Candida and severe acute pancreatitis: We won’t be fooled again

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Abstract
Several studies have suggested a role of candida in infected cases of severe acute pancreatitis (SAP). This commentary reports high incidence and mortality rates of candida infection in this setting and demonstrates the value of the colonization index to detect patients at risk for fungal infection. These findings indicate the need to review the place of antifungal therapy and prophylaxis.

Introduction
In the previous issue of Critical Care, Hall and colleagues [1] brought new insight to the pathogenic role of candida in severe acute pancreatitis (SAP). The first reports of pancreatic abscesses secondary to Candida albicans were published in the ‘80s [2], but a potential role of candida in SAP was suspected later [3,4]. Overall, a handful of articles have reported the presence of candida in infected pancreatic necrosis, but most reported only a few poorly documented cases that raised more questions than answers. Given the experience acquired with bacterial infections in SAP and the confusion generated by these reports, the relevance of published data must be clearly evaluated before therapeutic and prophylactic antifungal regimens can be prescribed.

The first points that need to be clarified are the prevalence and severity of positive candida cultures in SAP. Previous studies have reported various candida infection rates, ranging between 5% and 68.5% [5,6]. However, interpretation is difficult and depends on which population is analyzed; populations can be global [5,7] or confined to intensive care unit (ICU) cases [8,9] or all cases of SAP [9,10] or limited to infected cases [6,11]. In their well-documented ICU population, Hall and colleagues [1] reported that the an incidence of candida infection complicating SAP was 17.8% of cases. The authors also observed candidemia, which is rarely mentioned in the literature [5,8], in 27.8% of the cohort. The mortality rates reported in previous series of candida infection varied considerably (from 0% to 84% [12,13] of the cases) with increased [13], decreased [5], or identical [8,9] mortality rates compared with non-candida infections. Hall and colleagues [1] observed a twofold increase in mortality compared with non-infected SAP.

Discussion
Previous articles have frequently reported concomitant bacterial and candida microorganisms in surgical samples [5,8,9,12,14,15]. Positive candida cultures do not systematically imply active infection but might reflect simply fungal colonization. These results are difficult to interpret, leading some authors to define true and possible candida infections on the basis of dubious criteria [5]. Decreased mortality rates [5] or the absence of a difference [8,9,15] between SAP cases with positive fungal samples and those with pure bacterial cultures might be suggestive of colonization in some cases. This confusion emphasizes the value of the second issue addressed by Hall and colleagues [1]: evaluation of risk factors for candida infection and the risk scores used to assess the development of invasive candidiasis. These scores, validated in general ICU populations but not in patients with a presumed high risk such as SAP, are based on the assumption that the higher the score, the higher the probability of candida infection, while results situated in the middle range should represent colonization. The conclusions of Hall and colleagues [1], even if valid only in their institution, suggest that the most relevant tool for accurate detection of candida in SAP is the candida colonization index score. Patients with high candida colonization index scores can be considered to be at high risk for candida infection or are already infected.

These findings raise a number of additional issues. No clinical study has ever assessed the efficacy of an antifungal agent in the course of SAP. The pharmacokinetic
characteristics of antifungal drugs in necrotic pancreatic tissues are practically unknown. Previous studies have reported the therapeutic use of amphotericin B or triazoles or both [5,7-9,15], but no information on the use of echinocandins for curative purposes is currently available. However, the dose of antifungal agents, duration of treatment, and endpoints to assess clinical efficacy have never been published or even discussed.

Demonstrating that the colonization index is valid for detecting SAP patients at risk for candida infection raises the additional issue of antifungal prophylaxis. Antibacterial prophylaxis in the course of SAP has been a controversial issue since the ’70s and remains so. Several authors have proposed antifungal prophylaxis in SAP [5,7-9], although the most basic questions have yet to be resolved.

Conclusions
So that the mistakes of previous decades in the field of bacterial infection are not repeated, a step-by-step approach is required. Additional scientifically rigorous studies with accurate descriptions of cases similar to those in the article by Hall and colleagues [1] are required before prophylaxis or extensive therapeutic indications of antifungal agents in SAP can be proposed.

Abbreviations
ICU, intensive care unit; SAP, severe acute pancreatitis.

Competing interests
The authors declare that they have no competing interests.

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