

The clinical features and prognosis of infective endocarditis in the elderly from 2007-2016 in a tertiary hospital in China

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Abstract

Background Infective endocarditis (IE) is a serious disease, with a worse prognosis in the elderly. **Aims** To explore the clinical features and prognosis of old patients with IE in a tertiary hospital. **Methods** A retrospective cohort study was conducted. A total of 407 patients diagnosed as IE were divided into two groups: 348 patients under 65 years old and 59 patients over 65 years old. **Results** For older patients, clinical symptoms such as fever, anemia, and heart murmur were as common as in younger patients. Comorbidities like hypertension ($P=0.001$) and diabetes ($P=0.023$) were more common in older patients. Complications like renal insufficiency ($P=0.027$) and arrhythmia ($P=0.001$) were also more common in older patients. The old patients had a lower operation rate (40.7% vs 60.6%, $P=0.004$) and higher in-hospital mortality (20.3% vs 8.9%, $P=0.008$) compared with the younger patients. Pitt score ≥ 4 ($P=0.043$, OR=28.0, 95% CI 1.1-700.4) and renal insufficiency ($P=0.011$, OR=34.2, 95% CI 2.2-521.2) were independent risk factors of in-hospital mortality for older patients. Surgical treatment was a significant predictor of one-year mortality even after adjusting for the confounders (HR = 1.722, 95% CI 0.563-5.365, $P = 0.005$). The one-year survival rate was higher for older patients with surgical intervention than those without (95.8% vs 68.6%, $P=0.007$). **Conclusions** IE in older patients present with more comorbidities and complications as well as a higher mortality than younger patients. Surgery were underused in old patients and old patients with surgical treatment had better long-term prognosis.

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Conclusions IE in older patients present with more comorbidities and complications as well as a higher mortality than younger patients. Surgery were underused in old patients and old patients with surgical treatment had better long-term prognosis.

Keywords: Infective endocarditis; elderly; risk factors; surgery

Introduction

Infective endocarditis (IE) is a severe disease with a high burden of mortality and morbidity.[1] Over the past few decades, with the increase in life span, the increase in invasive procedures, as well as cardiovascular electronic devices and prosthetic valves implants, IE has become more and more frequent in the elderly.[2, 3] Mortality in older patients is higher than in the general population.[2, 3] The most frequent causative organism as previously reported is *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* has a high infection rate in older patients. [2, 3] Previous reports show that clinical presentations of IE in the elderly are often nonspecific and atypical, which often lead to the delay in diagnosis and treatment for this unique population.[4-6] And the proportion of patients undergoing surgical treatment is lower in older patients compared to younger patients because of the increased risk caused by aging.[7]

However, most of the reports derive from developed countries, and studies exploring the clinical features of older patients with IE in developing countries are scarce. The aim of this article is to investigate the clinical features and prognosis of IE in the elderly from a tertiary teaching hospital in east China.

Methods

Patient Selection and study design

The study 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. All patients were identified according to the modified Duke criteria [8] and patients without complete clinical data were excluded. Patients with IE who were admitted to the hospital more than once during the study period were considered as one case. All the patients included were separated into two groups according to their age: under 65 years old and over 65 years old. Then, patients over 65 years old were divided into the survival group and the mortality group according to their in-hospital outcome.

The analysis strategies were the followings: (1) Analysis of the clinical features of IE in the elderly, therefore, a comparison between the two groups was conducted; (2) Exploration of the prognostic risk factors of in-hospital mortality for older patients and a comparison between the survival group and mortality group was conducted; and (3) Evaluation of the effect of surgical treatment on older patients, and analysis of the one-year survival rate between patients with antibiotic therapy combined with surgical intervention and patients with antibiotic treatment alone.

Clinical parameters and definition

The data for each patient were obtained from the Electronic Medical Record of the First Affiliated Hospital of Zhejiang University. The data included general information, comorbidities, clinical manifestations,

complications, laboratory findings, causative microorganisms, echocardiography results, treatments and outcomes.

Surgical indications were based on the European Society of Cardiology (ECS) guidelines. [8, 9] Embolism events included both embolization diagnosed by imaging techniques and clinical performance. The main outcome was in-hospital all-cause mortality, and the second outcome was one-year all-cause mortality. The one-year follow-up data were collected from the patients' latest visits to our hospital. Transthoracic echocardiogram was performed routinely in all patients. Transesophageal echocardiogram (TEE) was used to detect cases with negative transthoracic echocardiography (TTE) results. Blood culture was performed in all the patients with aerobic, anaerobic and fungal blood cultures, but blood cultures 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

Univariate analysis was performed using Pearson's χ^2 test or Fisher's exact test as appropriate for categorical variables and independent Student's t-test or Rank sum test was used as appropriate for continuous variables. Categorical variables were expressed as frequencies and percentages of the specified group. Continuous variables were reported as the median and interquartile range. After univariate analysis, variables with $P < 0.05$ were included in the logistic regression to identify the risk factors of in-hospital mortality among older patients. Cox multivariate survival analysis was also performed to discover the predictors of one-year all-cause mortality. A Kaplan-Meier analysis was used to determine the one-year survival. All tests were 2-tailed, and $P < 0.05$ was considered statistically significant. All analyses were performed using the SPSS version 23 statistical software.

Results

Patient enrollment

There were 409 patients diagnosed as IE and 2 patients with incomplete data (whose blood culture results were unreachable) were excluded. There were 407 patients included in our study, 348 patients were in the <65 years old group and 59 patients were in the ≥ 65 years old group. During the follow-up, 92.8% (378 of 407) of patients taking part in the study completed a median follow-up of one year after infective endocarditis diagnosis. During this period, 45 (11.1%) patients died.

The clinical characteristics of IE in the two groups

The clinical characteristics of IE in the two groups are summarized in Table 1. There were no differences in the length of hospital stay, duration of symptoms before echocardiography and duration of symptoms before diagnosis between the two groups. There were more patients with previous cardiac surgeries ($P=0.001$) and degenerative heart disease ($P=0.001$) in the ≥ 65 years old group than in the <65

years old group. With regards to comorbidities, there were no significant differences between the two groups, except that older patients had a higher rate of hypertension ($P=0.001$) and diabetes mellitus ($P=0.023$) than the younger patients. In older patients, clinical symptoms such as fever, anemia and heart murmur were as common as in younger patients. There were more cases of arrhythmia and renal insufficiency in the older patients than in the younger ones ($P=0.001$, $P=0.027$, respectively).

Blood cultures were performed in all patients with IE. Two hundred and twenty two blood cultures had positive results. Patients with negative blood culture were diagnosed as IE by the following criteria: 180 patients had positive echocardiographic findings plus three minor criteria, and 5 patients were identified by positive histopathological findings. The main pathogen in older patients was streptococci with 13 patients (22.0%), followed by Staphylococci with 11 patients (18.6%), which was similar to the cases reported in younger patients ($P=0.876$). The rate of patients with surgical indications was similar between the two groups, but there were only 24 patients (40.7%) who underwent surgery in older patients which was much lower than in younger patients ($n=211$, 60.6%) ($P=0.004$). The in-hospital mortality in older patients was significantly higher than that in the younger patients (20.3% vs 8.9%, $P=0.008$).

The risk factors for in-hospital mortality in old patients

For patients ≥ 65 years old, multivariate analysis identified Pitt score ≥ 4 ($P=0.043$, OR=28.0, 95% CI 1.1-700.4) and renal insufficiency ($P=0.011$, OR=34.2, 95% CI 2.2-521.2) as independent risk factors of in-hospital mortality for ≥ 65 years old patients with IE. (Table 2)

The risk factors for one-year mortality in old patients

A one-year survival analysis was performed for patients ≥ 65 years old. The results are displayed in Table 3. Significant variables included man, hemodialysis, renal insufficiency, pulmonary arterial hypertension, Pitt score ≥ 4 , vegetation length ≥ 30 mm and surgical treatment. Surgical treatment [hazard ratio (HR) = 1.722, 95% CI 0.563-5.365, $P = 0.005$] was a significant predictor of one-year mortality even after adjusting for man, renal insufficiency, pulmonary arterial hypertension, Pitt score ≥ 4 and vegetation length ≥ 30 mm. The Kaplan–Meier survival curves revealed that cumulative one-year survival rate was significantly higher in old patients with antibiotic therapy combined with surgical intervention than that in patients with antibiotic treatment alone (95.8% vs 68.6%, $P=0.007$) (Figure).

Discussion

For older patients with IE, clinical symptoms were as common as in younger patients but comorbidities and complications more common in older patients. The in-hospital mortality in older patients was higher compared with the younger patients. Surgical treatment was a significant predictor for long-term mortality but the operation rate was lower in older patients with IE. The one-year survival rate was higher for older patients with antibiotic therapy combined with surgical intervention than those with antibiotic treatment alone (95.8% vs 68.6%, $P=0.007$).

The different clinical characteristics of old patients with infective endocarditis

According to the published researches, the clinical features in older patients were few and untypical, which often led to a delay in the diagnosis of IE. [5, 10, 11] While, Jean et al [12] found older people had a more severe clinical status than younger patients, which lead to the early diagnosis of older patients. However, in our study, we found that clinical presentations such as fever, anemia and heart murmur in older patients were as common as in younger patients and that the time to diagnosis was not significantly different compared to the younger patients.

In accordance with previous studies, cardiovascular and general comorbidities increased with aging. Older patients were more frail, which often lead to more comorbidities and complications than younger patients.[12-15] Similarly, we found that older people suffered from more comorbidities and complications in our study.

In our study, we found that the in-hospital mortality rate in older patients was much higher than that in the younger patients, and the finding was consistent with previous reports. [3, 14-17] As reported previously, older adults were prone to require complex care needs and suffer from multiple comorbidities, which made them vulnerable to health-associated exposure and poor outcomes. [14, 18-20] Besides, the lower operative rate in older patients compared with the younger in our cohort may be another important reason for the higher mortality in older patients. [7, 13, 14]

The in-hospital mortality and one-year mortality were lower in older patients in our study compared with previous studies.[5, 14, 16] Léopold Oliver et al reported that one-year mortality was higher in the ≥ 80 -year-old group (37.3%) than in the <65-year-old group (13%) and the 65-80-year-old group (19.7%), indicating that the mortality rate increased with aging.[13] The few number of very old patients in our study (there were only 5 patients who were over 80 years old) may be an important reason.

The risk factors of in-hospital mortality in patients ≥ 65 year old with infective endocarditis

Previous studies reported that in older patients, older age, renal failure, prosthetic valve endocarditis, neurological deficit, and cerebral embolism were independent risk factors for in-hospital mortality. [4, 21] In our study we found the independent risk factors were renal insufficiency and a Pitt score ≥ 4 . Pitt score was always a means to evaluate the severity of disease. A high Pitt score suggested the worse condition of the patients and it was an integrative barometer of multiple adverse events including neurological deficit, cerebral embolism and heart failure. These events have been confirmed to be risk factors for mortality in IE patients.[8, 22, 23]

Surgical treatment and prognosis in old patients with IE

We observed that elderly patients with surgical treatment had a lower mortality rate compared with non-operated patients during the one-year follow-up in our study. Other recent reports also reached the same conclusion.[13] However, surgery was performed less often in older patients in our study, although the rate of patients with theoretical indications of surgery was not significantly different compared to the

younger patients. This phenomenon was frequently presented in previous reports. [3, 24, 25] The main consideration may be the increasing risks during the perioperative period owing to the decline in organ function and the presence of comorbidities associated with aging. These factors made the choice of surgical treatment for elderly patients more difficult.

But these considerations could not prevent the old patients with surgical indications from suitable treatments in-time. There are many frailty scores to assess the physical condition of older patients, and some scores showed good reliability in the assessment of mortality independently of age. [18] Some studies have recently proven the utility of these scores for the evaluation of IE-related stroke and prognosis evaluation before cardiac surgery. [26] Therefore, surgery is appropriate in selected old patients with IE. And we recommend a more global patient evaluation and cooperation among multiple specialists to improve IE management in older populations in the future.

Limitations

There are several limitations in our study. First, it was performed in a referral teaching hospital where most patients were transferred from other medical centers leading to long-term disease and negative blood culture results. Therefore, these results should not be generalized to other patient groups. Second, as a retrospective study, the long-term follow-up was not possible and 29 patients were lost during the one-year follow-up. Finally, the study covered a long period of time in order to keep the enough sample sizes. Changes in treatment regimens and causative organisms could affect the patient prognosis during this period. Therefore, a multiple-center prospective cohort studies conducted in our region was suggested.

Conclusions

In conclusion, IE in older patients presents more comorbidities and complications with a higher mortality than in younger patients. Renal insufficiency and a Pitt score ≥ 4 were risk factors for in-hospital mortality. Surgery were underused in older patients and old patients with surgical treatment presented better long-term prognosis.

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

Ethical approval was granted from the Ethics Committees and review board of the First Affiliated Hospital, College of Medicine, Zhejiang University. As this study used secondary data, informed consent was not obtained from patients.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Conflicting of interest

The authors declare that they have no conflicts of interest.

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Authors' contributions

ZW designed the study and created study protocols, ZW and YC performed the data collection, data analysis and drafts the manuscript. YX supervised the study development, helped to review the manuscript and made critical revision to the paper. TX TN and QS performed data collection and helped to review the manuscript. All authors read and approved the final manuscript.

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