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The definition of starting point for evaluation of timely adequate antifungal therapy

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Dear Editor,
We read with interest the paper of Bassetti et al. [1] on *Candida* spp. septic shock. No difference in mortality was documented for patients starting antifungal therapy before or after the first 24 h of candidemia documentation (the first blood culture known to be positive for *Candida*).

On the other hand, Kollef et al. [2], in their *Candida* septic shock series, using the onset of septic shock as starting point, showed that antifungal therapy within 24 h plus source control strikingly decreased the mortality rate.

It is noteworthy that, in the majority of reports on candidemia, the starting point was represented by the collection time of the first blood cultures shown to be positive for *Candida* thereafter [3–5]. All but one showed that “timely” antifungal therapy (less than 48 h from this

starting point) reduced the mortality rate.

It is therefore not surprising that benefits of timely antifungal therapy seem to be evident in the case of an empirical approach (i.e. antifungal added before the blood culture results). In the case of a targeted antifungal strategy (after microbiological documentation), any benefit seems to be lost.

For a blood culture to become positive, hours or even days are required after blood collection from the patient: in our experience, the mean time to positivity (TTP) for *Candida* spp. (60 isolates) is 27.5 h, with differences among species: 8.8 h for *C. tropicalis* (6 isolates) and 48.8 h for *C. glabrata* (8 isolates) (Tascini, unpublished data).

Therefore a common definition of the starting point is crucial in order to understand the real effect of an appropriate antifungal therapy on mortality. In the case of septic shock, however, immediate intervention seems to be recommended.

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