Influence of Minimum Inhibitory Concentration in Clinical Outcomes of *Enterococcus faecium* Bacteremia Treated With Daptomycin: Is it Time to Change the Breakpoint?

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Abstract

Background. Daptomycin has become a front-line antibiotic for multidrug-resistant *Enterococcus faecium* bloodstream infections (BSIs). We previously showed that *E. faecium* strains with daptomycin minimum inhibitory concentrations (MICs) in the higher end of susceptibility frequently harbor mutations associated with daptomycin resistance. We postulate that patients with *E. faecium* BSIs exhibiting daptomycin MICs of 3–4 μg/mL treated with daptomycin are more likely to have worse clinical outcomes than those exhibiting daptomycin MICs ≤2 μg/mL.

Methods. We conducted a multicenter retrospective cohort study that included adult patients with *E. faecium* BSI for whom initial isolates, follow-up blood culture data, and daptomycin administration data were available. A central laboratory performed standardized daptomycin MIC testing for all isolates. The primary outcome was microbiologic failure, defined as clearance of bacteremia ≥4 days after the index blood culture. The secondary outcome was all-cause in-hospital mortality.

Results. A total of 62 patients were included. Thirty-one patients were infected with isolates that exhibited daptomycin MICs of 3–4 μg/mL. Overall, 34 patients had microbiologic failure and 25 died during hospitalization. In a multivariate logistic regression model, daptomycin MICs of 3–4 μg/mL (odds ratio [OR], 4.7 [1.37–16.12]; *P* = .014) and immunosuppression (OR, 5.32 [1.20–23.54]; *P* = .028) were significantly associated with microbiologic failure. Initial daptomycin dose of ≥8 mg/kg was not significantly associated with evaluated outcomes.

Conclusions. Daptomycin MICs of 3–4 μg/mL in the initial *E. faecium* blood isolate predicted microbiological failure of daptomycin therapy, suggesting that modification in the daptomycin breakpoint for enterococci should be considered.