Clinical Correlates of Enterococcal Bacteremia: Attributable or Associated?

Str—In their analysis of clinical outcomes that correlate with enterococcal bacteremia, Caballero-Granado et al. [1] correctly state that, in observational studies, we must account for potential confounding variables to protect against making false inferences of causation. This principle was observed in their analysis of mortality, which incorporated multivariate logistic regression analysis. Unfortunately, this principle was not observed in their analysis of duration of hospital stay, which provided the only (putatively) significant association between outcome and enterococcal bacteremia [1]. Adjustment or stratification for potential confounders is essential for this analysis as well, because, compared with the control group, the patients with bacteremia exhibited a significantly higher prevalence of several baseline characteristics (i.e., cirrhosis, neutropenia, history of organ transplantation, prolonged prior hospital stay, urinary catheter use, nasogastric tube use, receipt of parenteral nutrition, and prior antibiotic therapy) [1]. Although these characteristics possibly predispose patients to develop enterococcal bacteremia, they also would be expected to be associated with prolonged hospital stays, independent of bacteremia. Furthermore, even if analysis were to show an independent association between enterococcal bacteremia and duration of stay, the possibility that unmeasured confounding variables were responsible for the association could not be excluded (as inevitably is the case in observational studies).

Thus, the title of the article (“Attributable...Duration of Hospital Stay...” [1], p. 587) is potentially misleading, and the concluding sentence of the abstract (“Enterococcal bacteremia...extends the duration of hospital stay of patients who develop it” [1], p. 587) is inadequately supported by the data presented. Perhaps the authors could provide a multivariate analysis that includes the other clinical variables (i.e., in addition to enterococcal bacteremia) as predictors of duration of hospital stay, to convince skeptical readers that bacteremia remains a significant predictor after adjustment for other known host factors.

James R. Johnson
Infectious Diseases Section, Veterans Affairs Medical Center, Minneapolis

Reference

Reply
Str—We agree with Dr. Johnson [1] that several factors should be considered when carrying out appropriate analysis of the development of enterococcal bacteremia that is associated with a hospital stay, as we did when analyzing the mortality rate [2]. It is also true that case and control subjects in our study differed with respect to some epidemiological features, as shown in table 1 of our report [2]. Therefore, it may be concluded that a longer hospital stay could be associated with one or several of these epidemiological factors, rather than with enterococcal bacteremia itself.

We disagree with Dr. Johnson’s suggestion that we should combine case and control subjects into a single group to carry out a multivariate linear regression analysis and to demonstrate that enterococcal bacteremia is an independent risk factor for extending hospital stay. In matched case-control studies, the control group is not randomly selected from a population; rather, some criteria are used to ensure that it is similar to the case group (except for the variable of interest). In our series, these criteria were age, sex, hospitalization ward, time proximity between the performance of blood cultures (with respect to those for case patients), and blood culture negative for enterococci. Thus, multiple linear regression models are not appropriate in this setting, because they would not take into account the matching criteria [3].

We performed only a univariate analysis. We think that, for some subgroups (in particular, patients with neutropenia, patients with cirrhosis of the liver, and patients who have received parenteral nutrition), there were not enough pairs to carry out a qualified stratified analysis. This is the disadvantage of stratification. On the other hand, we found that there was no difference between case and control patients with respect to the severity of the underlying conditions.

We recently published a deeper analysis—one that includes multivariate analysis—of the epidemiological characteristics of this series [4]. Our 2 reports are complementary, but their subjects, as well as their lengths, justified publishing them separately. In our second report [4], we demonstrated that, of all the epidemiological features we considered, only 3 factors were overrepresented among patients with enterococcal bacteremia: use of a urinary catheter, prior administration of antimicrobials, and neutropenia. None of these factors seems to extend hospital stay. Therefore, an extended hospital stay must be due to enterococcal bacteremia itself.

F. J. Caballero-Granado, J. M. Cisneros, and J. Pachón
Infectious Diseases Department, Hospital Universitario “Virgen del Rocío,” Seville, Spain

References
2. Caballero-Granado FJ, Becerril B, Cuberos L, Bernabeu M, Cisneros JM, Pachón J. Attributable mortality rate and duration of hospital stay...