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COMMENTARY

Cautious application of targeted temperature management in a real-world OHCA population after "TTM2 trial"

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Systemic ischemia-reperfusion injury caused by cardiac arrest and subsequent resuscitation requires postcardiac arrest care, including hemodynamic support, mechanical ventilation, targeted temperature management (TTM), percutaneous coronary intervention, diagnosis and treatment of underlying causes, detection and management of seizures, treatment of infection, and general intensive care management. In light of the complexity of postcardiac arrest patients, the development of a comprehensive and multidisciplinary system of care should be implemented to optimize survival and neurological outcome of the patients.

To prevent ischemia-reperfusion brain damage in comatose cardiac arrest survivors, the current American Heart Association and European Resuscitation Council guidelines for cardiopulmonary resuscitation recommend TTM between 32 °C and 36 °C for at least 24 hours for all cardiac rhythms [1, 2]. However, some uncertainties within the topic of TTM persist, including whether temperature should vary on the basis of patient characteristics, how long TTM should be maintained, and how quickly it should be started.

The recently published TTM2 trial is an international, multicenter randomized superiority clinical trial that aimed to assess the beneficial and harmful effects of hypothermia at 33 °C as compared with targeted normothermia (≥37.8 °C) in patients with out-of-hospital cardiac arrest (OHCA) [3]. No significant difference in the primary outcome of 6-month mortality between targeted hypothermia and normothermia (50% vs. 48%) was found [3]. Hypothermia did not increase the frequency of pneumonia, sepsis, or bleeding, but arrhythmias causing hemodynamic compromise were more common in the hypothermia than in the normothermia (24% vs. 16%) [3].

Previously, in the TTM1 trial (33 °C vs. 36 °C), the argument focuses on those patients most likely to have a good outcome, which means a limitation of generalizability in the real world. In the TTM2 trial, adults who experienced OHCA, regardless of the initial rhythm, were included. Inclusion was done within 180 minutes of ROSC. However, patients with OHCA included in the trial do not reflect the general OHCA population we see in the clinical field. Multicenter registry data from the Cardiac Arrest Registry to Enhance Survival (CARES) reported that non-traumatic OHCA patients who survive to hospital admission had a witnessed arrest of 71.1% (2496/3512), bystander cardiopulmonary resuscitation (CPR) rate of 38.7% (1359/3512), an initial shockable rhythm rate of 32.6% (1145/3512) [4, 5]. Moreover, the Korean Hypothermia Network (KORHN) registry reported that OHCA survivors treated with TTM at 22 academic hospitals across South Korea between 2015 and 2018 had a witnessed arrest of 70.3% (804/1144), bystander CPR rate of 61.9% (708/1144), an initial shockable rhythm rate of 35.4% (241/1144), and an ST-segment elevation myocardial infarction rate of 12.1% (92/1144) [6]. Compared with data from CARES and KORHN, the demographic characteristics of included patients in the TTM2 trial showed a witnessed arrest rate of 91%, a bystander CPR rate of 82%, an initial shockable rhythm rate of 73.6%, and an ST-segment elevation myocardial infarction rate of 40.3%, implying selected OHCA patients with less severe brain injury and good neurological outcomes were included. Therefore, the high survival rate at 6-month of 49.2% in the TTM2 trial was not surprising. In addition, among the OHCA patients screened but not randomized after assessing the eligibility in the TTM2 trial, the most common reason for exclusion was a duration of over 180 minutes from ROSC (32.3%; 794/2455). Considering that all participating sites in this trial had previous experiences with the use of hypothermia, it might be not a small number, and their mortality rate needs to be reported.

Cardiac arrest results in heterogeneous injury in patients with postcardiac arrest. It is apparent that the one-size-fits-all approach to any therapy is imprecise. Recent systemic reviews suggest that lower temperatures may be uniquely helpful in brain injury [7, 8]. OHCA survivors with different severities of brain injury require different types of therapy such as proven effectiveness of prone positioning only in severe acute respiratory distress syndrome (ARDS) not in all ARDS patients [9–11].

Despite the valuable results in the TTM2 trial, concerns about the study population did not reflect a real-world OHCA

population; therefore, cautious interpretation and application of this result is warranted and clinicians should not be taken in misinterpreted the result as “No cool anymore in all OHCA population”.

AUTHOR CONTRIBUTIONS

YJK and WYK drafted the manuscript and contributed substantially to the revision.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

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