Can the Number of Coagulase-negative Staphylococci Specimens Detected be an Alternative Quality Indicator to the Blood Culture Contamination Rate?

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Research Article

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Abstract

**Purpose:** Coagulase-negative staphylococci (CoNS) are the most frequent contaminating bacteria; hence, we aimed to investigate an indicator of CoNS to predict the increase in blood culture contamination rate (ConR).

**Methods:** We performed a retrospective study of selected patients who underwent blood culture testing.

**Results:** Cases with CoNS-positive blood cultures correlated with ConR ($r=0.85$). The area under the receiver operating characteristic curves for the number of cases with ConR $\geq 2.5$ did not differ statistically from that of the number of cases contaminated by CoNS.

**Conclusion:** The number of CoNS-positive cases could help predict an increase in ConR $\geq 2.5$.

Introduction

Relevant culture tests are important for the appropriate use of antimicrobial agents to combat antimicrobial-resistant bacteria. However, these tests can result in increased contamination, leading to an excessive use of antimicrobial agents, contributing to longer hospital stays and higher costs [1, 2]. Although the blood culture contamination rate (ConR) is calculated retrospectively based on certain criteria [3], its calculation is time-consuming and requires some labour. Coagulase-negative staphylococci (CoNS) are the most frequently detected bacteria on blood culture contamination [2]. Therefore, we intended to investigate a simple real-time indicator of CoNS to predict the increase in ConR.

Results

A total of 104,853 sets of blood cultures were collected during the study period. Of these, 14,227 sets were culture-positive and 1,149 sets were excluded due to pending determination in 190 cases and no determination in 404 cases. A total of 2,142 cases were determined as contaminated; of these, 1,689 (78.9%) cases were contaminated with CoNS. The ConR was 2.5% or higher for 28 months of the total study period (25.9%) (Supplementary Fig. 1). The correlation coefficients with ConR for indicators A–D were 0.71, 0.85, 0.91, and 0.93, respectively (Fig. 1). The ROC curve is shown in Fig. 2, with AUCs (95% confidence interval) of 0.85 (0.78 to 0.93), 0.93 (0.88 to 0.98), 0.95 (0.92 to 0.99), 0.97 (0.93 to 1.00), respectively. On comparing the AUCs for each indicator, we found that A vs. B, A vs. C, and A vs. D were statistically significant with Holm correction (Supplementary Table 1). The sensitivity was 78.6%, 92.9%, 92.9%, and 100%, and the specificities were 78.7%, 80.0%, 87.5%, and 87.5%, with cut-off values of 33 sets, 23, 19, and 19 cases for indicators A–D, respectively; all with a high negative predictive value of 91.3–100%.

Discussion
These results suggest that the number of CoNS-positive cases correlated with ConR to predict a ConR of \( \geq 2.5 \), as well as the number of CoNS-contaminated cases. However, high negative predictive rates were observed for all indicators, indicating that if the number of cases with CoNS detection or CoNS positivity remained low, it was unlikely that the ConR would increase. Although the sensitivity and specificity for predicting \( \text{ConR} \geq 2.5 \) were higher when indicators C or D were used, the former requires time until another blood culture set collected at the same time is determined to be negative, and the latter requires human resources and time to determine contamination. In contrast, indicators A and B do not require much human resources and can be displayed in real time. As for the calculation of ConR, most hospitals do it once a month; however, only less than 30% of the facilities report it over a longer span of time [7]. Indicators A and B may be good predictors for ConR in such institutes.

ConR of \( \leq 3.0 \) is often used as a standard for the quality of blood culture tests [8]. In this study, we set the predicted ConR to be \( \geq 2.5 \). As the cut-off was increased, the predictive power of each index increased because the number of months covered decreased; however, there was no difference in the trend of AUC between 2.5% or higher and 3.0% or higher (Supplementary Table 2). ConR is related to disinfection of the puncture site, collection method, hand hygiene, education, and feedback methods regarding collection [9]. Recently, the usefulness of a blood collection device has also been reported [10]. These relevant factors can be reviewed when CoNS-positive cases increase. In addition, it has been reported that feedback from monitoring results alone can improve the ConR [9, 11]. Therefore, establishing a system that provides real-time feedback on the number of cases of CoNS detection may be a countermeasure to reduce contamination without requiring additional labour.

However, the situation regarding blood cultures varies from hospital to hospital [7]. For example, in facilities with many patients with central venous catheters, true infection by CoNS is more common. Therefore, the results of this study, especially the cut-off values, may not be directly applicable to other facilities. However, as CoNS is the most commonly detected organism in contamination, a similar result can be predicted. It would be desirable to set a cut-off and determine the correlation with ConR at least once at one’s own institution before using it as a simple indicator.

**Methods**

**Study design**

We performed a retrospective study of patients who underwent blood culture testing at the National Center for Global Health and Medicine between April 2012 and March 2021. The need for informed consent was waived due to the retrospective nature of the study design. The study information was presented on the Web for the possibility of opting out of consent. This was substituted for the participants’ consent. The protocol of this study including the opt-out consent method was approved by the Certificate Review Board of National Center for Global Health and Medicine (NCGM-G-004168-00) and conformed to the amended Declaration of Helsinki. The data were compiled from the registry of blood culture surveillance, including data on contamination, and the microbiology laboratory.
The registry data of blood culture surveillance

For every case, two or more infectious disease physicians of the National Center for Global Health and Medicine determined whether the case was contaminated from a clinical point of view by reviewing clinical records and laboratory data in accordance with the CUMITECH criteria [3]. Undetermined cases and those with pending determination were excluded from the study.

Identification of bacterial species

All blood culture samples were collected into standard aerobic and anaerobic culture bottles (92F or 94F and 93F, 23F or 20F and 24F Becton Dickinson Microbiology Systems, Sparks, MD, USA) and processed using the BACTEC 9240, 9120, and FX systems (Becton, Dickinson and Company, Franklin Lakes, NJ, USA). These samples were routinely monitored for at least 144 h. The bottles that tested positive were removed and subjected to Gram staining. The specimens were then inoculated into 5% sheep blood agar and BTB agar media (Nissui Pharmaceutical Co., Ltd., Tokyo, Japan), and incubated at 35°C (Depending on the situation, other media may be added or the environment may be changed, such as anaerobic incubation). Conventional bacterial identification and susceptibilities to the predefined antimicrobials were determined in accordance with the Clinical and Laboratory Standard Institutions criteria (M100) [4, 5] by matrix assisted laser desorption/ionization-time of flight mass spectrometry system (MALDI Biotyper system; Bruker, Billerica, MA, USA) and automated broth micro dilution system (MicroScan WalkAway 96 SI system; Beckman Coulter, Brea, CA, USA). All Staphylococci species, except Staphylococcus aureus and S. lugdunensis, were treated as CoNS.

Indicators

We calculated the monthly ConR [(total number of contaminated cases per month) / (total number of blood culture sets collected per month) × 100] [3]. The values of the four indicators were aggregated as follows: the number of CoNS-positive sets (Indicator A), CoNS-positive cases (Indicator B), cases with only one CoNS-positive blood culture set (Indicator C), and cases of CoNS contamination (Indicator D).

Statistical analysis

Correlation coefficients were calculated using Pearson's correlation test. Receiver operating characteristic (ROC) curves were prepared for all indicators with a ConR of ≥ 2.5, as the objective variable, and cut-off values were calculated using Youden's index. The area under the curves (AUCs) were compared using the Delong method with the Holm correlation. Statistical analysis was performed using EZR for Windows version 1.54 [6]. Figures were created using IBM SPSS Statistics software for Windows (version 26.0; IBM Corp., Armonk, NY, USA). The probability of significance was calculated to be 5%.

Declarations
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Authors' contributions

KY came up with the conception and design of the study, and analysed and interpreted data. KY and KM acquired data. KY wrote drafting the article, and KM and NO revised it critically for important intellectual content. All authors reviewed the manuscript and approved the final version to be submitted.

has nothing to declare.

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K.M. declare no competing interests.

Ethics approval:

The need for informed consent was waived due to the retrospective nature of the study design. The study information was presented on the Web for the possibility of opting out of consent. The protocol was approved by the institutional review board of the National Center for Global Health and Medicine (NCGM-G-004168-00).

Consent to participate:

The study information was presented on the Web for the possibility of opting out of consent.

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**Figures**
Figure 1

Scatter plot of correlation of ConR of each group (Indicator A–D) a: Number of CoNS detected per specimen b: Number of CoNS detected per case c: Cases with only one set of positive CoNS d: Contamination cases by CoNS ConR: contamination rate; CoNS: coagulase-negative staphylococci

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryFigure1.tif
- SupplementaryTable.pdf