Epidemiological analysis of infective endocarditis at the Gold Coast area health service, Australia

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Abstract:

Introduction: Infective endocarditis is known to be a condition which is associated with high mortality and morbidity. Some studies indicate an in-hospital mortality of 16% with a one-year mortality of 37% with infective endocarditis.

Aim: We aim to determine the risk factor profile, valve profile, complication rates, mortality, microorganisms involved and impact of antimicrobial resistance of patients with infective endocarditis at the Gold Coast area health service

Design: We performed a retrospective single-center analysis on 111 patients of 18 years old and above with echo-proven infective endocarditis who were followed at the department of cardiology, Gold coast area health service from January 2011 to December 2015.

Place and duration of study: Department of Cardiology, Gold coast area health service, January 2011 to December 2015

Inclusion criteria: Age > 18 years, index hospital stay with infective endocarditis, echocardiographic evidence of endocarditis

Results:

Median age**:** 59 years, median length of stay: 21 days, male predominance (68% males, 32% females), mitral valve was the most commonly involved valve, surgical intervention in 20%, mortality 16%

Risk factors: Intravenous drug use was the most common risk factor (28%).Presence of prosthetic heart valve (mechanical and bioprosthetic) was the second most common risk factor. Other risk factors-healthcare related endocarditis (14%), previous episodes of endocarditis (15%), rheumatic heart disease and intracardiac device (8%)

Methicillin-sensitive Staphylococcus aureus(MSSA) was the most commonly involved organism (46%) followed by streptococcus(26%), Enterococcus(11%). Methicillin-resistant Staphylococcus aureus(MRSA) was involved in 5% of the patients.

Septic emboli was the most common complication(42%).Heart failure which complicated endocarditis in 38% of patients had a relative risk of mortality of 2.83 (p=0.018, 95%[CI] 1.1-6.7). Arrhythmias happened in 11% of patients which posed a relative risk of mortality, (RR-2.71, p=0.037, 95% [CI] 1.0-6.9). The RR for mortality in the non-surgical group was 2.09 (RR-2.09, 95% [CI] 0.5-8.4, P= 0.3) compared to the surgical group.

Conclusion: The key findings in our single center study were that intravenous drug use and health care related endocarditis were the most common reversible risk factors of endocarditis with complications of heart failure and arrhythmias posing a significant risk of mortality.

Keywords: *Infective endocarditis, complications, risk factors, mortality*

Abbreviations

Infective endocarditis IE

Methicillin-sensitive Staphylococcus aureus MSSA

Methicillin-resistant Staphylococcus aureus MRSA

Intravenous drug use IVDU

Heart Failure HF

Relative risk RR

ICE-PCS International collaboration on endocarditis prospective cohort study

1. Introduction

Infective endocarditis is known to be a condition associated with high mortality and morbidity (1). Some studies indicate an in-hospital mortality of 16% with a one-year mortality of 37% with infective endocarditis (2). Despite advancements in diagnostic tools, antibiotics and surgical techniques, endocarditis has been associated with grave outcomes (3). The epidemiology of IE can vary depending on the demography and the risk factor profile of the patients. The rate and type of complications can vary significantly. Despite this, certain microorganisms are found to be associated with mortality. For example, Staphylococcus aureus endocarditis on the left-sided native valve is associated with a high one-year mortality (4). The international collaboration on endocarditis prospective cohort study (ICE-PCS) was one of the few multicenter studies in IE. It showed that complications like heart failure (HF) and intra-cardiac abscess are associated with increased mortality (5). Mitral valve is the most commonly affected valve and infected prosthetic valves attributed to significant mortality risk (5).

There have been studies to develop prognostic scores which indicate that six-month mortality of IE can be based on patient factors, culprit microorganisms and IE characteristics and complications (3). Some studies indicate early surgical interventions in patients with Staphylococcus infections showed better survival (6).

There is lack of local epidemiological data for IE in Australia. Gold Coast is a coastal city in Queensland, Australia with a total population of 576,918 with a median age of 38 year. The total indigenous population is approximately 6000. We aim to assess epidemiological factors and key risk factors, complication rates, culprit micro-organisms and mortality rates in our study population. This is a pilot project with an aim to develop an endocarditis registry in future.

1. Methods and materials:

This is a retrospective analysis of all infective endocarditis with echocardiographic evidence of endocarditis admitted to Gold coast area health service from January 2011 to December 2015.

This study was conducted as per the guidelines of the human research and ethics committee.The human research and ethics approval number is HREC/17/QGC/296

Inclusion criteria included patients with age above 18 years who had echocardiographically proven IE.

Patients with only echocardiographically proven endocarditis were included. Duke's criteria for diagnosis was not used due to lack of reliable reporting in the patient records. It also helps us make the data more reproducible and have diagnostic certainty. Only the index hospital stay of a particular patient was taken into account.

Data were collected by the study investigators and stored in secured filing locations that were only accessible to the study investigators. Data was collected on from electronic and paper medical records, pathology and echocardiography database. Patients diagnosed by transthoracic and trans-esophageal echocardiograms were included. The follow-up duration of these patients was one year.

The data collected included the age and sex of the patient, index hospital stay.

Risk factors like indigenous or aboriginal status, previous episodes of IE, history of intravenous drug abuse, history of rheumatic or congenital heart disease, prosthetic heart valves or intra-cardiac devices and recent invasive procedure were assessed and described as a continuous data in the form of percentages

We also looked at the frequency with which each cardiac valve was affected and reviewed the complications like heart failure, septic emboli, intracardiac or perivalvular abscess or arrhythmias. This frequency was described in percentages.

The significance of the association between the complications and mortality were assessed by Chi-square test.

As antibiotic resistance is a major issue in IE patients, we also examined the rates of antibiotic-resistant organisms in our patient cohort. The treatment strategy (medical therapy versus surgical intervention) was noted and mortality rates were also calculated.

2. Results and discussion

We performed a retrospective analysis of 111 echocardiographically proven cases of infective endocarditis.

2.1. Patient characteristics

The median age of the patients was 59 years. Also, the median length of inpatient stay was 21 days.

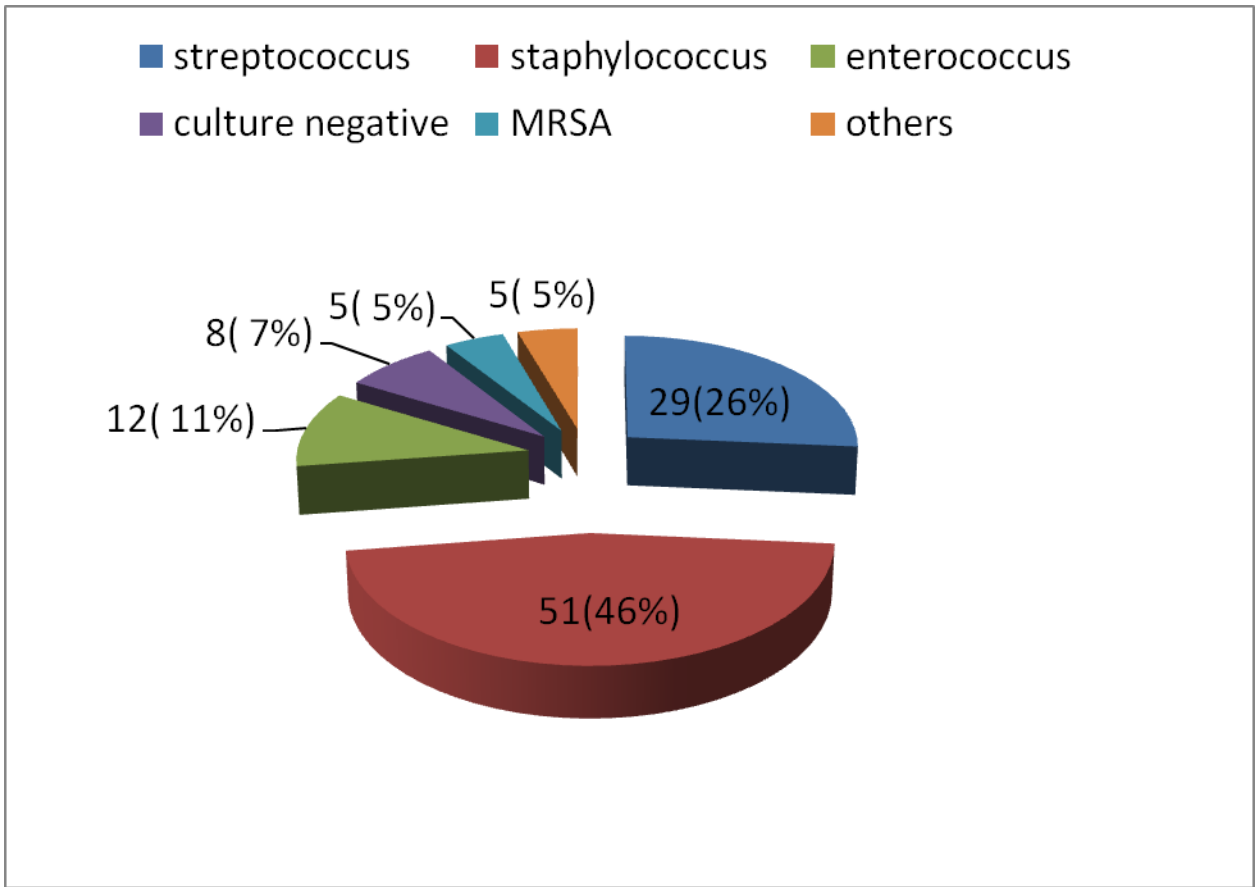
The sex distribution was male predominant with males affected in 68%of cases and females 32%

2.2. Micro-organisms (Fig 1)

Methicillin-sensitive Staphylococcus aureus (MSSA) was the most common culprit organism as it affected 51 patients (46%).It was noted the 71% of patients with Staphylococcus endocarditis had at least one or more major complication. These findings were consistent with the results of Fowler V et al in a study including 1779 patients (7). Methicillin-resistant Staphylococcus aureus (MRSA) was a causative organism in 5% of the patients. The incidence of MRSA was looked at separately as it significantly changes the patient management as well as infection control precautions during their hospital stay.

Streptococcus was the culprit organism in 26% of the patients.11% patients had enterococcus as a causative organism and 7% were culture negative. 5% of the patients had other organisms like Serratia, Burkholderia, erysipelothrix and Haemophilus.

Figure 1: Culprit micro-organisms



2.3. Risk factors (Fig 2)

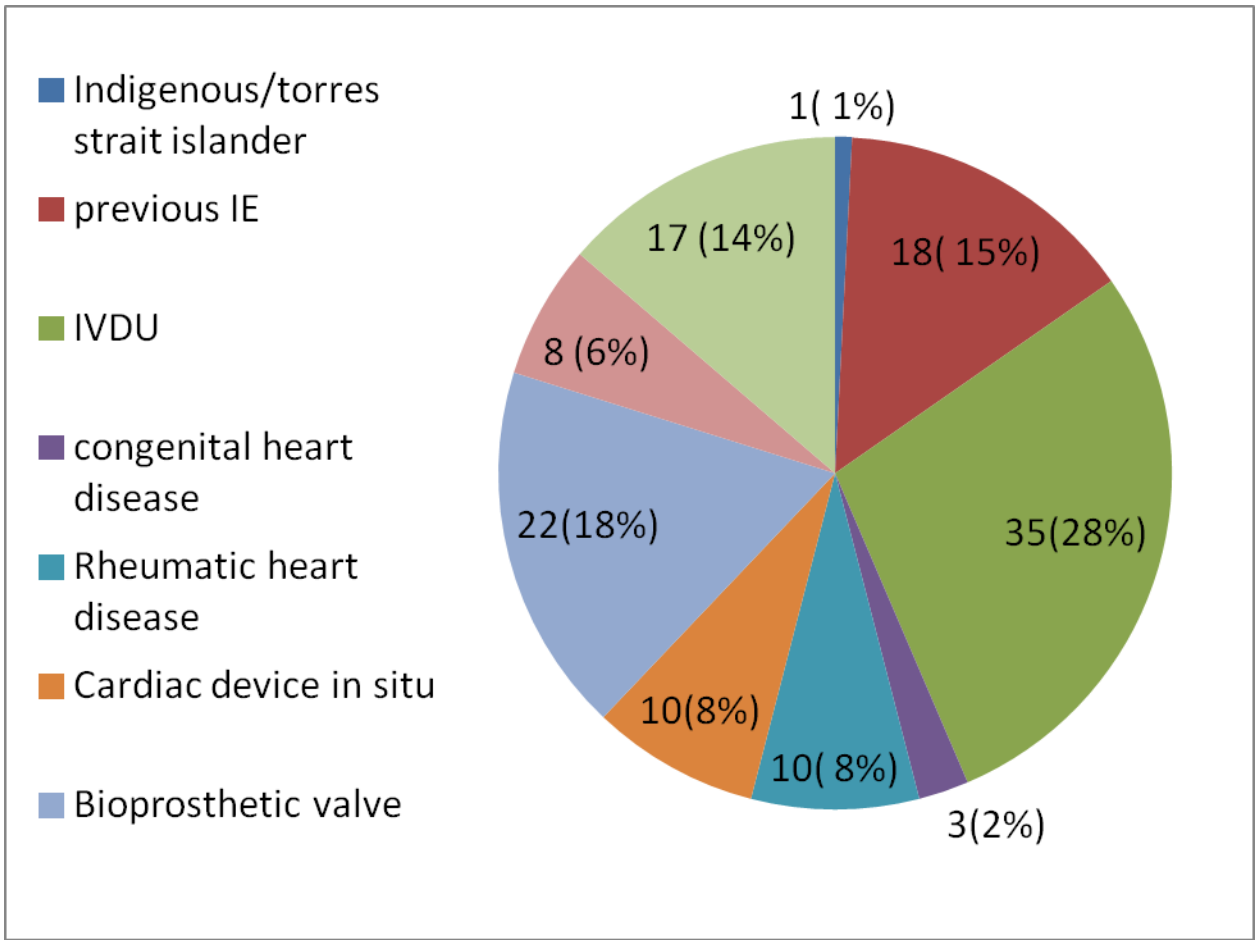
On the assessment of risk factors, it was found that only one patient in the cohort was Indigenous Australian in origin.

Intravenous drug use (IVDU) was the most common risk factor. It was present in 28% of the patients contributing to 83% of IE amongst patients under the age of 50 years. This was significantly higher than the rates of IVDU in the International collaboration of infective endocarditis prospective cohort study (ICE-PCS), possibly related to the differences in patient demographics (5). Presence of prosthetic heart valves was the second most common risk factor (24%). This was comparable to the ICE-PCS study.

Eighteen patients (15%) had a previous history of IE. Amongst the IE patients, 14% had an invasive procedure in the preceding 3 months amounting to the nosocomial risk of endocarditis. This group has been shown to have a worse prognosis in some studies (3).We define this group as patients with healthcare related endocarditis which is one of the potentially reversible risk factors of endocarditis.

Eight percent of the patients had an intra-cardiac device (permanent pacemaker or automated implantable cardiac defibrillator) and 8% had a history of rheumatic heart disease.

Figure 2: Risk factors



2.4. Valvular involvement

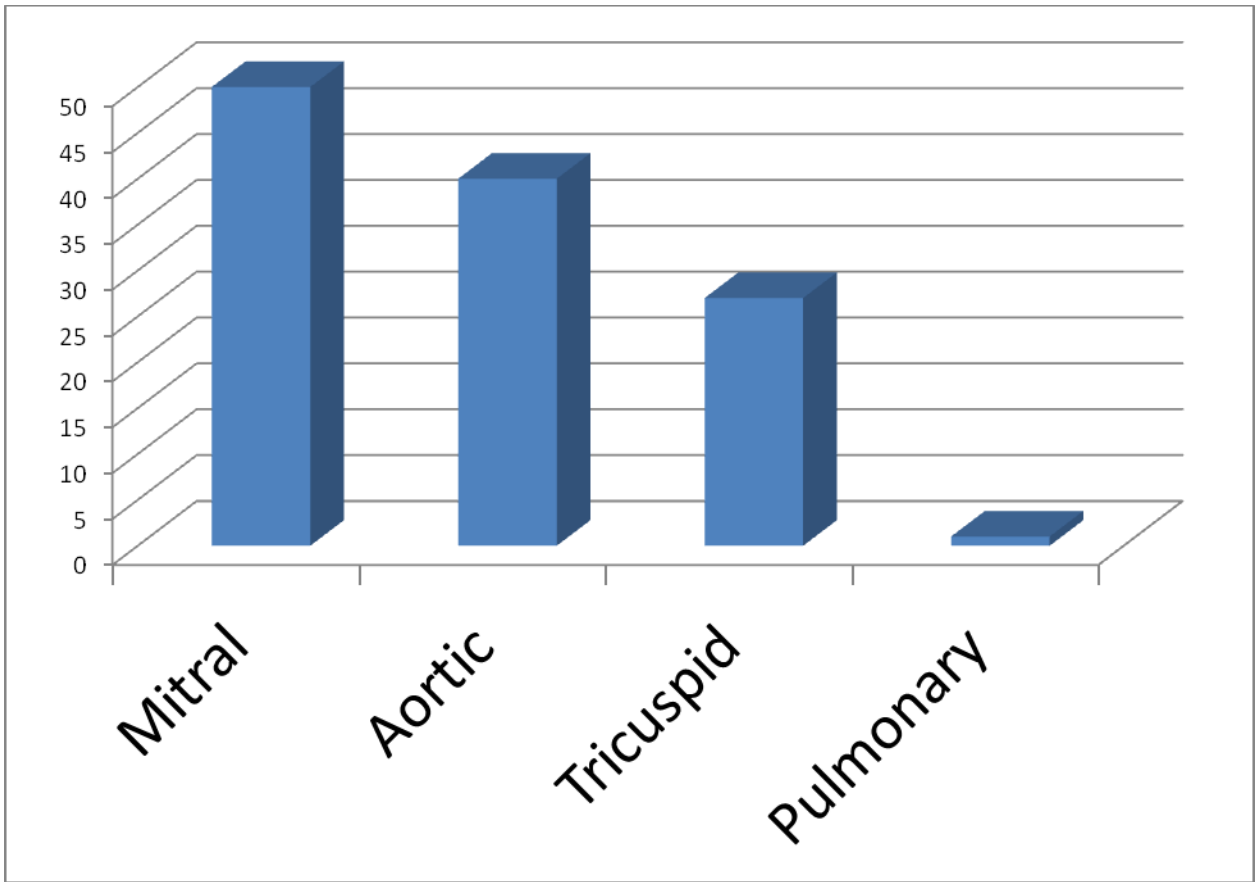
The frequency of valvular involvement was 45% for mitral, 36% for aortic, 24% for tricuspid and 1% for pulmonary valves (Fig 3). These rates are consistent with the findings of the ICE-PCS study where mitral

valve involvement occurred in 41% and aortic valve in 38% (5).Hasbun R et al also noted 50% of their 513 patients had mitral valve endocarditis(8). There was a higher incidence of tricuspid valve endocarditis (24%) noted in this cohort. Tricuspid valve endocarditis has been linked with IVDU use in the community. Studies have shown that native tricuspid valve endocarditis, when associated with IVDU may have an improved prognosis (9).

We had 27 patients with tricuspid valve endocarditis (24%) out of which 18 had associated IVDU. There was only one mortality amongst these patients; in a 25 year old female with Staphylococcus septicemia and complicating acute renal failure. Given the relatively small sample size of tricuspid valve endocarditis in our study, it is not possible to comment on improved prognosis in IVDU patients.

Another striking feature of the analysis was that all 9 patients with a paravalvular abscess had evidence of aortic valve vegetation giving a strong association between the two.(P =0.000 by Fischer exact test)

Figure 3: Frequency of valvular involvement



2.5. Complications

We reviewed the rates of four major complications amongst our patients which included heart failure, septic emboli, arrhythmias and para-valvular abscess (Fig 4).

Complications included heart failure in 40 patients (36%), septic emboli in 43 patients (42%), arrhythmias in 12 patients (11%) and para-valvular abscess in 9 patients (8%). Heart failure and septic emboli are documented to be some of the most common complications of IE in previous studies (5). Furthermore, heart failure was associated with increased mortality. The RR of mortality with HF was 2.83(p=0.02, 95% [CI] 1.1-6.7).This was consistent with previous studies suggesting heart failure as a poor prognostic marker for death (10).

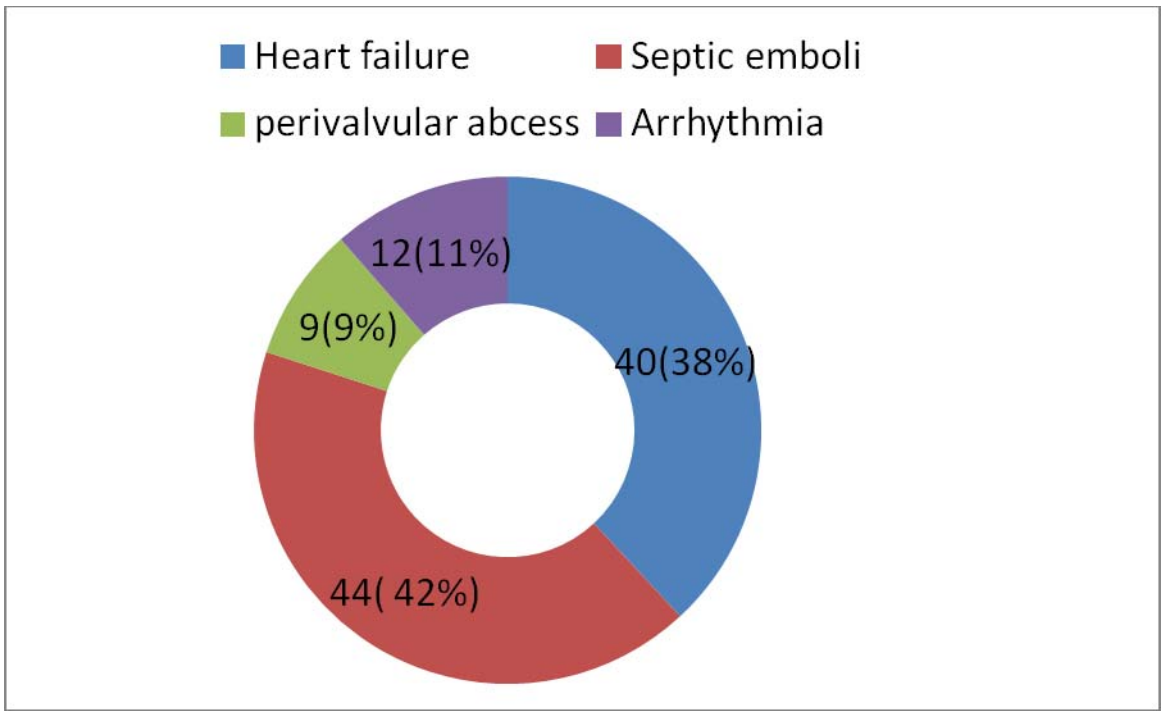
RR of mortality with arrhythmia: RR=2.71(95% [CI] 1-7.0, P=0.04)

Para-valvular abscess RR=1.4(95% [CI] 0.4-5.2, P=0.59) and septic emboli RR=0.98(95% [CI] 0.4-2.3, P =0.97 were not statistically significant for mortality.

Twenty three (20%) patients underwent surgical intervention. The surgical rates were lower compared to previous studies (3).

Overall mortality was 16% in this cohort. This was lower than the predicted mortality rates with IE in spite of lower surgical rates (5).The RR for mortality in the non-surgical group was 2.09(95%[CI] 0.5-8.4, P= 0.3) compared to the surgical group.

Figure 4: complication rates



3. Study Limitations

This was a single center retrospective study hence the findings cannot be extrapolated to the entire population in Australia. Despite being a single center analysis, some of the findings were comparable to a multicenter study indicating certain salient characteristics of the disease process.

The follow-up period was approximately one year which meant that long-term mortality and morbidity associated with IE could not be assessed.

Also, only patients with echocardiographic evidence of endocarditis were included to make the findings more reproducible. This meant that patients with IE who met Dukes criteria for definite or probable endocarditis but did not have echocardiographic evidence could have been missed. It could have possibly included a sicker cohort of patients in the study as most of them would either have a significant vegetation, valvular pathology or paravalvular abscess.

Ethical Approval:

This study was conducted as per the guidelines of the human research and ethics committee.The human research and ethics approval number is HREC/17/QGC/296

Consent: NA

4. Conclusion

Infective endocarditis is an infrequent pathology associated with high mortality and morbidity. There are definite risk factors which predispose patients to endocarditis and the risk factor profile changes with the population demographics. Staphylococcus is the most common causative organism and is associated with higher complications rates.

Heart failure is a common complication and is associated with grave prognosis. Aortic valve endocarditis has a strong association with para-valvular abscess

Rates of surgical interventions vary significantly amongst the previous studies and so do their outcomes.

Intravenous drug use and healthcare-associated infections are increasingly associated with IE while rheumatic heart disease is a less common risk factor. More multicenter studies are needed to assess the dynamic nature of the risk factor profile of the varied demographic populations. Further studies will also enable development of prognostication scores and guide us towards the better selection of patients needing early surgical intervention.

References:

1. Bonow RO, Carabello B, de Leon AC, Edmunds LH, Jr., Fedderly BJ, Freed MD, et al. ACC/AHA Guidelines for the Management of Patients With Valvular Heart Disease. Executive Summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients With Valvular Heart Disease). J Heart Valve Dis. 1998;7(6):672-707.
2. Cabell CH, Jollis JG, Peterson GE, Corey GR, Anderson DJ, Sexton DJ, et al. Changing patient characteristics and the effect on mortality in endocarditis. Arch Intern Med. 2002;162(1):90-4.

3. Park LP, Chu VH, Peterson G, Skoutelis A, Lejko-Zupa T, Bouza E, et al. Validated Risk Score for Predicting 6-Month Mortality in Infective Endocarditis. J Am Heart Assoc. 2016;5(4):e003016.
4. Lauridsen TK, Park L, Tong SY, Selton-Suty C, Peterson G, Cecchi E, et al. Echocardiographic Findings Predict In-Hospital and 1-Year Mortality in Left-Sided Native Valve Staphylococcus aureus Endocarditis: Analysis From the International Collaboration on Endocarditis-Prospective Echo Cohort Study. Circ Cardiovasc Imaging. 2015;8(7):e003397.
5. Murdoch DR, Corey GR, Hoen B, Miro JM, Fowler VG, Jr., Bayer AS, 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):463-73.
6. Bishara J, Leibovici L, Gartman-Israel D, Sagie A, Kazakov A, Miroshnik E, et al. Long-term outcome of infective endocarditis: the impact of early surgical intervention. Clin Infect Dis. 2001;33(10):1636-43.
7. Fowler VG, Jr., Miro JM, Hoen B, Cabell CH, Abrutyn E, Rubinstein E, et al. Staphylococcus aureus endocarditis: a consequence of medical progress. JAMA. 2005;293(24):3012-21.
8. Hasbun R, Vikram HR, Barakat LA, Buenconsejo J, Quagliarello VJ. Complicated left-sided native valve endocarditis in adults: risk classification for mortality. JAMA. 2003;289(15):1933-40.
9. Mi MY, Nelson SB, Weiner RB. Clinical and Echocardiographic Factors Associated With In-Hospital Mortality in Patients With Infective Endocarditis Affecting the Native Tricuspid Valve. Am J Cardiol. 2016;118(5):739-43.
10. McGiffin DC, Galbraith AJ, McLachlan GJ, Stower RE, Wong ML, Stafford EG, et al. Aortic valve infection. Risk factors for death and recurrent endocarditis after aortic valve replacement. J Thorac Cardiovasc Surg. 1992;104(2):511-20.