Using Electronic Data to Predict the Probability of True Bacteremia from Positive Blood Cultures

Samuel J Wang, MD, PhD[1,2], Gilad J Kuperman, MD, PhD[1], Lucila Ohno-Machado, MD, PhD[2], Andrew Onderdonk, PhD[3], Heidi Sandige[1], David W Bates, MD, MSc[1]

[1]Partners HealthCare System, Boston, MA

[2]Decision Systems Group, Harvard Medical School, Boston, MA

[3]Brigham & Women's Hospital, Boston, MA

Abstract

As part of a project to help physicians make more appropriate treatment decisions, we implemented a clinical prediction rule that computes the probability of true bacteremia for positive blood cultures and displays this information when culture results are viewed online. Prior to implementing the rule, we performed a revalidation study to verify the accuracy of the previously published logistic regression model. We randomly selected 114 cases of positive blood cultures from a recent one-year period and performed a paper chart review with the help of infectious disease experts to determine whether the cultures were true positives or contaminants. Based on the results of this revalidation study, we updated the probabilities reported by the model and made additional enhancements to improve the accuracy of the rule. Next, we implemented the rule into our hospital's laboratory computer system so that the probability information was displayed with all positive blood culture results. We displayed the prediction rule information on approximately half of the 2184 positive blood cultures at our hospital that were randomly selected during a 6-month period. During the study, we surveyed 54 housestaff to obtain their opinions about the usefulness of this intervention. Fifty percent (27/54) indicated that the information had influenced their belief of the probability of bacteremia in their patients, and in 28% (15/54) of cases it changed their treatment decision. Almost all (98% (53/54)) indicated that they wanted to continue receiving this information. We conclude that the probability information provided by this clinical prediction rule is considered useful to physicians when making treatment decisions.

Introduction

Differentiating between true positive and contaminant blood cultures is a challenge even for experienced clinicians[1]. Because bacteremia is such a potentially life-threatening condition, physicians take positive culture results seriously. However, because of the high rate of false positives due to contamination (approximately 50% by some estimates[2, 3]), it is sometimes difficult for clinicians to determine whether to initiate treatment when a preliminary report comes back positive. It has been shown that physicians' estimates of the true positive probability of blood cultures are often inaccurate[1] and that inappropriate treatment of false positives leads to a significant increase in resource use[4].

The long-term goal of this project is to determine if information from a clinical prediction rule can be used in clinical practice to help physicians make more appropriate decisions regarding the treatment of patients with positive blood cultures. We previously published the derivation of a clinical prediction rule[4-6] that stratifies positive blood cultures into risk categories based on factors that are known at the time of first report. In this paper, we report the results of a revalidation study that we performed to verify the accuracy of the model on recent blood culture results at our institution and describe the subsequent modifications we made to improve the performance of the model. We then describe our implementation of the model in our hospital's laboratory reporting system and present the results of a physician survey regarding this intervention.

Setting

This study was performed at the Brigham & Women's Hospital (BWH), a 750-bed tertiary care academic medical center that handles about 40,000 inpatient admissions per year. The BWH microbiology laboratory processes over 40,000 blood culture specimens per year.

Clinical Prediction Rule

We previously described[6] the derivation of a clinical prediction rule that uses a logistic regression model to stratify all positive blood cultures into 4 risk categories indicating the probability of true bacteremia. The independent predictors used by the model were organism category, time until the culture

1067—5027/00/$5.00

first turned positive, presence of other cultures positive for the same organism, and a clinical risk score. The model was also tested on an independent validation data set[6]. In order to implement this rule as an automated system, we wanted to be able to calculate the risk category solely from information available in electronic form, so we derived a modified version of the algorithm that did not require the use of the clinical risk score.

Table 1 shows the logistic regression beta coefficients for the 3 independent variables in this modified algorithm. The logistic regression model was then translated into a simple 3-step point system for ease of calculation. The first step is to determine the organism category as previously described[6] and assign the appropriate point value from Table 1. Step 2 is to add points based on time until first growth, and step 3 is to add 4 points if another culture grew the same organism. After adding up the points for these steps, one of 4 risk categories is assigned (Table 2) along with a corresponding true positive probability.

			LR Coeff	Points
Step 1	Organism Category	1	0.0	0
		2	1.5	2
		3	3.2	4
		4	3.8	5
		5	6.2	8
Step 2	Time until first positive	0-24	2.4	3
		24-48	1.6	2
		48-72	0.8	1
		>72	0.0	0
Step 3	Other matching culture		2.9	4
	Intercept		-4.1	

Table 1: Blood culture clinical prediction rule. (LR = logistic regression beta coefficient) To compute the risk score, add up the appropriate number of points for each of the 3 steps.

Revalidation

Prior to implementing this clinical prediction rule into a live clinical system, we felt that it was important to revalidate the model on current results at our institution to verify the accuracy of the probabilities and to determine if any modifications to the model would be needed. The original model was derived 10 years ago and some factors may have changed since then. For example, it is possible that microbial prevalence rates and virulence patterns may have changed sufficiently to affect the performance of the model. In addition, our laboratory now uses an improved automated incubation system that detects growth at an earlier stage and this could potentially have an impact on the model.

For our revalidation study, we reviewed the paper charts of selected patients with positive blood cultures to determine the accuracy of the model prediction. We used the opinion of infectious disease experts as our gold standard. All patients that had at least one positive blood culture processed at the BWH microbiology laboratory during the one-year period 3/18/98 to 3/17/99 were eligible for inclusion in the revalidation study. From this population, we picked a random sample of 114 patients stratified by risk category to ensure that we obtained at least 25 cases from each of the 4 risk categories. We performed a retrospective paper chart review on these cases using a two-pass review system. All charts were initially reviewed by a single reviewer using a detailed clinical abstract form. Equivocal cases were then reviewed by 2 infectious disease experts, with any discrepancies resolved by a third expert.

The results of the revalidation study showed that the prediction model was still valid, although the true positive probabilities for each risk category were slightly higher than in the original model. Table 2 shows the revised probabilities for each risk category.

When comparing the performance of our modified algorithm at preliminary report to the original algorithm that included the clinical risk score, we found only a slight degradation in performance. The area under the receiver operating characteristic curve for our modified algorithm was 0.83, compared to a value of 0.86 for the original algorithm[6].

Points	Risk Category	Probability	
		Prelim	Final
0-2	Low	16%	7%
3-5	Medium	48%	53%
6-7	High	71%	72%
>7	Very High	94%	97%

Table 2: Risk Category Table. Use the points calculated from Table 1 to look up the corresponding risk category and true positive probability at preliminary and final report. These probabilities have been updated to reflect the results of our revalidation study.

Modifications

Based on our revalidation study, we made the following improvements to the clinical prediction rule:

- Increased the episode time from 48 hours to 5 days. If there is a matching organism isolated from any other specimen, this is a strong implication of a true positive, even if that specimen was drawn several days ago.
- Required a susceptibility pattern match for coagulase-negative Staphylococcus. Because this is such a commonly occurring organism, we found that it was necessary to compare susceptibility patterns in order to determine a match.
- Reassigned some organisms into more appropriate organism categories based on a frequency analysis.
- Reported separate probability data for preliminary vs. final results to show better-calibrated probabilities.

We found it necessary to treat "Gram Positive Cocci in Clusters" as a special case. This is the most common preliminary report (55.8% of first reports). The issue is that coagulase status is not available for at least 12 hours after this preliminary report comes back, and this report can lead to outcomes with widely varying clinical significance—the two most common outcomes are coagulase-negative Staphylococcus, which is usually a contaminant, and Staphylococcus aureus, which usually represents true bacteremia. Since the prediction rule did not handle this type of divergence well, we excluded it from the model and handled it as a special case. Using information from our database review of recent results, we computed a true positive probability (37%) for this report based on a weighted average of the true positive probabilities of the typical organisms that result from this preliminary report. We emphasize on the message display that this probability will change when more specific organism identification becomes available.

Implementation

Microbiology results at BWH are reported through the Brigham Integrated Computing System (BICS)[7], which also houses the physician order entry system[7, 8] and other internally developed results reporting applications. We implemented our algorithm in BICS and display the risk category and probability information on the microbiology results screen for all blood cultures done at BWH. When a user looks up a blood culture result, s/he will also see the probability information from our clinical prediction rule (Figure 1). There is also an option for the user to press a key to see more detailed information about the prediction rule (Figure 2). The details screen gives an explanation of the algorithm used to compute the risk category and lists the specific factors that were used to arrive at the resulting risk category for this culture.

Microbiology Results

02/15/00 REC'D 3:00P BLOOD from TRIPLE LUMEN

----------Final BLOOD CULTURE Report----------

STAPHYLOCOCCUS, COAGULASE NEGATIVE From AEROBIC 'FAN' (BACT/ALERT)

****

True Positive Probability: LOW (7%) (based on final result)

There is a LOW probability that this result is a true positive. This result most likely represents a CONTAMINANT. Treatment decisions should NOT be based on this result alone, but on other results and the patient's clinical condition.

This probability may change if more information becomes available or if other culture results are pending.

Press 'D' to see detailed information about this alert.

****

Press <Enter>, or 'P' to print screen, or 'D' for alert Details:

Figure 1: Main Microbiology Results Screen.

********** Blood Culture Prediction Rule Details **********

True positive probabilities are determined using a clinical prediction model which classifies all preliminary or final results into 4 risk categories: LOW (7%-13%), MEDIUM (37%-57%), HIGH (75%-80%), VERY HIGH (94%-98%)

For this result, SUSPECTED STAPHYLOCOCCUS, COAGULASE NEGATIVE, the prediction model used the following factors:

1. Organism risk category (1-low probability to 5-high probability): 1
2. Time until culture turned positive: 37 hours
3. Other culture with same organism (drawn within 24 hours):
   05/25/99 8:18AM STAPHYLOCOCCUS, COAGULASE NEGATIVE

Resulting True Positive Probability: LOW (13%) (Preliminary)

This probability may change if more information becomes available or if other culture results are pending. Direct questions/comments to David Bates, M.D., x7063.

(Bates DW; Lee TH; "Rapid Classification of Positive Blood Cultures: Prospective Validation of a Multivariate Algorithm." JAMA, 1992, 267(14), pp. 1962-6.)

Figure 2: Alert Details Screen (optional).

Results of User Survey

We began the intervention in August, 1999. In the 6 month period that the intervention has been running (8/2/99 - 2/2/00), there have been a total of 20,474 blood culture specimens processed in the BWH microbiology laboratory (about 112 per day), and 1848 of these grew at least one organism (9% positive growth rate). There were a total of 2184 distinct isolates in this group. We displayed the risk category message for about half of these isolates that were randomly selected since we are preparing for a randomized controlled trial in the next phase of this

study. Table 3 shows the number of results that fell into each risk category at first report and at final report.

Risk Category	First Report	Final Report
1	534 (24.5%)	513 (23.5%)
2	263 (12%)	240 (11.0%)
3	709 (32.5%)	528 (24.2%)
4	661 (30.3%)	809 (37.0%)
Uncategorized	17 (0.8%)	94 (4.3%)
Totals	2184 (100%)	2184 (100%)

Table 3: Number of results in each risk category during 6 month study period.

During the study period, an average of 6.8 different users looked at each positive isolate, and there were an average of 14.6 total lookups per positive isolate. During this period, 429 users went to the details screen (about 1.5% of available lookups) to see more information about the alert message.

To determine user attitudes towards this intervention, we sent out a short email questionnaire to selected residents who saw the probability message. The survey questions were phrased in the context of the specific patient result that the physician had looked at, and were aimed at determining whether they found the information to be useful in the context of this particular patient result. To date, we have sent out 184 surveys and received 54 completed responses (response rate 29%). Table 4 shows the survey responses. Forty-six percent (25/54) of responses were from first year residents, and 74% (40/54) were from the medicine service.

Fifty percent (27/54) overall indicated that the intervention influenced their assessment of (either raised or lowered) the likelihood that the culture was a true positive; the other half indicated that the message confirmed what they already knew. Furthermore, 28% (15/54) indicated that the intervention actually caused them to change their treatment decision. Only 1 respondent indicated that he had not read the message at all.

We found that we obtained a higher return rate from surveys regarding the higher risk category blood cultures. This may indicate that physicians took more of an interest in this prediction rule for their sicker patients. In order to obtain a more representative sample across all risk groups, we subsequently sent out more surveys to the low risk group to compensate for this effect.

Q1: How did this information change your suspicion of the likelihood of true bacteremia in this patient?		
Raised my suspicion AND probably changed my treatment decision	11	20.4%
Lowered my suspicion AND probably changed my treatment decision	4	7.4%
Raised my suspicion BUT did not change my treatment decision	6	11.1%
Lowered my suspicion BUT did not change my treatment decision	6	11.1%
Confirmed what I already knew	26	48.1%
I believe it was incorrect	0	0.0%
I didn't read it	1	1.9%
Totals	**54**	**100.0%**
Q2: In the future, how would you like to receive these probability messages? (choose all that apply)		
By email	7	13.0%
By text pager	9	16.7%
Have lab tech or nurse page me	2	3.7%
On micro results screen (as is)	38	70.4%
Don't tell me at all	1	1.9%
Totals	**57**	

Table 4: User survey responses.

When asked if they would like to continue receiving this probability information, 98% (53/54) indicated that they would like to continue receiving the information in some form. Of these, 71% (38/53) said to continue to display the information as we were doing it. Seventeen percent (9/53) said they would like to receive the information via their alphanumeric text pagers, and 13% (7/53) said they would like to receive the information via email. Two respondents (4%) indicated that they would prefer to have a lab technician or nurse page them directly.

Discussion

We modified and implemented a published clinical prediction rule for bacteremia and found that clinicians appreciated the information and often changed their treatment decisions in response to the additional information.

One of the most challenging parts of the revalidation study was determining the true bacteremia standard. Since there is no universally accepted gold standard for true bacteremia, we relied upon the opinions of infectious disease experts to make the final determination. It may be considered more accurate to describe the probability information as the opinion of infectious disease experts as to the likelihood that the culture represents a true positive. Even so, the availability of this information as an

adjunct to an infectious disease consult may prove to be useful to clinicians when making their treatment decisions.

We did not make a specific recommendation for whether to treat at each risk level. More analysis would be needed to determine if there is a threshold percentage level at which we would recommend treatment. However, it would be important to emphasize that there are additional clinical factors not accounted for by the prediction rule that should be taken into consideration when deciding whether to treat. Some of these factors include clinical history and physical exam findings, intravascular catheter status, and the presence of an implantable hardware device.

When we analyzed user survey responses stratified by risk category, we found that a greater proportion of those in the very high-risk category (7/22) indicated that the intervention changed their treatment decision when compared to the low risk category (3/19). This may be an early indication that our intervention actually has a stronger influence for blood cultures in the higher risk categories and may encourage earlier antibiotic use in the appropriate situations.

Historically, it has been difficult to get practice guidelines and clinical prediction rules incorporated into daily clinical practice. There are a number of reasons that have been cited as barriers to the successful adoption of clinical prediction rules[9]. The results of our user survey indicate that physicians used and appreciated our blood culture prediction rule. There were a number of aspects that were probably key to the successful adoption of this rule. First, the informational message was incorporated into the physician's regular workflow (always displayed next to the culture result) so that the information was presented "just in time" at the time of decision-making, and they did not have to seek out the information. Also, the risk category information was automatically calculated based entirely on information available in the database—no user data entry was required. Our experience with this study indicates that clinicians are willing to make use of information from clinical prediction rules if it is integrated into their workflow and properly presented.

Conclusion

This study demonstrates that we were able to use electronic data to make calculations for a clinical prediction rule to help clinicians assess the probability that a given positive blood culture result represented true bacteremia. Clinicians nearly universally appreciated this information and reported that it often changed their decision making in this very important and common clinical circumstance. Aggregation of electronic data in ways that can help clinicians with decision-making is a key way that electronic records can improve care. Further evaluation is underway to determine the actual impact of this intervention on physicians' behavior and patient outcomes.

References

1. Poses RM, Anthony M. Availability, wishful thinking, and physicians' diagnostic judgments for patients with suspected bacteremia. Med Decis Making. 1991;11:159-68.

2. Weinstein MP, Reller LB, Murphy JR, Lichtenstein KA. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. I. Laboratory and epidemiologic observations. Rev Infect Dis. 1983;5:35-53.

3. MacGregor RR, Beaty HN. Evaluation of positive blood cultures. Guidelines for early differentiation of contaminated from valid positive cultures. Arch Intern Med. 1972;130:84-7.

4. Bates DW, Goldman L, Lee TH. Contaminant blood cultures and resource utilization. The true consequences of false-positive results. JAMA. 1991;265:365-9.

5. Bates DW, Cook EF, Goldman L, Lee TH. Predicting bacteremia in hospitalized patients. A prospectively validated model. Ann Intern Med. 1990;113:495-500.

6. Bates DW, Lee TH. Rapid classification of positive blood cultures. Prospective validation of a multivariate algorithm. JAMA. 1992;267:1962-6.

7. Teich JM, Glaser JP, Beckley RF, et al. The Brigham integrated computing system (BICS): advanced clinical systems in an academic hospital environment. Int J Med Inf. 1999;54:197-208.

8. Teich JM, Spurr CD, Schmiz JL, O'Connell EM, Thomas D. Enhancement of clinician workflow with computer order entry. Proc Annu Symp Comput Appl Med Care. 1995:459-63.

9. Weingarten S. Practice guidelines and prediction rules should be subject to careful clinical testing [editorial; comment]. JAMA. 1997;277:1977-8.