

Letter: Exploring the clinical utility of ammonia in critically ill patients with cirrhosis: More to do? Authors' reply

We appreciate the comments made about our study in the Letter from Dong et al.^{1,2}

Regarding the potential impact of infection on serum ammonia levels or patients' outcomes, in our derivation cohort of ACLF patients, we found no association between infection (vs other reason for intensive care unit (ICU) admission) and ICU days 1 (113 vs. 108 $\mu\text{mol/L}$; $p=0.30$) or 2 (85 vs. 91 $\mu\text{mol/L}$; $p=0.49$) serum ammonia levels. Furthermore, there was also no association between infection (vs other reason for ICU admission) and all-cause hospital mortality (37.3% vs. 32.9%; $p=0.31$). These data suggest that infection per se may not be as influential as other factors, namely liver failure, for serum ammonia levels or outcomes in ACLF patients. Unfortunately, we had no data to assess the potential differential impact of the type of infecting microorganisms, namely urease-producing bacteria, on serum ammonia levels or patients' outcomes. While our study was not aimed at studying such specifics, we acknowledge that further characterising infecting microorganisms could be interesting.³⁻⁵

Concerning the impact of kidney dysfunction on serum ammonia levels or patients' outcomes, in our derivation cohort of ACLF patients, we found no association between ICU day one serum creatinine and ICU days 1 ($p=0.85$) or 2 ($p=0.08$) serum ammonia levels. Nevertheless, as shown in our original manuscript, higher median ICU day one serum creatinine was associated with higher all-cause hospital mortality (1.98 vs. 1.32 mg/dL; $p<0.001$). These data suggest that kidney dysfunction per se may not be as relevant as other factors, such as liver failure, for serum ammonia levels in ACLF patients. Unfortunately, we were not able to capture chronic kidney disease (CKD) or acute kidney injury (AKI) occurrence properly due to centre-specific registry limitations, mainly related to prior to hospital stay serum creatinine levels (steady state or baseline, respectively) availability. However, in our derivation cohort of ACLF patients, kidney dysfunction, inferring from ICU day one serum creatinine levels, was associated with mortality. In fact, this is in agreement with the extensive literature describing the deleterious impact of kidney dysfunction on these patients' outcomes.^{6,7}

In conclusion, in our multicentre cohort of ACLF patients, neither infection nor kidney dysfunction per se significantly affected early serum ammonia levels.

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AUTHOR CONTRIBUTIONS

Filipe S. Cardoso: Conceptualization (lead); data curation (lead); formal analysis (lead); writing – original draft (lead). **Minjee Kim:** Data curation (equal); writing – review and editing (equal). **Rui Pereira:** Data curation (equal); writing – review and editing (equal). **Luís Bagulho:** Data curation (equal); writing – review and editing (equal). **Pedro Fidalgo:** Writing – review and editing (equal). **Anna Pawloski:** Writing – review and editing (equal). **Richard Wunderink:** Writing – review and editing (equal). **Nuno Germano:** Writing – review and editing (equal). **Sean Bagshaw:** Supervision (equal); writing – review and editing (equal). **Juan G Abraldes:** Formal analysis (equal); supervision (equal); writing – review and editing (equal). **Constantine Jason Karvellas:** Conceptualization (equal); data curation (equal); formal analysis (equal); supervision (equal); writing – review and editing (equal).

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CONFLICT OF INTEREST STATEMENT

None to be declared.

PATIENT CONSENT STATEMENT

Local ethics committees waived the need for individual informed consent (#CES371_2016, 16/12/2016, Central Lisbon University Hospital Center Ethics Committee; Pro00035429, 04/02/2013, University of Alberta Health Research Ethics Board; STU00204868, Northwestern University Institutional Review Board, 08/11/2017).


AUTHORSHIP

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