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Response to the letter to Editor

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Keywords

Ebola virus disease; Critical care; sepsis

We thank Kissoon *et al* (1) for their interest in our manuscript, and appreciate the opportunity to concur with them about the importance of early recognition of patients with sepsis. We also applaud the work of the Global Sepsis Alliance, which has highlighted the prevalence of the syndrome, and the importance of early recognition of sepsis and has been working on improving patient outcomes.

The major advantage of early recognition of sepsis is that it allows for delivery of timely antibiotics, fluid resuscitation, and infection source control. It is not clear to us that this treatment paradigm fits patients with Ebola virus disease (EVD). While we have few autopsy studies to suggest the mechanism of death in EVD patients (2, 3), electrolyte replenishment and volume resuscitation seem to play an important role in early treatment for these patients who usually present with copious gastrointestinal volume loss (4). However, 2 out of 3 of our patients developed acute kidney injury without developing significant hypotension or generation of lactic acid, suggesting that renal injury occurs independent of hypoperfusion in EVD. While some have made assumptions that in resource rich countries treatment goals for critically ill EVD patients should align with treatment for sepsis patients with therapies such

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as lung protective mechanical ventilation, at this time this remains just an assumption. It has been shown that patients with EVD may exhibit abnormal immunologic, inflammatory and coagulation responses to bacterial infection (3, 5–7). For example, Ebola virus targets macrophage-rich lymphoid tissues, liver, and adrenal glands, which is distinct from bacterial sepsis (5, 6). Most importantly, early administration of broad-spectrum antimicrobials therapy has been shown to improve outcome in patients with bacterial-induced sepsis while at this time there is no proven antiviral therapy specific for patients with EVD (8).

Furthermore, there may be differences in treatment effects for therapies in resource poor compared with resource rich countries as shown in the FEAST Trial (Uganda, Kenya, Tanzania), and the simplified EDGT Trial (Zambia), both of which demonstrate the complexities and harms associated with broad treatment protocol generalizations (8, 9). At this time, while patients with EVD may meet both the old and proposed new sepsis definitions, we are concerned that “lumping” EVD patients into this broad category may minimize important clinical differences between patients with EVD and other life threatening infections. The under recognition of these significant biological and clinical differences discussed above could have detrimental implications for the treatment and prognosis of patients with EVD.

In conclusion, we agree that sepsis still remains under-recognized worldwide with a high mortality rate and continue educating healthcare providers is important. We disagree that labeling EVD as “sepsis” is crucial for these patients and applying the same treatment algorithm may negatively affect both patient care and clinical trial design.

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