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### Case report

## Therapeutic hypothermia after prolonged cardiopulmonary resuscitation due to pulmonary thromboembolism. Case report<sup>☆</sup>



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#### ABSTRACT

This is a report of a 41-year-old patient undergoing femur osteosynthesis (OS) who develops intraoperative cardiac arrest (CA) with pulseless electrical activity (PEA). Massive pulmonary thromboembolism (PTE) was diagnosed as the cause for the CA and a thrombolysis performed 30 min later reestablished spontaneous circulation with no new CA events. Therapeutic hypothermia (TH) was then established with local measures for 18 h for brain protection. The patient was extubated 24 h later with no neurological deficit. There is an increasing evidence of TH and its protective mechanisms in patients with non-shockable arrest rhythms leading to a widespread use of the technique in various institutions around the world, with particular emphasis on neurological outcomes. This article discusses a review of the current literature on TH, in addition to describing each of the stages in TH and how to approach these stages.

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#### Hipotermia terapéutica post-reanimación cardiopulmonar prolongada en paro cardiaco debido a tromboembolismo pulmonar. Reporte de caso

#### RESUMEN

Se reporta un caso de un paciente de 41 años quien es llevado a osteosíntesis (OS) de fémur y que presenta paro cardiaco (PC) intraoperatorio con ritmo de actividad eléctrica sin pulso. Se diagnostica tromboembolismo pulmonar masivo como causa del PC y 30 min después se

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hace trombólisis, obteniéndose circulación espontánea sin nuevos episodios de PC. Posteriormente se instaura hipotermia terapéutica (HT) con medidas locales durante 18 h para protección cerebral. El paciente es extubado 24 h después sin ningún déficit neurológico. Es importante entender que la evidencia actual de la HT en pacientes con ritmos de paro no desfibrilables y sus mecanismos de protección es creciente, y que cada vez más se está implementando esta técnica en los diferentes centros del mundo, sobre todo haciendo énfasis en desenlaces neurológicos. En este artículo se hace una revisión de la literatura actual sobre HT, además de describir cada una de las etapas de la HT y la forma en que se deben abordar.

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## Introduction

Good neurological results following a CA are difficult to achieve. Any intervention during cardiopulmonary resuscitation (CPR) and in the next few hours after recovering spontaneous circulation (SC) is critical to reach this goal. Experimental trials both in humans and in animals show that therapeutic hypothermia (TH) improves the neurological and cardiovascular outcomes in these patients.<sup>1,2</sup> There is enough evidence to use moderate TH (32–34 °C) in ventricular tachycardia (VT) or ventricular fibrillation (VF), since it improves both, the neurological prognosis and mortality.<sup>1,3</sup>

## Clinical case

41-year-old patient with distal femoral shaft fracture referred two days later to the University Hospital San Vicente Fundación (HUSVF) in Medellín for osteosynthesis. The patient has a history of untreated diabetes mellitus type II. Paraclinical tests: HbA1c, blood count, glycaemia, ionogram, renal function, PT and PTT normal. Functional class and cardiovascular examination are normal.

The procedure is performed under spinal anesthesia, hyperbaric bupivacaine plus morphine, achieving a T10 level of anesthesia. 30 min into surgery, suddenly and unexpectedly, the patient develops cardiorespiratory arrest with PEA. CPR is administered, with capnography monitoring above 15 mmHg. The patient had not received thromboprophylactic treatment and the transthoracic ECG showed dilatation of the right ventricle and left-IV septal deviation, leading to a diagnosis of massive pulmonary thromboembolism (PTE). The patient received thrombolysis with tissue plasminogen activator as follows: initial 25 mg bolus followed by 25 mg in 30 min; then 50 mg in the next 30 min and 100 mg during the next hour, for a total of 200 mg.

After initiating the resuscitation maneuvers, the patient recovers spontaneous circulation; a femoral arterial catheter is inserted and esophageal temperature monitoring is established after CPR. When the patient was admitted to the ICU, the temperature reported was 33 °C (Philips Mx 600 monitor) just with exposure to the OR temperature. The patient is left uncovered, keeping the esophageal temperatures under control between 32.5 and 33.5 °C for 18 h. No inotropic support

was required and the norepinephrine vasopressors initiated during resuscitation were gradually tapered and well tolerated in the first 24 h. The patient received target CVP and diuresis-guided water therapy (approximately 7000 ml of crystalloids and transfusion of 2 leukocyte depleted red blood cells). During this time the patient did not develop any new episodes of CA or severe arrhythmia. Volume controlled mechanical ventilation was used – 6 ml/kg – and no additional neuromuscular relaxation was needed besides the rapid intubation sequence with 1.2 mg/kg rocuronium, sedation analgesia with 100 mg/h fentanyl plus midazolam 2 mg/h. At the end of 18 h, the patient was warmed up to 37 °C with blankets at room temperature. 6 h later the patient was extubated free of complications. The PTE was confirmed through ventilation/perfusion ultrasound, visualizing multiple apparently residual subsegmental thrombi. The patient experienced no significant bleeding and no neurological deficit.

## Discussion

Survival and neurological recovery following a CA are the most significant outcomes that vary depending on the underlying pathology, the time elapsed prior to receiving care after the arrest, the initial rhythm and the resuscitation modality.<sup>4,5</sup> The survival rate at discharge of the cases that achieve spontaneous circulation has been below 10%.<sup>6</sup>

The stages of the post-cardiac arrest syndrome are: phase one includes the period immediately after returning to spontaneous circulation and up to 20 min later. It is characterized by cardiovascular dysfunction, with a corresponding 63% mortality. During the intermediate phase – between 6 and 12 h – neurological damage develops accounting for 17% mortality and, to a larger extent, for morbidity at discharge. Finally, the recovery period accounts for 7% mortality from infectious complications and multiple organ failure (MOF). At the end of these three stages, the survival rate is 13%, of which 4% are free from any neurological damage.<sup>2,7</sup>

Neurological damage is mediated by several mechanisms.<sup>8</sup> Early on, the lack of cerebral blood flow depletes the ATP reserves. In the intermediate stage, the release of excitatory amino acids activates the cytotoxic pathways. Then at the late stage, the rupture of the blood-brain barrier worsens the cerebral edema and cell death.

The TH neuroprotective mechanisms are: 6–10% reduction in cerebral metabolism per every degree Celsius of temperature drop; attenuation of the cytotoxic cascade and oxygen reactive species; decreased apoptosis between 48 and 72 after the arrest; reduced inflammatory response; and finally, blood–brain barrier protection.<sup>9,10</sup>

There are some controversies about which method performs better in achieving the TH goal; however, there is strong literature support in favor of simple physical methods such as cold blankets, ice, or 4 °C isotonic solution. Regardless of the method chosen, the key is to have standardized institutional protocols.<sup>7,9</sup>

The following are the TH phases:

**Induction:** Lower the body temperature to between 32 and 34 °C as fast as possible; speed is not associated with adverse events. The recommendation is to start lowering the temperature when initiating the resuscitation maneuvers since this has shown to improve the hemodynamic profile of patients.<sup>10–12</sup> A 2000 cc 0.9% saline infusion at 4 °C is the first line approach at the University Hospital SVF for achieving the goal.

The TH-associated adverse events are: hypovolemia, diastolic dysfunction, hypokalemia, hypomagnesaemia, hypophosphatemia, hyperglycemia, coagulopathy, arrhythmias and endocraneal hypertension. Most of them are easily controllable.<sup>7</sup> Since TH causes dynamic changes that favor cardiovascular stability, if instability occurs the underlying cause must be identified.<sup>12</sup>

**Maintenance:** According to the AHA it should last between 12 and 24 h, maintaining a range between 32° and 34° with changes not exceeding 0.5 °C. When tremors occur, despite being a good prognostic sign, these should be tempered by improving the sedation or using neuromuscular relaxants.<sup>13,14</sup>

During this period, the clinical signs of infections will be weakened and so any mild indication of infection shall be studied and treated on a timely basis.<sup>6</sup>

**Re-Warming:** Inadequate re-warming remove the benefits of TH and is associated with cell injury, water–electrolyte disorders and increases insulin sensitivity. Consequently, active warming should not be faster than 0.5 °C/h.<sup>7</sup>

The good results in this particular case are due to the patient's age and little comorbidity that partially account for a faster and better cardiovascular recovery. Secondly, the arrest was witnessed and hence the response time was immediate and coordinate by expert practitioners. Third, though the arrest rhythm was PEA, this rhythm was not a degeneration of a malignant arrhythmia or a heart attack, which improves the prognosis. And lastly, the implementation of thrombolysis as specific treatment, considerably improved the patient's survival with little associated adverse events, despite the high dose used.

## Conclusions

TH is becoming increasing popular in situations beyond the non-shockable rhythms, mainly due to a better understanding of its protective mechanisms, particularly neuronal, and to the increasing evidence of the last few years. The indications for TH are not just growing, but the contraindications

are decreasing because the side effects are easily manageable. Nevertheless, the huge impact of this therapy is that it has been adopted as part of the institutional protocols, regardless of the method used. It should be kept in mind that the conventional cooling methods are probably the most cost-effective and easy to use in every scenario. Although the perioperative environment offers the least evidence, it is well known that the faster the TH is established, the short and long term outcomes are potentially improved. However, further trials with an improved epidemiological profile are needed to support this approach.

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## Conflicts of interest

The authors have no conflicts of interest to declare.

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