

## Letter to the Editor

## Factors Influencing Outcomes in Intensive Care Unit Patients with Nosocomial Infections

## Dear Editor,

We read with interest the article by Rejeb, et al. reporting the mortality associated with nosocomial infections in critically ill patients in a Tunisian intensive care unit (ICU) and we acknowledge their work.<sup>1</sup> The investigators reported mortality rates of 38.9%, 33.3%, and 43.5% for pneumonia, urinary tract infection and bacteremia, respectively. The authors correctly pointed out that one should distinguish associated mortality from attributable mortality, but this is difficult to assess as their study lacks a non-infected control group. In order to interpret the study outcomes, we wonder if the authors might provide us with some additional information. First, early detection of sepsis is pivotal to optimize the outcomes.<sup>2,3</sup> Therefore, an adequate staffing level of well-trained nurses seems essential. However, a recent survey showed that a formal critical care nursing program exists in only 17 out of 24 European countries, and in only 13 countries, critical care nursing is a recognized specialty.<sup>4</sup> We wonder what the average nurse-to-patient ratio is in the ICU reported by Rejeb, et al. and whether there exists a formal program for critical care nursing education in Tunisia. Second, a high rate of appropriate empiric therapy is essential to increase the odds of survival in critically ill septic patients.<sup>5</sup> High rates of appropriate empiric therapy (> 85% – 90%) have been associated with non-significant attributable mortality rates.<sup>6–8</sup> Vital to increase the rate of appropriate therapy is how the intensivists judge the risk of multidrug resistance involvement. Risk factors such as prior antibiotic exposure and prolonged hospitalization have been used in the past but these features have lost their predictive value, probably because multidrug resistance is no longer an exclusive concern of the hospital but rather widespread in the community.<sup>9</sup> As an alternative for the classic risk factors for multidrug resistance, use of routine surveillance cultures have been proposed to guide empiric therapy. In a diagnostic test accuracy meta-analysis, this strategy proved to have high accuracy with pooled sensitivities up to 75% and specificities up to 92%.<sup>10</sup> We wonder if the authors can provide the rate of appropriate empiric therapy in their series, and explain which strategy they use to guide empiric therapy. Finally, antibiotics should be adequately dosed to optimize bacterial killing rates.<sup>11</sup> Obviously, dose reductions might be necessary in case of overt renal or hepatic failure, but critical illness goes along with pathophysiologic alterations that might lead to underdosing as well, mainly through an increased volume of distribution of hydrophilic agents.<sup>12</sup> Therefore, discrete renal insufficiency may result in rather optimal antibiotic concentrations rather than toxic levels, thereby raising the question whether dose reduction is always required in severe sepsis.<sup>13</sup> Unfortunately, antibiotic concentrations are highly unpredictable in critically ill patients and therefore therapeutic drug monitoring (TDM) has come to the front in order to evolve to an individualized antibiotic dosing approach.<sup>14</sup> We wonder how the authors deal with this dosing dilemma and for which antibiotic agents they use TDM. We would greatly appreciate if the authors provide a more detailed insight to how severe infections are managed in their ICU.

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## Author's Reply

Sir, we would like to thank you for your remarkable comments. About severe sepsis management, we must note that in 2016, this pathological entity was withdrawn from the definition related to infections.<sup>1</sup> Indeed, the 3<sup>rd</sup> International Consensus Definition for

Sepsis and Septic Shock took into consideration the considerable advances that have been made in the pathology, management and epidemiology of sepsis, suggesting a need for re-examination.<sup>1</sup> Nevertheless, because our study was carried out between 2010 and 2011, we can still use the old nomenclature. In this regard, our management of severe sepsis and septic shock was based on the concept of Early Goal-Directed Therapy (EGDT) without sticking to the guidelines of Rivers, et al.<sup>2</sup> This means that in our daily clinical judgment, we keep in mind early sepsis detection and early appropriate empiric therapy as recommended in Surviving Sepsis Campaign.<sup>3</sup> Unfortunately, appropriate empiric therapy rate was only 36% in our institution in 2010.<sup>4</sup> This can be explained by the lack of antibiotic stewardship program and routine surveillance cultures which is expansive and without significant benefits.<sup>5</sup>

Furthermore, we agree that the antibiotics' pharmacokinetic in critically ill patients is different from others patients and therapeutic drug monitoring is pivotal. However, antibiotic dosing is done only for vancomycin and amino-glycosides in our organization. Regarding nursing staff, our nurse to patient ratio is lower than recommended (1: 3). Moreover, there is no critical care nursing speciality and formal program for critical care nursing education in Tunisia.

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