

Risk factors for mortality among older adults with hospital-acquired bloodstream infections in the intensive care unit: a multicenter cohort study.

Running title: Hospital-acquired bacteremia in elderly

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*** Supplementary data***

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Definitions

Site of acquisition was defined based on the unit in which the first positive blood cultured was sampled, as either ICU-acquired or ward-acquired.

Presumed source of BSI, categorized into 6 groups (vascular catheter-related, respiratory, intra-abdominal, urinary, primary BSI, and other), as determined by the treating clinician. Whenever more than single source was possible, we classified the source according to the source reported to as most likely.

Adequacy of the empirical therapy was defined as a regimen that was included ≥ 1 agent later on proved to be effective based on antimicrobial susceptibility test and administered within 24 hours from time of sampling.

Source control was defined as the performance of all necessary measures required to eradicate the bacterial inoculum within the origin of the BSI (catheter removal, percutaneous or surgical drainage, *etc.*) Source control was classified into three categories, as deemed by the treating physician. These categories included: source control measures were not indicated (or that an origin could not be defined, *i.e.*, primary BSI); source control measures were indicated and appropriately performed; source control measures were indicated and were not performed or incompletely performed. For analysis purposes, we combined the two former categories.

Difficult-to-treat resistance (DTR)

Difficult-to-treat resistance (DTR) was defined as resistance to all first line antimicrobials. To avoid over-reporting DTR for pathogens with incompletely reported antibiograms, the assessment required availability of antimicrobial susceptibility testing for at least one fluoroquinolone, one cephalosporin, one carbapenem. DTR was assessed for Enterobacterales, *Pseudomonas* spp., and *Acinetobacter* spp.

Sensitivity analyses (Tables S1-S8)

Table S1. Characteristics of 496 older adults diagnosed with bacteremia: sensitivity analysis by excluding those who were discharged from hospital.

	28-days mortality status		<i>p</i> ^a
	Alive N = 215 (43%)	Dead N = 281 (57%)	
Age (years), median (IQR)	80 (6)	81 (8)	0.079
Female gender, N (%)	85 (39.5)	111 (39.5)	0.994
Body mass index (BMI), median (IQR)	26.1 (6.7)	26.3 (6.3)	0.554
Comorbidities			
Charlson score, median (IQR)	2 (4)	2 (3)	0.516
COPD (moderate or severe), N (%)	51 (23.7)	55 (19.6)	0.264
Heart failure (NYHA classes 3-4), N (%)	39 (18.1)	59 (21.0)	0.428
Myocardial infarction, N (%)	29 (13.5)	36 (12.8)	0.825
Peripheral vascular disease, N (%)	23 (10.7)	29 (10.3)	0.892
Cerebrovascular disease, N (%)	37 (17.2)	41 (14.6)	0.427
Dementia, N (%)	28 (13.0)	35 (12.5)	0.851
Hemiplegia, N (%)	11 (5.1)	8 (2.8)	0.192
Diabetes mellitus, N (%)	74 (34.4)	84 (29.9)	0.284
Moderate renal disease, N (%)	31 (14.4)	39 (13.9)	0.864
Hemodialysis, N (%)	11 (5.1)	8 (2.8)	0.192
Connective tissue disease, N (%)	4 (1.9)	6 (2.1)	0.999 [§]
Peptic ulcer disease, N (%)	11 (5.1)	12 (4.3)	0.657
Severe liver disease, N (%)	3 (1.4)	2 (0.7)	0.657 [§]
AIDS, N (%)	0	1 (0.4)	0.999 [§]
Malignancy, N (%)	33 (15.3)	36 (12.8)	0.418
Metastatic solid tumor, N (%)	10 (4.7)	24 (8.5)	0.089
Hematological malignancy, N (%)	9 (4.2)	14 (5.0)	0.676
Transplant recipients, N (%)	0	0	
Corticosteroid therapy, N (%)	9 (4.2)	12 (4.3)	0.963
Functional status before hospitalization			0.217
No limitation, N (%)	60 (28.0)	78 (27.8)	
Mild to moderate limitation, N (%)	81 (37.9)	126 (44.8)	
Serious but not incapacitation restriction, N (%)	44 (20.6)	53 (18.9)	
Severe restriction including bedridden, N (%)	29 (13.6)	24 (8.5)	
Admission due to COVID-19, N (%)	17 (7.9)	59 (21.0)	<0.001
Bloodstream infection			
ICU-acquired bloodstream infection, N (%)	165 (76.7)	227 (80.8)	0.274
Duration of hospital stay prior to BSI detection, median (IQR)	15 (22)	14 (15)	0.206
Duration of ICU stay prior to BSI detection, median (IQR)	7 (18)	7 (11)	0.519
Most likely source of BSI			0.977
Respiratory, N (%)	61 (28.4)	77 (27.4)	
Primary, N (%)	39 (18.1)	60 (21.4)	
Vascular catheter-related, N (%)	49 (22.8)	61 (21.7)	
Intra-abdominal, N (%)	30 (14.0)	38 (13.5)	
Urinary, N (%)	18 (8.4)	22 (7.8)	
Other, N (%)	18 (8.4)	23 (8.2)	
SOFA at time of BSI, median (IQR)	8 (5)	10 (7)	<0.001

Maximal C-related protein (mg/L), median (IQR)	113 (161)	124 (179)	0.076
Maximal procalcitonin (ng/mL), median (IQR)	2.5 (10.4)	1.5 (8.1)	0.201
Maximal creatinine (mg/dL), median (IQR)	1.7 (3.1)	1.9 (2.7)	0.988
Ventilatory requirements during BSI			0.002
Invasive mechanical ventilation, N (%)	138 (64.2)	219 (77.9)	
Non-invasive ventilation, N (%)	13 (6.0)	17 (6.0)	
High flow oxygen, N (%)	16 (7.4)	15 (5.3)	
Low flow or no need for oxygen supplementation, N (%)	48 (22.3)	30 (10.7)	
Septic shock at presentation, N (%)	63 (29.3)	119 (42.3)	0.003
Glasgow Coma Scale, median (IQR)	12 (7)	10 (9)	0.010
Antimicrobial therapy during the 7 days prior to bloodstream infection, N (%)	145 (67.4)	219 (78.2)	0.007
Microbiology			
Causative pathogen			0.128
Gram negative bacteria, N (%)	108 (50.2)	142 (50.5)	0.947
<i>Enterobacteriales</i> ^b , N (%)	67 (31.2)	77 (27.4)	
<i>Pseudomonas aeruginosa</i> , N (%)	12 (5.6)	25 (8.9)	
<i>Acinetobacter baumannii</i> , N (%)	23 (10.7)	35 (12.5)	
Gram positive bacteria, N (%)	53 (24.7)	74 (26.3)	0.670
<i>Staphylococcus aureus</i> , N (%)	14 (6.5)	22 (7.8)	
Coagulase-negative <i>Staphylococci</i> , N (%)	18 (8.4)	18 (6.4)	
<i>Enterococcus</i> species, N (%)	15 (7.0)	33 (11.7)	
Candida, N (%)	20 (9.3)	28 (10.0)	
Other, N (%)	18 (8.5)	9 (3.2)	
Polymicrobial, N (%)	25 (11.6)	33 (11.7)	
Resistance pattern of the isolate ^c			0.536 [§]
Difficult to treat gram negative bacteria, N (%)	26 (12.1)	45 (16.0)	0.217
Methicillin-resistant <i>Staphylococcus aureus</i> , N (%)	5 (2.3)	13 (4.6)	
Methicillin-resistant <i>Staphylococcus epidermidis</i> , N (%)	12 (5.6)	16 (5.7)	
Vancomycin-resistant <i>Enterococcus</i> , N (%)	3 (1.4)	5 (1.8)	
Management			
Adequate therapy within 24 hours, N (%)	98 (45.6)	137 (48.8)	0.483
Source control indicated, N (%)	104 (48.4)	121 (43.1)	0.239
Source control accomplished, N (%)	92 (88.5)	79 (65.3)	<0.001
Failure to achieve source control ^d , N (%)	12 (5.6)	42 (14.9)	<0.001
Corticosteroid therapy, N (%)	43 (20.2)	83 (30.1)	0.013
Renal replacement therapy at onset of BSI, N (%)	33 (15.3)	63 (22.4)	0.048
Clinical status on day #7			
Renal replacement therapy, N (%)	28 (13.0)	36 (12.8)	0.944
Clinical failure, N (%)	22 (12.1)	57 (33.9)	<0.001
Persistent bacteremia ≥ 3 days, N (%)	24 (11.2)	25 (8.9)	0.402

^a Calculated using Chi-square test or Fisher's exact test (*) for categorical variables and the Mann-Whitney U test for continuous variables; ^b *Citrobacter* spp., *Enterobacter* spp., *Escherichia coli*, *Hafnia alvei*, *Klebsiella* spp., *Morganella morganii*, *Pantoea*, *Proteus* spp., *Providencia*, *Serratia* spp.; ^c Four individuals were diagnosed with polymicrobial bacteremia of with two resistant pathogens: 2 individuals with both carbapenem-resistant *Acinetobacter baumannii* and difficult to treat *Klebsiella* sp., 1 individual with carbapenem-resistant *Acinetobacter baumannii* and Methicillin-resistant *Staphylococcus epidermidis*, and 1 individual with difficult to treat *Klebsiella pneumoniae* and difficult to treat *Providencia* sp.; ^d those without appropriate source control vs those with either no indication for source control or appropriate source control.

AIDS = acquired immune deficiency syndrome; BSI = bloodstream infection; CI = confidence interval; COPD = Chronic obstructive pulmonary disease; ICU = intensive care unit; IQR = interquartile range; NYHA = New York Heart Association; SAPS = Simplified Acute Physiology Score.

Table S2. Independent risk factors for 28-days mortality among older adults diagnosed with bacteremia, multivariable analysis: sensitivity analysis by excluding those who were discharged from hospital.

Variable	aOR (95% CI) ^a	<i>p</i> ^a
Admission due to COVID-19	4.58 (1.56-13.48)	0.006
Failure to achieve source control	3.50 (1.64-7.50)	0.001
SOFA at time of BSI (per point)	1.17 (1.09 -1.26)	<0.001

^a Calculated using logistic regression model implemented through generalized estimating equations controlling for center-effect. Quasi likelihood information criterion for the model = 272.291.

CI = confidence interval; aOR = adjusted odds ratio.

Table S3. Characteristics of 482 older adults diagnosed with bacteremia: sensitivity analysis by excluding those who were diagnosed with COVID-19.

	28-days mortality status		<i>p</i> ^a
	Alive N = 260 (54%)	Dead N = 222 (46%)	
Age (years), median (IQR)	80 (7)	81 (8)	0.162
Female gender, N (%)	99 (38.1)	91 (41.0)	0.514
Body mass index (BMI), median (IQR)	26.0 (6.5)	26.2 (7.0)	0.316
Comorbidities			
Charlson score, median (IQR)	2 (4)	2 (4)	0.867
COPD (moderate or severe), N (%)	64 (24.6)	45 (20.3)	0.256
Heart failure (NYHA classes 3-4), N (%)	47 (18.1)	40 (18.0)	0.987
Myocardial infarction, N (%)	34 (13.1)	28 (12.6)	0.879
Peripheral vascular disease, N (%)	30 (11.5)	24 (10.8)	0.801
Cerebrovascular disease, N (%)	47 (18.1)	34 (15.3)	0.419
Dementia, N (%)	35 (13.5)	26 (11.7)	0.565
Hemiplegia, N (%)	15 (5.8)	6 (2.7)	0.100
Diabetes mellitus, N (%)	79 (30.4)	61 (27.5)	0.483
Moderate renal disease, N (%)	38 (14.6)	35 (15.8)	0.725
Hemodialysis, N (%)	14 (5.4)	6 (2.7)	0.141
Connective tissue disease, N (%)	4 (1.5)	5 (2.3)	0.739 [§]
Peptic ulcer disease, N (%)	15 (5.8)	12 (5.4)	0.863
Severe liver disease, N (%)	3 (1.2)	2 (0.9)	0.999 [§]
AIDS, N (%)	0	1 (0.5)	0.461 [§]
Malignancy, N (%)	37 (14.2)	31 (14.0)	0.933
Metastatic solid tumor, N (%)	13 (5.0)	23 (10.4)	0.026
Hematological malignancy, N (%)	9 (3.5)	14 (6.3)	0.144
Transplant recipients, N (%)	1 (0.4)	0	0.999 [§]
Corticosteroid therapy, N (%)	9 (3.5)	10 (4.5)	0.558
Functional status before hospitalization			0.347
No limitation, N (%)	66 (25.4)	60 (27.0)	
Mild to moderate limitation, N (%)	110 (42.3)	94 (42.3)	
Serious but not incapacitation restriction, N (%)	49 (18.8)	49 (22.1)	
Severe restriction including bedridden, N (%)	35 (13.5)	19 (8.6)	
Bloodstream infection			
ICU-acquired bloodstream infection, N (%)	195 (75.0)	170 (76.6)	0.687
Duration of hospital stay prior to BSI detection, median (IQR)	13 (21)	14 (15)	0.464
Duration of ICU stay prior to BSI detection, median (IQR)	5 (14)	7 (12)	0.581
Most likely source of BSI			0.801
Respiratory, N (%)	75 (28.8)	63 (28.4)	
Primary, N (%)	44 (16.9)	36 (16.2)	
Vascular catheter-related, N (%)	56 (21.5)	42 (18.9)	
Intra-abdominal, N (%)	40 (15.4)	37 (16.7)	
Urinary, N (%)	27 (10.4)	21 (9.5)	
Other, N (%)	18 (6.9)	23 (10.4)	
SOFA at time of BSI, median (IQR)	7 (5)	10 (6)	<0.001
Maximal C-related protein (mg/L), median (IQR)	121 (167)	127 (196)	0.203
Maximal procalcitonin (ng/mL), median (IQR)	2.9 (15.6)	2.9 (13.1)	0.779
Maximal creatinine (mg/dL), median (IQR)	1.9 (3.5)	2.0 (3.2)	0.411

Ventilatory requirements during BSI			<0.001
Invasive mechanical ventilation, N (%)	151 (58.1)	172 (77.5)	
Non-invasive ventilation, N (%)	20 (7.7)	16 (7.2)	
High flow oxygen, N (%)	19 (7.3)	13 (5.9)	
Low flow or no need for oxygen supplementation, N (%)	70 (26.9)	21 (9.5)	
Septic shock at presentation, N (%)	77 (29.6)	100 (45.0)	<0.001
Glasgow Coma Scale, median (IQR)	13 (7)	10 (8)	<0.001
Antimicrobial therapy during the 7 days prior to bloodstream infection, N (%)	173 (66.5)	174 (78.7)	0.003
Microbiology			
Causative pathogen			0.373
Gram negative bacteria, N (%)	140 (53.8)	113 (50.9)	0.519
<i>Enterobacteriales</i> ^b , N (%)	94 (36.2)	69 (31.1)	
<i>Pseudomonas aeruginosa</i> , N (%)	15 (5.8)	20 (9.0)	
<i>Acinetobacter baumannii</i> , N (%)	24 (9.2)	20 (9.0)	
Gram positive bacteria, N (%)	63 (24.2)	52 (23.4)	0.836
<i>Staphylococcus aureus</i> , N (%)	20 (7.7)	17 (7.7)	
Coagulase-negative <i>Staphylococci</i> , N (%)	17 (6.5)	15 (6.8)	
<i>Enterococcus</i> species, N (%)	18 (6.9)	19 (8.6)	
<i>Candida</i> , N (%)	20 (7.8)	26 (11.8)	
Other, N (%)	20 (7.8)	8 (3.6)	
Polymicrobial, N (%)	29 (11.2)	27 (12.2)	
Resistance pattern of the isolate ^c			0.862 [§]
Difficult to treat gram negative bacteria, N (%)	27 (10.4)	28 (12.6)	
Methicillin-resistant <i>Staphylococcus aureus</i> , N (%)	7 (2.7)	8 (3.6)	
Methicillin-resistant <i>Staphylococcus epidermidis</i> , N (%)	12 (4.6)	13 (5.9)	
Vancomycin-resistant <i>Enterococcus</i> , N (%)	4 (1.5)	2 (0.9)	
Management			
Adequate therapy within 24 hours, N (%)	125 (48.1)	109 (49.1)	0.823
Source control indicated, N (%)	119 (45.8)	102 (45.9)	0.969
Source control accomplished, N (%)	103 (86.6)	68 (66.7)	<0.001
Failure to achieve source control ^d , N (%)	16 (6.2)	34 (15.3)	0.001
Corticosteroid therapy, N (%)	52 (20.1)	66 (30.4)	0.011
Renal replacement therapy at onset of BSI, N (%)	41 (15.8)	52 (23.4)	0.034
Clinical status on day #7			
Renal replacement therapy, N (%)	32 (12.3)	32 (14.4)	0.497
Clinical failure, N (%)	21 (10.0)	46 (33.8)	<0.001
Persistent bacteremia ≥ 3 days, N (%)	26 (10.0)	23 (10.4)	0.896

^a Calculated using Chi-square test or Fisher's exact test ([§]) for categorical variables and the Mann-Whitney U test for continuous variables; ^b *Citrobacter* spp., *Enterobacter* spp., *Escherichia coli*, *Hafnia alvei*, *Klebsiella* spp., *Morganella morganii*, *Pantoea*, *Proteus* spp., *Providencia*, *Serratia* spp.; ^c Four individuals were diagnosed with polymicrobial bacteremia of with two resistant pathogens: 2 individuals with both carbapenem-resistant *Acinetobacter baumannii* and difficult to treat *Klebsiella* sp., 1 individual with carbapenem-resistant *Acinetobacter baumannii* and Methicillin-resistant *Staphylococcus epidermidis*, and 1 individual with difficult to treat *Klebsiella pneumoniae* and difficult to treat *Providencia* sp.; ^d those without appropriate source control vs those with either no indication for source control or appropriate source control.

AIDS = acquired immune deficiency syndrome; BSI = bloodstream infection; CI = confidence interval; COPD = Chronic obstructive pulmonary disease; ICU = intensive care unit; IQR = interquartile range; NYHA = New York Heart Association; SAPS = Simplified Acute Physiology Score.

Table S4. Independent risk factors for 28-days mortality among older adults diagnosed with bacteremia, multivariable analysis: sensitivity analysis by excluding those who were diagnosed with COVID-19.

Variable	aOR (95% CI) ^a	<i>p</i> ^a
Failure to achieve source control	2.92 (1.43-5.98)	0.003
SOFA at time of BSI (per point)	1.17 (1.09-1.26)	<0.001

^a Calculated using logistic regression model implemented through generalized estimating equations controlling for center-effect. Quasi likelihood information criterion for the model = 276.521.

CI = confidence interval; aOR = adjusted odds ratio.

Table S5. Characteristics of 486 older adults diagnosed with bacteremia, following exclusion of those whose death was preceded by a decision to avoid life-sustaining treatment.

	28-days mortality status		<i>p</i> ^a
	Alive N = 282 (58%)	Dead N = 204 (42%)	
Age (years), median (IQR)	80 (7)	81 (8)	0.066
Female gender, N (%)	108 (38.3)	85 (41.7)	0.454
Body mass index (BMI), median (IQR)	26.0 (6.3)	27.1 (6.2)	0.036
Comorbidities			
Charlson score, median (IQR)	2 (3)	2 (3)	0.538
COPD (moderate or severe), N (%)	68 (24.1)	39 (19.1)	0.190
Heart failure (NYHA classes 3-4), N (%)	51 (18.1)	50 (24.5)	0.085
Myocardial infarction, N (%)	37 (13.1)	28 (13.7)	0.847
Peripheral vascular disease, N (%)	30 (10.6)	21 (10.3)	0.903
Cerebrovascular disease, N (%)	48 (17.0)	31 (15.2)	0.590
Dementia, N (%)	41 (14.5)	33 (16.2)	0.620
Hemiplegia, N (%)	15 (5.3)	8 (3.9)	0.474
Diabetes mellitus, N (%)	90 (31.9)	70 (34.3)	0.579
Moderate renal disease, N (%)	40 (14.2)	27 (13.2)	0.765
Hemodialysis, N (%)	14 (5.0)	6 (2.9)	0.268
Connective tissue disease, N (%)	4 (1.4)	3 (1.5)	0.999 [§]
Peptic ulcer disease, N (%)	15 (5.3)	9 (4.4)	0.649
Severe liver disease, N (%)	3 (1.1)	1 (0.5)	0.643 [§]
AIDS, N (%)	0	0	
Malignancy, N (%)	40 (14.2)	26 (12.7)	0.648
Metastatic solid tumor, N (%)	13 (4.6)	17 (8.3)	0.092
Hematological malignancy, N (%)	9 (3.2)	7 (3.4)	0.884
Transplant recipients, N (%)	1 (0.4)	0	0.395 [§]
Corticosteroid therapy, N (%)	9 (3.2)	7 (3.4)	0.884
Functional status before hospitalization			0.761
No limitation, N (%)	78 (27.8)	54 (26.5)	
Mild to moderate limitation, N (%)	114 (40.6)	91 (44.6)	
Serious but not incapacitation restriction, N (%)	53 (18.9)	38 (18.6)	
Severe restriction including bedridden, N (%)	36 (12.8)	21 (10.3)	
Admission due to COVID-19, N (%)	22 (7.8)	54 (26.5)	<0.001
Bloodstream infection			
ICU-acquired bloodstream infection, N (%)	215 (76.2)	174 (85.3)	0.014
Duration of hospital stay prior to BSI detection, median (IQR)	13 (19)	13 (14)	0.832
Duration of ICU stay prior to BSI detection, median (IQR)	6 (15)	8 (11)	0.218
Most likely source of BSI			0.286
Respiratory, N (%)	80 (28.4)	57 (27.9)	
Primary, N (%)	52 (18.4)	49 (24.0)	
Vascular catheter-related, N (%)	61 (21.6)	49 (24.0)	
Intra-abdominal, N (%)	40 (14.2)	22 (10.8)	
Urinary, N (%)	28 (9.9)	11 (5.4)	
Other, N (%)	21 (7.4)	16 (7.8)	
SOFA at time of BSI, median (IQR)	7 (5)	10 (7)	<0.001
Maximal C-related protein (mg/L), median (IQR)	121 (163)	121 (155)	0.388
Maximal procalcitonin (ng/mL), median (IQR)	2.6 (13.3)	1.4 (6.2)	0.041

Maximal creatinine (mg/dL), median (IQR)	1.8 (3.4)	1.4 (1.8)	0.021
Ventilatory requirements during BSI			<0.001
Invasive mechanical ventilation, N (%)	165 (58.5)	165 (80.9)	
Non-invasive ventilation, N (%)	20 (7.1)	12 (5.9)	
High flow oxygen, N (%)	21 (7.4)	9 (4.4)	
Low flow or no need for oxygen supplementation, N (%)	76 (27.0)	18 (8.8)	
Septic shock at presentation, N (%)	84 (29.8)	88 (43.1)	0.002
Glasgow Coma Scale, median (IQR)	13 (7)	10 (9)	<0.001
Antimicrobial therapy during the 7 days prior to bloodstream infection, N (%)	189 (67.0)	160 (78.8)	0.004
Microbiology			
Causative pathogen			0.012
Gram negative bacteria, N (%)	150 (53.2)	102 (50.0)	0.487
<i>Enterobacteriales</i> ^b , N (%)	102 (36.6)	50 (24.6)	
<i>Pseudomonas aeruginosa</i> , N (%)	16 (5.7)	16 (7.9)	
<i>Acinetobacter baumannii</i> , N (%)	25 (9.0)	32 (15.8)	
Gram positive bacteria, N (%)	71 (25.2)	58 (28.4)	0.423
<i>Staphylococcus aureus</i> , N (%)	21 (7.5)	18 (8.9)	
Coagulase-negative <i>Staphylococci</i> , N (%)	21 (7.5)	14 (6.9)	
<i>Enterococcus</i> species, N (%)	21 (7.5)	26 (12.8)	
Candida, N (%)	22 (7.9)	21 (10.3)	
Other, N (%)	21 (7.5)	6 (3.0)	
Polymicrobial, N (%)	30 (10.8)	20 (9.9)	
Resistance pattern of the isolate			0.005
Difficult to treat gram negative bacteria, N (%)	28 (9.9)	41 (20.1)	
Methicillin-resistant <i>Staphylococcus aureus</i> , N (%)	8 (2.8)	13 (6.4)	
Methicillin-resistant <i>Staphylococcus epidermidis</i> , N (%)	14 (5.0)	12 (5.9)	
Vancomycin-resistant <i>Enterococcus</i> , N (%)	5 (1.8)	3 (1.5)	
Any resistance pattern, N (%)	55 (19.5)	69 (33.8)	<0.001
Management			
Adequate therapy within 24 hours, N (%)	136 (48.2)	90 (44.1)	0.370
Source control indicated, N (%)	127 (45.0)	89 (43.6)	0.758
Source control accomplished, N (%)	111 (87.4)	58 (65.2)	<0.001
Failure to achieve source control ^c , N (%)	16 (5.7)	31 (15.2)	<0.001
Corticosteroid therapy, N (%)	54 (19.3)	62 (31.2)	0.003
Renal replacement therapy at onset of BSI, N (%)	41 (14.5)	45 (22.1)	0.032
Clinical status on day #7			
Renal replacement therapy, N (%)	33 (11.7)	24 (11.8)	0.983
Clinical failure, N (%)	24 (10.5)	44 (36.4)	<0.001
Persistent bacteremia ≥ 3 days, N (%)	27 (9.6)	17 (8.3)	0.638

^a Calculated using Chi-square test or Fisher's exact test (*) for categorical variables and the Mann-Whitney U test for continuous variables; ^b *Citrobacter* spp., *Enterobacter* spp., *Escherichia coli*, *Hafnia alvei*, *Klebsiella* spp., *Morganella morganii*, *Pantoea*, *Proteus* spp., *Providencia*, *Serratia* spp.; ^c Those without appropriate source control vs those with either no indication for source control or appropriate source control.

AIDS = acquired immune deficiency syndrome; BSI = bloodstream infection; CI = confidence interval; COPD = Chronic obstructive pulmonary disease; ICU = intensive care unit; IQR = interquartile range; NYHA = New York Heart Association; SAPS = Simplified Acute Physiology Score.

Table S6. Independent risk factors for 28-days mortality among older adults diagnosed with bacteremia, multivariable analysis following exclusion of those whose death was preceded by a decision to avoid life-sustaining treatment.

Variable	aOR (95% CI) ^a	<i>p</i> ^a
Admission due to COVID-19	4.34 (1.39-13.52)	0.011
Failure to achieve source control	6.49 (2.12-19.85)	0.001
SOFA at time of BSI (per unit)	1.13 (1.02-1.26)	0.019
Maximal creatinine at time of BSI (per mg/dL)	0.91 (0.82-1.01)	0.081

^a Calculated using logistic regression model implemented through generalized estimating equations controlling for center-effect. Quasi likelihood information criterion for the model = 165.856.

CI = confidence interval; aOR = adjusted odds ratio.

Table S7. Characteristics of 292 older adults diagnosed with bacteremia: sensitivity analysis by including only Gram-negative bacteremia cases.

	28-days mortality status		<i>p</i> ^a
	Alive N = 150 (51.4%)	Dead N = 142 (48.6%)	
Age (years), median (IQR)	79 (7)	82 (9)	0.055
Female gender, N (%)	60 (40.0)	56 (39.4)	0.922
Body mass index (BMI), median (IQR)	26.2 (6.4)	26.6 (5.7)	0.762
Comorbidities			
Charlson score, median (IQR)	2 (4)	2 (3)	0.179
COPD (moderate or severe), N (%)	39 (26.0)	32 (22.5)	0.490
Heart failure (NYHA classes 3-4), N (%)	34 (22.7)	32 (22.5)	0.979
Myocardial infarction, N (%)	18 (12.0)	21 (14.8)	0.484
Peripheral vascular disease, N (%)	17 (11.3)	14 (9.9)	0.683
Cerebrovascular disease, N (%)	32 (21.3)	22 (15.5)	0.199
Dementia, N (%)	23 (15.3)	16 (11.3)	0.307
Hemiplegia, N (%)	11 (7.3)	4 (2.8)	0.081
Diabetes mellitus, N (%)	51 (34.0)	41 (28.9)	0.346
Moderate renal disease, N (%)	22 (14.7)	21 (14.8)	0.977
Hemodialysis, N (%)	10 (6.7)	3 (2.1)	0.059
Connective tissue disease, N (%)	3 (2.0)	4 (2.8)	0.717 [‡]
Peptic ulcer disease, N (%)	7 (4.7)	4 (2.8)	0.407
Severe liver disease, N (%)	5 (3.3)	4 (2.8)	0.999 [‡]
AIDS, N (%)	0	0	
Malignancy, N (%)	24 (16.0)	19 (13.4)	0.528
Metastatic solid tumor, N (%)	8 (5.3)	10 (7.0)	0.544
Hematological malignancy, N (%)	5 (3.3)	10 (7.0)	0.151
Transplant recipients, N (%)	1 (0.7)	0	0.999 [‡]
Corticosteroid therapy, N (%)	5 (3.3)	5 (3.5)	0.999 [‡]
Functional status before hospitalization			0.137
No limitation, N (%)	39 (26.0)	38 (26.8)	
Mild to moderate limitation, N (%)	54 (36.0)	66 (46.5)	
Serious but not incapacitation restriction, N (%)	34 (22.7)	26 (18.3)	
Severe restriction including bedridden, N (%)	23 (15.3)	12 (8.5)	
Admission due to COVID-19, N (%)	10 (6.7)	29 (20.4)	<0.001
Bloodstream infection			
ICU-acquired bloodstream infection, N (%)	115 (76.7)	116 (81.7)	0.291
Duration of hospital stay prior to BSI detection, media (IQR)	13 (24)	14 (15)	0.707
Duration of ICU stay prior to BSI detection, median (IQR)	7 (19)	9 (12)	0.910
Most likely source of BSI			0.688
Respiratory, N (%)	53 (35.3)	53 (37.3)	
Primary, N (%)	24 (16.0)	26 (18.3)	
Vascular catheter-related, N (%)	24 (16.0)	25 (17.6)	
Intra-abdominal, N (%)	15 (10.0)	16 (11.3)	
Urinary, N (%)	25 (16.7)	14 (9.9)	
Other, N (%)	9 (6.0)	8 (5.6)	
SOFA at time of BSI, median (IQR)	7 (6)	10 (6)	<0.001
Maximal C-related protein (mg/L), median (IQR)	138 (161)	129 (173)	0.679
Maximal procalcitonin (ng/mL), median (IQR)	4.2 (15.9)	1.8 (9.7)	0.190

Maximal creatinine (mg/dL), median (IQR)	1.8 (2.7)	1.9 (2.4)	0.951
Ventilatory requirements during BSI			<0.001
Invasive mechanical ventilation, N (%)	86 (57.3)	112 (78.9)	
Non-invasive ventilation, N (%)	13 (8.7)	9 (6.3)	
High flow oxygen, N (%)	13 (8.7)	5 (3.5)	
Low flow or no need for oxygen supplementation, N (%)	38 (25.3)	16 (11.3)	
Septic shock at presentation, N (%)	43 (28.7)	65 (45.8)	0.002
Glasgow Coma Scale, median (IQR)	12 (7)	9 (8)	<0.001
Antimicrobial therapy during the 7 days prior to bloodstream infection, N (%)	92 (61.3)	107 (75.9)	0.008
Microbiology			
Causative pathogen			0.064
<i>Enterobacteriales</i> ^b , N (%)	102 (68.0)	77 (54.2)	
<i>Pseudomonas aeruginosa</i> , N (%)	16 (10.7)	25 (17.6)	
<i>Acinetobacter baumannii</i> , N (%)	25 (16.7)	35 (24.6)	
Others, N (%)	7 (4.7)	5 (3.5)	
Resistance pattern of the isolate ^c			
Difficult to treat gram negative bacteria, N (%)	23 (15.3)	40 (28.2)	0.013
Management			
Adequate therapy within 24 hours, N (%)	81 (54.0)	76 (53.5)	0.935
Source control indicated, N (%)	64 (42.7)	48 (33.8)	0.119
Source control accomplished, N (%)	53 (82.8)	31 (64.6)	0.027
Failure to achieve source control ^d , N (%)	11 (7.3)	17 (12.0)	0.178
Corticosteroid therapy, N (%)	24 (16.0)	42 (30.4)	0.004
Renal replacement therapy at onset of BSI, N (%)	25 (16.7)	29 (20.4)	0.409
Clinical status on day #7			
Renal replacement therapy, N (%)	19 (12.7)	10 (7.0)	0.108
Clinical failure, N (%)	9 (7.6)	24 (32.0)	<0.001
Persistent bacteremia ≥ 3 days, N (%)	10 (6.7)	4 (2.8)	0.124

^a Calculated using Chi-square test or Fisher's exact test (*) for categorical variables and the Mann-Whitney U test for continuous variables; ^b *Citrobacter* spp., *Enterobacter* spp., *Escherichia coli*, *Hafnia alvei*, *Klebsiella* spp., *Morganella morganii*, *Pantoea*, *Proteus* spp., *Providencia*, *Serratia* spp.; ^c Four individuals were diagnosed with polymicrobial bacteremia of with two resistant pathogens: 2 individuals with both carbapenem-resistant *Acinetobacter baumannii* and difficult to treat *Klebsiella* sp., 1 individual with carbapenem-resistant *Acinetobacter baumannii* and Meticillin-resistant *Staphylococcus epidermidis*, and 1 individual with difficult to treat *Klebsiella pneumonia* and difficult to treat *Providencia* sp.; ^d those without appropriate source control vs those with either no indication for source control or appropriate source control.

AIDS = acquired immune deficiency syndrome; BSI = bloodstream infection; CI = confidence interval; COPD = Chronic obstructive pulmonary disease; ICU = intensive care unit; IQR = interquartile range; NYHA = New York Heart Association; SAPS = Simplified Acute Physiology Score.

Table S8a. Independent risk factors for 28-days mortality among older adults diagnosed with bacteremia, multivariable analysis: sensitivity analysis by including only gram-negative bacteremia cases.

Variable	aOR (95% CI) ^a	<i>p</i> ^a
Admission due to COVID-19	14.59 (1.22-173.93)	0.034
Source control accomplished	0.31 (0.12-0.81)	0.018
Corticosteroid therapy	2.97 (1.16-7.63)	0.023
Antimicrobial therapy during the 7 days prior to bloodstream infection	2.56 (1.01-6.51)	0.049

^a Calculated using logistic regression model implemented through generalized estimating equations controlling for center-effect. Quasi likelihood information criterion for the model = 136.761.

CI = confidence interval; aOR = adjusted odds ratio.

Table S8b. Multivariable logistic regression model following an introduction of corticosteroid therapy by septic shock.

Variable	aOR (95% CI) ^a	<i>p</i> ^a
Admission due to COVID-19	15.54 (1.92-125.63)	0.010
Source control accomplished	0.37 (0.14-0.98)	0.045
Corticosteroid therapy and septic shock (interaction variable)	6.36 (1.77-22.81)	0.005

^a Calculated using logistic regression model implemented through generalized estimating equations controlling for center-effect. Quasi likelihood information criterion for the model = 134.400.

CI = confidence interval; aOR = adjusted odds ratio.

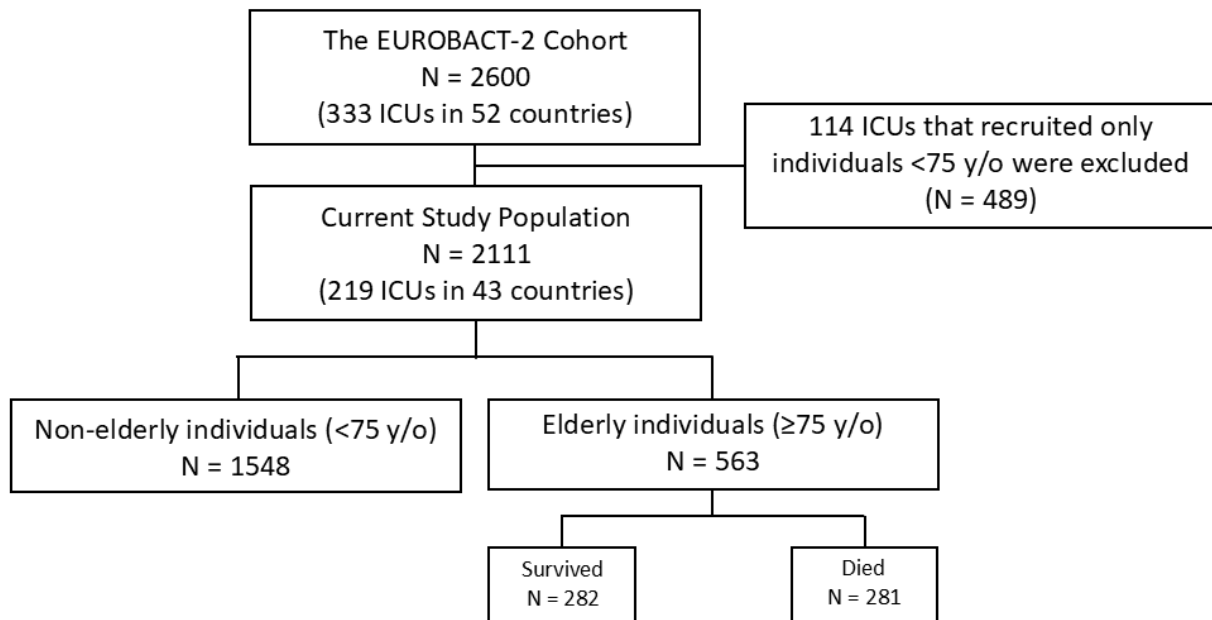
Table S9. Multivariable logistic regression model following the inclusion of additional variables

Variable	aOR (95% CI) ^a	<i>p</i> ^a
Admission due to COVID-19	4.12 (2.34-7.23)	<0.001
Failure to achieve source control	2.70 (1.40-5.15)	0.003
SOFA at time of BSI (per point)	1.16 (1.11-1.21)	<0.001
Gender (woman)	1.09 (0.76-1.57)	0.652
Pulmonary source for bacteremia	1.05 (0.70-1.59)	0.803
Adequate therapy within 24 hours	1.04 (0.73-1.48)	0.846

^a Calculated using logistic regression model implemented through generalized estimating equations controlling for center-effect.

CI = confidence interval; aOR = adjusted odds ratio.

Figure 1. Study flow diagram



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