

## ORIGINAL RESEARCH

# Predicting Bacteremia Based on Nurse-Assessed Food Consumption at the Time of Blood Culture

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**BACKGROUND:** Bacteremia and its complications are important causes of morbidity and mortality in hospitalized patients. However, the yield of blood cultures is relatively low, with many false-positive results from bacterial contamination.

**METHODS:** We investigated the relationship between patient food consumption and the presence of bacteremia. This was an observational analysis of a cohort of 1179 patients who underwent blood culture analysis between January 2005 and December 2009. Patients with anorexia-inducing conditions, such as gastrointestinal illness and malignant disease treated with chemotherapy, were excluded. Food consumption was rated by nurses as the percentage of food consumed during the meal preceding the blood culture. Groupings were as follows: low

consumption (<50%), moderate (>50% to <80%), and high (>80%).

**RESULTS:** Low consumption was observed in 39.8% of patients, moderate in 17.8%, and high in 41.6%. The average body temperature was  $38.1 \pm 1.1^\circ\text{C}$ . Bacteremia was present in 18.5%, 3.9%, and 1.4% of patients in the low, moderate, and high food consumption groups, respectively. The negative predictive value was 98.3%, suggesting that bacteremia is very unlikely in the setting of good food intake.

**CONCLUSION:** Bacteremia is an unlikely occurrence in hospitalized patients who maintain adequate food consumption at the time of blood culture. *Journal of Hospital Medicine* 2012;7:702–705. © 2012 Society of Hospital Medicine

Fever is a nonspecific phenomenon that can result from many inciting causes such as infection, inflammation, malignancy, thromboembolic disease, drugs, and endocrine disease. In hospitalized patients, one of the most important clinical considerations is bacteremia. Although vital signs compose 3 of the 4 current criteria for the diagnosis of Systemic Inflammatory Response Syndrome (SIRS),<sup>1,2</sup> they contribute little to the diagnosis of the cause, which can be inflammation or infection. Unfortunately, the physician's clinical diagnosis of bacteremia lacks both sensitivity and specificity.<sup>3–5</sup> Blood culture acquisition is a simple and basic diagnostic procedure routinely used in clinical practice that yields essential information for the evaluation of various infectious diseases.<sup>6</sup> Positive blood cultures can demonstrate not only an infectious cause of disease but also the microbiological response to an-

tibiotic therapy.<sup>7</sup> However, studies have reported that 35% to 50% of positive blood cultures are falsely positive owing to contamination.<sup>7–11</sup> False-positive cultures may lead to the use of inappropriate or unnecessary antibiotics, additional testing and consultation, and prolonged hospitalizations that increase patient care costs.<sup>9,12</sup>

Nursing staff caring for patients are generally able to assess oral intake, general clinical state, and care requirements. Moreover, the nursing staff are often able to identify problems with patients before physicians.<sup>13</sup> In Japan, nurse-assessed food consumption of every meal is standardized, and is frequently regarded as an indicator of the patient's clinical status, akin to a vital sign. In this context, we hypothesized that quantitative variations in food consumption could accurately distinguish those patients with or without bacteremia.

## MATERIALS AND METHODS

### Study Design

Between 2005 and 2009, we conducted a cross-sectional observational study at Juntendo University Nerima Hospital in Tokyo, Japan. We evaluated 1179 consecutive Japanese patients (mean age,  $67.8 \pm 16.8$  years; 51% male) who underwent blood cultures. Patients with anorexia-inducing conditions, such as gastrointestinal disease and those who were receiving

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chemotherapy for malignancy, were excluded. We also excluded patients who were not allowed to eat a regular diet. Patients aged <6 years old were also excluded. The indication for blood culture acquisition was at the discretion of the treating physicians. In general, when an axillary temperature >37.5–38°C developed, blood cultures were taken. The study was approved by the ethics committee of Juntendo University Nerima Hospital, and was conducted in accordance with the Helsinki Declaration of 1971, as revised in 1983.

### Definition of Bacteremia

In this study, bacteremia was defined as follows:

1. Identical organisms isolated from 2 sets of blood cultures (a set refers to 1 aerobic bottle and 1 anaerobic bottle).
2. If only 1 set of blood cultures was acquired and was positive for a pathogenic organism (such as enteric Gram-negative bacilli or *Streptococcus pneumoniae*) that could account for the clinical presentation, then the culture was considered positive.<sup>7,14,15</sup>

### Definition of Contamination

We considered as contaminants organisms common to skin flora, including *Bacillus* species, coagulase-negative staphylococci, *Corynebacterium* species, and *Micrococcus* species, without isolation of an identical organism with the same antibiotic susceptibilities from another potentially infected site in a patient with incompatible clinical features and no attributable risks.<sup>16</sup> Single blood cultures positive for organisms thought unlikely to explain the patient's symptoms were also considered contaminants.

### Assessment of Food Consumption and Inter-Assessor Reliability

Nursing staff assessed the patients' food consumption by estimating the percentage intake at each meal, and we characterized the patients' oral intake based on the meal immediately prior to the blood culture. We categorized the patients into 3 groups: low food consumption group (<50% consumed), moderate food consumption group (>50% to <80% consumed), and high food consumption group (>80% food consumed). To assess the reliability of the evaluations of food consumption, 100 patients (separate from this main study) were selected randomly and evaluated independently by 2 nurses. The kappa score of agreement between the nurses was 0.79 (95% confidence interval [CI], 0.77–0.80) indicating a high level of concordance.

### Other Predictor Variables

In addition to food consumption, we considered the following additional predictor variables: age, leukocyte count, C-reactive protein (CRP), systolic blood pressure, heart rate, and body temperature.<sup>17</sup> These predictor variables were obtained just prior to the blood culture acquisition. We defined systemic inflam-

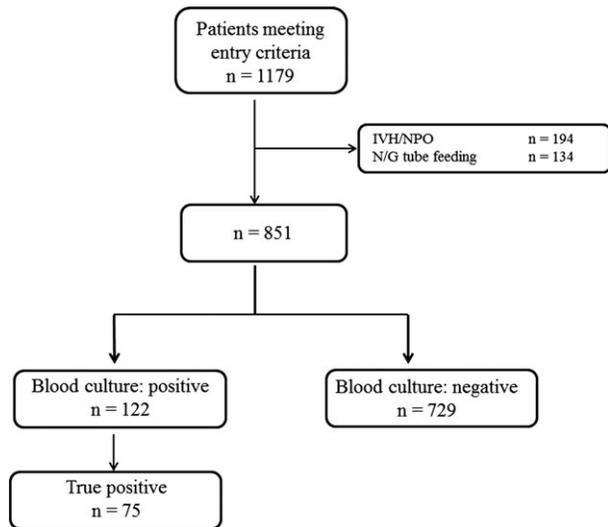
matory response syndrome (SIRS) based on standard criteria (heart rate of  $\geq 90$  beats/min, temperature of  $\leq 36$  or  $\geq 38^\circ\text{C}$ , and leukocyte level of  $\leq 4000$  or  $\geq 12,000$  cells/mL), and sepsis as SIRS in the context of clinical evidence or microbiological findings suggesting a primary focus of infection. Two investigators independently determined whether sepsis was present in each case, and the differences were resolved by consensus. Age subclassifications were categorized into 2 groups (<69 years and >70 years). CRP levels were dichotomized as above or below 10.0 mg/dL.

### Statistical Analysis

Continuous variables were presented as medians with the associated interquartile range. Univariate analysis was performed using the Student's *t* test for continuous variables and the Pearson chi-square test for categorical variables. Locally weighted regression analysis was applied for continuous variables significantly predictive of the outcome in univariate analysis, and the log odds of the outcome was performed to explore which cut-off points were the best predictors of true-positive blood culture results.<sup>18</sup> Evaluation of best fit was performed using a multivariate logistic regression model with a forward stepwise procedure, with significant multivariate predictors of the outcome kept in the model and expressed as adjusted odds ratios. Calibration was evaluated using the Hosmer-Lemeshow goodness-of-fit test. We calculated the sensitivity and specificity, and positive and negative predictive value for criteria to predict bacteremia. As a subgroup analysis, we repeated the above analytic approach after excluding those patients exposed to antibacterial drugs (which might independently impact food intake). All hypothesis testing was 2-tailed, and *P* values of less than 0.05 were considered statistically significant. Statistical analysis was performed using the SPSS v.16.0 software package (SPSS Inc, Chicago, IL).

## RESULTS

During the study period, 851 patients aged 16 to 99 years ( $66.8 \pm 16.6$ ), were eligible for inclusion (Figure 1). Baseline characteristics of the subjects are given in Table 1. The mean body temperature ( $\pm$  standard deviation [SD]) was  $38.1 \pm 1.1^\circ\text{C}$ , and the mean CRP level was  $8.7 \pm 8.1$  mg/dL. The results show that the patients had at least 2 SIRS criteria with elevations in temperature and heart rate. Of the 851 patients entered into the study, only 122 (14.3%) had positive blood cultures. Of these, 75 patients (8.8%) were considered to have true-positive blood culture. In this study, blood cultures were taken at the time of onset of fever, whether that was a new inpatient admission, or during the course of an admission to the hospital. On average, blood cultures were drawn 12 days after admission (SD, 5.6 days). Despite the variation in onset of fever, the inverse relationship of blood culture positivity to decreased food



**FIG. 1.** Study cohort. Abbreviations: IVH, intravenous hyperalimentation; N/G, nasal gastric; NPO, nil per oral.

consumption held true (data not shown). Gram-positive and Gram-negative organisms were obtained in near equal amounts. The main pathogens recovered from the true-positive blood cultures were Gram-positive cocci (26 patients [34.7% in true-positive blood cultures]), and Gram-negative bacilli (46 patients [61.3%]), as shown in Table 1. The underlying clinical diagnosis included 28 urinary tract infections; 9 catheter-associated infections; 5 cases each of pneumonia and abscess; 3 cases of phlebitis; 2 cases of meningitis and osteomyelitis; 1 case each of infective endocarditis, decubitus ulcer, and pelvic infection; and 17 cases of infection with an unknown focus.

**TABLE 1.** Characteristics of Patients (n = 851)

|                                 | Mean  | SD   |
|---------------------------------|-------|------|
| Age, years                      | 66.8  | 16.7 |
| Male (%)                        | 50.6  |      |
| Vital signs                     |       |      |
| Systolic blood pressure, mmHg   | 122.6 | 25.9 |
| Diastolic blood pressure, mmHg  | 65.3  | 14.6 |
| Heart rate, beats/min           | 91.1  | 19.2 |
| Body temperature, °C            | 38.1  | 1.1  |
| Laboratory results              |       |      |
| Leukocyte, × 100 µ/L            | 10.6  | 11.8 |
| C-reactive protein, mg/L        | 8.8   | 8.1  |
| Results of blood cultures       |       |      |
| Blood culture positive          | 122   | 14.3 |
| True positive                   | 75    | 8.8  |
| Gram-positive coccus            | 26    | 3.1  |
| Gram-negative bacilli           | 46    | 5.4  |
| Gram-negative coccus            | 1     | 0.1  |
| Fungus                          | 1     | 0.1  |
| Anaerobic                       | 1     | 0.1  |
| Contamination                   | 47    | 5.6  |
| Blood culture negative          | 729   | 85.7 |
| Food consumption                |       |      |
| Low food consumption group      | 344   | 4.4  |
| Moderate food consumption group | 152   | 17.9 |
| High food consumption group     | 354   | 41.4 |

Abbreviations: SD, standard deviation.

Low, moderate, and high food consumption groups consisted of 344 patients (40.4%), 152 patients (17.9%), and 354 patients (41.7%), respectively (Table 1). Of these, 63 patients, 6 patients, and 6 patients had bacteremia in the low, moderate, and high food consumption group, respectively. In order to distinguish those patients who had decreased food consumption compared to almost normal food consumption, low and moderate food consumption groups were combined and compared to the high food consumption group. Comparison of the combined low and moderate food consumption group versus the high food consumption group revealed a sensitivity of 92.0% and a negative predictive value of 98.3% for excluding true bacteremia. Conversely, the specificity (45.1%) and the positive predictive value (13.9%) were poor.

In the univariate analysis, the following variables were not statistically significantly associated with true bacteremia: age, heart rate, and leukocyte counts. Significant univariate predictors of bacteremia and their associated cut-off points were body temperature of  $\leq 36$  or  $\geq 38^\circ\text{C}$  (odds ratio [OR], 2.5; 95% CI, 1.5–4.4), CRP  $\geq 10.0$  mg/dL (OR, 2.0; 95% CI, 1.2–3.2), and food consumption (OR, 8.5; 95% CI, 3.8–18.6) (Table 2). There was no evidence of collinearity. In the final stepwise logistic regression (Table 3), the significant predictors of bacteremia were body temperature of  $\leq 36$  or  $\geq 38^\circ\text{C}$  (OR, 2.4; 95% CI, 1.4–4.2;  $P = 0.002$ ), C-reactive protein of  $\geq 10.0$  mg/dL (OR, 1.9; 95% CI, 1.2–3.0;  $P = 0.011$ ), and food consumption (OR, 7.5; 95% CI, 3.4–16.6;  $P < 0.001$ ). We identified only 6 patients with bacteremia in the high food consumption group. Three of the patients had been previously treated with antibiotics for conditions

**TABLE 2.** Univariate Correlates of Bacteremia

| Variables                                     | Blood Culture Result   |                   | P Value | OR (95% CI)    |
|---|------------------------|-------------------|---------|----------------|
|   | Negative (n = 729) (%) | Positive (n = 75) |         |                |
| Age, years                                    | 66.6                   | 69.0              |         |                |
| Mean ± SD                                     | 16.9                   | 13.5              |         |                |
| ≥70   | 408 (56.0)             | 43 (57.3)         | 0.7     |                |
| Heart rate, beats/min                         | 90.5                   | 96.3              |         |                |
| Mean ± SD                                     | 19.0                   | 20.3              |         |                |
| ≥90   | 368 (50.4)             | 43 (57.3)         | 0.3     |                |
| Temperature, °C                               | 38.0                   | 38.6              |         |                |
| Mean ± SD                                     | 1.0                    | 1.6               |         |                |
| ≤36, ≥38                                      | 444 (61.0)             | 61 (81.3)         | <0.001  | 2.5 (1.5–4.4)  |
| Leukocyte count, cells/µL                     | 10.1                   | 11.2              |         |                |
| Mean ± SD, × 100                              | 12.1                   | 7.4               |         |                |
| ≥120 × 10 <sup>3</sup> , <4 × 10 <sup>3</sup> | 336 (46.1)             | 38 (50.7)         | 0.4     |                |
| C-reactive protein                            |                        |                   |         |                |
| Mean ± SD                                     | 7.8                    | 10.0              |         |                |
| ≥10.0   | 245 (33.6)             | 39 (52.0)         | 0.0004  | 2.0 (1.2–3.2)  |
| Food consumption                              |                        |                   |         |                |
| Low and moderate                              | 426 (58.9)             | 69 (92.0)         |         |                |
| High  | 350 (48.0)             | 6 (8.0)           | <0.001  | 8.5 (3.8–18.6) |

Abbreviations: CI, confidence interval; OR, odds ratio; SD, standard deviation.

**TABLE 3.** Independent Predictors of Bacteremia

| Variables                                 | OR (95% CI)    | P Value |
|---|----------------|---------|
| Temperature, °C $\leq 36$ or $\geq 38$    | 2.4 (1.4–4.2)  | 0.002   |
| C-reactive protein, mg/dL $\geq 10.0$     | 1.9 (1.2–3.0)  | 0.011   |
| Food consumption High vs low and moderate | 7.5 (3.4–16.6) | <0.001  |

Abbreviations: CI, confidence interval; OR, odds ratio.

including infective endocarditis, osteomyelitis, and myelodysplastic syndrome.

On further analysis, we excluded patients who had received antibiotics before blood culture acquisition. There were 661 patients in this subanalysis. Low, moderate, and high food consumption groups consisted of 282 patients (41.4%), 118 patients (17.3%), and 261 patients (38.3%), respectively. Of these, 50 patients (17.7%), 5 patients (4.2%), and 4 patients (1.5%) had bacteremia in the low, moderate, and high food consumption groups, respectively. The sensitivity and negative predictive values were 93.2% and 98.5%, respectively. In the stepwise logistic regression, significant predictors of bacteremia were body temperature of  $\leq 36$  or  $\geq 38^\circ\text{C}$  (OR, 3.0; 95% CI, 1.5–5.6;  $P = 0.001$ ), CRP  $\geq 10.0$  mg/dL (OR, 2.1; 95% CI, 1.2–3.7;  $P = 0.006$ ), and food consumption (OR, 9.3; 95% CI, 3.3–26.1;  $P < 0.001$ ).

## DISCUSSION

We found that in a group of 851 Japanese patients who were suspected with bacterial infection, the estimated food consumption was negatively associated, both significantly and independently, with the subsequent isolation of microorganisms from their blood cultures. If validated in other studies, this simple rule of thumb can provide the clinician with reasonable confidence that a febrile patient has a low probability of being bacteremic, as long as the appetite remains normal. Both the sensitivity and the negative predictive value were extremely high at 92.3% and 98.3%, respectively, suggesting that adequate oral intake is a strong marker against the presence of bacteremia. In this study, it was the strongest predictor of bacteremia in multivariate analysis. After including only antibiotic-naïve patients, the sensitivity and the negative predictive values were 93.2% and 98.5%, respectively. Administration of antibiotics may lead to improved appetite in febrile patients despite bacteremia in the presence of fever, and therefore, inquiring about recent or current antimicrobial usage should be a requirement when considering oral intake as an indicator of bacteremia.

Our study has limitations. Since we did not make treatment decisions based on oral intake, we cannot conclude that it is safe to withhold antibiotic treatment on the basis of food intake alone. Additionally, this study would need to be repeated across many different age groups and racial groups to ensure applicability to the general population. It is also unknown whether this rule would be applicable to patients with

underlying immunosuppression. Finally, although inter-rater reliability was high in our center, nurses in other settings may not be as diligent in their assessment of food consumption. The high inter-assessor reliability in our setting, however, suggests that objective assessment of food intake can be performed reliably in settings in which accurate documentation of food consumption is expected.

In summary, we found that normal food intake was strongly and negatively associated with bacteremia in febrile patients. This observation, if validated in other settings, may serve as a simple aid to assist in the clinical diagnosis of bacteremia or for recruitment of patients with a high likelihood of bacteremia into clinical trials.

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