



## Reply to: “Is skin mottling a predictor of high mortality in non-selected patients with cirrhosis admitted to intensive care unit?”

### Do not misquote clinical signs

To the Editor:

We would like to thank Dr Coudroy and colleagues for their letter, which gives us the opportunity to clarify some important points.

First of all, when researchers aim to assess the prognosis value of a clinical sign or a biological tool, it is crucial to delineate a precise clinical context. Assessment of mottling prognosis value perfectly illustrates this point. Mottling is defined as patchy skin discoloration that usually starts around the knees due to heterogenic small vessel vasoconstriction, reflecting abnormal skin microperfusion [1]. More than 45 years ago, mottling was frequently noticed in patients with septic shock [2]. It has to be noticed that mottling is a dynamic clinical sign. The time of assessment may be crucial to define the mottling prognosis value.

We first reported the mottling score and its evolution during the first 24 h in the context of septic shock [3]. We found that, among hemodynamic parameters collected six hours after vasopressors infusion was started, mottling score was the strongest predictor of 14-day mortality (OR in univariate analysis: score 0–1: 1, score 2–3: 16, score 4–5: 74,  $p < 0.0001$ ). Moreover, 14-day mortality was different according the mottling score evolution between H0 and H6 (mortality when mottling score decrease: 23% vs. mortality when mottling score increase: 88%,  $p = 0.0005$ ). This illustrates the crucial importance to define the time of mottling assessment. In our study, H6 was chosen because it is the time to assess the efficacy of the initial hemodynamic management according to the recommendations of the Surviving Sepsis Campaign [4].

In another study, we assessed the mottling score during mechanical ventilation weaning to evaluate its predictive value on the weaning outcome [5]. We noticed that, during the spontaneous breathing trial, mottling could appear and the increase in the mottling score was predictive of trial failure. Once again, these results illustrates that mottling is a dynamic sign and that its prognosis value depends on the clinical context and the time of its assessment.

In our study recently published in the *Journal of Hepatology*, we focused on patients with cirrhosis and septic shock because we hypothesised that mottling score could have different prognosis value in patients with potentially cirrhosis-induced systemic vasodilation [6]. Similarly than in patients without cirrhosis in septic shock, mottling score assessed at H6 was the strongest hemodynamic parameters associated to 14-day mortality and mottling score evolution between H0 and H6 was strongly associated with 14-day mortality. Comparing these results with a population of 75 non-cirrhotic patients with septic shock, we highlighted some particularities of mottling in patients with cirrhosis. Due to higher skin perfusion in cirrhotic patients, mottling appearance was delayed in non-survivors and the sensitivity of

mottling score to predict 14-day mortality was lower whereas its specificity was excellent.

In the study by Coudroy and colleagues, the nurses recorded the presence of mottling in a non-selected population of ICU patients [7]. However, quantification of mottling and frequency of skin hypoperfusion recording were not standardized. Mottling was present at the day on admission in 19% and occurred later in 10% of included patients. Among patients with mottling, persistent mottling  $\geq 6$  h was associated with higher in-ICU mortality (76%, vs. 52%,  $p = 0.001$ ). In this study, only 32% of patients with mottling received vasopressors at mottling onset, vasopressors were started and fluid challenge was performed during the mottling episode in 9% and 26% respectively, and 60% had a mean arterial pressure  $\geq 65$  mmHg without vasopressors. This result confirms that mottling could occur aside from the shock context.

Among analyzed patients, 40 had cirrhosis. In their letter, Coudroy *et al.* report that 18 of them (45%) had at least one mottling episode during their ICU-stay. Mottling persisted more than six hours in 14 patients and four of them (29%) died. In their letter, the authors seem to be surprised of such a difference of mortality between their study and ours. However, as detailed above, mottling is a dynamic sign which can occur in various circumstances. Therefore, it is absolutely not surprising that mottling prognosis value is different aside from the septic shock context, which still associated with high mortality in patients with cirrhosis [8]. Generalizing the prognosis value of clinical signs or biological tools aside its validation context is always source of error.

### Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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