The Effect of Hospitalization Duration on Antimicrobial Resistance in Bloodstream Infections

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BACKGROUND:

Hospital-acquired bloodstream infection (BSI) is a common and important healthcare-associated infection. Decreasing antibiotic susceptibility with increasing length of hospital stay has been shown for the colonization or infection of selected organ systems (1,2). Only few investigators with modest numbers of isolates have scrutinized this question for BSI (3). We suspected a systematic relationship between duration of hospitalization and increasing antimicrobial resistance. Our goal was to determine the effect of hospitalization duration on antibiotic resistance rates in BSI.

METHODS I:

We performed a nationwide surveillance analysis of BSI pathogens recorded in the Swiss Centre for Antibiotic Resistance (ANRESIS) database. Only isolates from hospitals sending information on hospital length of stay at sampling were considered.

METHODS II:

We restricted the dataset to pathogens that occurred ≥50 times overall and in the first 30 days of hospitalization. Only the first isolate of a species per patient was eligible for the study (**Figure 1**). We applied generalized linear/additive and Poisson regression models to characterize these effects.
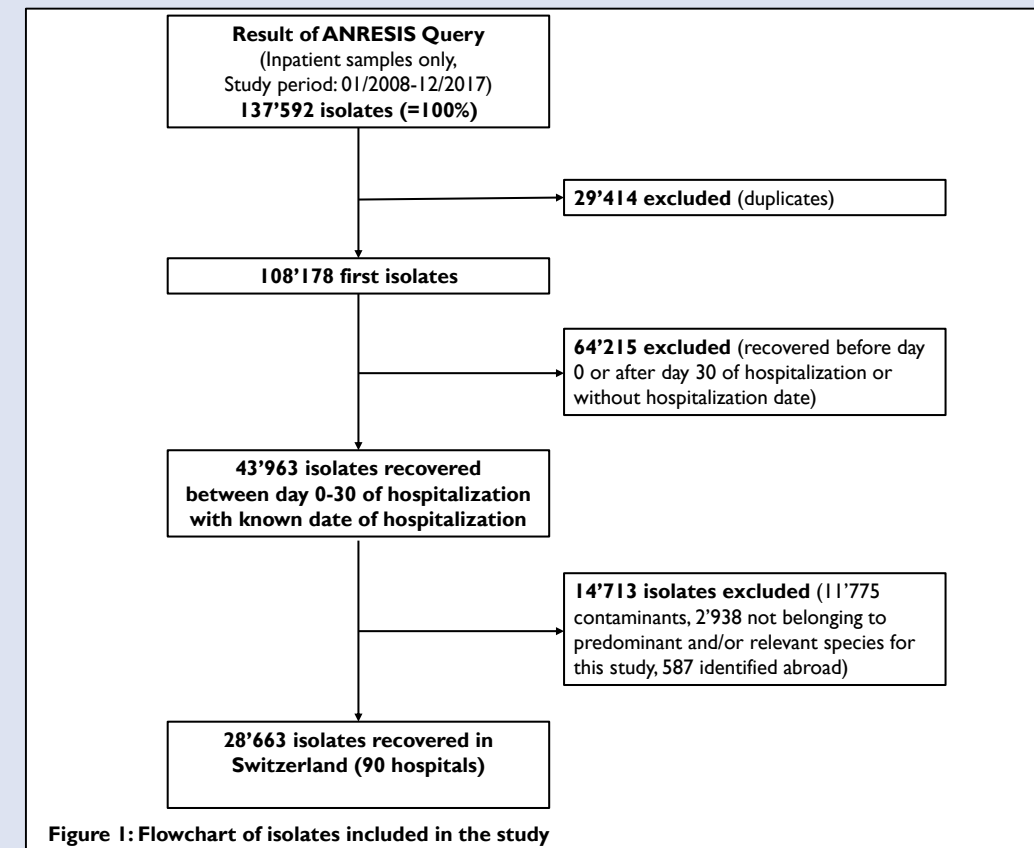

Figure 1: Flowchart of isolates included in the study

Table: Baseline epidemiological characteristics associated with the isolates included, Stratified by acquisition.

	Community-acquired	Early hospital-acquired	Late hospital-acquired	p-value
Episodes, n	14856	4508	9299	
Sex, male n (%)	8348 (56.2)	2825 (62.7)	5994 (64.5)	<0.001
Age, >59y n (%)	10751 (72.4)	3215 (71.3)	6576 (70.7)	0.018
Hospital type, university hospital n (%)	2345 (15.8)	1183 (26.2)	3268 (35.1)	<0.001
Department, non-ICU n (%)	13132 (88.4)	3727 (82.7)	7702 (82.8)	<0.001

Notes. Community acquired: 0-2 days after hospital admission. Early hospital-acquired: 2-5 days after the hospitalization. Late hospital-acquired: >5day after the hospitalization. ICU: Intensive Care Unit. y: years old.

RESULTS I:

A total of 28'663 BSIs identified in 90 hospitals were analyzed from January 2008 to December 2017. Sixty percent (17'167) of BSIs occurred in male and 76% (21'973) were observed in community hospitals.
Forty-eight percent were hospital-acquired (13'807), of which 32% (9'299) were late hospital-acquired (i.e., BSI >5 days after hospitalization [**Table**]).
The most common etiologies were *Escherichia coli* (32.9%, 9'431), *Staphylococcus aureus* (16.4%, 4'696), Enterococci (9.8%, 2'804) and *Klebsiella* spp (9.4%, 2'682).
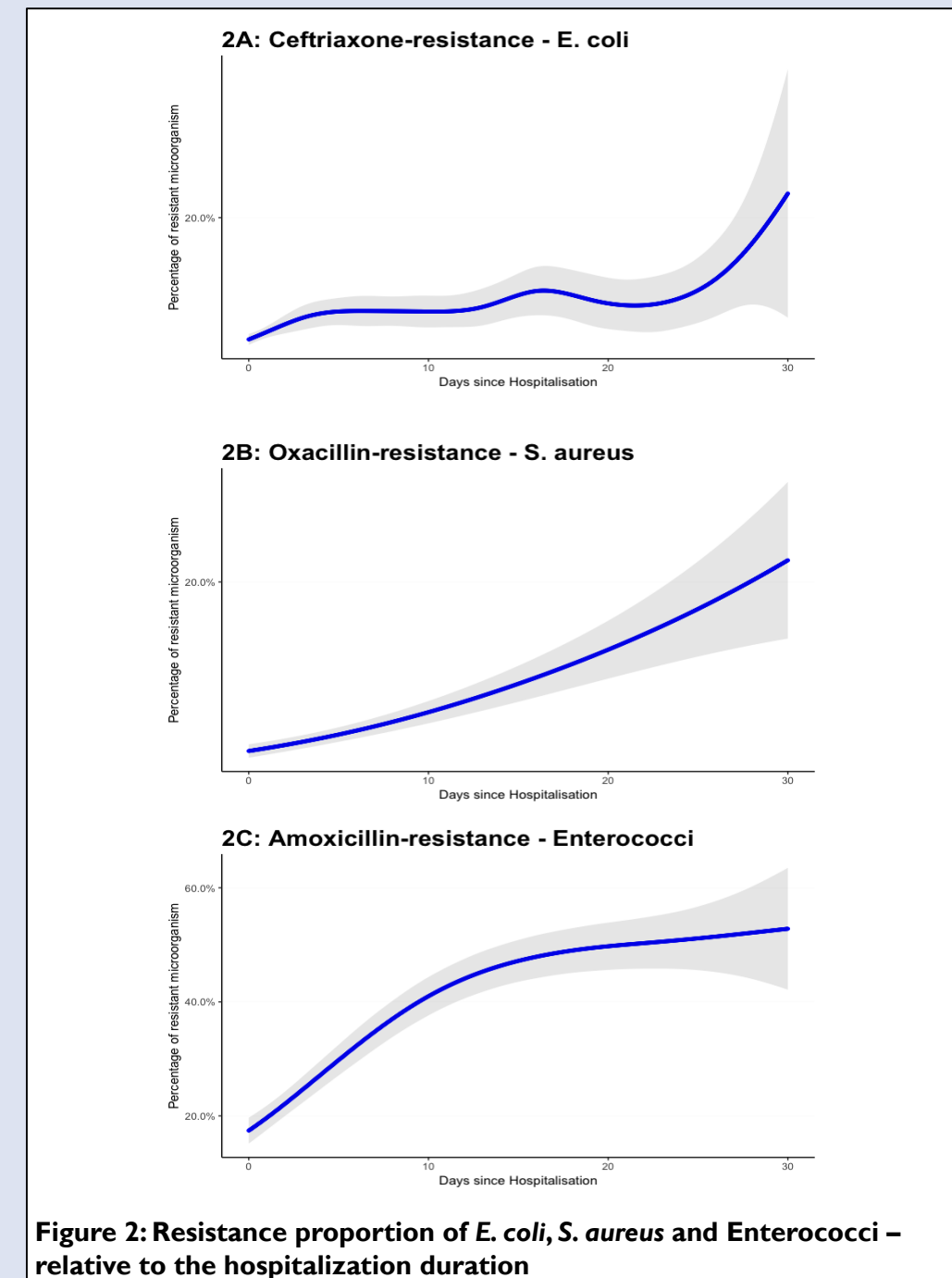

2A: Ceftriaxone-resistance - E. coli

2B: Oxacillin-resistance - S. aureus

2C: Amoxicillin-resistance - Enterococci

Figure 2: Resistance proportion of *E. coli*, *S. aureus* and Enterococci – relative to the hospitalization duration

RESULTS II:

Our models suggested that resistance patterns in function of hospitalization duration were pathogen-specific (**Figure 2**): for example Ceftriaxone resistance among *E. coli* remained stable for the first 15 days of hospitalization (Figure 2A). Antimicrobial resistance to first-line antibiotics (e.g., ceftriaxone for Gram-negative microorganisms, amoxicillin for Enterococci or oxacillin for *S. aureus*) was 13.4% at day zero and then increased daily at an adjusted relative rate of 4.2% (95% CI 3.8-4.5%, p<0.001, **Figure 3**).
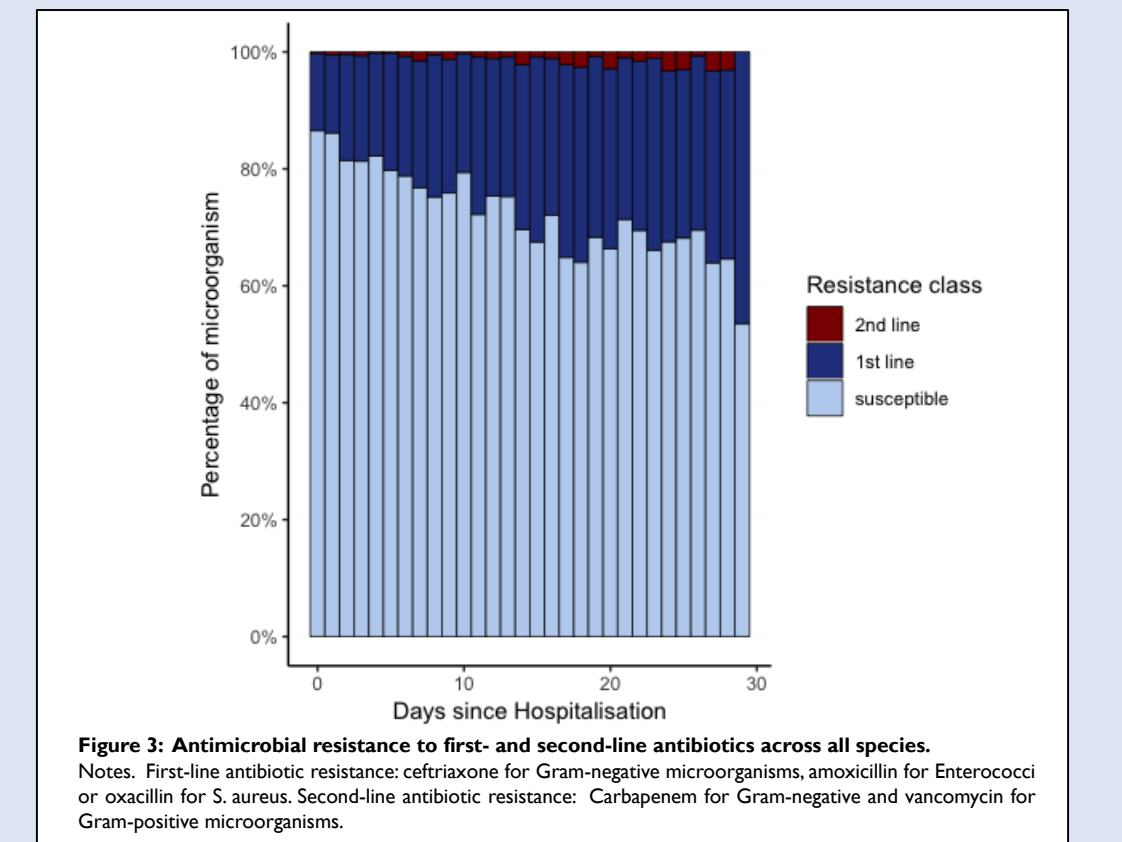

Figure 3: Antimicrobial resistance to first- and second-line antibiotics across all species. Notes. First-line antibiotic resistance: ceftriaxone for Gram-negative microorganisms, amoxicillin for Enterococci or oxacillin for S. aureus. Second-line antibiotic resistance: Carbapenem for Gram-negative and vancomycin for Gram-positive microorganisms.

CONCLUSIONS:

The duration of hospitalization appears to be associated with increasing antimicrobial resistance in BSI. We demonstrated that hospitalization duration exerted species/antibiotic specific effects that are essential for clinicians to know. The partially non-linear relationship suggests complex pathogen-specific adaption mechanisms that occur during hospitalization.

References:
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