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A comprehensive, predictive mortality score for patients with bloodstream infections (PROBAC): a prospective, multicentre cohort study

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Objectives: Bloodstream infections (BSI) are an important cause of mortality, although they show heterogeneity depending on patients and aetiological factors. Comprehensive and specific mortality scores for BSI are scarce. The objective of this study was to develop a mortality predictive score in BSI based on a multicentre prospective cohort.

Methods: A prospective cohort including consecutive adults with bacteraemia recruited between October 2016 and March 2017 in 26 Spanish hospitals was randomly divided into a derivation cohort (DC) and a validation cohort (VC). The outcome was all-cause 30-day mortality. Predictors were assessed the day of blood culture growth. A logistic regression model and score were developed in the DC for mortality predictors; the model was applied to the VC.

Results: Overall, 4102 patients formed the DC and 2009 the VC. Mortality was 11.8% in the DC and 12.34% in the CV; the patients and aetiological features were similar for both cohorts. The mortality predictors selected in the final multivariate model in the DC were age, cancer, liver cirrhosis, fatal McCabe underlying condition, polymicrobial bacteraemia, high-risk aetiologies, high-risk source of infection, recent use of broad-spectrum antibiotics, stupor or coma, mean blood pressure <70 mmHg and $PaO_2/FiO_2 \leq 300$ or equivalent. Mortality in the DC was <2% for ≤2 points, 6%–14% for 3–7 points, 26%–45% for 8–12 points and ≥60% for ≥13 points. The predictive score had areas under the receiving operating curves of 0.81 (95% CI 0.79–0.83) in the DC and 0.80 (0.78–0.83) in the VC.

Conclusions: A 30 day mortality predictive score in BSI with good discrimination ability was developed and internally validated.

Introduction

Bloodstream infections (BSI) are both frequent and important cause of death. In Europe and North America, the estimated rates of cases and mortality range 113 to 204 episodes and 20 to 38 deaths per 100 000 person-year, respectively, being among the top seven causes of death in these areas.[1] BSI are heterogeneous in terms of patients' features, sources of infection, microorganisms and severity of the inflammatory response, and therefore clinical management and follow-up needs are also heterogeneous, from episodes that can be managed in outpatient basis with minimum follow-up requirements to others needing intensive care and close, longer-term follow-up.[2]

Prognostic scores are useful for clinical situations with heterogeneous outcomes to help physicians in management-related decisions, to perform benchmarking and to inform the design and analysis of therapeutic studies.[3] Prognostic score development is different from causal research as scores do not pretend to explain how the variables act in causal pathways to reach the outcome, but just predict the outcome.[3] Some specific prognostic scores have been developed specifically for patients with BSI, however, most of them were developed only for specific aetiologies (e.g. Gram negatives, including antibiotic-resistance[4–6]) or groups of patients (e.g. haematological patients[7]); also, different studies validated the predictive ability of scores not specifically developed for BSI, such as MEDS, Charlson comorbidity index and sepsis-related organ failure assessment (SOFA) scores, or not including variables related to source or pathogens, such as the Pitt score.[8,9] Only recently, a comprehensive score was developed and validated in patients with all-cause bacteraemia in Germany.[10]

The objective of this study was to develop and internally validate a comprehensive 30-day mortality predictive score for patients with BSI regardless of the aetiology and source of infection, to be assessed at the bed side on the day of BSI diagnosis.

Methods

Study design and participants

A prospective cohort of consecutive adult patients with BSI diagnosed in 26 Spanish hospitals from October 2016 to March 2017 (PROBAC cohort, NCT03148769) was performed.[11] At the participating hospitals, blood cultures are typically indicated in admitted patients included with febrile disease and/or sepsis suspicion. Episodes in which a typical contaminant (e.g. coagulase-negative staphylococci or diphteroids) was isolated from only one blood sample were excluded. For this analysis, patients who died in <48 hours from blood cultures sampling date were also excluded as the intention was to develop a predictive model calculated when the BSI was diagnosed. Patients were included by daily reviewing the results of blood cultures at each participating site.

The PROBAC cohort, once closed, was randomly divided into a derivation cohort (DC) and an internal validation cohort (VC) with approximately two-thirds and one-third of patients, respectively, using the SPSS tool for random selection.

Study variables and data collection

The study endpoint was all-cause mortality at day 30; for patients discharged before day 30, in-person or telephone visits were performed according to local standard procedure for follow-up of patients with BSI. When a 30-day visit was not performed, the charts were checked for the last healthcare contact or mortality registries were consulted.

Exposure variables included demographics, underlying conditions, Charlson comorbidities index,[12] McCabe classification,[13] previous receipt of antibiotics, invasive procedures, type of acquisition of infection, Pitt score[14] and SOFA score[15] with their individual components, source of infection and aetiology of BSI. All variables were assessed with the information available on the day that bacterial growth was noted on blood cultures (typically, the day after the blood cultures were obtained) including aetiology of BSI, except in sites where MALDI was not used in which the aetiology was usually assessed the next day. Previous receipt of antibiotics was classified into a broad spectrum, including piperacillin-tazobactam, third- and fourth-generation cephalosporins, carbapenemens, fluoroquinolones and glycopeptides, and others. Other variables definitions were previously reported in detail.[11]

The data were collected from the charts by trained local teams and introduced in an electronic case report form. The data were monitored remotely for missing values and coherence.

The Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) guidance[16] was followed (Table S1, available as Supplementary data at *JAC* Online).

Ethical aspects

The PROBAC project was approved by the Ethical Boards of the coordinating hospital (Hospital Universitario Virgen Macarena, reference FIS-AMO-2016-01) and of the participant centres. Anonymized data were used. A waiver for obtaining informed consent was accepted because of the observational and epidemiological nature of the study.

Statistical analysis

To our knowledge, the largest previous study developing a comprehensive predictive score in BSI included 2568 patients in a DC, and therefore we consider the sample size of PROBAC adequate for this purpose. Missing data in exposure variables were checked (Table S2). Because of their lack of association with other observed variables, a P value for Little's test <0.05 and a non-monotone pattern, missing data were considered missing at random. Then, multiple imputation was performed using the Markov chain Monte Carlo method. The crude association of each

Table 1. Comparison of the baseline clinical and epidemiologic characteristics of patients included in the DC and VC

Variable	DC ($n=4102$)	VC ($n=2009$)
Median age in years (IQR)	71 (60–81)	71 (59–81)
Male sex	2357 (57.5)	1164 (57.9)
Nosocomial or healthcare-associated acquisition	2452 (60.6)	1121 (55.8)
Ward of admission		
Surgical	426 (10.4)	216 (10.8)
Emergency	2001 (48.8)	1027 (51)
Medical	1310 (31.9)	588 (29.3)
Intensive care	365 (8.9)	178 (8.9)
Source of infection		
Urinary tract	1360 (33.2)	648 (32.3)
Intra-abdominal, biliary tract	529 (12.9)	299 (14.9)
Catheter-related	528 (12.9)	229 (11.4)
Unknown	511 (12.5)	245 (12.2)
Intra-abdominal, non-biliary tract	335 (8.2)	179 (8.9)
Respiratory tract	333 (8.1)	174 (8.7)
Skin and soft tissue	169 (4.1)	79 (3.9)
Endocarditis	73 (1.8)	37 (1.8)
Osteoarticular	53 (1.3)	19 (0.8)
Central nervous system	33 (0.8)	10 (0.5)
Other	178 (4.3)	90 (4.5)
Aetiology		
Escherichia coli	1745 (42.5)	+884 (44)
Staphylococcus aureus	363 (8.8)	168 (8.4)
Klebsiella pneumoniae	304 (7.4)	138 (6.9)
Staphylococcus epidermidis	229 (5.6)	109 (5.4)
Pseudomonas aeruginosa	118 (2.9)	60 (3)
Streptococcus pneumoniae	183 (4.5)	84 (4.2)
Enterococcus faecalis	130 (3.2)	67 (3.3)
Enterococcus faecium	92 (2.2)	41 (2)
Proteus mirabilis	67 (1.6)	28 (1.4)
Enterobacter cloacae	73 (1.8)	30 (1.5)
Klebsiella oxytoca	52 (1.3)	20 (1)
Streptococcus agalactiae	29 (0.7)	15 (0.7)
Serratia marcescens	28 (0.7)	11 (0.5)
Streptococcus pyogenes	25 (0.6)	5 (0.2)
Klebsiella aerogenes	20 (0.5)	14 (0.7)
Morganella morganii	16 (0.4)	13 (0.6)
Salmonella spp.	17 (0.4)	9 (0.4)
Citrobacter freundii	18 (0.4)	10 (0.5)
Haemophilus influenzae	17 (0.4)	6 (0.3)
Listeria monocytogenes	12 (0.3)	6 (0.3)
Acinetobacter baumannii	8 (0.2)	4 (0.2)
Citrobacter koseri	9 (0.2)	3 (0.1)
Proteus vulgaris	4 (0.1)	2 (0.1)
Other microorganisms	543 (13.2)	282 (14)
Chronic underlying conditions		
Diabetes mellitus	997 (24.3)	465 (23.1)
Chronic pulmonary disease	496 (12.1)	246 (12.2)
Heart failure	476 (11.6)	234 (11.6)
Chronic pulmonary diseases	543 (13.2)	282 (14)
Liver cirrhosis	330 (8)	190 (9.5)
Cancer	1053 (25.7)	534 (26.6)
Dementia	353 (8.6)	171 (8.5)
Charlson, median (IQR)	2 (0–3)	2 (0–3)
Ultimately or rapidly fatal underlying disease	1198 (29.2)	594 (29.6)
Pitt score, median (IQR)	1 (0–2)	1 (0–2)
SOFA score, median (IQR)	3 (1–6)	3 (1–6)
Appropriate empirical therapy	2198 (53.58)	1088 (54.15)
30-day mortality	484 (11.8)	248 (12.3)

Data are number of patients (percentage) except where specified.
IQR, interquartile range.

exposure variable with 30-day mortality in the DC was explored; continuous variables were categorized according to the bivariate association of the strata with mortality. Also, categorical variables with multiple categories were simplified by grouping them according to their individual association with mortality; as an example, the McCabe classification, which includes three categories (rapidly fatal, ultimately fatal and non-fatal underlying condition) was simplified into fatal (if condition-related death was predicted to occur up to 5 years) and non-fatal (Table 2). OR with 95% CI were calculated, and P values were obtained by χ^2 or Fisher test as appropriate. Then, a predictive model was developed by logistic regression. Because the objective was to obtain a predictive and not a causal model, no causal relation among variables were predefined. Variables with a bivariable P value ≤ 0.2 and those considered potentially clinically significant were included and selected manually using a hierarchical stepwise backwards procedure. The hierarchies included the following groups: (i) demographics and underlying conditions; (ii) acquisition types, invasive procedures, exposure to antibiotics; (iii) aetiology and source of infection; (iv) acute severity and host response and (v) empirical treatment. We also explored interactions. Collinearity of variables in the final model was studied by calculating their variance inflation factor. The Akaike criterion and area under the receiving operating curve (AUROC) were used to select the final model, which was used to derive the predictive score by dividing each β regression coefficient by the smallest, rounded to the nearest unit. The sensitivity, specificity, positive and negative predictive values and positive and negative likelihood ratios were calculated for different cut-offs for the predictive score. The score was then applied to the DC, with calculation of the same diagnostic features and AUROC. The statistical analyses were performed with the SPSS software (IBM Statistics for Windows, v.25.0; IBM Corporation, Armonk, NY, USA).

Results

The PROBAC cohort included 6313 patients; 202 (3.2%) died in the first 48 hours and were excluded. Therefore, 6111 patients were analysed; the DC and the VC were composed of 4102 and 2009 patients, respectively (Figure S1). The median age of patients in the DC was 71 years; 2357 (57.5%) were males. The majority ($n=2001$, 48.78%) were attending the emergency department when BSI was diagnosed. The most frequent sources of BSI were the urinary tract ($n=1360$, 33.2%), the biliary tract ($n=529$, 12.9%) and vascular catheters ($n=528$, 12.9%). *Escherichia coli* and *Staphylococcus aureus* were the most

Table 2. Bivariate analysis of risk factors associated to all-cause 30-day mortality in the DC

Variable:	No. alive ($n=3618$)	No. dead ($n=484$)	OR (95% CI)	*P* value
Median age in years (IQR)	70 (59–81)	76 (65–85)	1.02 (1.01–1.03)	<0.001
Male sex	2079 (57.5)	278 (57.4)	1.01 (0.83–1.22)	0.92
Comorbidities				
Heart failure	391 (10.8)	85 (17.6)	1.75 (1.36–2.27)	<0.001
Chronic pulmonary disease	422 (11.7)	74 (15.3)	1.36 (1.04–1.78)	0.022
Diabetes mellitus	867 (24)	130 (26.9)	1.16 (0.94–1.44)	0.16
Liver cirrhosis	261 (7.2)	69 (14.3)	2.13 (1.6–2.84)	<0.001
Dementia	280 (7.7)	73 (15.1)	2.11 (1.60–2.79)	<0.001
Cerebrovascular disease	369 (10.2)	67 (13.8)	1.41 (1.07–1.87)	0.015
Chronic kidney disease	468 (12.9)	75 (15.5)	1.23 (0.94–1.60)	0.11
AIDS	31 (0.9)	3 (0.6)	1.38 (0.42–4.55)	0.59
Vascular disease	314 (8.7)	52 (10.7)	1.26 (0.92–1.72)	0.13
Solid cancer	874 (24.2)	179 (37)	1.84 (1.5–2.25)	<0.001
Haematology neoplasia	231 (6.4)	51 (10.5)	1.72 (1.25–2.37)	<0.001
Neutropenia (≤500 cells/μL)	123 (3.4)	21 (4.3)	1.29 (0.8–1.06)	0.29
Immunosuppressive treatment	381 (10.5)	65 (13.4)	1.31 (0.99–1.74)	0.055
Ultimately or rapidly fatal underlying condition (McCabe classification)	896 (24.76)	302 (62.4)	5.55 (4.46–6.91)	<0.001
Charlson index	2 (0–3)	2 (1–4)	1.11 (1.07–1.15)	<0.001
Recent use of broad-spectrum antibiotics[a]	570 (15.8)	127 (26.2)	1.9 (1.5–2.3)	<0.001
Invasive procedures				
Central venous catheter	629 (17.4)	124 (25.6)	1.63 (1.31–2.04)	<0.001
Urinary catheter	584 (16.1)	115 (23.8)	1.61 (1.29–2.03)	<0.001
Mechanical ventilation	140 (3.9)	33 (6.8)	1.81 (1.22–2.69)	0.003
Pitt score	1 (0–2)	2 (1–5)	1.27 (1.23–1.31)	<0.001
SOFA score	3 (1–5)	5 (3–8)	1.18 (1.15–1.21)	<0.001
Stupor or coma	269 (7.4)	139 (28.7)	4.97 (3.93–6.27)	<0.001
MBP <70 mmHg or vasoactive amines	759 (20.9)	198 (40.9)	2.59 (2.1–3.16)	<0.001
PaO_2FiO_2 < 300 or equivalent	335 (9.3)	141 (29.1)	4.02 (3.2–5.05)	<0.001
Creatinine >3.4 mg/dL	211 (5.8)	47 (9.7)	1.73 (1.24–2.41)	<0.001
Polymicrobial bacteraemia	233 (6.4)	49 (10.1)	1.62 (1.17–2.25)	0.003
High-risk aetiology[b]	607 (16.8)	144 (29.8)	2.10 (1.69–2.6)	<0.001
High-risk source of bacteraemia[c]	988 (27.3)	224 (46.3)	2.29 (1.89–2.78)	<0.001
Nosocomial or healthcare-associated infection	2094 (57.8)	358 (73.26)	1.99 (1.61–2.47)	<0.001
Appropriate empirical antibiotics	1954 (54)	244 (50.41)	0.84 (0.68–1.04)	0.11

MPB, mean blood pressure.

[a]Includes exposure during the last month to piperacilin-tazobactam, third- and fourth-generation cephalosporins, carbapenemens, fluoroquinolones and glycopeptides.

[b]Includes *S. aureus*, *P. aeruginosa*, *A. baumannii*, *S. marcescens*, *Enterococcus* spp. and *L. monocytogenes*.

[c]Includes respiratory tract, intra-abdominal other than biliary tract, central nervous system and unknown source.

frequent isolated pathogens ($n=1745$, 42.5%, and $n=363$, 8.8%, respectively). The most frequent comorbidities were cancer (n = 1053, 25.7%) and diabetes mellitus ($n=997$, 24.3%). The features of patients in the VC were similar, except for lower healthcare or nosocomial acquisition of BSI and admission to medical wards, and higher rate of biliary tract as a source of BSI (Table 1). The 30-day mortality rates were 11.8% (95% CI 10.7–12.9; 484 patients) in the DC and 12.3% (95% CI 10.6–13.9; 248 patients) in the VC.

A high number of variables were associated with 30-day mortality in bivariable analysis, including age, several underlying conditions, previous invasive procedures, acute-severity measures and nosocomial or healthcare-associated acquisition (Table 2). The 30-day mortality for specific aetiologies and sources of BSI are shown as Tables S3 and S4.

The final multivariable model included age, fatal McCabe condition, solid cancer, liver cirrhosis, high-risk aetiology, polymicrobial bacteraemia, source of infection, recent use of broad-spectrum antibiotics and several acute-severity variables (Table 3). Interactions were not significant, and variance inflation factor was <5 for all variables in the model, suggesting no relevant collinearity. The AUROC of this model for observed mortality was 0.82 (95% CI, 0.80–0.84) (Figure S2). Data about the calibration of the model are shown in Table S5 and Figure S3. Alternative models

Table 3. Final multivariate logistic regression model for 30-day mortality in the DC

Variable	B coefficient	Adjusted OR (95% CI)	*P*	Points
Age				
<65 years		Reference		0
65–80 years	0.37	1.45 (1.09–1.94)	0.01	1
>80 years	0.83	2.30 (1.70–3.11)	<0.001	2
Fatal McCabe underlying condition	1.47	4.34 (3.40–5.54)	<0.001	4
Solid cancer	0.34	1.41 (1.29–2.57)	0.006	1
Liver cirrhosis	0.60	1.82 (1.29–2.57)	0.001	2
High-risk aetiology[a]	0.71	2.05 (1.58–2.66)	<0.001	2
Polymicrobial bacteraemia	0.53	1.70 (1.15–2.51)	0.007	2
High-risk source of infection[b]	0.54	1.72 (1.36–2.18)	<0.001	2
Recent use of broad-spectrum antibiotics[c]	0.40	1.49 (1.17–1.90)	0.001	1
Stupor or coma	1.03	2.81 (2.10–3.76)	<0.001	3
MBP <70 mmHg or requirement of vasoactive amines	0.48	1.62 (1.26–2.08)	<0.001	1
$PaO_2/FiO_2 \leq 300$ or equivalent	0.84	2.33 (1.74–3.13)	<0.001	2

MBP, mean blood pressure.
[a]*S. aureus*, *P. aeruginosa*, *A. baumannii*, *S. marcescens*, *Enterococcus* spp. and *L. monocytogenes*.
[b]Includes respiratory tract, intra-abdominal other than biliary tract, central nervous system and unknown source.
[c]Includes exposure during the last month to piperacilin-tazobactam, third- and fourth-generation cephalosporins, carbapenemens, fluoroquinolones and glycopeptides.

developed included Charlson index instead of McCabe and the individual underlying conditions, Pitt or SOFA instead of the acute-severity variables, and excluding previous use of broad-spectrum drugs are shown in Tables S6 to S9; their AUROC ranged from 0.76 to 0.81 (Table S10).

A scoring system was calculated for the final model (Table 3); the system allowed a range of 0 to 18 points per episode. The AUROC of the scoring system was 0.81 (95% CI 0.79–0.83) (Figure S4). The sensitivity, specificity, positive and negative predictive values and positive and negative likelihood ratios were calculated for every cut-off of the score applied to the DC (Table 4). Mortality was <2% for ≤2 points, 6%–14% for 3–7 points, 26%–45% for 8–12 points and ≥60% for ≥13 points.

When the score was applied to the VC, the AUROC for observed data was 0.80 (95%CI 0.78–0.83) (Figure S5). The performance of the score when applied to the VC is shown in Table S11. Mortality was ≤3% for ≤2 points, 6%–19% for 3–7 points, 22%–47% for 8–12 points and >53% for ≥13 points.

Finally, to compare the predictive capacity of our model with that of the Pitt score, we applied the Pitt scale to our cohort and obtained the following result: AUROC was 0.68 (0.58–0.71).

Discussion

A mortality score for patients with BSI with good predictive ability was developed; this score can be applied the same day when growth is noted in blood cultures, particularly when a rapid system for pathogen identification such as MALDI is used. The score was developed from a large prospective, multicentre cohort and was internally validated in a different subgroup of randomly selected patients from the same cohort. The score includes 11 variables, comprising host-related variables that can be assessed at bedside, together with the aetiology of the BSI.

Despite the frequency and relevance of BSI, specific and comprehensive prognostic scores for all patients with BSI are lacking. Only recently, an important study performed in six university hospitals in Germany developed and validated a score with these features (BLOOMY).[10] The AUROC (95% CI) of the BLOOMY score was 0.87 (0.84–0.89) for 14-day mortality, which is only slightly higher than the AUROC of our model for 30-day mortality and 0.80 (0.78–0.83) for 6-month mortality. Of the 11 variables included in the 14-day BLOOMY mortality score, five referred to similar exposures to our score: age (but we did not find an interaction with mechanical ventilation), malignancy, aetiology, hypotension and altered mental state. Altered renal function, late nosocomial acquisition, high leukocyte or low platelets counts were not identified as independent variables in our model; the issue of platelets may be related to liver cirrhosis being included in our model. BLOOMY also included body mass index and C reactive protein, that we did not collect. Some predictors in the PROBAC model that were not in BLOOMY were polymicrobial bacteraemia, source of infection (it was included only in 6-month BLOOMY model), respiratory insufficiency (PaO2/FiO2 ≤ 300) and recent use of broad-spectrum antimicrobials. Important differences in the design of both studies are that the BLOOMY score was assessed at day 3 for 14-day mortality, while our score was assessed at day 1; we did not use machine-learning methods and our study included a higher number and variety of hospitals. Also, 14-day mortality in BLOOMY was higher than in our cohort, which may reflect a greater complexity of patients and/or a higher threshold for obtaining blood cultures in BLOOMY. Finally, while BLOOMY score was tested in an external cohort, the PROBAC score was only internally validated.

Table 4. Score performance as applied to the DC for the different cut-offs

Points	DC						
	Proportion of patients	Sensitivity	Specificity	PPV	NPV	PLR	NLR
≥1	92.4	99.6	8.6	12.7	99.4	1.0	0.04
≥2	80.7	99.0	21.7	14.5	99.4	1.3	0.04
≥3	65.7	96.7	38.5	17.4	98.9	1.6	0.08
≥4	54.2	90.3	50.6	19.7	97.5	1.8	0.2
≥5	44.5	84.1	60.7	22.3	96.6	2.1	0.3
≥6	36.1	75.0	69.1	24.5	95.4	2.4	0.4
≥7	27.0	65.5	78.2	28.7	94.4	3.0	0.4
≥8	19.4	56.8	85.5	34.5	93.7	3.9	0.5
≥9	13.3	43.0	90.7	38.2	92.2	4.6	0.6
≥10	8.9	32.6	94.2	43.3	91.3	5.7	0.7
≥11	5.8	25.8	96.9	52.5	90.7	8.2	0.7
≥12	3.7	18.6	98.3	60.0	90.0	11.2	0.8
≥13	1.5	13.0	99.2	70.0	89.5	17.4	0.9
≥14	1.3	8.7	99.6	76.4	89.1	24.1	0.9
≥15	0.9	6.0	99.8	80.5	88.8	31.0	0.9
≥16	0.4	3.1	100	93.7	88.5	112.1	0.7
≥17	0.02	0.2	100	100	88.2		1.0
≥18	0.02	0.2	100	100	88.2		1.0

PPV, positive predictive value; NPV, negative predictive value; PLR, positive likelihood ratio; NLR, negative likelihood ratio.

Some of the variables included in our score requires some explanation. First, we explored including only the combined indexes for the severity of underlying conditions (such as Charlson index or McCabe classification), only the individual chronic diseases or both. The models that fitted best were those including both, without causing significant collinearity. This is probably due to the insufficient capacity of the combined indexes to capture the importance of specific chronic diseases. Also, we tested whether it was better to include a hard variable such as Charlson instead of a softer one such as the McCabe classification. Both behave similarly and could probably be used instead of each other; in fact, there was a significant correlation between both variables. We opted for McCabe classification because of its simplicity. Regarding the acute-severity-related variables, we found that the inclusion of specific components of the Pitt or SOFA score provided a better prediction than the inclusion of the full scores. Finally, recent use of broad-spectrum drugs may be a proxy summarizing other patients' features (similarly to late nosocomial acquisition in BLOOMY), or be related to an increased risk of delay in active therapy. However, similar to BLOOMY, we did not find that active empirical therapy was a predictor; this might be due to the way the analysis was performed, as we did not investigate causal associations.

The PROBAC model allows recognizing patients with low, medium, high and very high risk of death. It might be applied to identify patients who might need early intense care if otherwise advisable, and also patients who might be suitable for early discharge if oral or ambulatory parenteral therapy are available and appropriate. However, further studies would be needed to test the clinical utility of the score.

Similar to other complex scores, incorporating the PROBAC predictive score in clinical practice is challenging. Knowledge from implementation science would help, but we think development of informatic tools such as easily accessible, user-friendly calculators and automated incorporation of data via informatic systems would help. Studies on the implementation and evaluating the impact of the use of the score are needed. Also, machine-learning techniques and artificial intelligence will help in refining the score and adapting it to epidemiological changes.

Our study has limitations. The results may not apply to areas with a different epidemiology of BSI; the proportion of *S. aureus* was somehow lower than in other studies, which may be related to exclusion of patients who died in the first 48 hours; although we used 30-day mortality as a frequently used endpoint in BSI, capturing most direct and indirect infection-related deaths,[17] it was not possible for us to assess longer-term mortality. The score might be less predictive for mortality in specific, underrepresented subpopulations; it would not be applicable to children, who were not included in the study cohort. Although our monitoring process was instrumental in obtaining a high-quality database, there were still some missing data. Finally, the score should still be validated in an external cohort. Some strengths of the study include the use of what is, to our knowledge, the largest prospective cohort of BSI cases, the inclusion of easy-to-collect variables and the internal validation obtained.

In summary, a predictive score for mortality in patients with bacteraemia, to be assessed at day of blood cultures growth, was developed and internally validated. The score showed a good prediction ability in both the DC and VC.

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Transparency declarations

None.

Supplementary data

Figures S1 to S5 and Tables S1 to S11 are available as Supplementary data at *JAC* Online.

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