CRITICAL CARE

COMMENTARY

Clinical prediction rules for invasive candidiasis in the ICU: ready for prime time?

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See related research by Hermsen et al., http://ccforum.com/content/15/4/R198

Abstract

Invasive candidiasis is a major source of morbidity and mortality in critically ill patients. The creation and validation of clinical prediction rules to identify patients at high risk has given clinicians access to advanced management strategies, such as targeted prophylaxis, pre-emptive therapy, and protocolized empirical therapy.

In the previous issue of *Critical Care*, Hermsen and colleagues [1] presented a validation of two clinical prediction rules for invasive candidiasis (IC) and propose a new one based on common risk factors found in ICU patients.

IC is the third to fourth most common cause of bloodstream infections in ICUs in the United States [2]. This infection is associated with substantial mortality (40%) and increased healthcare costs (approximately $40,000) [3]. Considerable research has been undertaken to identify patients at high risk for this infection and may benefit from prophylaxis or early therapy strategies, such as pre-emptive therapy and empirical therapy [4,5].

Hermsen and colleagues have attempted to validate two clinical prediction rules for IC in ICU patients in the setting of a case control study using contemporary patients from the Nebraska Medical Center. During the study period, the overall incidence of IC in patients with a length of stay ≥4 days was 2.3%, which is the typical incidence of IC seen in most ICUs in the US. Hermsen and colleagues selected patients with invasive candidiasis and matched them to three uninfected controls to validate the performance of the Paphitou [6] and Ostrosky-Zeichner rules [7]. These two rules were originally constructed through retrospective chart reviews and logistic regression to identify high risk patients for a multicenter clinical trial of antifungal prophylaxis in the ICU setting. In their validation, Hermsen and colleagues found that the Paphitou rule had sensitivity approximately 40%, specificity approximately 80%, and an unusually low positive predictive value (PPV) with a negative predictive value (NPV) >98%. The Ostrosky-Zeichner rule had sensitivity approximately 70%, specificity approximately 60%, with similar PPV and NPV performance. They then proceeded to create their own prediction rule (NMC rule), which includes any broad-spectrum antibiotic use, central venous catheter (D1 to D3), abdominal surgery (D-7 to D3), immunosuppressants (D-7 to D0), total parenteral nutrition (D1 to D3) and mean pre-ICU length of stay. The performance of their rule was reported as sensitivity 84.1%, specificity 60.2%, PPV 4.7%, NPV 99.4%, and area under the receiver operating characteristic curve (AUC ROC) 0.770.

Although the NMC rule shows very attractive risk prediction performance, one must approach these results with caution due to two important limitations of this study. The first is that the rule was derived from a single-center retrospective chart review study and it was created and validated in the same population. That was the same problem the Paphitou rule encountered, as performance in the original single-center study was quite predictive, but when we attempted to validate it in a multicenter data set, the rule lost a significant amount of sensitivity and specificity. The second limitation is more technical, and it has to do with attempting to evaluate PPV and NPV in case-control studies with an artificially created 'incidence' of disease. In the case-control study the incidence of IC would be 25%, which is 10 times higher than the incidence seen typically in patients who have an ICU length of stay ≥4 days.

Nevertheless, the NMC rule is a welcome addition to a set of clinical prediction rules that are currently in various stages of validation in prospective studies, such as the *Candida* score [8,9]and the MSG rule [10]. One can envision a near future in which ICU patients are systematically screened for risk of IC while in the ICU, giving them access to antifungal prophylaxis or enhanced

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surveillance with biomarkers and pre-emptive therapy of early disease, or as Hermsen and colleagues also propose, these rules can also be used to determine patients who would be less likely to benefit from these interventions and thus to discontinue antifungal prophylaxis in the evolution of antifungal stewardship.

Abbreviations

IC, invasive candidiasis; NPV, negative predictive value; PPV, positive predictive value.

Competing interests

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