Comparative Acute Kidney Injury Risk Across Antibiotics Commonly Used for Severe Infections in Hospitalized Patients

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Introduction

Antibiotics are among the most frequently prescribed medications in hospitalized patients, and several agents have been associated with an increased risk of acute kidney injury (AKI). However, AKI risk is not determined by antibiotic exposure alone; it is also influenced by patient-specific factors such as baseline renal function, comorbidities, concomitant medications, and clinical interventions. This study aims to evaluate differences in AKI risk according to antibiotic type using real-world clinical data and to assess potential effect heterogeneity by patient-level characteristics.

Data

Data Description

- Data source: Hospital-based clinical data from Kyung Hee University Medical Center, 2013–2025
- Initial population: 18,793 patients who received antibiotics for multidrug-resistant infections
- Antibiotics of interest: Vancomycin, Meropenem, Ertapenem, and Teicoplanin
- Same-day concurrent antibiotic administration was excluded, and antibiotic switching during hospitalization was analyzed as time-varying exposure
- Patients aged <18 years or those without laboratory or baseline clinical data were excluded
- Analytic variables (p = 52) included demographics, vital signs, laboratory tests, comorbidities, antibiotic exposure, and AKI outcome
- Final study population: 8,718 patients

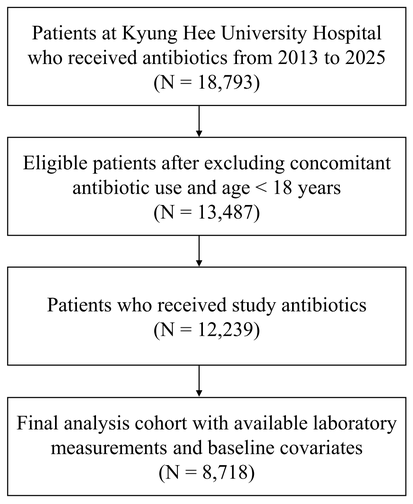

Figure 1. Flow chart

Definition of outcome

- Antibiotic-induced nephrotoxicity was assessed using acute kidney injury (AKI)
- AKI was defined as either:
  - an increase in serum creatinine of ≥ 0.3 mg/dL within 48 hours
  - ≥ 1.5 times from baseline value within 7 days after antibiotic administration

Antibiotic	Patients (N)	AKI events (n)	AKI incidence (%)
Vancomycin	4,112	451	11.0
Meropenem	3,463	736	21.3
Ertapenem	1,110	89	8.0
Teicoplanin	333	70	21.0

Table 1. AKI events by antibiotic group
Patients could be counted in more than one antibiotic group if they received multiple antibiotics at different time points during hospitalization.

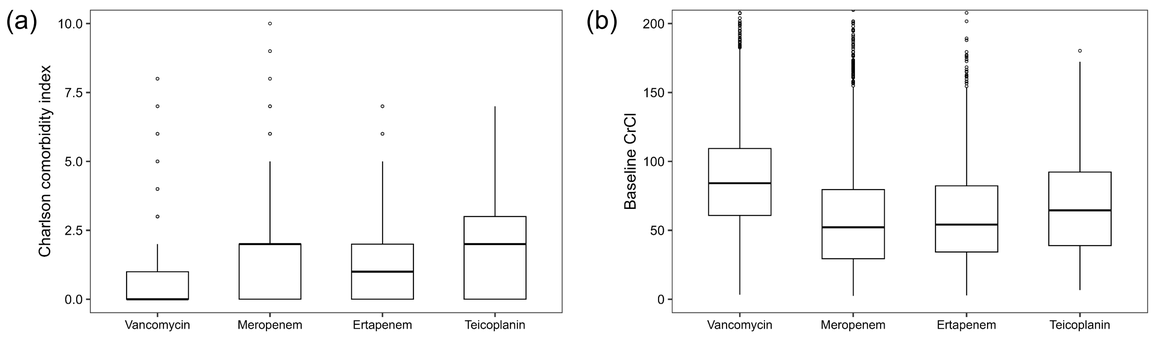

Figure 2. Baseline comorbidity burden and renal function by antibiotic group
(a) Charlson Comorbidity Index (CCI); (b) Creatinine clearance (CrCl)

- The distributions of baseline CCI and CrCl varied by antibiotic group, indicating differences in baseline comorbidity burden and renal function.

Method

Calculation of Weights for Marginal Structural Model (MSM)

- Stabilized inverse probability of treatment weights (IPW):

$$SW_{ik} = \prod_{k=0}^{K} \frac{P\left(A_{ik} = a_{ik} \middle| \bar{A}_{i(k-1)} = \bar{a}_{i(k-1)}\right)}{P(A_{ik} = a_{ik} | \bar{A}_{i(k-1)} = \bar{a}_{i(k-1)}, \bar{L}_{ik} = \bar{l}_{ik})}$$

- A_{ik}: antibiotic exposure for individual i at time k
- $\bar{A}_{i(k-1)}$: antibiotic exposure history before time k
- $\bar{L}_{ik}$: covariate history up to time k

Weighted Pooled Logistic MSM

- This model was fitted on the patient-day long-format data
- Each patient-day was weighted by the cumulative stabilized IPW
- Outcome model:

$$logit\{P(Y_{ik} = 1 | Y_{i,k-1} = 0)\} = \beta_0(t_k) + \beta_1 I(A_{ik} = Meropenem) + \beta_2 I(A_{ik} = Ertapenem) + \beta_3 I(A_{ik} = Teicoplanin)$$

- Y_{ik}: AKI event indicator for individual i at time k
- $\beta_0(t_k)$: time effect modeled using natural cubic splines
- This model estimates the marginal odds ratios for AKI associated with each antibiotic exposure

Result1 : Weighted Pooled Logistic MSM

$$OR_a = \frac{odds(AKI | A_{ik} = a)}{odds(AKI | A_{ik} = Vancomycin)} = \exp(\beta_a)$$

Antibiotic	OR	Confidence Interval	P-value
Meropenem	1.2225	(1.0550, 1.4165)	0.0075
Ertapenem	0.4705	(0.3569, 0.6201)	< 0.0001
Teicoplanin	1.4334	(1.0659, 1.9277)	0.0172

Table 2. IPW-weighted odds ratios for AKI by antibiotic exposure. Reference group: Vancomycin

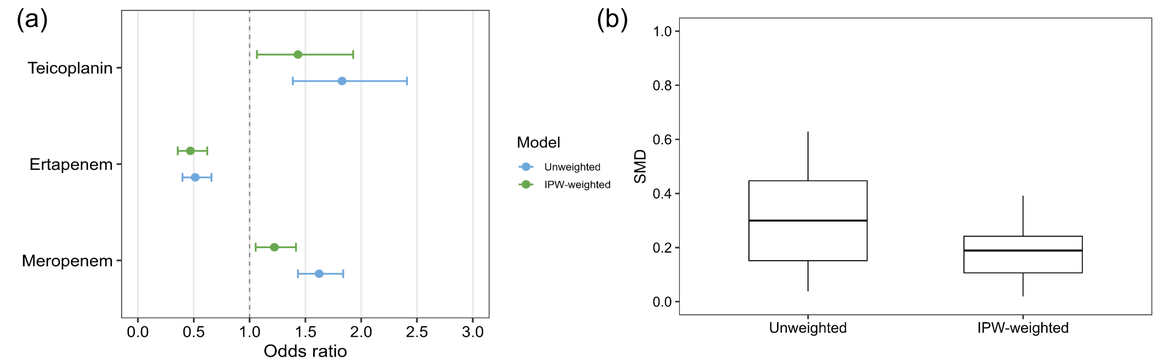

Figure 3. AKI odds ratios and covariate balance before and after IPW adjustment
(a) Odds ratios from unweighted and IPW-weighted models
(b) Maximum absolute Standardized Mean Differences (SMDs) before and after IPW

- After IPW adjustment, meropenem and teicoplanin showed significantly higher odds of AKI compared with vancomycin, whereas ertapenem showed significantly lower odds of AKI.
- IPW reduced maximum absolute SMDs, indicating improved covariate balance.

Result2 : Effect Modification by Comorbidities

$$logit\{P(Y_{ik} = 1 | Y_{i,k-1} = 0)\} = \beta_0(t_k) + \beta_a I(A_{ik} = a) + \gamma C_i + \delta_a I(A_{ik} = a) C_i$$

$$a \in \{Meropenem, Ertapenem, Teicoplanin\}$$

$$OR_{C=0} = \frac{odds(AKI | A_{ik} = a, C_i = 0)}{odds(AKI | A_{ik} = Vancomycin, C_i = 0)} = \exp(\beta_a),$$

$$OR_{C=1} = \exp(\beta_a + \delta_a),\ OR_{EM} = \frac{OR_{C=1}}{OR_{C=0}} = \exp(\delta_a)$$

- C_i: Comorbidity status, δ_a: antibiotic by comorbidity interaction coefficient

Antibiotic	$OR_{C=0}$	$OR_{C=1}$	OR_{EM}
Meropenem	1.29 (1.09, 1.52)	0.84 (0.61, 1.42)	0.65 (0.46, 0.93)
Ertapenem	0.55 (0.41, 0.74)	0.19 (0.10, 0.35)	0.34 (0.17, 0.69)
Teicoplanin	1.55 (1.12, 2.15)	0.91 (0.46, 1.78)	0.59 (0.28, 1.24)

Table 3. Stratified IPW-weighted odds ratios by cerebrovascular disease status

Antibiotic	$OR_{C=0}$	$OR_{C=1}$	OR_{EM}
Meropenem	1.37 (1.16, 2.15)	0.76 (0.56, 1.03)	0.56 (0.39, 0.79)
Ertapenem	0.54 (0.40, 0.74)	0.25 (0.13, 0.48)	0.45 (0.22, 0.93)
Teicoplanin	1.46 (1.04, 2.05)	1.29 (0.72, 2.31)	0.88 (0.45, 1.74)

Table 4. Stratified IPW-weighted odds ratios by diabetes without chronic complication status

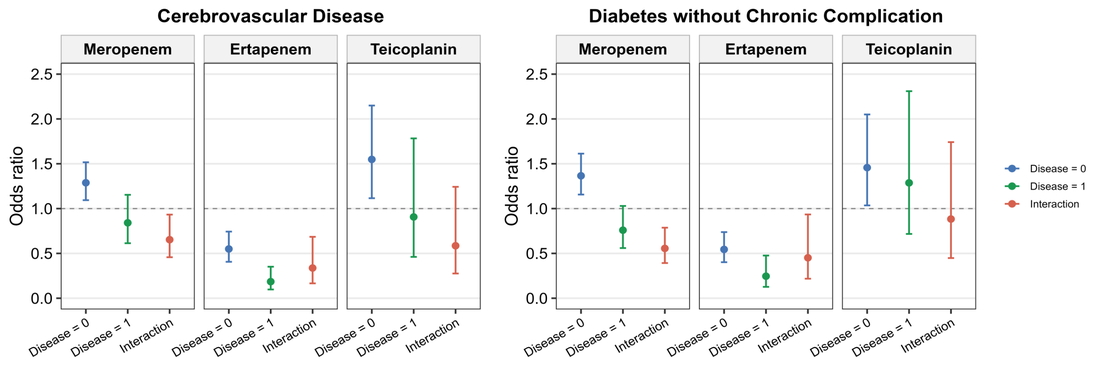

Figure 4. Stratified antibiotic-specific odds ratios and interaction effects by comorbidity status

- Cerebrovascular disease showed evidence of effect modification with lower relative AKI odds for meropenem and ertapenem compared with vancomycin in the disease subgroup.
- Diabetes without chronic complication showed a similar pattern, particularly for meropenem and ertapenem, suggesting that comorbidity status may modify antibiotic-specific AKI risk.

Conclusions

- In this time-varying causal analysis, AKI risk differed across commonly used antibiotics after IPW adjustment.
- Compared with vancomycin, meropenem and teicoplanin were associated with higher odds of AKI, whereas ertapenem showed lower odds.
- IPW reduced covariate imbalance, supporting improved comparability across antibiotic exposure groups.
- Cerebrovascular disease and diabetes without chronic complication showed potential effect modification in the association between antibiotic type and AKI risk.

References

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