

Cardiac Arrest, Mild Therapeutic Hypothermia, and Unanticipated Cerebral Recovery

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Objectives: Animal and human studies support mild therapeutic hypothermia as an effective means of preventing brain injury in comatose patients resuscitated from cardiac arrest. However, there is little clinical experience with predicting neurologic outcome in this patient population. We present 4 comatose patients resuscitated from cardiac arrest treated with mild hypothermia whose in-hospital neurologic prognosis was determined by board-certified neurologists to be grave, yet were ultimately discharged from the hospital with no or minimal neurologic sequelae.

Results: We report 4 comatose patients resuscitated from cardiac arrest treated with mild hypothermia. On hospital admission, all patients had a Glasgow Coma Score between 3 and 6 and a FOUR Score between 1 and 5. Mild hypothermia (32°C–33°C) was implemented for 24 to 40 hours. Examination by board-certified neurologists before and during hypothermia or the rewarming phase suggested a grave prognosis. All 4 patients had sudden and dramatic neurologic recovery 9 to 24 hours after rewarming to normothermia and were ultimately discharged with no or minimal neurocognitive sequelae.

Conclusion: This case series suggests that neurologic assessment-based prognosis of patients after cardiac arrest undergoing therapeutic mild hypothermia should be considered unreliable for at least the first 72 hours. Use of additional assessments such as brain injury markers or evoked potentials, in addition to clinical examination, should be strongly considered to help determine an estimated prognosis. Functional reversibility after a global insult could be an intrinsic potential of the brain, similar to myocardial stunning, and deserves investigation.

Key Words: cardiac arrest, neurologic outcomes, therapeutic hypothermia

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Each year, sudden cardiac death claims approximately 500,000 lives in the United States.¹ Nationally, the overall survival rate is about 5%.¹ For some of the few survivors, devastating sequelae include permanent and severe neurologic deficits.

Patients who suffer from anoxic-ischemic brain injury during cardiac arrest, develop varying degrees of neurologic dysfunction because of lack of blood flow and oxygen delivery to the brain. Normally, the brain receives about 15% of total cardiac output to meet its high metabolic demands. Within 20 seconds from the cessation of cardiac function, there is loss of cerebral oxygen stores and consciousness.² Within 5 minutes of cardiac arrest onset, there is depletion of glucose and ATP, resulting in membrane depolarization, acidosis, and eventually cell death.³

To decrease the effects of ischemia, anoxia, and reperfusion injury on brain tissue, therapeutic hypothermia (32°C–34°C) has been successfully implemented in animal^{4–9} and human trials.^{10,11} Two prospective, randomized clinical trials have demonstrated significant improvement in neurologic outcome and mortality using mild therapeutic hypothermia in patients who suffered an out-of-hospital ventricular fibrillation cardiac arrest and remained comatose after restoration of a perfusing rhythm.^{10,11} Based principally on these 2 studies (and a few nonrandomized clinical investigations),^{12–16} the American Heart Association (AHA) 2005 guidelines recommended mild hypothermia as a IIa recommendation for patients who meet these criteria. Mild hypothermia is also considered potentially beneficial for patients with nonventricular fibrillation arrest, or for in-hospital cardiac arrest (IIb recommendation).¹

Despite considerable efforts to accurately predict mortality and neurologic outcome after cardiac arrest, reliability of current methods is insufficient.^{17–20} Clinical evaluation, serum markers, imaging studies and evoked potentials have been studied in resuscitated normothermic patients.¹⁷ Relevant experience with therapeutic hypothermia and rewarming, is limited.^{18–20}

The clinical neurologic examination is the foundation for predicting outcome from cardiac arrest. Persistent brainstem dysfunction is usually considered unfavorable, although patients may recover.¹⁷ Conversely, patients with preserved brainstem function often die without awakening because of irreversible destruction of the cerebral cortex.¹⁷ Scales that rely solely upon brain stem function have limited utility in postresuscitation

TABLE 1. FOUR Score Neurologic Assessment and Scoring

FOUR Score	Glasgow Coma Scale
Eye response	Eye response
4 = eyelids open or opened, tracking, or blinking to command	4 = eyes open spontaneously
3 = eyelids open but not tracking	3 = eye opening to verbal command
2 = eyelids closed but open to loud voice	2 = eye opening to pain
1 = eyelids closed but open to pain	1 = no eye opening
0 = eyelids remain closed with pain	
Motor response	Motor response
4 = thumbs-up, fist, or peace sign	6 = obeys commands
3 = localizing to pain	5 = localizing pain
2 = flexion response to pain	4 = withdrawal from pain
1 = extension response to pain	3 = flexion response to pain
0 = no response to pain or generalized myoclonus status	2 = extension response to pain
	1 = no motor response
Brainstem reflexes	Verbal response
4 = pupil and corneal reflexes present	5 = oriented
3 = one pupil wide and fixed	4 = confused
2 = pupil or corneal reflexes absent	3 = inappropriate words
1 = pupil and corneal reflexes absent	2 = incomprehensible sounds
0 = absent pupil, corneal, and cough reflex	1 = no verbal response
Respiration	
4 = not intubated, regular breathing pattern	
3 = not intubated, Cheyne-Stokes breathing pattern	
2 = not intubated, irregular breathing	
1 = breathes above ventilator rate	
0 = breathes at ventilator rate or apnea	

FOUR indicates Full Outline of Unresponsiveness.

evaluation. Because the best verbal response is a significant component of the Glasgow Coma Scale (GCS), accuracy of this approach is limited after intubation. Recently a new Scale has been demonstrated to be prognostically superior to the GCS because of assessment of brainstem reflexes, breathing patterns and recognizing different stages of herniation. It is termed the Full Outline of UnResponsiveness (FOUR) Score (Table 1).²¹

All 4 patients had sudden and rapid improvement of their neurological status several hours after rewarming and all were discharged home with either no or minor neurocognitive deficits.

We report a series of 4 patients resuscitated from cardiac arrest and treated with mild hypothermia. All 4 patients had severe neurologic deficits before and during hypothermia as well as the rewarming phase that led to the clinical diagnosis of severe ischemic-anoxic encephalopathy. However, all 4 patients had sudden and rapid improvement of their neurologic status several hours after rewarming and all were discharged home with either no or minor neurocognitive deficits. Grouped information from all the cases for the duration of untreated cardiac arrest, cardiopulmonary resuscitation (CPR), and hypothermic treatment characteristics are seen in Table 2.

METHODS AND RESULTS

The study was approved by the Institutions Research Committee at the University of Minnesota, Minneapolis, and St. Cloud Hospital.

Case 1

A 38-year-old African American man collapsed in the emergency department waiting room. Immediate defibrillation was unsuccessful for an initial cardiac arrest rhythm of ventricular fibrillation and CPR was performed for 35 minutes. Sinus bradycardia was eventually restored after the 14th biphasic shock. Epinephrine, vasopressin, atropine, bicarbonate and amiodarone were given intravenously according to the AHA 2000 guidelines. The 12-lead electrocardiogram demonstrated ST elevation consistent with an acute anterior myocardial infarction. He was immediately transferred to the cardiac catheterization laboratory at a University Hospital. On arrival in the cardiac catheterization laboratory his brief neurologic FOUR Score examination was 1 (Table 3). Coronary angiography demonstrated a totally occluded proximal left anterior descending coronary artery with thrombolysis in myocardial infarction (TIMI) flow 0. An intra-aortic balloon pump was introduced on a 1:1 QRS gated pressure augmentation. During the percutaneous coronary intervention (PCI) of the culprit lesion, the patient redeveloped ventricular fibrillation that was converted immediately to normal sinus tachycardia by a single 150 J biphasic shock. The patient had TIMI 3 flow after successfully stenting the lesion. The patient had been completely unresponsive, intubated, and ventilated throughout the procedure. No medications were given to alter mentation and neurologic evaluation. Because of significant hypotension, dopamine and epinephrine infusions were started. The patient was then transferred to the intensive care unit. Transthoracic echocardiography revealed anterior akinesis, severe diffuse hypokinesis, moderate to severe ischemic mitral regurgitation, a pulmonary artery pressure of 40 mm Hg above right atrial pressure, and an ejection fraction visually estimated to be 15% to 20%. During the 2 first days, the patient's core temperature measured at the tympanic membrane and rectum was intentionally maintained at 33°C by direct exposure to the cooled air in the intensive care unit (permissive hypothermia with no sheets, bedclothes, or covers). There were no signs of shivering, and no anesthetics or sedatives were administered. Neurologic examination was performed by a board-certified neurologist the second postresuscitation day, and the FOUR score examination was again 1, suggestive of severe anoxic encephalopathy. Pertinent findings are shown in Table 3.

TABLE 2. Cerebral Perfusion and Therapeutic Hypothermia Factors

Patient	Duration of No Flow (min)	Duration of CPR (min)	Time to Target Temperature From Cardiac Arrest (h)	Duration of Hypothermia (h)	Duration of Rewarming (h)	Target Temperature (°C)	Major Recovery After Rewarming (hr)
1	2	35	Unknown	40	18	33	20
2	Unknown	24	3	24	12	32–33	9
3	~10	18	3	24	14	32	>26
4	~7	15	5	26	14	32	36

TABLE 3. Neurologic Assessments

Neurologic Examination	Patient 1	Patient 2	Patient 3	Patient 4
Initial	<ol style="list-style-type: none"> 1. Eyes closed to pain 2. Extension response to pain 3. Absent pupil, corneal, and cough reflex 4. Apnea. FS = 1/GCS = 4	<ol style="list-style-type: none"> 1. Eyes closed to pain 2. Flexion response to pain 3. Absent pupil, corneal, and cough reflex 4. Apnea FS = 2/GCS = 5	<ol style="list-style-type: none"> 1. Eyelids closed but open to pain 2. Flexion to pain 3. Pupil and corneal reflexes absent but positive cough reflex 4. Breathes above the ventilator's rate FS = 5/GCS = 6	<ol style="list-style-type: none"> 1. Eyes closed to pain 2. No response to pain 3. Absent pupil, corneal, and cough reflex Breathes above the ventilator's rate FS = 1/GCS = 3
After rewarming	<ol style="list-style-type: none"> 1. Eyes closed to pain 2. Extension response to pain 3. Absent pupil, corneal, and cough reflex 4. Apnea FS = 1/GCS = 4	Absent pupil, corneal, and cough reflex, on neuromuscular blockade FS = N/A 9 h later FS = 15/GCS = 14	<ol style="list-style-type: none"> 1. Eyelids closed but open to pain 2. Flexion to pain 3. Pupil, corneal and cough reflexes absent 4. Breathes above the ventilator's rate FS = 4/GCS = 6	<ol style="list-style-type: none"> 1. Eyes closed but open to pain 2. Extension response to pain 3. Absent pupil, corneal, and cough reflex Breathes above the ventilator's rate FS = 3/GCS = 5
Predischarge	4th day after arrest Normal motor and brain stem examination Minor neurocognitive deficits FS = 16/GCS = 15	4th day after arrest Major neurocognitive deficits that improved within 3 d before discharge FS = 16/GCS = 15	4th day after arrest <ol style="list-style-type: none"> 1. Eyelids closed but open to loud voice 2. Localizing to pain 3. Pupil and corneal reflexes present 4. Intubated, breathing over ventilator FS = 10/GCS = 10	4th day after arrest Normal motor and brain stem examination Minor neurocognitive deficits FS = 15/GCS = 14
Late	Normal exam one month later	Minor deficits in short memory and basic calculus	8 d later, normal neurologic evaluation	Normal exam one month later

Because of improved hemodynamics, the intra-aortic balloon pump and inotropic support were discontinued on the morning of day 3. Eighteen hours after rewarming to 36.5°C, an EEG was ordered but never obtained because of the course of events. A board-certified neurologist reevaluated the patient at 9:30 AM that same day and documented severe anoxic brain injury with a FOUR score of 1. The patient had normal liver and renal function. At 11 AM, the patient moved his feet and at 11:20 opened his eyes, sat up in the bed and tried to self-extubate. Mild sedation was initiated and extubation performed that evening. Neuropsychiatric evaluation before discharge revealed minimal neurocognitive deficits. His recovery was uneventful. One-month clinical follow-up revealed a normal neurologic examination and unchanged neurocognitive function.

Case 2

A 56-year-old woman who was resuscitated from ventricular fibrillation cardiac arrest was admitted to the inten-

sive care unit in a postresuscitation coma. In the emergency department, the patient received CPR for 24 minutes. Return of spontaneous circulation occurred on the 10th biphasic, 150 J shock. Upon arrival in the intensive care unit, the patient was unresponsive to commands and painful stimuli. The FOUR score was 2 (Table 3). Therapeutic hypothermia was started within 1 hour of resuscitation with cooling blankets and 2 L of 4°C intravenous normal saline. Target temperature was achieved in 2 hours and was maintained between 32°C to 33°C for 24 hours with cooling blankets and frequent temperature checks by dedicated nursing staff guided by rectal and tympanic membrane recordings. On the morning of the second day, the patient was on minimal sedation (1 mg of Morphine IV every 6 hours and 1 mg of Lorazepam IV every 12 hours). A cisatracurium drip was used for neuromuscular blockade. During the evening of the second day, the patient was rewarmed. Liver and renal function was normal. After the paralytic agent was discontinued for 12 hours and the

patient had been normothermic for 6 hours, evaluation by a board-certified neurologist of the corneal, pupillary, and gag reflexes was suggestive of severe brain stem dysfunction. Three hours after the neurology evaluation, spontaneous movements returned. Twelve hours later, she was extubated. Pupils were reactive to light bilaterally and a cough reflex was present. Her neurologic examination showed significant neurocognitive defects that were reversed significantly within the next 3 days. After implantable cardioverter defibrillator placement, the patient was discharged home. Follow-up evaluation in cardiology clinic one month later demonstrated no neurologic deficits. There was no neuropsychiatric testing during that visit, so subtle neurocognitive dysfunction could have been missed. The patient refused neurology clinic follow-up.

Case 3

A 49-year-old otherwise healthy man had an out-of-hospital cardiac arrest and was resuscitated after 18 minutes of CPR. A postresuscitation 12-lead electrocardiogram demonstrated precordial ST elevation consistent with an acute anterior myocardial infarction. The patient was taken to the cardiac catheterization laboratory. A proximal left anterior descending artery occlusion was identified and successful PCI resulted in TIMI 3 flow. After PCI, the patient remained comatose, withdrawing from painful stimuli. A FOUR score was calculated to be 5 (Table 3). After transfer to the intensive care unit, therapeutic hypothermia was instituted as described in Case 2. The target temperature of 32°C was maintained for 24 hours with cooling blankets and frequent temperature checks by dedicated nursing staff. Liver and renal function was normal as well as electrolytes. After rewarming was achieved and neuromuscular blockade was discontinued for 12 hours, neurologic evaluation demonstrated a FOUR score of 4 (Table 3). The second day after rewarming, neurologic evaluation by a board-certified neurologist showed significant improvement with a FOUR score of 10 (Table 3). The patient was extubated on day 4. After 3 days in the cardiac step down unit (complicated by a pneumonia), he was discharged home with a normal neurologic evaluation.

Case 4

A 52-year-old otherwise healthy man suffered an out-of-hospital cardiac arrest. Paramedics performed CPR for 15 minutes followed by continued CPR using an inspiratory impedance threshold device.^{1,22-24} Ventricular fibrillation was converted to normal sinus rhythm followed by pulseless electrical activity. Intravenous epinephrine (1 mg) and 40 units of vasopressin were given with a return of acceptable blood pressure (116/88 mm Hg) before admission to the emergency department. The patient was unconscious after return of spontaneous circulation with a FOUR Score of 1 (Table 3). Decorticate arm motion was recorded by a neurologist when the patient was in the emergency department. The 12-lead electrocardiogram did not reveal ST elevation, but there was diffuse ST depression in the precordial leads V₂-V₅. Intravenous amiodarone 150 mg was administered in the emergency department followed by an intravenous drip of

1mg/min for 12 hours. Emergent echocardiography was performed and showed a significantly decreased ejection fraction of 15% and global systolic dysfunction without any regional wall motion abnormalities. Left ventricular end systolic dimension was 55 mm and there was 3+ mitral valve regurgitation. A decision was made to perform coronary angiography, which showed no significant coronary artery disease. The diagnosis of idiopathic dilated cardiomyopathy was therefore established. The patient was still unresponsive and his FOUR score was now 3 (Table 3). One and a half hours after his cardiac arrest he was cooled with cooling blankets. A target temperature of 32°C was achieved 4 hours later. The patient was placed on cisatracurium for paralysis and intravenous propofol and morphine sulfate for pain control as needed. Forty hours after initial cooling, the patient was rewarmed to a normal temperature (30 hours of target hypothermia and ~10 hours of rewarming to normothermia). Liver and renal function was normal. Sedation and neuromuscular blockade were discontinued. Twelve hours later, the FOUR score was 3 (Table 3). The diagnosis of severe anoxic encephalopathy with a grim prognosis was established by a board-certified neurologist and the patient was restarted on sedation. One day later, the patient began spontaneous movements. He was extubated later the same day and was eventually discharged from the hospital after 4 days with a normal neurologic evaluation.

DISCUSSION

We present 4 cases indicating that decerebration, decortication, fixed and dilated pupils, and absence of gag and corneal reflexes immediately after cardiac arrest, during mild hypothermia and within 24 hours after rewarming to normothermia after cardiac arrest, do not appear to have prognosticating clinical significance. All 4 patients were evaluated by neurologists 2 to 4 days after cardiac arrest and were diagnosed with severe ischemic-anoxic encephalopathy. The significant neurologic dysfunction persisted after rewarming. Spontaneous neurologic recovery with dramatic improvement was observed within one to 2 days after return to normothermia. All 4 patients were discharged home without significant neurologic deficits.

Even under optimal conditions, CPR generates no more than 20% of normal cardiac output.²⁵ The brain is very sensitive to a lack of oxygen and blood supply. Furthermore, as time of untreated cardiac arrest increases, higher cerebral perfusion pressure is needed to maintain forward blood flow to the brain because of astrocytic and glial edema that results in an increase in intracranial pressure and blood flow resistance.⁸ Endocranial hypertension may persist after resuscitation.^{26,27} Depending on the duration of no blood flow, the damage to the neurons and glial cells can be minimal, reversible or irreversible and result in brain death. As ischemia and anoxia have a global effect, the brain injury usually manifests as loss of consciousness. During that period, clinical signs and examination findings are usually suggestive of multilevel injury. The cortex appears to be more sensitive than the brainstem to low oxygen tension and loss of consciousness is the first manifestation.^{8,28}

Reperfusion is another critical component of neurologic injury. A sudden increase of cerebral blood flow with high oxygen content has been shown to cause significant reperfusion injury. Over a period of time that can extend to days after the restoration of spontaneous circulation, mechanisms that include calcium shifts, lipid peroxidation, other free-radical reactions, DNA damage and inflammation, lead to further neuronal damage.^{2,29,30} Several pharmacological manipulations (thiopental, corticosteroids, lidoflazine, nimodipine) have been tested in clinical trials in an effort to alter the natural history of coma after resuscitation from cardiac arrest, without significant demonstrated benefit.³¹⁻³⁴

Therapeutic hypothermia has been shown to protect neurologic recovery and brain function in animal models when it is applied just before, during or after cardiac arrest. The earlier hypothermia is established, the greater the benefits.^{27-29,35,36} Studies have focused on starting cooling either during CPR or immediately after cardiac arrest. Hypothermia instituted after restoration of spontaneous circulation may protect against this evolving damage by lowering endocranial pressure and thereby preserving cerebral perfusion. It may also benefit by decreasing oxygen demand in low flow regions and by protecting against the destructive effects of reperfusion injury.³⁷ The optimal time of onset, duration, and extent of hypothermia have not yet been established.²⁸

Although hypothermia has been studied as a neuroprotective measure for victims of cardiac arrest for more than 50 years,^{38,39} interest in its use has been recently renewed based on experimental work in animal models^{4,5,9} and 2 prospective randomized clinical trials.^{10,11} These studies have concluded that induction of mild hypothermia was safe and improved mortality and neurologic outcome.^{40,41} Accordingly, the 2003 Adult Trauma Life Support task force as well as the 2005 AHA guidelines recommend therapeutic mild hypothermia for patients who remain comatose after resuscitation from out-of-hospital cardiac arrest due to ventricular fibrillation and possibly for in-hospital cardiac arrest and arrest due to different rhythm abnormalities.^{1,42}

Recently, the prognostic value of the FOUR scale in comatose patients has been evaluated.²¹ There has been good correlation with the Glasgow Coma Scale because it can also be applied when patients are intubated. Low scores have been found to reflect a poor prognosis, including in patients resuscitated from cardiac arrest.²¹ However, in our 4 cases, an initially poor FOUR score immediately after resuscitation and 24 hours after rewarming from mild hypothermia, did not predict death or severe neurologic dysfunction.

Other methods of predicting neurologic outcome have been studied.⁴³ Clinical evaluation is generally available, repeatable, and simple to apply, but may be unreliable.^{17,43,44} Examination of brain stem reflexes and motor responses could give a reliable prognosis after 24 hours, whereas in 72 hours, a poor outcome can be predicted with accuracy.¹⁷ A recent meta-analysis suggested that absent corneal reflexes, absent pupillary reflexes, absent motor response or withdrawal to pain at 24 hours and absent motor response at 72 hours accurately predicted death or poor neurologic outcome in normothermic patients.^{17,45} These recommendations are

mainly based on the work of Levy et al⁴⁶ from 1985; he described that in normothermic patients absence of motor response at 72 hours predicted death and absence of possible independent living. Combining findings such as the GCS were not more helpful.³ The combination of serum neuron specific enolase, somatosensory evoked potentials, and the electroencephalogram has been proposed as superior to clinical evaluation alone in offering a more accurate prognosis in the first 24 to 72 hours.^{17,43,44} Our 4 patients were not evaluated with these laboratory investigations.

The clinical neurologic evaluation of patients in hypothermia is not extensively described. Even less studied is the neurologic recovery during rewarming. In accidental hypothermia, rectal temperature has been inversely related to the level of consciousness and pupillary response. However, great variability has been observed between patients with some of them retaining consciousness during deep hypothermia with others being lethargic during mild hypothermia. Similar findings were recorded with pupillary responses. With mild hypothermia, patients can be confused or even lethargic but reflexes are likely to be normal and pupillary responses intact.^{47,48} In patients with accidental hypothermia, permanent deficits of clinical relevance were either preexisting or attributed to injuries sustained during the accident.^{18,20,49} Findings in victims of accidental hypothermia cannot be extrapolated to induced hypothermia after resuscitation from cardiac arrest because of the different sequence of events leading to cell damage. However, the validity of somatosensory evoked potentials and serum neuron specific enolase is shown to be preserved in the context of mild hypothermia.^{18,19}

This case series represents patients with signs of severe irreversible anoxic brain injury and severe brain stem malfunction who, after therapeutic hypothermia after resuscitation from cardiac arrest, regained normal (or near normal) neurologic function. They demonstrate both the increased opportunity to help restore neurologic function in patients otherwise thought to have no chance for recovery as well as the challenge in predicting outcomes with current assessment tools. The sudden and near complete reversibility of such severe cerebral deficits reflects our poor understanding of cerebral function and hibernating properties of brain tissue in response to hypoxia and low blood flow states such as cardiac arrest. To our knowledge, this phenomenon has not been previously reported for victims of cardiac arrest treated with hypothermia. The neurologic response seen in these patients may represent a pathophysiologic state in the brain similar to myocardial stunning after resuscitation from cardiac arrest.⁵⁰ Irrespectively, these cases demonstrate that neurologic assessment should be considered unreliable for at least the first 72 hours. In our patients functional motor recovery occurred after >78, 48, 67, and 81 hours for patients 1, 2, 3, and 4 respectively (Table 2, summation of the hours in each patient). Functional reversibility after a global insult could be an intrinsic potential of the brain and deserves investigation. Because induction of therapeutic hypothermia post cardiac arrest involves intubation, sedation, and neuromuscular

blockade, prognostication with a 24-hour neurologic evaluation is impossible. In addition, because the duration of therapeutic hypothermia may vary between institutions and physicians and the rewarming period may take variable time, neurologic assessment for prognosis should be performed well after 3 days or 72 hours. Although in our case series medications were discontinued at least 12 hours before neurologic evaluation after rewarming, we are unable to say how the metabolism of those agents was altered by hypothermic conditions despite the normal liver and kidney function in all patients.

Limitations

This study has limitations that deserve mention. The small number of patients reported in this convenience sample without a comparison group precludes determination of the incidence of this phenomenon and direct application to large groups of patients with cardiac arrest. Nonetheless, the remarkable neurologic recovery seen in these patients is worthy of notice and supports consideration of larger, controlled studies to further characterize this experience.

CONCLUSION

This case series suggests that neurologic assessment-based prognosis of patients after cardiac arrest undergoing therapeutic mild hypothermia cannot and should not be performed for at least the first 72 hours. Use of additional tools such as brain injury markers, or evoked potentials, should be strongly considered to help determine an estimated prognosis. Functional reversibility after a global insult could be an intrinsic potential of the brain, similar to myocardial stunning, and deserves investigation. These cases demonstrate the need for better methods of predicting neurologic outcome in patients successfully resuscitated from cardiac arrest and treated with mild therapeutic hypothermia.

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