Ninety-Day Adverse Events Following Systemic Antibiotic Treatment for Early, Delayed, and Late Periprosthetic Joint Infection After Total Hip Arthroplasty

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BACKGROUND

- Systemic antibiotics are fundamental to the treatment of periprosthetic joint infection (PJI) following total hip arthroplasty (THA), yet their adverse-event burden remains incompletely characterized.
- While most PJI studies emphasize infection eradication, reoperation, and implant retention, antibiotic-associated renal, hepatic, hematologic, gastrointestinal, allergic, and cardiac complications may also meaningfully affect treatment tolerance and recovery.
- This study evaluated 90-day adverse events following systemic antibiotic treatment for THA PJI and compared event profiles according to the timing of infection.

METHODS

- A retrospective cohort study was performed using a federated, de-identified electronic health record network.
- Adults who developed hip PJI following THA were identified using procedural and diagnosis codes.
- To improve diagnostic specificity, inclusion required:
  - ≥2 PJI diagnosis codes
  - Systemic antibiotic exposure within 1 month of the first PJI diagnosis.
- Patients were stratified according to the timing of PJI after the index THA:
  - Early PJI: <3 months
  - Delayed PJI: 3 months to 1 year
  - Late PJI: >1 year
- The primary analysis evaluated the 90-day incidence of adverse events following systemic antibiotic treatment.
- Outcomes included C. difficile testing and infection, acute kidney injury, elevated AST/ALT, elevated BUN/creatinine, hematologic abnormalities, allergic reactions, toxic liver disease, and cardiac events including long-QT syndrome/torsades de pointes.
- For each outcome, patients with the adverse event before systemic antibiotic exposure were excluded from the corresponding at-risk population.
- As a secondary analysis, adverse-event rates were compared across early, delayed, and late PJI cohorts using Pearson chi-square testing.

RESULTS

- 2,076 patients met inclusion criteria: 810 early PJI; 524 delayed PJI; and 742 late PJI.
- Renal and hepatic laboratory abnormalities were the most frequently observed adverse events.
  - Elevated BUN/creatinine: 17.8% early, 21.0% delayed, and 26.7% late
  - Elevated AST/ALT: 18.7%, 16.0%, and 14.6%, respectively.
- Acute kidney injury occurred in 6.1%, 4.8%, and 4.6% of early, delayed, and late PJI patients, respectively.
- C. difficile testing occurred in 5.2%, 3.7%, and 4.7%, while hematologic abnormalities occurred in 2.9%, 3.7%, and 3.4%.
- Most adverse-event rates were similar across PJI timing groups.
- Allergic reactions were significantly more frequent in early PJI than in delayed or late PJI (3.7% vs 0% vs 0%; p<0.001).
- Diagnosis-coded C. difficile infection, toxic liver disease, and cardiac events were infrequent or not reportable because of small cell counts.

Table 1. Ninety-day incidence of adverse outcomes following antibiotic treatment for periprosthetic joint infection

Adverse Outcome	Early PJI[a] n/N (%)	Delayed PJI[b] n/N (%)	Late PJI[c] n/N (%)	P value[d]
C. difficile infection (lab)	39/757 (5.2)	18/492 (3.7)	32/684 (4.7)	0.466
C. difficile infection (diagnosis)	11/794 (1.4)	NR	NR	—
Acute kidney injury	36/595 (6.1)	19/399 (4.8)	24/523 (4.6)	0.491
Elevated AST/ALT	83/444 (18.7)	48/300 (16.0)	46/314 (14.6)	0.314
Elevated BUN/creatinine	45/253 (17.8)	35/167 (21.0)	56/210 (26.7)	0.067
Hematologic abnormalities	21/723 (2.9)	17/458 (3.7)	21/622 (3.4)	0.737
Allergic diagnoses	21/561 (3.7)	0/522 (0.0)	0/742 (0.0)	<0.001
Toxic liver disease	NR	0/523 (0.0)	NR	—
Cardiac (Long QT/TdP)	NR	NR	NR	—

CONCLUSION

- Among patients receiving systemic antibiotics for THA PJI, renal and hepatic laboratory abnormalities represented the most commonly recorded 90-day adverse events.
- Overall adverse-event profiles were broadly similar across early, delayed, and late PJI.
- These findings demonstrate a measurable short-term morbidity associated with systemic antibiotic treatment and reinforce the importance of considering treatment-related toxicity alongside infection control.
- This is particularly relevant because the duration of antibiotic therapy for PJI is often guided by limited and heterogeneous evidence, emphasizing the need to balance treatment benefit with potential adverse effects.