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Endocarditis 2014: An update

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ABSTRACT

The epidemiology of infective endocarditis is changing due to a number of factors, including more frequent and varied antibiotic use, the emergence of resistant microorganisms, and an increase in the implantation of cardiovascular devices. This review outlines and consolidates the most recent guidelines, including the 2007 and 2010 AHA/ACC guidelines and scientific statements for the prevention and management of infective endocarditis and for the management of cardiovascular device infections. The evidence-based guidelines, including the 2009 HRS consensus document, for the treatment of patients with cardiovascular device-related infections are also reviewed. Only patients with prosthetic valves, patients with prior endocarditis, cardiac transplant patients with a valvulopathy, and certain congenital heart disease patients now require endocarditis prophylaxis. There is an increasing incidence of cardiovascular device-related infections due to the higher frequency of implanted devices and higher morbidity and mortality rates in older patients.

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Introduction

Infective endocarditis has been recognized as a clinical entity since the 1950s. In 1955, the American Heart Association (AHA) first established guidelines for the treatment of infective endocarditis.¹ Since that time, the development of powerful antimicrobial therapy and implantable cardiac devices has changed the face of this disease. Today, patients with endocarditis are older and have more comorbidities. These changes present challenges for the prevention and management of endocarditis. This monograph reviews these challenges while continuing to incorporate the current AHA guidelines for the prevention of infective endocarditis¹ and for the management of implantable cardiovascular device infections.²

Diagnosis of infective endocarditis

Infective endocarditis (IE) is a clinical diagnosis and requires a high index of suspicion because patients may present with non-specific symptoms such as fevers, chills, fatigue, malaise, and weight loss. Some patients may present with stroke-like symptoms due to embolic events or with congestive heart failure. Elderly patients, patients with renal failure or patients previously treated with antibiotics may not present with fevers, creating a diagnostic challenge. The Duke Criteria for the diagnosis and management of IE

were initially drafted in 1994 for use in clinical trials and epidemiology studies – however, they were not designed for use in clinical patients.³ Nonetheless, the Duke Criteria have become the gold standard for the diagnosis of IE and were subsequently modified in 2002 to include echocardiographic evidence of IE (Table 1).⁴ A definitive diagnosis of IE may be made with either pathological or clinical criteria. The two major clinical criteria are abnormal blood cultures and evidence of endocardial involvement. The five minor clinical criteria are a predisposition to IE, fever of greater than 38 °C, vascular phenomena, immunologic phenomena, or microbiological evidence of IE not meeting major criteria (Table 1). Requirement for a clinical diagnosis of IE are 2 major clinical criteria, 1 major and 3 minor clinical criteria, or 5 minor clinical criteria.

Endocarditis prevention guidelines

The most recent revision of the AHA Guidelines for IE was published in 2007.¹ They were a clarification of the previous guidelines from 1997.⁵ There were several logical rationale for the revision of the guidelines. Firstly, regarding oral hygiene and procedures, IE was more likely to occur with everyday activities such as teeth brushing and flossing rather than with a single medical or dental procedure. Secondly, prophylaxis with antibiotics for dental procedures prevented very few IE cases. Furthermore, the risk of adverse events and cost of antibiotic therapy significantly outweighed the benefit of such prophylaxis. Thirdly, consistently good oral hygiene is more beneficial in preventing IE than a single dose of antibiotics.

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Table 1
Modified Duke Criteria for the diagnosis of infective endocarditis.

Pathological criteria (1 needed)
1. Microorganism identified by culture or histology from a vegetation, an embolized vegetation or in a cardiac abscess.
2. A histological specimen from a vegetation or an intracardiac abscess showing active endocarditis.
Clinical criteria (2 major, 1 major and 3 minor, or 5 minor needed)
Major criteria
1. Two positive blood cultures with typical microorganisms drawn at least 12 h apart (or one positive blood culture for <i>Coxiella Burnetii</i>)
2. Evidence of endocardial involvement (new murmur, echocardiographic evidence of a cardiac mass, abscess or valve dehiscence)
Minor criteria
1. Fever > 38 °C
2. Vascular phenomena (systemic emboli, Janeway lesions)
3. Immunological phenomena (Osler's nodes, Roth spots)
4. Predisposition to infective endocarditis (previous infective endocarditis or intravenous drug abuse)
5. Microbiological evidence not meeting major criteria

Adapted from Li JS, Sexton DJ, Mick N, et al. Clin Infect Dis 2000; 30:633–638.⁴

The number of patients requiring IE prophylaxis according to the 2007 guidelines has been greatly reduced.¹ Only the four following groups now require prophylaxis: patients with prosthetic valves, patients with prior IE, cardiac transplant patients with a valvulopathy, and certain congenital heart disease patients. These groups include patients with cyanosis, palliative shunts and conduits, patients with residual defects around a cardiovascular patch site and patients within 6 months of a complete repair of a congenital anomaly. For patients with a successful cardiovascular repair, adequate endothelialization of the repair is assumed after 6 months and prophylaxis is no longer needed. Patients with mitral valve prolapse with or without mitral regurgitation and patients with bicuspid aortic valves no longer require prophylaxis under the revised 2007 guidelines.

The number of dental procedures that require prophylaxis under the 2007 guidelines is also reduced. Antibiotic prophylaxis is a Class IIa (LOE C) recommendation for dental procedures that involve manipulation or perforation of the oral mucosa.¹ This does not include routine anesthetic injections through non-infected tissue, dental radiographs, placement or adjustment of orthodontic devices or trauma to the lips and teeth. For respiratory procedures, antibiotic prophylaxis is a Class IIa (LOE C) recommendation for any invasive procedures that involves incision or biopsy of the respiratory mucosa (such as tonsillectomy). An exception is bronchoscopy, which requires no prophylaxis.

Antibiotic choices are influenced by the patient's ability to tolerate oral medication, by medication allergies, and by the most likely pathogen. For dental and respiratory procedures, the most common bacteria are the various streptococcus viridans species. The recommended prophylactic antibiotic is amoxicillin 2 g orally 1 h prior to the procedure.¹ If the patient requires intravenous medication, ampicillin or ceftriaxone may be substituted. Cephalixin, clindamycin or azithromycin may be used in patients with a penicillin allergy. However, there is emerging penicillin resistance of the streptococcus viridans species, with percentage resistances in some studies ranging from 17% to 50%.^{6–10} The prescribing physician must consider the resistance in his/her area of practice when selecting the appropriate antibiotic. In cases where staphylococcus aureus is suspected, an anti-staphylococcal penicillin or vancomycin is recommended.¹

There are no published data linking gastrointestinal (GI) and genitourinary (GU) procedures to IE.¹¹ Consequently the 2007 guidelines recommend that antibiotic prophylaxis is no longer necessary during these procedures (Class III, LOE B).¹ It is stated, however, that if a patient has an established GI or GU infection and is undergoing elective GI or GU tract manipulation, any infection

should be eradicated prior to the procedure (Class IIb, LOE B).¹ The most common pathogens causing a GI or GU infection are the enterococcus species, which also have emerging antibiotic-resistant strains.¹ Penicillins are preferred for these infections, although piperacillin and vancomycin should be considered when a resistant enterococcus is suspected. In these cases, consultation with an infectious disease specialist may be warranted.

Currently, there is no indication for dental, GI or GU procedural prophylaxis for patients with implantable cardiovascular devices (Class III, LOE C).² However, prophylaxis with an anti-staphylococcal antibiotic is indicated at the time of a cardiovascular device implantation and any subsequent manipulation of the surgical created device pocket (Class I, LOE A).²

Treatment of endocarditis

Treatment of IE should be tailored to in-vitro susceptibility of the pathogen identified, and consultation with an infectious disease specialist can be considered. In general, antibiotics such as penicillin, ampicillin, ceftriaxone, rifampin, vancomycin and daptomycin are used. The length of treatment is dependent on the pathogen and type of valve (native vs. prosthetic). Antibiotic selection and duration of therapy is addressed in the 2005 AHA Scientific Statement.³ Viridans group streptococci endocarditis should be treated for 4 weeks for native valve IE and 6 weeks for prosthetic valve IE. For the more virulent staphylococcus aureus, treatment duration is 6 weeks, regardless of valve type. However, prosthetic valves require the addition of rifampin or gentamicin for synergy. Enterococcus endocarditis requires combination antimicrobial therapy for 4–6 weeks, regardless of valve type. Generally, ampicillin is used in combination with either gentamicin or ceftriaxone, depending on the patient's renal function. Treatment duration for the HACEK organisms (*Hemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella*, *Kingella*) is 4 weeks for native valves and 6 weeks for prosthetic valves.

Cardiovascular non-valvular device infections

IE associated with a cardiac pacemaker was first reported in the early 1970s.¹² Infection rates of these implanted devices in the 1970s–1980s ranged from less than 1%–19.9%.^{13,14} Subsequently, the numbers of implanted cardiac devices has significantly increased.¹⁵ Defibrillators are now implanted for primary prevention, and cardiac-resynchronization therapy has increased the total number of implanted intracardiac leads. Furthermore, the average patient with an implanted cardiac device is older and sicker. Zhan and colleagues have reported that among the patients receiving implantable cardiovascular devices, 70% are older than 65 years and at least 75% have more than one coexisting disease.¹⁵ Inevitably these characteristics lead to an increasing number of cardiovascular device-related infections, and a significant increase in associated morbidity and mortality.

Guidelines were initially drafted for the management of cardiovascular device-related infections by the ACC/AHA in 2003.¹⁶ Since the publication of these guidelines, there has been a substantial increase in the number of reports reviewing the incidence and clinical management of patients with cardiovascular device-related infections.^{17–19} As a result, a scientific statement from the AHA issued in 2010 updated the evidence-based guidelines for treatment of patients with cardiovascular device-related infections.²

Clinical presentation and diagnosis

The clinical presentation of a patient with a cardiac device-related infection can be subtle and patients may present with

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