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Original Contribution

Incidence of bacteremia and antimicrobial resistance, and associated factors among patients transferred from long-term care hospital

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ABSTRACT

Objective: To evaluate the prevalence of bacteremia and antimicrobial resistance, and associated factors among infectious patients transferred from long-term care hospitals (LTCHs).
Methods: Consecutive adult patients who were transferred for suspected infection from affiliated LTCH's to study hospital emergency department (ED) over a 12 month period from January to December 2016 were included retrospectively. Patients with positive blood cultures (excluding contaminants as clinically determined) were defined as primary measure and subjected to further analysis according to antimicrobial resistance pattern. The latter was categorized into 4 subgroups based on groups of antimicrobial choices for empiric choices of suspected bloodstream infections. R-Group 0: bacteria susceptible to penicillin and amoxicillin; R-Group 1: bacteria resistant to penicillin/amoxicillin, first, second, or third generation cephalosporins. R-Group 2: ESBL-producing bacteria or bacteria resistant methicillin, fourth generation cephalosporin, or fluoroquinolone. R-Group 3: highly resistant pathogens including vancomycin resistant enterococci, carbapenem or colistin resistant Gram negatives. Blood culture isolate could therefore be included in >1 group.
Results: Among 756 patients who were transferred from LTCHs, we excluded 278 patients who were not suspicious of infection and 65 patients who were not checked blood culture at ED. In total, 422 patients were enrolled. The incidence of bacteremia was 20.4% (n = 86). The most frequent pathogen was *E. coli* (n = 25) followed by *S. aureus* (n = 10), *S. epidermidis* (n = 8), and *K. pneumonia* (n = 6). The incidences of the R-Group 1, 2, and 3 groups were 16.8% (n = 71), 14.4% (n = 61), and 1.4% (n = 6), respectively. Of the Gram-positive pathogens (n = 44), the R-Group 1, 2, and 3 groups were 84.1% (n = 37), 75.0% (n = 33), and 9.1% (n = 4), respectively. Of the Gram-negative pathogens (n = 46), the R-Group 1, 2, and 3 groups were 82.6% (n = 38), 69.6% (n = 32), and 4.3% (n = 2), respectively. Among tested variables, initial serum procalcitonin level was significantly associated with the presence of bacteremia (AOR 1.03, 95% confidence interval 1.00–1.05), R-Group 1 (1.04, 1.01–1.07) and the R-Group 2 (1.04, 1.00–1.06).
Conclusions: The prevalence of bloodstream infections in patients admitted from LTCH was high (20.4%) with majority of these infections from resistant bacteria. Procalcitonin levels were significantly higher in bacteremic patients with an increasing trend towards bacteria in the antimicrobial resistant groups.

1. Introduction

The increasing complexity in medical care in developed countries over the last few decades has improved longevity. However, an unintended consequence is people with chronic illnesses that are residing in long term care facilities (LTCF) or hospitals (LTCH). In Korea, LTCHs are distinguished from LTCF by increased staffing of both doctors and nurses up to 24 h a day. LTCH patients who are suspected of infection usually receive treatment that includes empirical antimicrobials during their initial illness courses. Patients who respond poorly to the treatment are frequently transferred to the emergency department (ED) of tertiary care or referral hospitals. Once these patients show

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improvement, they return to the LTCHs. Once this link between LTCHs and tertiary care hospital is established and repeated, it eventually becomes a cycle.

Thus, notable features should be present among infectious LTCH patients. First, considering the advanced age and high rate of comorbidities of LTCH patients, the incidence of bacteremia should be significant. Second, considering the cycle between LTCHs and tertiary care hospitals, the incidence of antimicrobial resistant microorganisms should be high. Since the tertiary care hospital is the primary location where antimicrobial resistance occurred [1,2], the antimicrobial resistance acquired at the tertiary care hospital can subsequently be spread into LTCHs. Previous studies have already supported these propositions [3-6]. Bacteremia itself and infection by antimicrobial resistant pathogens can cause significant mortality and morbidity, which makes substantial demands on health care resources [7-10]. Additionally, selection of appropriate empiric antimicrobials in patients from LCTH is clinically challenging due to a higher risk of colonization with multi-resistant bacteria. Therefore, the incidence of bacteremia, antimicrobial resistance and other associated factors are important areas of concern.

Korea, like many developed nations, is challenged with an increasing elderly population with a proportionate rise in people residing in LTCH. In fact, the need for long-term care beds in Korea has increased the most among all OECD countries since 2000 [11].

To our knowledge, there are no local studies on the prevalence of infections including bacteremias, and multi-resistant pathogens in residential care facilities. Furthermore, previous world-wide studies regarding this issue were reported decades ago [3-6]. Therefore, this issue is worthy of being revisited and would be helpful for determining treatment, especially in the choice of empirical antimicrobials. In the present study, the authors evaluated the incidence of bacteremia and antimicrobial resistance, and associated factors among infectious patients transferred from LTCHs.

2. Methods

2.1. Study design and setting

This was a single center, retrospective observational study conducted at a local university hospital, a 1200-bed urban, academic, tertiary-care center with the highest ED referral service in the region. All patients transferred from approximately 50 neighboring LTCHs between January 1st and December 31st, 2016 for suspected infection were screened. This study was approved by the local Institutional Review Board (IRB) and informed consent was waived for all subjects in this study. We referred to the Standards for Reporting of Diagnostic Accuracy Studies (STARD) recommendations when analyzing the results [12].

Blood cultures were obtained before starting antimicrobials at the study hospital ED. At least two sets of 10 mL blood samples were collected in two sets of bottles – BacT/ALERT® FA Plus (for detection of aerobic and facultative microorganisms) and BacT/ALERT® FN Plus (for detection of anaerobic microorganisms) – and were incubated under aerobic and anaerobic conditions in an automated blood culture analyzer (BacT/ALERT® 3D, BIOMERIEUX, Durham, NC, USA). The bacterial growth was automatically monitored by the instrument.

In the study hospital, department of laboratory medicine take authority with the results of blood culture. VITEK MS (bioMérieux, Marcy l'Etoile, France) which is an automated microbial identification system based on matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) is used. Isolated were inoculated into the cards and were run on the VITEK 2 (bioMérieux, Hazelwood, MO, USA) system to assess the antimicrobial susceptibility test. After the system report, faculties of department of laboratory medicine who are sub-special for infectious disease confirm the result of blood culture. They have authorization to view clinical data of a patient to assess the actual pathogenicity after all.

There is no specifically distinct policy for antimicrobial prescription for infectious patients in LTCHs or transferred patients from LTCHs to study hospital ED who are suspicious of infection in this area.

2.2. Selection of participants

Consecutive all adult (aged 18 or above) patients transferred from the LTCHs to the study hospital ED between January 1, 2016 and December 31, 2016 were screened for this study. To determine whether a patient was suspected of infection or not, the senior resident of emergency medicine reviewed the ICD 10 code diagnosis at discharge from ED of screened patients. The senior resident was blinded to the aim of the study and patients' final outcome. Those who were compatible with infection-related diagnosis were only eligible (Fig. 1). Patients who

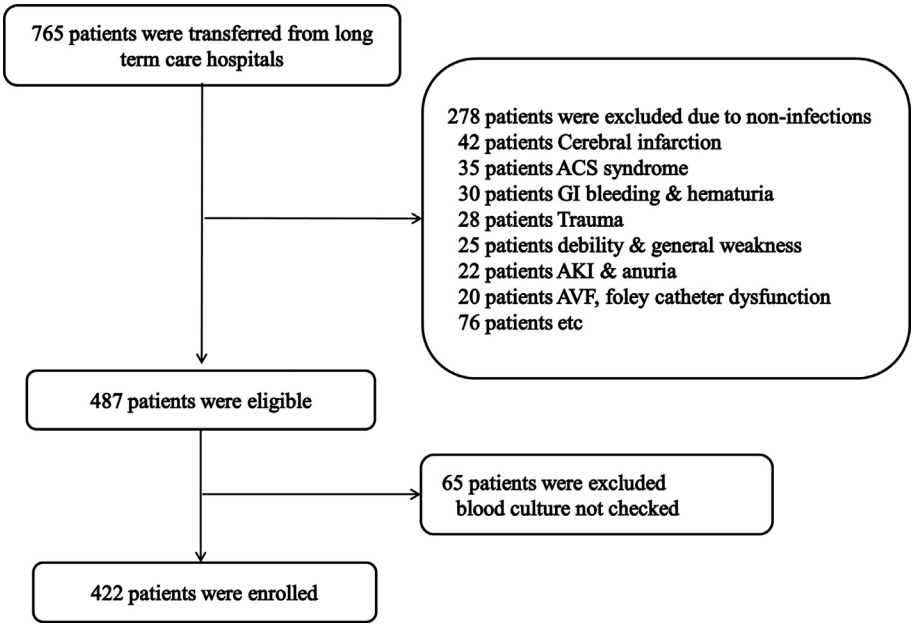


Fig. 1. STARD flow diagram.

Table 1
Characteristics of enrolled patients.

	All (N = 422)	Non-bacteremia group (N = 336)	Bacteremia group N (=86)	*p*-Value
Age, yr	77.5 ± 10.7	77.6 ± 11.1	77.5 ± 9.1	0.926
Age category				0.608
<65 yr	45 (10.7)	36 (10.7)	9 (10.5)	
65–74 yr	82 (19.4)	63 (18.8)	19 (22.1)	
75–84 yr	189 (44.8)	148 (44.1)	41 (47.7)	
≥85 yr	106 (25.1)	89 (26.5)	17 (19.8)	
Male sex, %	200 (47.4)	160 (47.6)	40 (46.5)	0.854
Hemiplegia, %	53 (12.6)	43 (12.8)	10 (11.6)	0.770
Sore	158 (37.4)	122 (36.3)	36 (41.9)	0.343
L-tube, %	45 (10.7)	32 (9.5)	13 (15.1)	0.134
Foley catheter, %	91 (21.6)	68 (20.2)	23 (26.7)	0.191
PEG, %	21 (5.0)	15 (4.5)	5 (5.8)	0.780
Tracheostomy, %	18 (4.3)	15 (4.4)	3 (3.5)	0.689
PICC, %	27 (6.4)	15 (4.5)	12 (13.9)	<0.01
AVF, %	19 (4.5)	16 (4.7)	3 (3.8)	0.776
PTGBD, %	2 (0.5)	1 (0.3)	1 (1.3)	0.366
ECOG				0.066
0	58 (13.7)	51(15.2)	7(8.1)	
1	110 (26.1)	92 (27.4)	18 (20.9)	
2	53 (12.6)	43 (12.8)	10 (11.6)	
3	79 (18.7)	63 (18.8)	16 (18.6)	
4	122 (28.9)	87 (25.9)	35 (40.7)	
Hypertension, %	219 (51.9)	172 (51.2)	47 (54.6)	0.567
Diabetes mellitus, %	114 (27.0)	94 (28.0)	20 (23.3)	0.379
Uncomplicated	48(11.4)	38(11.3)	10(11.6)	0.934
End-organ damage	66(15.6)	56(16.7)	10(11.6)	0.251
Chronic liver disease, %	12 (2.8)	9 (2.7)	3 (3.5)	0.716
Mild	1 (0.2)	1 (0.3)	0 (0.0)	0.612
Moderate to severe	11 (2.6)	8 (2.4)	3 (3.5)	0.565
Chronic kidney disease, %	45 (10.7)	40 (11.9)	5 (5.8)	0.119
Stroke, %	169 (40.1)	135 (40.2)	34 (39.5)	0.913
Dementia, %	167 (39.6)	127 (37.8)	40 (46.5)	0.140
Heart failure, %	45 (10.7)	33 (9.8)	12 (14.0)	0.268
Malignancy, %	78 (18.5)	61 (18.2)	17 (19.8)	0.731
Any leukemia or localized solid tumor	36 (8.5)	27 (8.0)	9 (10.5)	0.472
Metastatic solid tumor	42 (10.0)	34 (10.1)	8 (9.3)	0.821
Myocardial infarction, %	25 (5.9)	22 (6.6)	3 (3.5)	0.441
Chronic airway disease, %	49 (11.6)	41 (12.2)	8 (9.3)	0.454
Peptic ulcer disease, %	9 (2.1)	5 (1.5)	4 (4.7)	0.088
Charlson comorbidity	5.4 ± 1.9	5.4 ± 2.0	5.5 ± 1.9	0.97
Fever, %	225 (53.3)	171 (50.9)	54 (62.8)	0.048
Chill, %	71 (16.8)	48 (14.3)	23 (26.7)	<0.01
Respiratory symptoms, %	210 (49.8)	173 (51.5)	37 (43.0)	0.161
Abdominal symptoms, %	131 (31.0)	110 (32.7)	21 (24.4)	0.137
Urinary symptoms, %	40 (9.5)	26 (7.7)	14 (16.3)	0.016
Other symptoms, %	153 (36.3)	117 (34.8)	36 (41.9)	0.226
Previous antibiotics use, %	119 (28.2)	100 (29.2)	19 (23.8)	0.330
Sepsis				<0.01
None	179 (42.4)	157 (46.7)	22 (25.6)	
Sepsis without septic shock	193 (45.7)	154 (45.8)	39 (43.4)	
Septic shock	50 (11.9)	25 (7.4)	25 (29.1)	
SBP, mmHg (missing at 6)	120.5 ± 33.7	122.7 ± 31.4	112.7 ± 40.3	<0.01
DBP, mmHg (missing at 6)	69.3 ± 18.1	70.5 ± 16.8	64.5 ± 22.2	<0.01
PR, bpm (missing at 3)	92.1 ± 24.2	91.1 ± 22.3	96.0 ± 30.2	0.096
RR, bpm (missing at 3)	19.8 ± 3.1	19.9 ± 3.1	19.6 ± 3.1	0.439
Body Temperature, °C (missing at 2)	36.7 ± 2.7	36.7 ± 2.2	36.6 ± 4.2	0.752
SpO2, % (missing at 0)	95.6 ± 5.3	95.5 ± 5.7	96.3 ± 3.7	0.221
Mentality (missing at 0)				0.097
Alert. %	277 (65.6)	229 (68.2)	48 (55.8)	
Verbal. %	72 (17.1)	56 (16.7)	16 (18.6)	
Pain. %	62 (14.7)	44 (13.1)	18 (20.9)	
Unresponsive, %	11 (2.6)	7 (2.1)	4 (4.7)	
NEWS (missing at 0)	4.8 ± 3.8	4.6 ± 3.7	5.8 ± 4.1	<0.01
KTAS (missing at 0)				0.019
1	21 (5.0)	14 (4.2)	7 (8.1)	
2	74 (17.5)	51 (15.2)	23 (26.7)	
3	167 (39.6)	138 (41.1)	29 (33.7)	
4	148 (35.1)	121 (36.0)	27 (31.4)	
5	12 (2.8)	12 (3.6)	0 (0)	
White blood cell, 10^3/μL (missing at 3)	11.9 ± 6.6	11.7 ± 6.4	12.3 ± 7.4	0.502
SEG NEU, % (missing at 4)	79.2 ± 14.3	78.3 ± 13.8	82.9 ± 15.7	<0.01
Hematocrit, % (missing at 3)	32.1 ± 6.2	32.2 ± 6.3	31.6 ± 5.9	0.448
Hemoglobin, g/dL (missing at 3)	10.7 ± 2.2	10.8 ± 2.2	10.6 ± 2.1	0.652
Platelet, 10^3/μL (missing at 3)	236.4 ± 114.5	249.4 ± 108.9	186.1 ± 122.2	<0.01

Table 1 (*continued*)

	All (N = 422)	Non-bacteremia group (N = 336)	Bacteremia group N (=86)	*p*-Value
Sodium, mmol/L (missing at 2)	136.5 ± 6.1	136.5 ± 6.2	136.3 ± 6.1	0.709
Albumin, g/dL (missing at 2)	3.1 ± 0.6	3.2 ± 0.6	2.9 ± 0.7	<0.01
BUN, mg/dL (missing at 2)	26.5 ± 20.5	25.9 ± 21.2	29.1 ± 17.3	0.188
Creatinine, mg/dL (missing at 2)	1.3 ± 1.7	1.3 ± 1.9	1.3 ± 1.2	0.916
eGFR, mL/min/1.7 (missing at 2)	72.9 ± 37.2	75.1 ± 37.4	64.3 ± 35.4	0.016
Glucose, mg/dL (missing at 6)	144.3 ± 63.7	145.6 ± 63.6	139 ± 64.3	0.410
HbA1c, % (missing at 40)	5.8 ± 1.0	5.8 ± 0.9	5.6 ± 1.1	0.092
pH (missing at 6)	7.4 ± 0.1	7.4 ± 0.1	7.4 ± 0.1	0.674
HCO_3, mmol/L (missing at 6)	20.6 ± 4.5	21.0 ± 4.4	19.0 ± 4.7	<0.01
Lactate, mmol/L (missing at 7)	2.2 ± 2.6	2.0 ± 2.4	3.1 ± 3.0	<0.01
hs-CRP, mg/L (missing at 2)	98.0 ± 82.3	95.0 ± 78.9	109.7 ± 93.8	0.138
PCT, ng/mL (missing at 82)	6.7 ± 18.3	3.0 ± 9.6	19.4 ± 31.3	<0.01
UA category (missing at 81)				0.004
<5	127 (37.2)	106 (39.4)	21 (29.2)	
6–30	95 (27.9)	81 (30.1)	14 (19.4)	
>30	119 (34.9)	82 (30.5)	37 (51.4)	
ED LOS, h (missing at 0)	36.9 ± 36.1	36.8 ± 36.0	37. ± 36.6	0.947
Hospital LOS, day (missing at 0)	11.6 ± 14.7	11.4 ± 13.7	12.4 ± 18.7	0.592
ICU admission, % (missing at 0)	55 (13.0)	45 (13.4)	10 (11.6)	0.664
Ward admission, % (missing at 0)	231 (54.7)	181 (53.9)	50 (58.2)	0.478
Hospital death, % (missing at 0)	87 (20.6)	66 (19.6)	21 (24.1)	0.329

Abbreviations L-tube, Levin tube; PEG, percutaneous endoscopic gastrostomy; PICC, peripherally inserted central catheter; AVF, arteriovenous fistula; PTGBD, percutaneous transhepatic gallbladder drainage; ECOG, Eastern Cooperative Oncology Group; SBP, systolic blood pressure; DBP, diastolic blood pressure; PR, pulse pressure; RR, respiratory pressure; SpO_2, blood oxygen saturation; NEWS, national early warning score; KTAS, Korean triage and acuity scale; SEG NEU, segmented form neutrophil; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; HCO_3, bicarbonate; hs-CRP, high sensitive C-reactive protein; PCT, procalcitonin; UA, urine analysis; ED LOS, emergency department length of stay; ICU, intensive care unit.

did not have blood cultures taken in the ED were excluded. Before he reviewed the medical chart, he was trained to select patient who were compatible with infection based on ICD 10 code diagnosis and 20% of the randomly selected patients' data were reviewed by another author. In addition, patients who did not have blood cultures taken in the ED were excluded because we could not identify bacteremia.

2.3. Measurement and data collection

Data were collected from the patients' electronic charts using a structured form for data collection according to the guidelines recommended by Gilbert et al. [13]. The senior resident of emergency medicine reviewed and abstracted the data. Data included the following: age; sex; concurrent conditions (hemiplegia, sore, Levin tube in situ, Foley catheter in situ, percutaneous endoscopic gastrostomy (PEG) in situ; tracheostomy in situ, peripherally inserted central catheter (PICC) in situ, arteriovenous fistula (AVF) in situ, and percutaneous transhepatic gallbladder drainage (PTGBD) in situ; Eastern Cooperative Oncology Group (ECOG) scale; comorbidities [hypertension (HTN), diabetes mellitus (DM) – uncomplicated vs. end-organ damage, chronic liver disease (CLD) – mild vs. moderate to severe, chronic kidney disease (CKD), stroke, dementia, heart failure (HF), malignancy – any leukemia or localized solid tumor vs. metastatic solid tumor, myocardial infarction, chronic airway disease, and peptic ulcer disease]; Charlson comorbidity index; presentation symptoms (fever, chill, respiratory symptoms, abdominal symptoms, urinary symptoms, other symptoms); previous antimicrobial use; sepsis (none vs. sepsis without septic shock vs. septic shock); physiology at ED presentation [systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), respiratory rate (RR), body temperature, blood oxygen saturation(SpO_2)], mentality using Alert Verbal Pain Unresponsive (AVPU) scale, and national early warning score (NEWS); Korean triage and acuity scale (KTAS); initial laboratory findings of white blood cell (WBC) count, segmented neutrophil count, hematocrit (Hct), hemoglobin (Hb), platelet, sodium, albumin, blood urea nitrogen (BUN), creatinine, estimate glomerular filtration rate (eGFR), glucose, hemoglobin A1c (HbA1c), pH, bicarbonate (HCO_3), lactate, high sensitivity C-reactive protein (hs-CRP), procalcitonin (PCT); pyuria (<5 vs. 6–30 vs. >30); ED length of stay(LOS); hospital LOS; disposition [admission to the intensive care unit (ICU) or ward]; and, hospital death.

Comorbidity status was based on the physician's medical record. Most information were based on the guardian's statement. Sepsis and septic shock diagnosis is based on the recent international consensus (Sepsis-3) [14].

2.4. Study measures

The primary measure was patients with confirmed blood stream infection. Isolation of coagulase-negative *Staphylococcus*, *Corynebacterium*, *Propionbacterium* sp., *Bacillus* non-anthracis, or *Micrococcus* in a single blood culture was considered contaminant and therefore excluded from the case definition. However, single isolate of *S. epidermidis* among patients with prosthesis or pacemaker was not regarded as contamination. Additionally, we determined the proportion of bacteremias from antimicrobial-resistant bacteria according to a pragmatic antimicrobials classification. R-Group 0: bacteria susceptible to penicillin and amoxicillin; R-Group 1: bacteria resistant to penicillin/amoxicillin, first, second, or third generation cephalosporins (e.g. cefazolin, ceftriaxone, cefotaxime). R-Group 2: ESBL-producing bacteria or bacteria resistant methicillin, fourth generation cephalosporin (e.g. cefepime), or fluoroquinolone (e.g. ciprofloxacin). R-Group 3: highly resistant pathogens including vancomycin resistant enterococci, carbapenem (e.g. meropenem) or colistin resistant Gram negatives. A single patient could therefore be included in >1 group for analysis. For example, a patient with an ESBL producing *Klebsiella pneumoniae* bacteremia from an isolate which is also resistant to ciprofloxacin was included in both groups, R-Groups 1 and 2. A patient with pan-resistant *Pseudomonas* bacteremia was included in R-Groups 1, 2 and 3.

2.5. Analysis

All continuous data are presented as the mean and standard deviation (SD), and discrete data are presented as both the count and percentage. The results of logistic regression analyses are presented as the odds ratio with a 95% confidence interval. Statistical significance was defined as a two-sided $p < 0.05$.

Comparison of normally distributed data was performed using an independent sample *t*-test. For non-normally distributed data, comparisons were performed using the Mann-Whitney *U* test or the Kruskal-Wallis test. For categorical data, the Chi-square test was used. If necessary, the Chi-square test with a Fischer exact test for 2 × 2 tables was use. The results were considered significant at a threshold of $p < 0.05$ (two-tailed).

Associations between the presence of each measure (except R-group 0) and each potential variable were first quantified using univariate logistic regression analysis. Next, multivariable logistic regression analysis was performed for trend factors ($p < 0.05$) in the univariate analysis. Regression results are expressed as ORs with 95% confidence intervals (CI).

For the variable of interest, the area under the receiver operating characteristic (AUROC), sensitivity (SN), specificity (SP), positive likelihood ratio (+LR), negative likelihood ratio (−LR), positive predictive value (+PV), and negative predictive value (−PV) at various clinical cut-off points were examined.

For the missing information, discrete variables were treated as dummy variable and continuous variable were imputed as the mean value of each variable. Thus all of the subjects were included in the final multivariate analysis. A sensitivity analysis was conducted with the complete data to identify whether the creating dummy variable and imputation would affect the result.

All analyses were performed using STATA 11.1 (StataCorp LP, TX, USA) and SAS 9.1 (SAS Institute Inc., Cary, NC, USA).

3. Results

Four hundred and eighty-seven (63.7%) of 765 patients transferred from LTCH during the study period were suspected of having an infection. A total of 422 patients were enrolled in the study after exclusion of 65 patients who did not have 2 or more sets of blood cultures performed at ED (Fig. 1).

Table 1 showed the characteristics of the enrolled patients. Mean age was 77.5 ± 10.7 years, and males ware 200 of the 422 enrolled (47.4%). There were 53 (12.6%) patients with hemiplegia and 158 (37.4%) with sores. Regarding catheters or any tube in situ, a Foley catheter was the most common (n = 91, 21.6%) followed by L-tube (n = 45, 10.7%) and PICC (n = 27, 6.4%). HTN was the most frequent chronic disease (n = 219, 51.9%), followed by stroke (n = 169, 40.1%) and dementia (n = 167, 39.6%). Respiratory symptoms were the most frequent symptom (n = 210, 49.8%) followed by abdominal symptoms (n = 131, 31.0%) and urinary symptoms (n = 40, 9.5%). Fifty patients (11.9%) had septic shock and 193 patients (45.7%) had sepsis without septic shock. Fifty-five patients (13.0%) were admitted to the ICU and 231 patients (54.7%) were admitted to the ward. Hospital death occurred in 87 patients (20.6%). Most of the baseline characteristics and comorbidities were not significantly different between the bacteremia group and the non-bacteremia group. PICC in situ, fever/chill, urinary symptoms, and septic shock were more frequent in the bacteremia group. SBP and DBP were lower and NEWS and acuity as measured by KTAS was higher in the bacteremia group. Segmented neutrophil count, procalcitonin, and lactate level were higher, and platelet count, albumin, and bicarbonate level were lower, in the bacteremia group. Pyuria was more frequent in the bacteremia group. There were no significant difference in ED LOS, hospital LOS, ICU or ward admission, and hospital death between the two groups.

Table 2 shows the microbiological characteristics of 86 patients with bacteremia. Among Gram (+) bacteria, *S. aureus* was the most frequently isolated ($n = 10$) followed by *S. epidermidis* ($n = 8$), *S. capitalis* ($n = 5$) and *S. hominis* ($N = 5$). Forty-four Gram (+) bacteria were identified. Among Gram (−) bacteria, E.coli was the most frequently isolated ($n = 25$), and followed by *K. pneumonia* ($n = 6$). Forty-six Gram (−) bacteria were identified. Thus, when considering duplicate cases ($n = 4$), the actual number of bacteremic patients was 86. Majority were classified as R-Group 1 (37/44 (84.1%) in Gram (+), 38/46 (82.6%) in Gram (−), and 75/90 (83.3%)). There was a significant

Table 2
Microbiology of 90 bacterial isolates from 86 patients.

Species	Bacteria classification		Total	R-Group 0	R-Group1	R-Group 2	R-Group 3
Gram (+)	*Staphylococcus aureus*		10[a]		10	7[a]	
	Coagulase negative *Staph.*	*epidermidis*	8[b,c]	1	7[c]	6[b]	
		capitis	5[c]		5[c]	5	
		hominis	5		5	5	
		auricularis	2		1	1	
		caprae	1		1	1	
		wnarneri	1		1	1	
	Coagulase negative *Staphylococcus*		2		1	1	
	Enterococcus	*faecalis*	3		3	3	3
		faeceum	2		2	2	1
	Streptococcus	*constellatus*	1	1			
		gordonii	1	1			
		mitis	1	1			
		pneumoniae	1		1	1	
		viridans group	1	1			
Total			44	5	37	33	4
Gram (−)	*Escherichia coli*		25[a,b,d]	2	23	22[a,b,d]	
	Klebsiella pneumoniae		6[d]		2	2[d]	
	Proteus mirabilis		2		2	2	1
	Serratia marcescens		2		2		
	Stenotrophomonas maltophilia		2				
	Acinetobacter baumannii complex		1		1	1	
	Alcaligeness faecalis spp		1		1	1	
	Burkholderia cepacia		1		1		
	Elizabethkingia meningoseptica		1		1	1	1
	Enterobacter agrogenes		1		1		
	Hemophilus influenza		1		1	1	
	Morganella morganni		1		1		
	Providencia stuartii		1		1	1	
	Psedomonas aeruginosa		1		1	1	
Total			46	2	38	32	

a, b, c, and d denote that bacteria of same alphabet was isolated from the same patient.

overlap in bacterial species belonging to both R-Groups 1 and 2 with *E. coli* (22 of 23 isolates) due to quinolone resistance, and *Staphylococci* (22 of 26 isolates) due to both quinolone and methicillin resistance. Seven out of 10 *S. aureus* isolates (70%) were methicillin resistant (MRSA). There were only 6 bacteria in R-Group 3 including 3 vancomycin resistant *Enterococci*.

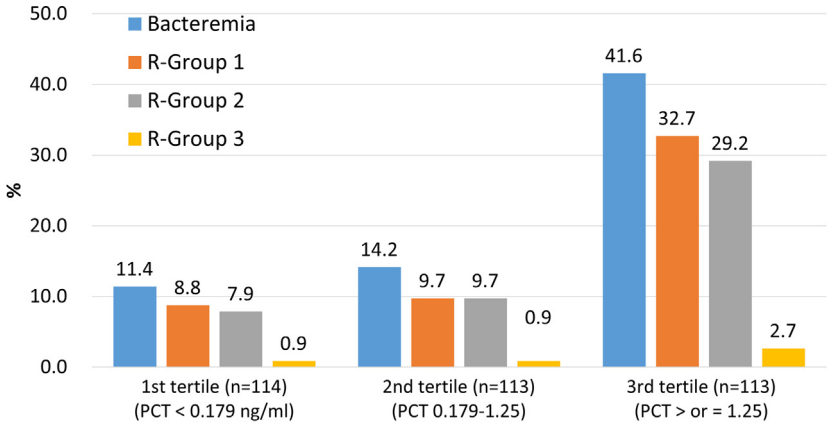
Results of multivariable logistic regression analysis are shown in Table 3. Although various potential factors showing a trend in univariable logistic analysis were tested, only procalcitonin level showed a significant relationship with bacteremia (AOR 1.03, 95% CI 1.00–1.05, $p = 0.010$), while the PICC and septic shock showed a trend (AOR 2.63, 95% CI 0.98–7.04, $p = 0.055$, and AOR 2.93, 95% CI 0.85–10.14, $p = 0.089$, respectively). Procalcitonin level and abdominal symptoms were significantly associated with R-Group1 (AOR 1.03, 95% CI 1.01–1.05, $p = 0.005$, and AOR 0.40, 95% CI 0.18–0.90, $p = 0.026$, respectively). Procalcitonin level and chill were significantly associated with R-Group 2 (AOR 1.02, 95% CI 1.00–1.04, $p = 0.030$, and AOR 2.33, 95% CI 1.01–5.35, $p = 0.047$, respectively). Septic shock showed a trend for R-Group 2 (AOR 3.64, 95% CI 0.93–14.29, $p = 0.064$). Urinary symptoms showed a significant association with R-Group (AOR 8.37, 95% CI 1.53–45.74, $p = 0.014$). We confirmed that the results were not much different after a sensitivity analysis which was conducted with the complete data to identify whether the creating dummy variable and imputation would affect the result (Appendix Table 1).

Next, we evaluated the characteristics of procalcitonin level further. Fig. 2 shows the distribution of each measure according to the tertile of procalcitonin level. Incidence of bacteremia was 11.4% at 1st tertile, 14.2% at 2nd tertile, and 41.6% at 3rd tertile. Incidence of R1 group was 8.8% at 1st tertile, 9.7% at 2nd tertile, and 32.7% at 3rd tertile. Incidence of R2 group was 7.9% at 1st tertile, 9.7% at 2nd tertile, and 29.2% at 3rd tertile. Incidence of R3 group was 0.9% at 1st tertile, 0.9% at 2nd tertile, and 2.7% at 3rd tertile. The AUROC was determined to be 0.729 (95% CI 0.657–0.800) for the presence of bacteremia, 0.733 (95% CI 0.653–0.812) for R-Group 1, 0.728 (95% CI 0.646–0.809) for R-Group 2, and 0.691 (95% CI 0.351–1.000) for R-Group 3. Table 4 showed the diagnostic performance of procalcitonin at the various clinical cut-off values for each outcome. +LRs for each outcome at procalcitonin levels of 5.0 and 10.0 were approximately 3.0 and 5.0, respectively. Multivariable logistic regression analyses using procalcitonin as tertile were shown in Appendix Tables 2 and 3.

Table 3
Logistic regression analysis for antibiotic resistance (422 patients were entered into analysis).

Variable	Bacteremia (n = 86) AOR	*p*-Value	R-Group 1 (n = 71) AOR	*p*-Value	R-Group 2 (n = 61) AOR	*p*-Value	R-Group 3 (n = 6) AOR	*p*-Value
L-tube, %			2.26 (0.79–6.47)	0.128	1.91 (0.66–5.57)	0.233		
PICC, %	2.63 (0.98–7.04)	0.055	1.48 (0.45–4.83)	0.520	1.48 (0.44–4.94)	0.526		
ECOG								
0	Reference		Reference		Reference			
1	1.11 (0.38–3.23)	0.844	0.86 (0.27–2.72)	0.792	0.61 (0.18–2.06)	0.429		
2	1.39 (0.42–4.51)	0.585	1.14 (0.31–4.16)	0.842	0.90 (0.23–3.45)	0.872		
3	1.52 (0.51–4.54)	0.452	0.97 (0.29–3.28)	0.966	0.78 (0.23–2.71)	0.701		
4	1.97 (0.70–5.89)	0.201	1.68 (0.54–5.21)	0.370	1.43 (0.46–4.47)	0.537		
Fever, %	1.21 (0.57–2.54)	0.623						
Chill, %	1.66 (0.75–3.71)	0.213	2.02 (0.92–4.46)	0.081	2.33 (1.01–5.35)	0.047		
Abdominal symptoms, %			0.40 (0.18–0.90)	0.026				
Urinary symptoms, %	1.42 (0.55–3.66)	0.470	1.34 (0.51–3.55)	0.553	2.16 (0.82–5.75)	0.121	8.37 (1.53–45.74)	0.014
Other symptoms, %					0.99 (0.47–2.07)	0.983		
Sepsis								
None	Reference		Reference		Reference			
Sepsis without septic shock	1.18 (0.57–2.48)	0.655	0.68 (0.30–1.55)	0.361	0.94 (0.39–2.24)	0.889		
Septic shock	2.93 (0.85–10.14)	0.089	2.38 (0.65–8.68)	0.188	3.64 (0.93–14.29)	0.064		
Systolic blood pressure, mm Hg	1.00 (0.99–1.01)	0.701	1.00 (0.98–1.01)	0.647	1.00 (0.98–1.01)	0.639		
Body temperature, °C	1.18 (0.78–1.79)	0.438						
Mentality								
Alert, %	Reference		Reference		Reference			
Verbal, %	1.12 (0.45–2.81)	0.804	1.79 (0.66–4.83)	0.253	2.39 (0.85–6.72)	0.098		
Pain, %	1.04 (0.34–3.18)	0.944	1.28 (0.36–4.52)	0.704	1.50 (0.40–5.56)	0.547		
Unresponsive, %	2.18 (0.31–15.61)	0.437	3.05 (0.26–36.23)	0.377	3.43 (0.29–40.13)	0.326		
NEWS	0.98 (0.87–1.09)	0.694	0.95 (0.83–1.08)	0.429	0.93 (0.81–1.07)	0.294		
KTAS								
1			2.12 (0.28–15.85)	0.464	1.27 (0.17–9.32)	0.817		
2			1.15 (0.17–8.00)	0.887	0.80 (0.12–5.47)	0.818		
3			2.01 (0.31–12.81)	0.461	1.69 (0.27–10.28)	0.571		
4 & 5			Reference		Reference			
SEG NEU %	1.01 (0.99–1.03)	0.317						
Platelet, 10^3/uL	1.00 (0.99–1.00)	0.021	1.00 (1.00–1.00)	0.291	1.00 (0.99–1.00)	0.142		
Albumin, g/dl	0.61 (0.37–1.03)	0.065	0.67 (0.38–1.18)	0.169	0.69 (0.38–1.24)	0.213		
eGFR, mL/min/1.7	1.00 (0.99–1.01)	0.825	0.99 (0.98–1.00)	0.186	1.00 (0.99–1.01)	0.642		
HCO_3, mmol/L	0.94 (0.87–1.03)	0.179	0.95 (0.86–1.04)	0.237	0.94 (0.86–1.03)	0.216		
Lactate, mmol/L	0.99 (0.85–1.16)	0.921	0.92 (0.78–1.09)	0.336	0.91 (0.76–1.08)	0.279		
PCT, ng/mL	1.03 (1.01–1.05)	0.010	1.03 (1.01–1.05)	0.005	1.02 (1.00–1.04)	0.030	1.02 (0.99–1.04)	0.193
UA category								
<5	Reference		Reference		Reference			
6–30	0.66 (0.29–1.54)	0.341	0.77 (0.31–1.96)	0.590	0.78 (0.28–2.19)	0.639		
>30	1.27 (0.58–2.73)	0.548	1.25 (0.54–2.88)	0.604	1.67 (0.68–4.10)	0.264		
99	1.12 (0.47–2.65)	0.804	0.69 (0.24–1.97)	0.487	0.89 (0.30–2.64)	0.833		

Abbreviations AOR, adjusted odd ratio; L-tube, Levin tube; PICC, peripherally inserted central catheter; ECOG, Eastern Cooperative Oncology Group; SBP, systolic blood pressure; DBP, diastolic blood pressure; PR, pulse pressure; RR, respiratory pressure; SpO_2, blood oxygen saturation; NEWS, national early warning score; KTAS, Korean triage and acuity scale; SEG NEU, segmented form neutrophil; eGFR, estimated glomerular filtration rate; HCO_3, bicarbonate; PCT, procalcitonin; UA, urine analysis; ED LOS, emergency department length of stay; ICU, intensive care unit.



Unadjusted odd ratio (95% confidential interval, p-value)			
Variable	1st tertile	2nd tertile	3rd tertile
Bacteremia	Reference	1.28 (0.59-2.80, p=0.535)	5.53 (2.78-11.01, p<0.001)
R-Group 1	Reference	1.12 (0.46-2.76, p=0.802)	5.06 (2.37-10.81, p<0.001)
R-Group 2	Reference	1.26 (0.50-3.16, p=0.625)	4.81 (2.18-1063, p<0.001)
R-Group 3	Reference	1.01 (0.06-16.33, p=0.995)	3.08 (0.32-30.08, p=0.333)

Fig. 2. Distribution of each outcome according to the procalcitonin level tertile.

The incidence of bacteremia of the top five LTCHs was compared. There were no significant differences in the incidence of bacteremia between the top five LTCHs. (Table 5).

4. Discussion

Our study provides insight about the prevalence of bacteremia, antimicrobial resistance and characteristics of bacteremic patients transferred from LTCHs with suspected infection. Key findings from our cohort can be summarized as follows. Firstly, 1 in 5 patients with suspected infection were bacteremic. Secondly, multi-resistant pathogens causing blood stream infections were very common, mostly ESBL producing Enterobacteriaceae, MRSA and fluoroquinolone resistant Gram negatives. Thirdly, an elevated procalcitonin level was a significant factor for the presence of bacteremia, as well as R-Group 1 and 2. These findings potentially have important implications in deciding empiric antibiotic treatment in this selected high risk patient group.

Table 4
Diagnostic performance of procalcitonin for each outcome.

Procalcitonin level	Outcome	SN (95% CI)	SP (95% CI)	+LR (95% CI)	−LR (95% CI)	+PV (95% CI)	−PV (95% CI)
>0.507 ng/mL	G1	72.4 (60.9–82.0)	59.5 (53.3–65.4)	1.8 (1.5–2.2)	0.5 (0.3–0.7)	34.0 (26.7–41.8)	88.2 (82.5–92.5)
	G2	74.1 (61.0–84.7)	57.8 (51.8–63.6)	1.8 (1.4–2.2)	0.5 (0.3–0.7)	26.5 (19.9–34.0)	91.6 (86.5–95.2)
	G3	73.6 (59.7–84.7)	57.1 (51.2–62.9)	1.7 (1.4–2.1)	0.5 (0.3–0.7)	24.1 (17.7–31.4)	92.1 (87.2–95.6)
	G4	80.0 (28.4–99.5)	52.8 (47.3–58.3)	1.7 (1.1–2.7)	0.4 (0.1–2.2)	2.5 (0.7–6.2)	99.4 (96.9–100.0)
>1 ng/mL	G1	64.5 (52.7–75.1)	72.4 (66.5–77.7)	2.3 (1.8–3.0)	0.5 (0.4–0.7)	40.2 (31.4–49.4)	87.6 (82.5–91.7)
	G2	65.5 (51.9–77.5)	70.2 (64.5–75.5)	2.2 (1.7–2.8)	0.5 (0.3–0.7)	31.1 (23.1–40.2)	90.8 (86.2–94.3)
	G3	64.2 (49.8–76.9)	69.3 (63.6–74.6)	2.1 (1.6–2.7)	0.5 (0.4–0.7)	27.9 (20.1–36.7)	91.3 (86.7–94.7)
	G4	60.0 (14.7–94.7)	64.5 (59.1–69.6)	1.7 (0.8–3.5)	0.6 (0.2–1.8)	2.5 (0.5–7.0)	99.1 (96.7–99.9)
>4.62 ng/mL	G1	46.1 (34.5–57.9)	87.5 (82.9–91.2)	3.7 (2.5–5.5)	0.6 (0.5–0.8)	51.5 (39.0–63.8)	84.9 (80.1–89.0)
	G2	46.6 (33.3–60.1)	85.5 (80.8–89.4)	3.2 (2.2–4.8)	0.6 (0.5–0.8)	39.7 (28.0–52.3)	88.6 (84.2–92.1)
	G3	45.3 (31.6–59.6)	84.7 (80.0–88.6)	3.0 (2.0–4.4)	0.7 (0.5–0.8)	35.3 (24.1–47.8)	89.3 (85.0–92.7)
	G4	60.0 (14.7–94.7)	80.6 (75.9–84.7)	3.1 (1.5–6.5)	0.5 (0.2–1.5)	4.4 (0.9–12.4)	99.3 (97.4–99.9)
>10.15 ng/mL	G1	35.5 (24.9–47.3)	93.2 (89.4–95.9)	5.2 (3.0–8.9)	0.7 (0.6–0.8)	60.0 (44.3–74.3)	83.4 (78.6–87.5)
	G2	39.7 (27.0–53.4)	92.2 (88.4–95.0)	5.1 (3.0–8.5)	0.7 (0.5–0.8)	51.1 (35.8–66.3)	88.1 (83.9–91.6)
	G3	39.6 (26.5–54.0)	91.6 (87.8–94.6)	4.7 (2.9–7.9)	0.7 (0.5–0.8)	46.7 (31.7–62.1)	89.2 (85.0–92.5)
	G4	60.0 (14.7–94.7)	87.5 (83.4–90.8)	4.8 (2.2–10.3)	0.5 (0.2–1.3)	6.7 (1.4–18.3)	99.3 (97.6–99.9)

Table 5
Comparison of bacteremia and antibiotic resistance between the top 5 long term care hospitals.

Hospital	N	G1	G2	G3	G4
A	44	10 (22.7%)	8 (18.2%)	8 (18.2%)	
B	26	7 (26.9%)	6 (23.1%)	5 (19.2%)	
C	24	5 (20.8%)	5 (20.8%)	4 (16.7%)	1 (4.2%)
D	21	2 (9.5%)	1 (4.8%)	1 (4.8%)	1 (4.8%)
E	18	3 (16.7%)	2 (11.1%)	2 (11.1%)	
p-Value		0.657	0.444	0.614	0.313

Long-term care (LTC) is defined as a variety of medical and non-medical services for people with a chronic illness or disability who cannot care for themselves for long periods of time [15]. Therefore, LTC services encompass non-skilled care, such as daily activity assistance including dressing, feeding, or bathing, as well as medical care up to prolonged mechanical ventilator support. Provision of LTC can happen at home, in the community, in assisted living facilities, in nursing homes, in long-term care facilities, or in long-term care hospitals. In Korea, LTCH are distinguished from others because they are staffed with doctors and nurses 24 h a day.

In the United States, chronic, critically ill patients accounted for a substantial number of ICU resources, up to 40% [16]. Since 1983, this burden has been relieved substantially by the rapid growth of LTCHs [17]. Many patients requiring prolonged mechanical ventilation after acute illness have been adequately managed in LTCHs. However, in Korea, illnesses do not appear to be as severe as they are in the US. In the present study, approximately 40% of patients were ECOG grade 0–2, meaning that they were ambulatory and capable of all self-care at a minimum [18,19]. Co-morbidity status appears to be the reason for the admission to the LTHC in this cohort, considering that their Charlson comorbidity point was relatively high (5 point) [20,21].

Acute exacerbation of a previous disease or a newly occurring illness can be managed initially in the LTCHs in Korea because they are staffed by doctors and nurses, and empirical antimicrobials could be started for the infectious patients. However, if the patients were insufficiently responsive, they were transferred to the referral center. After the patient's condition is stabilized, almost of all return to the LTCHs where they were admitted previously. Since the pre-conditions were not changed, though they were discharged from the referral center, they were still intrinsically vulnerable to acute exacerbation of a previous disease or a newly occurred illness. Therefore, the cycle between LTCHs and the referral center is initiated. The transfer of infected or colonized patients with antimicrobial resistant pathogens from acute-care facilities to LTCHs is already a well-known phenomenon [22].

Therefore, notable and unique features can be found in LTCH patients related to infection: 1) elderly with many comorbidities, 2) excessive exposure to broad-spectrum antimicrobials, and 3) likely to be exposed to patients infected with antimicrobial resistant pathogens or to surroundings colonized with antimicrobial resistant pathogens. As a consequence, it can be expected that the rate of infective complications would be high and in particular, bacteremia caused by antibiotic-resistant bacteria.

Studies that evaluated the incidence of bacteremia among LTC facilities were reported decades ago. In 1994, Nicolle et al. reported a rate of bacteremia of 6.3% (29/459) in long-term care facilities over an 8-year periods [4]. In 1992, Murder et al. reported a bacteremia rate of 0.20 to 0.36 cases/1000 patient-days from 1985 to 1989 [5]. In 1984, Setia et al. reported a bacteremia rate of 0.3 cases/1000 patient-days [6]. In the present study, we revisit the incidence of bacteremia among LTCH patients and a higher rate of bacteremia, approximately 20%, was found. This finding suggests that the severity of infectious patients in LTCHs has been worsening.

The issue of infection by antimicrobial resistant bacteria among LTC facilities came to light more recently. Regers et al. reported the annual incidence of antimicrobial-resistant infection was 12.7 cases per 1000 long-term residents in California, Florida, Michigan, New York and Texas [23]. Recent studies focus on the rate of colonization of various antimicrobial resistant bacteria, such as VRE [24], CRE [25], or multi-drug resistant strains [26]. In the present study, approximately 70% of isolates were either ESBL-producing or fluoroquinolone resistant Gram negatives, or MRSA (R-Group 2). Prevalence of VRE, and carbapenem and colistin resistant Gram negatives was relatively low (6.7%). This finding has important implications for an emergency or acute physician in terms of appropriate empiric antibiotic choices, especially considering a significantly higher rate of septic shock (29.1%) and trend towards high in-hospital mortality (24.1%) in the bacteremic group.

The findings of the present study have a notable clinical implication. Approximately 70% of the bacteria isolated from blood cultures were from the R-Group 2, meaning they were ESBL-producing or resistant to methicillin or fluoroquinolone. Therefore, if the result of the Gram stain was reported, physicians should carefully consider changing the empirical antimicrobials to vancomycin or carbapenem. Of course, antimicrobial change should be based on multifaceted and meticulous consideration, not a single factor. Additionally, misuse of vancomycin or carbapenem can lead to the emergence of resistant bacteria, such as VRE or CRE. However, from Gram stain to bacterial identification and antimicrobial susceptibility testing generally takes 24–48 h, and this would be the “golden time” for patients in critical condition [27]. Physicians should consider these two conflicting possibilities carefully in their practice. The other point is that the higher the initial procalcitonin level is, the higher the incidence of bacteremia is, as well as that of R-Group 2.

Additionally, among potential factors including well-used inflammatory markers, only procalcitonin was associated exclusively with bacteremia and R-Group 1 and 2. Several studies have examined the performance of procalcitonin as a biomarker for predicting bacteremia [28,29]. In addition with those studies, we noted a trend towards relatively higher procalcitonin levels in R-Groups 1 and 2. Physicians should carefully choose the empirical antimicrobials for patients transferred from LTCHs whose procalcitonin level is high.

Our study had several notable limitations. First, this is a retrospective chart review single center study. Incidence of bacteremia and antimicrobial resistant bacteria would differ between regions and nations according to baseline characteristics, co-morbidities, and national systems. Local epidemiological surveillance systems would also differ. Therefore, multicenter and multi-national studies are warranted. Second, there would be unknown confounding factors, although we collected extensive variables. We did not collect data on the type of empirical antimicrobials started before transfer or the patients' colonization history. Factors related to baseline characteristics or co-morbidities were found not to be associated with outcomes in the present study, raising concerns with other potential pre-morbid conditions of LTCH patients. Notably, the rate of antimicrobial use in LTCHs before transfer was 28.2% in the present study, seemingly a low rate, considering that LTCHs were staffed with doctors. Missed documentation or mal- or under-medical practice was possible causes. Third, the number of R-Group 3 was very small, thus the statistical results regarding the R-Group 3 should be interpreted carefully.

In conclusion, the prevalence of bloodstream infections in patients admitted from LTCH was high (20.4%) with majority of these infections from resistant bacteria. Procalcitonin levels were significantly higher in bacteremic patients with an increasing trend towards bacteria in the antimicrobial resistant groups.

Declaration of interest

The authors report no conflicts of interest. The authors are responsible for the content and writing of the paper.

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Conflict of interests

None.

Funding and support

None.

Authors' contributions

S.K. and S.J. designed this study. S.K. collected the data. S.J. supervised the overall data collection process, had full access to all data in the study, and takes responsibility for the integrity of the data. B.P. conducted the data analysis. S.J. and H.B. wrote the initial draft of the article. All authors provided substantial review and feedback on the final version of the article. S.J. takes responsibility for the paper as a whole.

All authors have read and approved the submitted manuscript. This manuscript has not been submitted or published elsewhere in whole or in part, except as an abstract (if relevant).

Appendix Table 1
Logistic regression analysis for antibiotic resistance with complete data.

Variable	Bacteremia (*n* = 61) AOR (available at 285)	*p*-value	R-Group 1 (*n* = 49) AOR (available at 276)	*p*-value	R-Group 2 (n = 45) AOR (available at 276)	*p*-value	R-Group 3 (n = 6) AOR (available at 422)	*p*-value
L-tube, %			4.22 (1.24–14.42)	0.022	3.97 (1.11–14.22)	0.034		
PICC, %	3.54 (0.95–13.15)	0.060	1.50 (0.34–6.62)	0.595	1.23 (0.25–5.93)	0.799		
ECOG								
0	Reference		Reference		Reference			
1	1.13 (0.43–4.05)	0.869	1.39 (0.28–6.79)	0.687	0.82 (0.16–4.32)	0.816		
2	2.46 (0.56–10.88)	0.236	2.80 (0.52–15.20)	0.232	1.96 (0.33–11.74)	0.461		
3	2.48 (0.60–10.22)	0.208	2.21 (0.42–11.49)	0.346	1.85 (0.34–10.07)	0.477		
4	2.12 (0.54–8.35)	0.281	2.43 (0.50–11.89)	0.272	1.95 (0.40–9.49)	0.407		
Fever, %	1.39 (0.58–3.34)	0.465						
Chill, %	1.89 (0.77–4.65)	0.163	1.77 (0.68–4.57)	0.236	2.17 (0.78–6.09)	0.140		
Abdominal symptoms, %			0.32 (0.11–0.90)	0.031				
Urinary symptoms, %	1.04 (0.33–3. 27)	0.953	0.96 (0.29–3.19)	0.951	1.71 (0.49–6.01)	0.404	10.24 (2.00–52.57)	0.005
Other symptoms, %					1.02 (0.38–2.74)	0.972		
Sepsis								
None	Reference		Reference		Reference			
Sepsis without septic shock	1.25 (0.49–3.22)	0.636	0.84 (0.30–2.30)	0.731	1.44 (0.46–4.47)	0.531		
Septic shock	2.08 (0.46–9.47)	0.344	2.06 (0.43–9.86)	0.366	3.87 (0.67–22.20)	0.129		
Systolic blood pressure, mm Hg	1.00 (0.99–1.01)	0.955	0.99 (0.98–1.01)	0.421	0.99 (0.97–1.01)	0.210		
Pulse rate, bpm			1.01 (0.99–1.03)	0.439	1.01 (0.99–1.03)	0.339		
Mentality								
Alert, %	Reference		Reference		Reference			
Verbal, %	1.14 (0.37–3.50)	0.824	1.59 (0.48–5.25)	0.446	2.53 (0.69–9.26)	0.160		
Pain, %	1.83 (0.44–7.54)	0.404	1.36 (0.28–6.59)	0.702	2.02 (0.36–11.26)	0.422		
Unresponsive, %	0.99 (0.08–11.58)	0.992	0.85 (0.05–14.88)	0.914	0.73 (0.04–12.63)	0.828		
NEWS	0.92 (0.79–1.08)	0.305	0.87 (0.73–1.04)	0.126	0.81 (0.66–1.00)	0.047		
KTAS								
1			1.05 (0.09–12.49)	0.968	0.53 (0.41–6.79)	0.625		
2			0.87 (0.08–9.26)	0.907	0.55 (0.05–6.05)	0.625		
3			1.32 (0.14–12.25)	0.809	1.05 (0.12–9.45)	0.968		
4 & 5			Reference		Reference			
SEG NEU %	1.02 (0.99–1.05)	0.228						
Platelet, $10^3/\mu L$	1.00 (0.99–1.00)	0.045	1.00 (0.99–1.00)	0.062	0.99 (0.99–1.00)	0.009		
Albumin, g/dL	0.55 (0.28–1.07)	0.079	0.79 (0.39–1.62)	0.527	0.87 (0.40–1.85)	0.711		
eGFR, mL/min/1.7	1.00 (0.99–1.01)	0.746	0.99 (0.98–1.01)	0.384	1.00 (0.99–1.01)	0.992		
HCO_3, mmol/L	0.91 (0.82–1.02)	0.093	0.93 (0.83–1.04)	0.206	0.91 (0.80–1.03)	0.116		
Lactate, mmol/L	0.97 (0.80–1.17)	0.742	0.95 (0.77–1.15)	0.593	0.92 (0.74–1.14)	0.456		
PCT, ng/mL	1.03 (1.01–1.05)	0.014	1.03 (1.01–1.06)	0.003	1.02 (1.00–1.04)	0.035		
UA category								
<5	Reference		Reference		Reference			
6–30	0.43 (0.16–1.18)	0.101	0.72 (0.24–2.16)	0.556	0.63 (0.18–2.25)	0.476		
>30	1.24 (0.53–2.90)	0.625	1.28 (0.49–3.33)	0.612	1.71 (0.60–4.93)	0.317		

Abbreviations AOR, Adjusted odd ratio; L-tube, Levin tube; PICC, peripherally inserted central catheter; ECOG, Eastern Cooperative Oncology Group; SBP, systolic blood pressure; DBP, diastolic blood pressure; PR, pulse pressure; RR, respiratory pressure; SpO_2, blood oxygen saturation; NEWS, national early warning score; KTAS, Korean triage and acuity scale; SEG NEU, segmented form neutrophil; eGFR, estimated glomerular filtration rate; HCO_3, bicarbonate; PCT, procalcitonin; UA, urine analysis; ED LOS, emergency department length of stay; ICU, intensive care unit.

Appendix Table 2
Logistic regression analysis for antibiotic resistance using procalcitonin as tertile (422 patients were entered into analysis).

Variable	Bacteremia (n = 86) AOR	*p*-value	R-Group 1 (n = 71) AOR	*p*-value	R-Group 2 (n = 61) AOR	*p*-value	R-Group 3 (n = 6) AOR	*p*-value
L-tube, %			2.34 (0.80–6.86)	0.120	1.98 (0.67–5.88)	0.217		
PICC, %	2.99 (1.06–8.43)	0.038	1.58 (0.48–5.17)	0.452	1.65 (0.50–5.50)	0.415		
ECOG								

Appendix Table 2 (*continued*)

Variable	Bacteremia (n = 86) AOR	*p*-value	R-Group 1 (n = 71) AOR	*p*-value	R-Group 2 (n = 61) AOR	*p*-value	R-Group 3 (n = 6) AOR	*p*-value
0	Reference		Reference		Reference			
1	0.95 (0.33–2.74)	0.929	0.73 (0.23–2.28)	0.587	0.57 (0.17–1.91)	0.366		
2	1.12 (0.34–3.65)	0.850	0.89 (0.24–3.26)	0.864	0.77 (0.20–2.97)	0.702		
3	1.24 (0.41–3.74)	0.700	0.79 (0.23–2.65)	0.697	0.71 (0.20–2.46)	0.586		
4	1.64 (0.64–4.19)	0.291	1.50 (0.49–4.58)	0.474	1.37 (0.44–4.26)	0.582		
Fever, %	1.12 (0.52–2.41)	0.767						
Chill, %	1.65 (0.72–3.78)	0.235	1.89 (0.85–4.21)	0.121	2.21 (0.95–5.14)	0.067		
Abdominal symptoms, %			0.45 (0.21–0.98)	0.044				
Urinary symptoms, %	1.64 (0.64–4.19)	0.305	1.69 (0.65–4.37)	0.279	2.48 (0.94–6.49)	0.065	10.24 (2.00–52.67)	0.005
Other symptoms, %					1.03 (0.49–2.17)	0.945		
Sepsis								
None	Reference		Reference		Reference			
Sepsis without septic shock	1.07 (0.51–2.25)	0.860	0.62 (0.27–1.41)	0.255	0.85 (0.36–2.03)	0.719		
Septic shock	2.18 (0.63–7.58)	0.220	1.74 (0.48–6.33)	0.402	2.78 (0.71–10.79)	0.140		
Systolic blood pressure, mm Hg	1.00 (0.99–1.01)	0.666	1.00 (0.98–1.01)	0.590	1.00 (0.98–1.01)	0.511		
Body temperature, °C	1.18 (0.77–1.82)	0.444						
Mentality								
Alert, %	Reference		Reference		Reference			
Verbal, %	1.04 (0.40–2.67)	0.937	1.74 (0.64–4.77)	0.279	2.29 (0.82–6.44)	0.116		
Pain, %	1.05 (0.33–3.27)	0.937	1.34 (0.38–4.69)	0.649	1.48 (0.40–5.45)	0.557		
Unresponsive, %	2.59 (0.27–24.67)	0.407	3.86 (0.34–44.19)	0.277	4.02 (0.36–45.60)	0.261		
NEWS	0.97 (0.86–1.09)	0.626	0.95 (0.83–1.08)	0.437	0.93 (0.81–1.07)	0.308		
KTAS								
1	1.03 (0.16–6.61)	0.977	1.68 (0.26–10.87)	0.588	1.07 (0.16–7.07)	0.946		
2	0.79 (0.13–4.68)	0.795	0.89 (0.15–5.42)	0.903	0.66 (0.11–4.06)	0.650		
3	1.54 (0.28–8.51)	0.621	1.79 (0.32–10.08)	0.507	1.55 (0.28–8.56)	0.616		
4 & 5	Reference		Reference		Reference			
SEG NEU %	1.01 (0.99–1.03)	0.351						
Platelet, 10^3/μL	1.00 (0.99–1.00)	0.020	1.00 (0.99–1.00)	0.197	1.00 (0.99–1.00)	0.087		
Albumin, g/dL	0.58 (0.34–0.99)	0.044	0.68 (0.38–1.19)	0.178	0.70 (0.39–1.26)	0.232		
eGFR, mL/min/1.7	1.00 (0.99–1.01)	0.996	0.99 (0.98–1.00)	0.274	1.00 (0.99–1.01)	0.750		
HCO_3, mmol/L	0.95 (0.87–1.04)	0.250	0.95 (0.86–1.04)	0.259	0.94 (0.86–1.04)	0.211		
Lactate, mmol/L	1.03 (0.88–1.20)	0.718	0.96 (0.82–1.13)	0.620	0.93 (0.79–1.11)	0.424		
PCT, ng/mL								
1st tertile	Reference		Reference		Reference			
2nd tertile	1.17 (0.56–2.43)	0.672	1.75 (0.76–4.01)	0.187	1.75 (0.73–4.15)	0.207		
3rd tertile	3.45 (1.36–8.76)	0.009	4.48 (1.63–12.29)	0.004	2.97 (1.03–8.56)	0.043		
UA category								
<5	Reference		Reference		Reference			
6–30	0.65 (0.27–1.54)	0.325	0.70 (0.27–1.79)	0.455	0.73 (0.26–2.05)	0.552		
>30	1.27 (0.58–2.79)	0.546	1.25 (0.54–2.90)	0.610	1.67 (0.68–4.12)	0.264		
99	1.25 (0.52–2.99)	0.622	0.79 (0.28–2.23)	0.651	0.97 (0.33–2.86)	0.951		

Abbreviations AOR, Adjusted odd ratio; L-tube, Levin tube; PICC, peripherally inserted central catheter; ECOG, Eastern Cooperative Oncology Group; SBP, systolic blood pressure; DBP, diastolic blood pressure; PR, pulse pressure; RR, respiratory pressure; SpO_2, blood oxygen saturation; NEWS, national early warning score; KTAS, Korean triage and acuity scale; SEG NEU, segmented form neutrophil; eGFR, estimated glomerular filtration rate; HCO_3, bicarbonate; PCT, procalcitonin; UA, urine analysis; ED LOS, emergency department length of stay; ICU, intensive care unit.

Appendix Table 3
Logistic regression analysis for antibiotic resistance using procalcitonin as tertile with complete data.

Variable	Bacteremia (n = 61) AOR (available at 285)	*p*-Value	R-Group 1 (n = 49) AOR (available at 276)	*p*-Value	R-Group 2 (n = 45) AOR (available at 276)	*p*-Value	R-Group 3 (n = 6) AOR (available at 422)	*p*-Value
L-tube, %			4.08 (1.17–14.15)	0.027	3.78 (1.05–13.65)	0.042		
PICC, %	4.49 (1.15–17.63)	0.031	1.88 (0.42–8.42)	0.409	1.60 (0.34–7.61)	0.553		
ECOG								
0	Reference		Reference		Reference			
1	1.28 (0.33–5.03)	0.724	1.55 (0.34–7.02)	0.571	0.91 (0.18–4.59)	0.907		
2	2.53 (0.58–11.09)	0.218	2.70 (0.53–13.91)	0.234	1.88 (0.32–10.98)	0.483		
3	2.53 (0.62–10.29)	0.196	2.06 (0.42–10.07)	0.374	1.69 (0.32–8.94)	0.539		
4	2.24 (0.59–8.57)	0.237	2.50 (0.56–11.25)	0.231	2.03 (0.43–9.52)	0.367		
Fever, %	1.39 (0.58–3.34)	0.462						
Chill, %	1.79 (0.73–4.37)	0.203	1.64 (0.63–4.25)	0.309	2.05 (0.73–5.74)	0.171		
Abdominal symptoms, %			0.40 (0.15–1.03)	0.057				
Urinary symptoms, %	1.19 (0.39–3.64)	0.761	1.21 (0.38–3.90)	0.747	1.86 (0.54–6.38)	0.327	10.24 (2.00–52.57)	0.005
Other symptoms, %					1.04 (0.38–2.82)	0.944		
Sepsis								
None	Reference		Reference		Reference			

(continued on next page)

Appendix Table 3 (*continued*)

Variable	Bacteremia (n = 61) AOR (available at 285)	*p*-Value	R-Group 1 (n = 49) AOR (available at 276)	*p*-Value	R-Group 2 (n = 45) AOR (available at 276)	*p*-Value	R-Group 3 (n = 6) AOR (available at 422)	*p*-Value
Sepsis without septic shock	1.35 (0.51–3.53)	0.544	0.87 (0.31–2.41)	0.784	1.42 (0.46–4.42)	0.546		
Septic shock	1.84 (0.41–8.19)	0.422	1.42 (0.31–6.57)	0.653	2.71 (0.49–14.94)	0.251		
Systolic blood pressure, mm Hg	1.00 (0.99–1.01)	0.955	0.99 (0.98–1.01)	0.475	0.99 (0.97–1.01)	0.212		
Pulse rate, bpm			1.01 (0.99–1.03)	0.352	1.01 (0.99–1.03)	0.275		
Mentality								
Alert, %	Reference		Reference		Reference			
Verbal, %	1.02 (0.33–3.20)	0.967	1.46 (0.43–4.94)	0.545	2.40 (0.66–8.82)	0.185		
Pain, %	1.87 (0.46–7.59)	0.383	1.35 (0.29–6.41)	0.703	1.97 (0.37–10.64)	0.430		
Unresponsive, %	1.51 (0.14–15.79)	0.731	0.98 (0.06–15.54)	0.990	0.79 (0.05–13.10)	0.868		
NEWS	0.93 (0.80–1.07)	0.300	0.87 (0.73–1.03)	0.100	0.81 (0.67–0.99)	0.041		
KTAS								
1			0.49 (0.05–4.68)	0.537	0.33 (0.03–3.78)	0.370		
2			0.34 (0.04–2.95)	0.329	0.29 (0.03–2.91)	0.293		
3			0.78 (0.11–5.85)	0.813	0.74 (0.09–5.97)	0.777		
4 & 5			Reference		Reference			
SEG NEU %	1.02 (0.99–1.05)	0.322						
Platelet, $10^3/\mu L$	1.00 (0.99–1.00)	0.023	0.99 (0.99–1.00)	0.015	0.99 (0.99–1.00)	0.003		
Albumin, g/dL	0.56 (0.28–1.10)	0.090	0.81 (0.40–1.67)	0.572	0.87 (0.41–1.88)	0.728		
eGFR, mL/min/1.7	1.00 (0.99–1.01)	0.992	1.00 (0.98–1.01)	0.574	1.00 (0.99–1.02)	0.905		
HCO_3, mmol/L	0.92 (0.83–1.03)	0.154	0.94 (0.84–1.05)	0.291	0.12 (0.81–1.03)	0.138		
Lactate, mmol/L	1.02 (0.85–1.23)	0.828	1.01 (0.83–1.22)	0.931	0.97 (0.79–1.19)	0.755		
PCT, ng/mL								
1st tertile	Reference		Reference		Reference			
2nd tertile	0.84 (0.28–2.55)	0.762	0.64 (0.20–2.08)	0.461	0.70 (0.19–2.44)	0.553		
3rd tertile	2.36 (0.78–7.12)	0.127	2.49 (0.83–7.47)	0.103	1.58 (0.48–5.26)	0.457		
UA category								
<5	Reference		Reference		Reference			
6–30	0.45 (0.17–1.23)	0.121	0.81 (0.26–2.46)	0.705	0.71 (0.20–2.54)	0.598		
>30	1.39 (0.60–3.23)	0.446	1.47 (0.56–3.84)	0.429	1.95 (0.68–5.57)	0.214		

Abbreviations AOR, adjusted odd ratio; L-tube, Levin tube; PICC, peripherally inserted central catheter; ECOG, Eastern Cooperative Oncology Group; SBP, systolic blood pressure; DBP, diastolic blood pressure; PR, pulse pressure; RR, respiratory pressure; SpO_2, blood oxygen saturation; NEWS, national early warning score; KTAS, Korean triage and acuity scale; SEG NEU, segmented form neutrophil; eGFR, estimated glomerular filtration rate; HCO_3, bicarbonate; PCT, procalcitonin; UA, urine analysis; ED LOS, emergency department length of stay; ICU, intensive care unit.

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