Predicting Bacteremia in Hospitalized Patients

A Prospectively Validated Model

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Objective: To develop and validate a model for the prediction of bacteremia in hospitalized patients, and to identify subgroups of patients with a very low likelihood of bacteremia in whom a positive blood culture has a low positive predictive value.

Design: Prospective cohort study with clinical data on 1516 episodes collected from a random sample of all patients who had blood cultures done at one institution.

Setting: Urban, tertiary care hospital.

Patients: Derivation set: 1007 blood culture episodes sampled from all blood cultures done on patients at Brigham and Women's Hospital between October 1988 and February 1989. Validation set: 509 episodes, May 1989 to June 1989. The unit of evaluation was the episode, defined as a 48-hour period beginning after a blood culture was drawn.

Measurements and Main Results: True- and false-positive rates of blood cultures in the derivation set as assessed by independent reviewers were 7% (74 of 1007) and 8% (81 of 1007), respectively. Independent multivariate predictors of true bacteremia were temperature of 38.3 °C or higher, presence of a rapidly (< 1 month) or ultimately (< 5 years) fatal disease; shaking chills; intravenous drug abuse; acute abdomen on examination; and major comorbidity. In the low-risk group, defined by absence of these predictors, the misclassification rate of the model in the derivation set was 1% (4 of 303), and a positive blood culture had a positive predictive value of only 14% for true bacteremia. The model also identified a high-risk subset in which 16% (41 of 264) of episodes represented true bacteremia. The model was prospectively validated in 509 additional episodes, and the misclassification rate in the low-risk group was 2% (3 of 155).

Interventions: None.

Conclusion: These findings provide a means of stratifying hospitalized patients according to their risk for bacteremia. If prospectively validated in other settings, this model may be helpful when deciding whether or not to do blood cultures or start antibiotic therapy and, when evaluating a positive blood culture, to determine whether or not it is a true-positive.

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Despite the availability of antibiotics and other therapies, the approximately 200 000 cases of septicemia that occur in the United States annually are associated with 40% to 50% mortality (1). Because of the serious consequences of missing this diagnosis, physicians have a low threshold for doing blood cultures. Only about 5% of blood cultures, however, lead to true-positive results, and another 1.5% to 4.5% (2) result in contaminants, which may lead to increased testing, length of stay, and unnecessary therapy. The problem of false-positive isolates is particularly important in patients with a low pretest probability of bacteremia.

Relatively little is known about clinical predictors of bacteremia in adults (3-6), and physicians' estimates of the probability of bacteremia in hospitalized adults are often inaccurate (4, 7). The purposes of our study were to determine rates of true-positive and false-positive results for blood cultures in an inpatient population; to identify univariate and multivariate correlates of true bacteremia; to stratify patients into groups with varying likelihoods of bacteremia based on clinical characteristics; and to develop and validate a model for the identification of a subgroup of patients with a very low likelihood of bacteremia in whom a positive blood culture has a low positive predictive value.

Patients and Methods

All adults (≥ 15 years of age) who had blood cultures during two periods (November 1988 to February 1989, and May 1989 to June 1989) at Brigham and Women's Hospital were eligible. Data from the first period were used to develop a prediction algorithm; these patients represented the *derivation set* (the group used for deriving the model). Data from the later period were used to evaluate the algorithm's performance in an independent population, called the *validation set*.

The unit of evaluation was the blood culture episode, which was defined as a 48-hour period beginning when a blood culture was drawn. Other blood cultures drawn within the first 48 hours were considered part of the initial episode. If blood cultures were drawn after the end of the first episode, the patient was again eligible and this event was considered a new episode. Episodes were excluded if: any blood culture had been drawn within the previous week in a patient who was not already in the study; the reason for performing the blood culture was noted as follow-up of a previous positive blood culture; or the blood culture was one of routine weekly blood cultures done on the bone marrow transplant service. Data were collected on a minimum of ten new patients per day. Patients who had an episode beginning on a date when no patients were enrolled (some weekends, holidays) were excluded for that episode. When data could not be collected on all eligible patients on a given day, ten or more patients were randomly selected for evaluation.

Definitions and Bacteriologic Methods

A blood culture set was defined as any one blood drawing, regardless of the number of bottles filled. Blood cultures were drawn primarily by the phlebotomy teams during the day and by house officers and nurses at night. Two bottles per set (an aerobic bottle containing dextrose-phosphate broth and an anaerobic bottle containing thioglycolate medium) were routinely inoculated. Bottles were incubated for 7 days at 37 °C. The system for detection of growth included daily visual examination of bottles and routine subculturing at day 1 and day 6.

Data Collection

The hospital charts of all adults reported to have had blood cultures were reviewed the same day or the following morning by a single investigator. The bedside chart was reviewed for temperature data, and the patient was checked for the presence of intravascular devices and a urethral catheter. All evaluations were done before the results of the cultures were available.

Historical data recorded included presence of valvular heart disease; history of endocarditis; history of intravenous drug abuse; use of immunosuppressive drugs (grouped into none, chronic steroids, chemotherapy, and other); tests for human immunodeficiency virus (HIV); and presence of diabetes, the acquired immunodeficiency syndrome (AIDS), malignancy (not skin, except melanoma), leukemia, or foreign bodies. Shaking chills were considered present if they were noted in the chart; otherwise they were considered absent. Major comorbidity was defined as the presence of any of the following: coma or brain death, bowel perforation, multiple trauma or burns, cardiopulmonary arrest within the last 24 hours, cardiac or bone marrow transplantation, severe pancreatitis, the acute respiratory distress syndrome, or acute or chronic hepatic failure. The duration, type, and route of antibiotic therapy were recorded.

To account for differences related to severity of underlying disease, patients were prospectively stratified into three groups by one investigator using a modification of the criteria initially suggested by McCabe and Jackson (8). McCabe and Jackson's categories were rapidly fatal underlying disease, used only for patients with acute leukemia or blastic relapse of chronic leukemia; ultimately fatal underlying disease, used for all other patients whose underlying disease was likely to be fatal within 5 years; and nonfatal underlying disease. We defined rapidly fatal disease as predicted chance of fatality within 1 month greater than 50% secondary to any underlying disease, for example, the hepatorenal syndrome or acute leukemia in relapse with no further therapy planned; ultimately fatal disease as predicted chance of fatality within 5 years greater than 50%, for example, metastatic colon cancer or AIDS; and nonfatal as no underlying disease likely to be fatal within 5 years. Analysis of agreement between two independent reviewers for 56 randomly selected episodes yielded a kappa statistic of 0.75.

Physical examination data included temperature recorded by the nursing staff at the time that the blood culture was drawn, occurrence and timing of previous fevers, presence of hypotension (systolic blood pressure <90 mm Hg or use of vasopressor agents), and presence of focal findings on examination. An acute abdominal examination was defined as presence of rebound tenderness or guarding, or at least moderate tenderness. Laboratory data included leukocyte count, percent bands, erythrocyte sedimentation rate, urinalysis, chest roentgenogram, and all other relevant culture results. For all blood cultures, time and site of drawing (through a central venous catheter, arterial line, arteriovenous fistula, or peripheral vein) were recorded.

Reasons for drawing the blood culture were abstracted prospectively from the chart and assigned to one of six categories: fever (no source), suspected focal infection (therapy not started), suspected focal infection (on therapy at time of blood culture), suspected endocarditis, other, and unknown. Follow-up clinical data, including evaluation of the presence of focal bacterial infection and all relevant culture data, were collected from the medical record and the hospital laboratory 2 to 4 days after the episode began, and then at weekly intervals until discharge.

Definition of Endpoints

The primary outcome of interest was the blood culture result. Positive cultures were classified according to the criteria of MacGregor and Beaty (9), which include clinical criteria (many of which were withheld from the reviewers) and laboratory criteria, including presence of multiple positive cultures, organism type, and results of other cultures. Positive blood cultures were evaluated initially by two independent reviewers who were blinded to data on potential predictors, and who classified cases as true-positives, equivocal, or contaminants. To be classified as a contaminant by these initial reviewers, the organism had to be one that usually represents a contaminant, and the patient had to have received no antibiotic therapy and have done well. Any case on which there was disagreement or that was thought to be equivocal by either reviewer was then reviewed and classified by three infectious disease specialists, who were given a summary of MacGregor and Beaty's criteria (9) and brief synopses containing only pertinent follow-up data and intravenous line and prosthetic device status. Intravenous line and prosthetic device status were included because the consultants felt that they could not make determinations about some isolates without this information. If all three infectious disease specialists agreed on a result, it was classified as definite bacteremia (true-positive) or contaminant (false-positive). If two of three agreed, a result was considered probable. In the remainder of the analysis, probable and definite results were combined. In secondary analyses, two other potential definitions of bacteremia were used: if any reviewer felt bacteremia was present; or if all three reviewers agreed it was present. Because the resulting models were similar using all three definitions, only the primary analysis is presented.

Focal bacterial infection was considered documented if any of the following culture results were found: for urinary tract infections, more than 4 leukocytes/high power field and 100 000 organisms/mL or more; for pneumonias, presence of a new lobar infiltrate on chest roentgenogram, and pure growth of a recognized respiratory pathogen or 4+ growth of a recognized respiratory pathogen in the presence of mixed growth; and, for other sites, culture of a pathogen from a normally sterile site. An infection was categorized as presumed but not documented if a patient had a syndrome such as cellulitis or pneumonia but cultures were not diagnostic. Bacteremia that was classified by the reviewers as a true-positive but without a focal source was considered a documented infection.

Statistical Methods

The univariate relationships between true bacteremia and categorical and continuous variables in the derivation set were evaluated using the chi-square test with appropriate degrees of freedom and the Student *t*-test, respectively. Three odds ratios were compared using the Breslow-Day test for homogeneity of the odds ratio. In the initial analysis, 60 categorical and 10 continuous variables were evaluated. Univariate correlates of bacteremia ($P < 0.05$) were then entered into a stepwise logistic regression analysis, which identified the independent predictors of bacteremia. Shaking chills were assumed to be absent if not recorded as present; otherwise, there were no missing data for predictors that entered the model.

The results of the multivariate analysis were then used to develop a clinical prediction model. Each beta coefficient was divided by 0.32 (one half the beta coefficient for ultimately fatal disease, which was one of the correlates) and rounded to the nearest integer. The risk score for an individual patient was determined by assigning points for each factor present and adding the results. The model's performance was then tested in the validation set. Performance of the model in the derivation set and the validation set were compared using receiver-operating characteristic (ROC) curve analysis (10).

Patients were eligible to be in the study more than once; there were 1.24 episodes per patient in the derivation set. In this group, however, only three patients had two true-positive episodes, and in one of these instances this occurred during a

Table 1. *Comparison of Characteristics of Patients in the Derivation Set and in the Validation Set*

Characteristic	Derivation Set (n = 1007)	Validation Set (n = 509)
Mean age (± SD), *y*	50 ± 20	49 ± 20
Male, *n (%)*	434(43)	221(43)
Hospital service, *n (%)*		
Medical	562(56)	264(52)
Surgical	298(30)	159(31)
Obstetrics-Gynecology	147(14)	86(17)
Reason for obtaining blood cultures, *n (%)*		
Fever (no source)	293(29)	145(28)
Suspected focal infection, therapy not yet started	297(29)	148(29)
Suspected focal infection, therapy started	200(20)	87(17)
Suspected endocarditis	46 (5)	18 (4)
Other	92 (9)	64(13)
Unknown	77 (8)	47 (9)

separate hospitalization. A secondary multivariate analysis in which these episodes were excluded yielded similar findings to the primary analysis, and therefore is not presented.

Results

The derivation set of 1007 blood culture episodes comprised data from 809 patients who had a total of 2295 individual blood culture sets (Table 1). The validation set of 509 episodes included 416 patients and 1105 individual blood culture sets. The samples of patients in the derivation set and validation set were similar with respect to age, sex, service, and reason for which blood cultures were obtained (Table 1). In 49% (497 of 1007) of the episodes in the derivation set, patients either had a suspected focal bacterial infection (*see* Patients and Methods) at initial evaluation or were already being treated for a focal bacterial infection. In the derivation set, 7% of episodes resulted in true-positives and 8% in contaminants (Table 2); in the validation set, 8% of episodes resulted in true-positives and 5% resulted in contaminants.

Derivation Set: Correlates of True-Positive Blood Cultures

Univariate correlates of true-positives in the derivation set included presence of intravenous drug abuse, shaking chills, major comorbidity, a rapidly fatal disease, a temperature of 38.3 °C or higher, hypotension, an acute abdominal examination, leukocyte count of less than 1×10^9/L or more than 15×10^9/L, and band count of greater than 10% (Table 3). Of 349 episodes in which patients were receiving antibiotics at the time of culture, 22 (6%) represented true bacteremia, compared with 8% (52 of 658) of episodes in which patients were not on antibiotics ($P = 0.36$).

Physicians had a lower temperature threshold for doing blood cultures in elderly patients; thus, the mean (± SD) temperature among the 489 patients of 50 years of age or more was 37.9 ± 1.0 °C compared with 38.3 ± 1.1 °C in the 518 younger patients ($P < 0.0001$). Bacteremic patients over 50 years of age ($n = 40$) had a lower mean temperature of 38.5 ± 0.8 °C compared with bacteremic patients under 50 years ($n = 34$; mean temperature, 38.9 ± 1.1 °C; $P = 0.09$). However, when we stratified by age (categories: age < 50, age 50 to 70, and age >70), the effect of temperature on bacteremia was independent of age ($P = 0.895$, Breslow-Day test for homogeneity of the odds ratio). Other factors not significantly correlated with bacteremia included sex; service; and presence of malignancy, diabetes, leukemia, or immunosuppressive drug therapy.

When univariate correlates were entered into a stepwise logistic regression analysis, the independent correlates of a true-positive blood culture were a temperature of 38.3 °C or higher, rapidly or ultimately fatal underlying disease, presence of shaking chills, intravenous drug use, acute abdominal examination, and major comorbidity (Table 4).

Clinical Prediction Model

When points were assigned to each of the predictors (*see* Patients and Methods), the model identified groups with increasing probability of true bacteremia (Table 5). A patient with none of the risk factors, for example, would have a score of 0 (the lowest-risk group), and a patient who used intravenous drugs and had shaking chills and a temperature of 38.3 °C would have a score of 10 (highest-risk group).

Of 1007 episodes in the derivation set, 303 (30%) fell in the low-risk group, which was defined by absence of all predictors except ultimately fatal disease. This low-risk group had a 1% probability (4 of 303) of true bacteremia whereas the high-risk group had a 16% probability of true bacteremia.

Episodes in which patients had temperatures of 38.3 °C or higher had a probability of bacteremia of 10% (54 of 529) and, within this group, we could not identify a group at very low risk for bacteremia. A subset of patients, defined by absence of all predictors mentioned above and a leukocyte count of less than 1×10^9/L or more than 15×10^9/L still had a probability of bacteremia of 4% (5 of 134).

Prospective Testing of the Model: Validation Set

When the model was applied prospectively to the validation set, it successfully stratified patients according to risk for bacteremia (Table 5). The low-risk group again included 30% of all episodes and had a probability

Table 2. *Blood Culture and Infection Results*

Results	Derivation Set	Validation Set
Total episodes, *n*	1007	509
Positive blood cultures, *n (%)*	155(15)	64(13)
True-positive, *n (%)*	74(7)	41(8)
Definite bacteremia	63(6)	37(7)
Probable bacteremia	11(1)	4(1)
Contaminant, *n (%)*	81(8)	23(5)
Definite contaminant	67(7)	19(4)
Probable contaminant	14(1)	4(1)
Any infection, *n (%)*	536(53)	264(52)
Documented infection	247(25)	130(26)
Presumed infection	289(29)	134(26)

Table 3. *Univariate Correlates of True-Positive Blood Cultures in Derivation Set*

Variable	True-Positive (n = 74)	All Other Results (n = 933)	P Value
History, *n (%)*			
Intravenous drug abuse	5 (7)	22 (2)	0.03
Chills	20(27)	121(13)	0.001
Major comorbidity	17(23)	79 (8)	0.001
Severity of underlying disease			0.001
Rapidly fatal disease (<1 month)	22(30)	114(12)	
Ultimately fatal disease (>1 mo but <5 y)	25(34)	315(34)	
No fatal disease	27(36)	504(54)	
On antibiotics	22(30)	327(35)	0.36
Physical examination			
Mean maximum temperature (± SD), °C	38.7 ± 0.9	38.1 ± 1.1	0.0001
Maximum temperature ≥ 38.3 °C, *n (%)*	54(73)	475(51)	0.001
Hypotension, *n (%)*	10(14)	63 (7)	0.04
Intravenous catheter present, *n (%)*	32(43)	222(24)	0.001
Acute abdomen on examination, *n (%)*	15(20)	88 (9)	0.003
Laboratory results			
Leukocyte count <1 × 10^9/L or >15 × 10^9/L, *n (%)*	30(45)	238(27)	0.002*
Bands >10%, *n (%)*	10(33)	53(13)	0.003†
Mean erythrocyte sedimentation rate (± SD), *mm/h*	92 ± 27	62 ± 39	0.008‡

* Seven patients with true-positive results and 49 other patients were excluded, 48 because leukemia was diagnosed and 8 because no leukocyte count was available.

† Forty-four patients with true-positive results and 533 other patients were excluded, 48 because leukemia was diagnosed and 529 because no band count was available.

‡ Data were available for 13 patients with true-positive results and for 145 other patients.

of true bacteremia of 2% (3 of 155). In the high-risk group, the probability of true bacteremia was 14% (21 of 145). When the ROC curves for the model in the derivation and validation sets were compared (Figure 1), the area in the derivation set was 0.72 ± 0.03, and the area in the validation set was 0.69 ± 0.04, suggesting nearly identical performance.

Positive Predictive Values in Risk Groups

The model may also be used to define the positive predictive values of a positive blood culture for the different risk groups, although this rate reflects the prevalence of contaminants in addition to the sensitivity and specificity of the model. In the entire study population, true bacteremia was present in only 7 of 39 positive episodes in the low-risk group (positive predictive value, 18%). In contrast, true bacteremia was present in 62 of 96 episodes in the high-risk group (positive predictive value, 65%).

Further Characterization of the Low-Risk Group

Because physicians may elect to withhold blood cultures in some patients with suspected bacteremia, which could have adverse consequences, we further characterized the low-risk group. In the entire study population, episodes that were low risk were more frequent on the medicine service (68% compared with 49% in all other risk groups, $P < 0.001$) and patients were older (mean age, 54 ± 20 compared with 47 ± 19 years, $P < 0.001$). The mean temperature for the low-risk group was 37.1 ± 0.9 °C, and a temperature between 37.9 and 38.3 °C was present in only 104 of 458 (23%) episodes. None of the 126 episodes in which the reason for doing blood cultures was unknown were true-positive; 100 of these were low risk.

Of the seven patients in the entire study population who had true bacteremia and were misclassified by the model into the low-risk group, three had bacterial infections apparent on initial examination (which in all instances grew a predicted pathogen sensitive to the antibiotic therapy started). Three others were either receiving antibiotics for suspected infection or started them immediately after their blood cultures were done, and the remaining patient had a positive urine culture and received antibiotics before the blood culture turned positive; none of the seven had a complication of bacteremia. For four of these patients misclassified by the model, the blood culture results were helpful (for example, prompting a change in antibiotic therapy or leading to an arterial line being changed).

Discussion

We have identified independent clinical predictors of bacteremia in hospitalized adults with suspected bacteremia, and used them to derive and validate a clinical prediction model that allows stratification of patients according to their risk for bacteremia. The independent predictors of true bacteremia, all of which were available at the time of evaluation when the decision to draw blood cultures was made, were temperature of 38.3 °C or higher, presence of a rapidly or ultimately fatal disease, intravenous drug abuse, presence of shaking chills, acute abdominal examination, and major comorbidity. Absence of all predictors (other than ultimately fatal disease) identified a low-risk group of hospitalized patients representing 30% of the study population. In these patients, the probability of bacteremia was only 2%, and even positive cultures had a low positive predictive value for true bacteremia.

Table 4. *Independent Predictors Identified by Multivariate Analysis*

Variable	Beta	Odds Ratio	95% CI	Points*
Intercept	−4.14			
Maximum temperature ≥38.3 °C	0.91	2.5	(1.4 to 4.3)	3
Rapidly fatal disease (<1 mo)	1.40	4.0	(2.1 to 7.9)	4
Ultimately fatal disease (>1 mo but <5 y)	0.65	1.9	(1.0 to 3.5)	2
Presence of chills	0.96	2.6	(1.4 to 4.8)	3
Intravenous drug abuse	1.28	3.6	(1.2 to 10.9)	4
Acute abdomen on examination	1.03	2.8	(1.4 to 5.4)	3
Major comorbidity	0.96	2.6	(1.4 to 5.0)	3

* Calculated by dividing beta coefficient by 0.32 and rounding to the nearest integer.

Table 5. *Performance of the Prediction Rule*

Variable	Risk Score			
	0 to 2	3	4 to 5	≥ 6
Derivation set (n = 1007), *n (%)*				
Bacteremia absent	299(99)	225(95)	186(91)	223(84)
Bacteremia present	4(1)	11(5)	18(9)	41(16)
Validation set (n = 509), *n (%)*				
Bacteremia absent	152(98)	113(93)	79(90)	124(86)
Bacteremia present	3(2)	8(7)	9(10)	21(14)

Comparison with Other Studies

This study has two main methodologic differences compared with previous studies of bacteremia in hospitalized patients (4, 11-13). First, data were collected on all patients with suspected bacteremia by a blinded reviewer before the outcome was known, whereas most previous studies were retrospective (11-13), and blinding with respect to predictors was not reported. Second, the sample size (1516 episodes) was larger than the only other prospective study (4), which included 344 patients. This sample size allowed greater statistical power for identifying a group at low risk for an uncommon outcome.

Two previous studies have evaluated prediction of bacteremia in outpatients (5, 6). Mellors and colleagues (5) developed an index to identify occult bacterial infection in outpatients with a temperature of 37.9 °C or higher; predictors included age of 50 years or more, diabetes, leukocyte count over 15 × 10^9/L, band count over 1.5 × 10^9/L, and a Wintrobe erythrocyte sedimentation rate of 30 mm/h or more. None of these entered our index; age and diabetes were not strong correlates of bacteremia in our population, and the other three predictors are laboratory values that are not always available at the time when the decision to draw blood cultures is made. We chose a temperature cutoff of 38.3 °C because it provided the best discrimination between bacteremic and nonbacteremic patients; this cutoff is higher than that used in a previous study of fever in hospitalized patients (4) and higher than that often used clinically. High or low leukocyte count was close to being statistically significant as an independent predictor in our population, but because this information is not always available at the time the patient is evaluated to determine whether a blood culture should be drawn, we chose not to include it in the index.

Even fewer data are available about prediction of bacteremia in hospitalized adults. In the study by Makadon and colleagues (4) of hospitalized adults, only febrile patients (temperature, 37.9 °C) were evaluated, and no low-risk group could be identified. As discussed, in our study, patients with temperatures of 38.3 °C or higher had a probability of bacteremia of 10%, and we could not identify a subset of patients within this group with a probability of bacteremia below 4%. Blood cultures were not drawn on all patients with temperatures of 38.3 °C or higher (in particular, on patients with early postoperative fever), and it is possible that such a group could be defined in future studies. In our study, however, 47% of episodes in which blood cultures were done were associated with temperatures of less than 38.3 °C.

Clinical Implications

Risk stratification allows identification of low-risk patients, which may be helpful both at the time of blood culture drawing and later when results are obtained. Because septicemia is a serious disorder, physicians are likely to have a low threshold for doing blood cultures. In previous studies (4, 5, 7), physicians' intuitive judgment for predicting bacteremia at the time of blood culture drawing has been poor. In one study (7), physicians consistently overestimated the likelihood of bacteremia, and their poor discriminating ability was reflected in an ROC curve with an area of 0.58.

In addition to helping clinicians identify patients with a low risk for bacteremia in whom blood cultures might be deferred in favor of further observation, the index can also be used to identify a group of patients with a high probability of bacteremia. Although definition of the threshold for beginning empiric antibiotics will require future cost-effectiveness analyses, this approach to stratification of patients according to risk for bacteremia may help identify those in whom empiric therapy should be considered after initial blood cultures are obtained.

When blood culture results become available, identification of risk groups may also be helpful in interpreting positive tests, because the positive predictive value of a test depends on the pretest probability of disease. This relationship is apparent from rates of true bacteremia in patients with positive cultures in the four risk classes; for example, for patients with a 1.5% pretest

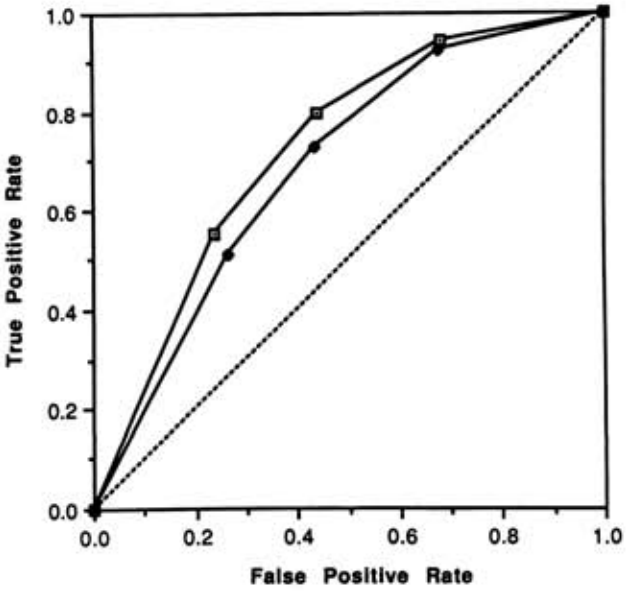

Figure 1. Comparison of the receiver-operating characteristic (ROC) curves for the derivation set (*open symbol*) and validation set (*closed symbol*). The area under the curve was 0.72 ± 0.03 for the derivation set and 0.69 ± 0.04 for the validation set, suggesting little degradation of the model's performance in prospective testing. The dashed line represents a test of no discriminative ability.

probability, the positive predictive value of a positive culture is only 18%; and for patients with a 15% pretest probability, the positive predictive value is 65%.

Limitations

These data must be interpreted in light of several limitations inherent in the study design. The investigation was done at a tertiary care institution, and the results may not be generalizable to other types of hospitals or clinical settings. The relationships between bacteremia and clinical predictors may not be generalizable to all patients with suspected bacteremia, because all data were from patients who actually had blood cultures done and whom physicians felt were most likely to have bacteremia. This potential selection bias would be expected to make identification of a low-risk subset more difficult. We do not have information on other patients who may, for example, have been febrile but did not have blood cultures done; thus, this study provides more insight into when not to draw blood cultures than into when to draw them.

The absence of a criterion standard for bacteremia raises the possibility of misclassification bias because of misclassification of the outcome, but we have attempted to minimize this bias by referring all equivocal cases to a panel of experts and by prospectively validating our predictive model. The misclassification rate of the model—that is, the percentage of patients classified as low risk who actually have bacteremia—is low. None of the seven patients who were misclassified into the low-risk group and who had bacteremia subsequently had a complication of bacteremia. It is possible that the costs of doing large numbers of blood cultures on all patients in this low-risk subset to identify a rare positive outweigh the benefit, especially because an alternative strategy to drawing blood cultures is continued observation, with blood cultures being drawn if clinical changes occur. Furthermore, the high frequency of contaminants in the low-risk group may lead to increased costs through further testing and treatment of these patients. However, this hypothesis requires formal cost-effectiveness analysis.

Although this type of model can be useful as a decision aid, it is important to use it with discretion. Some clinical findings that correlate with bacteremia may occur too rarely to have been identified as risk factors in our patient population, yet be powerful predictors—for example the combination of a new regurgitant murmur and peripheral embolic lesions. The study population from which the model was derived is heterogeneous, and the model cannot capture the fine level of clinical detail available for every patient. Furthermore, physicians must adjust their thresholds for doing blood cultures when the potential consequences of bacteremia are great, for example, in patients with prosthetic devices.

Conclusions

This study gives physicians a rational basis for estimating risk for bacteremia in adult hospitalized patients, and may be helpful in deciding whether to draw blood cultures or to start antibiotic therapy. Doing fewer blood cultures would save not only the costs of the blood cultures themselves (the charge is $60 for two sets at Brigham and Women's Hospital) but also the costs resulting from contaminants. Our recommendations based on these data are that until more data are available most, if not all, hospitalized patients with temperatures of 38.3 °C or higher should have blood cultures done; in patients with temperatures of less than 38.3 °C, with none of the other risk factors for bacteremia we have described, and with no other finding highly suggestive of bacteremia (for example, new peripheral emboli), physicians should consider withholding blood cultures; and that physicians should consider empiric antibiotics in patients with high-risk scores. Further questions of interest include whether subsets of hospitalized febrile adults can be identified who may not need blood cultures, and which patients are likely to benefit from empiric antibiotics.

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