Gräsner and colleagues, in the previous issue of Critical Care, perform an intriguing analysis on the combined approach of mild therapeutic hypothermia (MTH) and immediate percutaneous coronary intervention (PCI) for post-resuscitation care of patients with out-of-hospital cardiac arrest (OHCA) [1].

OHCA is a leading cause of death in developed countries and early resuscitation attempts are crucial to improve survival rates and neurological outcome. Gräsner and colleagues performed an intriguing analysis on the combined approach of mild therapeutic hypothermia (MTH) and immediate percutaneous coronary intervention (PCI) for post-resuscitation care of 584 patients with out-of-hospital cardiac arrest from the German Resuscitation Registry. PCI was independently associated with good neurological outcome at hospital discharge after successful resuscitation, and MTH was associated as an independent factor with increased chance of 24-hour survival. Moreover, a binary logistic regression analysis did not show statistical significance for MTH, in addition to PCI, as an independent predictor for good neurological outcome. The present study supports the evidence that post-resuscitation care based on standardized protocols is beneficial after successful resuscitation. Further prospective and randomized studies are warranted to elucidate criteria for a better selection of candidates for those strategies and to evaluate the potential, in terms of neurological outcome at hospital discharge, of a prehospital cooling strategy in patients who cannot be referred to immediate PCI.

**Abstract**

Out-of-hospital cardiac arrest is a leading cause of death in developed countries and early resuscitation attempts are crucial to improve survival rates and neurological outcome. Gräsner and colleagues performed an intriguing analysis on the combined approach of mild therapeutic hypothermia (MTH) and immediate percutaneous coronary intervention (PCI) for post-resuscitation care of patients with out-of-hospital cardiac arrest (OHCA) [1].

Since techniques in resuscitation have improved, the population of patients with anoxic brain injury is growing. The induction of MTH (32 to 34°C) for 24 hours has been shown to improve neurologic outcome of patients successfully resuscitated after cardiac arrest [8-10]. This improvement was demonstrated in two randomized controlled trials in patients with ventricular fibrillation as the initial cardiac rhythm [8,9]. Two meta-analyses found that MTH improves short-term neurologic outcome and survival in patients resuscitated from OHCA of presumed cardiac origin, with ventricular fibrillation/ventricular tachycardia as the initial rhythm [11,12].

The German Resuscitation Registry is a large registry started in 1998 for the collection of preclinical datasets on the attempts of out-of-hospital resuscitation. Since 2004 this database has been extended to the post-resuscitation datasets [1]. Despite obvious limitations, data from large-scale registries provide useful insights on the feasibility and safety of new therapeutic strategies, as well as on off-label indications. These insights are particularly useful in settings such as emergency care in which randomized
controlled trials are challenging, primarily because of ethical concerns. Gräsner and colleagues evaluated 584 patients from the German Resuscitation Registry with complete pre-resuscitation and post-resuscitation datasets [1]. The authors described the effects of a combined approach for the early treatment of OHCA patients with or without a shockable rhythm. They found that both PCI and MTH were associated with good neurological outcome and increased survival at 24 hours after return of spontaneous circulation, in line with previous reports [4-6]. The authors evaluated the effects of both MTH and PCI used alone and in combination: they found a beneficial effect even for PCI alone, while in a large previous report immediate PCI after OHCA was associated with MTH in 85% of patients [4]. Interestingly, data from binary logistic regression analysis showed that MTH was not an independent predictor of good neurologic recovery, when used in addition to PCI [1].

Some details are lacking in the present study, however, such as timing and the devices used to achieve cooling, as well as PCI details. Moreover, data on the potential advantage of the combination of PCI and MTH versus PCI alone or MTH alone are lacking.

In the PRINCE study, induction of hypothermia with intranasal cooling devices in a prehospital setting may be useful in reducing time intervals required to cool the patients [13]. An outcome difference in comparison with in-hospital cooling was not found; a post-hoc analysis of patients in which cardiopulmonary resuscitation (CPR) was started within 10 minutes demonstrated a significant effect of prehospital cooling on survival rate and neurological recovery. The potential of this approach in patients not immediately undergoing PCI due to lack of catheterization facilities is worth studying.

Some other interesting factors deserve further attention, particularly the association of fibrinolysis with a worse outcome. This association is in contrast to a previous report by Böttiger and colleagues, who found no difference of outcome in comparison with placebo using thrombolysis during resuscitation [7], without adjunctive antithrombotic therapies. Fibrinolysis is usually considered relatively contraindicated after prolonged CPR, because of the increased risk of bleeding. It could be useful to establish whether factors such as the timing of fibrinolysis administration, the duration of CPR and adjunctive antithrombotic therapies could have influenced the unfavorable effects observed in the present study.

Post-resuscitation care based on more standardized protocols including PCI and MTH may be beneficial after successful resuscitation. Further studies are warranted to elucidate criteria for a better selection of candidates, and to demonstrate whether a prehospital rapid cooling strategy during early CPR may be independently associated with an improvement of neurological outcome in patients who cannot be referred for immediate coronary angiography.

Abbreviations
CPR, cardiopulmonary resuscitation; MTH, mild therapeutic hypothermia; OHCA, out-of-hospital cardiac arrest; PCI, percutaneous coronary intervention.

Competing interests
The authors declare that they have no competing interests.

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