Is Transesophageal Echocardiography Dispensable in Hospital-Acquired *Staphylococcus aureus* Bacteremia?

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(See the article by Kaasch et al., on pages 1–9.)

*Staphylococcus aureus* is an important cause of community, health care–associated, and hospital-acquired bacteremia. In a study from US hospitals that reviewed >6000 episodes of bloodstream infection, *S. aureus* was the most common pathogen, accounting for 23% of all episodes, and was more strongly associated with death than any other bacterial pathogen [1]. Although gram-negative bacteria are increasing as a cause of hospital-acquired bacteremia, *S. aureus* is still responsible for 10%–15% of all cases for which intravascular catheters are the most common source [2]. The management guidelines of *S. aureus* bacteremia (SAB) recommend 2 and 4–6 weeks of antimicrobial therapy for uncomplicated and complicated bacteremia, respectively [3, 4]. The problem is that complicated bacteremia includes infectious endocarditis (IE), and an early diagnosis of this entity requires performance of an echocardiograph. For this reason, the recent guidelines for catheter-related SAB recommend transesophageal echocardiography (TEE) for guiding the duration of antibiotic therapy. This issue is under continuous debate because TEE is not widely available, could be associated with complications, and is an expensive technique. The recommendation to perform a TEE is derived from clinical experiences that select patients with a high risk of IE [5, 6]. For instance, in a study by Fowler et al [5], the prevalence of IE was 25%; however, the authors excluded 73 patients with SAB for whom TEE was not performed either because the patient or the attending physician refused it. It is possible that, in these cases, the prevalence of IE was lower [5]. Another series included mainly community-acquired SAB, and the authors also found a high prevalence (22%) of IE [6]. Indeed, the community acquisition of SAB has been recognized as a risk factor for IE and currently is generally accepted as an indication for TEE [6]. However, according to different reports, the prevalence of IE among patients with hospital-acquired SAB is 6%–9% [7, 8], and it is unknown whether it is possible to identify a subgroup of patients with a very low probability of IE for whom TEE is dispensable.

The article by Kaasch et al [9] addresses this important question with use of results from 2 large, well-conducted and prospective cohorts of consecutive patients with hospital-acquired SAB from 2 hospitals in Europe (Invasive *S. aureus* Infection Cohort [INSTINCT]) and the United States (*S. aureus* Bacteremia Group [SABG]). To select patients with low risk of IE, the authors evaluated a criteria set applied 6–8 days after the first positive blood culture result. The criteria consisted of the following: (1) prolonged bacteremia, when >4 days elapsed between the first blood culture yielding *S. aureus* and the first negative result of a follow-up blood culture (“documented”) or when follow-up blood cultures were not performed (“possible”); (2) the presence of a permanent intracardiac device (eg, prosthetic heart valve, pacemaker, or cardioverter-defibrillator); (3) hemodialysis dependency; and (4) spinal infection (eg, vertebral osteomyelitis epidural, subdural, or intraspinal empyema; or abscess) or nonvertebral osteomyelitis. Both cohorts were similar, except the rate of methicillin-resistant strains was significantly lower in the INSTINCT cohort (15.5%) than in the SABG cohort (65.7%). The prevalence of IE in both cohorts was in agreement with previous reports of hospital-acquired SAB (4.3% and 9.3%, respectively). The main finding is that the negative predictive value of these criteria was 99.5% (100% in INSTINCT and 99.2% in SABG), which means that only 1 of 208 patients...
(including both cohorts), without fulfilling any of the criteria, had IE. It could be questioned that 60% of the patients in the INSTINCT cohort and 43% of those in the SABG cohort did not have an echocardiograph performed to rule out IE, but the authors followed up with all patients for 3 months. Theoretically, patients who received prolonged treatment or those who suddenly died during follow-up could correspond to a missed case of IE; however, the authors convincingly describe the reasons that this option was unlikely. In addition, the mean duration of antimicrobial treatment was 14 days in the INSTINCT cohort and 17 days in the SABG cohort, with a 30-day mortality rate of 17% and 21%, respectively; these data are in agreement with the mortality rate reported by other authors [10–12]. As a consequence, the criteria of Kaasch et al allowed a one-third reduction in the number of TEE indications. The authors were prudent by considering patients who did not have surveillance blood culture performed as having possible prolonged bacteremia. However, if surveillance blood cultures had been performed for all patients, the number of TEE indications would have been even lower. It seems reasonable to repeat the blood cultures only for those patients with persistent fever; however, physicians should be aware that Khatib et al [13] observed that up to 54% of patients with documented persistent bacteremia had no fever performing at the time that surveillance blood cultures were performed. In addition, in a prospective study of SAB, persistent bacteremia was the best predictor of any complication, including septic metastasis and death [13].

The positive predictive value of the same criteria to predict patients with IE in the study by Kaasch et al was very low, but some differences between the INSTINCT and SABG cohorts were found. The only criterion that was significantly more frequent in patients with IE in the INSTINCT cohort was the presence of prosthetic heart valve, and in the SABG cohort, documented prolonged bacteremia, presence of a prosthetic heart valve, hemodialysis dependency, and spinal or nonvertebral osteomyelitis were significantly more prevalent. These differences could be attributable to the higher prevalence of methicillin-resistant S. aureus infection (MRSA) in the SABG cohort; however, the authors reject this explanation because prolonged bacteremia was similar in patients with methicillin-susceptible S. aureus and MRSA IE in the SABG cohort. Furthermore, the authors did not provide information about antibiotic treatment or differences in empirical use of β-lactams and vancomycin between Europe and the United States. This information is important because the most likely reason for the worse outcome in SABG is the lower efficacy of glycopeptides [15, 16]. Indeed, in a cohort of 424 patients with S. aureus IE, MRSA-infected patients (n = 141) experienced higher rates of persistent bacteremia than did patients with methicillin-susceptible S. aureus (MSSA) IE (42.6% vs 8.8%; P = .001) [17].

The study by Kaasch et al indicates again the relevance of catheters as a source of IE. In fact, in their study, 14 (26%) of 53 cases of hospital-acquired S. aureus IE were the consequence of a catheter-related bacteremia. This finding is in agreement with a recent report from the International Collaboration on Endocarditis Prospective-Cohort Study [16] that revealed that S. aureus was the most common pathogen among the 1779 cases of definite IE (558 patients; 31.4%) and that health care–associated infection was the most common form of S. aureus IE (218 patients; 39.1%). Although the medical community is making an effort to reduce the incidence of catheter-related infection in intensive care units, short-term catheters in general wards have been forgotten as important and avoidable sources of IE. In the future, in addition to well-known measures to prevent catheter infection, it will be necessary to evaluate other interventions, such as decolonization of nasal carriers of S. aureus, catheters loaded with antibiotics, or use of antibiogram lock solutions directed to patients with high-risk of IE (eg, with heart valve disease, presence of a prosthetic heart valve, or presence of an intracardiac device) who need an intravascular catheter.

In conclusion, the study presented in this issue of Clinical Infectious Diseases provides important information that should be consider in future guidelines of SAB bacteremia.

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