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Letter to the Editor

“Cold War”: Why does the debate continue?



To the Editor,

We thank Granfeldt et al.¹ for this comprehensive meta-analysis on Targeted Temperature Management (TTM) for cardiac arrest patients, which concluded that the use of moderate hypothermia, when compared to normothermia, did not result in improved outcome. However the pooled estimates of survival and favourable neurological outcome all skewed towards moderate hypothermia and heterogeneities among studies were high (please refer to Figure 2 of the meta-analysis by Granfeldt et al.). Numerous studies on TTM have been carried out for more than a decade with variable patient characteristics, cooling regimens and even prognostication models. These all may contribute as sources of heterogeneity of performing a meta-analysis. As a result, the validity of the conclusion drawn would be questionable. On the other hand, we have to ask whether TTM should be considered as a pure temperature control exercise or a bundle of care. If TTM should be considered as a care bundle, meta-analysis focusing on temperature alone may not resolve the controversy of the temperature debate. The variation in sedation protocol implementation would be a good example in illustrating this concept.

For the studies included in estimating effect on “Survival to hospital discharge” (Figure 2 of the meta-analysis by Granfeldt et al.), there was a significant variation in sedation regimen among those studies (Table 1 of this manuscript). In HACA² trial, sedation was given for “mechanical ventilation management”. We can presume it was mainly given to hypothermia group patients for shivering control and the associated patient-ventilator dyssynchrony. In the study by Bernard et al.³, sedation and paralysis was mainly given to the hypothermia group to suppress shivering for the first 18 to 24 hours during active cooling and rewarming phases. In the study by Lascarrou et al.⁴, deep sedation was given to the hypothermia group for at least 24 hours to maintain a Richmond Agitation-Sedation score (RASS) of –5 during active cooling phase. But normothermia group only received light sedation during the first 12 hours to maintain a RASS of 0. Beneficial effects for therapeutic hypothermia were revealed in these three studies. However, in the study by Dankiewicz et al.⁵, mandatory deep sedation for 40 hours was implemented in

Table 1 – A summary of various sedation protocols in the four major targeted temperature management trials.

	Deep sedation in hypothermic group	Deep sedation in normothermic group	Outcome difference
Dankiewicz, 2021 ⁵	✓	✓	Negative
HACA, 2002 ²	✓	X	Positive
Bernard, 2002 ³	✓	X	Positive
Lascarrou, 2019 ⁴	✓	X	Positive

both normothermia and hypothermia groups to maintain a RASS of –4. Negative result was revealed in this trial. Although the effect of sedation on post cardiac arrest patients would need further studies to verify, this served as an example that we may need to consider TTM as a bundle of care: the combination of sedation, paralysis and good temperature control may improve patients’ outcome, instead of temperature control alone. This is similar to catheter related infection prevention bundle: the sterile gloves alone cannot reduce the infection rate, but the bundle as a whole, which includes hand-washing, gowns and meticulous post catheter insertion care, reduces infection rate. This concept may also explain why the conflict on TTM did not settle even after more than a decade of research. The “cold war” just continues.

Author contribution

All authors contribute equally in preparing this manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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