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EDITORIAL

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# Predicting nosocomial pneumonia in the ICU . . . an ongoing challenge

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Pneumonia is the most frequent manifestation of infection in Intensive Care Units (ICUs); its incidence varies between 7 and 44 episodes per 100 admissions, according to the study population, type of surveillance and infection definition [1, 2]. Nosocomial pneumonia significantly affects the outcome of ICU patients [3] and is associated with significant morbidity and economic burden [4, 5]. Crude mortality rates from ventilator-associated pneumonia range from 20 to 70% with an attributable mortality accounting for a third of all deaths [1, 6]. Early identification of patients at higher risk for infection would help in the designing and testing of effective prevention strategies; such a challenge requires risk assessment based on reliable scoring systems that integrate all significant predisposing factors for infection, consider the dynamics of disease progression and may finally become a useful tool for clinical decision-making.

The objective of the study by A. Kropec and collaborators in the present issue of *the Journal* was to develop a scoring system for identifying patients at risk for nosocomial pneumonia in adult medical and surgical ICUs. They conducted a 2-year prospective cohort study involving a total of 756 ICU patients; 129 met the study definition for nosocomial pneumonia (17 episodes per 100 admissions). Independent risk factors for infection were identified using multivariate analysis. The model was developed applying the proportional hazards regression model proposed by Cox in 1972 for the event-specific hazard functions that takes the timing of events (pneumonia, death or discharge from the unit) into account. The authors applied statistical modeling appropriate for time-to-event data, but using information available on admission to the unit. Independent variables retained in the scoring system included the absence of infection on ICU admission, the need for thoracic drainage, the use of antacids, oxygen tension ($pO_2$) greater than 110 mmHg, and therapy with fresh frozen plasma or antithrombin 3; additional variables that predicted nosocomial pneumonia occurring in the 2nd week after ICU admission were male gender, emergency surgery and the presence of neurologic disease. Points (derived from the regression equations) were attributed to each of these variables and summed up: the higher the score, the higher was the probability of developing the infection. Sophisticated statistical techniques were applied to develop and cross-validate the scoring systems presented: internal validation was good.

In the past decade, several groups have used multivariate techniques to identify independent risk factors for pneumonia in ventilated and non-ventilated patients [1, 7–9]. Variables independently associated with nosocomial pneumonia included age greater than 70 years, underlying disease, shock, depressed consciousness, the use of intracranial pressure monitoring, chronic lung disease, chest or upper abdominal surgery, use and duration of mechanical ventilation, more frequent changes of ventilator circuits (daily vs every 48–72 h), reintubation, large volume tube feedings or gastric aspiration, use of $H_2$ blockers with or without antacids, and fall or winter season. Bronchoscopy was also identified as an independent risk factor for infection. Host factors such as obesity, poor nutrition, smoking, intravenous drug use, male gender, as well as defects in cell-mediated immune response may constitute additional predisposing factors. A number of these factors were taken into account in the study presently published in *the Journal* and some independently predicted the occurrence of pneumonia when recorded on admission.

Importantly, the scoring system developed by Kropec and collaborators has to be computed on admission to the unit, can only be applied to patients residing in the ICU

for at least 48 h and does not include time-dependent factors. In particular, the duration of intubation and/or mechanical ventilation could not be used to derive the proposed models because the score developed is aimed at predicting nosocomial pneumonia at the time of admission to the unit. Obviously, it is not possible to include the duration of ventilation in the score. The fact that intubation (at time of admission) was not selected as an independent factor for infection in this study does not mean that duration of intubation would not increase the risk for infection, as suggested in other studies [1]. The risk increase should be estimated using the number of endotracheal tube-days before infection develops; the variables should be analyzed in multivariate models using techniques that allow the inclusion of time-dependent factors; we strongly encourage intensive care investigators to conduct further studies in the field using appropriate design and analytical methods to answer this question properly.

Patients with endotracheal or nasotracheal tubes experience local trauma to the trachea, impaired swallowing, and compromised cilial clearance. Leakage of bacteria around the cuff of the endotracheal tube, which leads to colonization of the upper airway and purulent tracheobronchitis, may be the initial step in the progression to lower respiratory tract infection; the incidence of nosocomial pneumonia can be reduced by the continuous aspiration of subglottic secretions preventing frequent microaspirations through the cuff of the endotracheal tube in mechanically-ventilated patients [10]. Such a pathogenic process, for example, was not taken into account in the design of this study aimed at developing the predicting scores.

The scoring systems built using multivariate techniques only constitute rough estimates of some of the risk factors for nosocomial pneumonia. The population studied by Kropec and collaborators is heterogeneous (two types of ICU, intubated and non-intubated patients, various primary conditions and both early and late onset pneumonia were included). As a result, the variables selected by the models differ somewhat from previously published independent risk factors. Another limitation, recognized by the authors, is the criteria used for the diagnosis of pneumonia. Although all patients with pneumonia had fever, leukocytosis, purulent sputum or tracheal secretion and a pulmonary infiltrate, the value of those criteria for the diagnosis of infection in ICU patients is somewhat doubtful; bronchoalveolar lavage and protected brush specimens are usually required for a definite diagnosis in this study population.

The probability of disease, given the results of a test or a score, is called the predictive value of the test. Positive predictive value is the probability of infection in a patient with a score predicting a high risk of pneumonia. The positive predictive value expresses the real clinical validity of the proposed scores to predict nosocomial pneumonia; in this study it was only 42% in the category of patients with the highest risk group (highest score). These results indicate that important risk factors were probably not assessed in the model presented; further research is required to improve the clinical validity of the proposed score, in particular by including time-dependent factors, which may improve outcome prediction. Finally, as recognized by the authors, their model maintained a reasonable predictive ability when internal validity was tested on the same patient cohort (cross-validation), but further validation on a separate cohort of patients (external validity) is needed to establish its clinical utility in the decision-making process.

The investigation by Kropec and collaborators should promote further work to develop and test models and predictive scores with the ultimate goal to prevent nosocomial infection.

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