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The Role of Transthoracic Echocardiography in *Staphylococcus aureus* Bacteremia; A Retrospective Chart Review

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Abstract

Background:
Evaluation for endocarditis is an essential step in the management of patients with *Staphylococcus aureus* bacteremia (SAB). A common approach, consistent with preeminent national guidelines, is to perform transthoracic echocardiography (TTE) followed by transesophageal echocardiography (TEE) in the majority of patients with SAB. It is unclear how often patient management decisions are influenced by the results of TTE versus TEE.

Methods:
This retrospective chart review evaluated adult veterans at a single large Veterans Affairs medical center who had SAB and completed both TTE and TEE (n = 206 episodes of SAB). The timing of key patient-management decisions was correlated to the timing of each patient's TTE and TEE. It was then inferred whether each management decision could have been informed by TTE alone versus TTE plus subsequent TEE. Management decisions included: documentation of antibiotic treatment duration, initiation of synergistic antibiotics, consultation of relevant specialists, ordering of relevant imaging studies, and performance of valve surgery or cardiac device explantation.

Results:
The primary outcome (any of the five management decisions taking place) occurred after completion of TTE but prior to TEE in 27 SAB episodes (13.1%). The primary outcome occurred after both TTE and TEE in 178 SAB episodes (86.4%).

Conclusion:
Among patients with SAB who are felt to warrant TEE imaging for endocarditis evaluation, performance of a TTE prior to the TEE rarely prompts patient management decisions.

Introduction

Background:
Evaluation for endocarditis is an essential step in the management of patients with *Staphylococcus aureus* bacteremia (SAB). Preeminent national guidelines recommend that patients with SAB undergo both transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) as part of their workup to evaluate for infectious endocarditis¹⁻³.

Numerous studies have shown that TEE is a more sensitive study than TTE for the detection of endocarditis⁴⁻¹² and other cardiac complications^{5, 13-14} in the setting of SAB. Cost-analyses have found that TEE is more cost-effective than TTE for guiding patient management^{15, 16}. It is unclear how often patient management decisions are influenced by the results of TTE versus TEE.

Study Aims:
This retrospective chart review looked at patients with an episode of SAB who underwent both TTE and TEE and measured the timing of key management decisions relative to the time of TTE and TEE completion. The specific aim was to explore how often important management decisions were made following TTE but prior to TEE.

This study has implications for improving patient safety in the Veteran population. By offering insight into the usefulness of current endocarditis testing, we hope to improve resource utilization and expedite effective endocarditis workup at this VA hospital and other hospitals.

List of Abbreviations:
ICD Implantable cardioverter-defibrillator
SAB *Staphylococcus aureus* bacteremia
TEE Transesophageal echocardiography
TTE Transthoracic echocardiography

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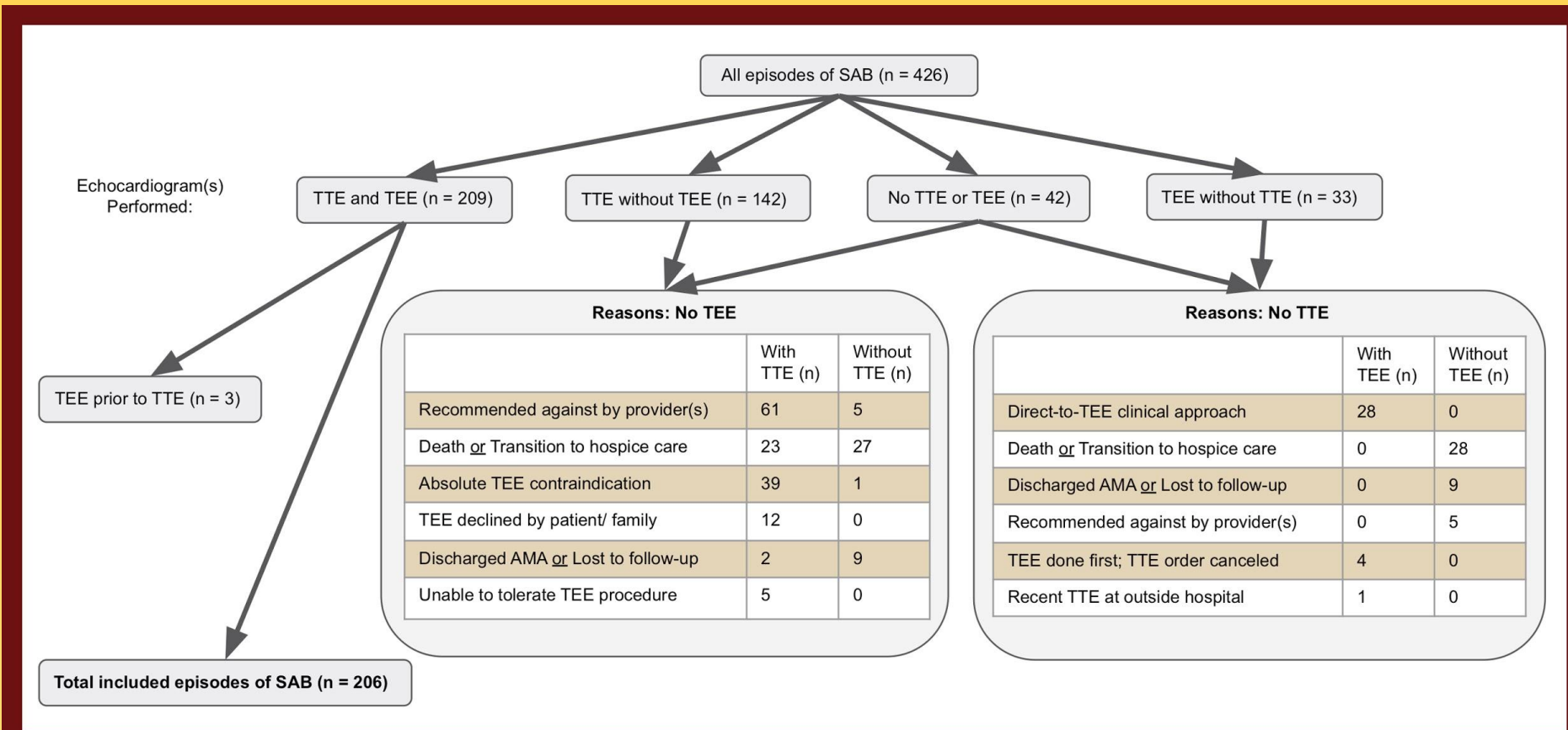


Figure 1: Flow Diagram of All Patients with an Episode of *Staphylococcus aureus* Bacteremia. All excluded patients who did not undergo TTE and/or TEE have the reason for not undergoing one or both studies listed.

Baseline Characteristics: Included Patients	Percent of Patients
Patient Demographics & Background	
Age- median (years)	67.5
Age (years)	
18-34	2 1.0%
35-49	6 2.9%
50-64	70 34.0%
65-79	104 50.5%
80+	24 11.7%
Sex- female	3 1.5%
Sex- male	203 98.5%
Relevant cardiac history	
Presence of implantable cardioverter-defibrillator (ICD) or pacemaker	26 12.6%
Presence of prosthetic heart valve (mechanical or bioprosthetic)	8 3.9%
History of endocarditis	3 1.5%
Bacteremia Characteristics	
MSSA	150 72.8%
MRSA	55 26.7%
MSSA and MRSA	1 0.5%
Bacteremia duration- average (days)	3.1
Bacteremia duration- median (days)	2
Bacteremia duration (days)	
≤1 day	97 47.1%
2-3 days	42 20.4%
4-5 days	36 17.5%
5-9 days	21 10.2%
10+ days	10 4.9%
Diagnosis of endocarditis	35 17.0%
Initial bacteremia source	
Skin and soft tissue (with or without underlying osteomyelitis)	76 36.7%
Vascular access (central line/ venous access port/ AV graft)	32 15.5%
Genitourinary	15 7.2%
Primary septic arthritis (with or without orthopedic hardware)	14 6.8%
Other sources	18 8.7%
Unclear/ unidentified	52 25.1%
Bacteremia associated with IV drug use	3 1.4%

Table 1: Baseline Patient Characteristics and Bacteremia Characteristics.

Echocardiography Timing	Time of Number of Patients	Percent of Patients
Timing Between Echocardiography Order & Completion		
Average time between TTE order and TTE completion	0d 16h 38m	
Average time between TEE order and TEE completion	1d 23h 26m	
Relative Timing of TTE & TEE Completion		
Average time between TTE completion and TEE completion	2d 23h 32m	
Time between TTE completion and TEE completion:		
< 24 hours	49	23.8%
24- 48 hours	41	19.9%
48- 72 hours	35	17.0%
72- 96 hours	28	13.6%
96- 120 hours	24	11.7%
> 120 hours (> 5 days)	29	14.1%
Relative Timing of TTE & TEE Orders		
Average time between TTE order and TEE order	1d 16h 44m	
Time between TTE order and TEE order:		
TEE ordered at same time (within 1 hour) as TTE	28	13.6%
TEE ordered 1-24 hours after TTE ordered	89	43.2%
TEE ordered > 24 hours after TTE ordered	117	56.8%
TEE order placed after TTE completion	164	79.6%

Table 2: Observed Echocardiography Timing

Primary & Secondary Outcomes	Number of Patients	Percent of Patients
Primary Outcome: Occurrence of any of the Five Secondary Outcomes		
All SAB episodes (n = 206)		
After TTE, prior to TEE	27	13.1%
After TTE & TEE	178	86.4%
Primary Outcome: Stratified: Occurrence of any of the Five Secondary Outcomes		
Patient ultimately diagnosed with endocarditis (n = 35)		
After TTE, prior to TEE	6	17.1%
After TTE and TEE	34	97.1%
Secondary Outcomes: Management Decision Timing Relative to Echocardiography		
1. Antibiotic treatment duration documented		
Prior to TTE	3	1.5%
After TTE, prior to TEE	8	3.9%
After TTE and TEE	176	85.4%
2. Synergistic antibiotics ordered		
Prior to TTE	2	1.0%
After TTE, prior to TEE	1	0.5%
After TTE and TEE	16	7.8%
3. Relevant consult(s) ordered		
Prior to TTE	11	5.3%
After TTE, prior to TEE	14	6.8%
After TTE and TEE	19	9.2%
4. Relevant imaging ordered		
Prior to TTE	2	1.0%
After TTE, prior to TEE	4	1.9%
After TTE and TEE	10	4.9%
5. Valve surgery or ICD/ pacemaker removal performed		
Prior to TTE	0	0.0%
After TTE, prior to TEE	0	0.0%
After TTE and TEE	6	2.9%

Table 3: Primary and Secondary Outcomes: The timing of key patient-management decisions relative to completion of TTE & TEE

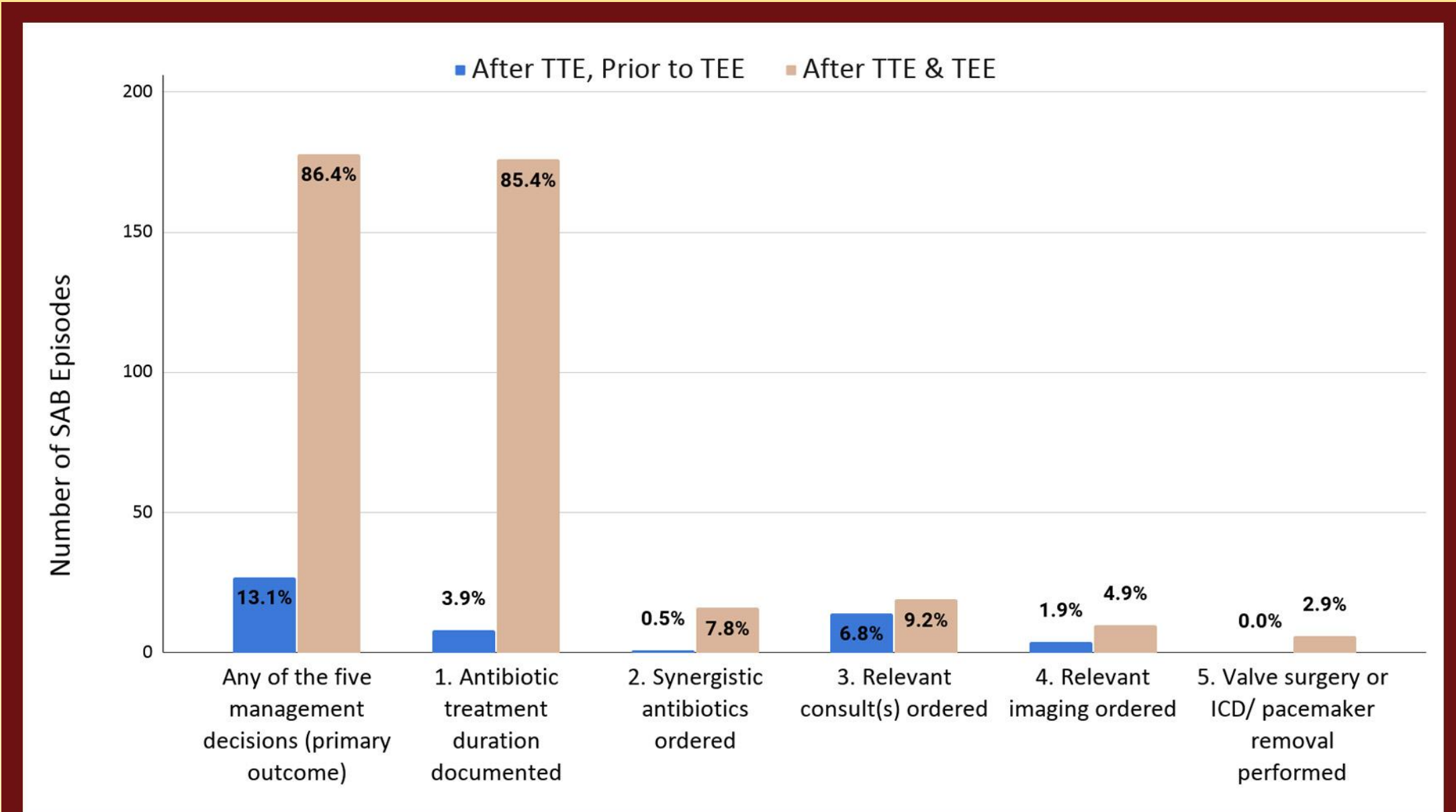




Figure 2: Primary and Secondary Outcomes- Exploring the timing of key patient-management decisions relative to completion of TTE & TEE. Blue bars reflect patient-management decisions made after completion of TTE but prior to TEE. Brown bars represent patient-management decisions made after completion of both TTE and TEE.

QR code link to complete methods and study protocol:



QR code link to additional results and discussion:



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Methods

This was a retrospective chart review performed at the Minneapolis VA Medical Center, a large tertiary-care hospital serving the Veteran population. Adult patients who had an episode of SAB (at least 1 blood cultures positive for *Staphylococcus aureus*) between April 2012 and December 2019 were screened. Patients who underwent sequential TTE and TEE as part of an inpatient endocarditis workup were eligible for inclusion. Exclusion criteria included (1) not completing both TTE and TEE at the Minneapolis VA Hospital within 6 weeks from the time of the initial positive *Staphylococcus aureus* blood culture or (2) completing TEE prior to TTE.

Among the patients who met all inclusion criteria, we recorded the occurrences and timing of 5 key patient-management decisions which were considered to be potentially influenced by echocardiography results:

- (1) **Documentation of antibiotic treatment duration**- The formal recommendation of a defined antibiotic treatment course in an ID consult note without preceding caveats such as "at least..." or "likely will need..." (Hospital protocol required ID consultation for all patients with SAB)
- (2) **Ordering of synergistic antibiotics**- The addition of rifampin, gentamicin, daptomycin, and/or ceftaroline to a primary antistaphylococcal antibiotic.
- (3) **Ordering of relevant consultation(s)**- Consults to Cardiology and Cardiac Surgery were considered "relevant" in all patients. Consults to Cardiology-Electrophysiology were considered "relevant" only in patients with an implantable cardioverter-defibrillator (ICD) or pacemaker.
- (4) **Ordering of relevant imaging**- "Relevant imaging" was defined as any CT or MRI study which requested evaluation for "septic emboli," "metastatic infection," and/or "seeding" as per the listed indication or as documented anywhere else in the imaging order.
- (5) **Performance of valve surgery or ICD/ pacemaker explantation**- Valve surgeries included valve replacement, valve repair, and/or myocardial abscess drainage.

The time of each management decision was simply compared to the time the patient completed TTE and TEE to infer which of the echocardiograms *could* have influenced each management decision. The primary outcome was a composite of any of the five management decisions occurring during a SAB episode. Each of the five management decisions was an individual secondary outcome.

This study was reviewed by the Institutional Review Board (IRB) and determined to be IRB-Exempt. See QR code (below center) for full study protocol.

Results

There were 426 episodes of SAB identified at our hospital between April 2012 and December 2019. Of these, 206 episodes met all inclusion criteria (involving 190 unique patients). 220 SAB episodes were excluded (**Figure 1**). Of the included patients, the median age was 67.5 years old. The vast majority of Veteran patients were male: 203 (98.5%). An ICD or permanent pacemaker was present in 26 patients (12.6%). Prosthetic heart valves were present in 8 patients (3.9%). Average bacteremia duration was 3 days; median duration was 2 days. The most common source was skin/ soft tissue infections (with or without underlying osteomyelitis) which accounted for 76 SAB episodes (36.7%). 52 SAB episodes were of unclear source (25.1%). IV drug use was determined to play a role in 3 SAB episodes (1.5%). In 35 SAB episodes (17.0%), the patient was ultimately diagnosed with endocarditis per ID documentation using the Modified Duke Criteria (**Table 1**). Serious TEE complications occurred in 0 patients (0.0%). The average time between TTE completion and TEE completion was 72.0 hours. (**Table 2**).

The primary outcome (any of the five management decisions taking place) occurred after TTE but prior to TEE in 27 SAB episodes (13.1%). The primary outcome occurred after both TTE and TEE in 178 SAB episodes (86.4%). Antibiotic treatment duration was documented after TTE but prior to TEE in 8 SAB episodes (3.9%) and after both TTE and TEE in 176 SAB episodes (85.4%). Synergistic antibiotics were ordered after TTE but prior to TEE in 1 SAB episode (0.5%) and after both TTE and TEE in 16 SAB episodes (7.8%). Relevant consults were ordered after TTE but prior to TEE in 14 SAB episodes (6.8%) and after both TTE and TEE in 19 SAB episodes (9.2%). Relevant imaging was ordered after TTE but prior to TEE in 4 SAB episodes (1.9%) and after both TTE and TEE in 10 SAB episodes (4.9%). Valve surgeries, ICD explantation, and/or pacemaker explantation always took place after both TTE and TEE and occurred in 6 patients (2.9%) (**Table 3**) (**Figure 2**).

Conclusion

Among patients with *Staphylococcus aureus* bacteremia who are felt to warrant TEE imaging for endocarditis evaluation, performance of a TTE prior to the TEE rarely prompts patient management decisions.



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