Initial Empirical Therapy and De-escalation in Hospitalized Community-Acquired Pneumonia : Clinical Outcomes from Korean National Health Insurance Claims and CAP Quality Assessment Data

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INTRODUCTION

Use of broad-spectrum empirical antibiotics for community acquired pneumonia (CAP) have increased in Korea. Previous studies have shown that consumption of 4th-generation cephalosporins and carbapenems doubled from 2010 to 2015, with especially high use among patients over 65 years. Nevertheless, real-world evidence on the clinical effectiveness of guideline-concordant empirical therapy and culture-guided de-escalation remains limited. We therefore evaluated clinical outcomes according to the initial empirical antibiotic regimen and subsequent spectrum changes in hospitalized patients with CAP.

METHODS

We conducted retrospective cohort study using Korean National Health Insurance claims data linked to Quality Assessment Program for CAP. Initial empirical antibiotics prescribed on the pneumonia diagnosis date were categorized into guideline-concordant or broad-spectrum. Among patients initially treated with broad-spectrum antibiotics, spectrum change was assessed by comparing the initial and final regimens according to antibiotic spectrum rank and the number of agents. Patients were classified as continuation, de-escalation, or escalation. Spectrum ranks are presented in Table 1, and definitions of de-escalation, and escalation are provided in Table 2.

Table 1. Antibiotics spectrum ranks

De-escalation	Escalation
Lower spectrum rank	Higher spectrum rank
Or Unchanged spectrum rank with fewer antibiotics	Or Unchanged spectrum rank with more antibiotics
Or Both lower spectrum rank and fewer antibiotics	Or Both higher spectrum rank and more antibiotics

Table 2. Definitions of de-escalation and escalation

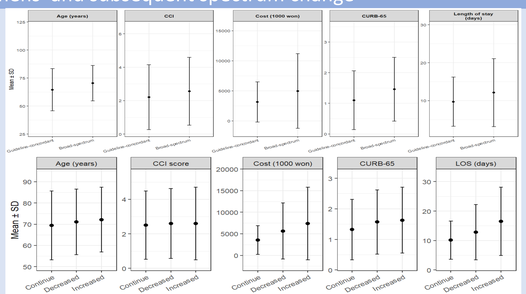
Rank	Antibiotics
Rank 6 : Agents for highly resistant organisms	Ceftolozane/tazobactam, Colistin, Tigecycline, Ceftazidime/avibactam
Rank 5 : Carbapenem	Ertapenem, Imipenem/cilastatin, Meropenem, Doripenem, Imipenem
Rank 4 : Anti-pseudomonal ß-lactam	Cefpirome, Cefepime, Cefoperazone/ sulbactam,, Ceftazidime
Rank 3 : 3rd cephalosporin or Fluoroquinolone	Cefcapene, Cefdinir, Cefditoren, Cefixime, Cefozidime, Cefotaxime, Cefpiramide, Cefpodoxime, Ceftizoxime, Ceftriaxone
Rank 2 : Ampicillin with β-lactamase inhibitors	Amoxicillin/clavulanate, Amoxicillin/ sulbactam, Ampicillin/sulbactam
Rank 1 : Other β-lactams & Macrolide	Ampicillin, Amoxicillin, Cefaclor, Cephalexin, , Cefazedone, Cefazolin, Cefbuperazone, Cefbuperazone, Cefmetazole, Cefradine, Cefminox, Cefotetan, Cefotiam, Cefoxitin, Cefprozil, Cefroxadine, Ceftezole, Cefuroxime, Flomoxef, Azithromycin, Clarithromycin, Roxithromycin

After 1:1 propensity score (PS) matching, logistic regression evaluated all-cause and 30-day mortality, 30-day pneumonia readmission, and clostridium difficile infection (CDI) according to initial empirical regimen and spectrum change. A tertiary-hospital subgroup analysis was performed. Antibiotic exposure was measured as defined daily doses (DDD).

RESULTS

Among total of 58,030 CAP episodes, the initial broad-spectrum and de-escalation groups showed significantly higher age, disease severity, and comorbidity profiles compared to the guideline-concordant and continuation cohorts (Figure.1).

Figure 1. Baseline characteristics according to initial empirical regimens and subsequent spectrum change



RESULTS

After PS matching, total antibiotic consumption (DDD per episode) was comparable between the broad-spectrum and guideline-concordant groups (19.6±13.5 vs, 19.7±13.0, p=0.253), whereas antibiotics consumption density (DDD per 100patient-days) was higher in the guideline-concordant group reflecting a shorter length of stay (201.5 vs. 181.5, p<0.001). Despite similar total antibiotics consumption, initial broad-spectrum therapy was associated with higher in-hospital mortal, 30-day mortality and, 30-day pneumonia readmission, while CDI did not differ significantly (Table 3).

Table 3. Clinical outcomes by initial empirical antibiotic therapy after propensity score matching

Outcome	PS-matched Odds Ratio (95% CI)* (Broad vs Guideline-concordant[reference])	P-value
Mortality		
In-hospital mortality	1.71 (1.45–2.01)	<0.001
30-day mortality	1.51 (1.35–1.68)	<0.001
30-day pneumonia readmission	1.25 (1.14–1.37)	<0.001
C. difficile infection	1.21 (0.98–1.50)	0.083

In the broad-spectrum cohort, de-escalation was associated with a higher PS-matched DDD per episode compared with continuation (21.1 ± 13.1 vs. 20.3 ± 12.2, p = 0.020), while DDD per 100 patient-days was lower (184.5 vs. 213.4, p < 0.001). This discrepancy may be explained by differences in hospitalization duration. De-escalation was most frequently undertaken in patients with higher initial severity and was observed most often in tertiary hospitals (45.9%), possibly reflecting more active or better-established antimicrobial stewardship programs (ASPs) in these settings. Therefore, a subgroup analysis for tertiary hospitals was also performed. In the PS-matched analysis of patients initially treated with broad-spectrum antibiotics, de-escalation was not associated with worse clinical outcomes, including in-hospital mortality, 30-day mortality, or 30-day pneumonia-related readmission. No significant difference was observed in CDI (Figure 2). Similar findings were observed in the tertiary hospital subgroup (Figure 3).

Figure 2. Clinical outcomes by comparing de-escalation versus continuation after propensity score matching

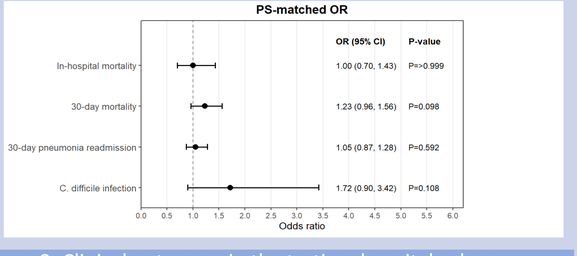
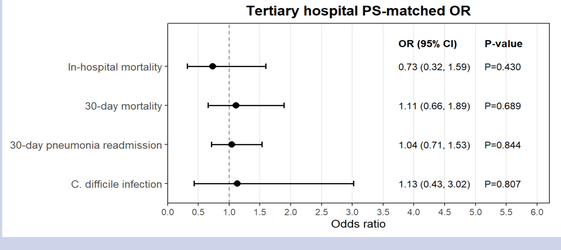


Figure 3. Clinical outcomes in the tertiary hospital subgroup: comparison of de-escalation and continuation after propensity score matching



CONCLUSION

In hospitalized patients with CAP, guideline-concordant empirical antibiotic therapy was not associated with worse clinical outcomes. In addition, de-escalation was not associated with worse outcomes compared with continuation after propensity score matching. Subgroup analyses in tertiary-care hospitals—where patients were most severely ill and de-escalation was most frequently practiced—demonstrated no significant differences in major clinical outcomes, supporting the safety of de-escalation even in the highest acuity settings. These findings support antimicrobial stewardship strategies that prioritize guideline concordant initial empirical therapy and encourage timely de-escalation when clinically appropriate. This strategy may reduce unnecessary exposure to broad-spectrum antibiotics while maintaining clinical safety.