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Role of echocardiography in uncomplicated *Staphylococcus aureus* catheter-related bloodstream infections

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Abstract

Uncomplicated bacteremia and catheter-related bloodstream infection (CRBSI) are frequently suggested as factors associated with low risk of infective endocarditis in *Staphylococcus aureus* bacteremia (SAB). Nevertheless, guidelines recommend that echocardiography in all patients with SAB. We evaluated the effects of echocardiography on patient outcomes. Patients with uncomplicated *S. aureus* CRBSI were retrospectively identified between January 2013 and June 2018 at a 1950-bed, tertiary-care university hospital. Treatment failure was defined as any case of relapse or all-cause death within 90 days. Of 890 SAB patients, 95 with uncomplicated *S. aureus* CRBSI were included. Thirty-two patients underwent echocardiography within 30 days of their first positive blood culture. Two patients who underwent echocardiography revealed right-sided infective endocarditis. One patient who did not undergo echocardiography experienced recurrent SAB (peripheral CRBSI) 85 days after his first positive blood culture. There were no SAB-related deaths. The Kaplan–Meier curves of treatment failure showed no significant differences between patients who did and did not undergo echocardiography ($P = .77$). In multivariable analysis, risk factors for treatment failure were liver cirrhosis (hazard ratio: 9.60; 95% confidence interval: 2.13–43.33; $P = .003$) and other prostheses (hazard ratio: 63.79; 95% confidence interval: 5.05–805.40; $P = .001$). This study did not verify the putative association between treatment failure and implementation of echocardiography in patients with uncomplicated *S. aureus* CRBSI. Given the low observed rates of adverse outcomes, routine echocardiography might not be obligatory and could be performed on an individual basis.

Abbreviations: CRBSI = catheter-related bloodstream infection, IE = infective endocarditis, IQR = interquartile range, SAB = *Staphylococcus aureus* bacteremia, TEE = transesophageal echocardiography, TTE = transthoracic echocardiography.

Keywords: catheter-related bloodstream infection, echocardiography, *Staphylococcus aureus*, uncomplicated bacteremia

1. Introduction

Staphylococcus aureus bacteremia (SAB) is a serious infection associated with high morbidity and mortality because it often causes metastatic infections and complications including infective endocarditis (IE).[1] *S. aureus* is one of the most common pathogens of IE, and the frequency of IE among SAB ranges between 2.7% and 23.4%.[2–4] Because of the risk of IE, current guidelines recommend echocardiography in all patients with SAB.[2,5] However, despite these recommendations, the frequency and strategy of echocardiography in patients with SAB vary among hospitals, and management decisions are often made without echocardiography.[6,7] Furthermore, many studies have attempted to identify groups at low risk of IE among patients with SAB and evaluated the necessity of echocardiography, especially transesophageal echocardiography (TEE).[8–20] These studies have identified factors associated with IE and suggested that patients at low risk of IE may need not TEE or even transthoracic echocardiography (TTE).

Among the factors associated with low risk of IE in patients with SAB, uncomplicated bacteremia and catheter-related bloodstream infection (CRBSI) have been frequently suggested, although the definitions of those were different among studies.[11–14] Furthermore, uncomplicated CRBSI can be treated with a minimum of 14 days of antibiotic, even if TEE shows silent vegetation.[5,21,22] Therefore, implementation of echocardiography may offer minimal or no benefit to these patients. We

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performed the present study to evaluate the role of echocardiography in patients with uncomplicated *S. aureus* CRBSI by comparing clinical outcomes depending on the implementation of echocardiography.

2. Methods

2.1. Study population

We retrospectively identified patients (age ≥ 18 years) with *S. aureus* isolated from ≥1 blood culture and symptoms or signs of infection (fever ≥ 38°C, chills, or hypotension) who were treated from January 2013 to June 2018 at Samsung Medical Center, a 1950-bed tertiary-care university hospital in Seoul, South Korea. Only the first episodes were included in the study. We excluded patients with complicated bacteremia, polymicrobial bacteremia (isolation of more than 1 microbial species from an episode), and cases that were not treated for SAB considered to represent contamination. The patients who had only 1 positive blood culture collected from the central catheter were excluded, because their positive blood culture may represent colonization of the catheter rather than true bacteremia. Patients who were discharged or died within 7 days from initial positive culture also were excluded. Follow-up data were collected for 90 days, if not until death or loss of follow-up.

2.2. Definition and data acquisition

Complicated bacteremia was identified if patients satisfied at least one of the following criteria[5]:

1) persistent bacteremia;
2) no defervescence within 3 days of initiating effective therapy;
3) evidence of metastatic sites of infection;
4) presence of implanted intracardiac prostheses.

Endocarditis was excluded from the criteria because occurrence of IE was one of the outcomes in this study. Only patients who met the modified Duke criteria for definite IE were considered to represent IE.[23] Persistent bacteremia was defined as persistently positive blood cultures for ≥4 days (documented) or no negative follow-up blood culture within 4 days (possible).[9] Initial effective therapy was defined as intravenous antibiotics with in vitro activity against isolated *S. aureus* excluding single aminoglycoside or rifampicin.[24] Defervescence was defined as an afebrile state in which tympanic body temperature remained lower than 38.0°C for at least 48 hours. Metastatic infection was defined as deep-seated infection caused by hematogenous seeding, including osteomyelitis, psoas muscle abscess, septic pulmonary embolism, mycotic aneurysm, septic cerebral emboli, and suppurative thrombophlebitis. If metastatic infection was not clearly distinguished from primary infection, the decision depended on the clinician's judgement. The onset of bacteremia was classified as nosocomial, healthcare associated, or community acquired.[25] Nosocomial bacteremia was defined as positive blood culture obtained from patients who had been hospitalized for 48 hours or longer. Healthcare-associated bacteremia was defined as positive blood culture obtained within 48 hours of admission from a patient who fulfilled any of the following criteria:

1) received intravenous therapy at home, received wound care or specialized nursing care through a healthcare agency, or received intravenous medical therapy in the previous 30 days;
2) attended a hospital or hemodialysis clinic or received intravenous chemotherapy in the previous 30 days;
3) was hospitalized in an acute care hospital for at least 2 days in the previous 90 days;
4) or resided in a nursing home or long-term care facility.

Otherwise, we classified the infection as community acquired. Definite CRBSI was defined by any of following[12,22]:

1) growth of $>10^2$ colony-forming units from a catheter tip by quantitative culture;
2) differential time to positivity meeting CRBSI criteria;
3) evidence of inflammation at the catheter insertion site and absence of another identified source of bacteremia.

Primary bacteremia in patients with intravascular catheter without other definitive source of bacteremia was considered to represent probable CRBSI.[12]

Additional collected data were the following: age, sex, microbiologic and echocardiographic data, underlying diseases, laboratory data, immunosuppression, and duration of antibiotic treatment. Echocardiographic data were included within 30 days of the first positive blood culture and classified as negative, equivocal, or positive findings.[26] The equivocal findings included no visible vegetation but native valves with more than mild thickening, calcification, or valvular regurgitation and extremely poor or non-diagnostic views. Positive findings were defined by visible vegetations.

2.3. Blood culture and antibiotic susceptibility testing

All blood cultures were obtained from peripheral veins or central venous catheters (CVCs). A Bactec-9240 system (Becton Dickinson, Sparks, MD) or a BacT/Alert 3D system (bioMérieux Inc., Marcy l'Etoile, France) was used for blood cultures. A Vitek II automated system (bioMérieux Inc.) was used for antibiotic susceptibility testing.

2.4. Study outcomes

To evaluate the usefulness of echocardiography in uncomplicated cases of *S. aureus* CRBSI, the outcome measures were occurrence of IE, relapse, SAB-related death, all-cause death, and treatment failure within 90 days after initial positive blood culture. Relapse was defined as reappearance of SAB with an organism showing an identical antimicrobial susceptibility profile.[27] SAB-related death was considered if death occurred within 10 days of SAB, with sepsis continuing up to death and no other infectious cause.[7] Treatment failure included any cases of relapse or all-cause death.

2.5. Statistical analysis

Continuous variables are presented as median (interquartile range [IQR]) or mean ± standard deviation, and categorical variables as frequency count (percentage). Comparisons of continuous variables between patients who did and did not undergo echocardiography were performed using Student's *t* test or the Mann–Whitney *U* test according to the results of normality tests. Fisher's exact test or chi-square test was used to compare categorical variables. The relationship between treatment failure and the implementation of echocardiography was evaluated by the Kaplan–Meier method using the log-rank test. Univariate Cox proportional hazard models were used to identify risk

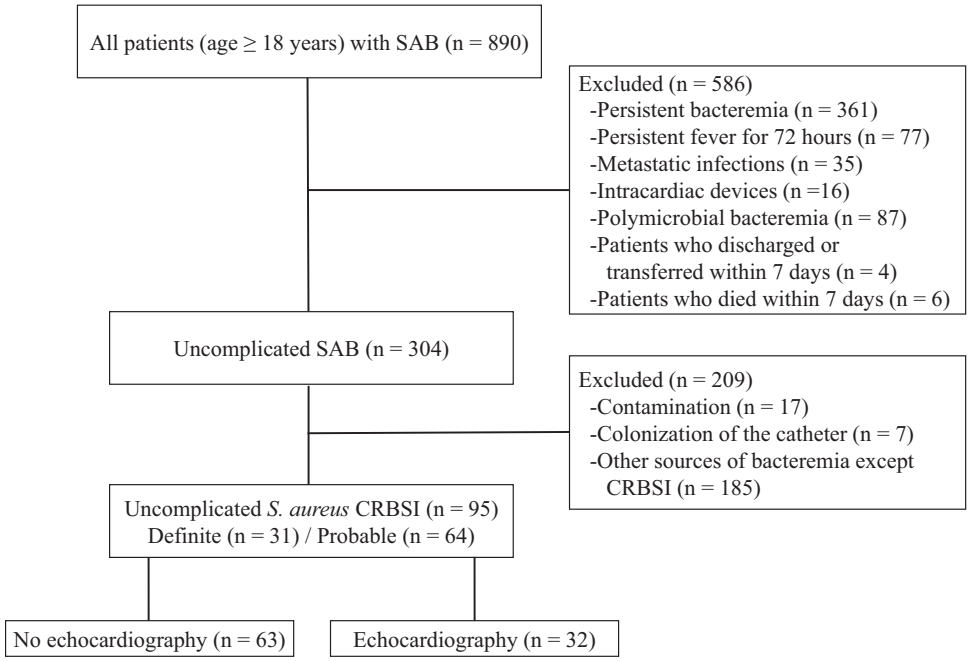

Figure 1. The study population. CRBSI = catheter-related bloodstream infection, SAB = *S. aureus* bacteremia.

factors associated with treatment failure. Variables with P value $< .05$ in the univariate analysis and implementation of echocardiography were included in multivariable analysis using the forward conditional method. If the variable did not satisfy the proportional hazard assumption verified by log minus log plot, time-dependent covariate was included in the model. P values were two-tailed, and those lower than 0.05 were considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (2017, IBM Corp., Armonk, NY).

3. Results

3.1. Study population

A total of 890 patients with SAB were identified during the study period. Four hundred eighty-nine patients who satisfied at least 1 criterion defining complicated bacteremia were excluded (Fig. 1). Overall, 95 patients with uncomplicated *S. aureus* CRBSI were included (Table 1). Nine cases were censored before relapse or death within 90 days, including 4 patients who underwent echocardiography (follow-up duration of censored cases: median 28 days).

3.2. Demographic characteristics and echocardiographic data

None of the patients had history of previous IE or intravenous drug use. Fifty-five patients had metastatic tumor or hematologic malignancy, and 58 were immunocompromised or neutropenic. The group that did not undergo echocardiography included more neutropenic patients and lower Charlson comorbidity index scores, shorter duration of total treatment, and greater tendency toward retention of central venous catheter.

Echocardiography was performed in 32 patients (time to echocardiography: median 4.5 days [IQR 2.25–8 days]; TTE: 28 patients, TEE: 1 patient, both: 3 patients). Echocardiographic findings were 19 negative, 11 equivocal, and 2 positive (6.3%) results. Eleven equivocal findings included 6 valve abnormalities and 9 poor echo views. One patient with a positive finding showed a catheter tip with vegetation in the right atrium (Table 2, patient 1). The other patient with a positive finding showed a negative finding on TTE, but TEE showed vegetation on the tricuspid valve (Table 2, patient 2). Both patients had leukemia and history of immunosuppression and did not have murmur or any peripheral signs of IE.

3.3. Outcomes

Two patients were diagnosed with right-sided IE although the sources of bacteremia were classified as probable CRBSI (Table 2). Relapse of SAB occurred in 1 patient who did not undergo echocardiography after 85 days from initial positive blood culture. Relapse event was identified as peripheral CRBSI. The first SAB of this patient was treated with vancomycin for 12 days. He was retreated with vancomycin for 14 days without performance of echocardiography and showed resolution without complications or further relapse.

Seven patients died within 90 days of onset of SAB, including 3 patients who underwent echocardiography (Supplementary Table 1, http://links.lww.com/MD/G57). Median time to death from onset of SAB was 24 days (IQR: 20–66 days). There were no SAB-related deaths. Overall 30-day and 90-day mortality rates were 4.4% and 8.1%, respectively. Kaplan–Meier curves of treatment failure showed no significant differences between groups (Fig. 2, $P = .77$).

3.4. Risk factors for treatment failure

In a univariate Cox proportional hazard model, possible risk factors were liver cirrhosis, other prostheses, and Charlson

Table 1

Characteristics of 95 patients with uncomplicated *S. aureus* CRBSI.

Variable, n (%) or median (IQR)	No echocardiography (n = 63)	Echocardiography (n = 32)	*P*
Mean age ± SD, yr	52.40 ± 18.95	56.78 ± 17.01	.27
Male	37 (58.7)	18 (56.3)	.82
Comorbidities			
Diabetes mellitus	16 (25.4)	5 (15.6)	.28
Liver cirrhosis	6 (9.5)	3 (9.4)	>.99
CKD	11 (17.5)	5 (15.6)	.82
HD dependence	4 (6.3)	2 (6.3)	>.99
Solid tumors	21 (33.3)	14 (43.8)	.32
Metastatic tumors	8 (12.7)	8 (25.0)	.13
Hematologic malignancies	29 (46.0)	10 (31.3)	.17
SOT	0 (0)	1 (3.1)	.34
HSCT	12 (19.0)	4 (12.5)	.43
Neutropenia (neutrophil < 500 μL)	24 (38.1)	4 (12.5)	.01
Immunosuppression*	36 (57.1)	21 (65.6)	.61
Prostheses			
Orthopedic devices	6 (9.5)	2 (6.3)	.71
Long-term CVCs†	35 (55.6)	14 (43.8)	.29
Intravascular devices‡	2 (3.2)	0 (0.0)	.55
Other prostheses§	1 (1.6)	1 (3.1)	>.99
Onset of bacteremia			.25
Nosocomial	43 (68.3)	18 (56.3)	
Healthcare-associated	20 (31.7)	14 (43.8)	
Charlson comorbidity score	5 (2–6)	5 (3.25–7.75)	.008
Pitt bacteremia score	2 (1–3)	2 (1–4)	.83
CRP (mg/dL)	5.49 (2.19–12.05)	4.86 (2.45–10.31)	.30
MRSA	18 (28.6)	13 (40.6)	.24
Time to positivity, h	14 (11–18)	13 (11–19)	.95
Two or more positive blood cultures	50 (79.4)	27 (84.4)	.56
Probable CRBSI	44 (69.8)	20 (62.5)	.47
Presence of CVC¶	52 (82.5)	23 (71.9)	.23
Removal of CVC	37/52 (71.2)	20/23 (87.0)	.10
Antibiotic lock therapy	9/52 (17.3)	0/23 (0)	.10
Time to CVC removal, d	1 (0.5–7)	1 (0–2.75)	.22
Total treatment duration, d	14 (10–16)	15 (14–18)	.001
Total treatment < 14 d	30 (47.6)	6 (18.8)	.006
IV treatment duration, d	11 (8–14)	10 (7.25–14)	.97
Infective endocarditis	0 (0)	2 (6.3)	.11
90-d relapse (n = 86)	1 (1.7)	0 (0)	>.99
30-d mortality (n = 90)	2 (3.3)	2 (6.7)	.60
90-d mortality (n = 86)	4 (6.9)	3 (10.7)	.68
Treatment failure‖ (n = 86)	5 (8.6)	3 (10.7)	.71

CKD = chronic kidney disease, CRBSI = catheter-related bloodstream infection, CRP = C-reactive protein, CVC = central venous catheter, HD = hemodialysis, HSCT = hematopoietic stem cell transplantation, IQR = interquartile range, IV = intravenous, MRSA = methicillin-resistant *Staphylococcus aureus*, SD = standard deviation, SOT = solid organ transplantation.

* Immunosuppression was defined as a history of any immunosuppressive medication, radiation, or corticosteroid (analogous to 20 mg prednisone for at least 7 d) within 30 d before the first positive blood culture.

† Long-term CVC was defined as cuffed tunneled intravascular catheter or subcutaneous port catheter.

‡ Intravascular devices included vascular grafts and inferior vena cava filters.

§ Other prostheses included ommaya reservoirs.

¶ CVC was defined as short-term CVC, long-term CVC, and peripherally inserted central catheter.

‖ Treatment failure included relapse and all-cause mortality cases within 90 d.

comorbidity index (Table 3). Because implementation of echocardiography did not satisfy the proportional hazard assumption, time-dependent Cox regression analysis was conducted for multivariable analysis. Independent risk factors were liver cirrhosis (hazard ratio: 9.60; 95% confidence interval: 2.13–43.33; $P = .003$) and other prostheses (hazard ratio: 63.79; 95% confidence interval: 5.05–805.40; $P = .001$). Implementation of echocardiography was not associated with treatment failure.

4. Discussion

This study did not show a significant association between the implementation of echocardiography and treatment failure in patients with uncomplicated *S. aureus* CRBSI. Furthermore, overall rates of relapse and IE were low in our study population. These results are similar to those of a previous study.[12] Of 62 patients with uncomplicated *S. aureus* CRBSI and primary nosocomial bacteremia, only 20 underwent echocardiography, and none developed IE during 3 months of follow-up.[12] However, the criteria used to identify complicated bacteremia were different from those used in the present study in that persistent bacteremia and defervescence were evaluated from the day of catheter removal.[12] We evaluated the actual duration of bacteremia and defervescence from initiation of effective therapy, stricter criteria than in the previous study. Furthermore, because our criteria were according to the guideline, the results of this study could reflect actual clinical situations.[5]

Multiple factors influence mortality of SAB, including host factors, pathogen–host interactions and pathogen-specific factors.[28] Liver cirrhosis and the presence of other prostheses were independent risk factors for treatment failure in this study. These results are consistent with previous studies that the patients with liver cirrhosis showed higher mortality than those with other diseases and the presence of one or more comorbidities has been associated with mortality of SAB.[28,29] However, because SAB-related death was not identified in this study, it may be that underlying diseases rather than SAB contributed to the outcomes (Supplementary Table 1, http://links.lww.com/MD/G57).

Most previous studies evaluating the benefits of echocardiography in SAB included substantial groups of patients who did not undergo echocardiography (range: 13–79%).[8–11,13–20] Such patients were excluded[8,14,19,20] or assessed by occurrence of SAB or IE during varying follow-up durations.[9–13,15–18] However, these studies included heterogeneous sources of bacteremia, and the duration of treatment was either prolonged or was not considered, factors that could conceal undetected IE and obscure the benefits of echocardiography in patients with SAB.[8–11,13–20] We evaluated patients with uncomplicated CRBSI to enable shorter treatment duration and verified 2 weeks of duration, steps that would highlight the effects of echocardiography. Nonetheless, this study did not verify a beneficial role of echocardiography on treatment outcome.

The prevalence of IE in patients with low risk is very low, between 0% and 5%.[8–20] These results are similar to those of the present study that identified 2 IE patients among the study population. Interestingly, both patients were diagnosed with right-sided IE. Intravenous drug user and intravascular catheter are major risk factors for right-sided IE, the manifestations of which are considerably different from those of left-sided IE.[30] Furthermore, right-sided IE has more favorable outcomes probably because right-sided valve dysfunction and pulmonary emboli cause minimal hemodynamic derangement.[30] Because of these differences from left-sided IE, criteria for identifying complicated bacteremia may be insufficient for excluding right-sided IE. Nonetheless, 2-week therapy, the current recommended treatment for uncomplicated SAB, could be used

Table 2

Clinical characteristics of 2 patients with infective endocarditis and 1 patient with relapse.

Patient	Age, yrs	Sex	Source (methicillin-resistance)	Onset	Underlying diseases	Immunosuppression/ neutropenia	Prostheses/ hemodialysis	Time to CVC removal, d	Time to TTE/TEE, d	Comments	Duration of treatment, (IV), d
1	31	F	Probable CRBSI (MSSA)	Healthcare-associated	ALL	Chemotherapy/Y	Long-term CVC/N	11	5/11	Both TTE and TEE showed vegetation-like lesions (1.59 × 0.91 cm) in the right atrium.	29 (19)
2	54	F	Probable CRBSI (MSSA)	Nosocomial	AML, allogenic HSCT	Steroid/N	N/N	NA	5/7	TEE showed oscillating linear material (2.4 cm) on tricuspid valve.	34 (34)
3	54	M	Definite CRBSI (MRSA)	Nosocomial	Lymphoma	Chemotherapy/N	Long-term CVC/N	1	NA	Peripheral CRBSI occurred after 85 d.	12 (12)

ALL = acute lymphocytic leukemia, AML = acute myeloid leukemia, CRBSI = catheter-related bloodstream infection, CVC = central venous catheter, IV = intravenous, MRSA = methicillin-resistant *Staphylococcus aureus*, MSSA = methicillin-susceptible *Staphylococcus aureus*, NA = not available, TEE = transesophageal echocardiography, TTE = transthoracic echocardiography.

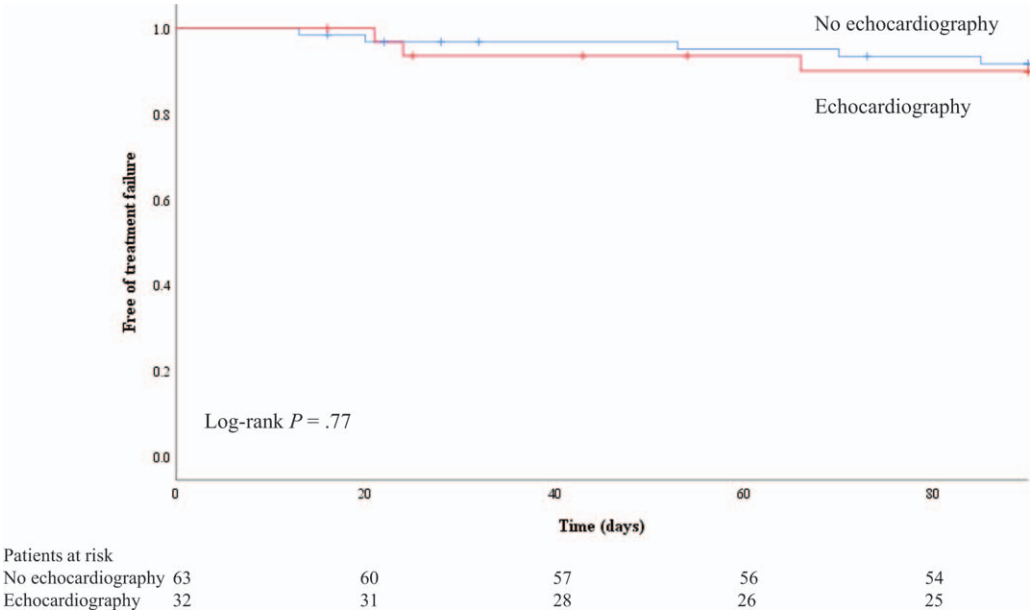

Figure 2. Kaplan–Meier curves of treatment failure in patients with uncomplicated *S. aureus* catheter-related bloodstream infection (CRBSI) according to the implementation of echocardiography.

to treat undiagnosed right-sided IE in CRBSI. One previous study showed that a 2-week monotherapy regimen of intravenous cloxacillin was equivalent to cloxacillin plus gentamicin administered for 2 weeks to treat right-sided IE.[31]

Relapse of SAB occurred in only 1 patient, who had a hematologic malignancy and immunocompromised state. Calculating from first negative blood culture, the treatment duration of the first episode was 10 days, less than the 14 days recommended.[2] Furthermore, if the patient had silent vegetation, treatment with vancomycin might have been insufficient due to its limited bactericidal activity and poor penetration into vegetation.[32] Such factors might contribute to relapse of SAB. However, given the long interval between the 2 SAB events, and the second episode was related with peripheral catheter, there

Table 3

Factors associated with treatment failure of uncomplicated *S. aureus* CRBSI.

	Univariate analysis		Multivariable analysis	
Factor	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
Liver cirrhosis	7.46 (1.77–31.47)	.006	9.60 (2.13–43.33)	.003
Other prostheses	35.70 (3.15–404.84)	.004	63.79 (5.05–805.40)	.001
Charlson comorbidity index (per 1 point)	1.28 (1.02–1.60)	.03		
No echocardiography	1.00 (0.97–1.03)	.98		

CI = confidence interval, CRBSI = catheter-related bloodstream infection, CVC = central venous catheter, HR = hazard ratio, IV = intravenous, MRSA = methicillin-resistant *Staphylococcus aureus*.

is the possibility of reinfection. Although echocardiography was not performed for second SAB, endocarditis was less likely considering there was no another relapse after treatment of the second bacteremia.

Despite many previous studies, it remains uncertain whether echocardiography is beneficial in SAB patients at low risk of IE. Heriot et al[33] stated that the testing threshold for TEE was a 1.1% probability of IE, and that none of the available criteria could be reduced below this probability. On the contrary, they showed that the survival benefit of any echocardiography strategy compared with 2 weeks of empirical therapy was marginal in patients at low risk of IE, using decision analysis and Monte Carlo simulation.[34] It may be difficult to statistically demonstrate the non-inferiority of outcomes depending on testing strategy in a population with a low prevalence of the disease.[34]

Our study has several limitations. First, the influence of selection bias could not be excluded because of inherent limitations of our study design. Second, we used broad criteria to define CRBSI, and a certain portion of the study population may represent cases of primary nosocomial or healthcare-associated bacteremia. However, intravascular catheters, including peripheral catheters, are significant contributors to *S. aureus* primary nosocomial bacteremia.[35,36] Third, it is difficult to draw clear conclusions because the sample size was small and the outcome events were rare. However, it would be difficult to include enough patients at low risk of IE in the study to ensure sufficient statistical power.[34]

In conclusion, we did not verify an association between treatment failure and the implementation of echocardiography in patients with uncomplicated *S. aureus* CRBSI. Given the observed low rates of adverse outcomes, empirical treatment without echocardiography may be an alternative treatment option for such patients in resource-limited settings.

Author contributions

Seok Jun Mun: Conceptualization, Investigation, Formal analysis, Writing – original draft.
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Kyungmin Huh: Investigation, Methodology.
Sun Young Cho: Investigation, Methodology.
Cheol-In Kang: Validation, Writing – Review and Editing.
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References

[1] Kern WV. Management of *Staphylococcus aureus* bacteremia and endocarditis: progresses and challenges. Curr Opin Infect Dis 2010;23:346–58.
[2] Holland TL, Arnold C, Fowler VGJr. Clinical management of *Staphylococcus aureus* bacteremia: a review. JAMA 2014;312:1330–41.
[3] Chang FY, MacDonald BB, Peacock JEJr, et al. A prospective multicenter study of *Staphylococcus aureus* bacteremia: incidence of endocarditis, risk factors for mortality, and clinical impact of methicillin resistance. Medicine (Baltimore) 2003;82:322–32.
[4] Jensen AG, Wachmann CH, Espersen F, et al. Treatment and outcome of *Staphylococcus aureus* bacteremia: a prospective study of 278 cases. Arch Intern Med 2002;162:25–32.
[5] Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the infectious diseases society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. Clin Infect Dis 2011;52:e18–55.
[6] Heriot GS, Tong SYC, Cheng AC, et al. Clinical variation in the use of echocardiography in *Staphylococcus aureus* bacteraemia: a multi-centre cohort study. Eur J Clin Microbiol Infect Dis 2018;37:469–74.
[7] Holden E, Bashir A, Das I, et al. *Staphylococcus aureus* bacteraemia in a UK tertiary referral centre: a 'transoesophageal echocardiogram for all' policy. J Antimicrob Chemother 2014;69:1960–5.
[8] Heriot G, Yeoh J, Street A, et al. Echocardiography has minimal yield and may not be warranted in *Staphylococcus aureus* bacteremia without clinical risk factors for endocarditis. Eur J Clin Microbiol Infect Dis 2015;34:1231–6.
[9] Kaasch AJ, Fowler VGJr, Rieg S, et al. Use of a simple criteria set for guiding echocardiography in nosocomial *Staphylococcus aureus* bacteremia. Clin Infect Dis 2011;53:1–9.
[10] Palraj BR, Baddour LM, Hess EP, et al. Predicting risk of endocarditis using a clinical tool (PREDICT): scoring system to guide use of echocardiography in the management of *Staphylococcus aureus* bacteremia. Clin Infect Dis 2015;61:18–28.
[11] Khatib R, Sharma M. Echocardiography is dispensable in uncomplicated *Staphylococcus aureus* bacteremia. Medicine (Baltimore) 2013;92:182–8.
[12] Pigrau C, Rodriguez D, Planes AM, et al. Management of catheter-related *Staphylococcus aureus* bacteremia: when may sonographic study be unnecessary? Eur J Clin Microbiol Infect Dis 2003;22:713–9.
[13] Gow N, Lowe BS, Freeman J, et al. The role of echocardiography in *Staphylococcus aureus* bacteraemia at Auckland City Hospital. N Z Med J 2015;128:28–35.
[14] Joseph JP, Meddows TR, Webster DP, et al. Prioritizing echocardiography in *Staphylococcus aureus* bacteraemia. J Antimicrob Chemother 2013;68:444–9.
[15] Rasmussen RV, Host U, Arpi M, et al. Prevalence of infective endocarditis in patients with *Staphylococcus aureus* bacteraemia: the value of screening with echocardiography. Eur J Echocardiogr 2011;12:414–20.
[16] Buitron de la Vega P, Tandon P, Qureshi W, et al. Simplified risk stratification criteria for identification of patients with MRSA bacteremia at low risk of infective endocarditis: implications for avoiding routine transesophageal echocardiography in MRSA bacteremia. Eur J Clin Microbiol Infect Dis 2016;35:261–8.
[17] Tubiana S, Duval X, Alla F, et al. The VIRSTA score, a prediction score to estimate risk of infective endocarditis and determine priority for echocardiography in patients with *Staphylococcus aureus* bacteremia. J Infect 2016;72:544–53.
[18] Barton T, Moir S, Rehmani H, et al. Low rates of endocarditis in healthcare-associated *Staphylococcus aureus* bacteremia suggest that echocardiography might not always be required. Eur J Clin Microbiol Infect Dis 2016;35:49–55.
[19] Longobardo L, Klemm S, Cook M, et al. Risk assessment for infected endocarditis in *Staphylococcus aureus* bacteremia patients: when is transesophageal echocardiography needed? Eur Heart J Acute Cardiovasc Care 2019;8:476–84.
[20] Van Hal SJ, Mathur G, Kelly J, et al. The role of transthoracic echocardiography in excluding left sided infective endocarditis in *Staphylococcus aureus* bacteraemia. J Infect 2005;51:218–21.
[21] DiNubile MJ. Transesophageal echocardiograms in patients with catheter-derived *Staphylococcus aureus* bacteremia. Am J Med 2012; 125:628–9.
[22] Mermel LA, Allon M, Bouza E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009;49:1–45.
[23] Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 2000;30:633–8.

[24] Paul M, Kariv G, Goldberg E, et al. Importance of appropriate empirical antibiotic therapy for methicillin-resistant *Staphylococcus aureus* bacteraemia. J Antimicrob Chemother 2010;65:2658–65.
[25] Friedman ND, Kaye KS, Stout JE, et al. Health care-associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections. Ann Intern Med 2002;137:791–7.
[26] Barton TL, Mottram PM, Stuart RL, et al. Transthoracic echocardiography is still useful in the initial evaluation of patients with suspected infective endocarditis: evaluation of a large cohort at a tertiary referral center. Mayo Clin Proc 2014;89:799–805.
[27] Chong YP, Moon SM, Bang KM, et al. Treatment duration for uncomplicated *Staphylococcus aureus* bacteremia to prevent relapse: analysis of a prospective observational cohort study. Antimicrob Agents Chemother 2013;57:1150–6.
[28] van Hal SJ, Jensen SO, Vaska VL, et al. Predictors of mortality in *Staphylococcus aureus* bacteremia. Clin Microbiol Rev 2012;25: 362–86.
[29] Park HJ, Lee YM, Bang KM, et al. Clinical significance of *Staphylococcus aureus* bacteremia in patients with liver cirrhosis. Eur J Clin Microbiol Infect Dis 2012;31:3309–16.
[30] Akinosoglou K, Apostolakis E, Marangos M, et al. Native valve right sided infective endocarditis. Eur J Intern Med 2013;24:510–9.
[31] Ribera E, Gómez-Jimenez J, Cortes E, et al. Effectiveness of cloxacillin with and without gentamicin in short-term therapy for right-sided *Staphylococcus aureus* endocarditis. A randomized, controlled trial. Ann Intern Med 1996;125:969–74.
[32] Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications: a scientific statement for healthcare professionals from the American Heart Association. Circulation 2015;132: 1435–86.
[33] Heriot GS, Tong SYC, Cheng AC, et al. What risk of endocarditis is low enough to justify the omission of transoesophageal echocardiography in *Staphylococcus aureus* bacteraemia? A narrative review. Clin Microbiol Infect 2018;24:1251–6.
[34] Heriot GS, Tong SYC, Cheng AC, et al. Benefit of echocardiography in patients with *Staphylococcus aureus* bacteremia at low risk of endocarditis. Open Forum Infect Dis 2018;5:ofy303.
[35] Saginur R, Suh KN. Staphylococcus aureus bacteraemia of unknown primary source: where do we stand? Int J Antimicrob Agents 2008;32 (Suppl 1):S21–5.
[36] Kovacs CS, Fatica C, Butler R, et al. Hospital-acquired *Staphylococcus aureus* primary bloodstream infection: a comparison of events that do and do not meet the central line-associated bloodstream infection definition. Am J Infect Control 2016;44:1252–5.