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LETTER

NSE concentrations and haemolysis after cardiac arrest

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Dear Editor,

We read with great interest the editorial by Nielsen et al. [1] regarding our recent publications in *Intensive Care Medicine* [2, 3]. We thank the authors for their opinions and agree with most of the expressed views. However, we feel that the critique against the neuron-specific enolase (NSE) analyses and our definition of haemolysis is not justified.

Briefly, we obtained 463 serum samples for the analyses of NSE concentrations at ICU admission and 24, 48 and 72 h after cardiac arrest. In seven samples (1.5%), the Roche haemolysis index was over 50 (corresponding to 500 mg of free haemoglobin per litre). We excluded these samples from the analyses. In the samples taken at the Danish centre ($n=26$), the NSE concentration was analysed immediately and haemolysis was not assessed.

Of the remaining 430 samples, there was detectable haemolysis (haemolysis index ≥ 10) in 150 samples (34.9%). The mean haemolysis index $\pm$ standard deviation in these samples was 19.0 ± 9. The amount of these moderately haemolytic samples was comparable in all the intervention groups. Notably, our main findings remained unchanged after exclusion of all samples with detectable haemolysis: the study interventions had no impact on the NSE concentrations (Table 1). Accordingly, we conclude that our results are not biased because of the impact of haemolysis on NSE concentrations.

Nielsen et al. claimed that our original threshold for defining significant haemolysis, 500 mg of free haemoglobin per litre, was too high. However, the very same threshold has been used in previous studies [4], including the TTM trial. Furthermore, in other studies using NSE as the primary outcome, haemolysis was not assessed at all [5].

Table 1 Median (inter-quartile range) serum neuron-specific enolase concentrations at 48 h after cardiac arrest with all samples with detectable haemolysis (Roche haemolysis index ≥ 10) excluded

Intervention group	NSE (µg/l)	*p* value
Low-normal $PaCO_2$	17.3 (13.3–25.0)	0.156
High-normal $PaCO_2$	21.8 (13.8–34.9)	
Normoxia	18.4 (13.4–25.2)	0.232
Moderate hyperoxia	18.8 (13.6–34.9)	
Low-normal MAP	19.1 (13.9–33.8)	0.433
High-normal MAP	17.3 (13.5–30.3)	

NSE neuron-specific enolase, *PaCO2* arterial carbon dioxide tension, *MAP* mean arterial pressure

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Compliance with Ethical Standards

Conflicts of interest
None.

Ethical approval
An approval by an ethics committee was not applicable.

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