Comparative Sensitivity of Transthoracic and Transesophageal Echocardiography in Diagnosis of Infective Endocarditis Among Veterans With Staphylococcus aureus Bacteremia

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Background. Echocardiography is fundamental for diagnosing infective endocarditis (IE) in patients with Staphylococcus aureus bacteremia (SAB), but whether all such patients require transesophageal echocardiography (TEE) is controversial.

Methods. We identified SAB cases between February 2008 and April 2012. We compared sensitivity and specificity of transthoracic echocardiography (TTE) and TEE for evidence of IE, and we determined impacts of IE risk factors and TTE image quality on comparative sensitivities of TTE and TEE and their impact on clinical decision making.

Results. Of 215 evaluable SAB cases, 193 (90%) had TTE and 130 (60%) had TEE. In 119 cases with both tests, IE was diagnosed in 29 (24%), for whom endocardial involvement was evident in 25 (86%) by TEE, vs only 6 (21%) by TTE (P < .001). Transesophageal echocardiography was more sensitive than TTE regardless of risk factors. Even among the 66 cases with adequate or better quality TTE images, sensitivity was only 4 of 17 (24%) for TTE, vs 16 of 17 (94%) for TEE (P < .001). Among 130 patients with TEE, the TEE results, alone or with TTE results, influenced treatment duration in 56 (43%) cases and led to valve surgery in at least 4 (6%). It is notable that, despite vigorous efforts to obtain both tests routinely, TEE was not done in 86 cases (40%) for various reasons, including pathophysiological contraindications (14%), patient refusal or other patient-related factors (16%), and provider declination or system issues (10%).

Conclusions. Patients with SAB should undergo TEE when possible to detect evidence for IE, especially if the results might affect management.

Keywords. diagnosis; echocardiography; infective endocarditis; Staphylococcus aureus bacteremia; transesophageal echocardiography.

The incidence of infective endocarditis (IE) in patients with Staphylococcus aureus bacteremia (SAB) ranges from 6% to 32% [1–4]. Sensitivity of transthoracic echocardiography (TTE) for detection of IE-consistent valvular abnormalities ranges from 40% to 80%, compared with 93% to 100% for transesophageal echocardiography (TEE) [3, 5–7]. However, TEE is less well tolerated than TTE, associated with ~0.5% risk of major complications and death, and more expensive [8, 9].

Recommendations for echocardiography in SAB cases vary. Infectious Diseases Society of America (IDSA) guidelines for diagnosis of IE [1] recommend echocardiography when IE is suspected, with the choice of TTE or TEE depending on the clinical scenario. Models to identify SAB cases with substantial IE risk have been developed, but the predictive risk factors vary in different studies [7, 10]. The IDSA recommends TEE in all cases of methicillin-resistant S aureus bacteremia [11]. Some experts recommend TEE only when IE is suspected clinically or when TTE image quality is inadequate to exclude IE [12–15]. Others recommend that all patients with SAB undergo TEE [3, 16].

To determine the best approach for patients at the Minneapolis Veterans Affairs Medical Center (MVAMC), physicians from Cardiology and Infections Diseases (ID) Sections agreed to recommend both TTE and TEE for all patients with SAB. In this study, we analyze TTE and TEE test performance in relation to patient characteristics and the impact of TTE and TEE on clinical management. In addition, because we noticed early on that TEE was not done in a large proportion of SAB cases despite our recommendations, for each case without TTE and/or TEE we determined why these tests were not done.

METHODS
The MVAMC is a 320-bed, academically affiliated, tertiary care hospital. Since 2008, MVAMC has required that all patients...
with SAB have ID consultation, because this is associated with improved patient outcomes [17–23]. Infections Diseases consultants recommended both TTE and TEE in almost all cases. The MVAMC Institutional Review Board considered analysis of these data for publication exempt under Title 38 Code of Federal Regulations 16.101(b).

Case Selection
We used microbiology laboratory logs to identify MVAMC patients who, between February 2008 and April 2012, had ≥1 blood culture (BC) yielding S aureus. An SAB case was defined as isolation of S aureus from blood for periods of 1–30 days without gaps lasting ≥10 days. Cases were excluded if the patients died before BCs became positive, the patient was assigned to comfort care within 72 hours after BCs turned positive, providers considered a single BC yielding S aureus to be a contaminant, or the patient was admitted elsewhere or transferred to a different hospital before BCs were positive.

Data collection for each case began promptly after the first BC became positive and included the following: age; gender; underlying medical conditions; and clinical description, including risk factors for endocarditis, laboratory data, and echocardiographic findings. If TTE or TEE was not done, we recorded the reason. Definite IE was diagnosed according to modified Duke Criteria [24]. Antimicrobial courses of <21 days were considered short, and courses of ≥21 days were considered long. Cases were classified as (1) “healthcare-associated” if within the previous year patients resided in a nursing home or had hemodialysis, an indwelling catheter, or an outpatient medical procedure, (2) nosocomial if the onset was ≥72 hours after admission [2, 16, 25], and (3) community-onset if none of these conditions were present.

Cases were considered at risk for relapse if the patient lived until after S aureus therapy was completed. Relapses were defined as a new clinical episode of deep or systemic S aureus infection within 1 year of the case's SAB diagnosis, provided the new S aureus isolate had the same oxacillin susceptibility as the initial isolate. Cases were excluded from analysis for relapses if focal infections present during the initial SAB were not adequately drained or if infected prostheses were not removed and infection recurred at the same site.

Risk factors for IE identified in previous studies were recorded. These included presence of a cardiac implantable electronic device (CIED) [26], persistent fever (≥48 hours after initiation of adequate antimicrobial therapy) [16], prolonged bacteremia (>4 days between the first positive BC reported and the first negative follow-up BC) [26], presence of a prosthetic valve [16], unknown bacteremia source [14, 16], intravenous drug use [3], hemodialysis dependency [26], pre-existing valvular heart disease [4, 27, 28], bacteremia that was not nosocomial [7, 25], and spine infection or nonvertebral osteomyelitis [26].

Echocardiography
Board-certified cardiologists specializing in imaging interpreted each echocardiogram using conventional criteria [29]. Findings suggesting IE (mobile, echo-dense masses attached to valve leaflets, mural endocardium, or CIED leads; perianular abscesses; or new dehiscence of a valvular prosthesis) were identified [24, 29, 30]. Study quality was considered adequate or better when the aortic, mitral, and tricuspid valve anatomy and perivalvular tissues were seen well in multiple views.

Statistical Analysis
We planned to consider 212 SAB cases in order to detect a sensitivity difference between TTE and TEE of 35%. Assumptions included that 15% of SAB cases would not meet inclusion criteria, that 80% of fully evaluable cases would have both TTE and TEE, and that 20% of patients with SAB would have IE [1–6]. We compared sensitivity of TTE and TEE for findings supporting a diagnosis of definite IE [24] with a modified McNemar test [31]. We described group characteristics with means, standard deviations, medians, interquartile ranges, and proportions. We used χ², Fisher’s exact, or Mann-Whitney U tests to compare groups.

RESULTS
During the study period, 239 SAB cases occurred in 219 patients. Twenty-four cases were excluded for reasons listed (Supplementary Figure 1), leaving 215 evaluable SAB cases in 196 patients. Of these, 16 patients had 2 separate SAB cases and 2 had 3 separate cases during the study period. Among the 215 evaluable cases, TTE was done in 193 (90%) and TEE was done in 130 (60%). Transesophageal echocardiography was done in 13 of 48 (21%) community-onset cases, 66 of 66 (100%) healthcare-associated cases, and 50 of 88 (57%) nosocomial cases. Definite IE was diagnosed in 37 of 215 (17%) cases.

The 196 evaluable case patients had a median age of 67 years and 97% were males. Age and selected clinical conditions were distributed similarly among patients who had both TTE and TEE, TTE only, TEE only, or neither TTE nor TEE (Table 1). The median number of positive BCs, median number of days with positive BCs, and percentage of patients with prolonged bacteremia were significantly greater for patients who had both TTE and TEE than for other patients.

Comparative Performance of Transthoracic Echocardiography and Transesophageal Echocardiography
The 119 cases in which both TTE and TEE were done allowed a direct comparison of the sensitivity of these techniques for detection of IE (Table 2). Of 29 (24%) cases with definite IE, endocardial involvement was evident by TEE in 25 cases (86%), but by TTE in only 6 (21%, P < .001). All cases with evidence for IE on TTE also had evidence on TEE. In the 4 (14%) IE cases
without echocardiographic evidence of endocardial involvement, IE was diagnosed because vegetations were found on extracted CIED leads in 1 case and on heart valves at autopsy in another; in the other 2 cases, 1 major and 3 minor modified Duke criteria were fulfilled.

Regarding specificity, there were no false-positive TTE results (Table 2). For TEE, 3 of 90 cases without definite IE had apparent evidence of endocardial involvement (specificity, 97%). All 3 had a single BC yielding *S aureus* and 1 or 2 minor criteria, qualifying as possible but not definite IE [24]. Positive predictive value (PPV) was 6 of 6 (100%) for TTE and 25 of 28 (89%) for TEE. Negative predictive value (NPV) was 90 of 113 (80%) for TTE and 87 of 91 (96%) for TEE.

Comparisons of TTE versus TEE for sensitivity and specificity in relation to IE risk factors showed that TEE was significantly more sensitive than TTE in patients with prolonged bacteremia, persistent fever, pre-existing valvular disease, an unknown source of bacteremia, or at least 1 risk factor for IE. The single IE case that was diagnosed among 14 patients without an IE risk factor was identified by TEE; TTE was negative.

Similarly, TEE was significantly more sensitive than TTE whether patients had nosocomial or healthcare-associated SAB (Table 2). For the 9 community-associated cases, 2 had endocarditis; of these, 1 had positive TEE, and neither had positive TTE. Among the 44 nosocomial SAB cases, TEE was significantly more sensitive than TTE in cases with any IE risk factor and, within this group, in those with a pre-existing valve abnormality and/or possible or documented prolonged bacteremia. Twelve of these 44 cases met none of the clinical prediction criteria associated previously with increased IE risk [26]. Among these 12 low-risk cases, the single IE case was detected by TEE; TTE was negative.

Performance characteristics of TTE and TEE for identification of IE were also assessed in relation to image quality. Of the 193 TTE tests, image quality was judged adequate, good, or excellent in 103 (53%), technically difficult in 57 (30%), and poor or less than adequate in 17 (9%), and was not recorded in 16 (8%). Among the cases with adequate, good, or excellent TTE images, TTE exhibited a sensitivity of 6 of 19 (32%), specificity of 84 of 84 (100%), PPV of 6 of 6 (100%), and NPV of 84 of 97 (87%). In contrast, of the 129 TEE tests, image quality was judged adequate, good, or excellent in 127 (98%) and less than adequate in 2 (2%). Among the former, TEE exhibited sensitivity of 27 of 31 (87%), specificity of 92 of 96 (96%), PPV of 27 of 31 (87%), and NPV of 92 of 96 (96%).
adequate or better quality TTE images, sensitivity was only 4 of 17 (24%) for TTE vs 16 of 17 (94%) for TEE (P < .001). Among the 43 cases with poor or less than adequate quality TTE images, sensitivity was only 2 of 8 (25%) for TTE vs 6 of 8 (75%) for TEE (P = .03).

Previous investigators have attempted to identify IE risk factors that would indicate the need for TEE. Possible IE risk factors in our population were entered into multivariable logistic regression. Among cases with both TTE and TEE, a history of endocarditis, presence of underlying heart disease known to predispose to endocarditis, history of endocarditis, intravenous illicit drug use, source of bacteremia unknown, prolonged bacteremia, prolonged fever, spinal infection, or osteomyelitis.

### Table 2. Sensitivity and Specificity of TTE and TEE for Evidence of Infective Endocarditis

| Population | Infective Endocarditis Rate (%) | Sensitivity (%) | Specificity (%) | Sensitivity (%) | Specificity (%) | P Valuea, Sensitivity of TTE vs TEE |
|------------|---------------------------------|----------------|----------------|----------------|----------------|-----------------------------------|
| All patients | 29/119 (24) | 6/29 (21) | 90/90 (100) | 25/29 (86) | 87/90 (97) | <.001 |
| Bacteremia source unknown | 12/25 (50) | 3/12 (25) | 13/13 (100) | 11/12 (92) | 13/13 (100) | .008 |
| CIED | 6/18 (33) | 1/6 (17) | 12/12 (100) | 4/6 (67) | 12/12 (100) | .25 |
| Hemodialysis | 7/17 (41) | 1/7 (14) | 10/10 (100) | 5/7 (71) | 10/10 (100) | .13 |
| History of endocarditis | 7/9 (78) | 2/7 (29) | 2/2 (100) | 6/7 (86) | 2/2 (100) | .13 |
| Intravenous illicit drug use | 3/5 (100) | 0/3 (0) | 2/2 (100) | 2/2 (100) | 2/2 (100) | NCb |
| Preexisting valvular disease | 18/45 (40) | 3/18 (17) | 27/27 (100) | 15/18 (83) | 27/27 (100) | <.001 |
| Prosthetic heart valve | 1/11 (11) | 0/1 (0) | 8/8 (100) | 1/1 (100) | 8/8 (100) | NCb |
| Septic emboli | 6/6 (100) | 2/6 (33) | 0/0 | 4/6 (66) | 0/0 | .50 |
| Spinal infection or nonspecial osteomyelitis | 2/17 (12) | 1/2 (50) | 15/15 (100) | 2/2 (100) | 14/15 (93) | NCb |
| Persistent fever | 12/44 (27) | 3/12 (25) | 32/32 (100) | 10/12 (83) | 32/32 (100) | .016 |
| Prolonged bacteremia | 18/55 (33) | 3/18 (17) | 37/37 (100) | 14/18 (78) | 37/37 (100) | .001 |
| Nosocomial | 13/44 (30) | 2/13 (15) | 31/31 (100) | 10/13 (77) | 31/31 (100) | .008 |
| Nosocomial, prolonged bacteremia (documented and possible) | 11/25 (44) | 2/11 (18) | 14/14 (100) | 8/11 (73) | 14/14 (100) | .03 |
| Nosocomial, pre-existing heart valve abnormality | 11/23 (48) | 1/11 (9) | 12/12 (100) | 9/11 (82) | 12/12 (100) | .008 |
| Nosocomial, any risk factor for endocarditis | 13/41 (32) | 2/13 (15) | 28/28 (100) | 10/13 (77) | 28/28 (100) | .008 |
| Healthcare-associated | 14/86 (21) | 4/14 (29) | 52/52 (100) | 14/14 (100) | 49/52 (94) | <.001 |
| Any risk factor | 28/105 (27) | 6/28 (21) | 77/77 (100) | 24/28 (86) | 76/77 (99) | <.001 |
| No risk factor | 1/14 (7) | 0/1 (0) | 13/13 (100) | 1/1 (100) | 11/13 (85) | NCb |

Abbreviations: CIED, cardiac implantable electronic device; NC, not calculable; TEE, transeophageal echocardiography; TTE, transthoracic echocardiography.

aModified McNemar test [31]. The data were not corrected for multiple comparisons because of limitations of correction methods with the available sample sizes.

bNot calculable with modified McNemar test.

### Table 3. Risk Factors for Infective Endocarditis in Patients Who Had Both TTE and TEE

| Variable | Odds Ratio | 95% CI | P Value |
|----------|------------|--------|---------|
| History of endocarditis | 10 | 1.5–66 | .017 |
| Source of bacteremia not known | 4.3 | 1.4–13 | .01 |
| Underlying heart disease known to predispose to endocarditis | 3 | 1.0–9 | .045 |

Variables included hemodialysis, presence of underlying heart disease known to predispose to endocarditis, history of endocarditis, intravenous illicit drug use, origin of infection (community associated, healthcare associated, nosocomial), whether source of bacteremia was known, whether Staphylococcus aureus were methicillin resistant, and presence of prolonged bacteremia [26] or prolonged fever [16]. Omnibus Test of Model Coefficients P < .001; Nagelkerke R2 = 0.362, Cox and Snell R2 = 0.243; Hosmer Lemeshow test P = .59. There was no interaction between terms.

IE, the presence of underlying heart disease known to predispose to IE, and unknown source of bacteremia were independent IE risk factors (Table 3). Among 60 patients with 1 or more of these 3 factors, sensitivity was only 5 of 24 (21%) for TTE vs 21 of 24 (88%) for TEE (P < .001). Both had good specificity, ie, 36 of 36 (100%). Although PPV was 5 of 5 for TTE and 21 of 21 for TEE, NPV was only 36 of 55 (66%) for TTE vs 36 of 39 (92%) for TEE. Among the 59 patients without any of these 3 factors, sensitivity was only 1 of 5 (20%) for TTE vs 4 of 5 (80%) for TEE. Specificity was 54 of 54 (100%) for TTE vs 51 of 54 (94%) for TEE. The PPV was 1 of 1 for TTE vs 4 of 7 (57%) for TEE. The NPV was 54 of 58 (93%) for TTE vs 51 of 52 (98%) for TEE.

### Effects of Transthoracic Echocardiography and Transesophageal Echocardiography Results on Management

To quantify the impact of echocardiogram results on clinical management, we determined whether they influenced treatment duration and/or a decision to perform surgery. Among the 8 cases with positive TTE and no TEE, therapy was lengthened in all 8 (Table 4). Among the 66 cases with negative TTE and no TEE, therapy was shortened in 23 (35%). Surgery was not performed in any case with TTE and no TEE. Among the
In the case with relapse, IE was diagnosed contemporaneously with initial SAB, and duration of therapy was 6 weeks. Ten weeks later, SAB recurred with IE and discitis.

In the 2 cases with relapse, IE was not diagnosed initially, and duration of therapy was 2 weeks. SAB recurred within 4 months, and IE was indicated by the presence of vegetations.

Definitions: At risk for relapse = patient lived until after therapy was completed; relapse = new clinical episode of deep or systemic bacteremia; TEE, transthoracic echocardiography.

NOTE: No cases had positive TEE and negative TEE.

**Comparative Sensitivity of TTE and TEE in Diagnosis of Infective Endocarditis**

Infective endocarditis was present contemporaneously with the initial episode in only 1 case, TTE and TEE were both positive in 2. Definite IE was diagnosed in 2 of the 22 cases without TEE. Therefore, the sensitivity of TTE was 82% (22/27), and TEE was 100% (22/22). The specificity of TTE was 97% (21/22), and TEE was 100% (22/22). The positive predictive value of both TTE and TEE was 96% (22/23), and the negative predictive value of both TTE and TEE was 99% (21/21). The positive and negative predictive values of TEE were both 100% (22/22) and 100% (21/21), respectively.

**DISCUSSION**

Our main goal was to compare the performances of TTE versus TEE for detecting evidence of IE among patients with SAB. Among the 119 SAB cases in which both TTE and TEE were done, IE was diagnosed in 29 (24%). For these 29 cases, TEE was significantly more sensitive than TTE (86% vs 21%; P < .001), similar to previous reports [3–5, 32]. This was especially true for the 105 cases among patients with IE risk factors (Table 2). In addition, 14 of the 119 patients who underwent both TEE and TEE were positive in 6, therapy was lengthened in all 6, and surgery was performed in 4 (67%). Transthoracic echocardiography was negative and TEE was positive in 22, therapy was lengthened in 16 (73%), and surgery was performed in 4 (18%). Transthoracic echocardiography and TEE were both negative in 91, therapy was shortened in 38 (42%), and surgery was not performed in any of the 91. In the 38 cases in which therapy was shortened, provider notes and/or the timing of the decision suggested that it was the TEE results that led to shorter therapy. Among the 11 cases that had only TEE, positive TEE results (n = 3) led to lengthened therapy in 2, whereas negative results (n = 8) led to shortened therapy in 2.

Out of concern that short therapy courses might result in relapse, we quantified relapse frequency among the 191 at-risk cases (Table 4). Overall, relapse occurred in 13 cases (7%). Infective endocarditis was present contemporaneously with the initial episode in only 1 case, TTE and TEE were both positive, therapy lasted 6 weeks, and then IE recurred along with discitis 10 weeks later. Four relapses occurred in cases with negative TTE results and no TEE. Of these, 2 of the 4 relapses occurred in 23 cases with short courses, and in both instances SAB relapsed along with evidence for IE. The other 2 relapses occurred among the 33 with long courses, and neither had evidence of IE. Seven relapses occurred among the 89 at-risk cases with negative results in both TTE and TEE. Of these, 5 relapses occurred among the 38 cases with short courses, and the other 2 relapses occurred among the 51 cases with long courses. None of these 7 cases had evidence of IE. Finally, 1 relapse occurred in a case in which no echocardiograms were done, and there was no evidence of IE.

**Reasons Why Echocardiography Was Not Performed**

Transthoracic echocardiography was not done in 86 (40%) of the 215 evaluable cases. In 31 cases (14%), TEE was not done because of pathophysiological contraindications (Table 5); TTE was done in all 31. In 35 cases (16%), TEE was not done because of patient refusal or other patient-related factors; TTE was done in 29 (83%) of these patients but not in 4 patients in comfort care status and 2 who had TTE within the previous 10 days. Finally, TEE was not done in 20 cases (9%) and TTE was done in 16 cases (7%) because of provider declination or system issues. Definite IE was diagnosed in 6 of the 86 cases (7%) without TEE. In these 6, TEE was not done because of increased risk in 4 and patient refusal or intolerance in 2. Definite IE was diagnosed in 2 of the 22 cases without TTE. In both, TTE was not done because of provider error or cancellation.

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and TTE had a low prior probability of IE, and in the single such case that was diagnosed with IE, TEE was crucial for diagnosis.

Infective endocarditis is uncommon among patients without IE risk factors [1, 13, 14, 26, 33–35]. For example, in one study, IE occurred in only 1 of 208 cases of nosocomial SAB among patients without prolonged bacteremia, a permanent intracardiac device, hemodialysis dependency, spinal infection, or non-vertebral osteomyelitis [26]. An unresolved question is whether IE is uncommon enough in patients without IE risk factors that the risks and costs associated with TEE outweigh the benefits of the improved diagnostic certainty it provides regarding presence/absence of IE. If a patient with no risk factors for IE has another need for prolonged therapy, it would probably be acceptable to not perform TEE. However, if such a patient had an indication for valve surgery, this might be missed without TEE.

We compared the performance characteristics of TTE and TEE according to image quality for the 119 cases in which both TTE and TEE were done. As expected, in the 43 cases in which TTE image quality was less than adequate, sensitivity was much worse for TTE (2 of 8, vs 6 of 8 for TEE). However, this was true even in the 66 cases in which TTE image quality was adequate or better (4 of 17 for TTE, vs 16 of 17 for TEE). Others have advocated that TEE is needed only when TTE image quality is inadequate [1, 5, 6, 12–14, 16, 33, 36]. In our study, 13 of 17 IE cases were missed by TTE despite adequate or better quality images, and TEE was positive in 12 of these 13.

Transesophageal echocardiography results influenced IE management. Of the 130 patients with TEE, results of TEE, by themselves or combined with TTE results, led to longer antimicrobial courses in at least 18 (14%) cases, shorter courses in 38 (42%), and surgery in 8 (6%) (Table 4). In 16 cases, TEE demonstrated IE when TTE was negative, and therapy was extended as a result. In most of the 38 cases in which TTE and TEE results were both negative and therapy was shortened, providers were confident enough to do so only when they had negative TEE results. Although relapses occurred in 7 cases in which therapy was shortened, in no case was a negative TEE result followed by a diagnosis of IE during follow up.

We systematically encouraged providers to request both TTE and TEE in almost all SAB cases. Echocardiography was done in 205 of 216 (95%) cases, a much greater percentage than in previous reports [14, 26, 34, 37–40]. We anticipated that at MVAMC, the absence of financial barriers and strong encouragement from ID consultants would lead providers to obtain

Table 5. Reasons Why TTE and/or TEE Were Not Done in 96 Cases of Staphylococcus aureus Bacteremia

| Reasons Why TEE and/or TEE Were Not Done | No TEE (n = 74) | No TTE (n = 10) | No TEE or TTE (n = 12) |
|-----------------------------------------|----------------|----------------|-----------------------|
| **Increased risk of TEE**               |                |                |                       |
| Gastrointestinal                        |                |                |                       |
| Dysphagia                               | 6 (8%)         | 0              | 0                     |
| Anatomic abnormality                    | 4 (5%)         | 0              | 0                     |
| Bleeding                                | 1 (1%)         | 0              | 0                     |
| Prior esophagectomy                     | 1 (1%)         | 0              | 0                     |
| Pulmonary                               |                |                |                       |
| Respiratory distress                    | 6 (8%)         | 0              | 0                     |
| Musculoskeletal                         |                |                |                       |
| Cervical spine instability              | 2 (3%)         | 0              | 0                     |
| Unable to position patient with arthritis | 2 (3%)     | 0              | 0                     |
| Otolaryngological                       |                |                |                       |
| Prior oropharynx or larynx cancer       | 3 (4%)         | 0              | 0                     |
| Hematologic                             |                |                |                       |
| Thrombocytopenia or coagulopathy        | 3 (4%)         | 0              | 0                     |
| Psychiatric or neurological             |                |                |                       |
| Delirium or dementia                    | 3 (4%)         | 0              | 0                     |
| **Subtotal**                            | 31 (42%)       | 0              | 0                     |
| **Patient refusal or intolerance or recent TTE** |            |                |                       |
| Patient refused                         | 21 (28%)       | 0              | 0                     |
| Patient transitioned to comfort care    | 4 (5%)         | 0              | 4* (33%)              |
| Patient intolerant of TEE              | 5 (7%)         | 0              | 0                     |
| TTE within previous 10 days             | 0              | 2 (20%)        | 0                     |
| Patient transferred to another hospital | 1 (1%)         | 0              | 0                     |
| **Subtotal**                            | 31 (42%)       | 2 (10%)        | 4 (33%)               |
| **Provider or ID decision or system issue** |            |                |                       |
| Cancelled by primary provider           | 0              | 3 (30%)        | 0                     |
| No TEE or TTE order, despite ID recommendation | 6 (8%)      | 3 (30%)        | 3* (25%)              |
| No ID consult                           | 0              | 0              | 5* (42%)              |
| ID consultant did not recommend TEE     | 3 (4%)         | 0              | 0                     |
| Error in order process                  | 3 (4%)         | 2 (20%)        | 0                     |
| **Subtotal**                            | 12 (16%)       | 8 (80%)        | 8 (66%)               |

Abbreviations: ID, infectious diseases; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

*aData are expressed as n (column percent).

*bIn each of these cases, TTE and TEE were not done for the same reasons.*
both TTE and TEE in most patients. On the contrary, although TTE was done in 90% of cases, TEE was done in only 60%.

Our analysis of the reasons why TTE or TEE was not done implicated provider-related factors in 16 (73%) of 22 cases in which TTE was not done but in only 21 (24%) of 86 cases in which TEE was not done (Table 5). Pathophysiological and patient-related factors accounted for most cases in which TEE was not done. Some of the pathophysiological contraindications appeared relative or modifiable (eg, thrombocytopenia or impaired coagulation), such that TEE might have been done safely. Many provider-related factors could be anticipated and overcome, but it is still unlikely that TEE will be obtained in all patients. These data add considerably to the scant available information about why TEE is not performed in some SAB cases [3, 34, 37].

This study has multiple strengths. First, the Veterans Affairs (VA) electronic health record system enabled excellent case ascertainment. Second, ID consultants assessed all patients with SAB and encouraged both TTE and TEE for all. Third, echocardiograms were interpreted by clinical cardiologists assigned to read echocardiograms within 1 day after test performance, consistent with typical clinical practice. Fourth, most VA patients receive consistent care and follow up, which probably increased the likelihood that S aureus infection diagnosed after discharge would be recognized.

The study also has limitations. First, despite encouragement by ID consultants, TTE was done in only 90% and TEE in only 60% of SAB cases. Second, interpretation of echocardiograms is subjective and reader-dependent, which limits generalizability. Third, the study was observational. The patients in whom both TTE and TEE were done had more BCs and more often had prolonged bacteremia, suggesting that their IE incidence was greater than among patients with only 1 or no echocardiogram. Consequently, the observed comparative performance of TTE vs TEE likely applies best to patients at moderate or high risk for IE; the likely smaller yield among patients at lower risk for IE may be insufficient to justify the risk and expense of doing both tests. Fourth, the study included only veterans, which limits its generalizability but increases its relevance to veterans. Fifth, echocardiography results were used to make IE diagnoses, which were then used to assess test performance for TTE versus TEE. This inherent circularity, which confounds all studies of the value of echocardiography in SAB, reflects the absence of a practical external standard. Sixth, the readers of the second echocardiogram in individual cases were not blinded to the results of the first echocardiogram, although this reflects typical clinical practice.

CONCLUSIONS

This study contributes 3 important new insights. First, among the 119 cases with both TTE and TEE, in 19 (16%) cases TEE demonstrated valvular vegetations not seen on TEE. In no identifiable subset would TTE have sufficed to exclude IE with confidence; TEE added important information for all subsets. Second, TEE results impacted management for from 13% to 49% of cases, indicating that the added information it provided was regarded as actionable. Third, explanations were found for why TEE is unlikely to be performed in a large minority of patients; this should be reflected in management strategies [1] and patient-specific diagnostic and management plans. Although a subset of patients will likely refuse or have unavoidable contraindications to TEE, we recommend TEE for all other patients with SAB if diagnosing IE would affect management [1, 29].

Supplementary Data

Supplementary materials are available at Open Forum Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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