FOCUS EDITORIAL

Focus on immunocompromised patients

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Introduction

Clinicians face several challenges treating critically ill patients. In this context, immunocompromised patients are a special population requiring specific knowledge, management and attention from the staff. Immunocompromised patients are being increasingly admitted to intensive care units (ICU), requiring complex and ideally multidisciplinary management [1]. Here, we summarize the most important recently published papers in this field.

Epidemiology and outcomes

The definition of an immunocompromised status is heterogeneous, has multiple causes and usually the degree of immunosuppression is dynamic. Indeed, there are new drugs or targeted therapies raising new challenges and changing immune defences in previously well-described populations. Accordingly, the changing landscape of malignancies, both in terms of molecular diagnosis and therapeutic options, has raised new questions regarding both diagnosis and outcomes of critically ill immunocompromised patients [2].

Mokart et al. assessed outcomes in neutropenic critically ill cancer patients [3]. Beyond usual risk factors of poor prognosis (older age, organ failure, sepsis, allogeneic stem cell transplantation), this study identified neutropenic enterocolitis as a factor independently associated with survival. In addition, in a case–control analysis, the authors failed to demonstrate any prognostic impact of neutropenia, confirming that neutropenia per se should probably not be used for triage of cancer patients [3]. Future studies may, however, be needed in this field, in particular aimed at differentiating mechanisms of

neutropenia, taking into account functional neutropenia along with associated immune defects.

Adequate empirical antibiotic treatment and source identification are cornerstones for sepsis treatment, and immunocompromised patients have poor outcome when infection fails to be identified. Progress in diagnostic procedures can prove useful in these patients. Among novel potential diagnosis strategy, 18-fluorodeoxyglucose positron emission tomography combined with computed tomography may be of help in identifying infection site in patients with sepsis and unclear infection site [4]. Although available data only suggest feasibility and potential benefits of such an approach in selected patients, additional studies are needed to validate both benefits and input of this diagnostic strategy.

Molecular oncology is definitely the appropriate tool to identify cancer patients likely to benefit from immunotherapy and targeted therapies. Toffart et al. reported in a case–control study that patients with advanced non-small cell lung cancer harbouring oncogenic mutation may be targeted by specific drugs leading to trustworthy ICU and hospital survival (57 and 50%, respectively), despite having a poor performance status, being frequently admitted for acute respiratory failure with two-thirds of them requiring invasive mechanical ventilation [5]. These results, although reported in highly selected patients and a small sample size, are a plea toward evaluation of larger ICU admission policies in these specific patients.

Finally, in a retrospective study, Wan et al. assessed the incidence of acute respiratory distress syndrome (ARDS) within 6 months of renal transplantation at their institution [6]. At 6 months after transplantation, 5% of the 1369 evaluated renal transplant recipients developed features of ARDS. The main etiologies were bacterial infection (74%), cytomegalovirus infection (12%) and invasive fungal infection (8%). Interestingly, beside underlying renal function and ARDS severity, tacrolimus-based regimen were associated with poor outcome, a finding that certainly deserves to be further explored [6].

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Table 1 Gaps in research for immunocompromised patients in critical care

Area	Potential research question
Epidemiology	Adequate description of patients' immune status along with updated epidemiology of specific population underlying condition in the era of targeted therapies Systematically assess selection bias by more systematically assessing population at risk when compared to admitted/treated population in forthcoming studies Change in immune status
Diagnostic	Adequately designed diagnostic test input of new procedures (PET-CT, multiplex PCR, point-of-care testing) in immunocompromised patients
Management	Optimizing chemotherapy/immunosuppressant agents in immunocompromised patients Assessing performance of bundle strategies aiming to improve resource use and outcome in this setting Centre effect and impact of units' expertise in managing immunocompromised patients Benefits from early and systematic palliative care in critically ill cancer patients

Treatments

Optimal oxygenation strategy in patients with acute hypoxemic respiratory failure remains controversial [7, 8]. In critically ill cancer patients at high risk of mortality, there is an urgent need for additional data. In a retrospective cohort study matched and adjusted for potential confounders, Mokart et al. found patients receiving both non-invasive ventilation (NIV) and high-flow nasal cannula oxygen therapy (HFNC) to have a lower mortality and more days free from invasive mechanical ventilation at day 28 [9]. This study should be taken cautiously as regard to unmeasured confounders that may have participated in treatment choice, but it does underline the need to perform trials specifically dedicated to this population [7–9].

Extracorporeal membrane oxygenation for refractory hypoxia is being increasingly studied in the general ICU population with a hospital mortality of 35%, as discussed in a recent report by Serpa Neto et al. [10]. Benefits of extracorporeal membrane oxygenation in immunocompromised patients remain uncertain, although an increasing body of evidence suggests feasibility in selected cases. Following a case series suggesting feasibility and some long-term survival in adult patients with haematological malignancies [11], Smith et al. reported similar results in nine paediatric critically ill neutropenic patients, the majority of whom had high-grade haematological malignancies [12]. In this setting, hospital mortality was found to be as high as 44% with long-term survival of 22% [12]. However, the studied population displayed a high rate of veno-arterial extracorporeal life support (ECLS), was highly selected, and bleeding rates were tremendously high [12]. Along the same line, Legras et al. reported a case of a patient with anti-glomerular basement membrane disease with isolated pulmonary involvement who failed to recover from pulmonary involvement and who received prolonged ECMO followed by double lung transplantation; this confirmed the feasibility of ECMO as bridge to lung transplantation not only in patients

with acute exacerbation of chronic diseases but also in selected patients with de novo lung diseases [13]. Additional studies might be required both in adult and paediatric settings to confirm these data and define those patients in whom ECMO might deserve to be considered and ultimately tested as a rescue strategy.

After demonstrating organizational factors associated with improved outcome in critically ill cancer patients (namely presence of clinical pharmacist, daily meeting with oncologist and implemented clinical protocols) [1], Soares et al. demonstrated an association between liberal visiting policies for family members and implemented processes to improve communication with families in units with higher performance as assessed by standardized mortality ratio or resource use as assessed by standardized resource use [14].

Conclusion and perspective

In many ways, the presented studies both raise questions and give answers, each step forward carrying uncertainties, challenges and underlining the changing complexity of this rapidly moving field. We are currently facing new challenges that may deserve full attention of clinicians (Table 1). Demonstrating feasibility of PET-CT or ECMO in this setting raises concerns regarding unmeasured selection bias, optimal patient selection and ultimately the risk of inappropriate care. But more importantly, a global approach aiming to evaluate and improve outcome and resource use through organizational processes or integrating palliative care early in ICU patients is probably among the next steps to be taken and assessed.

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Compliance with ethical standards

Conflicts of interest

The authors declare that they have no competing interest.

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