Journal of Intensive Medicine 2 (2022) 56–60

Contents lists available at ScienceDirect

Journal of Intensive Medicine

journal homepage: www.elsevier.com/locate/jointm

Original Article

Impact of satellite blood culture on early diagnosis of sepsis ☆

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ARTICLE INFO

Keywords:
Blood culture
Sepsis
Intensive care unit
Antibiotic switching
Turnaround time
Gram stain

ABSTRACT

Background: The aim of this study was to assess whether satellite blood culture (SBC) can improve turnaround times, antibiotic switching, and patient prognosis, relative to laboratory blood culture (LBC).

Methods: Patients with sepsis treated in the intensive care units (ICUs) of Henan Provincial People's Hospital from February 5, 2018 to January 19, 2019 who met the inclusion criteria were recruited to the study and divided into the SBC group and LBC group according to different blood culture methods. Patient demographics, blood culture, antibiotic adjustment, and prognosis data were collected and compared between the two groups.

Results: A total of 204 blood culture sets from 52 ICU patients, including 100 from the medical microbiology LBC group and 104 from the SBC group, were analyzed in this study. There was no significant difference in the positive rates between the two groups. Time from specimen collection to incubation was significantly shorter in the SBC group than that in the LBC group (1.65 h *vs.* 3.51 h, $z=-4.09$, $P<0.001$). The median time from specimen collection to notification of blood culture positivity was 24.83 h in the SBC group and 27.83 h in the LBC group. Median times from adjustment of antibiotics according to the first report were 26.05 h and 51.71 h in the SBC and LBC groups, respectively, while those according to the final report were 97.17 h and 111.45 h, respectively. Median ICU lengths of stay were 15.00 days and 17.00 days in the SBC and LBC groups, respectively, and median ICU lengths of stay were 18.00 days and 23.50 days, respectively. Mean hospitalization costs were 157.99 and 186.73 thousand yuan in the SBC and LBC groups, respectively.

Conclusion: SBC can significantly reduce blood culture turnaround times; however, there were no significant differences between the two blood culture methods in initial reporting of positive cultures, time to adjustment of antibiotic therapy, or medical costs, despite a trend toward improvement.

Introduction

Sepsis describes life-threatening organ dysfunction caused by a dysregulated host response to infection[1] and is a leading cause of death worldwide.[1–4] It is important to improve the outcomes of patients with sepsis by early detection and timely treatment.[5] Each hour of delay in antimicrobial administration is associated with an average decrease in survival of 7.6%.[6] Antibiotic treatment is a key component of therapy for sepsis. Early targeted therapy relies on the identification of the underlying pathogen. Further, identification and antibiotic susceptibility tests from positive blood cultures are needed to shift from empiric to directed antibiotic treatment; however, the current gold standard diagnostic method, culture-based pathogen detection, is limited by a delayed time to result.[7] Shorter time to positivity may be achieved using satellite blood culture (SBC), where blood cultures are set up in a clinical department outside the hospital microbiology laboratory (i.e., cultures are incubated at the site of collection) to meet the requirement for timely specimen incubation; however, evidence that SBC can

☆ Given his role as Editorial Board Member, Prof. Bingyu Qin had no involvement in the peer-review of this article and has no access to information regarding its peer-review. Prof. Dechang Chen who is the co-editor-in-chief took the responsibility for peer-review progress and made the final decision.

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https://doi.org/10.1016/j.jointm.2021.11.003
Received 3 September 2021; Received in revised form 28 October 2021; Accepted 17 November 2021. Managing Editor: Jingling Bao
Available online 21 December 2021

significantly reduce the time to obtaining test results and perform antibiotic adjustment in patients with sepsis is from limited studies and remains weak and insufficient.[8,9]

This study extended previous investigations of patients with sepsis and examined the impact of SBC on time to results, length of stay (LOS), and medical costs.

Methods

Study design, specimen collection, and processing

This retrospective study was performed in the Department of Critical Care Medicine, Henan Provincial People's Hospital, China. Enrollment commenced on February 5, 2018 and concluded on January 19, 2019. Patient inclusion criteria were as follows: (1) age, 18 to 85 years; (2) met the sepsis 3.0* diagnostic criteria;[1] (3) ICU LOS >48 h; (4) at least one blood culture bottle was positive (positive: positive blood culture bottle ≥ 1, negative: positive blood culture bottle = 0). The exclusion criteria were as follows: (1) discharged or died within 48 h after admission; (2) pregnancy or lactation; (3) malignant tumor; (4) lack of complete clinical data.

Ethics approval was obtained from the Human Research Ethics Committee at Henan Provincial People's Hospital (Number: (2020) Ethical Review No. (143)).

Specimens were collected and processed according to the Clinical and Laboratory Standards Institute guidelines.[10] Before culture, blood samples were stored at room temperature. Blood samples were sent to the medical microbiology laboratory (laboratory blood culture [LBC group]) for culture or were cultured in the intensive care units (ICUs) (SBC group) [Figure 1]. The ICU is located on the 5th floor, while the medical microbiology laboratory is on the 2nd floor of the same building. The working hours of the medical microbiology laboratory are from 08:00 to 18:00 everyday, and specimens were collected and cultured only during those working hours; at other times, blood samples were incubated in the ICU.

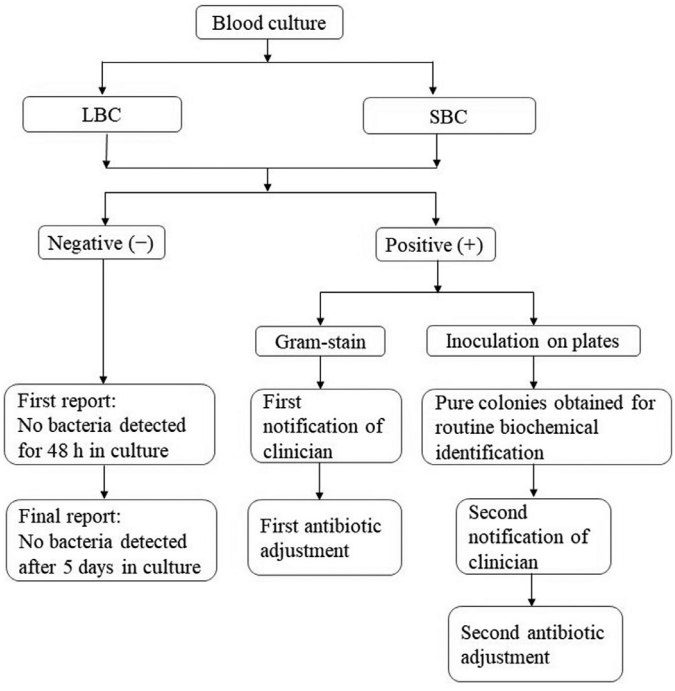

Figure 1. Flowchart of blood culture processing. LBC: Laboratory blood culture; SBC: Satellite blood culture.

Positive cultures were Gram-stained and transferred onto blood agar plates, chocolate agar plates, and MacConkey agar plates simultaneously (Autobio Diagnostics Ltd). Pure colonies were identified for routine biochemical tests. A Phoenix 100 automatic biochemical identification system (BD Diagnostics) was used for routine biochemical analyses, including strain identification and susceptibility testing [Figure 1].

When a positive signal was detected, the blood culture instrument alarmed and recorded the time of the positive report. The staff on duty verified the result and reported it, including whether the organism was gram negative or positive and anaerobic or aerobic, to clinicians via telephone. Clinicians then adjusted the antibiotics administered based on Gram staining results, inflammation indicators, and clinical manifestations [Figure 1]. After the final report, the clinicians adjusted the antibiotics again, according to susceptibility testing, if necessary. If blood culture was negative, cultures were incubated in the BACTEC FX40 for 5 days, and clinicians could access the final report through the hospital computer system [Figure 1].

All blood culture sets comprised an aerobic and an anaerobic bottle, and at least one set of blood cultures was collected for each patient. All blood culture bottles (BACTEC Aerobic Plus/F, BACTEC Anaerobic Lytic/F) were incubated in a BACTEC FX40 instrument.

Data collection and definitions

Data on the following parameters were collected and compared: patient demographics, inflammation indicators, temperature, Acute Physiology and Chronic Health Evaluation II score (APACHE II score), infection site, blood collection site, blood culture outcomes, time interval between blood culture collection and incubation, positive report, ICU LOS, hospital LOS, and medical costs.

The following time intervals were recorded:

TCI: time from specimen collection until incubation.
TCK: time from specimen collection until instrument reporting positive.
TFA: time from specimen collection until antibiotic adjustment, according to first report.
TSA: time from specimen collection until antibiotic adjustment, according to final report.

Statistical analysis

All data were statistically analyzed using SPSS software(version 21, IBM, NY, USA). The Kolmogorov-Smirnov method was used to test data normality. Continuous variables were expressed as mean ± standard deviation or median and interquartile range (IQR). Categorical variables were expressed as numbers and percentages. For continuous variables, comparisons between two groups with normally distributed data were conducted using the *t*-test; otherwise, the Mann–Whitney test was used. For categorical variables, methods used included Pearson's chi-squared test, continuity correction, Fisher's exact

test, or likelihood ratio. Two-sided *P*-values <0.05 were considered statistically significant.

Results

Baseline characteristics

Patients with sepsis who met the inclusion criteria were recruited to the study and divided into two groups according to different blood culture methods. In total, 204 blood culture sets from 52 patients with sepsis were analyzed: 100 cultures from 26 patients in the LBC group and 104 cultures from 26 patients in the SBC group.

Comparisons between demographic and clinical characteristics of each group are presented in Table 1. There were no significant differences between the two groups, including in age, sex, temperature before culture, APACHE II score, infection site, blood collection site, or inflammatory markers (white blood cell count [WBC], procalcitonin [PCT], and C-reactive protein [CRP]).

Blood cultures

As shown in Table 2, 45 (45.00%) of 100 blood culture sets were positive in the LBC group, while 57 (54.81%) of 104 blood culture sets were positive in the SBC group.

Antibiotic adjustment and prognosis

Comparisons of time intervals are shown in Table 2. TCI in the SBC group was significantly shorter than that in the LBC group (1.65 h *vs.* 3.51 h, $P < 0.001$). Median TCK, TFA, and TSA in the SBC and LBC groups were 24.83 h and 27.83 h, 26.05 h and 51.70 h, and 97.17 h and 111.45 h, respectively.

Prognosis variables for patients in the two groups are shown in Table 2. Median ICU and hospital LOS were 15.00 days and 17.00 days and 18.00 days and 23.50 days in the SBC and LBC groups, respectively. The medical costs were 157.99 thousand yuan in the SBC group and 186.73 thousand yuan in the LBC group.

Discussion

Our data indicate that incubation of blood cultures at the site of collection (SBC) significantly reduced the TCI ($P<0.001$). In the current study, compared with the LBC group, TCI and TCK were reduced by 1.86 h ($P<0.001$) and 3.00 h, respectively, in the SBC group. TFA and TSA were also reduced by 25.66 h and by 14.28 h, respectively, although the difference was not significant, probably due to the small sample size. The ICU and Medical Microbiology departments are located in the same building; therefore, the advantage of SBC was not obvious, and the small distance between the laboratories may be another factor contributing to the lack of significance of some detected differences between groups. The results of our study were consistent with those of previous reports showing that incubation of cultures at the collection site can significantly reduce the time to detection of positive cultures, pathogen identification, and reporting of antimicrobial susceptibility test results.[8,9] Unfortunately, the decreased time to detection of positive cultures found in this study did not translate into corresponding significant decreases in either ICU or hospital LOS nor was there a decrease in total hospital costs. A decrease in each of these parameters was

Table 1
Baseline characteristics of patients with sepsis.

Characteristic	LBC group (n = 26)	SBC group (n = 26)	$Z/\chi^2/F$	*P*-value
Age (years)	45.00 (30.00, 70.00)	56.50 (44.75, 70.25)	1.50	0.13
Sex				
Male	17 (65.38)	22 (84.62)	2.56	0.11
Female	9 (34.62)	4 (15.38)		
WBC* (10^9/L)	14.95 ± 8.61	11.84 ± 5.09	13.66	0.12
PCT (ng/mL)	4.61 (0.74, 21.18)	4.65 (1.49, 8.23)	−0.51	0.61
CRP (mg/L)	160.15 (84.18, 200.00)	173.14 (122.78, 200.00)	−0.49	0.62
Temperature	38.00 (37.05, 38.10)	37.65 (37.00, 38.50)	−0.18	0.85
APACHE II score	17.00 (10.75, 20.00)	16.50 (15.00, 21.50)	−1.14	0.26
Infection site*			6.12	0.41
Pneumonia	16 (61.54)	12 (46.15)		
Abdominal cavity	6 (23.08)	6 (23.08)		
Pancreatitis	2 (7.69)	2 (7.69)		
Biliary	1 (3.85)	3 (11.54)		
Urinary tract	1 (3.85)	0 (0.00)		
Hematogenous	1 (3.85)	0 (0.00)		
Nervous system	0 (0.00)	3 (11.54)		
Blood collection site			1.15	0.78
Central vein	1 (3.85)	0 (0.00)		
Peripheral	12 (46.15)	14 (53.85)		
Both	13 (50.00)	12 (46.15)		

Data are presented as mean ± standard deviation, median (Interquartile range), or n (%).

* One patient suffered a urinary tract infection and pneumonia; therefore, the total number of infection sites in the LBC group was 27.APACHE II score: Acute Physiology and Chronic Health Evaluation II score; CRP: C-reactive protein; LBC: Laboratory blood culture; PCT: Procalcitonin; SBC: Satellite blood culture; WBC: White blood cell count.

Table 2
LBC and SBC group blood culture, antibiotic adjustment, and prognosis data.

Outcome	LBC group (n = 26)	SBC group (n = 26)	χ^2/Z	P-value
Positive	45 (45.00)*	57 (54.81)*	1.96	0.21
Negative	55 (55.00)*	47 (45.19)*		
TCI (h)	3.51 (1.43, 5.12)	1.65 (0.98, 3.17)	−4.09	<0.001
TCK (h)	27.83 (22.92, 48.66)	24.83 (18.81, 43.25)	−1.14	0.26
TFA (h)	51.71 (41.29, 67.77)	26.05 (20.67, 46.53)	−1.82	0.07
TSA (h)	111.45 (93.18, 117.52)	97.17 (80.81, 103.11)	0.30	0.30
ICU LOS (days)	17.00 (4.75, 27.25)	15.00 (7.00, 24.25)	−0.18	0.86
Hospital LOS (days)	23.50 (9.75, 38.50)	18.00 (9.75, 29.00)	−0.67	0.50
Cost (Yuan)	186,733.88 (74,025.69, 327,015.03)	157,993 (74,607.03, 264,347.58)	−0.66	0.51

Data are presented as median (Interquartile range) or n (%).

* 100 blood culture sets in the LBC group, and 104 blood culture sets in the SBC group.Hospital LOS: Time from patient admission to the hospital to leaving the hospital; ICU LOS: Time from patient admission to the ICU to leaving the ICU; LBC, Laboratory blood culture; SBC: Satellite blood culture; TCI: Time from specimen collection until incubation; TCK: Time from specimen collection until instrument reporting positive; TFA: Time from specimen collection until antibiotic adjustment, according to first report; TSA: Time from specimen collection until antibiotic adjustment, according to final report.

detected in the SBC group; however, they did not reach statistical significance, partly due to the wide variation among individual patients and the small sample size. Based on our experience, these results underscore a fundamental problem confronting laboratories. If possible, laboratories should select rapid and accurate diagnostic methods. Further, it is equally important for laboratories to communicate these results to clinicians in a timely manner to ensure more effective patient management. The medical management of patients with sepsis is complex, with decisions based on experience and data from various diagnostic tests, including blood cultures. Laboratories are challenged to adapt their workflow practices and to prioritize the rapid communication of blood culture data.

It has been reported that, when TCI was only 1.86 h earlier, TCK was 3.00 h earlier, which was related to laboratory workflows.[11] Schwarzenbacher et al.[9] controlled the incubation time to within 1 h in the SBC group, and even in the LBC group, the incubation time did not exceed 8 h. In contrast, the incubation time obtained in the present study was much longer, possibly because staff were not trained to incubate blood cultures as soon as possible. In support of this speculation, a recent study showed that improving awareness of sepsis in staff was associated with enhancement of pre-analytical phase blood culture collection procedures, and isolation of bacteria by blood culture increased 3.25-fold;[12] this approach will guide us in making future improvements. Janapatla et al.[13] reported that there was no difference in time to positive detection of pathogens in bottles processed during the day or after overnight delay, which contrasts with our hypothesis and warrants further study.

In the study reported by Schwarzenbacher et al.,[9] the time to determining positivity was longer than that in our study, which may be because clinicians are on 24-h duty in our hospital; hence, positive outcomes could be obtained quickly for the SBC group, while there were no staff on duty at night in the medical microbiology laboratory (LBC group). This could explain why TFA was much longer than TCK in the LBC group, while TFA was only slightly longer than TCK in the SBC group; however, regarding TFA and TSA, SBC was not superior to LBC, although the median time from specimen collection to antibiotic adjustment was reduced by 25.66 h and 14.28 h in the SBC group. Inconsistencies between the study reported by Schwarzenbacher et al.[9] and our investigation may be attributable to the difference in sample size.

Lack of staff during off-hours increases the risk of death among patients hospitalized during off-duty periods.[14] Further, timely intervention for patients with positive blood culture results during weekends, and durations of hospital stay for patients with hospital-acquired bacteremia were significantly reduced after controlling for confounders.[15]

The probability of culture positivity decreased by 16% when the laboratory was closed. Further, the positive rates of blood cultures may decrease by 0.3% for every 1-hour delay from blood sample collection to incubation.[11] We found that, although the positive rate was increased in the SBC group, there was no significant difference between the two groups inconsistent with a previous study.[9] The limited number of patients may account for the differences in findings between the studies. Further, blood cultures that were collected within 24 h after admission yield more positive results than those collected later.[16] Also, if blood cultures remain negative for 24 h, the probability of bacteremia is 1.8%, which may contribute to antimicrobial therapy decisions.[17] When the time of culture incubation is >48 h, few true bloodstream infections can be detected.[18] In addition, evaluation of blood volume can improve rates of blood culture positivity;[19,20] therefore, clinicians can adjust empirical antibiotic coverage at this time, with little risk of subsequent bacterial pathogen detection.

Shortening the processing time from specimen collection to positive blood culture detection can decrease hospital LOS and mortality rate;[8,21] however, in the current study, there were no significant differences in the duration of ICU and hospital LOS or medical cost between the two groups, although all three factors were lower in the SBC group. This may be because of over-representation of older patients in the SBC group in our study; the small sample size in our study may also be a reason. Therefore, further research is needed to explore the impact of shortening processing time on hospital LOS, mortality rate, and medical costs.

Many studies have focused on rapid diagnostics using new technologies, such as multiplex Polymerase Chain Reaction(PCR), matrix-assisted laser desorption ionization-time of flight mass spectrometry, and next-generation sequencing, such as metagenomic sequencing.[22–25] These technologies may track pathogens more quickly than SBC, but the reliability of these new technologies needs further verification.

The current study was non-randomized controlled; thus, analytical bias cannot be excluded. Further, the sample size in this

study was relatively small. Therefore, we will design a randomized controlled study, with increased sample size, to provide more robust evidence on the outcomes associated with SBC.

Conclusions

In conclusion, SBC can significantly reduce turnaround times of blood cultures; however, we did not detect significance differences between the LBC and SBC groups in initial reporting of positive cultures, time to adjustment of antibiotic therapy, or medical costs, despite trends toward improvement.

Ethical Approval

The study was approved by the Human Research Ethics Committee at Henan Provincial People's Hospital. All experiments in this study were performed in accordance with relevant guidelines and regulations.

Availability of Data and Materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors thank Patrick Murray, Xia Shan, Yanhong Liu, and Yang Liu for providing medical writing support and Jingge Zhao for guidance on statistics.

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