Residual rates of mortality in patients with severe sepsis: a fatality or a new challenge?

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Residual rates of mortality in patients with severe sepsis: a fatality or a new challenge?

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Résumé en anglais
Phase III clinical trials on severe sepsis and septic shock published during the past decade have failed to reveal the superiority of any therapeutic intervention on mortality compared with evolving standards of care, with the exception of the Early-Goal Directed Therapy reported in 2001. This viewpoint paper presents an analysis of these studies in order to understand what lessons can be learned and proposes perspectives for future study designs. A total of 102 studies were selected among clinical trials published in the field of severe sepsis and septic shock from 2001 to 2013, based on the assessment of a therapeutic intervention and mortality as an outcome. Studies were further selected according to randomized, controlled trial (RCT) quality criteria and analysed according to reported data. Most (n = 61) were excluded because they did not comply with RCT quality criteria or did not report inclusion criteria or patient severity (n = 22). The 19 remaining studies were categorized into three groups depending on whether the intervention assessed led to better, worse, or equivalent outcomes. It appears that the mortality rate in the control arm, ranging from 17% to 61%, impacted the results, with a benefit reported in the studies with the highest rates. Both heterogeneous studied populations and uncontrolled diversity of care among participating centres probably contributed to discrepancies between studies assessing the same intervention. The new challenge to enhance the probability of decreasing mortality rates should include a more appropriate definition of sepsis based on more specific criteria involving biomarker use and accurate patient phenotypes.

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