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Value of the Pitt Bacteraemia Score to predict short-term mortality in *Staphylococcus aureus* bloodstream infection: a validation study

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Summary

BACKGROUND AND AIMS: The widely used Pitt Bacteraemia Score (PBS) has repeatedly been described as a risk factor for short-term mortality in *Staphylococcus aureus* bloodstream infection (BSI), but little is known about its overall predictive performance. We therefore aimed to externally validate the PBS in *S. aureus* BSIs.

METHODS: We performed a retrospective validation study at the University Hospital Basel. Adult patients with a first episode of methicillin-susceptible *S. aureus* BSI between January 2008 and December 2013 were eligible for the study. We measured the overall discriminative power of the PBS at day of BSI onset in predicting 30-day all-cause mortality by receiver-operating characteristics analysis. For each PBS cut-off, we calculated the corresponding sensitivity, specificity and predictive values for prediction of 30-day all-cause mortality.

RESULTS: A total of 329 patients were included in the final analysis: The median PBS at BSI onset was 0 (interquartile range, 0–2) with patients suffering from various comorbidities (Charlson Comorbidity Index median 3, interquartile range 1–5). Thirteen percent of patients (43/329) died within 30 days from any cause. At BSI onset, 52% (170/329) of patients had a PBS of zero; the concomitant specificity and positive predictive value for prediction of 30-day all-cause mortality were 0% and 13%, respectively. The overall performance of the PBS in predicting the 30-day all-cause mortality was lower than published, with an area under the curve of 0.711 (95% confidence interval 0.614–0.807; p <0.001).

CONCLUSIONS: For short-term mortality, the PBS had a low predictive value in a patient population with methicillin-susceptible *S. aureus* BSI. There is a need to improve simple clinical scores to better predict mortality, in particular for *S. aureus*.

Key words: *Bloodstream infection*, *predictive performance*, *Pitt Bacteraemia Score*, Staphylococcus aureus, *validation*

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Introduction

Staphylococcus aureus is a leading cause of bloodstream infections (BSIs), associated with a high mortality in spite of adequate antimicrobial and supportive measures [1–3]. Hence, mortality risk scores in *S. aureus* BSI may have a profound impact on clinical decision support and risk adjustment in observational studies.

The Pitt Bacteraemia Score (PBS) is a widely used severity-of-illness score, which is mainly used to estimate short-term mortality in gram-negative BSIs [4, 5] and is not pathogen-specific. The PBS is calculated at initial patient evaluation from distinct clinical variables (range 0–14 points): temperature of 35.1–36.0°C or 39.0–39.9°C (1 point), temperature of ≤35°C or ≥40°C (2 points), mental status (alert, 0 points; disoriented, 1 point; stuporous, 2 points; comatose, 4 points), hypotension (2 points), receipt of mechanical ventilation (2 points) and cardiac arrest (4 points) [5]. In *S. aureus* BSIs, the PBS has repeatedly been reported to reflect risk for short-term mortality [6–8], but little is known about its overall predictive performance, as studies validating the PBS and modified versions of the PBS have been performed solely in patients with intensive care unit-acquired sepsis and in patients with gram-negative BSIs [9–11]. We therefore aimed to externally validate the PBS in *S. aureus* BSIs.

Materials and methods

This was a retrospective validation study performed at the University Hospital Basel, an 800-bed tertiary care centre in Northwestern Switzerland. We extracted relevant data from our prospective in-house BSI database, which includes microbiological, laboratory and clinical data of all patients with a positive blood culture.

Patients aged ≥18 years with a first episode of methicillin-susceptible *S. aureus* BSI between January 2008 and December 2013 were eligible for the study. We excluded patients with a missing PBS at BSI onset. The Ethics Committee of Northwestern and Central Switzerland approved this study (EKNZ BASEC 2016–01515).

A *S. aureus* BSI was defined as the growth of *S. aureus* in one or more blood cultures. The time-stamp of the first positive blood culture by the in-house laboratory was defined as the day of BSI onset. Onset of BSI after more than two days of hospitalisation was interpreted as hospital-acquired BSI. Immunosuppression was defined as stated elsewhere [12]. The PBS at BSI onset was calculated retrospectively from clinical information in written/electronic medical records and our in-house BSI database [5].

During the entire study period, rapid processing of the blood cultures round the clock was ensured by use of one blood culture system (BacT/ALERT; bioMérieux, Durham, NC, USA).

At our institution, beta-lactam antibiotics constitute the first-line empirical treatment for patients presenting with sepsis. Antimicrobials with activity against methicillin-resistant *S. aureus* (MRSA) are added only in patients who are known carriers or patients with recent hospitalisation in a high-burden region.

For our primary outcome parameter, 30-day all-cause mortality, we measured the overall discriminative power of the PBS at BSI onset by receiver-operating characteristics analysis, with an area under the curve (AUC) of 0.5 indicating a random prediction and a value of 1.0 denoting a perfect prediction; for the validation, only the highest PBS was taken at BSI onset. For each PBS cut-off, we calculated the corresponding sensitivity, specificity and predictive values for prediction of 30-day all-cause mortality. In a univariable logistic regression model, we assessed the calibration of the PBS using the Hosmer-Lemeshow goodness-of-fit statistic [13] with a p-value ≥0.05 reflecting a good model fit. We analysed all data using SPSS, version 22 (IBM, Chicago, IL, USA).

Results

In the 6-year study period, 7 of 336 eligible patients were excluded because of a missing PBS at onset of *S. aureus* BSI; the remaining 329 patients were included in the final analysis. The median age of the study population was 67 years (interquartile range [IQR] 51–78 years) (table 1). The median PBS at BSI onset was 0 (IQR 0–2), with patients suffering from various comorbidities (Charlson Comorbidity Index median 3, IQR 1–5). Overall, the most frequent source of BSI was skin/soft tissue (34%; 113/329) and intravascular catheters / foreign materials (27%; 90/329). At BSI onset, 98% of patients (316/323) received adequate empirical antimicrobial therapy. Thirteen percent of patients (43/329) died within 30 days from any cause.

At BSI onset, 52% (170/329) of patients had a PBS of zero; the concomitant specificity and positive predictive value for prediction of 30-day all-cause mortality were 0% and 13%, respectively (table 2). One percent of patients (4/329) exhibited a PBS of ≥7 points, and 3 of these 4 patients died within 30 days from any cause. The PBS cut-off with the highest combined sensitivity and specificity for prediction of 30-day all-cause mortality was ≥2 (sensitivity, 63%; specificity, 76%).

In receiver-operating characteristics analysis, the AUC of the PBS in predicting the 30-day all-cause mortality was 0.711 (95% confidence interval [CI] 0.614–0.807; p <0.001) (fig. 1). Hosmer-Lemeshow statistics revealed a good calibration of the PBS with a corresponding insignificant p-value (chi-square goodness-of-fit test = 2.9, p = 0.234).

Discussion

This is the first study investigating the discrimination and calibration of the PBS in *S. aureus* BSIs. More than 50% of patients had zero scoring points at BSI onset, which re-

Table 1: Demographic and clinical characteristics of patients with a *Staphylococcus aureus* bloodstream infection (n = 329).

Variable	Value
Age in years, median (IQR)	67 (51–78)
Female gender, n (%)	122 (37)
Risk scores and comorbidities	
Pitt Bacteraemia Score at BSI onset, median (IQR)	0 (0–2)
Charlson Comorbidity Index at BSI onset, median (IQR)	3 (1–5)
Diabetes mellitus type 2, n (%)	81 (25)
Any surgery in the last 30 days*, n (%)	85 (26)
Intravenous drug use, n (%)	46 (14)
Immunosuppression†, n (%)	155 (47)
Infection and treatment characteristics	
Hospital-acquired BSI, n (%)	114 (35)
Focus of BSI, n (%)	
Intravascular catheters / foreign material	90 (27)
Respiratory tract	25 (8)
Skin and soft tissue	113 (34)
Osteomyelitis/arthritis	35 (11)
Endocarditis	11 (3)
Other/unknown	55 (17)
Adequate empirical antimicrobial therapy, n (%)	316 (98)‡
30-day all-cause mortality, n (%)	43 (13)

BSI = bloodstream infection; IQR = interquartile range * Prior to bloodstream infection onset. † As defined in [12]. ‡ Valid percentage (data missing for six patients).

Table 2: Sensitivity, specificity, and predictive values of the Pitt Bacteraemia Score for prediction of 30-day all-cause mortality in *Staphylococcus aureus* bloodstream infection (n = 329).

Score* at BSI onset	Total n (%)	Death within 30 days n (%)	Sensitivity† % (95% CI)	Specificity† % (95% CI)	PPV† % (95% CI)	NPV† % (95% CI)
0	170 (52)	13 (8)	100 (75–100)	0 (0–1)	13 (10–17)	–
1	63 (19)	3 (5)	70 (54–83)	55 (49–61)	19 (13–26)	92 (87–96)
2	54 (16)	8 (15)	63 (47–77)	76 (70–81)	28 (19–38)	93 (89–96)
3	10 (3)	4 (40)	44 (29–60)	92 (88–95)	45 (30–61)	92 (88–95)
4	15 (5)	7 (47)	35 (21–51)	94 (91–96)	47 (29–65)	91 (87–94)
5	6 (2)	2 (33)	19 (8–33)	97 (94–99)	47 (23–72)	89 (85–92)
6	7 (2)	3 (43)	14 (5–28)	98 (96–99)	55 (23–83)	88 (84–92)
≥7	4 (1)	3 (75)	7 (1–19)	100 (98–100)	75 (19–99)	88 (84–91)

BSI = bloodstream infection; CI = confidence interval; NPV = negative predictive value; PPV = positive predictive value * The Pitt Bacteraemia Score ranges from 0 to 14 points. † The total of scoring points was used as cut-off (e.g. a total score of 2 resulted in a cut-off of ≥2 points).

sulted in a low predictive value of the non-pathogen-specific PBS. Our study population was very homogenous: a single pathogen was involved, almost all antibiotics given for empirical therapy were active against *S. aureus*, MRSA cases were excluded since empirical therapy did not cover MRSA, and vancomycin is considered to be inferior in terms of activity against *S. aureus* compared to beta-lactams. Therefore, the circumstances for validation of the PBS are in favour of such a score, because confounding variables such as different pathogens with variable susceptibility patterns, sources of infection and classes of antimicrobial therapy have been minimised.

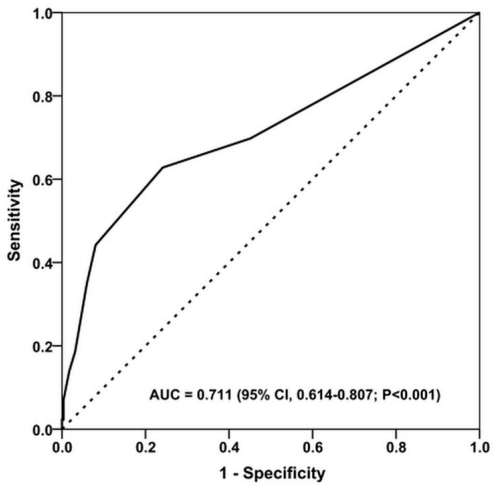
Our results challenge other, mainly small observational, studies indicating that the PBS is –at least in high-risk populations –a good predictor of death in BSI or sepsis: In a Korean study, the PBS had a high discriminative power in predicting mortality in intensive care unit-acquired sepsis (AUC 0.8, 95% CI 0.7–0.9), which was comparable to the performance of the Charlson Comorbidity Index and the Acute Physiology and Chronic Health Evaluation II scoring system [9]. In a prospective study performed on an adult population in New Zealand, a PBS ≥2 was independently associated with death related to *S. aureus* BSI (overall 30-day mortality 19%) [8]. These results are in line with investigations in emergency room patients with *S. aureus* BSI and in patients with haematogenous *S. aureus* meningitis, in which the PBS was an independent predictor of short-term mortality [7, 14].

Variables other than acute severity of illness have been associated with mortality in *S. aureus* BSI, such as age, presence of comorbidities and source of infection [6]. Inclusion of such strong predictors of all-cause and infection-related 30-day mortality in *S. aureus* BSI could significantly improve the discriminative power of the PBS. For gram-negative BSIs, the PBS has already been modified by addition of distinct clinical variables, which resulted in an excellent predictive performance of the adapted PBS in external validation (AUC for 28-day mortality 0.9) [11]. In line, modification of the PBS parameters and its associated scoring weights could improve the predictive accuracy of the PBS in gram-positive BSIs.

Our study has limitations. First, we investigated the predictive performance of the PBS solely in *S. aureus* BSI; however, for infectious agents with lower pathogenicity and concomitant lower case fatality rates, the discriminatory capacity of the PBS might be lower, as even a higher proportion of patients could have a low PBS of 0 or1 points. Second, we did not analyse the predictive power of the different PBS components. Third, we did not compare the predictive performance of the PBS with other well-established clinical scores.

In conclusion, for short-term mortality, the PBS had a low predictive value in a patient population with methicillin-susceptible *S. aureus* BSI. There is a need to improve simple clinical scores to better predict mortality, in particular for *S. aureus*.

Figure 1: Receiver-operating characteristics curve of the Pitt Bacteraemia Score for prediction of 30-day all-cause mortality in *Staphylococcus aureus* bloodstream infection (n = 329).



Disclosure statement

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