsis.

Within the limits of the available sample size, the data showed that; age, prosthetic valve, DM, other comorbidities, *S. aureus* infection did not show significant association with in-hospital mortality.

Echo findings (large vegetation, severe left-sided regurgitation, and severe prosthetic valve dysfunction) and clinical complications (heart failure and renal impairment) also showed no significant relation to in-hospital mortality.

Heart Failure

In our study, congestive heart failure occurred in different situations; chronic valve regurgitation, acute severe valve regurgitation, underlying cardiomyopathy, or transiently due to fluid over resuscitation in the early phase of presentation in septic patients which contribute to the occurrence of CHF in these vulnerable patients. Each had different treatment, and some had other fatal complications.

Wallace et al.[18] performed a study to identify early available (within the first 2 days of admission) clinical findings that are associated with poor outcomes in infective endocarditis. Fifty-two years (with range 1.2) was the mean age of the studied group (208 patients). One-hundred and ninety-four patients out of 208 (93%) were positive for Duke criteria. Their related data showed that mortality at discharge was 18% age, left ventricular function and the infecting organism were not predictors of adverse outcomes.

On the other hand, Gálvez-Acebal et al.[19] conducted an observational multicenter study. They included 705 IE patients (left-sided IE). The overall mortality was 29.5%. Prosthetic valve, Age, presence of underlying comorbidity, especially chronic liver disease, *S. aureus* and fungal infection, and clinical consequences (heart failure, neurologic manifestations, septic shock, perivalvular extension of infection, and renal impairment) were associated with increased mortality in univariate analysis.

Alkhawam et al.[20] identified diabetes mellitus and renal failure on dialysis to be significant risk factors in an analysis of 209 who were found to meet IE diagnosis on the base of modified Duke criteria. The average age was 59 years.

Remadi et al.[21] attributed the bad prognosis in IE patients with *S. aureus* as the causative microorganism to the underlying comorbidities, development of heart failure, flare-up of infection ending in severe sepsis, severe neurologic complications, and prosthetic valve endocarditis.

Comorbidities

We assessed the relation of some chronic diseases with the outcome. These comorbidities included DM, IHD, chronic compensated liver disease, HTN, and chronic kidney disease, not on dialysis.

A combination of multiple comorbidities and other varieties of chronic diseases were not represented in the study (end-stage renal disease on dialysis, malignancy, immune-compromised patients).

Recurrence in our study was evident in two cases due to incomplete extraction of pacemaker leads.

Diabetes, *S. aureus* infection, and especially signs of persistent infection, as well as vegetation size ≥10 mm, and acute renal insufficiency have been associated with the progression to septic shock. Surgery in this complicated situation usually is much less frequently performed and so, these patients have higher mortality than those without these circumstances.[22]

Bishara et al.,[23] in a study on 213 definite or possible IE patients through 9 years, diabetes mellitus was found in 39 (18%). On multivariate analysis, they reported that DM *per se* did not affect mortality.

Regarding Age and DM

A high prevalence of prosthetic and degenerative valves is found in old-aged patients; also, diseases with immune-suppression states like diabetes mellitus and malignancy are common and so the higher rates of nosocomial endocarditis and an increase in enterococci and *S. bovis* infections.

Susceptibility to severe infections in hospitalized patients with diabetes is attributed to many factors; of these, frequent colonization by *S. aureus* due to dysfunction of phagocytes and defects in cell-mediated immunity.[24]

Conclusion

Septic shock, neurological complications (especially cerebral hemorrhage), reduced LV EF, and indicated nonperformed surgery are associated with in-hospital mortality in critical illness due to IE.

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References

1. Thuny F, Grisoli D, Cautela J, Riberi A, Raoult D, Habib G. Infective endocarditis: prevention, diagnosis, and management. Can J Cardiol 2014;30(9):1046–1057. DOI: 10.1016/j.cjca.2014.03.042.
2. Li JS, Sexton DJ, Mick N, Netles R, Fowler Jr VG, Ryan T, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 2000;30:633–663. DOI: 10.1086/313753.
3. Karalis DG, Bansal RC, Hauck AJ, Ross J Jr, Applegate PM, Jutzy KR, et al. Transesophageal echocardiographic recognition of subaortic complications in aortic valve endocarditis. Circulation 1992;86(2): 353–362. DOI: 10.1161/01.cir.86.2.353.
4. San Roman JA, Vilacosta I, Zamorano JL, Almeria C, Sanchez-Harguindey L. Transesophageal echocardiography in right-sided endocarditis. J Am Coll Cardiol 1993;21:1226–1230. DOI: 10.1016/0735-1097(93)90250-5.
5. Habib G, Badano L, Tribouilloy C, Vilacosta I, Zamorano JL, Galderisi M, et al. Recommendations for the practice of echocardiography in infective endocarditis. Eur J Echocardiogr 2010;11(2):202–219. DOI: 10.1093/ejechocard/jeq004.
6. Tornos P, Almirante B, Olona M, Permanyer G, González T, Carballo J, et al. Clinical outcome and long-term prognosis of late prosthetic valve endocarditis: a 20-year experience. Clin Infect Dis 1997;24(3):381–386. DOI: 10.1093/clinids/24.3.381.
7. Selton-Suty C, Celard M, Le Moing V, Doco-Lecompte T, Chirouze C, Iung B, et al. Preeminence of *Staphylococcus aureus* in infective endocarditis: a 1-year population-based survey. Clin Infect Dis 2012;54(9):1230–1239. DOI: 10.1093/cid/cis199.
8. Sy RW, Kritharides L. Health care exposure and age in infective endocarditis: results of a contemporary population-based profile of 1536 patients in Australia. Eur Heart J 2010;31(15):1890–1897. DOI: 10.1093/eurheartj/ehq110.
9. Habib G, Hoen B, Tornos P, Thuny F, Prendergast B, Vilacosta I, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). Eur Heart J 2009;30(19):2369–2413. DOI: 10.1093/eurheartj/ehp285.
10. Chu VH, Cabell CH, Benjamin Jr DK, Kuniholm EF, Fowler Jr VG, Engemann J, et al. Early predictors of in-hospital death in infective endocarditis. Circulation 2004;109(14):1745–1749. DOI: 10.1161/01.CIR.0000124719.61827.7F.
11. García-Cabrera E, Fernández-Hidalgo N, Almirante B, Noureddine M, Plata A, Lomas JM, et al. Neurological complications of infective endocarditis: risk factors, outcome, and impact of cardiac surgery: a multicenter observational study. Circulation 2013;127(23): 2272–2284. DOI: 10.1161/CIRCULATIONAHA.112.000813.
12. Heiro M, Helenius H, Hurme S, Savunen T, Metsärinne K, Engblom E, et al. Long-term outcome of infective endocarditis. Arch Intern Med 2000;160(18):2781. DOI: 10.1001/archinte.160.18.2781.
13. Revilla A, López J, Vilacosta I, Villacorta E, Rollán MJ, Echevarría JR, et al. Clinical and diagnostic profile of patients with infective endocarditis. Eur Heart J 2007;28(1):65–71. DOI: 10.1093/eurheartj/ehl315.
14. Moreira RI, Cruz MC, Branco LM, Galrinho A, Miranda LC, Fragata J, et al. Infective endocarditis: surgical management and prognostic predictors. Rev Port Cardiol (Engl Ed) 2018;37(5):387–394. DOI: 10.1016/j.repce.2017.08.007.16.
15. Krecki R, Drozdz J, Ibata G, Lipiec P, Ostrowski S, Kasprzak J, et al. Clinical profile, prognosis and treatment of patients with infective endocarditis. Clin Infect Dis 2000;30(4):633–638. DOI: 10.20452/pamw.224.
16. Cresti A, Chiavarelli M, Scalese M, Nencioni C, Valentini S, Guerrini F, et al. Epidemiological and mortality trends in infective endocarditis, a 17-year population-based prospective study. Cardiovasc Diagn Ther 2017;7(1). DOI: 10.21037/cdt.2016.08.09.
17. Batoo AM, Waleed A, Sameh B, Wafaa E, Hussein R. Predictors of in hospital mortality in patients with infective endocarditis. Egypt Heart J 2013;65(3). DOI: 10.1016/j.ehj.2012.09.002.
18. Wallace SM, Walton BI, Kharbanda RK, Hardy R, Wilson AP, Swanton RH, et al. Mortality from infective endocarditis: clinical predictors of outcome. BMC Infect Dis 2008;8:49. DOI: 10.1186/1471-2334-8-49.
19. Gálvez-Acebal J, Rodríguez-Baño J, Martínez-Marcos FJ, Reguera JM, Plata A, Ruiz J, et al. Prognostic factors in left-sided endocarditis: results from the Andalusian multicenter cohort. BMC Infect Dis 2010;10:17. DOI: 10.1186/1471-2334-10-17.
20. Alkhawam H, Sogomonian R, Zaiem F, Vyas N, El-Hunjul M, Jolly J, et al. Morbidity and mortality of infective endocarditis. Investig Med 2016;64(6):1118–1123. DOI: 10.1136/jim-2015-000040.22.
21. Remadi JP, Habib G, Nadji G, Brahim A, Thuny F, Casalta JP, et al. Predictors of death and impact of surgery in Staphylococcus aureus infective endocarditis. Ann Thorac Surg 2007;83(4):1295–1302. DOI: 10.1016/j.athoracsur.2006.09.093.
22. Olmos C, Vilacosta I, Fernández C, López J, Sarriá C, Ferrera C, et al. Contemporary epidemiology and prognosis of septic shock in infective endocarditis. Eur Heart J 2013;34(26):1999–2006. DOI: 10.1093/eurheartj/ehs336.
23. Bishara J, Peled N, Samra Z, Sagie A, Leibovici L, Pitlik S. Infective endocarditis in diabetic and non-diabetic patients. Scand J Infect Dis 2004;36:795–798. DOI: 10.1080/00365540410025384.25.
24. Calvet HM, Yoshikawa TT. Infections in diabetes. Infect Dis Clin North Am 2001;15(2):407–421. DOI: 10.1016/s0891-5520(05)70153-7.