



CLINICAL RESEARCH STUDY

# The degree of chills for risk of bacteremia in acute febrile illness

Yasuharu Tokuda, MD, MPH, FACP,<sup>a,b</sup> Hitoshi Miyasato, MD,<sup>a</sup>  
Gerald H. Stein, MD, FACP,<sup>c,d</sup> Tomokazu Kishaba, MD, FACP<sup>a</sup>

<sup>a</sup>Department of Medicine, Okinawa Chubu Hospital, Okinawa, Japan; <sup>b</sup>Harvard School of Public Health, Boston, Mass;  
<sup>c</sup>Department of Medicine, College of Medicine, University of Florida, Gainesville; and <sup>d</sup>University of Hawaii, Honolulu.

**KEYWORDS:**

Chills;  
Shivering;  
Bacteremia;  
Sepsis;  
Bacterial infections

**ABSTRACT**

**PURPOSE:** Patients with acute febrile illness may experience different degrees of chills. To evaluate the different degrees of chills in predicting risk of bacteremia in patients with acute febrile illness, we performed a single-center prospective observational study.

**METHODS:** We enrolled consecutive adult patients with acute febrile illness presenting to our emergency department. We defined mild chills as cold-feeling equivalent such as the need of an outer jacket; moderate chills as the need for a thick blanket; and shaking chills as whole-body shaking even under a thick blanket. We estimated risk ratios of the different degrees of chills for bacteremia using multivariable adjusted Poisson regression.

**RESULTS:** Of a total 526 patients, 40 patients (7.6%) had bacteremia. There were 65 patients (12.4%) with shaking chills, 100 (19%) with moderate chills, and 105 (20%) with mild chills. By comparing patients with no chills, the risk ratios of bacteremia were 12.1 (95% confidence interval [CI] 4.1-36.2) for shaking chills, 4.1 (95% CI 1.6-10.7) for moderate chills, and 1.8 (95% CI 0.9-3.3) for mild chills. Shaking chills showed a specificity of 90.3% (95% CI 89.2-91.5) and positive likelihood ratio of 4.65 (95% CI 2.95-6.86). The absence of chills showed a sensitivity of 87.5% (95% CI 74.4-94.5) and negative likelihood ratio of 0.24 (95% CI 0.11-0.51).

**CONCLUSION:** Evaluation of the degree of chills is important for estimating risk of bacteremia in patients with acute febrile illness. The more severe degree of chills suggests the higher risk of bacteremia.

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Bacteremia is a cause of high mortality and morbidity in patients with acute febrile illness.<sup>1-3</sup> Blood cultures are mandatory tests for proving bacteremia and obtaining bacteriological identity and its antibiotics sensitivity.<sup>4</sup> Thus, most physicians have low thresholds for drawing blood cultures and initiating empiric antibiotics for patients with acute febrile illness.<sup>5</sup> However, it is often difficult to esti-

mate the probability of bacteremia based on clinical judgment.<sup>6,7</sup> Therefore, the yield of blood cultures is relatively low, and there are many false positive contaminants that may lead to unnecessary therapy.<sup>8</sup>

Previous studies have established several clinical predictors of bacteremia. Of these, baseline predictors include old age, major comorbidity, poor functional status, and intravenous drug abuse.<sup>5,8</sup> Vital sign predictors were high fever, tachycardia, and low blood pressure.<sup>8,9</sup> Predictors in clinical examination included the signs of acute abdomen, altered mental status, and the presence of chills.<sup>5,6,8,10</sup> Laboratory

Requests for reprints should be addressed to Yasuharu Tokuda, MD, MPH, FACP, 281 Miyasato, Uruma City, Okinawa 904-2293 Japan.  
E-mail address: tokuyasu@orange.ocn.ne.jp.

predictors were high blood leukocyte count, low platelet count, low serum albumin, and high serum creatinine.<sup>5,9</sup> However, the clinical prediction rules using these predictors were only partially successful for predicting bacteremia.<sup>7,9,11</sup> Recent interest seemed to be shifted to expensive laboratory measurements such as C-reactive protein, procalcitonin and cytokines.<sup>12-14</sup>

Of the predictors mentioned above, the presence of chills was one of the most powerful single predictors.<sup>15-18</sup> In addition, we observed that the severest form of chills, namely shaking chills, would be more predictive for bacteremia compared with the minor form of chills.<sup>19,20</sup> We also practiced interviewing the patients to specifically ask about the qualitative degree of their chills.<sup>19</sup> However, no previous studies evaluated the association of different degrees of chills with bacteremia. Thus, our study objective was to determine risk ratios of the different qualitative degrees of chills for bacteremia and to analyze statistical characteristics in patients with acute febrile illness. These simple clinical observations would report for the first time that basic bedside findings may help clinicians identify high-risk patients in whom the blood cultures are most likely to yield a bacterial pathogen.

## Methods

### Patient assembly and data collection

In our prospective observational study, we enrolled consecutive patients (aged 15 years and older) who presented with acute febrile illness and were admitted to the emergency department of Okinawa Chubu Hospital, Japan. The hospital is a major community hospital and provides primary and specialty care to a population of approximately 400 000. Patient enrollment was from 2 periods (May to July and January to March) to include both summer and winter seasons.

The patient inclusion criteria were all of the following: axillary or oral temperature  $\geq 38.0^{\circ}\text{C}$  by patient self-report or at the hospital emergency department (some bacteremic patients might have no fever at the time of hospital arrival); a febrile illness of less than 2 weeks' duration before presenting to the emergency department; admitted through the acute care outpatient division to the admission division of the emergency department to evaluate suspected bacterial infection. These criteria were based on the study method of Leibovici et al.<sup>5</sup>

We analyzed baseline clinical characteristics including demographics, comorbidity, antibiotic use during the 4 days before hospital arrival, vital sign data, and blood leukocyte count. We recorded blood leukocyte count data performed within 24 hours after patient presentation. For medical comorbidity, we used the modified classification based on the *ICD-9-CM (International Classification of Diseases, Ninth Revision, Clinical Modification)* coding scheme.

We evaluated the patients' chills from the clinical history during the 24 hours before presenting to the emergency

department. We used qualitative degree criteria of chills based on our practice and classified them into the following: "mild chills": feeling cold with equivalent of the need for an outer jacket; "moderate chills": feeling very cold with equivalent of the need for a thick blanket; "shaking chills": feeling extremely cold with rigor and generalized bodily shaking even under a thick blanket. The physicians had instructional sessions of interviewing for chills before serving in the emergency department. These emergency physicians were required to record the degree of chills when they ordered blood cultures. When patients had reasons not to be interviewed (eg, mental status change), the family or accompanying persons were interviewed specifically regarding chills of the patient.

### Definition of bacteremia

Our primary outcome was a positive blood culture indicating bacteremia. The physicians performed blood culture collections within 12 hours after patient presentation to the emergency department. They were instructed to draw 10 milliliters of blood aseptically and inoculate them into an aerobic and anaerobic bottle, respectively; this procedure was repeated for drawing another blood sample from the different superficial vessels. As a result, we obtained 2 sets of blood cultures for each patient.<sup>4,21</sup> The bottles were incubated at  $37^{\circ}\text{C}$ , sub-cultured daily, and inspected for bacterial growth for 7 days. Positive bottles underwent microbiologic techniques for bacterial identification and antibiotics sensitivity testing.<sup>22</sup>

We defined bacteremia when a pathogenic microorganism was detected in at least one blood culture bottle and met the criteria of MacGregor and Beaty.<sup>23</sup> The episodes of bacterial contaminants were counted as negative cultures. The contamination criteria included all cultures that grew only *Corynebacterium* species, *Propionibacterium* species, or *Bacillus* species, and all cultures that grew *Staphylococcus epidermidis* and alpha-hemolytic *Streptococci* unless they were identified in 2 sets of blood cultures among patients with an intravascular device and otherwise no infectious site.<sup>24</sup>

We also collected postadmission data about the specific infective sites. For instance, we confirmed a urinary tract infection when the identical pathogenic bacteria were recovered from urine culture in the patient who was suspected to have this infection clinically.

### Statistical analysis

We used risk ratios as the primary measure of association for bacteremia of patients with different degrees of chills in reference to patients with no chills. We estimated risk ratios by multivariable Poisson regression rather than by using logistic regression in which odds ratio may overestimate true relative risk when analyzing common outcome.<sup>25</sup> Risk

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