251. High prevalence of the cefazolin inoculum effect in methicillin-susceptible Staphylococcus aureus causing bloodstream infections in a hospital network in Houston, TX

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Background: Anti-staphylococcal β-lactams, such as anti-staphylococcal penicillins (AsPen) or cefazolin are the drugs of choice for methicillin-susceptible Staphylococcus aureus (MSSA) bloodstream infections. However, cefazolin has seen increasing use due to its better tolerance, lower cost, ease of administration and possibly better outcomes when compared to AsPen. Nevertheless, its efficacy may be compromised by the cefazolin inoculum effect (CzIE), defined as an increase in the minimum inhibitory concentration (MIC) of cefazolin to ≥16mg/L when a high inoculum ($5x10^7$ CFU/ml) is present. Previous studies have suggested that the prevalence of the CzIE varies geographically, with high prevalence in some Latin American countries. Prospective data evaluating the presence of the CzIE in deep-seated MSSA infections across the United States are lacking.

Methods: We performed a prospective observational study of MSSA bacteremia in a network of 13 hospitals in Houston, TX. Patients ≥ 18 years old, with a positive blood culture with MSSA, with at least one follow-up blood culture confirming clearance of the bacteremia, who received cefazolin or nafcillin as definitive therapy (72 hours or longer after culture results known) and whose original isolate was available for evaluation of the CzIE, were included. Patients with polymicrobial BSI, or those who received another antibiotic with activity against MSSA in the definitive therapy period were excluded. Cefazolin MICs were determined by broth microdilution at standard and high inoculum.

Results: We report the results of 50 patients enrolled from February 15, 2020-April 30, 2020. The baseline characteristics of each group are outlined in **Table 1**. A total of 37/50 (74%) received cefazolin as definitive therapy, and complicated bacteremia was seen in 27/50 (54%). A total of 16/50 (32%) of the MSSA isolates exhibited the CzIE. Two patients in our cohort died: both of whose isolates exhibited the CzIE and received cefazolin as definitive therapy.

Table 1: Baseline characteristics

	Inoculum effect n=16	No Inoculum effect n=34	P value
Age	60.4	57.3	0.471
Male gender	11 (68.75)	24 (70.59)	1
Race			1
African American	3 (18.75)	7 (20.59)	
American Indian	0	1 (2.94)	
Caucasian	6 (37.50)	11 (32.35)	
Asian	1 (6.25)	1 (2.94)	
Other	4 (25)	9 (26.47)	
Unknown	2 (12.50)	5 (14.71)	
Ethnicity			0.882
Hispanic	4 (25)	11 (32.35)	
Charlson comorbidity index ≥ 5	10 (62.5)	13 (38.24)	0.136
On dialysis before admission	5 (25)	13 (38.24)	0.524
Immunocompromised	1 (6.25)	3 (8.82)	1
qSOFA ≥ 1	10 (62.5)	16 (47)	0.372
Jackson/McCabe			1
Non-fatal	14 (87.50)	28 (82.35)	
Ultimately fatal	2 (12.50)	6 (17.65)	
ICU admission	3 (18.75)	5 (14.71)	0.861
Source			0.546
Primary	3 (18.75)	14 (41.18)	
Secondary	13 (81.25)	20 (58.82)	
Sites of infection			0.486
Bone/joint	2 (12.5)	4 (11.76)	
CNS	0	2 (5.88)	
Endovascular	4 (25)	5 (14.71)	
Respiratory	2 (12.5)	0	
Skin and soft tissue	5 (31.25)	9 (26.47)	
Complicated bacteremia	6 (37.50)	21 (61.76)	0.136

Conclusion: We report a high prevalence of the CzIE in MSSA BSIs in a major US urban hospital network. Further evaluation of the clinical implications of the CzIE is urgently needed.

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252. Increased incidence rates of positive blood cultures shortly after chemotherapy treatment initiation among individuals treated for solid malignant tumours

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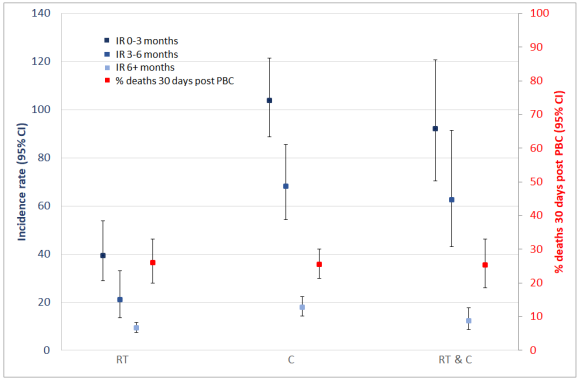
Background: Cancer treatments suppress immune function and are associated with increased risk of infections, but the overall burden of serious infectious diseases in treated patients has not been clearly elucidated.

Methods: All patients treated for solid malignant tumours with curative intent radiotherapy (RT) and/or standard first line chemotherapy (C) at the Department of Oncology at Rigshospitalet between 01/1/2010 to 31/12/2016 were included. Patients were followed from treatment initiation to new cancer treatment, end of follow up or death whichever came first. We calculated incidence rates (IR) of positive blood culture (PBC) per 1000 person years follow up using Kaplan-Meier methods, and examined the proportion who died within 30 days of PBC.

Results: 13,275 individuals were included, 4,372 (33%), 6,349 (48%), and 2,554 (19%) treated with RT, C, or concomitant RT&C, respectively, contributing 21,493 person years follow-up. 6,930 (52%) were female, the median (IQR) age was 63 (53, 70), and the most common cancer diagnoses were breast (n = 2,593 [19%]), colorectal (n=1,422 [11%]), and stomach (n=1,246 [9%]).

Overall, 564 individuals (4%) experienced 746 unique episodes of PBC, 188, 408, and 150 events in 143, 311 and 110 individuals treated with RT, C, and RT&C, of which 49 (26%), 104 (25%), 38 (25%) died within 30 days of PBC, respectively. IR of PBC significantly varied by treatment: 13.0 (95% confidence interval 11.1, 15.4), 43.9 (39.3, 49.0) and 32.0 (26.5, 38.5) per 1000 person-years follow up in the RT, C and RT&C groups, respectively (IR ratio = 3.36 (2.75, 4.10) and 2.45 (1.91, 3.14) for C and RT&C compared to RT, respectively) and time since treatment (figure). *Escherichia coli* (n=185, 25%), *Staphylococcus aureus* (n=102, 14%), *Klebsiella pneumoniae* (n=76, 10%), *Enterococcus faecium* (n=48, 6%), and *Enterococcus faecalis* (n= 37, 5%) were the top 5 microorganisms identified and did not vary by treatment category, p = 0.11, there were 31 (4%) cases of *Candida*.

Incidence rate of positive blood culture (PBC) by time since treatment initiation (0–3 months, 0–6 months and >6 months) and the proportion who died within 30 days of PBC by treatment type among individuals treated for solid malignant tumours with radiotherapy [RT], chemotherapy [C] and concomitant RT&C at Department of Oncology at Rigshospitalet, University of Copenhagen between 01/1//2010 to 31/12/2016.



Conclusion: PBCs are seen more often within 3 – 6 months after C than after RT alone. PBCs are not common, but when they occur, mortality is high. More precise risk factors for PBC and prophylactic means and empiric treatments in selected high-risk patients should be investigated.

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