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EDITORIAL

Clinical management of sepsis can be improved by artificial intelligence: no

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Artificial intelligence (AI) is a branch of computer science that generates multifaceted algorithms and rules as tools to solve complex problems that would be difficult—or almost impossible—for humans. But, can computers reason? They can certainly calculate—with astonishing speed and ever-increasing power—and they have driven scientific advances that would have been impossible without them. Even so, we are eager to believe that, for some puzzles, there's no substitute for old-fashioned human knowledge and intuition. But this view may be changing. One of the most challenging puzzles is sepsis. Sepsis is a common and life-threatening syndrome, and a leading cause of morbidity and mortality. Early identification of patients who would benefit from rapid initiation of individualized sepsis-related interventions is crucial to reduce associated mortality. Regrettably, neither clinical signs nor laboratory tests are specific of sepsis as the previous clinical case illustrates. Although many biomarkers have been assessed for ruling out or confirming sepsis, none has sufficient accuracy to be routinely employed in clinical practice [1].

Critical care patients are technologically dependent on monitoring and life-sustaining medical equipment. This context generates quantitative measurements of a huge number of physiological and analytical parameters. These large amounts of data that are captured daily and almost continuously are ripe for the application of AI. Early diagnosis of complex diseases, outcome prediction, drug development and personalize treatments are the top applications of AI in medicine today [2].

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In the field of sepsis, early detection, mortality prediction, and AI-derived algorithms aim at optimizing management of sepsis and septic shock are the main applications of AI [3]. Thus, it has been demonstrated that, using only vital sign inputs available in the ICU in real-time, an AI algorithm can predict the onset of sepsis 4–12 h prior to clinical recognition [4]. Moreover, machine learning (ML) technology has derived and validated a new "Risk of Sepsis Score" in a large emergency department (ED) population with a high discriminant capacity at the first hour of ED admission [5]. This is of the utmost importance since early identification enables anticipation and prompt management. AI methods have also demonstrated their accuracy for mortality prediction in sepsis, improving the sensitivity and specificity of the currently available scoring systems [6].

A recent randomized controlled trial has concluded that, compared with the standard clinical management, a ML-algorithm for sepsis detection in patients already admitted to the ICU resulted in a significant lower mortality rate and length of stay [7]. These findings cannot be generalized to other populations especially patients in the emergency department or in the general wards that were not included in this trial.

AI-based techniques have paid much attention to early sepsis detection and mortality prediction. Notwithstanding, information about its use for guiding sepsis shock management is not so abundant. Management of sepsis includes primarily fluid resuscitation and prompt administration of adequate antimicrobials to revert tissue hypoperfusion and eradicate invading micro-organisms. The AI Clinician, a computational model using reinforcement learning, which is able to dynamically suggest optimal treatments for adult patients with sepsis in the intensive care unit (ICU) has been validated in an independent cohort. Of note, mortality was reduced in patients in whom clinicians'

Table 1 Current barriers to implement AI in daily clinical practice

Pitfalls AI	Comments
It needs time to set up	Automation and machine learning need to be adequately validated in external cohorts
There are many statistical analyses	Different methods can be taken from AI to evaluate the interventions
Technical input	It is not possible with the current training of physicians to run this kind of tests
Technical limitations	hospitals' information systems are not prepared for these heavy systems
Ethical concerns	Algorithms will not be free of charge

prescriptions matched the AI decisions [8]. Very recently, AI-derived techniques have demonstrated to be capable of predicting response to fluid administration in sepsis using urinary output as outcome measure [9]. AI has also developed models for antibiotic resistance prediction, for the choice of empirical regimen, and for prediction of treatment response with dissimilar successes [10].

Despite these promising experiences, AI-derived systems cannot replace the physician in the clinical management of sepsis. Thus, the selection of the most appropriate treatment strategies would still require the physician clinical judgement, the patient's physical examination, and a profound knowledge of his/her medical history. Septic patients are highly heterogeneous and include vulnerable patients who have an important burden of underlying diseases. Therefore, therapy ought to be necessarily personalized and tailored to meet the requirements of each single patient [11].

Bedside examination is of the utmost importance in patients with sepsis and septic shock. Absence of key signs of infection is not uncommon in patients with sepsis. Thus, 55% of patients with sepsis in the emergency department had a body temperature below 38.3 °C and 23% had less than 37 °C. Importantly, septic patients with body temperature below 37 °C received worse quality of care with a strong and linear association between decreased body temperature and mortality [12]. Furthermore, vital signs as tachycardia or laboratory abnormalities as leukocytosis or leucopenia may not be present in patients with sepsis even in those who subsequently die.

In a recently published randomized controlled trial, a resuscitation strategy targeting normalization of capillary refill time (CRT), an easy and bedside method to assess peripheral perfusion, was associated with a strong trend towards a lower mortality and less organ dysfunction at 72 h than a lactate level-targeted resuscitation [13]. Moreover, abnormal CRT in hyperlactatemic septic patients has been shown to be a good risk stratification parameter during very early resuscitation [14].

Many clinicians are reluctant to incorporate AI algorithms into daily clinical practice, the scientific evidence is still very low, and the implementation of these tools present a great number of challenges (Table 1). It is always difficult to successfully translate advances in research innovations into clinical practice [15]. Of note, reinforcement learning approaches based on purely associative relationships (all data-driven) are difficult to be externally validated. Apart from these barriers to the implementation of these AI-derived tools, we do consider that clinical management of this complex puzzle termed sepsis requires physical examination of the patient, evaluation of imaging, and a profound awareness of the physiology and physiopathology of sepsis as well as a thoughtful knowledge of infectious diseases. Thus, in the last decade, without the support of AI, although the crude mortality rates of severe sepsis have increased, the case-fatality has notably decreased [16].

In conclusion, at present AI cannot replace the medical clinical management of sepsis. Until AI-based algorithms can incorporate courses of actions compatible with known physiology and demonstrate to prospectively modify outcomes across multiple environments, they should remain as tools in development.

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Compliance with ethical standards

Conflicts of interest

The authors declare that they have no competing interests.

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