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The use of hypothermia and outcome post cardiopulmonary resuscitation in 2014

O uso de hipotermia e desfechos após ressuscitação cardiopulmonar em 2014

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THE PAST

In animal trials clinical outcome and histopathological damage of the brain tissue due to hypoxia after cardiac arrest was found to be reduced by mild therapeutic hypothermia.^(1,2)

The clinical milestone trials in 2002 also have found mild therapeutic hypothermia at 32°-34 °C for 12-24 hours to be neuroprotective in treatment of the post-cardiac arrest syndrome.⁽³⁻⁵⁾ The last update of the international guidelines for resuscitation in 2010 stressed the benefit of hypothermia to almost all patients after cardiac arrest that remain comatose after return of spontaneous circulation (ROSC).⁽⁶⁾ Over the past much data have been published showing a significant benefit for neurological outcome in clinical practice besides large trials.

In our own centre we were able to reduce the rate of patients remaining in a persistent coma after cardiac arrest by an impressive number of approximately 50% after implementation of mild therapeutic hypothermia and to double therefore the group discharged with good outcome. But of course nowadays it is due to more than temperature management because we know that a complete treatment bundle, including early invasive coronary angiography, optimal ventilation, mean arterial pressure, glucose control, monitoring of diuresis and avoiding a severe acidosis will enlarge the numbers with good outcome.^(7,8)

Following a consensus statement of five different societies for critical care we now refer to targeted temperature management (TTM) instead of hypothermia.⁽⁹⁾

THE PRESENT

Implementation of TTM greatly varies between different countries or even between different hospitals although severe life-threatening side effects have never been reported to be significant.^(10,11) Therefore, for no reason, a high number of cardiac arrest survivors will not receive any kind of post-cardiac arrest temperature management.

A problem is still the unguided practice of withdrawal of treatment in those patients without reliable signs or markers predicting poor outcome with 100%. This could also bias outcomes in many trials as self-fulfilling prophecy. For the future, implementation has to be enhanced worldwide as well as the need for more research to gain the knowledge for difficult prognostication.

Conflicts of interest: None.

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However three main questions are still open: (1) what subgroup benefits most from TTM, (2) how long to cool, and (3) what should the optimal target temperature be. The TTM-trial recently published by Nielsen and co-workers in the *New England Journal of Medicine* therefore compared two different target levels (33° and 36 °C) and measured overall mortality and outcome.⁽¹²⁾ This randomized multicentre trial analyzed 939 patients in 12 countries (n=473 at 33 °C and n=466 at 36 °C). The main result was no statistical significant difference between both targeted temperature levels for mortality and neurological outcome, the overall mortality rate was 50% in the 33 °C group and 48% in the 36 °C group respectively. By misinterpreting these results some hospitals stopped TTM in all patients or feel justified in not implementing TTM if they had not in the past. An important question is whether the results can be transferred worldwide or not. Why is that? Most participants were located in Scandinavia where Basic Life Support (BLS) is part of school education, resulting in a very high bystander rate of cardiopulmonary resuscitation (CPR) of 73%. A further possible confounder could be the long time needed in the 33 °C group to reach the target temperature (>8 hours respectively). The results of the TTM trial are neutral in fact. There is no evidence to stop TTM completely and no doubt that pyrexia following cardiac arrest needs to be avoided at any time after cardiac arrest. On one hand it seems problematical to apply the results of the TTM trial to all patients after cardiac arrest because some cohorts might be different, e.g. long downtime and prolonged start of BLS or no bystander BLS at all. For example the bystander rate performing BLS in Germany is 16%.⁽¹³⁾ It is well known that especially

early start of CPR is a significant predictor for good outcome.⁽¹⁴⁾ On the other hand the results may open the possibility to cool those who will not tolerate 33 °C due to various reasons (e.g. hemodynamic instability or severe bleeding) at 36°. However the range between 36 °C and pyrexia (>37 °C) is small and therefore the temperature management has to be precise and should be facilitated by the use of a computer-feedback device.

However a final conclusion cannot be drawn by the TTM trial data and we have to raise the question whether our own cohort of patients after cardiac arrest is comparable to those analyzed in the study or not and the question about the optimal or individual best target temperature has still to be answered. The German Society for Intensive Care and Emergency Medicine released a current statement about the results of the TTM trial with the strong recommendation to continue using 32 °C-34 °C as reliable target temperature. This has also been supported by the current International Liaison Committee on Resuscitation (ILCOR) statement that recommends following the still valid guidelines for post-arrest care.⁽¹⁵⁾

THE FUTURE

Keeping this in mind, the most interesting questions for the future are to find a way to characterize the severity of the hypoxic brain damage to adjust TTM in depth and duration.

It will also be beyond any doubt that TTM implementation needs to be increased despite the open questions. In addition a promising new field of indication might be in ST-elevation myocardial infarction patients for treatment of the reperfusion injury of the myocardium.

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