Use of Transthoracic Echocardiography in the Management of Low-Risk *Staphylococcus aureus* Bacteremia

Results From a Retrospective Multicenter Cohort Study

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ABSTRACT

OBJECTIVES The aim of this study was to develop a prediction model to identify patients with low-risk *Staphylococcus aureus* bacteremia (SAB), in whom infective endocarditis (IE) can be ruled out based on transthoracic echocardiogram (TTE).

BACKGROUND *S. aureus* is a major cause of bacteremia and often leads to IE. Current guidelines recommend performing transesophageal echocardiography on all patients or treating all patients empirically with prolonged intravenous antibiotics; however, this approach is resource intensive, many physicians do not adhere to guidelines, and recent studies suggest that low-risk patients may not require transesophageal echocardiography.

METHODS We conducted a retrospective cohort study of 833 consecutive hospitalized patients with SAB from 7 academic and community hospitals in Toronto, Canada, over a 3-year period (2007 to 2010). Patients who received a TTE within 28 days of bacteremia (n = 536) were randomly divided into derivation and validation cohorts. Multivariable logistic regression analysis was used to determine high-risk criteria for IE in the derivation cohort, and criteria were then applied to the validation cohort to determine diagnostic properties.

RESULTS Four high-risk criteria predicted IE: indeterminate or positive TTE (p < 0.001), community-acquired bacteremia (p = 0.034), intravenous drug use (p < 0.001), and high-risk cardiac condition (p < 0.004). In the validation cohort, the presence of any 1 of the high-risk criteria had 97% sensitivity (95% confidence interval [CI]: 87% to 100%) and 99% negative predictive value (95% CI: 96% to 100%) for IE. The negative likelihood ratio was 0.05 (95% CI: 0.007 to 0.35).

CONCLUSIONS A normal TTE ruled out IE in patients without community-acquired SAB, high-risk cardiac conditions, and intravenous drug use. This study provides evidence that clinical risk stratification combined with a normal TTE may be adequate to rule out IE in most patients with SAB. (J Am Coll Cardiol Img 2015;8:924–31) © 2015 by the American College of Cardiology Foundation.

Staphylococcus aureus is a major cause of bacteremia and commonly leads to severe complications (1-3). Infective endocarditis (IE) occurs in up to 25% of cases and is associated with lengthy hospitalization, relapsing bacteremia, and high mortality (3-9). Identification of IE is crucial because patients require a more complex approach to management, which includes prolonged use of intravenous antibiotic therapy (10,11). The majority of patients with IE do not have clinically evident disease at the time of bacteremia, which makes early diagnosis challenging (4,8,12).

Current guidelines for management of *S. aureus* bacteremia (SAB) assume IE, requiring at least 4 weeks of intravenous antibiotic therapy unless a transesophageal echocardiogram (TEE) is negative (13). This is based on historical studies demonstrating that transthoracic echocardiography (TTE) may not be sufficiently sensitive to rule out IE (4). However, performing a TEE on all patients is resource intensive, and clinicians frequently deviate from current guidelines according to TEE availability, patient refusal, and comorbid critical illness (8,14,15).

Modern echocardiographic techniques and equipment have improved TTE sensitivity in SAB, particularly in low-risk patients (16-18). TTE might therefore exclude IE in many patients and eliminate the need for more invasive testing with TEE (19). Thus, we sought to describe the current use of echocardiography in a multicenter SAB cohort in Toronto, Canada. We then tested the potential of a multivariable model to identify low-risk patients, in whom IE can be ruled out based on TTE alone.
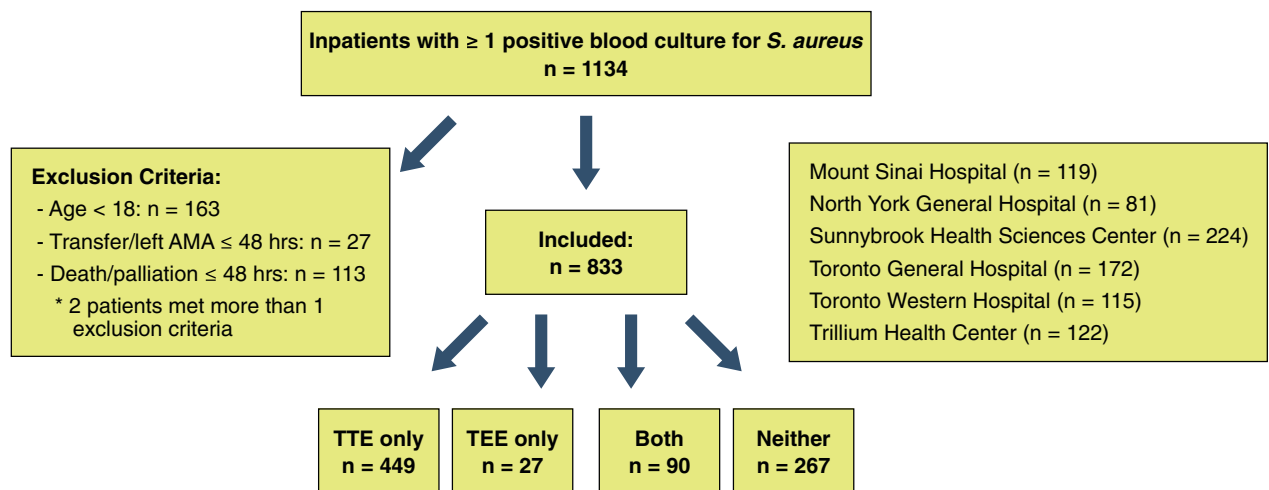
METHODS

PATIENTS AND SETTING. We conducted our study at 7 university-affiliated and community hospitals in the Greater Toronto area. The 7 sites accounted for a total of 3,338 acute care beds and approximately 160,000 annual patient admissions. We obtained approval from the research ethics boards at all sites. We retrospectively identified all inpatients with at least 1 positive blood culture for *S. aureus* from each hospital's microbiology laboratory information system during a 3-year period from April 1, 2007, through March 31, 2010. Five microbiology laboratories provided results for the 7 study sites. All sites used standard methods that conformed to Clinical and Laboratory Standards Institute guidelines for *S. aureus* identification and antimicrobial susceptibilities (20).

We included only adult inpatients (age ≥18 years) with a first SAB episode and excluded patients who died, were deemed suitable for palliative care only, were transferred to another facility, or left against medical advice within 48 h of bacteremia. We entered each patient in the study only once, using the first positive blood culture as the index isolate. Request

FIGURE 1 Flow Diagram of Patients With *Staphylococcus aureus* Bacteremia, Including Type of Echocardiography Performed

Inpatients with ≥ 1 positive blood culture for *S. aureus*
n = 1134

Exclusion Criteria:
- Age < 18: n = 163
- Transfer/left AMA ≤ 48 hrs: n = 27
- Death/palliation ≤ 48 hrs: n = 113
  * 2 patients met more than 1 exclusion criteria

Included:
n = 833

Mount Sinai Hospital (n = 119)
North York General Hospital (n = 81)
Sunnybrook Health Sciences Center (n = 224)
Toronto General Hospital (n = 172)
Toronto Western Hospital (n = 115)
Trillium Health Center (n = 122)

TTE only n = 449 | **TEE only** n = 27 | **Both** n = 90 | **Neither** n = 267

Echocardiography performed within 28 days of bacteremia

AMA = against medical advice; TEE = transesophageal echocardiogram; TTE = transthoracic echocardiogram.