CASE REPORT

The Importance of Early Cooling for Patients with Hyperthermia

- Experience with Intravascular Temperature Management (IVTM) -

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Summary

- Severe (3rd degree) hyperthermia may cause sequelae such as disseminated intravascular coagulation (DIC), infections, multiple organ failure, impairment of cerebral function, and cerebellar ataxia.
- Complications and sequelae are factors that have a major influence on patient outcomes, and rescuing patients from hot environments and controlling core body temperature with more rapid cooling are crucial.
- Cooling methods include chilled transfusions, the evaporation method (covering the body surface with moistened gauze, etc. and using air flow to remove the heat of evaporation) and methods in which the patient's entire body is immersed in cold water (cold-water immersion).

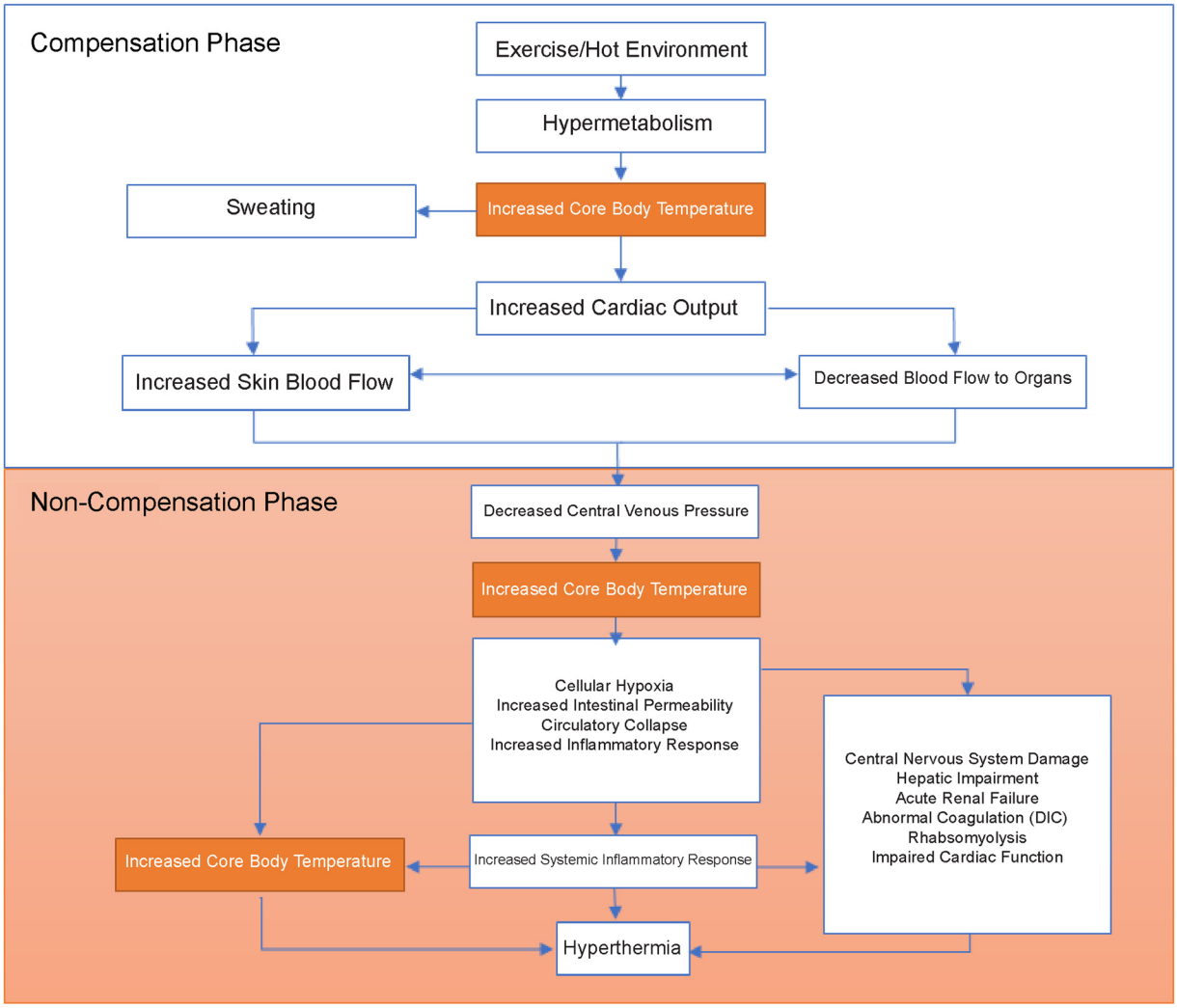
What is Hyperthermia?

Pathophysiology of Hyperthermia: Hyperthermia is an elevated body temperature that can no longer be controlled and causes organ damage.

The body adjusts body temperature using functions such as those listed below.

- Conduction: Direct exchange of heat with gases and liquids that come into contact with the skin
- Radiation: Diffusion of heat between the skin and the external environment
- Evaporation: Removal of heat when sweat and other forms of moisture evaporate from the skin
- Convection: Promotion of the movement of heat through conduction and evaporation that result from the flow of surrounding air

Figure 1: Pathology of Hyperthermia [1)]



- The increase in core body temperature caused by exercise or a hot environment is suppressed by conduction, radiation, and convection due to increased blood flow in the skin resulting from factors such as sweat (evaporation) and redistribution of blood flow (compensation phase).
- The ability of the body to lower core body temperature reaches its limit (non-compensation phase), resulting in further increase in core body temperature, which further promotes a systemic inflammatory reaction, increasing core body temperature even further, leading to various types of organ damage.

  - Promptly getting the patient to rest, removing him or her from the hot environment, and lowering core body temperature as rapidly as possible is the best treatment for preventing progression of the pathology of hyperthermia.

  - Severe hyperthermia causes complications and sequelae such as disseminated intravascular coagulation (DIC), infections, multiple organ failure, impairment of higher function, and cerebellar ataxia, which have a major influence on patient outcomes. Outcomes are said to be poor when the patient's body temperature is 40.5°C or greater in the early stages. [1)]

  - When a group of patients with sequelae is compared to a group without sequelae, the time until cooling to 38°C is significantly longer in the group with sequelae (Table 1) [2)], showing that intensive therapy focused on rapid cooling, sound management of body temperature, and treatment and prevention of organ damage is vital, especially in patients with severe hyperthermia.

Table 1: Occurrence of Sequelae and Time to Reach 38°C [2)]

	Sequelae Group	Control Group
Heatstroke STUDY 2006/2008	108.3 ± 93.5	67.2 ± 85.0
Heatstroke STUDY 2010	118.0 ± 111.5	78.6 ± 131.1
Heatstroke STUDY 2012	234.6 ± 362.2	130.7 ± 232.1

($p < 0.05$ for all in Mann-Whitney test)

Types of Hyperthermia and Selection of Cooling Method

Hyperthermia is broadly divided into 2 types: exertional and non-exertional (Table 2). [1)]
Japan has a characteristically high proportion of non-exertional hyperthermia in the aged.

Table 2: Types of Hyperthermia and Selection of Treatment

Characteristic	Non-Exertional	Exertional
Age	Elderly	Young
Onset Type	Seasonal (heat waves, etc.)	Sporadic
Patient's Activities of Daily Living	Inactive	Active
Health	Chronic complications present	Healthy
Medication Status	Regular medication use	No regular medication use
Clinical Condition	Retention of heat and impaired dissipation of heat due to environmental factors	Excessive production of heat due to exercise
Sweating	Often lacking	Often prominent
Central Nervous System Damage	Yes	Yes
Rhabdomyolysis	Rare	Frequent
Liver Failure	Mild	Moderate-severe
Renal Impairment	Rare (<5%)	Frequent (25-30%)
DIC	Mild	Moderate-severe
ARDS	Yes	Yes
Treatment	IVTM/evaporation method	Cold-water immersion

- Cooling methods for patients include:
  - Chilled transfusions
  - Transpiration method (moistening the body surface and providing air flow)
  - Cold-water immersion: Methods include immersing the patient in cold water
- Japan is characterized by high levels of non-exertional hyperthermia in the aged. [3)]
- Methods such as cold-water immersion that are poorly adjustable can cause hypothermia due to excessive cooling in the elderly and require caution.
- In elderly patients, the use of IVTM and the evaporation method, which are less invasive and more easily adjustable than cold-water immersion, are recommended. [1)]

Catheter Insertion Location, Target Temperature Setting, Use of Sedatives, Analgesics, and Muscle Relaxants, and Timing

- In Japan, the Cool Line IVTM catheter, which has 2 cooling balloons, is available for use in the treatment of hyperthermia under the Japanese reimbursement system. Similar to conventional central venous catheters, insertion from the femoral area, jugular vein, or subclavian vein using the Seldinger technique is possible.
- No certain temperature setting has been established, but in our facility the target temperature is set to 37°C in order to prevent excessive cooling of patients. [4)]
- Reliable securing of the airway (tracheal intubation) is to be carried out before the start of IVTM, particularly in patients with impaired consciousness, shock, or multiple organ failure. Intubation is to remain in place until a normal body temperature is achieved. Systemic management is to be provided using sedatives, analgesics (fentanyl), and even muscle relaxants in some cases.
- Even when no sufficient decrease in body temperature is achieved despite the introduction of IVTM, muscle relaxants such as rocuronium are used in addition to tracheal intubation. This can be expected to result in dilation of the peripheral blood vessels and control of the generation of heat by shivering and bodily movements.
  (At this point, the efficacy of dantrolene has not been proven.)[1)]

Intensive Care and Temperature Management Therapy for Hyperthermia: Hints and Risks

It is important to maintain the airway, respiration, and circulation.

Continuously monitor core body temperature (rectal temperature, bladder temperature, esophageal temperature, etc.) and continue cooling until body temperature is below 38°C. Administer 4°C chilled extracellular fluid from a central venous catheter. (1000 mL/30 min. at 4°C in adults. Caution is necessary in the elderly due to poor cardiac function.)

Unlike ordinary fever, hyperthermia is not a high temperature that results from an abnormal set point for the body temperature. Therefore, antipyretics like NSAIDs or acetaminophen are ineffective. Furthermore, they should not be used because they may cause decreased blood pressure, renal impairment, or hepatic impairment. [1)]

There are no wonder drugs for the treatment of hyperthermia. In order to save the patient's life, it is vital to maintain proper vital signs by reliably securing the airway and providing proper transfusion management and to quickly remove the patient from the hot environment and provide rapid cooling.

Cases and Research

In Japan, Thermogard XP® and the Cool Line® catheter is covered by insurance for the treatment of patients with hyperthermia.

We have also confirmed the efficacy and safety of IVTM in multicenter research.

Design: Prospective observational study

Change in temperature, Sequential Organ Failure Assessment (SOFA) score, incidence of complications, and neurological outcomes in an arm receiving conventional cooling alone and an arm receiving IVTM in addition to conventional cooling were compared.

Figure 3

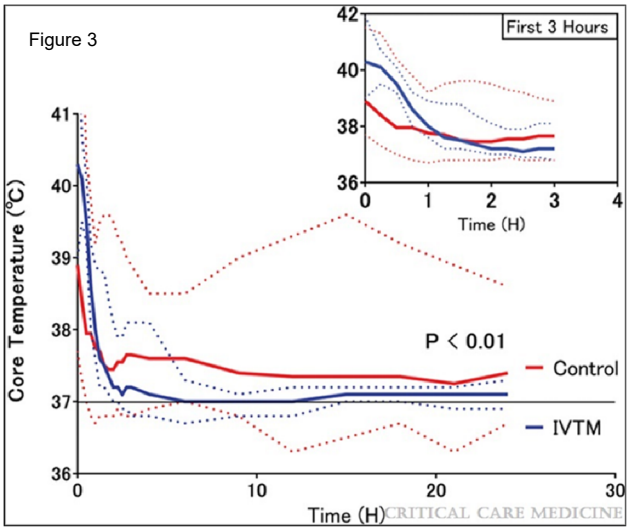
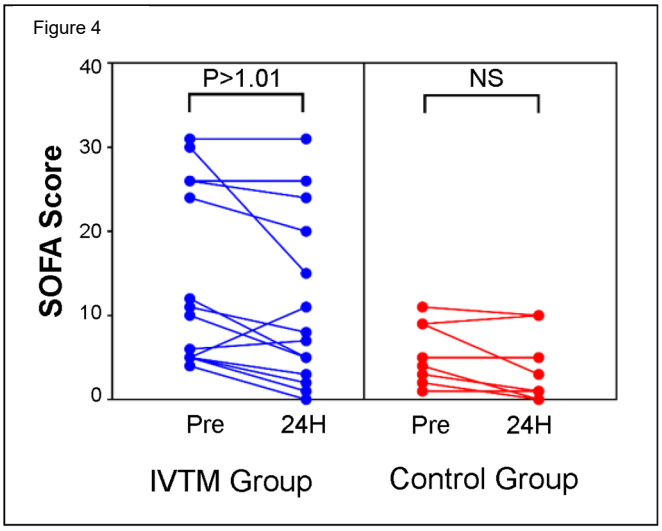
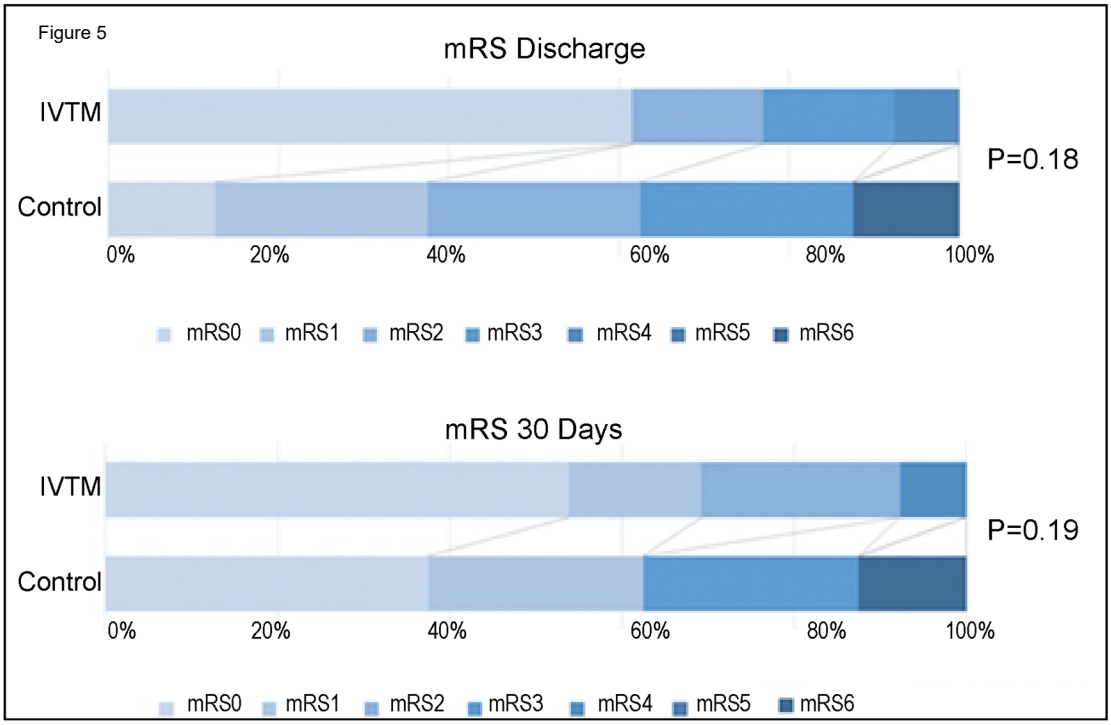


Figure 4



- All patients for whom IVTM was used (blue line) reached a temperature of 37°C within 24 hours, while only 50% of patients in the control arm (red line) were able to reach normal temperature (Fig. 3; solid lines indicate medians, dotted lines indicate 95% confidence intervals).
- SOFA scores were significantly lower in patients for whom IVTM was used.
(Median: 4.0 vs. 1.5; p = 0.04)
- There were no cases of death in IVTM patients, and they were confirmed to have superior neurological findings at the time of discharge and 30 days later.
(Fig. 5: mRS at Discharge and After 30 Days)

Figure 5



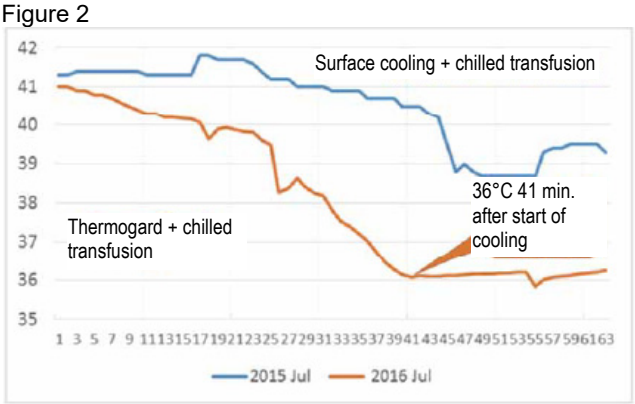
The mean age of patients in this study was 75 years.
Thus, it can be surmised that IVTM (Thermogard XP and Cool Line catheter) is a safe treatment even for patients with severe hyperthermia in Japan, a country with an especially large aged population. [4)]

Case Presentation

85 years of age, female.

Comparison of IVTM treatment in patients transported to the hospital with grade III severe hyperthermia in 2 consecutive years (Fig. 2)

Figure 2



Consent has been obtained.

Compared to the cooling methods used before the introduction of IVTM (blue line: ice packs on the body surface, mist, and fan cooling with chilled transfusion), cooling methods using Thermogard and chilled transfusion (orange line: Thermogard and chilled transfusion) made it possible to provide more rapid and reliable temperature management, which was associated with earlier patient discharge.

Advantages of IVTM

- Unlike conventional cooling methods like cold-water immersion, ice packs and evaporation, and gel pad cooling, IVTM does not directly cool the skin. It avoids reduced efficacy of radiation from the skin resulting from constriction of the peripheral blood vessels due to excessive cooling of the peripheral skin. IVTM can provide efficient body temperature management through the indwelling of a direct cooling catheter in the superior vena cava and “direct cooling of the blood and direct reduction of core body temperature.”
- Unlike conventional temperature management devices, which cool the surface of the body, IVTM does not cover the precordial region and does not moisten the body during cooling. This makes access easier when responding to sudden changes in patient condition, such as emergency defibrillation.

Disadvantages of IVTM

- Although problems like DIC are likely in hyperthermia and there is little risk of thrombus formation, there is a risk of deep vein thrombosis and catheter infection, as with conventional central venous catheters. It is also important not to indwell the catheter for longer than necessary.
  (At our facility, the catheter is removed at an early stage (within 24 to 48 hours) if body temperature management is complete.)

References

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4) Yokobori S, Koido Y, and Yokota H, *et al*
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