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ICU-acquired pneumonia in immunosuppressed patients with acute hypoxemic respiratory failure: A post-hoc analysis of a prospective international cohort study

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ABSTRACT

Objective: Intensive Care Units (ICU) acquired Pneumonia (ICU-AP) is one of the most frequent nosocomial infections in critically ill patients. Our aim was to determine the effects of having an ICU-AP in immunosuppressed patients with acute hypoxemic respiratory failure.
Design: Post-hoc analysis of a multinational, prospective cohort study in 16 countries.
Settings: ICU.
Patients: Immunosuppressed patients with acute hypoxemic respiratory failure.
Intervention: None.
Measurements and main results: The original cohort had 1611 and in this post-hoc analysis a total of 1512 patients with available data on hospital mortality and occurrence of ICU-AP were included. ICU-AP occurred in 158 patients (10.4%). Hospital mortality was higher in patients with ICU-AP (14.8% vs. 7.1% $p < 0.001$). After adjustment

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for confounders and centre effect, use of vasopressors (Odds Ratio (OR) 2.22; 95%CI 1.46–3.39) and invasive mechanical ventilation at day 1 (OR 2.12 vs. high flow oxygen; 95%CI 1.07–4.20) were associated with increased risk of ICU-AP while female gender (OR 0.63; 95%CI 0.43–94) and chronic kidney disease (OR 0.43; 95%CI 0.22–0.88) were associated with decreased risk of ICU-AP. After adjustment for confounders and centre effect, ICU-AP was independently associated with mortality (Hazard Ratio 1.48; 95%CI 14.–1.91; $P = 0.003$).
Conclusions: The attributable mortality of ICU-AP has been repetitively questioned in immunosuppressed patients with acute respiratory failure. This manuscript found that ICU-AP represents an independent risk factor for hospital mortality.

1. Introduction

Immunocompromised patients often require intensive care (ICU) admission. Acute respiratory failure (ARF) may be the cause for admission or develop during the hospital course and is one of the most concerning complications in this population, carrying high morbidity and mortality. Patients with ARF may develop hospital acquired pneumonia in the Intensive Care Unit called ICU acquired pneumonia (ICU-AP). The prevalence and risk factors for ICU-AP and the impact on mortality are less known in immunocompromised patients [1]. The aim of the manuscript is to report the characteristics of ICU-AP in a large, multicentre cohort of immunosuppressed patients with acute hypoxemic respiratory failure, to define its risk factors and to assess whether it affects hospital mortality. Our hypothesis is that ICU-AP in immunosuppressed patients with acute hypoxemic respiratory failure might not represent an independent risk factor for hospital mortality.

2. Patients and methods

Efraim was a multinational, observational prospective cohort study performed by the Nine-I (Caring for critically ill immunocompromised patients) study group [1]. Statistical analyses were performed with R statistical software [2]. Further details can be found elsewhere, and full methods is reported as supplementary appendix. (Supplementary Appendix).

3. Results

The original cohort had 1611 and in this post-hoc analysis a total of 1512 immunosuppressed patients with acute hypoxemic respiratory failure with available data on hospital mortality and occurrence of ICU-AP were included. ICU-AP occurred in 158 patients (10.4%). Male gender, previous chronic kidney disease (CKD) and poor performance status Eastern Cooperative Oncology Group (ECOG) score > 2 were significantly more frequent in the group of patients with ICU-AP. The presence of neutropenia was not significantly different between patients with and without ICU-AP. Invasive mechanical ventilation was associated with higher rate of ICU-AP as compared to other types of oxygen provided. Patients with ICU-AP received more vasopressors than those without it and, bronchoalveolar lavage (BAL) was more often performed in ICU-AP patients (59.5% vs. 34.9%, $p < 0.001$). Hospital mortality was 44.1% ($n = 682$) in the total population. Risk factors associated with hospital mortality are displayed in table 1. Patients who died were older, presented a higher degree of organ failure (manifested by a higher SOFA score) and more often had a poor performance status (ECOG > 2) and neutropenia. The prevalence of ICU-AP was also higher in non survivors (14.8% vs 7.1%; $P < 0.001$). We further analysed the prognostic impact of ICU-AP and found a significantly higher mortality in immunosuppressed patients with acute hypoxemic respiratory failure with ICU-AP after ICU admission. After adjustment in a mixed model taking into account centre effect, use of vasopressors (OR 2.22; 95%CI 1.46–3.39) and invasive mechanical ventilation at day 1 (OR 2.12 vs. high flow oxygen; 95%CI 1.07–4.20) were associated with increased risk of ICU-AP while female gender (OR 0.63; 95%CI 0.43–94) and chronic kidney disease (OR 0.43; 95%CI 0.22–0.88) were associated with decreased risk of ICU-AP. When forced in the final model, neutropenia did not change the model and was not selected (OR 0.72; 95%CI 0.35–1.34). ICU-AP was also independently associated with hospital mortality in a frailty model with random effect on centres (HR 1.48, p 0.003; 95%CI 1.14.–1.91). Further details can be found in the supplementary appendix.

4. Discussion

ICU-AP is a frequent complication for immunosuppressed patients with acute hypoxemic respiratory failure. In this manuscript, we report the main findings from a large, multicentre study of ICU patients admitted across the world. Interestingly, only 10% of the patients were diagnosed with ICU-AP. A recent manuscript by Moreau et al. reported a higher incidence of ventilator associated lower respiratory tract infections (VA-LRTI) in immunosuppressed patients (16.6%), which was still lower than in the general population (24%) [3]. Regarding the type of ventilatory support, invasive mechanical ventilation showed the highest rate whilst non-invasive ventilation (NIV) showed the lowest rate for ICU-AP development. This might have important clinical implications as the development of ICU-AP in mechanically ventilated patients is associated with worse outcomes. However, this finding is difficult to interpret because of the observational nature of the study and the lack of data regarding the timing of ICU-AP with respect to intubation; whether invasive mechanical ventilation was a cause or a consequence of the higher rate of ICU-AP remains unclear.

The lack of documented aetiology for ARF was not found to be an independent risk factor for hospital mortality. These data confront a study published in 2015 that assessed the association between bacterial resistance and ICU mortality, showing that patients with clinically diagnosed and treated ICU-AP but without microbiological documentation had the best prognosis [4]. This finding opens the dilemma of how to achieve etiological diagnosis in immunosuppressed patients with ICU-AP. The use of invasive diagnostic procedures is not a risk-free approach and in light of our findings the performance of these techniques to obtain aetiology should be carefully weighted. Recently Bauer et al. found that bronchoscopy performed in immunosuppressed patients was associated with improved diagnosis and changes in management, but also with increased hospital mortality [5].

Data on Clinical pulmonary infection score (CPIS) and discrimination of ventilated vs. non ventilated pneumonia were not included as items in the database.

The key results were that poor performance status was significantly more frequent in the group of immunosuppressed patients with acute hypoxemic respiratory failure with ICU-AP, ICU-AP was independently associated with hospital mortality and the presence of neutropenia was not significantly different between immunosuppressed patients with acute hypoxemic respiratory failure with and without ICU-AP.

5. Conclusion

The attributable mortality of ICU-AP has been repetitively questioned in immunosuppressed patients with acute respiratory

failure. This manuscript found that ICU-AP represents an independent risk factor for hospital mortality.

Author statement

Please find attached the revision of a short report of patients with immunosuppression and respiratory tract infections. This is a subanalysis of a cohort study multicentric that aims to explore the mortality in patients with HAP.

We want to thank the reviewers for their time to review our manuscript.

The information has not been submitted elsewhere and all the authors approved the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2020.09.027.

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