Targeted Temperature Management: Surface vs. Intravascular Temperature Management Methods

Abstract
Targeted temperature management has been a subject of ongoing experimental and clinical investigations in various applications of patient care. Therapeutic hypothermia remains an important neuroprotectant, as it decreases cerebral metabolism and energy consumption processes. Therefore, the goal of TTM is to improve neurological outcomes in all patients with acute brain injury.

This whitepaper provides a comparison of surface cooling and intravascular temperature management (IVTM) methods. Factors that affect the rate of cooling include shivering, patient body mass, and cooling performance. A summary of clinical trials comparing surface cooling and IVTM methods shows differences in outcomes with regard to total patient survival as well as neurological outcome at hospital discharge, depending on the cooling method used. In addition, economic differences between surface and intravascular cooling exist in targeted temperature management.

Key Takeaways

1. All published clinical trials, which totaled over 1100 patients, showed that patients cooled via IVTM had better neurological outcomes at hospital discharge compared to patients cooled via surface cooling (39.4% vs 28.7%, $P<0.001$).
2. All published clinical trials, which totaled over 1400 patients, showed that IVTM had better survival to hospital discharge compared to surface cooling (50% vs. 44.9%, $P=0.028$).
3. IVTM shows better cooling performance, less sedation and paralytic used and significantly less nursing burden compared to surface cooling.
4. IVTM provides a better value proposition compared to surface cooling, based on both patient outcomes and economic impact to the healthcare facility.

Abbreviations

AIS: Acute Ischemic Stroke
CA: Cardiac Arrest
CVC: Central Venous Catheter
CVP: Central Venous Pressure
ICH: Intracranial Hemorrhage
ICU: Intensive Care Unit
IVTM: Intravascular Temperature Management
SAH: Subarachnoid Hemorrhage
TBI: Traumatic Brain Injury
TH: Therapeutic Hypothermia
TTM: Targeted Temperature Management

Background

Temperature is one of the four main vital signs. Targeted temperature management (TTM), which includes fever control, therapeutic hypothermia (TH) and warming, has been shown to improve outcomes, reduce complications and deliver a beneficial economic impact on society and hospitals.

TTM has been a subject of ongoing experimental and clinical investigations in different fields of application and patient care. Many studies published over the past two decades have shown that fever in patients with acute neurologic injury, regardless of its cause, is independently linked to higher mortality, poor neurologic outcomes, and increased length of stay in the intensive care unit (ICU) and hospital. This has been demonstrated for traumatic brain injury (TBI), acute ischemic stroke (AIS), subarachnoid hemorrhage (SAH), intracranial hemorrhage (ICH), and cardiac arrest (CA)[1,2]. Therapeutic hypothermia, introduced more than five decades ago, remains an important neuroprotectant. Hypothermia decreases cerebral metabolism and energy consumption and reduces the excitotoxic cascade in steps such as apoptosis, necrosis, and inflammation. Therefore, the goal of TTM is to improve neurological outcomes in all patients with acute brain injury.

Overview of Surface vs. Intravascular Temperature Management Methods

TTM can be induced and maintained with external surface cooling or intravascular systems. Review of technical and clinical data showed differences in performance and effectiveness of the two cooling methods.

Surface Cooling

TTM via surface cooling utilizes the skin as a mechanism to cool or warm a patient, where 90% of all heat exchange occurs through skin and heat transfer is directly proportional between the cooling pad/blanket to the skin surface area[3]. Surface cooling systems vary, from ice packs to alcohol rubs to thermally conductive skin blankets and pads. Thermally conductive skin blankets or pads connect to a console with a water reservoir which circulates cold or hot fluid (between 4°C to 42°C) throughout the blankets or pads. Some surface systems have built-in feedback loops where the system is regulated based upon the measured input temperature from patients.

Intravascular Cooling

Core cooling was first described in early 1950s during cardiothoracic surgery. By the late 1960s, deep hypothermia (less than 20°C) using bypass machines was widely applied during surgery[4,5]. In recent years, the renewed interest in therapeutic hypothermia has generated the demand in the development of more sophisticated cooling methods to address unmet clinical needs.

Intravascular Temperature Management (IVTM) technology utilizes an innovative proprietary catheter design and computer controlled console. Catheters are placed in the patient's venous system and use a "closed-loop" saline flow for internal thermoregulation. Thermoregulation of the core body temperature takes place based on feedback from a patient temperature probe. In addition, these catheters support standard critical care management similar to standard triple lumen central venous catheters (CVC) including medication delivery, central venous pressure measurements, and blood draws.

Comparison of Surface Cooling and IVTM Methods

Advantages for both surface and IVTM cooling methods are summarized in Table 1. ZOLL provides both surface and IVTM solutions for temperature management. The purpose of this comparison is to assist with choosing the most appropriate method to use for each individual patient.

Table 1. Comparison of Surface Cooling and IVTM Methods: Advantages

Surface Cooling	IVTM
• Cooling pads can be applied by nurses without physician presence • Non-invasive method of cooling • Can be used outside of the ICU setting • Faster time to initiate cooling	• Precise control of target temperature and less temperature fluctuation • Faster time to target temperature • Less shivering, which results in less sedation needed to control shivering and can be used in awake, non-intubated patients[6] • Significantly less nursing workload due to easy access to patient skin and reduction in skin check frequency[7,8]

The publication of two studies in NEJM 2002 on hypothermia after cardiac arrest, the HACA and Bernard trials, supported the recommendation of TH as an AHA and ERC level 1 guideline in 2010[9]. These guidelines were updated in 2015 to extend the range of target temperatures between 32°C and 36°C. TH can be induced and maintained with surface (external) cooling or core (internal) cooling methods. The selection of device is not only important in clinical practice, but it can also be instrumental in clinical trials. Significantly better outcomes were shown in a small randomized controlled trial (RCT) published in 2012 using a precise feedback-control system through intravascular cooling. The study compared 32.0°C to 34.0°C[10]. Alternatively, no difference was shown in a larger RCT that heavily used surface cooling. This trial, published in 2013, found no difference between strict temperature control at 36.0°C compared to 33.0°C[11]. The conclusions of this study have been criticized for problems such as prolonged time (10 hours) to target temperature, temperature fluctuations during the maintenance phase (only 7 hours target temperature separation between 33°C group and 36°C group during the 24 hours maintenance phase), excessively rapid re-warming, and other issues[12-15].

Despite disagreement on the optimal target temperature, general consensus on the importance of TTM focuses on the speed at reaching target temperature, precision of maintaining target temperature, a controlled rate of rewarming, and fever control. These are the key factors for TH resulting in better neurological outcomes. In this regard, the efficiency of temperature control device is becoming increasingly important. Although the AHA and ERC recommendation of TH is a class 1 guideline, it is used infrequently[16-19]. Potential reasons cited from physicians include technical and logistical difficulties as well as a lack of financial or personnel resources in TTM.

Factors Affecting Cooling Rate

Shivering

In order to understand the difference in surface cooling versus intravascular cooling to reduce body temperature, it is necessary to know how the human body works to maintain a constant core temperature of approximately 37°C. This extraordinary temperature stability requires the integration of temperature sensing, central processing and efferent responses to precisely balance heat loss and heat production. Both cold and warm receptors are widely distributed throughout the skin, while the central processing occurs in the hypothalamus. When the skin sensors inform the hypothalamus of cold below a certain threshold or set point (normally around 36.5°C), a strong sympathetic nervous system response occurs, causing vasoconstriction of skin vessels to conserve heat and increased muscle tension and shivering to generate heat[3]. The shivering threshold is 1°C below the vasoconstriction threshold so around 35.5°C. The shivering response peaks at core temperature near 35°C, decreases significantly at temperatures below 33°C, and ceases completely around 31°C in most patients[20,21]. Shivering can cause problems in the patient's TTM, such as increasing metabolic heat production up to 600% above basal level[22], even in febrile patients. At this point, it becomes difficult to achieve core temperature below 34°C without general anesthesia and neuromuscular blocking agents. Shivering is not only remarkably uncomfortable, but it also increases intracranial pressure[23]. Shivering can double or even triple oxygen consumption, causing hypoxemia, myocardial ischemia, and myocardial infarction in high-risk patients because of increased myocardial demands[24]. This has a particularly negative impact on a post cardiac-arrest patient whose heart has just been resuscitated. Therefore, American Heart Association (AHA) strongly recommends the avoidance of shivering during hypothermia induction, normothermia or rewarming periods[9].

Surface cooling has been shown to increase peripheral vasoconstriction and shivering as the body attempts to thermoregulate and conserve body heat. In one clinical study using a skin surface cooling device (Arctic Sun®, Bard), gel pads were applied directly to the skin of critically ill patients and cold water was circulated through the pads, simulating water immersion. Shivering occurred in 86% of febrile, mechanically ventilated, and sedated patients, all of whom were receiving propofol[25]. Another study of Arctic Sun in 69 post-cardiac arrest intubated paralyzed patients had a shivering occurrence of 96%[26].

Although surface cooling may seem easy to use and can be applied by nurses without a physician being present, the potential risks and disadvantages are outweighed by the benefits of TH and fever control. The effectiveness of surface cooling is limited to the maximum amount of skin coverage, the lowest temperature that circulates within the blankets or pads, and any counterproductive activity from shivering. When applying surface cooling methods, patients need continuous attention due to the risk of freezing-induced skin damage and shivering[27].

Patient Body Mass

Another important parameter affecting ease and speed of cooling is body mass; obese patients are more difficult to cool, especially with surface cooling, due to insulating properties of adipose tissue and because of the greater mass that needs to be cooled[28]. Obesity decreases the surface area-to-mass ratio and increases the size of the peripheral compartment. In a multicenter pilot clinical trial, Hindmann et al found that 12% of patients could not reach a target of 34.5°C with surface cooling despite patients being paralyzed and a cold operating room temperature. These obese patients (127 – 150 kg) have a reduced ability to dissipate internal energy because of the low thermal conductivity of their layers of fat[29]. In other words, obesity decreases the surface area-to-mass ratio and increases the size of the peripheral thermal compartment. These properties each diminish the ability to cool the core during surgery[29].

In another large observation cohort study in 1,086 patients who suffered post cardiac arrest, about one third of patients (32%) failed to achieve target temperature of 34°C with surface cooling[30]. The group with higher body weights (81 kg vs. 74 kg, $p<0.001$) took 17 hours

(Median) to reach target from arrest compared to 10 hours. High body weights (OR 1.02 per kg, 95% CI 1.01-1.03; p=0.007) was identified as one of the risk factors for failure of surface cooling in the multivariable analysis in this study.

Mechanical Factors

Differences in mechanical factors, such as the rate of heat transfer, differ between surface and intravascular temperature management methods. These differences can affect the efficiency of temperature management and are shown in Table 2.

Table 2. Factors that Affect the Rate of Heat Transfer: Surface Cooling vs. IVTM

Factor	Surface Cooling[31]	IVTM
Temperature differences	Between cooling blanket and patients skin	Between cooling catheter and patient blood flow
Material thickness	Cooling blanket	Catheter balloons
Material surface area	Skin coverage where blanket is applied	Catheter balloons
Flow rate and patterns of the coolant	Inside cooling blanket	Inside catheter balloons
Thermal conductivity of materials	Separating patient's skin and coolant	Separating patient blood flow and saline
Insulation from patient's peripheral tissues	Yes	Not an issue, cools patient blood directly

Cooling Performance

Due to the pathophysiology described above, surface cooling has limited cooling performance. The Rescue trial[32] was a prospective and randomized study and compared the Arctic Sun to other surface cooling. The Arctic Sun utilizes a higher flow rate than standard cooling blankets through the use of conductive adherent gel pads and an automatic temperature feedback mechanism. Despite these features, the cooling rate was 0.7°C/hr with Arctic Sun compared to 0.5°C/hr with standard surface cooling. In addition, 25% patients in Arctic Sun group failed to reach target temperature of 34°C after 4 hours. Wide fluctuations in temperature were also noted, as 31% of patients in the Arctic Sun group had temperatures outside the target range (±2°C).

Many studies have shown that intravascular cooling is superior to surface cooling in maintaining target temperature and being faster to reach target temperature. Hoedemaekers et al.[33] compared several different cooling modalities and demonstrated that IVTM was effective in maintaining target temperature and less time spent out of target range compared to other water circulating blankets and gel pads. Flemming et al. conducted a study comparing IVTM with an automated surface cooling device. All patients (100%) treated with IVTM achieved target temperature of 33C with a mean of 3.5 hours, only 9% patients in surface cooling group achieved target temperature with a mean of 9.2 hours[34].

Table 3 shows a list of studies comparing cooling performance of surface cooling and IVTM in post-CA patients.

Table 3. Comparison of Performance in Surface Cooling vs. IVTM

First Author	Study Type	Number of Patients	Surface Cooling Device	Time to Target Temperature	Precision Measure	Precision Result
Deye[8]	Multicenter RCT	400	Conventional	Surface: 510 min IVTM: 330 min P<0.0001	Time deviation from target	Surface: 330 min IVTM: 60 min P<0.0001
Ferreira[35]	Single center, retrospective	49	Conventional	Surface: 270 min IVTM: 96 min P<0.001		No over cooling with IVTM Better controlled rewarming P<0.0001
Tømte[36]	Single-Center Observational	92	Arctic Sun	Surface: 273 Min IVTM: 270 min P=0.479	NA	NA
Flemming[34]	Single center observation	80	TheraCool, KCI	Surface: 9.2 hrs IVTM: 3.48 hrs	% achieving target temperature	Surface: 4/49 (9%) IVTM: 31/31 (100%)
Gillies[37]	Retrospective cohort study	83	Theracool, Criticool System	Target not reached Surface: 10/41 (24%) IVTM: 3/42 (7%) P=0.04	Time at target temp (hours) Occurrence of overcooling (%)	Surface: 17.5±12.3 IVTM: 22.4±6.1 P=0.02 Surface: 27% CG 10% P=0.049
Pittl[38]	Single center RCT	78	Arctic Sun	Surface: 242 min IVTM: 180 Min P=0.13	Mean Temp during maintenance	Surface: 32.7C (32.4-32.9) IVTM: 33 (32.9-33C) P<0.001
Waard[27]	Retrospective study	173	Med-Therm Gaymar	Surface: 178 Min IVTM: 180 min P=0.31	Mean temperature Temperature variation	Surface 32.5+0.5C IVTM: 33.1+0.3C P<0.0001 Surface: 0.85 IVTM: 0.35 P<0.0001
Schwab[39]	Retrospective	49	ThermoWrap	Surface: 268 min IVTM: 154 Min P=0.0002	Temperature deviation from target	Surface:0.60±0.61C IVTM: 0.19±0.23C P=0.00006
OH[40]	Retrospective Registry	803	Blanketrol, MediTherm Arctic Sun	Surface: 240 min IVTM: 211 min P=0.1	Occurrence of overcooling	Surface: 23.5% IVTM: 9.2% P<0.01
Forkmann[41]	Prospective observational	63	Medutek cooling blanket	IVTM: 100% achievement 159 min Surface: lowest temp was 35.2C after 436 min	NA	NA

Differences in Outcomes

Table 4 provides a summary of studies comparing outcomes of surface cooling vs. IVTM in cardiac arrest patients.

Table 4. Comparison of Outcomes: Surface Cooling vs. IVTM

First Author	Study Type	No. of Patients	Surface Cooling Device	Survival at Discharge	Outcome Measure	Outcome Results
Ferreira[35]	Single center, retrospective	49	Conventional	Surface: 16 (64%) IVTM: 17 (71%)	Good Neurological outcome (CPC 1-2) at hospital discharge	Surface: 10/25 (40%) IVTM: 15/24 (63%) P=0.12
Tømte[36]	Single-Center Observational	92	Arctic Sun	Surface: 44/92 (48%) IVTM: 35/75 (47%)	Good neurological outcome (CPC1-2) at final hospital discharge	Surface: 34/92 (37%) IVTM: 34/75 (45%) P=0.27
Flemming[34]	Single center observation	80	TheraCool, KCI	Surface: 38/49 (78%) IVTM: 23/31 (74%) P=0.2	NA	NA
Gillies[37]	Retrospective cohort study	83	Theracool, Criticool System	Surface: 17/41 (41%) IVTM: 21/42 (50%)	Good neurological outcome (CPC 1-2) at hospital discharge	Surface: 16/41 (39%) IVTM:18/42 (43%) P=0.82
Pittl[38]	Single center RCT	78	Arctic Sun	Surface: 21/39 (53.8% IVTM: 24/39 (61.5%) P=0.65	Good neurological outcome (CPC 1-2) at hospital discharge	Surface: 14/39 (35.9%) IVTM: 14/39 (35.9%) P=0.99
Waard[27]	Retrospective study	173	Med-Therm Gaymar	Surface: 38/76 (50%) IVTM: 59/97 (60%)	GCS at discharge	Surface: 10 (4-13) IVTM: 15 (3-15) P=0.008
Schwab[39]	Retrospective	49	ThermoWrap	Surface: 14/23 (61%) IVTM: 18/26 (69%) P=0.5	NA	NA
OH[40]	Retrospective registry	803	Blanketrol, MediTherm AS	Surface: 218/559 (39%) IVTM: 92/244 (37.7%) P=0.73	Good neurological outcome (CPC 1-2) at hospital discharge	Surface cooling: 143/559 (25.6%) IVTM: 86/244 (35.4%) P=0.01
Summary (survival and outcomes at hospital discharge)				**Surface**	**IVTM**	**P-value**
Total survival at hospital discharge (N=1482)				406/904 44.9%	289/578 50.0%	P=0.028
Total good neurological outcome at hospital discharge (N=1180)				217/756 28.7%	167/424 39.4%	P<0.001
First Author	**Study Type**	**No. of Patients**	**Surface Cooling Device**	**Survival at 30 Days**	**Outcome Measure**	**Outcome Results**
Deye[8]	Multicenter RCT	400	Conventional cooling tent and ice packs	Surface:75/197 (38%) IVTM: 85/203 (42%)	Good neurological outcome (CPC 1-2) at 90 days	Surface: 47/181 (26%) IVTM 66/191 (35%) P=0.07
Forkmann[41]	Single center, randomized observation	63	Medutek cooling blanket	Surface: 12/23 (52%) IVTM: 28/40 (70%)	NA	NA
Summary (total survival and outcomes)				**Surface**	**IVTM**	**P-value**
Total survival (N=1945)				493/1124 43.8%	402/821 49.0%	P=0.013
Total good neurological outcome (N=1552)				264/937 28.2%	233/615 37.9%	P<0.001

Table 5 is a list of studies comparing surface cooling vs IVTM in normothermia.

Table 5. Comparison of Performance in Normothermia: Surface Cooling vs. IVTM

First Author	Study Type	Number of Patients	Surface Cooling Device	Population	Fever Burden	Other Outcomes
Hinz[42]	Single center RCT	26	Conventional	SAH (21) TBI (5)	Surface: 1.05-2.34 (1.41) IVTM: -0.49-1.22 (-0.06) P<0.001	Antipyretic drugs Surface: 12 g/d IVTM: 0 P<0.001
Puccio[43]	Case control study	42	Conventional	TBI	Surface: 10.6% IVTM: 1.6% p=0.03	ICP> 25 mmHg Surface: 9.4±11.4% IVTM: 2.3±2.8% p=0.03
Broessner[44]	RCT	102	Blanketrol	SAH with HH grade 3-5 CH, ICH	Surface: 4.3C IVTM: 0 P<0.0001	NA
Diringer[45]	RCT	296	Conventional	SAH, TBI ICH, CH	Surface: 7.92 C/hrs IVTM: 2.87 C/hrs P<0.0001	Any antipyretic use Surface: 89% IVTM: 61% P<0.0001

In a longitudinal study by Keller[46] in 20 severe SAH patients with Hunt & Hess grade 3-5, hypothermia was induced either with surface cooling (Blanketrol, and ice bags on groin, axilla) or IVTM (Cool Line or Icy catheters in combination with Coolgard). Table 6 below shows the results.

Table 6. Survival of Patients in a Single Center Comparison of Surface to IVTM Treatment

First Author	Study Type	Number of Patients	Time of reach target	On target range	Survival	Median GOS*
Keller[46]	Single center Longitudinal study	20	Surface: 375 min IVTM: 186 min P=0.023	Surface: 84% IVTM: 95% P<0.001	Surface: 7/10 (70%) IVTM: 10/10 (100%) P=NS	Surface: 2.5 IVTM: 4.5 P=NS

*GOS: Glasgow outcome score: 1 = death, 5 = normal

Fever was recently shown to be linked to cerebral metabolic distress, which is known as an independent predictor of worse outcome post traumatic brain injury. A study conducted by Vespa et al[47] showed that patients in IVTM group had statistically significant better temperature control (p<0.001) and shorter time in metabolic crisis (p<0.001) compared to the surface cooling group. Intracranial pressure (ICP) was well controlled in the IVTM group.

Economic Impact

Effects on economics can also be represented by both indirect and direct economic impact measures. Indirect impact measures include the complications that could potentially arise from the cooling method chosen, resulting in higher costs for the healthcare facility, or potentially having better outcomes with the cooling method and thus higher hospital reimbursement. Direct impact measures include the patient's length of stay in a healthcare facility and the amount of nursing workload reduction due to the chosen method of cooling.

Studies have shown that elevated body temperature (fever) in NICU resulted in 3.2 additional ICU stays and 4.3 additional hospital days overall[48]. It is important to note that the selection of cooling technology may impact the effectiveness of fever control. A retrospective case-control study conducted at Columbia Presbyterian[49] where a total of 80 patients were admitted with intracerebral hemorrhage (ICH) received fever control with a target of 37°C. The data were analyzed in two groups: 40 patients in a control group whose treatment included acetaminophen and water-circulating blankets, and 40 patients in a "TTM" group who, in addition to the acetaminophen and water-circulating blankets, received treatment using the Arctic Sun surface cooling device. The outcomes and complication rates are shown in Table 7 below. The conclusion of this study stated that the increased length of ventilation rate and tracheostomy are related to the sedation often needed for shivering control in surface cooling. It can be inferred that all of these factors could contribute to high hospital costs.

Table 7. Complication Rates and Outcomes: Surface Cooling Compared to Standard Fever Control[49]

Complication	TTM (n=40)	Control (n=40)	P-value
Number of patients intubated	40 (100)	35 (88)	0.03
Tracheostomy*	22 (55)	9 (26)	0.010
Days of mechanical ventilation	14 [8-21]	6 [2-16]	0.003
Sedation days	8 [5-11]	1 [0-3]	<0.001
NICU length of stay (days)	15 [11-18]	10 [6-17]	0.003
Glasgow Coma Score (GCS) at discharge	9 [3-11]	11 [3-15]	0.06

All data are N (%), median [IQR]
*% of intubated patients receiving tracheostomy

TTM in post resuscitation care has been shown to improve the number of neurologically intact patients. Patients who survive this event neurologically intact are candidates for cardiac interventions including PTCA, CABG and implant of a cardiac defibrillator. Those procedures are generally economically favorable for hospitals, as a Medicare model has been shown that the reimbursement between a non-survivor and neurologically intact survivor average nearly $50,000 per case[50]. An independent study of survivors of SCA treated with aggressive post resuscitation care validated this model showing that on average intact survivors generate approximately $57,700 in revenue and approximately $21,000 in direct margin[51]. IVTM provides more rapid cooling and precise temperature maintenance. 12 studies in table 3 showed a better neurological outcome with IVTM than surface cooling, therefore the positive economic impact from IVTM to hospital is larger than surface cooling. In addition, studies also showed shorter length of stay (LOS) in ICU associated with using IVTM than surface cooling[27,52].

Because IVTM technology is more efficient, decreased workload on nursing staff has been demonstrated. Schmuthard and coworkers used the Coolgard system in a pilot study of 51 patients in NICU to maintain normothermia and fever control. They found that IVTM catheter was easy to insert and incorporate into the usual ICU routine[53]. In a randomized controlled trial by Deye et al.[8] where 400 post-CA patients were cooled, the IVTM group showed a 74% nursing time reduction on time spent for patient-specific target temperature management using IVTM vs. surface cooling technology. As the survey stated, the challenges of infrequently utilizing TH are the technical and logistical difficulties along with a lack of financial or personnel resources in TTM. Thus, reduction in nursing workload can be an impact on resources and cost saving for the hospital, and nurses can focus on other critical matters related to patient care[8].

Data show that surface cooling methods are logistically difficult to administer for hospital staff, require significant nursing attention and reduce overall access to critically ill patients. In addition, a CVC is required to measure CVP per the AHA guideline[54], as post-CA ischemia and reperfusion response causes intravascular volume depletion relatively soon after the heart is restarted, and volume expansion is usually required. The potential for persistent precipitating pathology could cause elevated CVP independent of volume status, such as the case with right-sided acute myocardial infarction. CVP only can be measured via a central venous line; therefore there are additional needs for post-CA patients to receive a standard CVC even with surface cooling. Studies have shown no difference in complications rate (i.e. DVT, infection, etc.) compared to cooling catheters than standard central line[8,46].

With regards to future technological development, surface cooling has reached its technical limitation while IVTM has the potential for greater power in the future. The only practical way to increase the power with surface is to increase the surface area covered. With the torso and thighs covered, that leaves the only the head, chest, lower legs and arms accessible, which would bring modest gains while adding to the burden and risk around skin checks. Alternatively, expanding the surface area with IVTM is possible by using novel serpentine designs that add to surface area without increasing catheter length. This approach may significantly increase the heat-exchange capacity and with it open new applications and the ability to cool with greater speed and precision.

Conclusion

TTM is complex as the circumstances and patients are highly varied; thus, hospitals should follow guideline-driven, institution-specific protocols for temperature management. When making a choice regarding cooling devices, institutions should select the most appropriate means of TTM based on patient outcomes, economics, and the maximum potential for a wide range of applications.

Although surface cooling may seem easy to use and can be applied by nurses without a physician being present, the potential risks and disadvantages are outweighed by the benefits of TH and fever control. The effectiveness and performance of surface cooling is limited to the maximum amount of skin coverage, the lowest temperature that circulates within the blankets or pads, and any counterproductive activity from shivering. When applying surface cooling methods, patients need continuous attention due to the risk of freezing-induced skin damage and shivering[27].

IVTM offers more controlled cooling and is faster to target temperature. Better temperature control is associated with fever reduction[39,42,46] and better neurological outcomes[8,27]. IVTM has direct thermoregulation to the core instead of using the skin as a conduit, and therefore less medication may be needed to control shivering. In addition, skin counterwarming can be utilized to significantly reduce or eliminate shivering response[55-57]. The strategy of using IVTM provides the ability to induce TH in awake, non-intubated and non-paralyzed patients (i.e for the treatment of acute ischemic stroke or acute myocardial infarction) because of better patient tolerance and less shivering. In conclusion, IVTM provides a better value proposition compared to surface cooling, based on both patient outcomes and economic impact to the healthcare facility.

References

1. Polderman KH. Induced hypothermia and fever control for prevention and treatment of neurological injuries. Lancet. 2008;371:1955–1969.
2. Polderman KH. An injured brain needs cooling down: yes. Intensive Care Med. 2015 May 14.
3. Sessler DI. Perioperative thermoregulation and heat balance. Ann NY Acad Sci 1997;813:757-777
4. Bigelow WG et al: Hypothermia its possible role in cardiac surgery. Ann Surg 1950;132
5. Delorme EJ: Experimental cooling of the blood-stream. Lancet 1952;2:914-915.

6. Erlinge D et al: a pilot study of rapid cooling by cold saline and endovascular cooling before reperfusion in patients with ST-elevation myocardial infarction. Circulation aug, 2010
7. Vaga A et al: A pilot study of key nursing aspects with different cooling methods and devices in the ICU. Resuscitation 2008
8. Deye N et al: Endovascular versus External Targeted Temperature Management for Out-of Hospital Cardiac Arrest Patients: A Randomized Controlled Study. CIRCULATIONAHA.114.012805
9. AHA guideline. Circulation. 2010
10. Lopez-de-Sa E, Rey JR, Armada E, et al. Hypothermia in comatose survivors from out-of-hospital cardiac arrest: pilot trial comparing 2 levels of target temperature. Circulation. 2012;126:2826–2833.
11. Nielsen N, Wetterslev J, Cronberg T, et al; TTM Trial Investigators. Targeted temperature management at 33°C versus 36°C after cardiac arrest. N Engl J Med. 2013;369:2197–2206
12. Polderman KH, Varon J. How low should we go? Hypothermia or strict normothermia after cardiac arrest? Circulation. 2015;131:669–675
13. Polderman KH, Varon J. Interpreting the Results of the Targeted Temperature Management Trial in Cardiac Arrest. The Hypothermia Temp Manag. 2015;5:73–76.
14. Perchiazzi G, D'Onghia N, Fiore T. Targeted temperature management after cardiac arrest. N Engl J Med. 2014;370:1356–1361.
15. Varon J, Polderman K. Targeted temperature management after cardiac arrest. N Engl J Med. 2014;370:1358–1359
16. Abella BS, Rhee JW, Huang KN, et al. Induced hypothermia is underused after resuscitation from cardiac arrest: a current practice survey. Resuscitation 2005;64:181–186.
17. Merchant RM, Soar J, Skrifvars MB, et al. Therapeutic hypothermia utilization among physicians after resuscitation from cardiac arrest. Crit Care Med 2006;34:1935–1940.
18. Jena AB, Romley JA, Newton-Cheh C, et al. Therapeutic hypothermia for cardiac arrest: real-world utilization trends and hospital mortality. J Hosp Med 2012;7:684–689.
19. Mikkelsen ME, Christie JD, Abella BS, et al. Use of therapeutic hypothermia after in-hospital cardiac arrest. Crit Care Med 2013;41:1385–1395.
20. Polderman KH, Herold I. Therapeutic hypothermia and controlled normothermia in the intensive care unit: practical considerations, side effects, and cooling methods. Crit Care Med. 2009;37:1101–1120.
21. Polderman KH. Mechanisms of action, physiological effects, and complications of hypothermia. Crit Care Med. 2009;37:S186–202.
22. Giesbrecht G. Sessler D et al: treatment of immersion hypothermia by direct body-to body contact. J Appl Physiol 1994;76
23. Rosa G: control of post anesthetic shivering with nefopa, hydrochloride in mildly hypothermic patients after neurosurgery. Acta Anesthesiol Scand 1996
24. Frank SM, Fleisher LA, Breslow MJ, et al. Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. A randomized clinical trial. JAMA. 1997:277:1127-1134.

25. Carhuapoma JR, et al. Journal of Neurosurgical Anesthesiology. 2003;15(4):313-318.
26. Jarrah Neurocritical Care 2011
27. Waard MC et al: Intravascular versus surface cooling speed and stability after cardiopulmonary resuscitation. Emerg Med J 2014;0:1–6.
28. Ricome et al, Intensive Care Med 2013
29. 46. Hindman BJ et al:Mild Hypothermia as a protective therapy during intracranial aneurysm surgery: a randomized prospective pilot trial. Neurosurgery 1999; 44:23-32. Discussion 32-33
30. Ricome S, et al: Ricome et al, Intensive Care Med 2013. Intensive Care Med
31. De Georgia et al; Chapter: Method to induce hypothermia. Therapeutic Hypothermia. Marcel Dekker, New York, 2004
32. Heard K, et al: A randomized controlled trial comparing the Arctic Sun to standard cooling for induction of hypothermia after cardiac arrest. Resuscitation 81 (2010) 9nte
33. Hoedemaekers CC, EzzahtiMM, et al: Comparison of different cooling methods to induce and maintain normo-and hypothermia in ICU patients: a prospective intervention study. Critical Care. 2007,11:R91
34. Flemming K, et al: Comparison of external and intravascular cooling to induce hypothermia in patients after CPR. GMS Ger Med Sci 2006;4:Doc04
35. Therapeutic mild hypothermia improves outcome after out-of-hospital cardiac arrest. Netherlands Heart Journal, Volume 17, Number 10, October 2009
36. A comparison of intravascular and surface cooling techniques in comatose cardiac arrest survivors. Crit Care Med 2011 Vol. 39, No. 3
37. Gillies MA: Therapeutic hypothermia after cardiac arrest: A retrospective comparison of surface and endovascular cooling techniques. RESUS-4349; 2010
38. Pittl U: Invasive versus non-invasive cooling after in- and out-of-hospital cardiac arrest: a randomized trial. Clin Res Cardiol, March 2013
39. Schwab KF. Endovaskuläre Kühlung oder Oberflächenkühlung? Anaesthesist 2008

40. Oh SH, Oh JS, Kim YM, et al; Korean Hypothermia Network Investigators. An observational study of surface versus endovascular cooling techniques in cardiac arrest patients: a propensity-matched analysis. Crit Care. 2015;19:85.
41. Forkmann M et al: Target temperature management of 33C exerts beneficial haemodynamic effects after out-of-hospital cardiac arrest. Acta Cardiol 2015; 70(4): 451-459
42. Hinz J: Effectiveness of an Intravascular Cooling Method Compared With a Conventional Cooling Technique in Neurologic Patients. J Neurosurg Anesthesiol 2007;19:130–135)
43. Puccio AM: Induced Normothermia Attenuates Intracranial Hypertension and Reduces Fever Burden after Severe Traumatic Brain Injury. Neurocrit Care (2009) 11:82–87
44. Broessner G et al: Prophylactic, Endovascularly Based, Long-Term Normothermia in ICU Patients With Severe Cerebrovascular Disease. Bicenter Prospective, Randomized Trial. Stroke published online Sep 17, 2009;
45. Diringer MN, et al: Treatment of fever in the neurologic intensive care unit with a catheter-based heat exchange system. Crit Care Med 2004 Vol. 32, No. 2
46. Keller E. et al: Endovascular cooling with heat exchange catheters: a new method to induce and maintain hypothermia. Intensive Care Med (2003) 29:939–943
47. Vespa et al: Therapeutic intravascular normothermia reduces the burden of metabolic crisis. Neurocritical care (2015) 22:265-272
48. Diringer MN Reaven NL et al. Elevated body temperature independently contributes to increased length of stay in neurological intensive care unit patients. Crit. Care. Med 2004 Vo l32 No. 7
49. Lord A; et al: Therapeutic Temperature Modulation for Fever After Intracerebral Hemorrhage. Neurocrit Care (2014) 21:200–206

50. Medicare cost analysis data supplied by Freudman Healthcare Consulting LLC, 2008
51. Jancin, Bruce. Cardiac Arrest Centers Boost Survival, Profits WWW. E C A R D I O L O G Y NEWS . C OM January 2009
52. Fink K. Et al: Endovascular or surface cooling? Theraputic hypothermia after cardiac arrest. Anaesthesist 2008
53. Schmutzhard E et al: Safety and efficacy of a noval intravascular cooling device to control body temperature in neurologic intensive care patients: a prospective pilot study. Cirit Care med 2002; 30:2481
54. Neumar RW et al: Post Cardiac Arrest Syndrome. Epidemiology, Pathophysiology, Treatment, and Prognostication a consensus statement *Circulation* published online Oct 23, 2008
55. Polderman KH, Herold I. Therapeutic hypothermia and controlled normothermia in the intensive care unit: practical considerations, side effects, and cooling methods. *Crit Care Med*. 2009;37:1101–1120.
56. Polderman KH. Mechanisms of action, physiological effects, and complications of hypothermia. *Crit Care Med*. 2009;37:S186–202.
57. van Zanten AR, Polderman KH. Blowing hot and cold? Skin counter warming to prevent shivering during therapeutic cooling. *Crit Care Med*. 2009;37:2106–2108