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EDITORIAL

Severe community-acquired pneumonia: in search of the guiding star

Pedro Póvoa[1,2,3*], Saad Nseir[4,5] and Jorge Salluh[6,7]

Community-acquired pneumonia (CAP) is a very common entity ranking as the first cause of sepsis [1]. The history and impact of CAP follows the history of humanity, being described by William Osler as the "Captain of the men of death". In 2017 there were 1.8 million sepsis-related deaths attributable to lower respiratory infections [2].

The first CAP guidelines were endorsed by the American Thoracic Society in 1993 [3]. Since then, several national and international medical societies have published guidelines on the management of outpatient and hospitalized CAP patients. Interestingly, despite the significant burden of CAP in the intensive care unit (ICU) and the fact that it differs from non-ICU CAP and general sepsis in terms of diagnostic and therapeutic management, only in 2023 guidelines on severe (S) CAP were published [4].

CAP is the leading cause of sepsis and it encompasses very particular etiologies, viral, bacterial, fungal and co-infections [1]. It has a seasonal variation and, in adults, affects predominantly men and older age groups, with multiple risk factors like chronic pulmonary disease, alcohol and/or tobacco consumption, renal failure and malnutrition [5, 6]. In addition, CAP severity varies, with 5–10% of hospitalized CAP patients being admitted in ICU for respiratory failure and/or septic shock presenting a mortality ranging to around 50% [5, 7, 8].

In the current issue of the Intensive Care Medicine (ICM), Martin-Loeches and colleagues provide the recommendations of 4 major European and South American societies on sCAP in patients without immunosuppression [4]. The authors should be commended for the publication of the first guidelines on such an important topic. The methodology used is stringent, even though the quality of evidence is rather low for the majority of the 8 questions raised by the authors (Table 1). However, this may represent not only the quality of the available evidence but also an opportunity for future research in the field.

The guidelines recommend using corticosteroids in sCAP specific patients when shock is present, except in severe acute respiratory syndrome (SARS), middle east respiratory syndrome (MERS) and influenza pneumonia. This recommendation is based on the results of the meta-analysis performed for the guidelines, showing a beneficial effect on mortality. A recent large multicenter randomized controlled double-blind trial in sCAP found no significant impact of methylprednisone on 60-day mortality [9]. However, it is important to stress that the study was stopped early due to recruitment difficulties and lacked the power to detect the expected difference between the two groups. In addition, a recent large randomized controlled double-blind trial in sCAP patients without septic shock, published after the guidelines were prepared, showed that hydrocortisone significantly reduced 28-day mortality, with no significant side effects [10]. The data from these two large trials suggest that currently there is no strong evidence to issue a recommendation for OR against routine administration of corticosteroids to all sCAP patients. It is also fundamental to stress that this recommendation does not apply to patients with viral pneumonia (other than SARS CoV-2), due to the adverse outcomes associated with the use of corticosteroids in this population [11].

In the recent guidelines, multiplex PCR testing (viral and bacterial) on respiratory specimen and serum procalcitonin (PCT) are also recommended aiming to reduce antibiotic use (low to very low quality of evidence).

*Correspondence: pedrorpovoa@gmail.com
[3] Department of Intensive Care, ICU-4, São Francisco Xavier Hospital, CHLO, Estrada Do Forte Do Alto Do Duque, 1449-005 Lisbon, Portugal
Full author information is available at the end of the article

Table 1 Recommendations and level of evidence

Recommendation	Level of recommendation	Level of evidence
Multiplex PCR testing (virus and/or bacterial detection) whenever non-standard sCAP antibiotics are prescribed or considered	Conditional	Very low
HFNO instead of standard oxygen in patients with acute hypoxaemic respiratory failure not needing immediate intubation	Conditional	Very low
NIV might be an option in certain patients with persistent hypoxaemic respiratory failure not needing immediate intubation, irrespective of HFNO	Conditional	Low
Addition of macrolides, not fluoroquinolones, to beta-lactams as empirical antibiotic therapy	Conditional	Very low
Use of PCT to reduce the duration of antibiotic treatment	Conditional	Low
Use of oseltamivir for sCAP due to influenza confirmed by PCR	Conditional	Very low
Use of empirical oseltamivir during the influenza season, when PCR is not available to confirm influenza,	Conditional	Very low
Use of corticosteroids if shock is present	Conditional	Low
Integrating specific risk factors based on local epidemiology and previous colonization to guide decisions regarding drug-resistant pathogens and empirical antibiotic prescription	Conditional	Moderate
Standard CAP therapy regimen and not specific therapy targeting anaerobic bacteria, when risk factors for aspiration are present	Ungraded, good practice statement	Absent

HFNO high flow nasal oxygen, *PRC* polymerase chain reaction, *PCT* procalcitonin, *NIV* noninvasive ventilation, *sCAP* severe community-acquired pneumonia

Although PCT use could be helpful in centers using long courses of antimicrobials when combined with clinical data [12], multiplex PCR might be of limited value in this situation, especially in patients without risk factors for multidrug resistant (MDR) pathogens. Further, the cost-effectiveness of multiplex PCR in sCAP is still to be demonstrated, as available studies have limited data to inform on outcomes improvement of this strategy [13].

We also observed that the authors recommended a similar antimicrobial strategy when risk factors for aspiration are present. One should keep in mind that aspiration pneumonia is mainly due to chemical lesions and bacteria are responsible for approximately 50% of all episodes [14]. In addition, anaerobic bacteria, even though difficult to isolate, are commonly responsible for this infection and should probably be covered at least for a short period. Therefore, the usefulness of combination therapy, including macrolides or fluoroquinolones, is still to be proven by evidence from well-designed studies for this indication.

Finally, although the guidelines have many merits, they also indirectly highlight some major shortcomings of the current literature on sCAP, especially regarding the origin of the studies backing the recommendations. Most evidence is derived from studies performed in high-income countries, especially from the northern hemisphere. The disproportional under-representation of some geographic and economic regions has major implications for the wide applicability of the present guidelines. Thus, it is legitimate to question the external validity and even feasibility of the present recommendations in low and middle-income countries (LMICs). In addition, it demonstrates that even though sCAP is one of the main causes of death in LMICs [2], few studies were performed in these settings to provide epidemiologic, etiologic, or treatment-related evidence.

Also, there are potential differences in the etiology of CAP, rates of co-infections as well as individual risk factors for poor outcomes. Higher frequency of MDR pathogens as well as less usual conditions such as tuberculosis and melioidosis must be considered in the guidelines due to their relative importance in specific geographic areas.

Lastly, some unmet needs in the present guidelines are related to the post-ICU landscape. In this scenario, as previously known in sepsis and coronavirus disease 2019 (COVID-19), understanding post-ICU clinical and functional outcomes is of utmost importance to understand its burden and properly design and implement rehabilitation and prevention strategies [15]. Among some of the prevention measures, checking the vaccination status and recommending vaccination (both pneumococcal and influenza) after discharge could potentially reduce the future risk of CAP or severe diseases.

In conclusion, as clinicians caring for critically ill patients, we are seeking a "guiding star" to help us implement the best available evidence for patients with sCAP. In this aspect, the present guidelines represent a major advance in the field and an opportunity for researchers and experts to delineate future research priorities in the field to outcome the present shortcomings.

Author details
[1] NOVA Medical School, CHRC, New University of Lisbon, Lisbon, Portugal.
[2] Research Unit of Clinical Epidemiology, Institute of Clinical Research,

University of Southern Denmark Centre for Clinical Epidemiology, Odense University Hospital, Odense, Denmark. [3] Department of Intensive Care, ICU-4, São Francisco Xavier Hospital, CHLO, Estrada Do Forte Do Alto Do Duque, 1449-005 Lisbon, Portugal. [4] CHU de Lille, Centre de Réanimation, 59000 Lille, France. [5] Team Fungal Associated Invasive & Inflammatory Diseases, Université de Lille, INSERM U995, Lille Inflammation Research International Center, Lille, France. [6] Postgraduate Program, D'Or Institute for Research and Education (IDOR), Rio de Janeiro, Brazil. [7] Postgraduate Program of Internal Medicine, Federal University of Rio de Janeiro, Rio de Janeiro, UFRJ, Brazil.

Declarations

Conflicts of interest

PP received honoraria for lectures and advisory boards from Abionic, Merck Sharp & Dohme, Sanofi, Gilead, Mundipharma and Pfizer; SN received honoraria for lectures and DSMB from Pfizer, Gilead, MSD, Biomerieux, Bio Rad, Fisher and Paykel; JS has nothing to declare.

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