To the editor,

We wish to thank *the correspondent* for their observations related to our study in their letter to the editor. They shared concerns about our statements [1] regarding the risk of rapid blood pressure (BP) reduction in critically ill children with initial hypertension on admission to Paediatric Intensive Care (PICU). Many of the concerns raised by *the correspondent* were discussed in our paper, but we are grateful for the opportunity to expand in these.

The *correspondent* highlights the risk of blood pressure reduction in patients *with* known pre-existing hypertension. This is not the population we studied. Our cohort was defined by a high blood pressure within the first hour of admission to PICU when the origin of the hypertension may, or may not, be known. This population has a higher PICU mortality; abnormal blood pressure an important contributor to the widely used (and in the UK mandated) risk adjustment score the Paediatric Index of Mortality 3 [*Pediatr Crit Care Med 2013; 14:673–681*]. We chose to focus on this population, which reflects that in which intensive care staff have to decide on the risks and benefits of treatment of abnormal blood pressure. Our hypothesis was that the risk of an adverse outcome was associated not with the initial blood pressure, but the blood pressure distribution in the first 24-hours of PICU admission.

Our study is observational. We did not compare different BP reduction strategies. Within our cohort were children who received continuous infusions of vasoconstrictors/inotropes, and those who received continuous infusions of anti-hypertensive drugs (n=29 in the analysed cohort). Therefore, there may have been more than one strategy employed. Our aim was to observe the effect of a reduction below the cited threshold value. We chose a BP reduction of more than 25% of the admission value, based on treatment guidelines, in the first 24 hours. The use of a threshold effect has been criticised by the correspondent – albeit acknowledging this is also variably used in published guidelines. We agree that a threshold from the admission value, in children, could still be above the hypertensive value (or may rarely even be below a normotensive value). Whilst an alternative may be to use a fixed value above a population-based centile, the cerebral circulation of an individual may not defer to a population distribution, rather be relative to the measurement it has adapted to. Both approaches may be problematic when individual blood pressure profiles and targets prior to presentation are not known.

Where the clinician had pre-specified a different value, for example to target a known cerebral perfusion pressure, or a pre-existing baseline systolic blood pressure, this was used instead (n=9 where there was a documented pre-specified target). The time spent, and mean distance, from the target was not significantly associated with our primary outcome of a composite of death and organ support free days at day 28. Since several studies claim rapid reduction in blood pressure can worsen end-organ function [3] the requirement of organ support during PICU admission seems a valid outcome. Significant neurological injury is likely to be reflected in the duration of organ support in this population – for example, as difficulty in liberation from ventilation. This is supported by the use of *duration of organ support or organ dysfunction* as an outcome measure in clinical trials in PICU [4]. We completely agree long-term (neurological) status, or any neurological injury, would be valid outcome. These data were not available to us.

Hypertension defined as a SBP higher than the 95th centile was based on the Fourth Report [2]. We agree that many of the children in our cohort do not meet the thresholds for 'hypertensive emergency or encephalopathy' that the correspondent describes in their forthcoming review (which they have kindly shared with us) [5]. This was not the premise of our study. We acknowledge this definition does not necessarily correlate with the increased risk of mortality described in the PICU population – the PIM3 score assigns the risk of mortality to be lowest at a systolic blood pressure of 120mmHg.

However, we have previously shown that the risk of mortality is better defined by an age-associated blood pressure. [Mattetore ref]. This is why we used an age-associated threshold to define a high blood pressure.

We point out that 4.9% (26/534), not 26/3069 i.e. 0.8%, of our patients had pre-existing hypertension. A sensitivity analysis using a higher a priori risk in this population – up to a 100-fold higher - did not show increased risk of harm in that specific group. This does not mean the risk in this population is not high – it could mean that in this population the blood pressure was more tightly controlled. This is a limitation of observational data. The claim for reducing the BP in a controlled manner over a period of at least 48 hours in children with severe hypertension, without demonstrable recent normotension, is based mainly on two observational studies: adult data from 1979 [6] and a study by Deal [7] et al based on data 1975 -85 that retrospectively compared rapid BP normalisation with bolus therapy versus slower reduction through continuous infusion therapy. They found 4 patients with permanent visual loss in the rapid group (0 in the slow group). All 4 patients had neurological symptoms on presentation and had average BP reduction of nearly 50% (20%-68%) in the first 24 hours. Regarding the sound physiological grounds, the changed cerebral autoregulation in hypertensive patients is acknowledged in our paper, however there is also evidence the rate of normalisation of cerebral autoregulation is unaffected in patients with pre-existing hypertension [8].

Our data suggest that the blood pressure measurements at admission, or in the first 24-hours after PICU admission, cannot define the risk in isolation. We believe hypertension in acute critically illness can be an adaptive response, a para-phenomenon with little significance or a major contributor to pathology. Acknowledging this complexity is necessary to improve decisions about blood pressure management.

There are no prospective or randomised data available regarding the management of patients with hypertension, either those that we describe, nor those alluded to by the correspondent. We would welcome such data. We believe it would be a mistake to assume we know the answer in advance of such results.

References

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