

# Neurologic outcome in patients with cardiac arrest complicating ST elevation myocardial infarction treated by mild therapeutic hypothermia: The experience of a tertiary institution

## ST yükselmeli miyokart enfarktüsü sonrası gelişen kalp durması nedeniyle tedavi amaçlı hipotermi uygulanan hastalarda nörolojik sonlanım: Üçüncü basamak merkez tecrübesi

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### ABSTRACT

**Objective:** Therapeutic hypothermia improves neurologic prognosis after cardiac arrest. The aim of this study was to report clinical experience with intravascular method of cooling in patients with cardiac arrest resulting from ST-segment elevation myocardial infarction (STEMI).

**Methods:** Thirteen patients (11 male, 2 female; mean age was 39.6±9.4 years) who had undergone mild therapeutic hypothermia (MTH) by intravascular cooling after cardiac arrest due to STEMI were included. Clinical, demographic, and procedural data were analyzed. Neurologic outcome was assessed by Cerebral Performance Category (CPC) score.

**Results:** Anterior STEMI was observed in 9 patients. One patient died of cardiogenic shock complicating STEMI. Mean cardiopulmonary resuscitation (CPR) duration and door-to-invasive cooling were 32.9±20.1 and 286.1±182.3 minutes, respectively. Precooling Glasgow Coma Scale score was 3 in 9 subjects. Twelve patients were discharged, 11 with CPC scores of 1 at 1-year follow-up. No major complication related to procedure was observed.

**Conclusion:** In comatose survivors of STEMI, therapeutic hypothermia by intravascular method is a feasible and safe treatment modality.

### ÖZET

**Amaç:** Kalp durması sonrası tedavi amaçlı hipotermi uygulamasının nörolojik prognoz üzerine olumlu etkisi gösterilmiştir. Bu yazıda, ST yükselmeli miyokart enfarktüsüne (STEMI) bağlı kalp durması geçiren hastalarda damar içi yöntemle yapılan soğutma tedavisine ilişkin çalışmamız sunuldu.

**Yöntemler:** ST yükselmeli miyokart enfarktüsü sonrası kalp durması nedeniyle damar içi yöntemle tedavi amaçlı hipotermi uygulanan 13 hasta (11 erkek, 2 kadın; ortalama yaş 39.6±9.4 yıl) çalışmaya dahil edildi. Klinik, demografik ve soğutma işlemine ait veriler incelendi. Nörolojik takipler Serebral Performans Kategorisi skorlaması kullanılarak yapıldı.

**Bulgular:** Dokuz hastada akut ön duvar miyokart enfarktüsü tespit edildi. Bir hasta kardiyojenik şok nedeniyle kaybedildi. Ortalama kardiyopulmoner canlandırma süresi ve kapı invaziv soğutma süresi sırasıyla 32.9±20.1 ve 286.1±182.3 dakikaydı. Soğutma öncesi dokuz hastada Glasgow Koma Skalası 3 bulundu; 12 hasta taburcu edildi, 11 hastanın bir yıllık takipte Serebral Performans Kategorisi skoru 1 olarak saptandı. Soğutma işleminden kaynaklanan ciddi komplikasyon gözlenmedi.

**Sonuç:** ST yükselmeli miyokart enfarktüsü sonrası koma halinde bulunan hastalarda damar içi yöntemle yapılan tedavi amaçlı hipotermi faydalı ve güvenli bir tedavi seçeneğidir.

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Mild therapeutic hypothermia (MTH) is indicated in comatose patients with resuscitated cardiac arrest due to ST-segment elevation myocardial infarction (STEMI).<sup>[1]</sup> Patients with STEMI have better survival rates than those with other causes of cardiac arrest.<sup>[2]</sup> Therefore, it is crucial to improve neurologic prognosis by methods of cooling. Hypothermia can be induced by intravascular or external methods. However, external cooling may lead to overcooling, fluctuating temperatures, and increased adverse outcomes.<sup>[3]</sup> Although clinically indicated, MTH is not commonly utilized in Turkey. The aim of the present study was to share our experience with therapeutic hypothermia induced by intravascular cooling.

## METHODS

### Patient selection

Thirteen comatose patients referred for primary percutaneous coronary intervention (PCI) between May 2012 and July 2013 were assigned to receive MTH after restoration of spontaneous circulation. Exclusion criteria were unwitnessed arrest, Glasgow Coma Score >8, pregnancy, hypothermia <34°C, any terminal illness precluding advanced life support, and preexisting neurologic dysfunction. The study was approved by the local ethics committee.

### Cooling

Patients were treated with therapeutic hypothermia using an intravascular cooling system that included an external heat exchanger (CoolGard System 3000; Zoll Medical Corp., Chelmsford, MA, USA; Figure 1). It also included a closed-loop heat exchange catheter (Thermogard XP; Alsius Corp., Irvine, CA, USA; Figure 2). Catheter was placed in the inferior vena cava through the femoral vein. Measurement of core body temperature was obtained by sensor probe via urinary catheter. To achieve immediate cooling, 2000 or 30 cc/kg cold (4°C) saline was administered in 30 minutes before the aforementioned catheter-based method if no signs of lung edema were present. Cooling was initiated following coronary procedure. Subjects were cooled to 33°C, and this temperature was maintained for 24 hours. Rewarming was conducted at a rate of 0.2°C/h, followed by controlled normothermia (37°C) for 12 hours.

Analgesia and sedation were induced by infusion of fentanyl (0.05 mg/h) and midazolam (0.1 mg/kg/h).

Vecuronium, a neuromuscular blocking drug, was routinely administered (1 mcg/kg/min) to prevent shivering. All patients were intubated and received mechanical ventilation. The drugs were terminated when core temperature reached 36 °C. After 6 hours, neurologic examination was performed, then repeated daily.

Neurologic and functional statuses of patients were assessed at 30-day, 6-month, and 1-year outpatient visits.

### Definitions

Cerebral Performance Category (CPC) 1: conscious, no neurologic disability; CPC 2: conscious, moderate neurologic dysfunction, can work; CPC 3: conscious, severe neurologic dysfunction, dependent; CPC 4: permanent vegetative status.<sup>[4]</sup>

Door-to-invasive cooling time: Time interval between hospital admission and start of invasive cooling following PCI.

#### Abbreviations:

CPC	Cerebral Performance Category
CPR	Cardiopulmonary resuscitation
MTH	Mild therapeutic hypothermia
PCI	Percutaneous coronary intervention
STEMI	ST-segment elevation myocardial infarction



Figure 1. Intravascular cooling system.

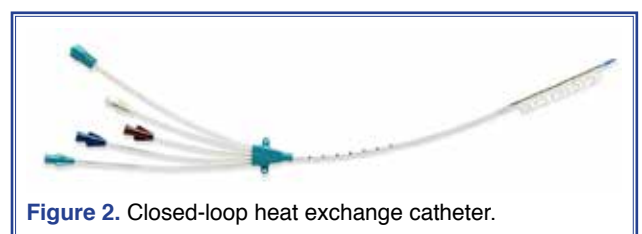


Figure 2. Closed-loop heat exchange catheter.

**Table 1. Baseline, procedural and outcome data**

No	Age	Sex	STEMI	CPR (min)	OHCA	Door to cooling time (min)	Precooling GCS	Discharge GCS	1 year CPC	Rebound fever	Creatinin on admission (mg/dL)	Lactate on admission (mmol/L)	Vasopressor treatment	LV EF $\leq 30\%$
1	28	Male	Anterior	25	-	120	3	15	1	-	1.5	9.0	+	+
2	33	Male	Inferolateral	30	-	600	6	15	1	+	1.1	7.6	-	+
3	31	Male	Anterior	18	+	180	4	15	1	-	0.9	12	-	-
4	54	Male	Inferior	10	-	240	6	15	1	-	1.0	13	+	-
5	35	Male	Anterior	10	+	120	3	15	1	-	0.9	6.0	-	-
6	41	Male	Anterior	30	+	720	3	-	-	-	1.7	17	+	+
7	51	Male	Inferior	60	-	300	3	15	1	-	1.0	19	+	-
8	43	Male	Anterior	65	-	300	3	15	1	+	1.7	22	+	+
9	32	Male	Anterior	25	+	150	3	15	1	-	0.9	2.5	-	+
10	32	Male	Anterior	25	+	240	3	15	1	-	1.1	12	-	+
11	57	Male	Anterior	50	+	210	5	15	1	-	1.5	6.9	+	+
12	36	Female	Inferior	15	-	360	6	15	1	-	1.4	6.7	-	-
13	42	Female	Anterior	65	+	180	5	9	3	-	1.1	12	+	+

CPC: Cerebral Performance Category; CPR: Cardiopulmonary resuscitation; OHCA: Out-of-hospital cardiac arrest; STEMI: ST-segment elevation myocardial infarction; GCS: Glasgow Coma Scale; LVEF: Left ventricular ejection fraction at admission.

## RESULTS

Thirteen patients were included. Baseline clinical, demographic, and procedural characteristics are shown in Table 1. Eleven male subjects, with a mean age of  $39.6 \pm 9.4$ , were included. Mean CPR duration and door-to-invasive cooling time were  $32.9 \pm 20.1$  and  $286.1 \pm 182.3$  minutes, respectively. Two patients (numbers 2 and 6) had longer door-to-invasive-cooling times. These delays were attributed to lack of standard treatment protocol and length of time to communication with cooling catheter supplier. The majority of patients (9/13) had baseline Glasgow Coma Scale scores of 3. Anterior STEMI, observed in 9 patients, was the leading diagnosis. Non-shockable initial rhythms were detected in 2 patients (numbers 6 and 13). One patient (number 6) died of cardiogenic shock complicating STEMI; others were discharged. Seizures due to brain hypoxia were observed in 5 subjects, but good neurologic recovery was observed in 11 subjects at 30 days. Valproic acid and phenytoin were administered as antiepileptic agents. Poor neurologic outcome (CPC 3) was observed in 1 patient. Transfer time of this patient to our hospital was 70 minutes, and she was hypotensive. Intravenous vasopressor support was administered in 7 patients, 4 of whom developed recurrent ventricular arrhythmias and cardiac arrest during cooling. No procedure related clinically adverse events, such as insertion site bleeding or catheter thrombosis were seen. Two patients experienced rebound hyperthermia, which complicated hypothermia therapy.

## DISCUSSION

The primary finding was that MTH by intravascular cooling had favorable effect on neurologic recovery in patients with cardiac arrest due to STEMI. This treatment was found to decrease mortality and morbidity in patients who received successful resuscitation after cardiac arrest.<sup>[5,6]</sup> Limited reperfusion injury, reduced release of toxic sub-

stances including glutamate, decreased rate of brain metabolism, and inhibited apoptosis are thought to be the main mechanisms.<sup>[7]</sup>

Previous studies analyzed data of patients with acute coronary syndromes, and these data were compared with historical uncooled control group. It was observed that a combination of PCI and therapeutic hypothermia in comatose patients was safe and reasonable.<sup>[8–10]</sup> Referred patients whose neurologic status did not improve after CPR was successfully performed at another hospital were also cooled. As a long-term outcome, a normal neurologic status was observed in 11 patients at 1 year.

Apart from procedural complications, hypothermia can induce metabolic disturbances, including hypokalemia, hypomagnesemia, and hyperglycemia. Leukopenia and thrombocytopenia may also occur.<sup>[7]</sup> Therefore, regular measurement of electrolytes and glucose is necessary. Complete blood count and basic coagulation parameters should be checked. Only 1 patient developed thrombocytopenia, but bleeding episodes, which were mainly gastrointestinal, occurred in 9. Sepsis was shown to be likely in hypothermia patients.<sup>[5]</sup> Standard prophylactic antibiotics were administered in a study.<sup>[8]</sup> In our population, antibiotic treatment was administered to 7 subjects, 2 of whom had sepsis. Most common diagnosis was pneumonia.

Hyperthermia predicts poor neurologic recovery after successful CPR.<sup>[11]</sup> Rebound hyperthermia is a poorly emphasized phenomenon in therapeutic hypothermia. In the present study, 2 patients developed pyrexia (>38°C) after completion of rewarming phase, but good neurologic recovery was observed. In this situation, cooling system recooled patients to suppress hyperthermia. An additional 10 hours were necessary to recool patient number 8. Any infectious process should be excluded when the cooled patient experiences fever. Rebound hyperthermia was predictive of increased mortality and morbidity in patients treated with therapeutic hypothermia.<sup>[12]</sup> Another study found higher maximal temperatures (>38.7°C) to be associated with poorer neurologic outcome.<sup>[13]</sup> These studies were retrospective; further research is needed to delineate the importance and management of rebound fever.

Door-to-invasive cooling time was longer in the present study, compared with previous studies.<sup>[8]</sup> In

order to compensate for this delay, intravenous cold saline was administered prior to invasive cooling. This approach was shown to be safe and effective.<sup>[14]</sup> Mean time to start therapeutic hypothermia and achieve target temperature was reduced by implementing hypothermia protocols.<sup>[15]</sup>

In the present study, mortality and morbidity were relatively low, compared with previous studies.<sup>[8,16]</sup> Younger age, good neurologic and functional status prior to arrest, successful coronary intervention, and enrollment of patients with in-hospital arrest are thought to be the major contributing factors. MTH via intravascular cooling is not routinely implemented in Turkey,<sup>[17]</sup> though it improves neurologic outcome after cardiac arrest due to STEMI. Further studies enrolling more patients are warranted to integrate MTH into clinical practice.

**Conflict-of-interest issues regarding the authorship or article: None declared**

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**Keywords:** Cardiac arrest; therapeutic hypothermia; myocardial infarction.

**Anahtar sözcükler:** Kalp durması; terapötik hipotermi; miyokart enfarktüsü.