EDITORIAL

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S aureus bacteremia: TEE and infectious disease consultation

MORBIDITY AND MORTALITY rates in patients with *Staphylococcus aureus* bacteremia remain high even though diagnostic tests have improved and antibiotic therapy is effective. Diagnosis and management are made more complex by difficulties in finding the source of bacteremia and sites of metastatic infection.

See related article, page 517

S aureus bacteremia is a finding that demands further investigation, since up to 25% of people who have it may have endocarditis, a condition with even worse consequences.[1] The ability of *S aureus* to infect normal valves[2,3] adds to the challenge. In the mid-20th century, Wilson and Hamburger[4] demonstrated that 64% of patients with *S aureus* bacteremia had evidence of valvular infection at autopsy. In a more recent case series of patients with *S aureus* endocarditis, the diagnosis was established at autopsy in 32%.[5]

Specific clinical findings in patients with complicated *S aureus* bacteremia—those who have a site of infection remote from or extended beyond the primary focus—may be useful in determining the need for additional diagnostic and therapeutic measures.

In a prospective cohort study, Fowler et al[6] identified several factors that predicted complicated *S aureus* bacteremia (including but not limited to endocarditis):

- Prolonged bacteremia (> 48–72 hours after initiation of therapy)
- Community onset
- Fever persisting more than 72 hours
- Skin findings suggesting systemic infection.

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THE ROLE OF ECHOCARDIOGRAPHY

Infective endocarditis may be difficult to detect in patients with *S aureus* bacteremia; experts recommend routine use of echocardiography in this process.[7,8] Transesophageal echocardiography (TEE) detects more cases of endocarditis than transthoracic echocardiography (TTE),[9,10] but access, cost, and risks lead to questions about its utility.

Guidance for the use of echocardiography in *S aureus* bacteremia[1,10–14] continues to evolve. Consensus seems to be emerging that the risk of endocarditis is lower in patients with *S aureus* bacteremia who:

- Do not have a prosthetic valve or other permanent intracardiac device
- Have sterile blood cultures within 96 hours after the initial set
- Are not hemodialysis-dependent
- Developed the bacteremia in a healthcare setting
- Have no secondary focus of infection
- Have no clinical signs of infective endocarditis.

S aureus bacteremia demands further investigation, since up to 25% of people who have it may have endocarditis

Heriot et al[14] point out that studies of risk-stratification approaches to echocardiography in patients with *S aureus* bacteremia are difficult to interpret, as there are questions regarding the validity of the studies and the balance of the risks and benefits.[1] The question of timing of TEE remains largely unexplored, both in initial screening and in follow-up of previously undiagnosed cases of *S aureus* endocarditis.

In this issue of the *Journal*, Mirrakhimov et al[15] weigh in on use of a risk-stratification model to guide use of TEE in patients with *S aureus* bacteremia. Their comments about avoiding TEE in patients who have an alternative explanation for *S aureus* bacteremia and a

low pretest probability for infectious endocarditis and in patients with a disease focus that requires extended treatment are derived from a survey of infectious disease physicians.[16]

ROLE OF INFECTIOUS DISEASE CONSULTATION

Infectious disease consultation reduces mortality rates and healthcare costs for a variety of infections, with endocarditis as a prime example.[17] For *S aureus* bacteremia, a large and growing body of literature demonstrates the impact of infectious disease consultation, including improved adherence to guidelines and quality measures,[18–20] lower in-hospital mortality rates[18–21] and earlier hospital discharge.[18] In the era of "curbside consults" and "e-consultation," it is interesting to note the enduring value of bedside, in-person consultation in the management of *S aureus* bacteremia.[20]

Many people with *S aureus* bacteremia should undergo TEE. Until the evidence becomes more robust, the decision to forgo TEE must be made with caution. The expertise of infectious disease physicians in the diagnosis and management of endocarditis can assist clinicians working with the often-complex patients who develop *S aureus* bacteremia. If the goal is to improve outcomes, infectious disease consultation may be at least as important as appropriate selection of patients for TEE.

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ONE MINUTE CONSULT

BRIEF ANSWERS TO SPECIFIC CLINICAL QUESTIONS

Q: When does *S aureus* bacteremia require transesophageal echocardiography?

A: *Staphylococcus aureus* is the most common infective agent in native and prosthetic valve endocarditis, and 13% to 22% of patients with *S aureus* bacteremia have infective endocarditis.[1]

See related editorial, page 521

Transthoracic echocardiography (TTE) is a good starting point in the workup of suspected infective endocarditis, but transesophageal echocardiography (TEE) plays a key role in diagnosis and is indicated in patients with a high pretest probability of infective endocarditis, as in the following scenarios:

- Clinical picture consistent with infective endocarditis
- Presence of previously placed port or other indwelling vascular device
- Presence of a prosthetic valve or other prosthetic material
- Presence of a pacemaker
- History of valve disease
- Injection drug use
- Positive blood cultures after 72 hours despite appropriate antibiotic treatment
- Abnormal TTE result requiring better visualization of valvular anatomy and function and confirmation of local complications
- Absence of another reasonable explanation for *S aureus* bacteremia.

Forgoing TEE is reasonable in patients with normal results on TTE, no predisposing risk factors, a reasonable alternative explanation for *S aureus* bacteremia, and a low pretest probability of infective endocarditis.[1] TEE may also be unnecessary if there is another disease focus requiring extended treatment (eg, vertebral infection) and there are no findings suggesting complicated infective endocarditis, eg, persistent bacteremia, symptoms of heart failure, and conduction abnormality.[1]

TEE also may be unnecessary in patients at low risk who have identifiable foci of bacteremia due to soft-tissue infection or a newly placed vascular catheter and whose bacteremia clears within 72 hours of the start of antibiotic therapy. These patients may be followed clinically for the development of new findings such as metastatic foci of infection (eg, septic pulmonary emboli, renal infarction, splenic abscess or infarction), the new onset of heart failure or cardiac conduction abnormality, or recurrence of previously cleared *S aureus* bacteremia. If these should develop, then a more invasive study such as TEE may be warranted.

TEE is usually not needed in patients with a low pretest probability of infective endocarditis

INFECTIVE ENDOCARDITIS: EPIDEMIOLOGY AND MICROBIOLOGY

The US incidence rate of infective endocarditis has steadily increased, with an estimated 457,052 hospitalizations from 2000 to 2011. During that period, from 2000 to 2007, there was a marked increase in valve replacement surgeries.[2] This trend is likely explained by an increase in the at-risk population—eg, elderly patients, patients with opiate dependence or diabetes, and patients on hemodialysis.

Although *S aureus* is the predominant pathogen in infective endocarditis,[2–5] *S aureus* bacteremia is often observed in patients with skin or soft-tissue infection, prosthetic device infection, vascular graft or catheter infection, and bone and joint infections. *S aureus* bacteremia necessitates a search for the source of infection.

S aureus is a major pathogen in bloodstream infections, and up to 14% of patients with *S aureus* bacteremia have infective endocarditis as the primary source of infec-

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TABLE 1

Modified Duke criteria for infective endocarditis

MAJOR CRITERIA
Positive microbiologic findings
Two separate blood cultures positive for typical microorganisms causing infective endocarditis: *Staphylococcus aureus*, *Viridans*-group streptococci, *Streptococcus gallolyticus*, enterococci, and "HACEK-group" organisms (*Haemophilus* species, *Aggregatibacter* species, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* species)
Persistently positive blood cultures: ie, 2 cultures at least 12 hours apart positive for typical pathogens, and at least 3 of 4 cultures positive for pathogens commonly considered as skin contaminants (*Staphylococcus epidermidis*)
A single blood culture positive for *Coxiella burnetii*, or an immunoglobulin G titer > 1:800
Echocardiographic findings
Valvular vegetation, abscess, dehiscence of prosthetic valve, or new valvular regurgitation
MINOR CRITERIA
Clinical predisposition: intravenous drug use, presence of a prosthetic heart valve or material, history of valvular disease
Microbiologic findings: positive findings on microbiologic study other than those in the major criteria
Body temperature ≥ 38.0 °C (100.4 °F)
Vascular findings: embolization, mycotic aneurysm, conjunctival hemorrhage, Janeway lesions
Immunologic findings: glomerulonephritis, Osler nodes, Roth spots, positive rheumatoid factor

Based on information in reference 7.

Infective endocarditis can present subtly, as a nonspecific infectious syndrome, or with overt cardiac manifestations or extracardiac organ damage

tion.[3] The pathogenesis of *S aureus* infective endocarditis is thought to be mediated by cell-wall factors that promote adhesion to the extracellular matrix of intravascular structures.[3]

A new localizing symptom such as back pain, joint pain, or swelling in a patient with *S aureus* bacteremia should trigger an investigation for metastatic infection.

Infectious disease consultation in patients with *S aureus* bacteremia is associated with improved outcomes and, thus, should be pursued.[3]

A cardiac surgery consult is recommended early on in cases of infective endocarditis caused by vancomycin-resistant enterococci, *Pseudomonas aeruginosa*, and fungi, as well as in patients with complications such as valvular insufficiency, perivalvular abscess, conduction abnormalities, persistent bacteremia, and metastatic foci of infection.[6]

RISK FACTORS

Risk factors for infective endocarditis include injection drug abuse, valvular heart disease, congenital heart disease (unrepaired, repaired with residual defects, or fully repaired within the past 6 months), previous infective endocarditis, prosthetic heart valve, and cardiac transplant.[2–4,6] Other risk factors are poor dentition, hemodialysis, ventriculoatrial shunts, intravascular devices including vascular grafts, and pacemakers.[2,3] Many risk factors for infective endocarditis and *S aureus* bacteremia overlap.[3]

DIAGNOSTIC PRINCIPLES

The clinical presentation of infective endocarditis can vary from a nonspecific infectious syndrome, to overt organ failure (heart failure, kidney failure), to an acute vascular catastrophe (arterial ischemia, cerebrovascular accidents, myocardial infarction). Patients may