Clinical outcomes and epidemiological characteristics of bacteremia in the older Japanese population

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Short title: Bacteremia in older Japanese individuals

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Authorship statement:

Keiji Nakamura, Shinya Tsuzuki, and Kayoko Hayakawa contributed to the study conception and design. They had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Keiji Nakamura, Shinya Tsuzuki, and Kayoko Hayakawa were responsible for the statistical analysis. Satoshi ide, Hidetoshi Nomoto, Gen Yamada, Takato Nakamoto, and Kei Yamamoto provided administrative, technical, and material support. Norio Ohmagari supervised the study. All the authors met the International Committee of Medical Journal Editors authorship criteria and have read and approved the final manuscript.

Abbreviations:

CA	Community-acquired
HCA	Healthcare-associated
HO	Hospital-onset
aOR	Adjusted odds ratio
BSIs	Bloodstream infections
NCGM	National Center for Global Health and Medicine
LOS	Length of stay
CLSI	Clinical and Laboratory Standards Institute
CoNS	Coagulase-negative *Staphylococci*

CLABSI	Central line-associated BSI
PVCR-BSI	Peripheral venous catheter-related BSI
UTIs	Urinary tract infections
BJIs	Bone and joint infections
IE	Infective endocarditis
IAIs	Intra-abdominal infections
LTRIs	Lower respiratory tract infections
SSTIs	Skin and soft tissue infections
IV	Intravenous
LTCF	Long-term care facility
ID	Infectious disease
IQR	Interquartile range
DM	diabetes mellitus

Abstract

Background

The characteristics and clinical consequences of bacteremia in older people, who are highly susceptible to infections, need to be clarified. This study aimed to determine the epidemiological characteristics, prognosis, and predictors of 7-day mortality in patients with community-acquired (CA), healthcare-associated (HCA), and hospital-onset (HO) bacteremia in older adults aged ≥65 years.

Methods

Patients aged ≥65 years with positive blood cultures between April 1, 2015, and March 31, 2018, were divided into three groups: pre-old (65–74 years), old (75–89 years), and super-old (≥90 years). Characteristics based on medical exposure, including CA, HCA, and HO, were also compared and factors related to mortality were identified.

Results

Overall, 1,716 episodes of bacteremia were identified in 1,415 patients. Of the 1,211 episodes without contamination, 32.8%, 54.3%, and 12.9% occurred in pre-old, old, and super-old patients. Central line-associated bloodstream infections were more common in pre-old patients and urinary tract infections in the old and super-old. The 7-day mortality rates in the pre-old, old, and super-old

groups were 7.4%, 5.8%, and 14.2% (P=0.002), respectively. Multivariable logistic regression showed that super-old age (adjusted odds ratio, aOR: 2.09 [1.13–3.88], P=0.019) and HO bacteremia (aOR: 1.97 [1.18–3.28], P=0.010) were independent risk factors for 7-day mortality. Infectious disease consultation had a protective effect on 7-day mortality (aOR: 0.59 [0.35–0.99], P=0.047).

Conclusions

The epidemiology of bacteremia differs among older people; thus, they should not be treated as a single entity. A careful approach is needed for the optimal management of bacteremia in these vulnerable patients.

Keywords: Older adults; Aging; Bloodstream infection; Community-Acquired; Health Care-Associated; Hospital-Onset

Introduction

Japan is a "super-aging" country, and the average life expectancy in 2020 was 87.7 years for women and 81.6 years for men [1]. Bloodstream infections (BSIs) are a major cause of morbidity and mortality in hospitalized patients [2] and the risk of mortality due to bacteremia increases with age [3-11]. Although bacteremia generally occurs in older adults, the actual age of the population can vary over a few decades. In addition, the degree of exposure to hospital environments varies greatly among community-acquired (CA), healthcare-associated (HCA), and hospital-onset (HO) bacteremia. Studies that examined the differences in epidemiological trends among older adult subgroups are limited. Although a study in Taiwan divided older adults into two groups (65–84 years and ≥85 years), its focus was limited to CA and community-onset (CO) infection [10, 11]. Hernandez et al. also divided older adults into three groups but limited the focus to CO [9]. In 2007, Crane et al. compared the epidemiology of CA, HCA, and HO in older adults but analyzed all ages together, and the epidemiological trends might have changed over the years [12]. Another study from Canada divided older adults into three groups (65–74 years, 75–84 years, and ≥85 years); however, it defined the incidence, clinical determinants, and risk factors for mortality from BSI in older adults with bacteremia but did not examine differences in medical exposure [13].

To the best of our knowledge, this is the first study to determine the epidemiological characteristics, prognosis, and predictors of 7-day mortality in patients with CA, HCA, and HO bacteremia by age group, in older adults aged ≥65 years.

Patients and Methods

Hospital setting and study design

This retrospective cohort study was conducted at the National Center for Global Health and Medicine (NCGM) in Tokyo, Japan from April 1, 2015, to March 31, 2018.

Patient Consent and ethics approval

Patient consent was not deemed necessary because the study used de-identified data. The study was approved by the Ethics Committee of the NCGM (Approval No: NCGM-G-003151-01).

Data source

Using a microbiology laboratory database, all hospitalized patients aged ≥65 years with positive blood cultures were identified. The patient's sex, age, healthcare exposure, medical care received, and clinical manifestations of the infection that caused the bacteremia, along with isolated microorganisms, 7-day all-cause mortality after bacteremia, and length of stay after the onset of bacteremia (LOS after) were recorded. Patients who died at the hospital were excluded from the LOS calculation. Bacterial identification and susceptibility testing were performed according to the Clinical and Laboratory Standards Institute (CLSI) criteria (M100-S23) (Table 1).

Definitions

Age groups

As per the Japanese Society of Geriatrics and Gerontology, age was classified into three categories: pre-old (65–74 years), old (75–89 years), and super-old (≥90 years) [14].

Bacteremia and infectious clinical diseases

Episodes of bacteremia and fungemia were defined as positive blood cultures. The clinical significance of positive blood culture due to coagulase-negative *Staphylococci* (CoNS) was classified as either true infection (i.e., bacteremia) or contamination, based on the number of culture positives, presence of a plausible source of infection, and clinical presentation [15].

When similar organisms were detected in the same patient, at least two infectious disease physicians determined whether it was in the same series of the bacteremic episode or a new episode, and only the new episodes were included. Infectious clinical diseases (i.e., the focus of bacteremia) were categorized as central line-associated BSI (CLABSI), short-term peripheral venous catheter-related BSI (PVCR-BSI), urinary tract infections (UTIs), bone and joint infections (BJIs), infective endocarditis (IE), intra-abdominal infections (IAIs), lower respiratory tract infections (LTRIs), skin and soft tissue infections (SSTIs), and others (such as central and vascular infections). Two independent infectious disease physicians determined the type of infectious clinical disease based on the chart and review and/or patient examination.

Healthcare exposure at the onset of bacteremia

Healthcare exposure at bacteremia onset was classified into three categories: CA, HCA, and HO

groups [16]. CA was defined as positive blood cultures presented on admission or within 48 hours of admission in patients who did not meet the criteria for HCA [16].

HCA bacteremia onset was defined as [16]:

・Receipt of intravenous (IV) therapy, wound care, or nursing care in the 30 days before the bloodstream infection.

・Visit to a hospital or hemodialysis clinic or receipt of IV chemotherapy in the 30 days before the bloodstream infection.

・Hospitalization in an acute care hospital for 2 or more days in the 90 days before the bloodstream infection.

・Residence in a nursing home or long-term care facility (LTCF).

A positive blood culture obtained from a patient who was hospitalized for more than 48 hours was defined as HO. For patients transferred from other hospitals, the length of hospital stay was calculated from the date of the first admission [16].

Infectious disease (ID) consultation

ID consultation was defined as consultation within 7days after blood culture collection.

Statistical analyses

The parameters retrieved from the medical records were compared between the groups using the Chi-

squared test or Fisher's exact test and the Kruskal–Wallis test for LOS (Tables 2 and 3, S1 and S2). Comparisons among the three groups by age (pre-old, old, super-old) were considered statistically significant at P<0.05 (Tables 2 and S1). Comparison between CA, HCA, and HO by the institution was performed for CA and HCA, CA and HO, and HCA and HO, and P <0.0167 after Bonferroni correction was considered statistically significant (Tables 3 and S2). Factors associated with mortality were identified using multivariable logistic regression analysis. Variables included in the model were identified based on previous studies [9-13] (Table 4). All statistical analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA).

Results

During the study period, 1,716 positive blood culture samples were reported for 1,415 patients, of which, 505 (29.4%) positive blood culture episodes were considered contaminated (Fig 1).

Comparison of clinical characteristics of bacteremic episodes in each focus of bacteremia

Excluding contamination, the total number of bacteremic episodes was 1,211 (70.6%), of which 652 (53.8%) occurred in men with a median age (Interquartile range: IQR) of 79 years (72–86 years). The number of pre-old, old, and super-old cases was 397 (32.8%), 658 (54.3%), and 156 (12.9%), respectively (Table 1).

Demographics

Regarding the focus of BSI, 289 cases (23.9%) were UTIs, 277 cases (22.9%) were IAIs, 159 cases (13.1%) were CLABSIs, and 96 cases (7.9%) were PVCR-BSIs. The percentages of CLABSI by age group were 19.1% in pre-old, 10.8% in old, and 7.7% in super-old patients, which tended to decrease with increasing age. The proportion of PVCR-BSI by age group was 6.3% in pre-old, 8.2% in old, and 10.9% in super-old patients, which increased with increasing age (Table 1).

Healthcare exposure

Of the total bacteremic episodes, 468 (38.6%) were CA, 213 (17.6%) were HCA, and 530 (43.8%) were HO. CLABSI and PVCR-BSIs were common in HO (89.3% and 91.7%, respectively). UTIs, BJIs, IE, IAIs, LRTIs, and SSTIs were common in CA (49.1%, 60.9%, 63.2%, 48.4%, 45.9%, and 66.1%, respectively) (Table 1).

Microbiology

The most common bacteria identified was *Escherichia coli*. The most common causative microorganism of CLABSI was CoNS (n=94 [59.1%]), followed by *Candida* spp. (n=25 (15.7%)), and *Staphylococcus aureus* (n=22 [13.8%]). The most common causative microorganism of PVCR-BSIs was CoNS (n=51 [53.1%]), followed by *S. aureus* (n=16 [16.7%]). *E. coli* was the most common microorganism causing UTI (n=198 [68.5%]) and IAIs (n=85 [30.7%]) (Table 1).

ID consultation and outcomes

ID consultation was performed in 383 cases (31.6%), and the 7-day mortality rate was 89 (7.3%). The highest rate of 7-day mortality among foci of BSIs was observed in patients with LTRI (19.2%),

and the lowest rates in those with SSTI (1.7%). The median LOS after a bacteremic episode was 23 days (IQR: 14–46 days) (Table 1). Of the 89 deaths, the pathogens with the highest number of deaths were, from the top, *K. pneumoniae* 15 cases, *E. coli* 12 cases, CoNS 12 cases, and *S. aureus* 9 cases (MSSA 5 cases, MRSA 3 cases, MSSA/MRSA unknown 1 cases). Pathogens with high mortality rates were, from the top, *Candida* sp. 15.4%, *Enterobacter cloacae* 15%, and *K. pneumoniae* 13.2%. In the cases where polymicrobial species were detected, the number of deaths was 16 cases and the mortality rate was 12.2%.

Comparison of clinical characteristics of bacteremic episodes within each age category

Demographics and healthcare exposure

The male-to-female ratio was almost the same (652 men [53.8%] and 559 women [46.2%]); however, the ratio by age group was different, with more males in the pre-old (n=249 [62.7%]) and more females in the super-old (n=109, 69.9%) groups (Table 2). The proportion of HCA tended to be higher in the super-old (P=0.006), and HO tended to be higher in the pre-old age group (P=0.005). LOS before bacteremia (LOS before) was the longest in the pre-old (P<0.001) group, with a median of 3 days (IQR 0–21).

Comorbidities including immunosuppression

The frequency of comorbidities differed significantly among the groups (P=0.015). Super-old patients frequently had diabetes mellitus (DM) (13.5%) and pre-old patients had hematological

malignancies (6.8%, P=0.001). The super-old group had a significantly lower number of patients with solid cancers (11.5%, P <0.001) (Table 2).

Focus of bacteremia

IAIs were the most common cause of bacteremia in pre-old patients (22.4%), while UTIs were in old and super-old patients (28% and 25.5%, respectively). There was a significant difference in the proportion of BSI among the three age groups regarding CLABSI, UTI, IE, and lower respiratory tract infections. Among patients with CLABSI, 19.1% were pre-old, 10.8% were old, and 7.7% were super-old (P<0.001). The UTI prevalence was 16.4%, 28%, and 25.6% among the pre-old, old, and super-old groups, respectively (P<0.001). The prevalence of PVCR-BSI significantly increased with age (Table 2).

ID consultation and outcome

ID consultation was more frequent in pre-old patients (38.0%), followed by old (28.7%) and super-old (27.6%) patients, with a significant difference among the three groups (P=0.003). The median days from blood culture collection to ID consultation was 2 days (IQR: 0-3.75 days). Median days from blood culture collection to ID consultation by age group was 2 days (IQR: 0-3 days) for pre-old, 2 days (IQR: 1-4 days) for old, and 1 days (IQR: 0-2.75 days) for super-old, respectively. The median days from positive blood culture to ID consultation was 0 day (IQR 0-2 days).

The 7-day mortality rate was higher in the super-old group (pre-old: 7.4%; old: 5.8%; super-old: 14.2%), with a significant difference among the three groups (P=0.002). There was no significant

difference in LOS among the three groups (P=0.428) (Table 2).

Microbiology

The most common bacteremia-causing microorganism isolated in was *E. coli* (pre-old: 21.2%; old: 29.8%; super-old: 30.1%). Significant differences were observed among the three groups with respect to the isolation of methicillin-susceptible *S. aureus* (MSSA) (P=0.024), *E. coli* (P=0.006), and Enterobacteriales (P=0.028) (Table S1).

Comparison of clinical characteristics of bacteremia based on healthcare exposure

Demographics

The male-to-female ratio was similar in the CA and HCA groups, but males were higher in the HO (58.1%) group, with a significant difference between CA and HO groups (P=0.007) (Table S2).

Comorbidities including immunosuppression

The most common comorbidity in the CA group was DM (26.9%) and in the HCA (32.4%) and HO (36.8%) groups were solid cancers (Table S2).

Focus of bacteremia

In the CA and HCA groups, UTI was the most common focus of bacteremia (30.3% and 28.2%, respectively), followed by IAI (28.6% and 26.8%, respectively). In the HO group, CLABSI was the most common (26.8%), followed by PVCR-BSIs (16.8%) (Table S2).

ID consultation and outcome

ID consultation was significantly more common in the HO group than in the CA and HCA groups (P<0.001 and P=0.005, respectively). However, there was no significant difference between the CA and HCA groups. The 7-day mortality rates were 5.4%, 6.6%, and 9.5%, for the CA, HCA, and HO groups, respectively, with no significant differences among healthcare exposures (Table S2).

Microbiology

E. coli most commonly caused bacteremia in both the CA and HCA groups (37.2% and 35.2%, respectively). In contrast, CoNS (28.7%) was most frequently isolated in HO. In comparison between the CA and HCA groups, *Pseudomonas aeruginosa* (*P. aeruginosa*) and non-fermenter (NFGNB) were significantly more frequently detected in HCA (P≤0.001 and P=0.001, respectively). *Candida* sp. was detected significantly more in the HO group than in the CA and HCA groups (P≤0.001 and P<.001, respectively) (Table 3).

Clinical predictors of 7-day mortality

Multivariable logistic regression showed that bacteremia in the HO (adjusted odds ratio [aOR]: 1.97 [1.18–3.28], P=0.010) and super-old (aOR: 2.09 [1.13–3.88], P=0.019) groups were independent risk factors for 7-day mortality. ID consultation had a protective effect on 7-day mortality (aOR: 0.59 [0.35–0.99], P=0.047) (Table 4).

Discussion

The study found that patients ≥65 years were not a homogeneous group and that healthcare environment exposure has a complex effect on older adults based on subgroups.

In this study, 29.4% of the positive blood cultures were contaminated, similar to previous studies [15, 17–20]. The 7-day mortality rate in our study (5%) was lower than the previously reported 7-day mortality rate (13%) evaluated for *S. aureus* and 14-day mortality rate (7.3%) including non-older adult patients [21, 22]. In addition to the difference in days after BSI, this might be due to different patient populations, as both were single-center studies.

E. coli was the most frequently detected microorganism in all age groups, with higher detection rates in the older age group which was consistent with previous studies [6, 7, 9, 10]. This could be because the incidence of UTI and biliary tract infections increase with increasing age [7, 9]; our study also showed a higher proportion of UTI in old and super-old than in pre-old patients.

The prevalence of CLABSI tended to decrease with increasing age in our study, similar to previous studies [7, 9, 23, 24]. This might be due to a decreased opportunity to insert a central venous catheter with increasing age [23]. CoNS were the most common causative microorganisms of CLABSI in our study, similar to previous reports [25–27].

No studies focusing on BSIs in older adults have evaluated PVCR-BSIs. The present study compared

the occurrence of PVCR-BSIs in HO and BSIs in pre-old, old, and super-old patients and reported no significant difference between pre-old and old patients; however, the comparison between pre-old and super-old patients and old and super-old patients revealed that the prevalence of PVCR-BSIs was significantly higher in the super-old group ($P < 0.001$ and $P = 0.013$, respectively). In this study, CoNS were the most common causative microorganisms causing PVCR-BSIs. Although previous studies have reported similar findings [28], *S. aureus* was the most commonly detected causative microorganism in other studies, including a previous study from our hospital [25, 26, 29–32]. The previous study from our hospital was not limited to older adults, and the difference in patients' age and the study period might have caused a high number of CoNS reported in the present study.

A study on nosocomial BSIs not limited to older adults reported 4.4–6.3% of PVCR-BSIs [25, 29, 33], but this study revealed that 7.9% of PVCR-BSI cases are responsible for BSIs in older adults, and approximately 60% of PVCR-BSI cases were seen in ID consultations. PVCR-BSI may not be recognized as a device-related BSI as frequently as CLABSIs by non-ID specialists. In clinical practice in Japan, peripheral catheters might be used longer in older people because of difficulty in frequent insertions owing to the fragility of their skin and blood vessels which could compromise sterility leading to infections.

The 7-day mortality rate after BSI onset was the highest in the super-old group in this study. Previous studies that divided older adults into different age groups also reported similar findings, although the

number of days specified differed [6, 7, 9, 13]. In addition, in this study, the mortality rate of the oldest group was lower than that of the pre-old group, which is different from previous studies [9, 13]. On the other hand, a study by Wester et al. reported that the 3-day mortality after BSI was higher in the ≥85 years age group than in 65–84 years-old patients, and the 14-day mortality was higher in the 65–84 years age group than in those aged ≥85 years [11]. The difference in the duration from bacteremia to death may have influenced the results.

In this study, super-old age and HO were found to be independent risk factors for 7-day mortality. Previous studies also reported increasing age as a risk factor [3–5, 9, 11–13]. Kevin et al. found that HO is a risk factor for death [13]. This may be because of serious underlying conditions, such as hematological malignancies and solid cancers, that are more common in hospitalized patients than in those in the CA and HCA groups.

Previous studies reported that intervention by the Infectious Disease department improved the prognosis of bloodstream infections, though they were not specific to older patients [33-39]. ID intervention in this study showed an improvement in the 7-day mortality of BSIs in older patients, which suggests that early intervention may improve prognosis. ID consultation took place a median of 2 days after blood culture collection in our cohort, and recommendations such as antimicrobial modifications were provided on the same day.

The ID consultation rate in this study decreased with increasing age (as low as 26.3% in super-old) and the consultation rate was lower in CA and HCA when compared to HO. Thus, given the variation in ID consultation rates based on age and healthcare exposure, it is conceivable that the prognosis of bacteremia in older patients may be improved if ID consultation is actively performed regardless of their age or healthcare exposure.

This study has some limitations in addition to its retrospective nature and limited sample size. First, the findings may be influenced by the epidemiological variables of a single center and may not be generalized to other settings. Second, the information on the exact cause of death was not always available. Third, information on resistant organisms other than MRSA, nor other variables that may impact the outcome, such as time to appropriate antimicrobial therapy and the severity of bacteremia was not collected [40]. Fourth, the study did not assess the severity of comorbidities, by calculating the Charlson Comorbidity Index [41], for example, it cannot objectively assess the risk of death from comorbidities. Finally, 7-day mortality was reported as an outcome; however, some previous studies evaluated 28- or 30-days mortality [3, 5, 6, 9, 13] and some patients may have died later than 7 days after BSI.

In conclusion, the clinical features of bacteremia in older adults varied widely among the age groups and healthcare exposure types, and BSIs in patients >65 years are not uniform. Therefore, older

patients should not be treated as a single entity. The super-old patients were less likely to have an ID consultation and were more likely to die. Early intervention by ID specialists, and tailored preventive and therapeutic approaches for bacteremia are required to optimally manage the health of older patients.

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Conflict of Interests

Kei Yamamoto received research grants from Fujirebio, Inc. and Mizuho Medy, Co., Ltd., VisGene, Co., Ltd., Sanyo Chemical Industries Co., Ltd., and Canon Medical Systems Co., Ltd., outside the submitted work.

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References

1. Ministry of Health, Labour and Welfare. Life expectancies at birth in some countries, https://www.mhlw.go.jp/english/database/db-hw/lifetb20/dl/lifetb20-01.pdf; [accessed 20 January 2023].

2. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis 2004;39:309–17. https://doi/10.1086/421946.

3. Ayau P, Bardossy AC, Sanchez G, Ortiz R, Moreno D, Hartman P, et al. Risk factors for 30-day mortality in patients with methicillin-resistant Staphylococcus aureus bloodstream infections. Int J Infect Dis 2017;61:3–6. https://10.1016/j.ijid.2017.05.010.

4. Pastagia M, Kleinman LC, Lacerda de la Cruz EG, Jenkins SG. Predicting risk for death from MRSA bacteremia. Emerg Infect Dis 2012;18:1072–80. https://10.3201/eid1807.101371.

5. Gasch O, Camoez M, Dominguez MA, Padilla B, Pintado V, Almirante B, et al. Predictive factors for mortality in patients with methicillin-resistant Staphylococcus aureus bloodstream infection: impact on outcome of host, microorganism and therapy. Clin Microbiol Infect 2013;19:1049–57. https://10.1111/1469-0691.12108.

6. Lee CC, Wang JL, Lee CH, Hung YP, Hong MY, Chang CM, et al. Age-related trends in adults with community-onset bacteremia. Antimicrob Agents Chemother 2017;61:e01050-17. https://10.1128/AAC.01050-17.

7. Lee CC, Chen SY, Chang IJ, Chen SC, Wu SC. Comparison of clinical manifestations and outcome of community-acquired bloodstream infections among the oldest old, elderly, and adult patients. Medicine (Baltimore) 2007;86:138–44. https://10.1097/SHK.0b013e318067da56.

8. van Hal SJ, Jensen SO, Vaska VL, Espedido BA, Paterson DL, Gosbell IB. Predictors of mortality in Staphylococcus aureus bacteremia. Clin Microbiol Rev 2012;25:362–86. https://10.1128/CMR.05022-11.

9. Hernández C, Fehér C, Soriano A, Marco F, Almela M, Cobos-Trigueros N, et al. Clinical characteristics and outcome of elderly patients with community-onset bacteremia. J Infect 2015;70:135–43. https://10.1016/j.jinf.2014.09.002.

10. Reunes S, Rombaut V, Vogelaers D, Brusselaers N, Lizy C, Cankurtaran M, et al. Risk factors and mortality for nosocomial bloodstream infections in elderly patients. Eur J Intern Med 2011;22:e39–44. https://10.1016/j.ejim.2011.02.004.

11. Wester AL, Dunlop O, Melby KK, Dahle UR, Wyller TB. Age-related differences in symptoms, diagnosis and prognosis of bacteremia. BMC Infect Dis 2013;13:346. https://10.1186/1471-2334-13-346.

12. Crane SJ, Uslan DZ, Baddour LM. Bloodstream infections in a geriatric cohort: a population-based study. Am J Med 2007;120:1078–83. https://10.1016/j.amjmed.2007.08.028.

13. Laupland KB, Pasquill K, Steele L, Parfitt EC. Burden of bloodstream infection in older persons: a population-based study. BMC Geriatr 2021;21:31. https://10.1186/s12877-020-01984-z.

14. Ouchi Y, Rakugi H, Arai H, Akishita M, Ito H, Toba K, et al. (JGLS) and Japan Geriatrics Society (JGS) on the definition and classification of the elderly. Geriatr Gerontol Int 2017;17:1045–7. https://10.1111/ggi.13118.

15. Pien BC, Sundaram P, Raoof N, Costa SF, Mirrett S, Woods CW, et al. The clinical and prognostic importance of positive blood cultures in adults. Am J Med 2010;123:819–28. https://10.1016/j.amjmed.2010.03.021.

16. Friedman ND, Kaye KS, Stout JE, McGarry SA, Trivette SL, Briggs JP, et al. Health care--associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections. Ann Intern Med 2002;137:791–7. https://10.7326/0003-4819-137-10-200211190-00007.

17. Weinstein MP, Towns ML, Quartey SM, Mirrett S, Reimer LG, Parmigiani G, et al. The clinical significance of positive blood cultures in the 1990s: a prospective comprehensive evaluation of the microbiology, epidemiology, and outcome of bacteremia and fungemia in adults. Clin Infect Dis 1997;24:584–602. https://10.1093/clind/24.4.584.

18. Weinstein MP, Reller LB, Murphy JR, Lichtenstein KA. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. I.

Laboratory and epidemiologic observations. Rev Infect Dis 1983;5:35–53. https://10.1093/clinids/5.1.35.

19. Doern GV, Carroll KC, Diekema DJ, Garey KW, Rupp ME, Weinstein MP, et al. Practical guidance for clinical microbiology laboratories: A comprehensive update on the problem of blood culture contamination and a discussion of methods for addressing the problem. Clin Microbiol Rev 2019;33:e00009-19. https://10.1128/CMR.00009-19.

20. Story-Roller E, Weinstein MP. Chlorhexidine versus tincture of iodine for Reduction of Blood Culture Contamination Rates: a Prospective Randomized Crossover Study. J Clin Microbiol 2016;54:3007–9. https://10.1128/JCM.01457-16.

21. Bassetti M, Peghin M, Trecarichi EM, Carnelutti A, Righi E, Del Giacomo P, et al. Characteristics of Staphylococcus aureus Bacteraemia and Predictors of Early and Late Mortality. PLoS One 2017; **12**: e0170236.

22. Lee CC, Lin WJ, Shih HI, Wu CJ, Chen PL, Lee HC, et al. Clinical significance of potential contaminants in blood cultures among patients in a medical center. J Microbiol Immunol Infect 2007;40:438–44.

23. Gavazzi G, Mallaret MR, Couturier P, Iffenecker A, Franco A. Bloodstream infection: differences between young-old, old, and old-old patients. J Am Geriatr Soc 2002;50:1667–73. https://10.1046/j.1532-5415.2002.50458.x.

24. Lee XJ, Stewardson AJ, Worth LJ, Graves N, Wozniak TM. Attributable length of stay, mortality risk, and costs of bacterial health care-associated infections in Australia: A retrospective case-cohort study. Clin Infect Dis 2021;72:e506–14. https://10.1093/cid/ciaa1228.

25. Tsuboi M, Hayakawa K, Mezaki K, Katanami Y, Yamamoto K, Kutsuna S, et al. Comparison of the epidemiology and microbiology of peripheral line- and central line-associated bloodstream infections. Am J Infect Control 2019;47:208–10. https://10.1016/j.ajic.2018.08.016.

26. Pujol M, Hornero A, Saballs M, Argerich MJ, Verdaguer R, Cisnal M, et al. Clinical epidemiology and outcomes of peripheral venous catheter-related bloodstream infections at a university-affiliated hospital. J Hosp Infect 2007;67:22–9. https://10.1016/j.jhin.2007.06.017.

27. Marcos M, Soriano A, Iñurrieta A, Martínez JA, Romero A, Cobos N, et al. Changing epidemiology of central venous catheter-related bloodstream infections: increasing prevalence of Gram-negative pathogens. J Antimicrob Chemother 2011;66:2119–25. https://10.1093/jac/dkr231.

28. Sato A, Nakamura I, Fujita H, Tsukimori A, Kobayashi T, Fukushima S, et al. Peripheral venous catheter-related bloodstream infection is associated with severe complications and potential death: a retrospective observational study. BMC Infect Dis 2017;17:434. https://10.1186/s12879-017-2536-0.

29. Sasaki T, Harada S, Yamamoto S, Ohkushi D, Hayama B, Takeda K, et al. Clinical characteristics of peripheral venous catheter-associated gram-negative bloodstream infection among patients with malignancy. PLOS ONE 2020;15:e0228396. https://10.1371/journal.pone.0228396.

30. Guembe M, Pérez-Granda MJ, Capdevila JA, Barberán J, Pinilla B, Martín-Rabadán P, et al. Nationwide study on peripheral-venous-catheter-associated-bloodstream infections in internal medicine departments. J Hosp Infect 2017;97:260–6. https://10.1016/j.jhin.2017.07.008.

31. Coello R, Charlett A, Ward V, Wilson J, Pearson A, Sedgwick J, et al. Device-related sources of bacteraemia in English hospitals--opportunities for the prevention of hospital-acquired bacteraemia. J Hosp Infect 2003;53:46–57. https://10.1053/jhin.2002.1349.

32. Mermel LA. Short-term peripheral venous catheter-related bloodstream infections: A systematic review. Clin Infect Dis 2017;65:1757–62. https://10.1093/cid/cix562.

33. Bai AD, Showler A, Burry L, Steinberg M, Ricciuto DR, Fernandes T, et al. Impact of infectious disease consultation on quality of care, mortality, and length of stay in Staphylococcus aureus bacteremia: results from a large multicenter cohort study. Clin Infect Dis 2015;60:1451–61. https://10.1093/cid/civ120.

34. Burnham JP, Olsen MA, Stwalley D, Kwon JH, Babcock HM, Kollef MH. Infectious diseases consultation reduces 30-day and 1-year all-cause mortality for multidrug-resistant organism infections. Open Forum Infect Dis 2018;5:ofy026. https://10.1093/ofid/ofy026.

35. Chiong F, Wasef MS, Liew KC, Cowan R, Tsai D, Lee YP, et al. The impact of infectious diseases consultation on the management and outcomes of Pseudomonas aeruginosa bacteraemia in

adults: a retrospective cohort study. BMC Infect Dis 2021;21:671. https://10.1186/s12879-021-06372-5.

36. Ishikane M, Hayakawa K, Kutsuna S, Takeshita N, Ohmagari N. The impact of infectious disease consultation in candidemia in a tertiary care hospital in Japan over 12 years. PLOS ONE 2019;14:e0215996. https://10.1371/journal.pone.0215996.

37. Kobayashi T, Marra AR, Schweizer ML, Ten Eyck P, Wu C, Alzunitan M, et al. Impact of infectious disease consultation in patients with candidemia: A retrospective study, systematic literature review, and meta-analysis. Open Forum Infect Dis 2020;7:ofaa270. https://10.1093/ofid/ofaa270.

38. Lee RA, Vo DT, Zurko JC, Griffin RL, Rodriguez JM, Camins BC. Infectious diseases consultation is associated with decreased mortality in enterococcal bloodstream infections. Open Forum Infect Dis 2020;7:ofaa064. https://10.1093/ofid/ofaa064.

39. Vogel M, Schmitz RP, Hagel S, Pletz MW, Gagelmann N, Scherag A, et al. Infectious disease consultation for Staphylococcus aureus bacteremia - A systematic review and meta-analysis. J Infect 2016;72:19–28. https://10.1016/j.jinf.2015.09.037.

40. Hounsom L, Grayson K, Melzer M. Mortality and associated risk factors in consecutive patients admitted to a UK NHS Trust with community acquired bacteraemia. Postgrad Med J 2011;87:757–62. https://10.1136/pgmj.2010.116616.

41. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83. https://10.1016/0021-9681(87)90171-8.

Figure legends

Figure 1. Flow chart of patients subdivided based on age

Table 1. Clinical characteristics of contamination and bacteremic episodes among each focus of bacteremia

	Total bacteremic	CLABSI	PVCR-BSI	UTI	Bone & Joint infections	IE	Intraabdominal infections	Lower respiratory tract infections	Skin & soft tissue infections	Other (central and vascular infections etc)
Patients, n=	1,211	159	96	289	23	19	277	74	59	215
Male	652 (53.8)	94 (59.1)	54 (56.3)	113 (39.1)	15 (65.2)	10 (52.6)	151 (54.5)	53 (71.6)	32 (54.2)	130 (60.5)
Median age (IQR)	79 (72-86)	76(70-83)	81.5 (72.25-87)	81 (75-87)	75 (72-86)	72 (69-80)	79 (72.5-86)	80 (73.75-85)	78 (72-87)	79 (72-85)
Pre-Old	397 (32.8)	76 (47.8)	25 (26)	65 (22.5)	11 (47.8)	13 (68.4)	89 (32.1)	19 (25.7)	21 (35.6)	78 (36.3)
Old	658 (54.3)	71 (44.7)	54 (56.3)	184 (63.7)	9 (39.1)	6 (31.6)	149 (53.8)	51 (68.9)	30 (50.8)	104 (48.4)
Super-Old	156 (12.9)	12 (7.5)	17 (17.7)	40 (13.8)	3 (13)	0 (0)	39 (14.1)	4 (5.4)	8 (13.6)	33 (15.3)
LOS before	1 (0-19)	28 (12-51)	15.5 (7-33.75)	0 (0-9)	0 (0-2)	0 (0-1)	0 (0-8.5)	0 (0-14.5)	0 (0-1)	0 (0-14)
＜Healthcare exposure＞										
CA	468 (38.6)	3 (1.9)	5 (5.2)	142 (49.1)	14 (60.9)	12 (63.2)	134 (48.4)	34 (45.9)	39 (66.1)	85 (39.5)
HCA	213 (17.6)	14 (8.8)	3 (3.1)	60 (20.8)	4 (17.4)	4 (21.1)	57 (20.6)	18 (24.3)	10 (16.9)	43 (20)

HO	530 (43.8)	142 (89.3)	88 (91.7)	87 (30.1)	5 (21.7)	3 (15.8)	86 (31)	22 (29.7)	10 (16.9)	87 (40.5)
< **Microorganism** >										
Polymicrobial	143 (11.8)	20 (12.6)	6 (6.3)	21 (7.3)	3 (13)	0 (0)	49 (17.7)	8 (10.8)	9 (15.3)	27 (12.6)
MRSA	41 (3.4)	13 (8.2)	6 (6.3)	1 (0.3)	2 (8.7)	0 (0)	1 (0.4)	2 (2.7)	4 (6.8)	12 (5.6)
MSSA	62 (5.1)	9 (5.7)	10 (10.4)	0 (0)	6 (26.1)	5 (26.3)	4 (1.4)	10 (13.5)	8 (13.6)	10 (4.7)
Coagulase-negative staphylococci	229 (18.9)	94 (59.1)	51 (53.1)	12 (4.2)	4 (17.4)	2 (10.5)	7 (2.5)	6 (8.1)	10 (16.9)	43 (20)
Enterococcus species	89 (7.3)	11 (6.9)	4 (4.2)	17 (5.9)	1 (4.3)	4 (21.1)	30 (10.8)	1 (1.4)	5 (8.5)	16 (7.4)
Streptococcus pneumoniae	14 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	12 (16.2)	0 (0)	2 (0.9)
GBS	24 (2.0)	0 (0)	0 (0)	1 (0.3)	3 (13)	1 (5.3)	1 (0.4)	2 (2.7)	6 (10.2)	10 (4.7)
GGS	20 (1.7)	0 (0)	0 (0)	0 (0)	1 (4.3)	0 (0)	2 (0.7)	0 (0)	13 (22)	4 (1.9)
Streptococcus species	96 (7.9)	0 (0)	0 (0)	3 (1)	3 (13)	6 (31.6)	13 (4.7)	18 (24.3)	18 (30.5)	35 (16.3)
Bacillus species	21 (1.7)	1 (0.6)	9 (9.4)	1 (0.3)	1 (4.3)	0 (0)	4 (1.4)	1 (1.4)	0 (0)	4 (1.9)
Enterobacteriales*	566 (46.7)	14 (8.8)	8 (8.3)	258 (89.3)	6 (26.1)	1 (5.3)	187 (67.5)	24 (32.4)	8 (13.6)	60 (27.9)
Escherichia	327 (27)	3 (1.9)	1 (1)	198	3 (13)	0 (0)	85 (30.7)	6 (8.1)	3 (5.1)	28 (13)

coli				(68.5)						
Klebsiella pneumoniae	123 (10.2)	3 (1.9)	1 (1)	31 (10.7)	1 (4.3)	0 (0)	62 (22.4)	14 (18.9)	0 (0)	11 (5.1)
Pseudomonas aeruginosa	44 (3.6)	5 (3.1)	4 (4.2)	9 (3.1)	0 (0)	0 (0)	7 (2.5)	8 (10.8)	3 (5.1)	8 (3.7)
Non-fermenter	58 (4.8)	5 (3.1)	7 (7.3)	9 (3.1)	0 (0)	0 (0)	12 (4.3)	10 (13.5)	2 (3.4)	13 (6)
Bacteroides species	31 (2.6)	1 (0.6)	0 (0)	0 (0)	0 (0)	0 (0)	24 (8.7)	0 (0)	0 (0)	6 (2.8)
Candida species	39 (3.2)	25 (15.7)	6 (6.3)	2 (0.7)	0 (0)	0 (0)	1 (0.4)	0 (0)	0 (0)	5 (2.3)
<ID consultation>										
ID consultation	383 (31.6)	66 8 (41.5)	56 (58.3)	62 (21.5)	18 (78.2	15 (78.9)	46 (16.6)	20 (27)	35 (59.3	65 (30.2)
< Outcome >										
Outcome (7 days after blood culture)	89 (7.3)	9 (5.7)	8 (8.3)	8 (2.8)	1 (4.5)	2 (10.5)	20 (7.3)	14 (19.2)	1 (1.7)	26 (12.2)
LOS after, excluding death	23 (14-46)	36 (20.75-66)	32.5 (15-53.75)	16 (13-28)	62.5 (25.25-90)	62 (49-78)	21 (11.25-41)	28 (16-60.25)	25 (15.5-42.75)	24.5 (14-46)

IQR, interquartile range; LOS before, length of stay before the onset of bacteremia; CA, community-acquired bloodstream infection; HCA, healthcare-associated bloodstream infection; HO, hospital oncet bloodstream infection; LOS after, length of stay after the onset of bacteremia; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; GBS, group B streptococcus; GGS, Group G streptococcus; CLABSI, central line-associated bloodstream infection; PVCR-BSI, short-term peripheral venous catheter-related bloodstream infection; UTI, urinary tract infection; IE, infectious endocarditis

* including *Escherichia coli* and *Klebsiella pneumoniae*

Table 2. General characteristics and cause of bacteremia by age groups

	Pre-Old	Old	Super-Old	P-value
Patients, n=	397	658	156	
Male	249 (62.7)	356 (54.1)	47 (30.1)	<.001
Median age (IQR)	70 (68-72)	82 (78-85)	93 (91-95)	
＜Healthcare exposure＞				
CA	147 (37)	258 (39.2)	63 (40.4)	0.696
HCA	56 (14.1)	117 (17.8)	40 (25.6)	0.006
HO	194 (48.9)	283 (43)	53 (34)	0.005
IV therapy, wound care, nursing care (in 30 days)	8 (2)	19 (2.9)	5 (3.2)	0.621
Attended a hospital, hemodialysis clinic, IV chemotherapy (in 30 days)	10 (2.5)	13 (2)	4 (2.6)	0.808
Was hospitalized in an acute care hospital (>2 days in 90 days)	118 (29.7)	176 (26.7)	31 (19.9)	0.063
Resided in a nursing home or LTCF	4 (1)	21 (3.2)	14 (9)	<.001
LOS before median, IQR	3 (0-21)	0.5 (0-20)	0 (0-20)	<.001
＜Comorbidities/immunosuppression＞				
DM	91 (22.9)	159 (24.2)	21 (13.5)	0.015
CKD	40 (10.1)	60 (9.1)	12 (7.7)	0.675

CHF	35 (8.8)	78 (11.9)	29 (18.6)	0.006
COPD	17 (4.3)	15 (2.3)	2 (1.3)	0.076
Hematological malignancy	27 (6.8)	19 (2.9)	2 (1.3)	0.001
Solid cancer	143 (36)	188 (28.6)	18 (11.5)	<.001
Corticosteroid	29 (7.3)	37 (5.6)	4 (2.6)	0.096
＜Focus of infections＞				
CLABSI	76 (19.1)	71 (10.8)	12 (7.7)	<.001
PVCR-BSI	25 (6.3)	54 (8.2)	17 (10.9)	0.183
UTI	65 (16.4)	184 (28)	40 (25.6)	<.001
Bone & Joint infections	11 (2.8)	9 (1.4)	3 (1.9)	0.27
IE	13 (3.3)	6 (0.9)	0 (0)	0.003
Intraabdominal infections	89 (22.4)	149 (22.6)	39 (25)	0.792
Lower respiratory tract infections	19 (4.8)	51 (7.8)	4 (2.6)	0.021
Skin & soft tissue infections	21 (5.3)	30 (4.6)	8 (5.1)	0.856
Other (central and vascular infections, etc.)	78 (19.6)	105 (16)	33 (21.2)	0.162
<ID consultation>	65-74	75-89	90	
ID consultation	151 (38)	189 (28.7)	43 (27.6)	0.003
＜Outcome＞				
Outcome (7 days after Blood Culture)	29 (7.4)	38 (5.8)	22 (14.2)	0.002
LOS after, excluding death	24 (14-46)	24 (14-	21 (13-42)	0.428

	47)

IQR, interquartile range; CA, community-acquired bloodstream infection; HCA, healthcare-associated bloodstream infection; HO, hospital oncet bloodstream infection; IV chemotherapy, intravenous therapy chemotherapy; LTCF, long-term care health facility; LOS before, length of stay before the onset of bacteremia; DM, diabetes mellitus; CKD, chronic kidney disease; CHF, chronic heart failure; COPD, chronic obstructive pulmonary disease; CLABSI, central line-associated bloodstream infection; PVCR-BSI, short-term peripheral venous catheter-related bloodstream infection; UTI, urinary tract infection; IE, infectious endocarditis; LOS after, length of stay after the onset of bacteremia

Table 3. Microorganisms based on the healthcare exposure

	CA	HCA	HO	P-value CA vs. HCA	P-value CA vs. HO	P-value HCA vs. HO
n=	468	213	530			
＜Microorganisms＞						
Polymicrobial	57 (12.2)	29 (13.6)	57 (10.8)	0.601	0.48	0.27
MRSA	6 (1.3)	6 (2.8)	29 (5.5)	0.137	<.001	0.122
MSSA	29 (6.2)	13 (6.1)	20 (3.8)	0.963	0.077	0.163
Coagulase-negative staphylococci	46 (9.8)	31 (14.6)	152 (28.7)	0.071	<.001	<.001
Enterococcus species	23 (4.9)	16 (7.5)	50 (9.4)	0.176	0.006	0.405
Streptococcus pneumoniae	12 (2.6)	2 (0.9)	0 (0)	0.135	<.001	0.025
GBS	15 (3.2)	3 (1.4)	6 (1.1)	0.175	0.023	0.502
GGS	13 (2.8)	6 (2.8)	1 (0.2)	0.977	0.001	0.003
Streptococcus species	64 (13.7)	17 (8)	15 (2.8)	0.033	<.001	0.002

Bacillus species	12 (2.6)	1 (0.5)	8 (1.5)	0.051	0.235	0.219
Enterobacteriales*	256 (54.7)	112 (52.6)	198 (37.4)	0.607	<.001	<.001
Escherichia coli	174 (37.2)	75 (35.2)	78 (14.7)	0.621	<.001	<.001
Klebsiella pneumoniae	45 (9.6)	26 (12.2)	52 (9.8)	0.305	0.917	0.335
Pseudomonas aeruginosa	6 (1.3)	13 (6.1)	25 (4.7)	<.001	0.002	0.438
Non-fermenter	11 (2.4)	16 (7.5)	31 (5.8)	0.001	0.006	0.4
Bacteroides species	10 (2.1)	9 (4.2)	12 (2.3)	0.125	0.891	0.145
Candida species	2 (0.4)	2 (0.9)	35 (6.6)	0.371	<.001	0.001

IQR, interquartile range; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *S. aureus*; GBS, group B streptococcus; GGS, group G streptococcus

* including *Escherichia coli* and *Klebsiella pneumoniae*

The Bonferroni-corrected P < 0.01671 was deemed to be statistically significant.

Table 4. Multivariable analysis of risk factors for 7-day mortality of bacteremia

Variable	aOR (95% CI)	P-value
Male	0.99 (0.63, 1.56)	0.97
Old	0.78 (0.47, 1.30)	0.34
Super-old	2.09 (1.13, 3.88)	0.019*
HCA	1.18 (0.60, 2.33)	0.638
HO	1.97 (1.20, 3.33)	0.008*

DM	0.54	(0.28, 1.04)	0.065
ID consultation	0.59	(0.35, 0.99)	0.047*

aOR, adjusted odds ratio; CI, confidence interval; HCA, healthcare-associated bloodstream infection; HO, hospital-onset bloodstream infection; DM, diabetes mellitus; ID consultation, infectious diseases consultation

Note. We used all listed variables in the table to conduct multivariable analysis of risk factors for 7-day mortality of bacteremia.

Figure. 1

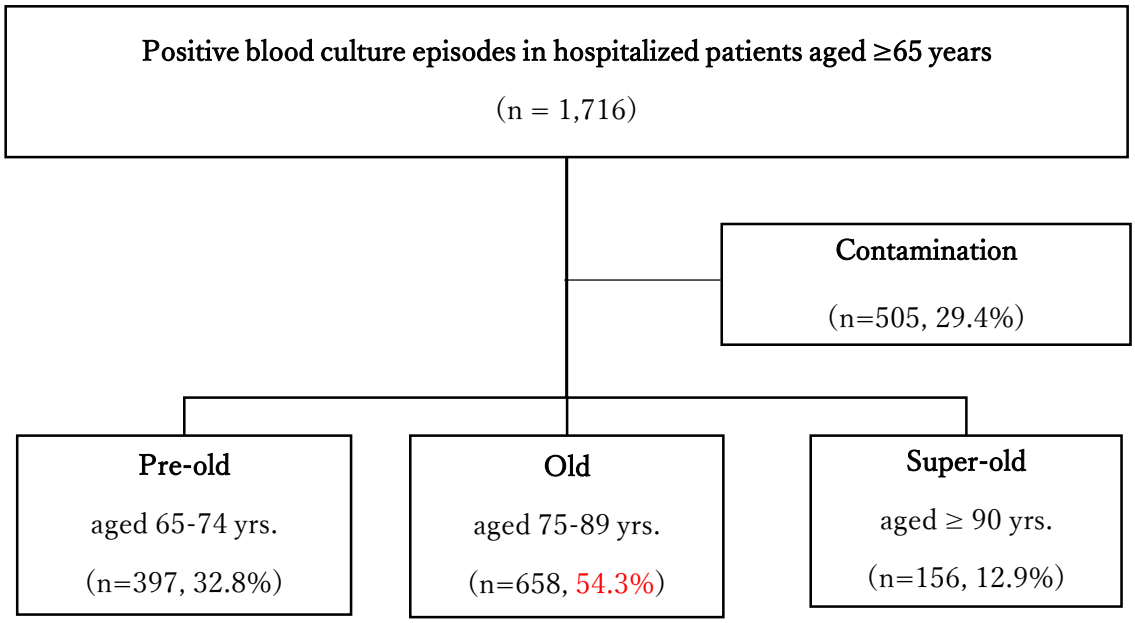
Positive blood culture episodes in hospitalized patients aged ≥65 years
(n = 1,716)
Contamination
(n=505, 29.4%)
Pre-old
aged 65-74 yrs.
(n=397, 32.8%)
Old
aged 75-89 yrs.
(n=658, 54.3%)
Super-old
aged ≥ 90 yrs.
(n=156, 12.9%)

Table S1: Causative microorganisms by age group

	Pre-Old	Old	Super-Old	P-value
Patients, n=	397	658	156	
＜Microorganism＞				
Polymicrobial	35 (8.8)	84 (12.8)	24 (15.4)	0.052
MRSA	12 (3)	22 (3.3)	7 (4.5)	0.69
MSSA	30 (7.6)	27 (4.1)	5 (3.2)	0.024
Coagulase-negative staphylococci	65 (16.4)	132 (20.1)	32 (20.5)	0.287
Enterococcus species	30 (7.6)	51 (7.8)	8 (5.1)	0.519
Streptococcus pneumoniae	3 (0.8)	11 (1.7)	0 (0)	0.141
GBS	10 (2.5)	11 (1.7)	3 (1.9)	0.632
GGS	8 (2)	8 (1.2)	4 (2.6)	0.388
Streptococcus species	31 (7.8)	52 (7.9)	13 (8.3)	0.979
Bacillus species	9 (2.3)	10 (1.5)	2 (1.3)	0.599
Enterobacteriales*	164 (41.3)	327 (49.7)	75 (48.1)	0.028
Escherichia coli	84 (21.2)	196 (29.8)	47 (30.1)	0.006
Klebsiella pneumoniae	30 (7.6)	73 (11.1)	20 (12.8)	0.091
Pseudomonas aeruginosa	15 (3.8)	24 (3.6)	5 (3.2)	0.948
Non-fermenter	18 (4.5)	33 (5)	7 (4.5)	0.922
Bacteroides species	11 (2.8)	17 (2.6)	3 (1.9)	0.85
Candida species	15 (3.8)	20 (3)	4 (2.6)	0.711

IQR, interquartile range; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *S. aureus*; GBS, group B streptococcus; GGS, group G streptococcus;

* including *Escherichia coli* and *Klebsiella pneumoniae*

Table S2: General characteristics and cause of bacteremia based on the Healthcare exposure

	CA	HCA	HO	P-value CA vs. HCA	P-value CA vs. HO	P-value HCA vs. HO
n=	468	213	530			
Male	232 (49.6)	112 (52.6)	308 (58.1)	0.466	0.007	0.169
median age (IQR)	79 (73-85)	82 (74-88)	78 (71-85)			
LOS before median (IQR)	0 (0-0)	0 (0-0)	24 (12-48)	0.291	<.001	<.001
＜Comorbidities/immunosuppression＞						
DM	126 (26.9)	44 (20.7)	101 (19.1)	0.08	0.003	0.619
CKD	30 (6.4)	33 (15.5)	49 (9.2)	<.001	0.098	0.014
CHF	50 (10.7)	29 (13.6)	63 (11.9)	0.268	0.549	0.518
COPD	13 (2.8)	9 (4.2)	12 (2.3)	0.322	0.604	0.145
Hematological malignancy	10 (2.1)	8 (3.8)	30 (5.7)	0.222	0.005	0.287
Solid cancer	85 (18.2)	69 (32.4)	195 (36.8)	<.001	<.001	0.257
Corticosteroid	13 (2.8)	12 (5.6)	45 (8.5)	0.066	<.001	0.186
＜Focus of bacteremia＞						
CLABSI	3 (0.6)	14 (6.6)	142 (26.8)	<.001	<.001	<.001
PVCR-BSI	5 (1.1)	3 (1.4)	88 (16.6)	0.481	<.001	<.001

UTI	142 (30.3)	60 (28.2)	87 (16.4)	0.565	<.001	<.001
Bone & Joint infection	14 (3)	4 (1.9)	5 (0.9)	0.401	0.018	0.239
IE	12 (2.6)	4 (1.9)	3 (0.6)	0.584	0.01	0.108
Intraabdomen infection	134 (28.6)	57 (26.8)	86 (16.2)	0.614	<.001	0.001
Lower respiratory tract infections	34 (7.3)	18 (8.5)	22 (4.2)	0.589	0.033	0.019
Skin & soft tissue infections	39 (8.3)	10 (4.7)	10 (1.9)	0.088	<.001	0.032
Other (central and vascular infections etc)	85 (18.2)	43 (20.2)	88 (16.6)	0.531	0.516	0.246
<ID consultation>						
ID consultation	123 (26.3)	58 (27.2)	202 (38.1)	0.769	<.001	0.005
＜Outcome＞						
Outcome (7 days after Blood Culture)	25 (5.4)	14 (6.6)	50 (9.5)	0.537	0.017	0.216
LOS after, excluding death	18 (12-41)	20 (13-36)	30 (16-57)	0.459	<.001	<.001

IQR, interquartile range; LOS before, length of stay before the onset of bacteremia; DM, diabetes mellitus; CKD, Chronic kidney disease; CHF, chronic heart failure; COPD, Chronic obstructive pulmonary disease; CLABSI, Central line-associated bloodstream infection; PVCR-BSI, Short-term peripheral venous catheter-related bloodstream infection; UTI, urinary tract infection; IE, Infectious endocarditis; LOS after, Length of stay after the onset of bacteremia; CA, Community-acquired bloodstream infection; HCA, Healthcare-associated bloodstream infection; HO, Hospital oncet bloodstream infection

The Bonferroni corrected $P < 0.01671$ was deemed to be statistically significant.