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Predictive factors of true bacteremia and the clinical utility of blood cultures as a prognostic tool in patients with community-onset pneumonia

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Abstract

Although blood cultures (BCs) are an important component of diagnostic practice for antibiotic management in patients with pneumonia, several studies have questioned whether they should be performed. The objective of this study was to evaluate the predictive factors of bacteremia and the role of BCs in patients with community-onset pneumonia (community-acquired pneumonia and healthcare-associated pneumonia).

This study was retrospectively conducted in patients with community-onset pneumonia who were hospitalized at Jeju National University Hospital between January 2012 and December 2014. A true bacteremia (TB) group and a contaminants or negative bacteremia (CNB) group were classified according to the bacterial growth on the BC media and were investigated for the clinical relevance of the BCs.

We enrolled 785 patients; the TB group and the CNB group contained 36 patients (4.5%) and 749 (95.4%) patients, respectively. Only 10 patients (1.2%) required a change in antibiotic therapy based on the BC results (3 patients with an escalation, 7 with a de-escalation). There was no significant difference between the community-acquired pneumonia and the healthcare-associated pneumonia groups with regard to the rate of antibiotic change due to the BC results (1.1% vs 1.4%; $P = 0.751$). Chronic liver disease (odds ratio [OR] 2.973, 95% confidence interval [CI] 1.099–8.037), a confusion, urea, respiratory rate, blood pressure, age ≥65 (CURB-65) score of 4 to 5 points (OR 3.484, 95% CI 1.304–9.307), and Pneumonia Severity Index (PSI) class V (OR 2.405, 95% CI 1.007–5.743) were independently associated with TB. In patients with PSI class V and a CURB-65 score of 4 to 5 points, the TB group tended to show a higher inhospital mortality rate than the CNB group (50.0% vs 29.4%; $P = 0.060$, 60.0% vs 42.5%; $P = 0.480$). The areas under the curve for PSI score and CURB-65 score for predicting TB revealed an increased tendency compared with that of C-reactive protein (0.72, 95% CI 0.630–0.809; and 0.72, 95% CI 0.622–0.819 vs 0.629, 95% CI 0.522–0.735, respectively).

It seemed reasonable to selectively conduct BC in patients hospitalized with severe community-onset pneumonia based upon its low overall positive rate, its effects on antimicrobial modification, and the associations of TB with the severity indices of pneumonia.

Abbreviations: ARP = antibiotic-resistant pathogens, AUC = area under the curve, BC = blood culture, CAP = community-acquired pneumonia, CI = confidence interval, CNB = contaminants or negative bacteremia, CO = community onset, CRP = C-reactive protein, CURB-65 = confusion, urea, respiratory rate, blood pressure, age ≥65, HCAP = healthcare-associated pneumonia, MDR = multidrug-resistant, PSI = Pneumonia Severity Index, TB = true bacteremia.

Keywords: bacteremia, health care, microbiology, pneumonia

1. Introduction

Microbiological studies in the management of pneumonia include bacterial cultures of clinical specimens, such as sputum, pleural effusion, and blood.[1] It has been widely debated as to when blood cultures (BCs) should be ordered in patients with pneumonia. In community-acquired pneumonia (CAP), the yield of BCs has been reported to be as low as 5% to 14%.[2–6] Positive BC results have not been associated with better outcomes in some studies.[3,7] False-positive results could even lead to prolonged hospital stays, higher costs, or the overuse of antimicrobial agents.[4,8] However, BCs offer information regarding the need for escalation or de-escalation of antibiotics. De-escalation can, in special cases, decrease the development of resistance and adverse effects due to antibiotics or medical costs.

There is a distinction among the different guidelines in terms of performing BCs in patients with CAP. The American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) in 2007 stated that BCs should be performed selectively.[1] British Thoracic Society (BTS) guidelines also recommended that BCs should be ordered in patients with moderate or severe CAP, but can be omitted in CAP patients with lower severity and no comorbidity.[9] On the contrary, the recent guidelines from the European Respiratory Society and the European Society of Clinical Microbiology and Infectious Diseases (ERS/ECCMID)

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state that BCs should be performed in all patients admitted with CAP.[10]

In 2005, the ATS/IDSA introduced the concept of healthcare-associated pneumonia (HCAP) as a type of community-onset (CO) pneumonia.[11] HCAP comprises a proportion of 17.3% to 73.7% of CO pneumonia.[12–19] And, compared with CAP, HCAP is known to be associated with higher rates of multidrug-resistant (MDR) pathogens which require broad-spectrum antimicrobial therapy or modification of an initial therapy.[11,20] However, studies about the clinical usefulness of BCs in patients with HCAP are very scarce.

Therefore, we aimed to examine the clinical usefulness of BCs in patients with CO pneumonia, including CAP and HCAP, and to investigate the predictive factors of bacteremia.

2. Methods

2.1. Study population and design

This retrospective observational study was performed at Jeju National University Hospital (a 600-bed, university-affiliated hospital in Jeju, South Korea). Adult patients (≥18 years) who were hospitalized due to CAP or HCAP from January 2012 through December 2014 were investigated. We reviewed their medical records and collected data. According to the US Centers for Disease Control and Prevention Criteria, the BC results were classified as positive, contaminated, or negative.[21] Based upon clinical relevance, we divided the participants into 2 groups: a true bacteremia (TB) group and a contaminants/negative bacteremia (CNB) group. Since contaminants do not generally have effects on patients' clinical outcomes, we decided to combine contaminants group with negative bacteremia group along with referring to previous studies.[22–24] We basically conducted statistical analysis based on 2 groups: TB group versus CNB group.

Clinical manifestations, underlying diseases, severity of the pneumonia, and the clinical outcomes were compared between the 2 groups. The study protocol was approved by the Ethical Review Committee of Jeju National University Hospital (approval number: 2015–11–011).

2.2. Definition

Pneumonia was defined as the presence of a new infiltrate on chest radiography and at least 1 of the following: fever (≥38.0°C) or hypothermia (<35.0°C); new-onset cough; pleuritic chest pain; dyspnea; or altered breath sounds on auscultation. HCAP was defined according to ATS/IDSA guidelines.[11] CAP was defined as a diagnosis of pneumonia in patients who did not meet any of the criteria for HCAP. The patients whose pneumonia developed after being hospitalized for >72 hours or who were readmitted due to pneumonia within 10 days of leaving the hospital or being transferred from other hospitals after a hospitalization lasting longer than >48 hours were excluded.

Changes in antibiotic regimens were classified as escalation, de-escalation, or no change after drug susceptibility tests (DSTs) were complete. When a new therapy was initiated to cover a broader spectrum of pathogens according to the results of the DSTs, it was regarded as an escalation of antimicrobial therapy. On the contrary, when the spectrum of an initial antimicrobial therapy became narrower, it was defined as a de-escalation.

Patients were determined to have TB if BCs performed within 36 hours of presentation to the hospital isolated organisms that were not defined as a contaminant.[8] According to previous reports, although many microorganisms (eg, *Enterococcus* species, non-pneumococcal *Streptococci*) do not cause pneumonia, we decided to include patients in our study who had TB due to these organisms.[8] BC results that grew coagulase-negative staphylococci, *Corynebacterium* species, *Clostridium* species, *Micrococcus* species, *Propionibacterium* species, and *Bacillus* species were defined as contaminated.[8]

2.3. Statistical analyses

The data are presented as median (interquartile range) for continuous variables and as number (%) for categorical variables. Continuous variables were compared using the Mann–Whitney *U* test, and categorical variables were compared using the Pearson chi-square test, and the Fisher exact test was used when any cell contained less than 5. Multivariate logistic regression analyses were performed to identify independent prognostic factors associated with bacteremia, as measured by the estimated odds ratio (OR) with 95% confidence interval (CI).

The discriminatory power of each factor for bacteremia was assessed by calculating the area under each receiver-operating characteristic (ROC) curve. The estimated area under the ROC curve (AUC) values were compared using the Hanley–McNeil test.[25] The cut-off point that showed the highest Youden index was considered the optimal cut-off value.[26] All tests were 2-sided, and P values <0.05 were considered statistically significant. All analyses were performed using the Statistical Package for the Social Sciences (SPSS) network version 18.0 (SPSS; Chicago, IL).

3. Results

3.1. Study population, bacteremia, and modification of antimicrobial regimens

We identified 920 patients who were admitted with CO pneumonia. As BCs were not performed in 135 of these patients, we analyzed the remaining 785 patients. Bacteremia was detected in 75 patients (9.5%). The culture results of 39 of these patients (5.2%) were found to be contaminated, whereas those from 36 (4.8%) were proven to contain pathogens (TB).

Since 6 (0.7%) patients died before the results of the BCs were available, they were excluded from the analysis of the effectiveness of antimicrobial therapy. Of the remaining 30 patients with bacteremia, antibiotic regimens were modified in 13 (1.6%). On the basis of the BC results, 3 (0.3%) experienced escalation of antibiotic regimen, and 7 (0.8%) required de-escalation. All patients with an escalation received vancomycin as an additional agent. The rates of regimen changes based on the BC results in patients with CAP and HCAP were 1.1% (6/504) and 1.4% (4/281), respectively ($P=0.751$; Fig. 1).

3.2. Clinical characteristics

There were 36 patients (4.5%) in the TB group and 749 (95.4%) in the CNB group. Table 1 shows the clinical characteristics and outcomes of both groups. The number of patients with HCAP and the distribution of categories of HCAP were similar between the 2 groups. Among several comorbidities, only chronic liver disease was frequently more reported in the TB group (16.6% vs 5.4%; $P=0.016$).

The TB group exhibited worse clinical parameters. Of the laboratory findings, initial median C-reactive protein (CRP) and procalcitonin levels were higher in the TB group (16.7 vs 11.1 mg/dL; $P=0.010$, and 7.8 vs 0.2 mg/dL; $P<0.001$). The median

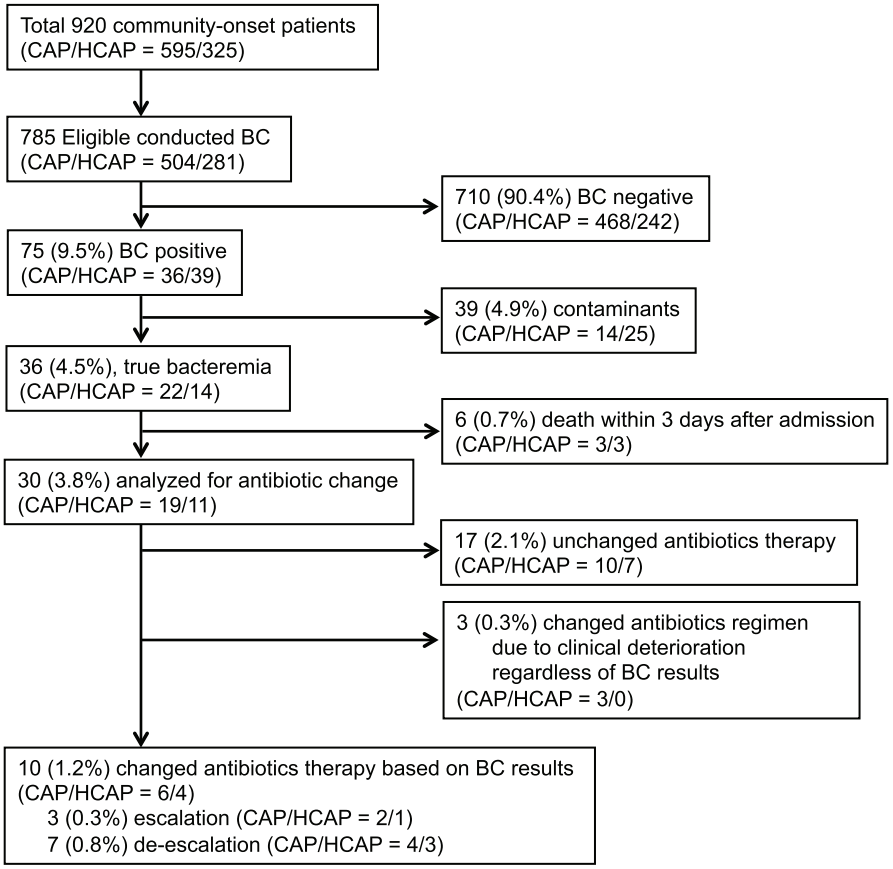

Figure 1. Flow diagram of the study population. BC = blood culture, CAP = community-acquired pneumonia, HCAP = healthcare-associated pneumonia.

confusion, urea, respiratory rate, blood pressure, age ≥65 (CURB-65) scores and PSI scores as severity indices of pneumonia were higher in the TB group (3 vs 1; $P < 0.001$, and 134 vs 102; $P < 0.001$). The TB group showed a higher inhospital mortality rate (30.5% vs 10.6%; $P = 0.001$).

3.3. Distribution of microorganisms

Table 2 shows the distribution of microorganisms isolated from the BCs. In the TB group, *Staphylococcus aureus* and *Escherichia coli* were most common, followed by *Streptococcus pneumoniae* and *Klebsiella pneumoniae*. *Staphylococcus epidermidis* was the most frequently isolated microorganism among the blood contaminants.

3.4. Risk factors of true bacteremia and its clinical implications

True bacteremia was more frequently observed in patients who belonged to PSI class V compared with classes I to IV (9.5% vs 2.8%; $P < 0.001$; Fig. 2A). Additionally, CURB-65 scores of 4 to 5 had a significantly higher TB rate of 20.0% (10/50) compared with a rate of 3.5% (26/735) for CURB-65 scores from 0 to 3 ($P < 0.001$; Fig. 2A).

The multivariate analysis for the risk factors of TB showed that 2 pneumonia severity scoring systems were independently associated with TB: a CURB-65 score of 4 to 5 points (OR 3.484, 95% CI 1.304–9.307) and PSI class V (OR 2.405, 95% CI 1.007–5.743). Chronic liver disease was also a significant risk factor of TB (OR 2.973, 95% CI 1.099–8.037). Age, tube feeding, HCAP, body temperature, and CRP were not associated with TB (Fig. 3).

In patients with PSI class V and CURB-65 score of 4 to 5, the TB group exhibited a higher inhospital mortality rate than the CNB group (50.0% vs 29.4%; $P = 0.06$, 60.0% vs 42.5%; $P = 0.48$; Fig. 2B).

3.5. Discriminatory power of the severity index for pneumonia associated with TB

Figure 4 shows the ROC curves for TB of each severity scoring system. Both the PSI and the CURB-65 scores had a high discriminatory power to predict TB. The AUC of the PSI score was 0.720 (95% CI 0.630–0.809), whereas that of the CURB-65 score was 0.720 (95% CI 0.622–0.819). These results were higher than those of the CRP (AUC 0.629, 95% CI 0.522–0.735), although the 3 did not statistically differ. The highest Youden index was shown at cut-off points of 116.5 (sensitivity 75.0%, specificity 62.0%) for the PSI and 2.5 (sensitivity 61.1%, specificity 79.7%) for the CURB-65 score.

4. Discussion

The ERS/ECCMID guidelines for CAP recommend that BCs should be conducted in all patients hospitalized with CAP. In contrast, the ATS/IDSA and BTS guidelines impose a limit on conducting BCs in patients with CAP. As a result, physicians could be confused about ordering BCs when they take care of

Table 1

Clinical characteristics of patients with community-onset pneumonia.

Variables	TB group (n = 36)	CNB group (n = 749)	*P*
Age, y	75 (63–81)	72 (61–80)	0.471
Male (n)	26 (72.2%)	446 (59.5%)	0.129
Tube feeding	2 (5.5%)	39 (5.2%)	0.712
Presence of HCAP	14 (38.8%)	267 (35.6%)	0.692
Hospitalization for ≥2 d in the past 90 d	6 (16.6%)	135 (18.0%)	0.836
Residence in a nursing home or long-term care facility	6 (16.6%)	118 (15.7%)	0.883
Recent outpatient intravenous therapy ≤30 d	3 (8.3%)	30 (4.0%)	0.189
Attendance at a dialysis center in the previous 30 d	2 (5.5%)	18 (2.4%)	0.232
Underlying diseases			
Malignancy	10 (27.7%)	143 (19.0%)	0.199
Chronic liver disease	6 (16.6%)	41 (5.4%)	0.016
Cardiovascular disease	7 (19.4%)	116 (15.4%)	0.523
Chronic kidney disease	8 (22.2%)	86 (11.4%)	0.064
Diabetes mellitus	12 (33.3%)	169 (22.5%)	0.134
Chronic lung disease	7 (19.4%)	192 (25.6%)	0.404
Central nervous system disorders	15 (41.6%)	205 (%)	0.062
Clinical parameters			
Body temperature, °C	37.9 (36.8–38.6)	37.6 (36.9–38.3)	0.398
Altered mentality	8 (22.2%)	81 (27.3%)	0.045
Respiratory failure	19 (52.7%)	272 (36.3%)	0.046
Severe sepsis or septic shock	15 (41.6%)	122 (16.2%)	<0.001
ICU admission	15 (41.6%)	105 (14.0%)	<0.001
Use of mechanical ventilator	12 (33.3%)	49 (6.5%)	<0.001
Radiological findings			
Multilobar involvement	19 (52.7%)	383 (51.1%)	0.847
Pleural effusion	11 (30.5%)	150 (20.0%)	0.126
Laboratory findings			
White blood cells, /mm^3	9700 (3875–16,250)	11,000 (8150–14,900)	0.092
C-reactive protein, mg/dL	16.7 (7.4–29.0)	11.1 (5.2–17.6)	0.010
Procalcitonin, mg/dL*	7.8 (1.0–49.1)	0.2 (0.1–0.8)	<0.001
Severity index of pneumonia			
CURB-65 score	3 (2–4)	1 (1–2)	<0.001
PSI score	134 (104–182)	102 (77–131)	<0.001
Clinical outcomes			
Duration of antibiotic therapy, d	11 (7–16)	10 (7–14)	0.459
Length of hospital stay, d	9 (4–16)	8 (5–13)	0.711
Inhospital mortality	11 (30.5%)	80 (10.6%)	0.001

Data are presented as median (interquartile range) or number (%).

CNB = contaminants/negative bacteremia, HCAP = healthcare-associated pneumonia, ICU = intensive care unit, PSI = Pneumonia Severity Index, TB = true bacteremia.

* Procalcitonin testing was performed in 32 patients in the TB group and 579 in the CNB group.

patients with CAP. Additionally, the concept of HCAP intensifies this confusion. Therefore, it is important to verify whether BCs have value as a tool to improve treatment outcomes, suppress resistance, and decrease medical costs in CO pneumonia. It would also valuable to identify which patients with CO-pneumonia would obtain the most benefit from BCs.

In our study, we calculated the TB rate for all patients hospitalized with CO-pneumonia; it was no more than 4.5%. Previous studies have included mostly patients with CAP and have reported that the incidence of the TB ranges from 3.7% to 16.0%.[2,3,22–24,27–33] Low overall TB rates indicate that it might not be necessary to perform BC in all hospitalized patients, which contrasts with the recent ERS/ECCMID guidelines. However, TB rates in patients with a high severity of illness such as PSI class V or CURB-65 scores of 4 to 5 points were 9.5% and 20.0%, respectively. This might indicate that the role of BCs increases as the severity of pneumonia increases.

In addition, we found that chronic liver disease was also 1 of the independent factors for predicting TB in patients with CO-pneumonia. Change in the immune system, including depression of the activity of the reticuloendothelial system and neutrophil leukocyte dysfunction, is likely to contribute to TB in these patients.[34] As a result, it could be reasonable to perform BCs selectively in a proportion of patients with CO-pneumonia. Although previous studies have tried to construct a more useful tool to predict bacteremia using clinical variables in patients hospitalized with CAP, these prediction model seems to be not easy to perform in clinical practice.[8,31,32] Our findings for prediction of TB may be helpful for clinicians in practice.

Normally, 1 of the indications for BCs is to determine whether antibiotic therapy should be altered based upon the results. However, several studies have reported that BCs rarely affect antibiotic therapy for patients with pneumonia.[2,27,28,35] On the whole, in our study, only 1.2% (10 of 785 patients) had their initial antibiotic regimens modified according to the BC results. A systematic review has revealed that TB rates were 0% to 14% among cases of CAP, which resulted in antibiotic narrowing in 0% to 3% of cases and broadening in 0% to 1%.[36] These results suggest that it would not be beneficial to routinely conduct BCs in all patients with CAP.

Pneumonia Severity Index and CURB-65 have been accepted as useful tools to help clinicians predict mortality in patients with

Table 2

Microorganisms identified from blood cultures in patients with community-onset pneumonia.

Microorganisms	Number of patients with microorganisms isolated from blood
True Pathogens	36 (48.0%)
Streptococcus pneumoniae	6 (8.0%)
Other *Streptococcus* species	2 (2.6%)
Staphylococcus aureus	10 (13.3%)
Methicillin-sensitive *S aureus*	5 (6.6%)
Methicillin-resistant *S aureus*	5 (6.6%)
Escherichia coli	10 (13.3%)
Klebsiella pneumoniae	5 (6.6%)
Enterococcus species	1 (1.3%)
Pseudomonas aeruginosa	1 (1.3%)
Other	1 (1.3%)
Contaminants	39 (52.0%)
Coagulase-negative staphylococci	36 (48.0%)
Staphylococcus epidermidis	15 (20.0%)
Staphylococcus hominis	14 (18.6%)
Staphylococcus capitis	4 (5.3%)
Other coagulase-negative staphylococci	3 (4.0%)
Clostridium perfringens	1 (1.3%)
Corynebacterium species	1 (1.3%)
Other	1 (1.3%)

Data are presented as number (%).

CAP.[1,9,10] Our study showed that in patients with PSI class V or CURB-65 scores of 4 to 5 points, the relative risk of mortality due to CO-pneumonia was about 1.5 to 2 times higher in the TB group compared with the CNB group (Fig. 4). At the same time, a positive correlation of PSI class or CURB-65 score with positive BCs was demonstrated (Figs. 2 and 3). These results suggest that BCs could be a useful prognostic tool for predicting of mortality in patients with high-severity indices of pneumonia.

A few studies have assessed the need for BCs in HCAP.[31,37] This is 1 reason why the guidelines did not refer to whether BCs should be performed in HCAP patients.[1,9–11] Our study found that HCAP was not a predictive factor of TB, and the rates of change in antibiotic therapy did not differ between CAP and HCAP. Therefore, we suggest that performing BCs on a routine basis in HCAP is not likely to be valuable. However, its usefulness needs to be evaluated through further well-designed studies.

A recent systematic review of 15 studies with a total of 3898 patients admitted with CAP reported the microorganisms in patients with positive BCs.[36] *S pneumoniae* was the most common pathogens, followed by *S aureus* and *E coli*.[36] Several previous studies have reported very low isolation rate of antibiotic-resistant pathogens (ARPs).[36] In contrast, a recent prospective, observational study revealed a relatively high rate of ARP bacteremia in CAP (30/2892 patients; 1.0%).[37] In our

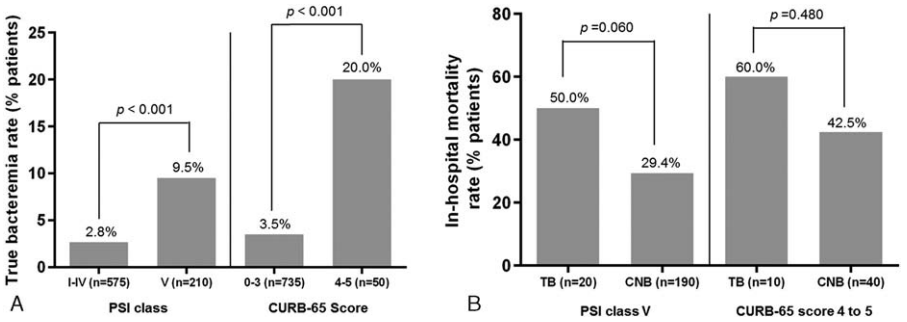

Figure 2. Relationship between severity of pneumonia and true bacteremia. A, Bacteremia rates according to PSI class and CURB-65 score. B, In-ospital mortality rates of true bacteremia in PSI class V and CURB-65 score of 4 to 5 points. CNB = contaminants or negative bacteremia, CURB-65 = confusion, urea, respiratory rate, blood pressure, age ≥65, PSI = Pneumonia Severity Index, TB = true bacteremia.

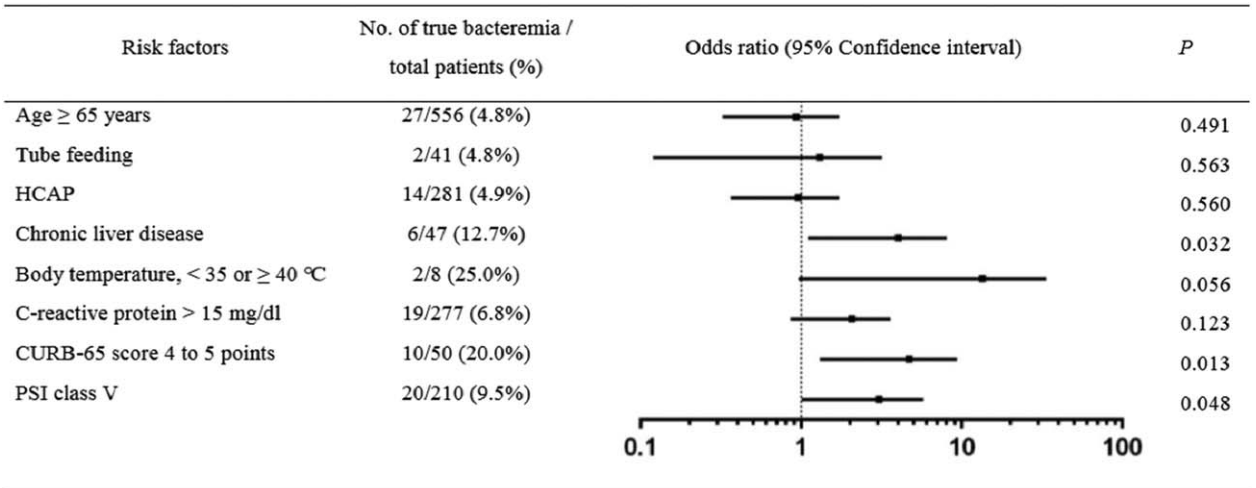

Figure 3. Logistic regression analysis for risk factors associated with true bacteremia in patients admitted with community-onset pneumonia. CURB-65 = confusion, urea, respiratory rate, blood pressure, age ≥65, HCAP = healthcare-associated pneumonia, PSI = Pneumonia Severity Index.

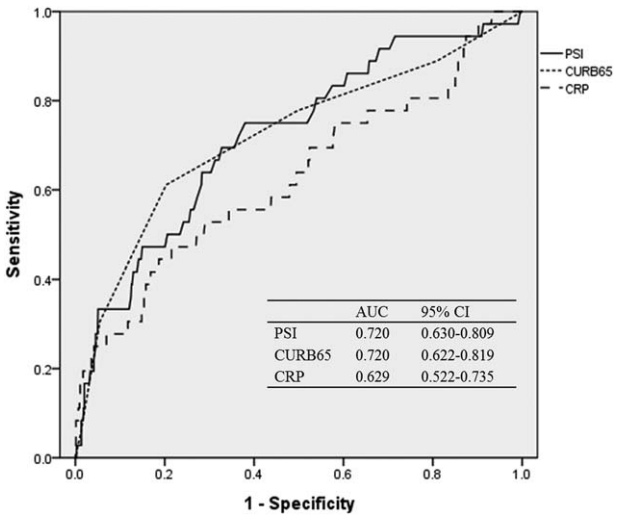

Figure 4. Comparison of ROC curves between PSI score, CURB-65 score, and CRP level for predicting true bacteremia. AUC = area under the curve, CI = confidence interval, CRP = C-reactive protein, CURB-65 = confusion, urea, respiratory rate, blood pressure, age ≥65, PSI = Pneumonia Severity Index, ROC = receiver operating characteristic.

study, the most common pathogens in the TB group were *S aureus* and *E coli*, followed by *S pneumoniae* and *K pneumoniae*. ARPs were isolated in only 6 patients (0.7%), although our study also included patients with HCAP.

4.1. Limitations

Our study had some limitations. Firstly, our study was a retrospective study performed at a single center. The results of this study should be carefully interpreted and might not be generalizable to other institutions. Secondly, the sample size of the TB group was less than optimal. Future subgroup analyses of patients with HCAP with larger sample sizes are needed. Thirdly, unusual microorganisms like *Enterococcus* species (n = 1) and nonpneumococcal *Streptococci* (n = 2) were included in the TB group as the etiology of pneumonia.[8] Although these microorganisms rarely cause pneumonia, some cases could actually have been due to specimen contamination. Although we additionally conducted a statistical analysis excluding 3 patients, we did not find a significant change of pneumonia severity or mortality. The risk factors for bacteremia were not changed as well. Finally, we used PSI and CURB-65 as prognostic factors in patients with HCAP. But, because a recent study demonstrated that the discriminatory powers of PSI and CURB-65 for 30-day mortality were significantly low in the HCAP group compared with the CAP group, more precise models for prediction of TB are demanded in patients with HCAP.[38]

5. Conclusions

The overall positive rate of BCs was very low in all patients hospitalized with CO-pneumonia. In addition, the rate of modification of antibiotic regimens according to the BC results was low. However, chronic liver disease, PSI class V, and a CURB-65 score of 4 to 5 points were the predictive factors associated with TB, which tended to show higher inhospital mortality that the CNB group. Accordingly, it is reasonable to perform BCs selectively in CO patients with a higher severity of pneumonia.

References

[1] Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007;44(suppl 2):S27–72.
[2] Campbell SG, Marrie TJ, Anstey R, et al. The contribution of blood cultures to the clinical management of adult patients admitted to the hospital with community-acquired pneumonia: a prospective observational study. Chest 2003;123:1142–50.
[3] Waterer GW, Wunderink RG. The influence of the severity of community-acquired pneumonia on the usefulness of blood cultures. Respir Med 2001;95:78–82.
[4] Houck PM, Bratzler DW, Nsa W, et al. Timing of antibiotic administration and outcomes for Medicare patients hospitalized with community-acquired pneumonia. Arch Intern Med 2004;164:637–44.
[5] Fine MJ, Smith MA, Carson CA, et al. Prognosis and outcomes of patients with community-acquired pneumonia. A meta-analysis. JAMA 1996;275:134–41.
[6] Metersky ML. Is the lateral decubitus radiograph necessary for the management of a parapneumonic pleural effusion? Chest 2003;124:1129–32.
[7] Yu VL, Chiou CC, Feldman C, et al. An international prospective study of pneumococcal bacteremia: correlation with in vitro resistance, antibiotics administered, and clinical outcome. Clin Infect Dis 2003;37:230–7.
[8] Metersky ML, Ma A, Bratzler DW, et al. Predicting bacteremia in patients with community-acquired pneumonia. Am J Respir Crit Care Med 2004;169:342–7.
[9] Lim WS, Baudouin SV, George RC, et al. BTS guidelines for the management of community acquired pneumonia in adults: update 2009. Thorax 2009;64(suppl 3):iii1–55.
[10] Woodhead M, Blasi F, Ewig S, et al. Guidelines for the management of adult lower respiratory tract infections: full version. Clin Microbiol Infect 2011;17(suppl 6):E1–59.
[11] American Thoracic Society, Infectious Diseases Society of America: Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171:388–416.
[12] Fukuyama H, Yamashiro S, Tamaki H, et al. A prospective comparison of nursing- and healthcare-associated pneumonia (NHCAP) with community-acquired pneumonia (CAP). J Infect Chemother 2013;19:719–26.
[13] Giannella M, Pinilla B, Capdevila JA, et al. Pneumonia treated in the internal medicine department: focus on healthcare-associated pneumonia. Clin Microbiol Infect 2012;18:786–94.
[14] Simonetti A, Viasus D, Garcia-Vidal C, et al. Timing of antibiotic administration and outcomes of hospitalized patients with community-acquired and healthcare-associated pneumonia. Clin Microbiol Infect 2012;18:1149–55.
[15] Nakagawa N, Saito Y, Sasaki M, et al. Comparison of clinical profile in elderly patients with nursing and healthcare-associated pneumonia, and those with community-acquired pneumonia. Geriatr Geronto Int 2014;14:362–71.
[16] Ishida T, Tachibana H, Ito A, et al. Clinical characteristics of nursing and healthcare-associated pneumonia: a Japanese variant of healthcare-associated pneumonia. Intern Med 2012;51:2537–44.
[17] Maruyama T, Fujisawa T, Okuno M, et al. A new strategy for healthcare-associated pneumonia: a 2-year prospective multicenter cohort study using risk factors for multidrug-resistant pathogens to select initial empiric therapy. Clin Infect Dis 2013;57:1373–83.
[18] Carratalà J, Mykietiuk A, Fernández-Sabé N, et al. Health care-associated pneumonia requiring hospital admission: epidemiology, antibiotic therapy, and clinical outcomes. Arch Intern Med 2007;167:1393–9.
[19] Koh SJ, Lee JH. Clinical characteristics of nursing home-acquired pneumonia in elderly patients admitted to a Korean teaching hospital. Korean J Intern Med 2015;30:638–47.
[20] Chalmers JD, Rother C, Salih W, et al. Healthcare-associated pneumonia does not accurately identify potentially resistant pathogens: a systematic review and meta-analysis. Clin Infect Dis 2014;58:330–9.

[21] Garner JS, Jarvis WR, Emori TG, et al. CDC definitions for nosocomial infections, 1988. Am J Infect Control 1988;16:128–40.
[22] Kennedy M, Bates DW, Wright SB, et al. Do emergency department blood cultures change practice in patients with pneumonia? Ann Emerg Med 2005;46:393–400.
[23] Corbo J, Friedman B, Bijur P, et al. Limited usefulness of initial blood cultures in community acquired pneumonia. Emerg Med J 2004;21: 446–8.
[24] Benenson RS, Kepner AM, Pyle DN2nd, et al. Selective use of blood cultures in emergency department pneumonia patients. J Emerg Med 2007;33:1–8.
[25] Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology 1982;143:29–36.
[26] Schisterman EF, Perkins NJ, Liu A, et al. Optimal cut-point and its corresponding Youden index to discriminate individuals using pooled blood samples. Epidemiology 2005;16:73–81.
[27] Abe T, Tokuda Y, Ishimatsu S, et al. Usefulness of initial blood cultures in patients admitted with pneumonia from an emergency department in Japan. J Infect Chemother 2009;15:180–6.
[28] Chalasani NP, Valdecanas MA, Gopal AK, et al. Clinical utility of blood cultures in adult patients with community-acquired pneumonia without defined underlying risks. Chest 1995;108:932–6.
[29] Ramanujam P, Rathlev NK. Blood cultures do not change management in hospitalized patients with community-acquired pneumonia. Acad Emerg Med 2006;13:740–5.
[30] Glerant JC, Hellmuth D, Schmit JL, et al. Utility of blood cultures in community-acquired pneumonia requiring hospitalization: influence of antibiotic treatment before admission. Respir Med 1999;93:208–12.
[31] Lee J, Hwang SS, Kim K, et al. Bacteremia prediction model using a common clinical test in patients with community-acquired pneumonia. Am J Emerg Med 2014;32:700–4.
[32] Falguera M, Trujillano J, Caro S, et al. A prediction rule for estimating the risk of bacteremia in patients with community-acquired pneumonia. Clin Infect Dis 2009;49:409–16.
[33] Bohte R, van Furth R, van den Broek PJ. Aetiology of community-acquired pneumonia: a prospective study among adults requiring admission to hospital. Thorax 1995;50:543–7.
[34] Navasa M, Rodes J. Bacterial infections in cirrhosis. Liver Int 2004; 24:277–80.
[35] Waterer GW, Jennings SG, Wunderink RG. The impact of blood cultures on antibiotic therapy in pneumococcal pneumonia. Chest 1999;116:1278–81.
[36] Afshar N, Tabas J, Afshar K, et al. Blood cultures for community-acquired pneumonia: are they worthy of two quality measures? A systematic review. J Hosp Med 2009;4:112–23.
[37] Torres A, Cillóniz C, Ferrer M, et al. Bacteraemia and antibiotic-resistant pathogens in community acquired pneumonia: risk and prognosis. Eur Respir J 2015;45:1353–63.
[38] Jeong BH, Koh WJ, Yoo H, et al. Performances of prognostic scoring systems in patients with healthcare-associated pneumonia. Clin Infect Dis 2013;56:625–32.