Infection, Disease & Health (2019) **24**, 49—55

Available online at www.sciencedirect.com

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Research paper

Appropriateness of blood culture: A comparison of practices between the emergency department and general wards

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Received 4 July 2018; received in revised form 16 October 2018; accepted 19 October 2018
Available online 26 November 2018

KEYWORDS
Blood culture;
Emergency department;
General ward;
Bacteremia;
Institutional practice

Abstract *Background:* The decision to perform a blood culture is influenced by factors, such as the pretest probability of bacteremia, resource availability and individual clinician's preference. The lack of formal guidelines results in inconsistencies in practices and an inappropriate or overuse of blood cultures. The primary aim of this study is to compare the rate of positive blood cultures in the emergency department (ED) and general ward. The secondary aim of this study is to analyze factors associated with a positive blood culture.
Methods: We compared 200 consecutive patients in the ED with 200 consecutive patients with first blood cultures done within 24 h of admission from ED to the general ward. We analyzed the clinical characteristics, proportion of positive blood cultures, and variables associated with a positive blood culture.
Results: The percentage of positive blood cultures was 13.5% (n = 27) in the ED group, compared with 6.0% (n = 12) in the general ward group. Contamination rates were higher in the ED compared to general ward (4% vs 0.5%). Heart rate and rigors were independently associated with a positive blood culture in a multivariate logistic regression model.
Conclusion: There was a lower rate of positive blood cultures in the general ward group. Reasons may include a lower threshold for performing blood cultures in the general ward, and prior antibiotics in the ED reducing the sensitivity of blood cultures taken in the general ward. Adherence to clinical decision rules and education of junior staff are needed to improve the efficiency of blood culture taking practices.

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https://doi.org/10.1016/j.idh.2018.10.003
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Highlights

- The threshold to do a blood culture depends on the pretest probability of bacteremia and factors such as resource availability.
- Tachycardia and rigors were associated with bacteremia and are useful markers instead of temperature alone.
- An awareness of factors influencing the decision to perform a blood culture may help to prevent the over use of blood cultures.

Introduction

The only indication for obtaining blood cultures is to detect blood stream infection. Despite this single goal, the decision to perform blood cultures is influenced by multiple factors that determine the pre-test probability of bacteremia, such as the patients' medical condition and clinical status [1]. Other non-medical issues, including cost-versus-benefit ratio and perceived lack of psychological safety [2] by junior doctors who may err on the side of caution by performing the blood culture, may also play a part in this decision-making process.

Although blood culture is the current gold standard for diagnosis of bacteremia, its drawbacks include the lengthy time required for a positive or negative growth, and false positive results from contamination [3]. False positive results can lead to repercussions through administration of unnecessary antimicrobial agents, escalation in healthcare cost and most importantly, exacerbating the incidence of antimicrobial resistance [4].

Predictive factors and models to predict bacteremia have been formulated, such as the combination of Shapiro score [1] and procalcitonin, with a positive predictive value ranging from 12.1% to 25.9% and negative predictive value from 96.5% to 99.2%, depending on the cut-off used [5]. However, such models have their limitations, including the lack of predictive capabilities across different hospitals and populations due to the heterogeneity of sepsis [6]. Even within a healthcare unit, providers have varying thresholds for testing based on personal preferences and clinical experience. Patients often pass through multiple physicians and departments in their hospital stay, which poses further conflict where there are inconsistencies in blood culture practices. These factors highlight the importance of examining institutional practices on a contextualized basis [7].

The aims of this study were to analyze and compare the practices of obtaining blood cultures in the ED and inpatient general wards, and to examine the clinical impact of such practices, with specific focus in Asia where formal guidelines are not available. We hypothesized that the rate of positive blood cultures and utility of blood cultures would be low when performed in the general ward for patients who did not have prior blood cultures taken in the ED.

Methods

Study design and setting

This retrospective contemporaneous comparative cohort study compared patients who had blood cultures taken at the ED and inpatient general wards of National University Hospital, Singapore. The hospital is a 1100-bed academic medical center with 130,000 adult ED visits annually. This study was approved by the Institutional Review Board (2013/01128), which granted waiver of informed consent.

Study population

We randomly selected the month of December 2013 for this comparative study. All consecutive patients presenting to the adult ED and had blood cultures obtained in the ED were included. Consecutive patients from the general ward who were admitted from the ED without blood cultures, and had the first blood cultures obtained in the ward within 24 h of admission were included as the comparative cohort. Only the first set of blood cultures taken for each patient was analyzed. Exclusion criteria included patients admitted from the outpatient clinics, elective admissions, transfers from other hospitals and patients admitted to intensive care facilities. We excluded first blood cultures done in the general ward after 24 h from admission, or repeated sets of blood cultures performed in the same patient due to the higher likelihood of a change in clinical condition, which may render these patients not be comparable to the ED cohort.

Data collection

Baseline demographics, comorbidities, presenting symptoms, clinical signs, diagnosis, laboratory values, radiological investigations, blood culture results including sensitivity to antibiotics, treatment administered and outcome information were collected from the electronic medical records.

Outcome measures

The primary outcome was the difference in proportion of true positive blood culture results between the two groups. Secondary outcomes were differences in characteristics of

patients in the ED and general ward who were deemed to require blood cultures. We also sought to identify possible predictors of positive blood cultures by comparing true positive culture results with the combination of true negative results and those with contaminants. A contaminant was defined based on the organism detected, as well as the clinical impression labeled by the treating medical team, taking into account the patient's clinical context, including presence of indwelling vascular and urinary catheters. The Shapiro score [1] is a validated clinical decision rule for obtaining blood cultures, and stratifies patients into high risk (positive score) indicating a blood culture, and low risk (negative score) where blood cultures can be omitted (Supplementary Table 1). A patient who fulfills at least 1 major or 2 minor criteria would be considered a high-risk patient. We applied this score post hoc to our cohort, to determine its diagnostic performance.

Data analysis

Categorical variables were reported in frequency and percentages and continuous variables in mean (SD). For continuous variables that were skewed, median (interquartile range [IQR]) values were reported instead. Proportions were compared using Fisher's exact test. The odds ratio (OR) of achieving the primary outcome was reported together with its 95% confidence interval (CI). Continuous outcomes, unless otherwise stated, were compared with the 2-sample *t* test. Skewed continuous outcomes were compared with the Mann–Whitney *U* test. To determine factors associated with a positive blood culture, we performed a univariate analyses, followed by a multivariate stepwise logistic regression model where variables with P-values of less than 0.10 were included. Data analysis was performed with Stata 14 (StataCorp LP, College Station, TX).

Based on a hospital audit in February 2013 (unpublished), the proportion of true positive blood cultures from all non-intensive care unit adult patients in the NUH was 14.7% (212/1439). We assumed that the ED would have a true positive blood culture proportion of 5.3%, similar to a previously published local study [8]. Three hundred sixty patients were required to detect a 9.4% difference in proportion of patients with true positive blood cultures with a power of 80% at a type I error of 5%. We decided to include consecutive samples of 200 patients in each group for the randomly-chosen month of December 2013 for this study.

Results

Comparison of ED and general ward cases

Two hundred ED patients from 1 December 2013 to 11 December 2013 and 200 general ward patients from 1 December 2013 to 13 December 2013 were included (Table 1). Age, gender and ethnic composition were similar between the two groups. Patients with blood cultures first taken from ED had higher temperatures and heart rates compared to the general ward patients when their blood cultures were being obtained. They were more likely to have a history of being immunocompromised and presence of focal site of infection.

Table 1 Demographic, baseline characteristics and medical history.

Variable	ED cases (n = 200)	General ward cases (n = 200)
Age (years), median (IQR)	67 (51–78)	65 (47–78)
Male gender, n (%)	85 (42.5)	104 (52.0)
Ethnicity, n (%)		
Chinese	109 (54.5)	133 (66.5)
Malay	55 (27.5)	38 (19.0)
Indian	20 (10.0)	19 (9.5)
Eurasian	1 (0.5)	2 (1.0)
Others	15 (7.5)	8 (4.0)
Temperature (°C), mean (SD)	37.70 (1.03)	36.96 (0.96)
Temperature ≥38 °C, n (%)	83 (41.5)	29 (14.5)
Heart rate (beats per min), median (IQR)	104 (91.5–120)	93 (79–108)
Heart rate >100 beats per min, n (%)	115 (57.5)	73 (36.5)
Mean arterial pressure (mmHg), median (IQR)	93.5 (80–105)	92 (82–103)
Comorbidities, n (%)		
Diabetes mellitus	85 (42.5)	78 (39.0)
Renal disease	37 (18.5)	41 (20.5)
Liver disease	11 (5.5)	15 (7.5)
Malignancy	36 (18.0)	30 (15.0)
Immunocompromised state	74 (37.0)	43 (21.5)
Risk factors, n (%)		
History of bacteremia	32 (16.0)	19 (9.5)
Recent invasive procedure	8 (4.0)	16 (8.0)
Antibiotic use prior to blood culture	21 (10.5)	19 (9.5)
Presence of indwelling urinary catheter	9 (4.5)	9 (4.5)
Presence of central venous or peripherally inserted central catheter	11 (5.5)	3 (1.5)
Presence of focal site of infection	140 (70.0)	72 (36.0)

Table 2 Symptoms.

Variable	ED cases (n = 200)	General ward cases (n = 200)	P value
Fever, n (%)	143 (71.5)	56 (28.0)	<0.001
Chills, n (%)	58 (29.0)	22 (11.0)	<0.001
Dizziness, n (%)	8 (4.0)	22 (11.0)	0.008
Rigors, n (%)	36 (18.0)	11 (5.5)	<0.001
Altered mental status, n (%)	20 (10.0)	18 (9.0)	0.733
Source of symptoms, n (%)			
Respiratory	85 (42.5)	40 (20.0)	<0.001
Gastrointestinal	37 (18.5)	48 (24.0)	0.179
Genitourinary	8 (4.0)	17 (8.5)	0.063
Cardiovascular	10 (5.0)	13 (6.5)	0.519
Neurological	10 (5.0)	13 (6.5)	0.519
Hepatobiliary	3 (1.5)	2 (1.0)	0.653

Patients with blood cultures first taken from the ED were more likely to have symptoms of fever, chills, dizziness, rigors, and a respiratory source of symptoms (Table 2). The general laboratory investigations were largely similar between both groups except for a higher neutrophil:lymphocyte ratio in the ED group (Table 3).

The primary outcome of true positive blood culture proportion was significantly higher in the ED group (13.5% (27/200) vs. 6.0% (12/200), P = 0.01), which also had a significantly higher proportion of false positive results (4.0% (8/200) vs. 0.5% (1/200), P = 0.02). General ward patients were less likely to receive empirical antibiotics after having their blood cultures taken (48.0% (96/200) vs. 89.0%, (178/200) P < 0.001). When empirical antibiotics were administered in the general ward, oral antibiotics were prescribed more often compared to the ED (9.4% (9/96) vs. 2.2% (4/178), P = 0.008).

Of 200 blood cultures done in the general ward within 24 h of admission, there were 12 (6.0%) true positive results. Based on the blood culture sensitivity results, 3

Table 3 Laboratory results, radiology investigations and treatment.

Variable	ED cases (n = 200)	General ward cases (n = 200)	P value
Blood culture results			
Positive	27 (13.5)	12 (6.0)	0.0115
Negative	165 (82.5)	187 (93.5)	0.0007
Contaminant	8 (4.0)	1 (0.5)	0.0183
Hemoglobin (mg/dL), median (IQR)	12.2 (10.1–13.7)	12.3 (10.45–13.8)	0.388
Total white cell count ($x10^9$/L), median (IQR)	11.63 (7.73–16.19)	10.83 (7.42–15.62)	0.293
Neutrophils (%), median (IQR)	n = 197 80.0 (70.2–87.9)	77.1 (67.0–84.6)	0.013
Lymphocytes (%), median (IQR)	10.1 (5.8–17.2)	12.7 (7.3–19.1)	0.021
Neutrophil:Lymphocyte, median (IQR)	8.03 (4.33–15.50)	6.05 (3.49–11.70)	0.020
Platelet ($x10^9$/L), median (IQR)	231 (166–322)	254.5 (171–315)	0.209
Creatinine (μmol/L), median (IQR)	75 (58–117)	81 (63.5–135)	0.089
Urea, (mmol/L), median (IQR)	5.7 (3.9–9.25)	5.95 (4.05–9.9)	0.546
C-Reactive Protein (mg/L), median (IQR)	n = 108 73.5 (29.5–123.5)	n = 132 52.5 (16.5–116.5)	0.098
Albumin (g/L), median (IQR)	n = 157 36 (32–41)	n = 140 36 (31–41)	0.337
Glucose (mmol/L), median (IQR)	n = 181 8.2 (6.1–11.3)	n = 165 7.8 (6.1–11.3)	0.531
$PaCO_2$ (mmHg), median (IQR)	n = 88 33.8 (29–40.15)	n = 57 34.6 (29.9–40.6)	0.640
PaO_2 (mmHg), median (IQR)	n = 88 74 (46–99)	n = 57 89 (66–124)	0.017
pH, median (IQR)	n = 88 7.43 (7.36–7.465)	n = 57 7.4 (7.32–7.46)	0.060
Lactate (mmol/L), median (IQR)	n = 122 1.6 (1.1–2.2)	n = 67 1.8 (1.1–2.8)	0.231
Urinary nitrite positive, n (%)	n = 101 19 (18.8)	n = 71 12 (16.9)	0.748
Urinary leukocyte positive, n (%)	n = 101 38 (37.6)	n = 71 30 (42.3)	0.541
Empiric antibiotics after blood culture taken, n (%)	178 (89.0)	96 (48.0)	<0.001
Antibiotics route, n (%)	n = 178	n = 96	
Oral	4 (2.2)	9 (9.4)	0.008
Intravenous	173 (97.2)	86 (89.6)	0.008
Intraperitoneal	1 (0.6)	1 (1.0)	0.656

patients had an appropriate antibiotic escalation, 8 patients had an appropriate step down to a narrower agent or from an intravenous to oral agent, while the last patient was kept on the initial empiric therapy despite blood culture results suggesting that it might be safe to step down. All patients were discharged well from hospital.

Factors associated with a positive blood culture

There were 39 (9.8%) true positive blood cultures results during the study period. Patients with a true positive blood culture were more likely to have a higher temperature, more rapid heart rate, lower median mean arterial pressure, presence of indwelling central catheter or peripherally-inserted central catheter, fever, chills or rigors than those with negative blood cultures. In a multivariate stepwise logistic regression model, the following two variables (odds ratio [OR]; 95% confidence interval [CI]) were found to be independently associated with true positive blood cultures: more rapid heart rate (1.02; 1.00 to 1.04) and presence of rigors (5.77; 1.34 to 24.88).

The Shapiro score was applied post hoc to all 400 patients, and stratified based on location of ED or general ward (Supplementary Table 2). A negative score was derived in 35.8% (143/400) of the cases and would have missed 1 patient (false negative) in the general ward who had a positive blood culture. A positive Shapiro score is not as useful in those with low pre-test probability of blood stream infections (likelihood ratio of positive score = 1.6).

Discussion

The lower proportion of true positive blood cultures in the general ward compared to the ED (6.0% vs. 13.5%) supports our hypothesis that utility of blood cultures performed in the general ward is lower than in the ED. The proportion of true positive blood cultures in our ED was also higher compared to majority of other international published studies, which range from 3.4% to 12.4% [1,9—12]. Hospital-wide studies generally had a higher positive blood culture rate of 8.3%—13.0% [13—15].

We postulate some reasons for the lower proportion of positive blood cultures in the general ward compared to ED. First, doctors in the ED may have a higher threshold to perform a blood culture than doctors in the general ward. Differences in the working environment including higher patient volume and consequently greater number of patients seen by each physician in the ED over a shorter contact time may have led to a more selective approach in obtaining blood cultures. In addition, the ED at our institution has continuous attending physician oversight that could have regulated the number of cultures performed. In contrast, the house staff or junior trainee who frequently attends to the patient first in the ward may order an array of tests beforehand, including blood cultures to expedite management. The perceived psychological safety of junior staff may also lead them to err on the side of caution by performing more rather than less blood cultures. Another reason may be the increasing recognition among emergency physicians on the limited utility of blood cultures, with few alterations in subsequent patient management [16,17]. In the general ward, the heterogeneity of practice, particularly with the presence of multiple medical and surgical disciplines may have led to the seemingly lower true positive proportion. While we did not investigate the volume of blood sampled, it is known that suboptimal volume of blood inoculated occurs frequently [14] and can reduce sensitivity [18]. Nevertheless, the non-differential misclassification of such cases in both the ED and general ward groups makes this factor less likely to explain our observed differences in true positive cases.

The use of clinical decision rules and scores such as the Shapiro score can provide a framework for junior doctors to reduce unnecessary blood cultures performed on low-risk patients. In our study, over a third of blood culture performed could have been avoided if such a score was used. However, it is extremely important to consider the overall clinical context of the patient, including other components of the history and physical examination, as a small proportion of patients with a negative score may have blood stream infections.

A second explanation of the lower true positive rate from those in the general ward is that the cultures were taken after antibiotic administration in the ED or when patients were less likely to be febrile after symptomatic medications. This emphasizes the importance of examining blood culture taking practices at an institutional level. Standardizing thresholds and situations for performing a blood culture may help to reduce suboptimal circumstances where a blood culture is deemed necessary by a new team of doctors after the administration of antibiotics by the prior team who felt it unnecessary. The usage of molecular diagnostic methods with improved sensitivity to detect bacteremia despite prior antibiotic administration may help to circumvent this limitation [19]. A study by Riedel et al. [20] interestingly found that the likelihood of a positive blood culture was not associated with the timing of collection relative to a fever spike, which disproves the preexisting notion that cultures have to be taken during a temperature spike to optimize its yield.

Tachycardia and rigors were found to be independently associated with a true positive blood culture in a multiple logistic regression analysis, emphasizing the importance of these clinical parameters in predicting bacteremia. An interesting point to note is that inflammatory markers such as C-reactive protein were not found to be associated with positive cultures. We did not analyze procalcitonin, which was not commonly tested at the point of data collection, but found in other studies to correlate well with bacteremia [21]. Guidelines and recommendations for performing a blood culture, can take into account factors such as heart rate and rigors, and pretest probabilities based on disease condition (e.g. low probability in community acquired pneumonia and cellulitis, higher probability in endocarditis and meningitis) [18] may be considered, instead of solely using fever as an indication to perform a blood culture.

Of the 12 (6.0%) positive cultures general ward, 3 had appropriate escalation of antibiotics while 8 had de-escalation. A study showed decreased costs of antibiotic therapy when there was appropriate de-escalation based on culture results and suggested the importance of avoiding unnecessary broad spectrum antibiotics to reduce antibiotic resistance [22]. However, this has to be balanced with the costs of false positive bacteremia including increased length of stay and financial costs [23]. A follow-

up prospective study on the clinical implications of blood cultures with an economic analysis would be beneficial. Manpower costs would need to be taken into consideration when determining if lower threshold of culturing in the general ward is appropriate.

The percentage of contaminants in blood cultures was much higher in the ED than general ward in our institute. We postulate that increased time constraints and overcrowding in the ED could have been associated with this increase [24,25]. A quality improvement project has since been commenced in the ED to improve the technique of doctors when performing a blood culture through use of checklists, direct observation and accreditation, showing sustained results of below 3% contamination rate in the last 24 months (results not published yet).

Novel molecular techniques using genetic amplification and mass spectrometry [26,27] have been gaining momentum in recent years as another diagnostic modality to allow rapid identification of large range of blood stream pathogens. These may change the role of blood cultures as the gold standard for the diagnosis of bacteremia, although the increased costs of these molecular techniques limit its current use for most patients.

Limitations

Our study has several limitations. First, although we randomly selected a month to include patients, the potential of selection bias cannot be ignored. Second, the retrospective nature of this study may have led to presence of bias due to missing information from clinical records. Third, selection of cases from the general ward may have been limited by patients with higher risk of bacteremia having already been included in the ED, thereby potentially skewing the results. Fourth, procalcitonin which has acceptable correlation with bacterial infection was not included in our study, and would be something useful to look at in future studies.

Conclusion

Positive blood cultures are useful in guiding antibiotic therapy in sepsis, however, excessive use can lead to increased costs, and taking blood cultures after antibiotic administration can lower its sensitivity. The proportion of true positive blood cultures was significantly lower in the general ward compared to the ED, which may arise from a lower threshold to do a blood culture in the general ward, and from cultures being taken after antibiotics have been administered. Adherence to best practice guidelines and standardization of practices are needed to improve the efficiency of blood culture taking practices in the hospital.

Conflicts of interest

There are no conflicts of interest to declare.

Sources of funding

There are no sources of funding to declare.

Ethics

This study was approved by the National Healthcare Group Institutional Review Board (2013/01128), which granted waiver of informed consent.

CRediT authorship contribution statement

Ellie Ci-En Choi: Conceptualization, Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Yet Hong Chia:** Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Yun Qing Koh:** Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Celestine Zi Qian Lim:** Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Jia Chen Lim:** Conceptualization, Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Shirley Beng Suat Ooi:** Conceptualization, Writing - review & editing. **Irwani Ibrahim:** Formal analysis, Writing - review & editing. **Win Sen Kuan:** Conceptualization, Data curation, Formal analysis, Writing - original draft, Writing - review & editing.

Acknowledgements

We would like to acknowledge A/Prof Arpana Vidyarthi for her advice and assistance in proofreading the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.idh.2018.10.003.

Provenance and peer review

Not commissioned; externally peer reviewed.

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