Epidemiology and risk factors of infective endocarditis in a tertiary hospital in China from 2007 to 2016

CURRENT STATUS: POSTED

Zhenzhu Wu
Zhejiang University First Affiliated Hospital State Key Laboratory for Diagnosis and Treatment of Infectious Diseases

Yi Chen
Zhejiang University School of Medicine First Affiliated Hospital

Tingting Xiao
Zhejiang University School of Medicine First Affiliated Hospital

Tianshui Niu
Zhejiang University School of Medicine First Affiliated Hospital

Qingyis Shi
Zhejiang University School of Medicine First Affiliated Hospital

Yonghong Xiao
Zhejiang University School of Medicine First Affiliated Hospital

Corresponding Author
xiaoyonghong@zju.edu
ORCID: https://orcid.org/0000-0003-2529-938X

DOI:
10.21203/rs.2.19349/v1

SUBJECT AREAS
General Microbiology

KEYWORDS
Infective endocarditis, epidemiology, risk factors, pathogen
Abstract
Background: To explore the trends in epidemiology and risk factors related to the prognosis of infective endocarditis in a teaching hospital over the past ten years. Methods: A retrospective cohort study was performed. A total of 407 consecutive patients were included. The clinical characteristics and risk factors related to the prognosis of infective endocarditis during this period were analyzed. Results: A total of 407 patients with infective endocarditis were included, the average age was 48 ±16 years old with an increasing trend and in-hospital mortality rate was 10.6% and one-year mortality rate was 12.2%. Among patients with underlying heart disease, congenital heart disease was the most common (25.8%), followed by rheumatic heart disease which showed a decreased trend during this period (P<0.001). There were 222 (54.5%) positive blood cultures and streptococci (44.1%) was the main pathogens with an increasing trend. There were 403 patients (99%) with surgical indications, but only 234 patients (57.5%) received surgical treatment. Hemodialysis (P = 0.041, OR = 4.697, 95% CI 1.068-20.665), pulmonary hypertension (P = 0.001, OR = 5.308, 95% CI 2.034-13.852), Pitt score ≥ 4 (P <0.001, OR = 28.5, 95% CI 5.5-148.1) and vegetation length ≥30mm (P = 0.011, OR = 13.754, 95% CI 1.832-103.250) were independent risk factors for in-hospital mortality. Conclusions: There was no significant change in the overall incidence of IE, the clinical features of IE have changed slightly during the past ten years. Streptococci IE was still the predominant. IE patients with hemodialysis, pulmonary hypertension, Pitt score ≥ 4 and vegetation length ≥30mm had an worse in-hospital outcome.

Background
Infective endocarditis (IE) is an infectious disease involving the heart valve or endocardium caused by causative microorganisms. It is a severe disease with high morbidity and mortality [1]. Serious complications such as heart failure and cerebral embolism are common. In developed countries, the annual incidence is between 3 and 9 patients per 100,000 persons with a slight increase between 1970 and 2013[1, 2]. Although the improvement of prevention, the progress of antibiotic therapy, the development of imaging technology and the intervention with surgery, the mortality is still 15–30% [3]. Over the past two decades, with the increase in life expectancy, the increased use of cardiac
Implant devices, and the frequency in invasive procedures, the epidemiology of IE in developed countries has changed significantly: older patients with IE gradually increased, prosthetic valve endocarditis (PVE) and IE associated with implanted devices increased, and Staphylococci has become the most predominated pathogen [4].

However, studies from developing countries such as Turkey showed a different epidemiological character[5,6]. In their study, although staphylococcal IE was increasing, streptococci was still the most predominant pathogen; rheumatic heart disease (RHD) and congenital heart disease (CHD) were still the most common underlying heart diseases, and the number of patients undergoing surgical treatment was increasing[5, 6]. In this study, we analyzed the changes in clinical features of IE over the past 10 years to explore the trend of IE and problems existing on diagnosis and treatment in our region.

Methods

Patients

A retrospective, consecutive case-series analysis was organized and performed in the First Affiliated Hospital of Zhejiang University, Hangzhou, China. Patients with a clinical diagnosis of IE from January 1, 2007 to December 31, 2016 were reviewed. The Modified Duke criteria [1] was used to evaluate patients reviewed. Patients who were admitted to the hospital more than one time for the same pathogen during the study period were considered as one case.

Clinical parameters and study design

The data were retrieved from the Electronic Medical Record. The data included in the analysis were patient demographic information, underlying heart diseases, comorbidities, clinical manifestations, complications, causative microorganisms, echocardiographic demonstrations, treatments, and outcomes. The following data analysis strategies were conducted: (1) The changing trend of clinical characteristics in IE was analyzed with every two year time periods; (2) To explore the prognostic risk factors, the comparison between the survival group and the death group was conducted.

Definition

Infective endocarditis was categorized based on disease types as native-valve endocarditis,
prosthetic-valve endocarditis, and cardiac device–related endocarditis [1]. Embolism events included both central nervous system embolism and non-central nervous system embolism. Transthoracic echocardiogram (TTE) was performed routinely in all patients. Transesophageal echocardiogram (TEE) was used to detect cases with negative TTE results. Blood culture was performed in all the patients with aerobic, anaerobic and fungal blood cultures, but blood culture for the HACEK group (Haemophilus spp, Aggregatibacter spp, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingae) and anti-legionella, mycoplasma and bartonella anti-body tests as well as PCR test were not performed when patients had negative blood culture results.

**Statistical analysis**

The trends in clinical characteristics was performed using the log-linear Poisson regression model. Univariate analysis was performed using the Pearson’s $\chi^2$ test or Fisher’s exact tests as appropriate for categorical variables and the independent Student’s $t$-test or the Rank sum test as appropriate for continuous variables. Categorical variables were expressed as frequencies and percentages of the specified group and continuous variables were reported as averages with standard deviations or medians and interquartile ranges. After univariate analysis, variables with P<0.05 were included in backward stepwise logistic regression to identify predictors for in-hospital mortality among IE patients. Odds ratios (OR) with 95% confidence interval (CI) were calculated in logistic regression. All tests were 2-tailed, and P <0.05 was considered statistically significant. All analyses were performed using SPSS version 23 statistical software.

**Results**

**Patient enrollment**

In our study, there were 409 patients with IE and 2 patients whose blood culture results were unreachable were excluded. A total of 407 IE patients were included. There were 43 patients (10.6%) died during hospitalization and 46 died (12.2%) in the one-year follow-up.

**The clinical characteristics of patient with IE**

Among the 407 patients, 262 patients were male (64.6%). The average age was 48±16 years old with an increasing trend during this period (P=0.001) (Table 1). The annual incidence of IE were between
0.33 and 0.72 patients per 1000 admissions and the incidence was stable over this period (Figure 1). There were 186 patients (45.7%) without underlying heart disease and the proportion increased over this time (P=0.044). CHD was the most common underlying heart disease, accounting for 25.8% of all patients, and the proportion of RHD decreased yearly during this period (P<0.001). Patients with degenerative valvular disease (DVD) accounted for 3.2% with a growing trend (P=0.001). Native valve IE was still the most dominant, with 370 patients (90.9%) and the proportion increased (P=0.002). Except for hypertension with a significant increase in the proportion (P=0.005), the proportion of other comorbidities did not change significantly. There were 215 patients (52.8%) with heart failure and 125 patients (30.7%) with cerebral embolization. The proportion of cerebral embolism was significantly increased in our study (P=0.001).

TEE was performed on 53 patients (13.0%) and 30 patients (7.4%) were diagnosed after TEE. The detection rate of vegetation was 86.7% with a significant growth trend (P<0.001). There were 72 patients (17.7%) with valve perforation and 30 patients (7.4%) with perivalvular abscess. Left-side IE was the most common with 356 patients (87.5%). A single valve being affected was more common, with 295 patients (72.5%), among which the mitral valve was affected in 134 patients (32.9%) and the aortic valve was affected in 143 patients (35.1%).

Blood cultures were performed in all patients with IE. Two hundred and twenty two (54.5%) blood cultures had positive results. Patients with negative blood culture were diagnosed as definite IE by the following criteria: 173 patients had positive echocardiographic findings plus three minor criterias, and 12 patients were identified by positive histopathological findings. Streptococci was the main pathogen, accounting for 24.1% of positive results with an increasing trend, followed by staphylococci, accounting for 18.9%. There were 40 patients (18.0%) of staphylococcus aureus IE, including 26 patients (11.7%) of methicillin-resistant staphylococcus aureus (MRSA) IE.

**The risk factors for in-hospital mortality**

Univariate analysis found that age, previous heart valve surgery, hemodialysis, hypertension, heart failure, cerebral embolism, cerebral hemorrhage, arrhythmia, hepatic insufficiency, renal insufficiency, pulmonary hypertension, prosthetic valve or pacemaker valve IE, *Staphylococcus*...
aureus infection, Pitt score≥4, surgical treatment were related to the in-hospital mortality (Table 2). Multi-factor analysis showed, Hemodialysis (P = 0.041, OR = 4.697, 95% CI 1.068-20.665), pulmonary hypertension (P = 0.001, OR = 5.308, 95% CI 2.034-13.852), Pitt score ≥ 4 (P <0.001, OR = 28.5, 95% CI 5.5-148.1) and vegetation length≥30mm (P = 0.011, OR = 13.754, 95% CI 1.832-103.250) were independent risk factors for in-hospital mortality (Table 3).

Discussion
Over the past decades, the epidemiology of IE has changed due to changes in demographic characteristics and risk factors. Researches from developed countries showed that the incidence of IE had increased in the past decades [4]. Cresti et al [7] found the incidence was 4.6/100,000 person-years with a significant linear increase between 1998 and 2014. Keller et al [8] found that the incidence of IE in Germany was 11.6/100,000 person-years between 2005 and 2015 and the incidence increased continuously during the study period, especially in the last five years. However, in our study, we found that the incidence of IE was between 0.33 and 0.72 patients per 1000 admissions and the incidence remained stable during the period, which was lower in comparison with the developed countries (approximately 1-1.3 patients per 1000 hospital admissions) [4, 7]. The difference in incidence of IE from different studies may be related to the geographical location of the study, the time period selected, and the difference in diagnostic techniques of different institutions.

In our study, we found that the mean age at the time of IE episodes were younger than those reported from developed countries, although the mean age increased during this period. The proportion of old patients with IE increased gradually in our study period, and this shown the same trend as the developed countries [7, 9]. Erichsen et al [10] found that the incidence increased substantially for elderly patients between 1994 and 2011, with the highest incidence rate of 3.38 for patients more than 80 years old at IE onset. In Oliver et al’s report [11], 49% of IE patients were over 65 years old and 11.2% were over 80 years old. The changes in the age of IE onset may owing to the aging population. And as a result of the older onset age, patients with IE in the latter part of the study period were more likely to have comorbidities compared with patients in the earlier part of the study period.
We found that CHD had become the most common underlying heart disease for patients with IE in our study. RHD was once the most common underlying heart disease in the 1990s according to Chao et al’s report [12]. But the proportion of RHD gradually decreased in our study. The results from other medical institutions in China also found the same change on underlying heart disease in patients with IE[13]. Previous reports from developed countries also presented that the proportion of RHD had dropped obviously, and DVD, PVE and implantable electronic devices related IE had gradually increased and replaced RHD as the leading heart disease [1, 4, 8]. This difference may contributed to the large number of patients with CHD and the relative low proportion of patients with prior cardiac surgery. According to the published reports, the risk of developing into IE increased in patients with CHD [14–16]. Darren et al [16] found that the IE risk exceeded 100 times in patients with ACHD compared to that of the general population and 2.5 times that of children with CHD [16, 17]. The proportion of patients with CHD in our study was as high as 25.8%.

TEE was performed in only 13% patients with IE in our study, as most patients diagnosed after TTE did not perform TEE routinely. Based on a review of the literature published from China on IE, the rate was similarly but it approached to other studies in our region [13, 18, 19]. But this rate was significantly lower than that reported by other studies from developed countries with 74%-100%[20, 21]. However, according to the 2015 European Association of Cardiology guidelines on IE, for TTE positive patients, TEE should be performed to exclude perivalvular complications[1]. The low utilization rate of TEE could directly resulted in the low detection rate of perivalvular complications such as valvular perforation and perivalvular abscess in our study. They were very important data for the cardiac surgeon. Besides, this could cause the missed diagnoses of IE in patients with unobvious valvular lesions or with basic valvular lesions. This underlined that our research institution still needs to strengthen the learning of the value of TEE in IE diagnosis, strengthen the study of the latest IE guidelines and improve the use of TEE in the diagnoses of IE to reduce missed diagnoses.

The positive rate of blood culture in our study was lower compared with other studies from developed countries, where the rate of a positive blood culture varied from 83–96%[2, 8, 11, 22]. However, the positive culture rate was approximate to other studies from China varied from 38.5–70.1%[13, 18,
This finding could be related to the use of antibiotics before blood culture, because in our study the proportion of patients with prior antibiotics use was as high as 81.7%. As a tertiary hospital, most patients in our hospital had been referred from other medical institutions. They usually had a history of antibiotic use prior to the blood cultures. Besides, the blood cultures of the HACEK group, serology tests for mycoplasma, bartonella, legionella and the polymerase chain reaction (PCR) were not performed in our hospital. All these factors resulted in the low microbiology detection rate. We suggested that patients with suspected bloodstream infection should receive blood cultures routinely before the use of antibiotics to rule out or confirm the diagnosis of bloodstream infection.

In our study, streptococci was the main pathogen accounting for 24.1%, followed by staphylococci accounting for 18.9%, which was the same as the report in the 1990s from China [12]. This was similar to other developing countries [5, 6] but different from developed countries [4]. For IE in developed countries, the proportion of staphylococci increased gradually and became the main pathogenic bacteria [4, 6]. The increase in staphylococcus IE was mainly due to the high incidence of intravenous drug addicts, hemodialysis patients and elderly patients with comorbidities [3, 4, 24]. However, in our study, the proportion of patients with intravenous drug addicts, hemodialysis patients and octogenarians was lower compared with developed countries. Besides, streptococcus IE was the main for community origin IE according to the previous reports, and most of patients in our study were community origin IE [19].

According to published studies, older age, prosthetic valve IE, heart failure, septic shock staphylococcus aureus, and large vegetation were predictors of poor outcome in patients with IE [1, 4]. In our study, we also found that hemodialysis and pulmonary arterial hypertension were independent risk factors of in-hospital mortality. The risk of in-hospital mortality in patients with Hemodialysis increased by 4.697 times and in patients with pulmonary arterial hypertension, the risk of in-hospital mortality increased by 5.308 times.

There are several limitations in our study. First, as a retrospective study, there exists information bias, and we were unable to obtain information on patient exposure to dental procedures and the use of antibiotic prophylaxis. Second, the study used a single-center cohort in a referral teaching hospital.
with possible selection bias that could not represent the entire Chinese condition. Finally, as a nonrandomised study, there were associated limitations and selection bias affecting comparisons between the in-hospital outcomes. Therefore, we suggest multiple-center prospective cohort studies performed in our region.

Conclusions
In conclusion, this study is currently a large sample research in IE from our region. It presents the clinical features of IE in currently in our region that the age at the time of IE episodes has being older, congenital heart disease is the predominant cardiac disease and streptococci is still the predominant pathogen. Besides, it showed that patients with hemodialysis, pulmonary hypertension, Pitt score ≥ 4 and vegetation length ≥ 30 mm had an worse in-hospital outcome. Our results will have an important impact in the improvement in the diagnosis and treatment of IE in our region in the future.

Abbreviations
IE: infective endocarditis; TTE: transthoracic echocardiography; TEE: transesophageal echocardiography; SD: standard deviation IQR: interquartile range; OR: odds ratios; HR: hazard ratio; CI: confidence interval

Declarations

Ethics approval and consent to participate
Ethics approval for this study was submitted and approved through Research Ethics Committee of the First Affiliated Hospital, College of Medicine, Zhejiang University. The consent to participate is not applicable because the study design is a retrospective data collection. The Research Ethics Committee of the Hospital was responsible for administrative permissions to access the raw data.

Consent for publication
Not applicable.

Availability of data and materials
The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Conflicting of interests
The authors declare that they have no conflicts of interest.
Funding

This work was partially supported by grants from the Key Research and Development Program of Zhejiang Province (No. 2015C03032). The funder was not involved in the design of the study, data collection, analysis and interpretation of the data and in writing the manuscript.

Authors’ contributions

ZZW designed the study and created study protocols, ZZW and YC performed the data collection, data analysis and drafts the manuscript. YHX supervised the study development, helped to review the manuscript and made critical revision to the paper. TTX TSN and QYS performed data collection and helped to review the manuscript. All authors read and approved the final manuscript.

Acknowledgements

We are very grateful to the staffs in the Medical record room in the First Affiliated Hospital of Zhejiang University for their support and assistance.

Authors' Information

State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, National Clinical Research Center for Infectious Diseases, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China

Zhenzhu Wu, Yi Chen, Tingting Xiao, Tianshui Niu, Qingyi Shi and Yonghong Xiao

References

1. Linhartova K, Benes J, Gregor P. 2015 ESC Guidelines for the management of infective endocarditis. Summary document prepared by the Czech Society of Cardiology. Cor Et Vasa. 2016;58(1):E107-E28.
2. Toyoda N, Chikwe J, Itagaki S, Gelijns AC, Adams DH, Egorova NN. Trends in Infective Endocarditis in California and New York State, 1998–2013. JAMA. 2017;317(16):1652–60.
3. Cahill TJ, Baddour LM, Habib G, Hoen B, Salaun E, Pettersson GB, Schafers HJ, Prendergast BD. Challenges in Infective Endocarditis. J Am Coll Cardiol. 2017;69(3):325–44.
4. Ambrosioni J, Hernandez-Meneses M, Tellez A, Pericas J, Falces C, Tolosana JM, Vidal B, Almela M, Quintana E, Llopis J, et al: The Changing Epidemiology of Infective Endocarditis in the Twenty-First Century. Curr Infect Dis Rep. 2017;19(5).
Elbey MA, Kalkan ME, Kaya MG, Bulur S, Ulus T, Elbey HK. A multicenter study on experience of 13 tertiary hospitals in Turkey in patients with infective endocarditis. Anadolu Kardiyol Derg. 2013;13(6):523–7.

6. Njuguna B, Gardner A, Karwa R, Delahaye F. Infective Endocarditis in Low- and Middle-Income Countries. Cardiol Clin. 2017;35(1):153–63.

7. Cresti A, Chiavarelli M, Scalese M, Nencioni C, Valentini S, Guerrini F, D’Aiello I, Picchi A, De Sensi F, Habib G. Epidemiological and mortality trends in infective endocarditis, a 17-year population-based prospective study. Cardiovasc Diagn Ther. 2017;7(1):27–35.

8. Keller K, von Bardeleben RS, Ostad MA, Hobohm L, Munzel T, Konstantinides S, Lankeit M. Temporal Trends in the Prevalence of Infective Endocarditis in Germany Between 2005 and 2014. Am J Cardiol. 2017;119(2):317–22.

9. Cecchi E, Chirillo F, Castiglione A, Faggiano P, Cecconi M, Moreo A, Cialfi A, Rinaldi M, Del Ponte S, Squeri A, et al. Clinical epidemiology in Italian Registry of Infective Endocarditis (RIEI): Focus on age, intravascular devices and enterococci. Int J Cardio. 2015;190:151–6.

10. Erichsen P, Gislon GH, Bruun NE. The increasing incidence of infective endocarditis in Denmark, 1994–2011. Eur J Intern Med. 2016;35:95–9.

11. Oliver L, Lavoute C, Giorgi R, Salaun E, Hubert S, Casalta JP, Gouriet F, Renard S, Saby L, Avierinos JF, et al. Infective endocarditis in octogenarians. Heart. 2017;103(20):1602–9.

12. Chao TH, Li YH, Tsai WC, Tsai LM, Lin LJ, Chen JH, Yang YJ. Prognostic determinants of infective endocarditis in the 1990s. J Formos Med Assoc. 1999;98(7):474–9.

13. Zhu W, Zhang Q, Zhang JP. The changing epidemiology and clinical features of infective endocarditis: A retrospective study of 196 episodes in a teaching hospital in China. BMC Cardiovasc Disord. 2017;17.

14. Diller GP, Baumgartner H. Endocarditis in adults with congenital heart disease: new answers-new questions. Eur Heart J. 2017;38(26):2057–9.

15. Moore B, Cao J, Kotchetkova I, Celermajer DS. Incidence, predictors and outcomes of infective endocarditis in a contemporary adult congenital heart disease population. Int J Cardiol. 2017;249:161–5.

16. Mylotte D, Rushani D, Therrien J, Guo L, Liu A, Guo K, Martucci G, Mackie AS, Kaufman JS, Marelli A. Incidence, Predictors, and Mortality of Infective Endocarditis in Adults With Congenital Heart Disease Without Prosthetic Valves. Am J Cardiol. 2017;120(12):2278–83.

17. Rushani D, Kaufman JS, Ionescu-ilatu R, Mackie AS, Pilote L, Therrien J, Marelli AJ. Infective endocarditis in children with congenital heart disease: cumulative incidence and predictors. Circulation. 2013;128(13):1412–9.

18. Wei XB, Liu YH, Huang JL, Chen XL, Yu DQ, Tan N, Chen JY, He PC. Prediabetes and diabetes are both risk factors for adverse outcomes in infective endocarditis. Diabet Med. 2018;35(11):1499–507.
19. Yang FF, Zhang BY, Yu J, Shao LY, Zhou P, Zhu LP, Chen S, Zhang WH, Weng XH, Zhang JM, et al: Epidemiology and the prognosis of healthcare-associated infective endocarditis in China: the significance of non-nosocomial acquisition. Emerg Microbes Infect. 2015;4.

20. van den Brink F, Hasenaar J, Winia V, Klomp M, Van Vlies B, Nicastia D, Groenmeijer B, Braam R, Jaarsma W, Kupper AJF. Prognostic factors in infective endocarditis in general hospitals in the Netherlands. Neth Heart J. 2016;24(12):717–21.

21. Lamas CC, Fournier PE, Zappa M, Brandao TJD, Januario-da-Silva CA, Correia MG, Barbosa GIF, Golebiovski WF, Weksler C, Lepidi H, et al. Diagnosis of blood culture-negative endocarditis and clinical comparison between blood culture-negative and blood culture-positive cases. Infection. 2016;44(4):459–66.

22. Fernandes E, Olive C, Inamo J, Roques F, Cabie A, Hochedez P. Infective Endocarditis in French West Indies: A 13-Year Observational Study. Am J Trop Med Hyg. 2017;97(1):77–83.

23. Xu H, Cai S, Dai H. Characteristics of Infective Endocarditis in a Tertiary Hospital in East China. PLoS One.2016;11(11).

24. Cahill TJ, Prendergast BD. Infective endocarditis. Lancet. 2016;387(10021):882–93.

Tables

| Variable, n(%) | Total | 2007-2008 | 2009-2010 | 2011-2012 | 2013-2014 | 2015 |
|---------------|-------|-----------|-----------|-----------|-----------|------|
| Male          | 262(64.4) | 40(64.5) | 42(66.7) | 53(67.9) | 56(62.9) | 71(62) |
| Age, mean±SD  | 48±16  | 45±15 | 42±15 | 47±16 | 50±16 | 52±15 |
| Comorbidities |        |         |         |         |         |      |
| Hypertension  | 82(20.1) | 9(14.5) | 9(14.3) | 11(14.1) | 20(22.5) | 33(22) |
| Diabetes mellitus | 37(9.1) | 3(4.8) | 5(7.9) | 6(7.7) | 8(9.0) | 15(10) |
| Chronic organ disease | 23(5.7) | 3(4.8) | 3(4.8) | 2(2.6) | 6(6.7) | 9(7.1) |
| Cancer | 12(2.9) | 2(3.2) | 2(3.2) | 4(5.1) | 2(2.2) | 2(1.4) |
| No-underlying heart disease | 186(45.7) | 18(29.0) | 29(46.0) | 42(53.8) | 40(44.9) | 57(44) |
| Underlying heart disease | 221(54.3) | 44(71.0) | 34(54.0) | 36(46.2) | 49(55.1) | 58(56) |
| Congenital heart disease | 105(25.8) | 17(27.4) | 16(25.4) | 18(23.17) | 26(29.2) | 28(21) |
| Rheumatic heart disease | 69(17.0) | 22(35.5) | 14(22.2) | 12(15.4) | 6(7.7) | 15(11) |
| Previous cardiac surgery | 44(10.8) | 11(17.7) | 6(9.5) | 6(7.7) | 15(16.9) | 6(5.3) |
| Degenerative heart disease | 13(3.2) | 0 | 0 | 2(2.6) | 2(2.2) | 9(7.1) |
| Hospital stay, mean±SD | 25±22 | 31±31 | 32±25 | 23±17 | 23±24 | 21±17 |
| Duration of Symptoms before echocardiography median(IQR), days | 13(4-35) | 17(7-48) | 14(6-30) | 15(4-40) | 9(3-50) | 15(4-30) |
| Duration of symptoms before | 25(12-62) | 26(12-68) | 24(9-42) | 25(14-62) | 28(10-75) | 26(10-76) |
| Diagnosis median (IQR, days) | Prior antibiotic use | Intravenous drug abuse | Symptons and signs | Fever | Anemia | Osler nodule | Janeway lesions or nailbed bleeding | TEE | Infection site | Right-side | Left-side | Left+ Right-side | Infection valve | Single valve | Mitral valve | Aortic valve | Multi-valve, n(%) | Endocardi or arterial intima | Type of IE | Native valve IE | Prosthetic valve IE or pacemaker valve IE |
|-----------------------------|----------------------|------------------------|-------------------|-------|-------|-------------|----------------------------------|-----|--------------|------------|----------|-----------------|----------------|------------|------------|-----------|-----------------|---------------------|----------------|----------------|-----------------------------|
| 321(81.7)                  | 48(81.4)             | 58(92.1)               | 65(90.3)          | 76(85.4) | 74(6) |
| 3(0.7)                     | 1(1.6)               | 1(1.6)                 | 0                 | 0     | 1(0).! |
| 365(89.7)                  | 57(91.9)             | 57(90.5)               | 70(89.7)          | 83(93.3) | 98(8) |
| 222(54.5)                  | 38(61.3)             | 43(68.3)               | 43(55.1)          | 58(65.2) | 40(3) |
| 7(1.7)                     | 2(3.2)               | 0                      | 3(3.8)            | 2(2.2) | 0     |
| 4(0.9)                     | 1(1.6)               | 3(4.8)                 | 0                 | 0     | 0     |
| 53(13.0)                   | 3(4.8)               | 4(6.3)                 | 5(6.4)            | 8(9.0) | 32(2) |
| 356(87.5)                  | 53(85.8)             | 54(85.7)               | 67(85.9)          | 79(88.8) | 9(7.1) |
| 31(7.6)                    | 7(11.3)              | 3(4.8)                 | 8(10.3)           | 4(4.5) | 6(6.7) |
| 20(4.9)                    | 2(3.2)               | 6(9.5)                 | 3(3.8)            | 6(6.7) | 3(2.1) |
| 295(72.5)                  | 38(61.3)             | 46(73.0)               | 55(70.5)          | 58(65.2) | 98(8) |
| 134(32.9)                  | 16(25.8)             | 20(31.7)               | 24(30.8)          | 30(33.7) | 44(3) |
| 143(35.1)                  | 18(29.0)             | 23(36.5)               | 25(32.1)          | 27(30.3) | 50(4) |
| 79(19.4)                   | 13(21.0)             | 15(23.8)               | 13(16.7)          | 24(27.0) | 14(1) |
| 33(8.1)                    | 11(17.7)             | 2(3.2)                 | 10(12.8)          | 7(7.9) | 3(2.1) |
| Native valve IE            | 370(90.9)            | 50(80.6)               | 58(92.1)          | 72(92.3) | 113(1) |
| Prosthetic valve IE or pacemaker valve IE | 37(9.1) | 12(19.3) | 5(7.9) | 6(7.7) | 12(13.5) | 2(1.1) |

**Complications**

| Embolic events | 125(30.7) | 14(22.6) | 16(25.4) | 16(20.5) | 34(38.2) | 45(3) |
|-----------------|-----------|----------|----------|----------|----------|-------|
| Cerebral embolism | 74(18.2) | 6(9.7) | 7(11.1) | 12(15.4) | 18(20.2) | 31(2) |
| Heart failure | 215(52.8) | 31(50.0) | 31(49.2) | 43(55.1) | 51(57.3) | 59(5) |
| Vegetation | 353(86.7) | 44(71.0) | 56(88.9) | 62(79.5) | 83(93.3) | 108(1) |
| Vegetation extent ≤10mm | 90(22.1) | 9(14.5) | 12(19.0) | 16(20.5) | 2(23.6) | 32(2) |
| ≥10mm≤20mm | 197(48.4) | 25(40.3) | 31(49.2) | 31(39.7) | 52(58.4) | 58(5) |
| ≥20mm≤30mm | 51(12.5) | 8(12.9) | 10(15.9) | 14(17.9) | 6(6.7) | 13(1) |
| ≥30mm | 12(2.9) | 2(3.2) | 1(1.6) | 1(1.3) | 3(3.4) | 5(4.4) |
| Perivalvular abscess | 72(17.7) | 3(4.9) | 7(11.1) | 11(14.3) | 21(23.6) | 30(2) |
| Perivalvular perforation | 30(7.4) | 0 | 1(1.6) | 3(3.9) | 12(13.5) | 14(1) |
| Positive rate blood culture Streptococci | 222(54.5) | 41(75.9) | 33(94.3) | 36(70.6) | 44(59.5) | 68(7) |
| Staphylococci | 98(24.1) | 17(27.4) | 9(14.3) | 14(17.9) | 20(22.5) | 38(3) |
| Surgical indications | 77(18.9) | 11(17.7) | 17(27.0) | 13(16.7) | 15(16.9) | 21(1) |
| Surgical treatment | 403(99.0) | 60(96.8) | 63(100.0) | 76(97.4) | 89(100.0) | 115(1) |
| In-hospital mortality | 43(10.6) | 12(19.4) | 3(4.8) | 2(2.6) | 10(11.2) | 16(1) |
| One-year mortality | 46(12.2) | 13(22.0) | 3(5.3) | 4(5.5) | 10(12.0) | 16(1) |

*percentage accounting for the positive results in each group
SD: Standard deviation
IQR: Interquartile range
IE: Infective endocarditis
TEE: Transesophageal echocardiography

Table 2: Risk factors of in-hospital outcome in patients with infective endocarditis univariate analysis
### Table 3  Risk factors of in-hospital outcome in patients with infective endocarditis multivariate analysis

| Variable                                      | P value | OR     | 95%CI     |
|-----------------------------------------------|---------|--------|-----------|
| Male                                          | .413    | 1.0    |           |
| Cerebral embolism                             | .137    | 1.3    | 1.0-1.7   |
| Hemodialysis                                  | .041    | 4.697  | 1.068-20.665 |
| Pulmonary arterial hypertension               | .001    | 5.308  | 2.034-13.852 |
| Pitt score ≥4                                 | .000    | 111.617| 28.255-440.934 |
| Vegetation length 30mm ≤10mm                  | .011    | 1.832  | 1.132-2.973 |
| Native valve IE                               | .337    | 3.72   | 1.11-11.573 |
| Prosthetic valve IE or pacemaker valve IE     | .001    | 10.23  | 3.06-32.83 |
| Prior antibiotic use                          | .204    | 1.37   | 0.98-1.903 |
| Causative organism                            | .033    | 1.07   | 1.00-1.141 |
| Streptococci                                  | .055    | 1.13   | 1.02-1.263 |
| Staphylococci                                 | .001    | 13.754 | 1.832-103.250 |
| Staphylococcus aureus                         | .004    | 0.92   | 0.84-1.01 |
| Pitt score                                    | .001    | 1.00   | 1.00-1.00 |
| Vegetation extent ≥4                          | .001    | 1.00   | 1.00-1.00 |
| Surgical treatment                            | .064    | 1.00   | 1.00-1.00 |
| Prosthetic valve IE or pacemaker valve IE     | .325    | 1.00   | 1.00-1.00 |

---

**Variable, n (%)**

| Survival | Death |
|----------|-------|
| n=364    | n=43  |

| Age, mean ±SD | 48±16 | 53±16 | .047 |
| Man          | 237(65.1) | 25(58.1) | .367 |
| Underlying heart disease | 176(48.4) | 25(58.1) | .225 |
| Rheumatic heart disease | 54(14.8) | 4(9.3) | .051 |
| Congenital heart disease | 70(19.2) | 8(18.6) | .921 |
| Previous cardiac surgery | 27(7.4) | 10(23.3) | .001 |
| Degenerative heart disease | 12(3.3) | 1(2.3) | .075 |
| Others       | 26(7.1) | 2(4.7) | .075 |

**Comorbidities**

| Chronic obstructive pulmonary disease | 5(1.4) | 1(2.3) | .491 |
| Cancer | 11(3.0) | 1(2.3) | .05 |
| Hemodialysis | 9(2.5) | 5(11.6) | .002 |
| Liver cirrhosis | 4(1.1) | 0 | .05 |
| Hypertension | 68(18.7) | 14(32.6) | .032 |
| Diabetes mellitus | 32(8.8) | 5(11.6) | .541 |

**Complications**

| Heart failure | 179(49.2) | 36(83.7) | .001 |
| Intracranial infection | 15(4.1) | 2(4.7) | .698 |
| Cerebral embolism | 55(15.1) | 19(44.2) | .001 |
| Cerebral hemorrhage | 16(4.4) | 7(16.3) | .001 |
| Arrhythmia | 65(17.9) | 15(34.9) | .008 |
| Hepatic insufficiency | 57(15.7) | 15(34.9) | .002 |
| Renal insufficiency | 60(16.5) | 21(48.8) | .001 |
| Pulmonary arterial hypertension | 92(25.6) | 24(57.1) | .001 |
| Valvular perforation | 64(17.7) | 8(18.6) | .881 |
| Perivalvular abscess | 26(7.2) | 4(9.3) | .544 |

| Vegetable length ≤10mm | 137(37.6) | 10(23.3) | .001 |
| ≥10mm to ≤20mm | 177(48.6) | 20(46.5) | .001 |
| ≥20mm to ≤30mm | 46(12.6) | 5(11.6) | .001 |
| ≥30mm | 4(1.1) | 8(18.6) | .001 |

| Vegetation extent | 142(39.0) | 16(37.2) | .819 |
| Native valve IE | 337(92.6) | 33(76.7) | .004 |
| Prosthetic valve IE or pacemaker valve IE | 27(7.4) | 10(23.3) | .001 |
| Prior antibiotic use | 291(80.2) | 30(69.8) | .204 |
| Causative organism | 75(20.6) | 3(7.0) | .033 |
| Streptococci | 53(14.6) | 12(27.9) | .001 |
| Staphylococci | 20(5.5) | 8(18.6) | .001 |
| Perivalvular abscess | 26(7.2) | 4(9.3) | .544 |
| Vegetation length ≥4 | 359(98.6) | 23(53.5) | .001 |
| ≥4 | 5(1.4) | 20(46.5) | .544 |

| Surgical treatment | 220(60.4) | 14(32.6) | .001 |

---

**Variable**

| Variable                                      | Survival | Death |
|-----------------------------------------------|----------|-------|
| Male                                          | n=364    | n=43  |
| Cerebral embolism                             | 137(37.6) | 10(23.3) | .001 |
| Hemodialysis                                  | 177(48.6) | 20(46.5) | .001 |
| Pulmonary arterial hypertension               | 46(12.6) | 5(11.6) | .001 |
| Cerebral embolism                             | 142(39.0) | 16(37.2) | .819 |
| Native valve IE                               | 337(92.6) | 33(76.7) | .004 |
| Prosthetic valve IE or pacemaker valve IE     | 27(7.4) | 10(23.3) | .001 |
| Prior antibiotic use                          | 291(80.2) | 30(69.8) | .204 |
| Causative organism                            | 75(20.6) | 3(7.0) | .033 |
| Valvular perforation                          | 53(14.6) | 12(27.9) | .001 |
| Perivalvular abscess                          | 20(5.5) | 8(18.6) | .001 |
| Vegetation extent ≥4                          | 359(98.6) | 23(53.5) | .001 |
| ≥4                                            | 5(1.4) | 20(46.5) | .544 |
| Surgical treatment                            | 220(60.4) | 14(32.6) | .001 |
Figures

Figure 1

Incidence of infective endocarditis from 2007 to 2016 in hospitalized patients (Linear regression showed $P=0.168$)