

Impact of ceftazidime-avibactam alone or as combination therapy on mortality and clinical response in patients with a carbapenem-resistant gram-negative infection



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Background

- Ceftazidime-avibactam (caz-avi), a novel β -lactam/ β -lactamase inhibitor, is commonly utilized for carbapenem-resistant gram-negative infections (CR-GNI)
- Benefits vs risks of combining caz-avi with other agents are unclear
- OBJECTIVE:** To evaluate the impact of caz-avi monotherapy (MT) vs combination therapy (CT; i.e., any concomitant use of gram-negative-active antibiotics)

Methods

- Retrospective cohort study, inpatients with CR-GNI treated with caz-avi were identified at 9 U.S. hospitals
- Data were populated using RedCap by chart review at individual centers
- Impact of caz-avi monotherapy (MT) vs combination therapy was studied using logistic regression, controlling for baseline patient and hospital factors
- Overlap weighting based on the propensity score was used to adjust for confounding in the comparison between two cohorts of caz-avi use
- An adjusted odds ratio (aOR) with 95% confidence interval (CI) was used to assess the primary and secondary outcomes

Primary and Secondary outcome

- The primary outcome was in-hospital mortality or discharge to hospice (death)
- Secondary outcomes were the length of stay (LOS), resolution of infectious signs and symptoms (clinical response), 90-day recurrent infection, and future infection with caz-avi-resistant organism

Table 1: Species Distribution of CR-GNI treated with ceftazidime-avibactam

Treated Organism	Frequency (%)
<i>Klebsiella spp.</i>	157 (39.3%)
<i>Pseudomonas aeruginosa</i>	94 (26.5)
<i>Enterobacter spp.</i>	43 (11.7%)
Other	42 (11.4%)
<i>Escherichia coli</i>	24 (6.5%)
<i>Achromobacter spp.</i>	9 (2.4%)

Results

Figure 1: Overlap weighting based on the propensity score

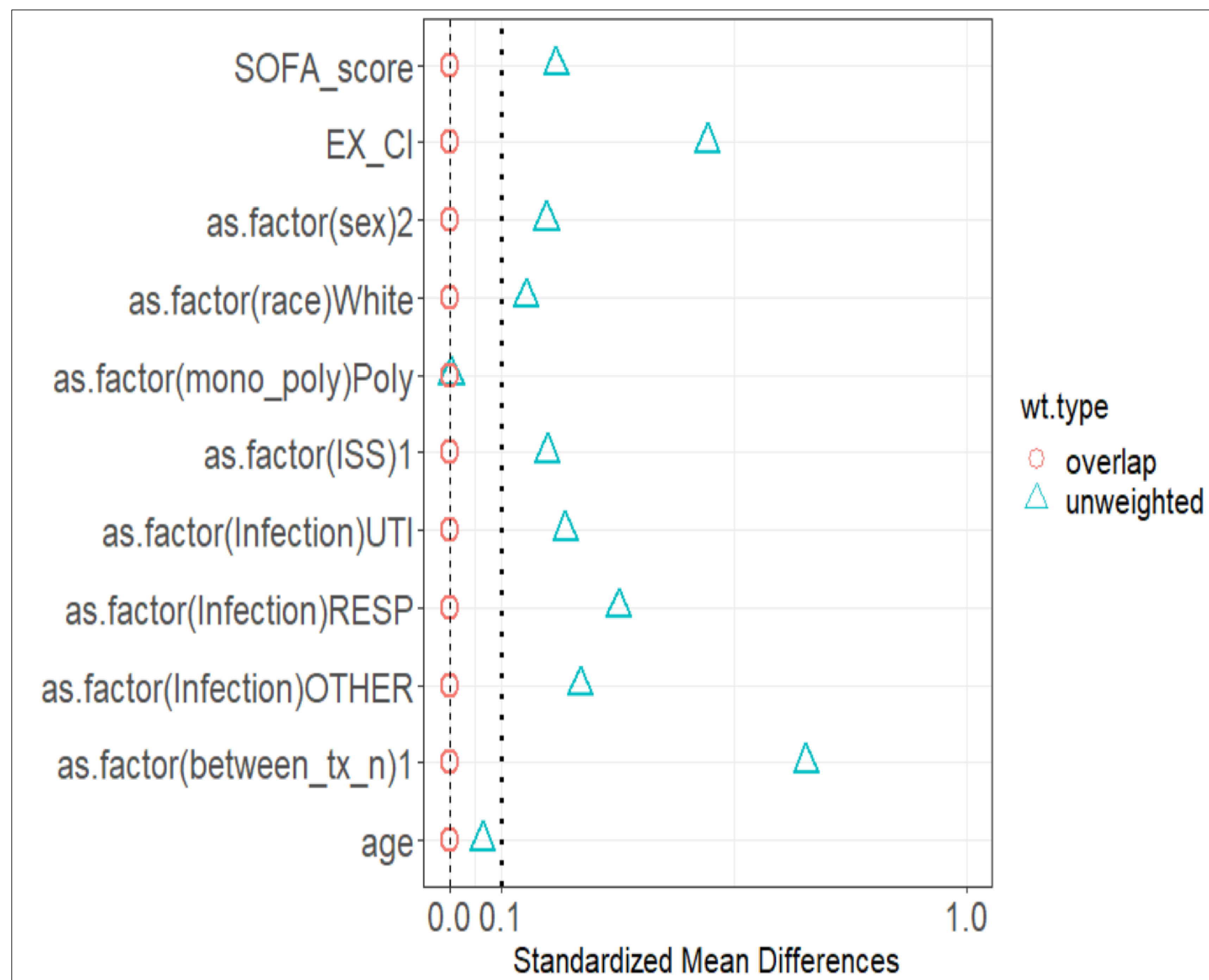


Table 2: Primary and secondary outcomes

	Outcome	Adjusted Odds Ratio	95% Confidence Interval
Combination therapy (CT) vs Mono Therapy (MT)	Death	0.87	0.47, 1.59
	Clinical response	1.80	1.03, 3.15
	90-day recurrent infection	1.57	0.89, 2.76
	Future infection with caz-avi-resistant organism	0.31	0.06, 1.51
	For LOS, the weighted log-rank test (stratified by center) gave p=0.29		

*Weighted logistic regression using overlap weighting was used to calculate adjusted mortality

- 369 patients received caz-avi as targeted therapy for a CR-GNI
- Overall, patients treated with MT and CT were similar at baseline and had comparable baseline demographics, although patients treated with CT were more likely to be in the ICU and receive a concomitant empiric in vitro-concordant antibiotic
- The most common organism was *Klebsiella* spp. (39.3%) followed by *Pseudomonas aeruginosa* (26.5%)
- CT most commonly included either aminoglycoside (12.7%), carbapenem (10.3%), colistin (9.8%), and quinolone (5.7%)
- Overall 88 (23.8%) patients died and CT (vs MT) displayed similar adjusted mortality risk (aOR [95%CI]: 0.87 [0.47-1.59])
- CT (vs MT) was associated with greater odds of clinical response (aOR: 1.80 [95%CI:1.03-3.15])
- CT and MT displayed similar rates of 90-day recurrent infection (aOR: 1.57 [95%CI:0.89-2.76])
- There is no significant difference between MT and CT in future infection with caz-avi-resistant organism (aOR: 0.31 [95%CI:0.06-1.51])
- For LOS, the weighted log-rank test (stratified by center) gave p=0.29 indicating no difference in LOS between CT and MT

CONCLUSION:

Patients with CR-GNI displayed similar survival and LOS when treated with caz-avi alone or as combination therapy although higher clinical response was observed in combination therapy users

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