

Evaluating the impact of antibiotic duration on superinfection after controlling for cumulative spectrum scores

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INTRODUCTION

- Superinfections (SIs) with resistant pathogens pose significant challenges in the treatment of critically ill patients.
- An antibiotic de-escalation strategy, as a key component of antibiotic stewardship, has been widely used to minimize exposure to broad-spectrum antibiotics, thereby reducing antibiotic resistance and SIs.
- In addition, an antibiotic spectrum score has been developed as an objective way of measuring an antibiotic regimen's degree of microbial activity patients are exposed to during hospitalization.
- However, evidence evaluating the impact of narrowing antibiotic spectrum on clinical outcomes is limited. Accordingly, the objective of this study was to examine the impact of antibiotic duration on the risk of SI development after adjusting for a cumulative antibiotic spectrum score (CASS).

METHODS

- This was a retrospective cohort study using electronic medical records between January 1, 2010 and December 31, 2017 from a tertiary care hospital in the U.S.
- Adult patients aged 18 or older with severe sepsis or septic shock who received at least one antibiotic during their hospitalization were included.
- Cohort entry was defined as the first day of any antibiotic use. Each patient in the cohort was followed from the first day until the occurrence of study outcome or censoring events, whichever came first. The primary outcome was the development of a SI (multi-drug resistance gram-negative or gram-positive bacteria, *Clostridioides difficile*, or *Candida* species) > 3 days after cohort entry. Patients were censored at 90 days following cohort entry, time of in-hospital mortality, or end of the study period. Also, patients identified with organisms in the period from 90 days prior to cohort entry through the first 3 days after cohort entry were censored.

METHODS (cont'd)

- After calculating spectrum scores for every antibiotic, we estimated a CASS for each day of exposure to antibiotics.
- Duration of antibiotic exposures was classified into four groups:
 - Group 1: 1-3 days
 - Group 2: 4-7 days
 - Group 3: 8-10 days
 - Group 4: 11-14 days
- Cox proportional hazard regressions were conducted to calculated the adjusted hazard ratio (HR) of SIs while controlling for numerous covariates.

RESULTS

- Of 10,221 patients included in the analysis, 2,107 (20.6%) developed a superinfection. The incidence rate of a superinfection was 0.495 per 100 person-days.
- (Table 1) Compared to those with no SI, the SI cohort was in more serious conditions (APACHE score: 17.0±5.8 vs. 16.2±5.7) and had higher comorbidities (Charlson score: 6.2±3.1 vs. 6.0±3.3).

Table 1. Baseline characteristics

	Superinfection (n=2,107)	No superinfection (n=8,114)	p-value
Age (years), median (IQR)	61.20 (51.52-70.05)	61.86 (51.69-71.28)	0.0135
Females, n(%)	916 (43.47%)	3609 (44.48%)	0.4424
Charlson score, mean±SD (range)	6.20±3.12 (0-18)	6.03±3.25 (0-20)	0.0468
Comorbidities, n(%)			
CAD	487 (23.11%)	1913 (23.58%)	0.6550
CHF	829 (39.35%)	2951 (36.37%)	0.0117
COPD	885 (42.00%)	2952 (36.38%)	< 0.0001
Cirrhosis	588 (27.91%)	1873 (23.08%)	<0.0001
Diabetes	823 (39.06%)	2989 (36.84%)	0.0601
CKD	814 (38.63%)	2755 (33.95%)	< 0.0001
HIV	26 (1.23%)	133 (1.64%)	0.1806
Neoplastic disease	479 (22.73%)	1353 (16.67%)	< 0.0001
APHACHE score, mean±SD (range)	17.00±5.78 (0-36)	16.21±5.72 (0-39)	< 0.0001
Antibiotic exposure 30 days before cohort entry, n(%)	581 (27.57%)	1833 (22.59%)	< 0.0001

RESULTS (cont'd)

- After cohort entry, patients with SI were found to have increased days of exposure to mechanical ventilation (mean difference [MD] 0.90 days, 95% CI: 0.35-1.44), urinary catheters (MD 0.72 days, 95% CI: 0.18-1.27), and vasopressors (MD 0.59 days, 95% CI: 0.17-1.01) that those with no SI.

Table 2. Results from Cox regression

CASS	Group	Adjusted HR (95% CI)
100 to 199	Group 1	Reference
	Group 2	2.520 (1.533-4.141)
	Group 3	2.458 (1.191-5.074)
	Group 4	1.792 (0.486-6.601)
200 to 299	Group 2	Reference
	Group 3	0.931 (0.742-1.169)
	Group 4	0.592 (0.365-0.960)
300 to 399	Group 2	Reference
	Group 3	1.035 (0.454-2.361)
	Group 4	1.014 (0.423-2.427)
400 to 499	Group 3	Reference
	Group 4	1.245 (0.745-2.081)

- Table 2 presents results from Cox proportional hazard regression analyses.
- When CASS is between 100-199, the adjusted HRs of SI were 2.52 (95% CI: 1.53-4.14) and 2.46 (95% CI: 1.19-5.07) for groups 2 and 3, respectively, compared to group 1.

DISCUSSION

- Patients who developed a SI were sicker at baseline, had higher rates of antibiotics exposure (before and after cohort entry), and required more invasive management than those without a SI.
- Results showed the risk for developing SIs appears to decrease as the daily spectrum scores decrease. In other words, the risk of SIs increased as the duration of antibiotic exposures increased.

CONCLUSIONS

- Study findings support the utility of antibiotic de-escalation. Further research is warranted to precisely measure the association of antibiotic de-escalation on the risk of SIs.