Clinical characteristics and predisposing risk factors for *Enterococcus faecalis* and *Enterococcus faecium* bloodstream infections: a prospective multi-centre cohort study from the PROBAC project

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Background
Enterococci are currently ranked second in terms of causative pathogens for gram-positive bloodstream infection (BSI) and are associated with significant morbidity and mortality. The two most common species are *Enterococcus faecium* and *E. faecalis*, which show important differences in terms of resistance patterns. Only a few studies have explored the differential risk factors for the two species. The study aimed to compare the predisposing risk factors for *E. faecalis* and *E. faecium* BSI and to explore the differences between them.

Methods
The study is a post-hoc analysis of the PROBAC project, a national multicenter, observational, prospective cohort study conducted in 26 Spanish hospitals between October 2016 and March 2017. For this sub-analysis, patients with a polymicrobial and monomicrobial BSI due to *E. faecalis* or *E. faecium* were eligible. Multivariable logistic regression model was performed to explore the independent predictors for BSI onset caused by *E. faecium* vs. *E. faecalis*.

Results
In total, 431 patients were included, with 267 BSI caused by *E. faecalis* and 166 by *E. faecium*, 128 (28.8%) BSI were polymicrobial. Median age was 72 (IQR 62-82), 33.4% female. The general characteristics and differences between *E. faecalis* and *E. faecium* are shown in Table1. In the bivariate analysis, no differences in BSI clinical presentation or clinical outcomes were observed. The source of infection and types of infection acquisition are shown in Figure1. In the multivariable analysis (Table2), Charlson comorbidity index ≥3 [adjusted OR=1.96(95%CI=1.07–3.58), p=0.03], previous use (<30 days) of penicillins [aOR=1.99(1.19-3.32), p=0.009] or carbapenems [aOR=2.46(1.16-5.23), p=0.002], hospital-acquired BSI [aOR=2.66(1.65–4.37), p<0.001], and biliary-tract source [aOR=3.28(1.79-6.02), p<0.001] were independent factors associated with *E. faecium* BSI. Instead, congestive heart failure [aOR=0.48(0.25-0.91), p=0.025], previous cerebrovascular incident [aOR=0.43 (0.20-0.92) p=0.03], and urinary-tract source [aOR=0.48 (0.25-0.91), p=0.024] were independent factors associated with *E. faecalis* BSI.

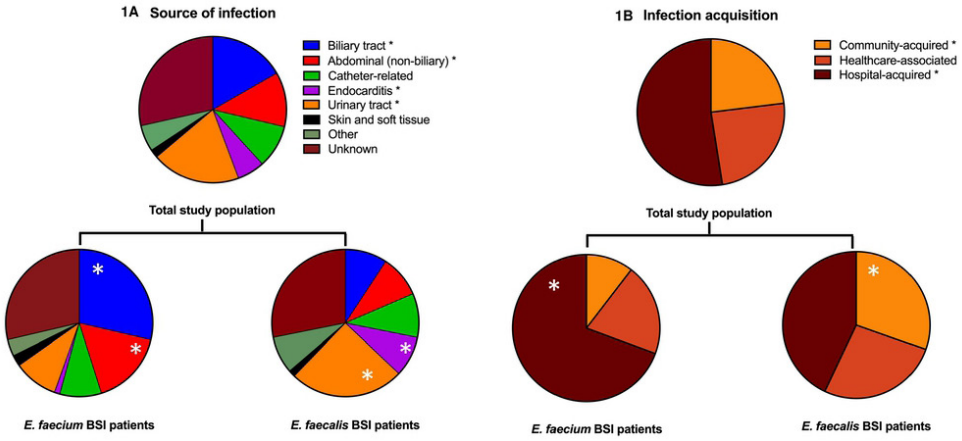
Conclusions
We found different predisposing factors for *E. faecium* and *E. faecalis* BSI, including comorbidities, type of acquisition, previous antibiotic therapy, and BSI source. These variables may help to suspect one or other species for empiric therapeutic decisions.

Table 1. General characteristic of study population

General characteristic of study population and differences between patients with a *E. faecalis* BSI and *E. faecium* BSI. The OR defined E. faecium vs E. faecalis

	All BSI (n = 431)	*E. faecalis* BSI (n = 267)	*E. faecium* BSI (n = 164)	OR (95% CI)	*p*-value
Demographic					
Age, median (IQR)	72 [62 - 82]	72 [63 - 83]	69.0 [60 - 81]	-	0.097
Male sex, n (%)	287 (66.6)	183 (68.8)	104 (63.8)	0.80 (0.53 - 1.21)	0.286
Comorbidities, n (%)					
Charlson comorbidity index (age-adjusted), median (IQR)	5.0 [3- 7]	5.0 [3- 7]	4.0 [3- 7]	-	0.360
Congestive heart failure	78 (18.1)	61 (22.8)	17 (10.4)	0.39 (0.22 - 0.70)	**0.001**
Hepatic disease	51 (11.8)	24 (9.0)	27 (16.5)	2.00 (1.11 - 3.59)	**0.020**
Solid tumor	133 (30.9)	70 (26.3)	63 (38.4)	1.76 (1.16 - 2.66)	**0.008**
Cerebrovascular disease	51 (11.8)	40 (15.0)	11 (6.7)	0.41 (0.20 - 0.82)	**0.010**
Obstructive uropathy	28 (6.5)	23 (8.6)	5 (3.0)	0.33 (0.12 - 0.90)	**0.023**
Obstructive biliary pathology	29 (6.7)	10 (3.7)	19 (11.6)	3.39 (1.53 - 7.44)	**0.002**
Use of antibiotics (in the previous 30 days), n (%)					
Any antibiotic	189 (43.9)	100 (37.5)	89 (54.3)	1.98 (1.34 - 2.94)	**<0.001**
Cephalosporin	64 (14.8)	38 (14.2)	26 (15.9)	1.14 (0.66 - 1.95)	0.646
Penicillin	100 (23.3)	45 (16.9)	55 (33.5)	2.48 (1.57 - 3.90)	**<0.001**
Carbapenem	42 (9.7)	14 (5.2)	28 (17.1)	3.72 (1.90 - 7.30)	**<0.001**
Vancomycin, linezolid or daptomycin	47 (10.9)	21 (7.9)	26 (15.9)	2.21 (1.20 - 4.07)	**0.010**
Quinolone	65 (13.0)	36 (13.5)	20 (12.2)	0.90 (0.50 - 1.60)	0.699
Other	45 (10.4)	26 (9.7)	19 (11.6)	1.22 (0.65 - 2.27)	0.543
Type of acquisition, n (%)					
Hospital-acquired	226 (52.5)	113 (42.9)	113 (69,3)	3.02 (2.00 - 4.58)	**<0.001**
Healthcare-associated	103 (24.5)	70 (26.6)	33 (20.2)	0.70 (0.44 - 1.12)	0.136
Community-acquired	97 (23.0)	80 (30.4)	17 (10.4)	0.27 (0.15 - 0.47)	**<0.001**
Intensive care units admission	54 (12.9)	25 (9.7)	29 (18.0)	2.05 (1.15 - 3.64)	**0.013**
Source of infection, n (%)					
Biliary tract	72 (16.7)	25 (9.4)	47 (28.7)	3.89 (2.28 - 6.63)	**<0.001**
Abdominal (non-biliary)	52 (12.1)	25 (9.4)	27 (16.5)	1.91 (1.91 - 3.42)	**0.028**
Catheter-related	41 (9.5)	26 (9.7)	15 (9.1)	0.99 (0.48 - 1.82)	0.839
Endocarditis	26 (6.0)	24 (9.0)	2 (1.2)	0.13 (0.03 - 0.54)	**0.001**
Bone and joint	1 (0.2)	1 (0.4)	0 (0.0)	-	1.000
Skin and soft tissue	8 (1.9)	4 (1.5)	4 (2.4)	1.64 (0.41 - 6.66)	0.486
Respiratory	16 (3.7)	14 (5.2)	2 (1.2)	0.22 (0.05 - 0.10)	**0.032**
Central nervous system	4 (0.9)	3 (1.1)	1 (0.6)	0.54 (0.06 - 5.23)	1.000
Urinary tract	84 (19.5)	68 (25.5)	16 (9.8)	0.32 (0.18 - 0.57)	**<0.001**
Other	4 (0.9)	1 (0.4)	3 (1.8)	4.96 (0.51 - 48.1)	0.156
Unknown	123 (28.5)	76 (28.5)	47 (28.7)	1.01 (0.66 - 1.55)	0.965
Etiology, n (%)					
Polymicrobial	124 (28.8)	81 (30.3)	43 (26.2)	0.82 (0.53 - 1.26)	0.359
Clinical presentation, n (%)					
Septic shock	47 (10.9)	24 (9.0)	23 (14.0)	1.65 (0.90 - 3.04)	0.103
Pitt score, median (IQR)	0 [0-1]	0 [0 – 1]	0 [0 – 1]	-	0.254
SOFA score, median (IQR)	0 [0 – 3]	0 [0 – 2]	0 [0-3]	-	0.450
Outcome, n (%)					
All-cause mortality	100 (23.2)	64 (24.0)	36 (22.0)	0.89 (0.56 - 1.42)	0.630
BSI-related mortality	60 (13.9)	36 (13.5)	24 (14.6)	1.10 (0.63 - 1.92)	0.738

Figure 1. A: type of infection; B: Area under the curve (AUROC) of the score



*: statistically significant difference (p<0.05). * in the graph: variables associated with the corresponding enterococcal BSI subgroup

Table 2. Multivariate analysis

Multivariable analysis for predisposing risk factors of enterococcal BSI.
Model for predicting the probability of BSI being caused by *E. faecium* BSI, in reference to *E. faecalis*.

	B -coefficient	OR (95% CI)	p-value
Charlson Comorbidity Index ≥ 3	0.670	1.96 (1.07 – 3.58)	**0.030**
Congestive heart failure	-0.737	0.48 (0.25 - 0.91)	**0.025**
Cerebrovascular disease	-0.854	0.43 (0.20 - 0.92)	**0.030**
Previous use of Penicillin	0.689	1.99 (1.19 - 3.32)	**0.009**
Previous use of Carbapenem	0.901	2.46 (1.16 - 5.23)	**0.002**
Hospital-acquired infection	0.978	2.66 (1.65 – 4.37)	**<0.001**
Focus Biliary	1.188	3.28 (1.79 - 6.02)	**<0.001**
Focus Urinary	-0.739	0.48 (0.25 - 0.91)	**0.024**

Predictive ability:
AUC 0.76 (95% CI 0.71 - 0.80)
Constant: -1.280 (p <0.001)

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Risk factors for bloodstream infections by carbapenem-resistant *Acinetobacter baumannii* in patients with colonisation by the same organism: a prospective observational study

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Background
Risk factors for bloodstream infection (BSIs) among patients colonized by carbapenem-resistant A. baumannii (CRAB) are poorly investigated[1-3]. Our aim was to evaluate the risk of BSI among patients with colonization by the same pathogen and identify factors independently associated with CRAB-BSI.

Methods
Observational, prospective study including patients with CRAB colonization at any body-site in the tertiary-care University Hospital of Pisa,Italy(June2020-June2023). Rectal swabs were performed for all hospitalized patients on admission and weekly during hospital stay. The surveillance of other sites beside stools was systematically performed in intensive-care unit (ICU). The primary outcome measure was CRAB-BSI. A multivariable regression analysis was conducted to identify factors independently associated with CRAB BSI. Odds-ratios (ORs) and 95% confidence intervals (CIs) were calculated. A sensitivity analysis was conducted in the subgroup of ICU patients.

Results
388 patients were included: the majority (67.8%) were rectal carriers, 44.1% had respiratory-tract, 18.8% skin and 15.2% urinary-tract colonization. The 53.1% of patients had more than 1 site of colonization. BSI occurred in the 30.2% (n=117/388) of patients (36.4% in ICU versus 13,3% in non-ICU wards, p<0.001). Comparison of patients who developed CRAB BSI and those who did not was shown in Figure 1. On multivariable analysis, burns affecting more than 35% of body surface (OR 8.9, 95%CI 2.38-33.87, p=0.001), intravascular device (OR 5.5, 95%CI 1.65-18.36, p=0.006), number of colonization sites (risk per each site) (OR 3.2, 95% CI 2.17-4.73, p<0.001) were factors independently associated with increased risk for CRAB-BSI. On sensitivity analysis, burns affecting more than 35% of body surface (OR 10.75, 95% CI 2.73-42.28, p<0.001), respiratory tract colonization (OR 3.81, 95% CI 2.01-7.22,p<0.001) and number of colonization sites (risk per each site) (OR 2.33, 95% CI 1.46-3.73, p<0.001) were independently associated with increased risk for BSI.

Conclusions
Multisite colonization by CRAB, together with respiratory-tract colonization in ICU patients, were associated with increased risk of BSI. A predictive model may be useful to identify patients at low risk of CRAB BSI and avoid overuse of new available antibiotics active against CRAB.