Predicting enteral feeding intolerance in patients with sepsis: Why and how?

Enteral feeding intolerance is a common problem in critically ill patients. It occurs in approximately one-third of patients in the intensive care unit (ICU) and is generally associated with adverse clinical outcomes.[1,2] In this issue of the journal, the study by Hu *et al*.[3] aimed at developing and validating a predictive model for enteral feeding intolerance in ICU patients with sepsis. The study was a dual-center retrospective study. Patients were included if they had sepsis as defined by the Sepsis 3.0 Consensus criteria and had no contraindications to enteral feeding.[3] Exclusion criteria were severe septic shock, gastrointestinal tumor, chronic diarrhea, gastrointestinal bleeding, gastrointestinal surgery, or length of ICU stay less than 7 days. The patients were fed through a nasoduodenal tube or nasogastric tube by intermittent (q4h, four times a day) or bolus feeding. The authors defined enteral feeding intolerance as vomiting, distension, high gastric residuals (gastric residual volume: ≥500 mL/24 h), diarrhea, and high intra-abdominal pressure (intra-abdominal pressure: >12 mm Hg). The study included 195 patients; data of 124 patients for 27 clinical indicators from one hospital were used to train the model, and data from 71 patients from another hospital were used for external validation. These models included logistic regression, naive Bayesian, random forest, gradient boosting tree, and deep learning (multilayer feed-forward artificial neural network (ANN) algorithm). Eighty-six (44.1%) patients were diagnosed with enteral feeding intolerance. The study found that the five models performed reasonably well with the areas under the receiver operating characteristic curve (AUC ROC) ranging between 0.70 and 0.94. The deep learning model achieved the best performance, with areas under the receiver operating characteristic curve of 0.82 (95% confidence interval (CI): 0.74–0.90) and 0.79 (95% CI: 0.68–0.89) in the training and external sets, respectively. Lower respiratory tract infection was the most important contributing factor, followed by peptide enteral nutrition and shock.[3]

The study by Hu *et al*.[3] is a welcome addition to the literature on enteral feeding intolerance. However, these results should be interpreted with a few considerations.

First, there has been no standard definition for enteral feeding intolerance. A systematic review identified 43 definitions of enteral feeding intolerance.[1,2] Therefore, the generalizability of the findings of the current study would be dependent on using the same definition used by Hu e*t al*.[3] This obviously begs the need to develop a uniform definition of enteral feeding intolerance, thereby leveling the playing field for measuring clinically relevant outcomes.

Second, with the wide variation in the definitions used, the reported prevalence of enteral feeding intolerance varied between 2% and 75% across different studies.[1,2] In the current study, the prevalence of enteral feeding intolerance is 44%. Again, the generalizability of the findings would greatly depend on the studied population and the prevalence of enteral feeding intolerance.[1]

Third, several studies have demonstrated that enteral feeding intolerance is associated with increased mortality.[4] In the current study, there is no association between enteral feeding intolerance and mortality. Data on other clinical outcomes such as length of stay are not reported. Therefore, the implications of predicting enteral feeding intolerance by using the reported models on clinically important outcomes are unclear based on the current study. Notably, the reported mortality in the current cohort (12/195, 6%) is lower than what would be expected for such a critically ill cohort with a mean acute physiology and chronic health evaluation (APACHE) II score of 23. Therefore, the prediction model would need to be validated in a larger multicenter cohort.

Fourth, predictive tools of enteral feeding intolerance would be clinically relevant if they can be used to guide interventions that are effective for prevention or early treatment. Unfortunately, the effectiveness of existing preventive or therapeutic options for enteral feeding intolerance, including, for example, prokinetic agents, is modest or limited.[5] A systematic review of 13 randomized controlled trials (n = 1341 critically ill patients) assigned to receive a prokinetic agent (metoclopramide, erythromycin, domperidone) or placebo, demonstrated that prokinetics reduced gastric residual volumes (RR: 0.69; 95% CI: 0.52–0.91) and enteral feeding intolerance (17.3%; 95% CI:

5–26.8) without any difference in vomiting, diarrhea, pneumonia, or mortality.[6] Prediction models for enteral feeding intolerance may be useful as a tool for randomized controlled trial enrichment by enrolling patients at risk for enteral feeding intolerance instead of enrolling all comers.

Fifth, patients were fed either by bolus or intermittent feeding, but none was fed by continuous feeding. Existing data suggest that continuous feeding is associated with a lower overall incidence of enteral feeding intolerance.[7]

Addressing enteral feeding intolerance is considered one of the research priorities in critical care nutrition.[8] Enrollment to randomized controlled trials for therapeutics can be enriched using effective predictive models for enteral feeding intolerance.

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