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Mild therapeutic hypothermia or targeted temperature management for cardiac arrest survivors?

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Out-of-hospital cardiac arrest (OHCA) is burdened with a high risk of death [1–5]. Following the results of the The Targeted Temperature Management Trial (TTM trial) — a randomized study published by Nielsen et al. [6] suggesting equivalent results of targeted temperature management (TTM) at 33°C and 36°C in comatose patients after OHCA, current guidelines recommend TTM in this subset of patients [7]. TTM covers a wider body's core temperature range (between 32°C and 36°C) than mild therapeutic hypothermia (MTH) (between 32°C and 34°C) [8–10]. However, while favorable clinical outcome of MTH was proven in several clinical studies [11–13], the impact of TTM remains less clear. A favorable effect of MTH on survival and neurological outcome was confirmed in a meta-analysis of data pooled from randomized and non-randomized studies [14]. Recently, Sobczyk et al. [15] published another report showing benefits of MTH in cardiac arrest survivors in the early phase of myocardial infarction. Taking into account the results of studies on MTH, it should be noted that the methodology of the TTM study — the largest available randomized trial — is questionable [6, 10]. The limitations were related to the non-uniform methodology of cooling (intravascular cooling was used in only 24% of patients) and the heterogeneity of the trial population (40% of patients with myocardial infarction). Moreover, a substantial proportion of patients in the MTH arm did not reach the target temperature, and the duration of hypothermia induction was unacceptably long (a mean of 8 h) [6]. These important shortcomings of the TTM study could have negatively affected the results, with a survival rate and neurological outcome being much worse than observed in MTH arms and similar to control arms of MTH studies [6, 11–15]. Nevertheless, European Society of Cardiology recommendations are based on results of the TTM study [6, 7]. Of note, also registries accepting the MTH's methodological diversity are burdened with a serious risk of result misinterpretations [16]. These observations strongly suggest the need for a new multicenter, methodologically uniform trial, free from the hoaxes of the TTM study. Acute coronary syndrome is the most common cause of OHCA [17]. In this context, when planning a new trial, the routine use of cangrelor in patients undergoing MTH should be considered due to the diminished antiplatelet effect of oral P2Y12 inhibitors [18–22].

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