Infective Endocarditis

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KEYWORDS

- Endocarditis • Fever • Murmur • Injection drug use (IDU) • Bloodstream infections
- Healthcare associated infections • Staphylococcal bacteremia

KEY POINTS

- Endocarditis should be considered in any patient with fever and risk factors, including significant valve damage, injection drug use, or an indwelling catheter.
- Blood cultures and echocardiography are the mainstays of diagnosis.
- Culture-negative endocarditis may result from certain fastidious or fungal organisms.
- Complications of endocarditis include heart failure, embolic stroke and metastatic infection, which may require cardiac surgery to control.

INTRODUCTION

Infective endocarditis (IE) is defined as an infection of a native or prosthetic cardiac valve, endocardial surface, or indwelling cardiac device.[1,2] Its incidence and mortality have not decreased in the past 30 years,[3] and it remains a challenging diagnosis to make and a difficult infection to treat despite new diagnostic and therapeutic strategies.[4]

The landscape of IE has changed in recent decades due to a shift in both the predominant pathogens and the most common predisposing conditions.[5] More virulent and resistant *Staphylococcus* species are becoming more common than penicillin-sensitive *Streptococcus*.[6] IE is occurring in an older, chronically ill population with more health care–associated and cardiac device–associated infections.[5] IE is no longer classified as acute versus subacute. Contemporary classification schemes vary but are all based on the distinction between native versus prosthetic valve endocarditis and community-acquired versus health care–associated infection; injection drug use (IDU)-related IE is generally considered separately.[7]

IE remains a disease with a highly variable and nonspecific presentation. Early diagnosis, particularly in the emergency department (ED) setting, depends on maintaining a high index of suspicion. IE should be suspected in any patient with a fever and unclear source of infection, new regurgitant heart murmur, and/or embolic events of unknown origin.[1] When IE is suspected, blood cultures and early formal

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echocardiography, the cornerstones for diagnosis, should be obtained immediately, usually while a patient is still in the ED.[8]

New consensus guidelines in the past decade have modified the approach to antibiotic therapy and prophylaxis.[8] Therapy recommendations, however, are still derived largely from expert opinion and observational cohort studies, due to the relatively low incidence of disease, lack of randomized controlled trials, and limited number of meta-analyses.[1,2] Although intravenous (IV) antibiotics are the mainstay of treatment, almost half of patients with IE eventually require surgery,[4] with common indications heart failure, perivalvular abscess formation, uncontrolled infection, and large or mobile vegetations.[8] Early consultation with cardiology and infectious disease specialists leads to improved diagnosis and management.[1]

EPIDEMIOLOGY

The annual incidence of IE is low, occurring in 3 to 10 per 100,000 people, with infection patterns varying according to geographic location. This incidence has remained stable over the past 2 decades. Globally, in 2010, IE caused the loss of 1.58 million disability-adjusted life-years (years of healthy life lost) as a result of death and illness or impairment.[4] In low-income countries, rheumatic heart disease is still the leading risk factor, underlying up to two-thirds of cases.[2,9,10] In the developed world, there has been an overall decrease in the proportion of cases related to rheumatic heart disease.[2] There is now a greater proportion of patients with other predisposing risk factors, including IDU, degenerative valve disease, congenital heart disease (CHD), prosthetic valves, and other cardiac devices.[11]

Overall, the mean patient age has increased, from approximately 45 years in the early 1980s to older than 70 in 2001 to 2006.[5] More IE patients now have comorbidities, such as chronic obstructive pulmonary disease, diabetes, cancer, and liver disease.[2] IE patients are more likely to be male. Although the overall incidence of IE has remained stable, the proportion caused by *S aureus* has steadily increased, now accounting for approximately 25% of cases in industrialized nations (**Table 1**). All of these shifts, in turn, highlight the growing importance of health care exposure as a risk factor for infection.[2]

A retrospective epidemiologic study examining 75,829 patients with first episodes of IE in California and New York State between 1998 and 2013 found that health care–associated IE accounted for more than half of all cases of native valve endocarditis (although in a contemporary French study the proportion of health care–associated disease was just 26.7%).[6,12] Health care–associated IE carried a 50% mortality at 1 year.[12] The proportion of patients who were dialysis dependent increased by 38.3% over the study period, accounting for 35% of health care–associated IE cases by 2010 to 2013.[12] Nosocomial (hospital-acquired) endocarditis cases actually declined over the study period, coinciding with large-scale efforts to reduce hospital-acquired infections, whereas non-nosocomial health care–associated endocarditis increased. These infections are acquired during outpatient health care encounters, for example, at dialysis and infusion centers, and often present first to the ED.

An increase in the proportion of patients with a history of valve surgery or implanted pacemakers or defibrillators has resulted in an increase in the incidence of prosthetic valve and cardiac device–related endocarditis, to 13% to 17% and 3% to 5%, respectively. Nonetheless, native valve IE still accounts for 71% to 78% of cases; 5% to 13% of cases are IDU related[1,7,12] (see **Table 1**).

Endocarditis remains rare in children, although improved survival in CHD has resulted in an increasing incidence of IE in this age group.[13] Pediatric IE is often a