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Enterococcal bloodstream infection. Design and validation of a mortality prediction rule

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SUMMARY

Background: To develop a prediction rule to describe the risk of death as a result of enterococcal bloodstream infection. **Methods:** A prediction rule was developed by analysing data collected from 122 patients diagnosed with enterococcal BSI admitted to the Clínica Universidad de Navarra (Pamplona, Spain); and validated by confirming its accuracy with the data of an external population (Hospital del Mar, Barcelona). **Results:** According to this model, independent significant predictors for the risk of death were being diabetic, have received appropriate treatment, severe prognosis of the underlying diseases, have renal failure, received solid organ transplant, malignancy, source of the bloodstream infection and be immunosuppressed. The prediction rule showed a very good calibration (Hosmer–Lemeshow statistic, $P = 0.93$) and discrimination for both training and testing sets (area under ROC curve = 0.84 and 0.83 respectively). **Conclusions:** The predictive rule was able to predict risk of death as a result of enterococcal bloodstream infection as well as to identify patients, who being below the threshold value, will have a low risk of death with a negative predictive value of 96%.

What is known

Enterococci cause bloodstream infections in patients with severe underlying diseases and numerous comorbidities. Enterococci compared with other Gram-positive cocci such as *S. aureus* or *S. pyogenes*, have low pathogenicity and fewer important virulence factors. Despite that, they are able to form biofilm associated with biomedical devices. During the last years, the number of episodes of bloodstream infection because of enterococci and the number of isolates of enterococci resistant to the major antimicrobials have increased.

What is new

The idea that a simple clinical variable in the general ward could help clinicians better predict Enterococcal BSI outcomes among patients admitted to the hospital.

Introduction

Enterococci are an important cause of serious infections such as bloodstream infection (BSI) and endocarditis (1–4). *Enterococcus* is the second most common cause of nosocomial BSI in the USA representing 10% of all isolates (5–9). This infection adds substantially to the morbidity and mortality rates of seriously ill patients (8–10). *Enterococcus* spp. represents 7% of all blood culture isolates in Europe, with a rising incidence (5–7). This is, in part, because it often occurs in patients with prolonged admissions, multiple comorbidities or who have undergone instrumental manipulation or are under antibiotic pressure (5–7,11).

Enterococcus spp. is by nature inherently resistant to certain antimicrobials (i.e. cephalosporins, cefamicins, clindamycin and trimethoprim–sulfamethoxazole) and also has an innate ability to acquire new resistance mechanisms against other antimicrobial as aminoglycosides or glucopeptides, especially in the case of *E. faecium* (7,12,13). Reported enterococcal BSI mortality rates range from 19% to 48% (1,14); with an attributable mortality, despite proper treatment, between 31% to 37% (15).

Models for prediction rules are widely used in medicine to quantify the relationship between disease and patient morbidity and mortality (16). A risk prediction model is a statistical model that combines information from several markers. Its purpose is to accurately stratify individuals into clinically relevant risk categories (17).

The aim of this study was to develop a simple scoring system (named 'Enteroscore') to assist clinicians to identify patients with high risk of death from those with low risk of death as a result of enterococcal BSI.

Patients and method

Design of study

The model has been developed in the Clínica Universidad de Navarra (CUN), a 300-bed University Hospital in Pamplona, Spain. From 1 January 1998 to 30 June 2011, we selected all patients diagnosed with *E. faecalis* o *E. faecium* BSI aged 18 or older admitted to the CUN, and with complete clinical data available. Of these, we collected demographic, clinical and microbiological data, previous antibiotic

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Disclosure
None.

exposure, current antimicrobial therapy and prognosis of underlying disease for every patient.

In order to validate the rule, we selected a testing set population from another hospital study group. It consisted of a population of 223 consecutive patients with enterococcal BSI from the Hospital del Mar, Barcelona, Spain (5).

Variables analysed

Data were collected from each patient by a previously designed form that gathered epidemiological, microbiological and clinical data.

Epidemiological data included the following: sex, age, hospitalisation ward (medical wards, surgical wards or ICUs), previous episodes of hospitalisation, antibiotic use, recent surgery or ICU admission (whether the patient was or had been a previous time at 72 h of BSI in an ICU). Site of acquisition [community or nosocomial (BSI was considered nosocomial when blood cultures were drawn after the first 48 h postadmission to hospital)], exogenous risk factor for acquiring the BSI, Charlson index score (18) and severity of the underlying disease (PUD) (19).

Clinical data included the following: source of the BSI, adequate treatment (when at least one of the drugs that the patient received was active *in vitro* against the organism isolated in the blood culture), other positive cultures; and also collected as a variable of the study if the patient had developed sepsis (sepsis, severe sepsis or septic shock) as a result of BSI. Finally, we calculated the total crude mortality and mortality attributable to BSI (death was attributable to BSI if, the patient died within 72 h after positive blood culture, if the BSI was the direct cause of death or if BSI was one of the causes of death).

Microbiological data included the following: mono- or polymicrobial BSI, enterococcal species isolated (*E. faecalis* or *E. faecium*), vancomycin MIC (μg/ml), ampicillin MIC (μg/ml) and high-level resistance to gentamicin. Identification of the isolates and susceptibility testing were performed using standard bacteriological methods and an automated system (Vitek II® System; bioMerieux, Durham, NC, USA), in accordance with the CLSI® guidelines (20).

Outcomes were defined as clinical cure, crude mortality (30-days mortality and 3-months mortality) and BSI-attributable mortality (if the patient died within 72 h after positive blood culture, if the BSI was the direct cause of death or if BSI was one of the causes of death). The follow-up was for up to 90 days, taking as day 0 the day that blood culture was drawn.

Statistical analysis

We performed a logistic regression model for the probability of death attributable to enterococcal BSI, with a stepwise selection algorithm. Variables with a score value (based on the first derivative of the log Likelihood function) of more than 0.05 were included into the model, and final Wald χ^2 p-values of less than 0.1 were retained in the final model. Predicted risks were categorised into seven groups. From these risk categories and for different selection of categories cut points, sensitivities, specificities, were calculated and displayed in the form of Receiver Operator Curve (ROC) and Area Under the Curve (AUC) values.

A prediction rule was created fitting a logit regression model with the variables selected through the stepwise selection as previously performed. The intercept and chosen coefficients (b) were used then to create prediction rules for the risk of death. In order to simplify the rule, all beta coefficients (b) were divided by the smallest beta value and rounded to integers. In this way, we obtained the new b″ coefficients that would take part in the prediction rule. A constant (18) was added in the formula, to create positive score results. We selected a cut-point to discriminate between high and low risk categories, and calculated the sensitivity, specificity, positive and negative prediction values of this rule.

Goodness of fit was calculated by the Hosmer–Lemeshow test with k-2 degrees of freedom based on deciles of risk. The Cragg & Uhler's R^2 (Nagelkerke's R^2 test) was measured, assessing the R^2 improvement from null model to fitted model, adjusting the Cox&Snell test so that the range of possible values extends to 1.

The predictive model development was carried out using Stata 12.0 statistical package.

Results

A total of 240 enterococcal BSI episodes were obtained, 78 episodes were excluded for not meeting the study criteria. Therefore, CUN population included 162 episodes obtained from 122 patients (Figure 1). Patients were divided into two different groups: those whose death was attributable to the enterococcal infection and those whose death was not. Table 1 outlines the baseline characteristics of the patients. A total of 102 patients (83.6%) had a higher Charlson index (more than '2'). It is noteworthy that both groups had similar baseline age, and comorbidities as well as previous admissions, as shown by the absence of differences found in previous diagnosis and Charlson Index. There was only a significant difference in the prognosis of the underlying disease, being worst in those who died as a result of enterococcal BSI (Table 1). Exogenous risk factors were also similar between both groups with the

exception of the prevalence of mechanical ventilation that was more frequent among those who died.

E. faecalis was the cause of BSI in 83 cases and *E. faecium* in 39. Vancomycin MIC_{50} and MIC_{90} were 0.5 mg/l and 2 mg/l respectively. Three of 122 strains were vancomycin resistant (two strains had a MIC = 64 mg/l and one had a MIC = 512 mg/l). Ampicillin MIC_{50} and MIC_{90} were 1 mg/l and 64 mg/l respectively. BSI episode was polymicrobial in 39.3%. BSI was nosocomial in 70.5%. BSI characteristics are described in Table 2. Fifty-six patients developed sepsis as a result of BSI, and 78.7% were receiving adequate empirical antimicrobial treatment at the moment of the identification of the *Enterococcus*. The global and attributable mortality of our series was 45.1% and 19.7% respectively; all the patients (four) who developed severe sepsis or septic shock died as its consequence (Table 2).

Testing set population (HM) included 228 patients (Table 3). The training and the testing populations exhibit major differences between them. Among HM cohort patients, 34% of the patients were diagnosed with a malignancy. Fifty two percent of the Hospital del Mar population was receiving the adequate treatment. The global and attributable mortality of the testing set was 33% and 13.6% respectively (Table S1).

Coefficients of the selected variables from the Logistic Multivariate Model on the risk of death attributable to enterococcal BSI on the training set (CUN population) are displayed in Table 4; [coefficients corrected are displayed in Table S2]. The appropriateness of the goodness of fit, calculated by the Hosmer–Lemeshow test, was not significant (p = 0.93) indicating an appropriate goodness of fit. The Nagelkerke's rescaled version of R^2cs was 0.386, suggesting that the model is able to account for only a small part of most of the variation in the data. The accuracy of the prediction rule was measured for both, training and testing population, calculating the Area Under ROC curve. The Area Under ROC curve for the training population was 0.848; whereas for the testing population it was 0.835 (Figure 2). Both values were included in the range 0.8–0.9 for which it is considered that the discrimination ability of the test is excellent.

The population was classified into seven groups according to their estimated risk of death, as follows: group 7 had an estimated risk of death of 60% or higher, and a risk reduction of 10% determined the rest of the groups. The results of the expected and observed mortality rates for both (training and testing population) are shown in appendix (Table S3).

Sensitivity and specificity cut-points of the different categories are shown in Figure 2. Additionally, when selecting a score cut-point of 10 following the coefficients shown in Table 4, a sensitivity of 91.7% and a NPV of 96.1%, was obtained (Table S4).

Table 5 shows the definitive table with the weighted relevance of each component of the prediction rule.

Discussion

We have designed and validated a new score (*Enteroscore*) which predicts the individual risk of death as

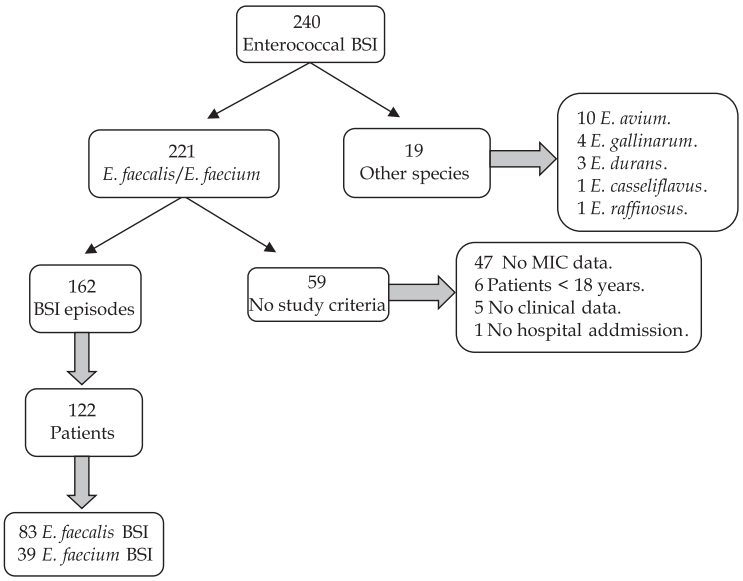

Figure 1 Patients included in the study

Table 1 Epidemiological features of patients with enterococcal bloodstream infection (BSI). Training set (CUN)

Factors	Total *N* = 122	Death AEI* *N* = 24	No death AEI* *N* = 98	p-value
Age (Me, IQR)	62.5 (54–71)	64 (57–69.5)	61 (52–71)	0.441
Gender (male)	77 (63.1)	12 (50)	65 (66.3)	0.141
Comorbidities				
Cirrhosis	16 (13.1)	2 (8.3)	14 (14.3)	0.445
COPD	11 (9)	4 (16.7)	7 (7.1)	0.156
Diabetes mellitus	33 (27)	9 (37.5)	24 (24.5)	0.202
Hypertension	54 (44.3)	9 (37.5)	45 (45.9)	0.458
Impaired renal function	52 (42.6)	13 (54.2)	39 (39.8)	0.205
Immunosuppression	12 (9.8)	14 (58.3)	49 (50)	0.465
Malignancy	70 (57.4)	11 (45.8)	59 (60.2)	0.560
Solid organ transplant	14 (11,5)	2 (8.3)	12 (12.2)	0.592
Ulcer	21 (17.2)	7 (29.2)	14 (14.3)	0.090
Prognosis underlying disease				
PUD 1	25 (20.5)	9 (37.5)	16 (16.3)	0.025*
PUD 2	70 (57.4)	13 (54.2)	57 (58.2)	0.471
PUD 3	27 (22.1)	2 (8.3)	25 (25.5)	0.185
Charlson Index				
26% mortality/year	20 (16.4)	3 (12.5)	17 (17.3)	0.567
52% mortality/year	33 (27)	6 (25)	27 (27.6)	0.801
85% mortality/year	69 (56.6)	15 (62.5)	54 (55.1)	0.513
Exogenous risk factors				
Biliary drain	25 (20.5)	2 (8.3)	23 (23.5)	0.117
Central intravenous catheter	72 (59)	15 (62.5)	57 (58.2)	0.158
Tunnelled	31 (43.1)	4 (26.7)	27 (47.4)	
No tunnelled	41 (56.9)	11 (73.3)	30 (60.7)	
Indwelling urinary catheter	45 (36.9)	13 (54.2)	32 (32.7)	0.054
Mecanic ventilation	20 (16.4)	10 (41.7)	10 (10.2)	0.001*
Nasogastric catheter	34 (27.9)	10 (41.7)	24 (24.5)	0.097
Nephrostomy	10 (8.2)	0	10 (10.2)	0.999
Neutropaenia	6 (4.9)	0	6 (6.1)	0.999
Other prosthesis	7 (5.7)	2 (8.3)	5 (5.1)	0.546
Parenteral nutricare	34 (27.9)	8 (33.3)	26 (26.5)	0.506
Previous cardiac valve replacement	12 (9.8)	2 (8.3)	10 (10.2)	0.783
Tracheostomy tube	12 (9.8)	4 (16.7)	8 (8.2)	0.219
Previous ICU admission	30 (24.6)	9 (37.5)	21 (21.4)	0.106
Previous 6-months hospitalisation	88 (72.1)	17 (70.8)	71 (72.4)	0.874
Previous 3-months antibiotic exposure	87 (71.3)	21 (87.5)	66 (67.3)	0.062
Recent surgery (3 months)	45 (36.9)	6 (25)	39 (39.8)	0.183

AEI, attributable to the enterococcal infection; PUD, prognosis underlying disease (Mc Cabe criteria); Charlson Index Score: prediction in mortality of short follow-up (≤ 3 years).

a result of enterococcal BSI. Malignancy, immunosuppression, life expectancy because of underlying disease, impaired renal function, previous solid organ transplantation, diabetes mellitus, enterococcal BSI source and proper antibiotic treatment when blood culture were drawn, are the makers which compound this new score (Table 5). We believe that it may help clinicians to improve the quality of care given to severely ill patients who develop such infections.

Enterococcus spp. is a microorganism that, despite having a low pathogenicity, is highly resistant to the main antimicrobial agents, which makes it a potential opportunistic pathogen (5,21,22). So far, there is no precedent of the prediction rule developed by our working group. There is only one study, published by Patterson y cols., in which are some predictors of mortality from enterococcal infection (23). According to this study (23), patients with the highest APACHE II score and ampicillin-resistant isolates

Table 2 Enterococcal bloodstream infection (BSI) characteristics. Training set (CUN)

Factors	Total *N* = 122	Death AEI* *N* = 24	No death AEI* *N* = 98	p-value
BSI source				
Endovascular	13 (7.10)	5 (20.8)	8 (8.2)	0.082
Genitourinary	24 (19.7)	2 (8.3)	22 (22.4)	0.136
Intra-abdominal	24 (19.7)	5 (20.8)	19 (19.4)	0.873
Primary	61 (50)	12 (50)	49 (50)	1
Acquired BSI				0.647
Community-associated	36 (29.5)	8 (33.3)	28 (28.6)	
Nosocomial	86 (70.5)	16 (66.7)	70 (71.4)	
Microorganism				0.873
E. faecalis	83 (68)	16 (66.7)	67 (68.4)	
E. faecium	39 (32)	8 (33.3)	31 (31.6)	
Polymicrobial	48 (39.3)	8 (33.3)	40 (40.8)	0.502
Other culture-positive specimens	50 (41)	12 (50)	38 (38.8)	0.318
Sepsis				0.176
Sepsis	52 (42.6)	10 (41.7)	42 (42.9)	
Severe sepsis	3 (2.5)	3 (12.5)	0	
Septic shock	1 (1.4)	1 (4.2)	0	
Adequate treatment	96 (78.7)	17 (70.8)	79 (80.6)	0.298
Ampicillin resistance	31 (25.4)	6 (25)	25 (25.5)	0.799
High-level gentamicin resistance	34 (27.9)	8 (33.3)	26 (26.5)	0.505
Vancomycin resistance	3 (2.5)	2 (8.3)	1 (1)	0.214
MIC vancomicyn > or =1.5 mg/l	34 (27.9)	9 (37.5)	25 (25.5)	0.244

were more likely to have an outcome of lack of cure than other patients. In our case, we have used more variables to build this rule and make it more accurate and useful. It should be noted that except for the "proper treatment", our rule is composed of unchangeable variables to the patient or the outbreak of BSI. We believe that this is the basis of the applicability of the model in different populations and it adds value to the objectivity of the determination.

One of the main strengths of our model relies on the external validation. Our predictive rule has been developed in patients diagnosed with enterococcal BSI who were admitted in our hospital. In agreement with others (7,11,24,25), our study population had a high prevalence of patients with multiple comorbidities, and a short life-expectancy resulting from an underlying disease, which is characteristic of patients with high risk of enterococcal BSI. On the other hand, HM population also showed a high number of comorbidities, but in contrast, the life-expectancy of their patients was longer than ours. This is most likely because of the elevated prevalence of malignancy in our population (57%) compared with the HM population (34%). Other difference between the two populations was the source of BSI; whereas in the CUN population, the principal source was primary or unknown, most episodes of BSI in the HM population were mainly intra-abdominal or genitourinary. There were also slight differences regarding the setting of the acquisition of the BSI, being nosocomial the most frequent in both populations, the second most common in the CUN population was community acquired, whereas the HM population was health care associated. Despite the major differences between both populations, AUC values of the ROC curve of both populations were similar (AUC = 0.848 CUN population; AUC = 0.835 HM population). This small difference certified that the model behaved similarly in both the study and the testing set population, which means that the discriminatory power of the model was optimal. Despite the differences between both populations, the validation was realised by the testing set (Hospital del Mar population) making the rule applicable to others populations. This point is very important because it allows us to assume that although the populations of other studies, centres or hospitals with characteristics very different from the population used as a model, the rule is applicable to any of them.

The idea that simple clinical variables available in the general ward could help clinicians better predict Enterococcal BSI outcomes among patients admitted to hospitals has stimulated the clinical investigation. If we observe each one of the selected

Table 3 Epidemiological features of patients with enterococcal bloodstream infection (BSI). Enterococcal bloodstream infection (BSI) characteristics. Testing set (HM)

Factors	Total *N* = 228	Death AEI* *N* = 31	No death AEI* *N* = 197
Age (Me, IQR)	66.3 (58–76)	73 (67.9–75.2)	70 (63.4–67.7)
Gender (male)	156 (68.4)	28 (64.5)	136 (69)
Comorbidities			
Cirrhosis	35 (15.4)	3 (9.7)	32 (16.2)
Diabetes mellitus	77 (33.8)	16 (51.6)	61 (31)
Impaired renal function	69 (30.3)	15 (48.4)	54 (27.4)
Immunosuppression	69 (30.3)	16 (51.6)	53 (26.9)
Malignancy	77 (33.8)	12 (38.7)	65 (33)
Solid organ transplant	5 (2.2)	0	5 (2.2)
Prognosis underlying disease			
PUD 1	14 (6.1)	3 (9.7)	11 (5.6)
PUD 2	94 (41.2)	22 (71)	72 (36.5)
PUD 3	120 (52.6)	6 (19.4)	114 (57.9)
Charlson Index			
26% mortality/year	228 (100)	31 (100)	197 (100)
52% mortality/year	0	0	0
85% mortality/year	0	0	0
BSI source			
Endovascular	55 (24.1)	4 (12.9)	51 (25.9)
Genitourinary	34 (14.9)	3 (9.7)	31 (15.7)
Intra-abdominal	61 (26.8)	6 (19.4)	55 (2.9)
Primary	60 (26.3)	15 (48.4)	45 (22.8)
Other focus	18 (7.9)	3 (9.7)	15 (7.6)
Acquired BSI			
Community-associated	0	0	0
Healthcare associated	63 (27.6)	3 (9.7)	60 (30.5)
Nosocomial	165 (72.4)	28 (90.3)	137 (69.5)
Microorganism			
E. faecalis	168 (73.7)	19 (61.3)	149 (75.6)
E. faecium	60 (26.1)	12 (38.7)	48 (24.4)
Polymicrobial	124 (54.4)	20 (64.5)	104 (52.5)
Adequate treatment	119 (52.2)	10 (32.3)	109 (55.3)

Table 4 Multivariable analyses of factors predicting death attributable to *Enterococcus* infection in training set ($N = 122$)

Factor	B	SE	OR	95% CI	p-value
Adequate treatment	−1.23	0.68	0.29	0.08–1.12	0.072
Diabetes mellitus	1.6	0.68	3.9	1.03–14.78	0.045
Cardiovascular source	0.8	0.82	2.23	0.44–11.25	0.329
Genitourinary source	−2.08	0.99	0.12	0.02–0.87	0.036
Impaired renal function	1.12	0.71	3.07	0.76–12.47	0.116
Intra-abdominal source	0.49	0.74	1.63	0.38–6.98	0.512
Immunosuppression	1.46	0.74	4.3	1.01–18.35	0.049
Malignancy	−2.65	0.85	0.07	0.01–0.38	0.002
PUD (2)	−2.51	0.81	0.08	0.02–0.40	0.002
PUD (3)	−4.26	1.18	0.01	0.01–0.14	< 0.001
Solid organ transplant	−3.46	1.34	0.03	0.01–0.43	0.01

variables, we could find that most of them have been previously defined by others studies as potential risk factors (7,11,24,25). Comorbidities like malignancy (7,11,24), immunosuppresion (15), solid organ transplantation (11) or the renal failure (8). Similar to it, the severity or prognosis of underlying

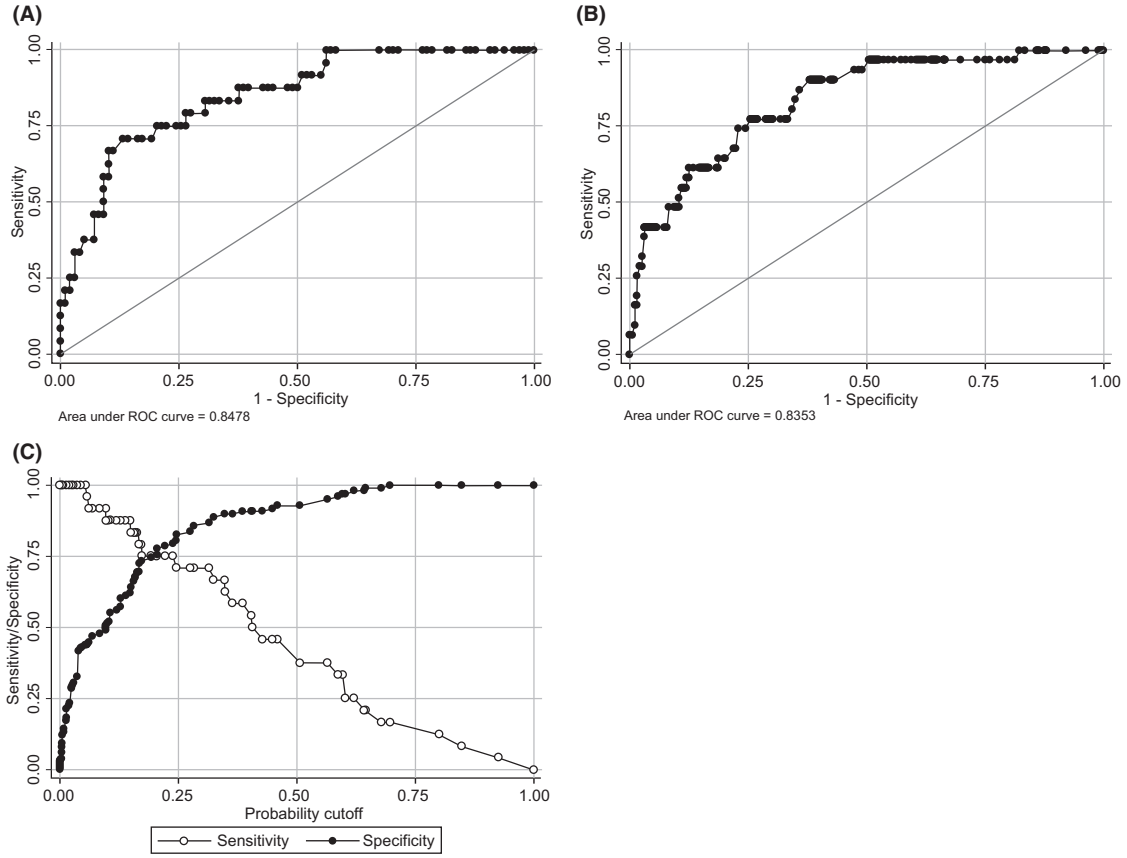

Figure 2 AUC ROC curve [training set (a), testing set (b)] and Sensitivity/specificity curve (c)

Table 5 Predictive rule of the risk of death by enterococcal bloodstream infection

Variables	Value
PUD > 5 years	−9
Solid organ transplantation	−7
Malignancy	−5
PUD 3 months-5 years	−5
Genitourinary BSI source	−4
Proper antibiotic source	−3
Intra-abdominal BSI source	1
Endovascular BSI source	2
Renal failure disease	2
Diabetes mellitus	3
Immunosuppression	3
Constant	18
Summary	Total

diseases (6–8,25,26), and the appropriated treatment (9,24,27).

Besides the clinical utilities, we believe that our score could be used as an internal quality control, for re-evaluation of retrospective series and compare the utility of newer clinical practices. It may also serve as a tool to compare with external series, in order to compare different populations and for clinical trials.

The relevance of our rule is to identify those subjects in whom aggressive measures are deemed disproportionate. Furthermore, it should be noted that except for the variable proper treatment, our rule is composed of variables which are all intrinsic to the patient or the outbreak of BSI, which means it cannot be changed and that new measures to establish must all be external to the patient or the aetiology of bloodstream infection.

This last point considered the rationale and need for new treatments and most measures and is critical to what the clinician has to face in situations where patients are usually in a serious or terminal state. In response, the physician must seek a balance between to perform or not to perform extraordinary measures. So far, some studies have sought the causes that influence these decisions. Most of them conclude that in almost all cases these are decisions which may be subjective such as family situations, the patient's own religious beliefs, the culture of a country and its own legislation (28,29). The main ethics committees do not differentiate between one type or another of mea-

sures, but in clinical practice the use of conservative treatment is more widespread (30).

Mathematical models are not intended to substitute or replace clinical judgment, but rather provide baseline data on which to base a presumptive diagnosis. The BSI model presented can help to change the attitude in the clinical and empirical and directed treatment. From here, more studies are necessary to establish, among other things, what are the measures to be taken to identify patients at high or low risk of mortality because of the enterococcal BSI and whether you can derive set standards or guidelines in the management of patients with enterococcal BSI.

Conclusions

We have designed and validated a predictive model for mortality of enterococcal bloodstream infection (*Enteroscore*) in our hospital with risk factors intrinsic to the patient. This model allows interhospital comparisons, quality analysis and is helpful for clinical decision-making routine clinical practice. The *Enteroscore*, which was calculated according to data collected in the CUN database and validated with an external population database, is an easy-to-calculate prediction rule. A score 10 will help clinicians select patients who will benefit from treatment and other kinds of care. A score greater than or equal to 10 in our rule (*Enteroscore*), correlates with a high probability of death as a result of the episode of BSI with a sensitivity of 91% and a specificity of 49%.

Author contributions

APG conceived the study and initial design with JDP. APG and AG under took the study (CUN population data), analysing and interpreting the data with MFL. DCE, JPH and SG analysed HM population variables. APG drafted the manuscript with critical approval from all authors. All authors gave final approval of the revision to be published.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Global and attributable mortality of CUN and HM populations.

Table S2. βCoefficients selected by the *stepwise* algorithm.

Table S3. Calibration table with the clinical model predicting risk of death attributable to *Enterococcus* spp. infection in the training and the testing set.

Table S4. Score value 10 cut-off point (Sensitivity, specificity, positive and negative prediction values) training set.

Table S5. Score value 10 cut-off point (Sensitivity, specificity, positive and negative prediction values) testing set.

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