Could Decisions to Limit Treatment Contribute to Mortality Differences between Patients with Different Presepsis Trajectories?

To the Editor:

We read Dr. Prescott and colleagues’ study describing pathways to sepsis (1) with great interest. Their identification of three distinct presepsis trajectories using latent profile analysis is robust and intuitively appealing. Moreover, the patients they describe belonging to “low,” “rising,” and “high use” classes are immediately recognizable to clinicians. But what are we to make of their finding that rising users have increased 90-day mortality (adjusted odds ratio, 1.2–2.2) compared with low users? Moreover, how to interpret the fact that high users, with more comorbidities and functional limitations, have similar survival to low users in their validation cohorts?

The authors speculate about reasons that rising use would uniquely predispose to vulnerability, and hence predict mortality, from impaired immunity to disruptions in the microbiome. These hypotheses involve two assumptions: First, that rising use is associated with excess mortality, and second, that this excess mortality is related to pathobiology.

Although it seems plausible that rising use would confer additional mortality risk compared with “low use,” it is harder to understand why rising use should predict higher mortality than high use. What if the issue is not that rising users are more likely to die but, instead, that high users are less likely to die? In addition, what if the survival advantage for high-use subjects is unrelated to pathobiology?

Mortality is determined by factors beyond an illness’ intrinsic survivability, including patients’ goals and treatment preferences. Indeed, most deaths among the critically ill, such as those who die of sepsis, occur after decisions to limit treatment (2). Therefore, when comparing 90-day mortality among groups of patients with different presepsis trajectories, it is important to consider whether varying tendencies to limit treatment contribute to survival differences.

Reconsidering the data through this lens, it may be that subjects in the high-use group died at a lower than expected rate because they were willing to undergo more aggressive interventions with the goal of prolonging life (e.g., intubation, tracheostomy, hemodialysis, etc.) These interventions could reduce mortality for high-use subjects while lengthening hospitalizations and yielding survivors with many comorbidities, functional limitations, and frequent use of skilled nursing facilities; in other words, survivors who look like the high users the authors describe. In contrast, rising users may not opt for such aggressive care, instead placing limits on life-sustaining treatment.

This explanation would seem to fit with prototypical patients: the patient with a new terminal malignancy who values independence and foregoes aggressive treatment for sepsis, versus the nursing home resident with a tracheostomy and feeding tube who keeps coming in with aspiration pneumonia and surviving. It is also supported by studies of how people accommodate increasing debility and factor present function into decisions about their goals and future quality of life (3).

We do not mean to suggest that goals of care mediate the entire relationship between presepsis trajectory and mortality. Clearly, decisions to limit treatment are typically made when the prognosis is grim. Still, goals and preferences could explain some of the observed survival differences, and thus warrant inclusion in multivariate models.

The authors could use information they already have to evaluate whether patient’s goals varied with presepsis trajectory. Among Health and Retirement Study decedents, there are data on whether treatment was limited at the end of life. Similarly, Health and Retirement Study surveys and Medicare claims could be used to ascertain whether rising use and high use patients used hospice at different rates. Given that many of the excess deaths in the rising use group occurred after hospital discharge, it may be that more rising users pursued hospice care. These data would strengthen the investigators’ ability to ascribe observed survival differences to underlying pathobiology.

Author disclosures are available with the text of this letter at www.atsjournals.org.

Brian L. Block, M.D.* Michael Matthey, M.D.
University of California, San Francisco
San Francisco, California

ORCID IDs: 0000-0002-0779-1170 (B.L.B.); 0000-0003-3039-8155 (M.M.).

*Corresponding author (e-mail: brian.block@ucsf.edu).

References

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