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Coolgard™ 3000 Catheter Thermal Regulation System: Endovascular hypothermia induction for treatment of comatose survivors of ventricular fibrillation cardiac arrest.

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PRIORITISING SUMMARY

REGISTER ID: **000173**

NAME OF TECHNOLOGY: **COOLGARD™ 3000 CATHETER THERMAL REGULATION SYSTEM**

PURPOSE AND TARGET GROUP: **ENDOVASCULAR HYPOTHERMIA INDUCTION FOR TREATMENT OF COMATOSE SURVIVORS OF VENTRICULAR FIBRILLATION CARDIAC ARREST**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☒	Yet to emerge	☐	Established
☐	Experimental	☐	Established *but* changed indication or modification of technique
☐	Investigational	☐	Should be taken out of use
☐	Nearly established		

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☒	Yes	ARTG number	80624
☐	No		

The CoolGard™ System received TGA approval in 2005, however is not yet available for purchase in the Australian market (personal communication, Alsius company representative). In addition, the device is approved and widely used for cardiac arrest patients in Canada and the European Union (United States Food and Drug Administration, 2005a). Aurora BioScience will manage the Australian launch in August/September 2005 (personal communication, Aurora BioScience).

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
United States	✓		
Austria	✓		
Switzerland	✓		

IMPACT SUMMARY:

Alsius has developed the CoolGard™ 3000 Catheter Thermal Regulation System with the aim of inducing hypothermia for the treatment of comatose survivors of out-of-hospital ventricular fibrillation (VF) cardiac arrest.

BACKGROUND

Induced Hypothermia is defined as the controlled lowering of core body temperature for therapeutic indications. That technique includes cooling subsets of patients to 32–34°C for 12 to

24 hours. Mild hypothermia decreases heart rate and increases systemic vascular resistance while stroke volume and mean arterial blood pressure are maintained (Bernard and Buist 2003). Hypothermia induction is commonly used for cerebral protection during cardiopulmonary bypass operations and has been recently investigated in infants after perinatal asphyxia (Batin et al 2002, Batin et al 2001, Gluckman et al 2004).

Previous studies (Level I, II, III-3 and IV intervention evidence) in Australia and overseas have demonstrated that treatment with moderate hypothermia appears to improve neurological outcomes in cardiac patients (Holzer et al 2005, Bernard et al 2002, Bernard et al 1997, Hypothermia after Cardiac Arrest Study Group 2002, Nolan et al 2003). In particular, mild therapeutic hypothermia (level I intervention evidence) has demonstrated favourable short-term neurologic recovery and survival in comatose patients resuscitated from cardiac arrest (Holzer et al 2005). Hypothermia in these studies was induced by external, surface cooling methods. Hypothermia methods to date have varied and included a mattress that delivered cold air (Hypothermia after Cardiac Arrest Study Group 2002), the application of cold packs to the head and torso (Bernard et al 2002), and cooling blankets. In Australia, treatment methods for hypothermia induction have been ice packs and or cooling blankets (Bernard et al 2002). The investigation of a cold liquid infusion is under investigation (Bernard et al 2003).

On the basis of the trials published in 2002previously mentioned, the International Liaison Committee on Resuscitation recognised the therapeutic value of hypothermia in the immediate treatment of comatose survivors of ventricular fibrillation sudden cardiac arrest (Nolan et al 2003). The Committee recommended that hypothermia be induced in unconscious adults with spontaneous circulation, who have experienced an out-of-hospital cardiac arrest. It is recommended that patients be cooled to 32-34°C for 12 to 24 hours when the initial rhythm is ventricular fibrillation (Nolan et al 2003).

The CoolGard™ 3000 Catheter Thermal Regulation System, using either the Icy or Fortius model catheter was first approved for use in cardiac surgery patients to achieve and or maintain normothermia during surgery and recovery/intensive care, and to induce, maintain and reverse mild hypothermia in neurosurgery patients in surgery and recovery/intensive care (Alsius 2005, United States Food and Drug Administration, 2005b).

In March 2005 the United States Food and Drug Administration approved the system for further use in the induction, maintenance and reversal of mild hypothermia in the treatment of unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest when the initial rhythm was ventricular fibrillation (United States Food and Drug Administration, 2005c).

The CoolGard™ Temperature Control System consists of a temperature monitor, temperature controller and heat exchanger units, and a pump (Figure 1), supplying the temperature controlled sterile saline to the patient via an indwelling catheter (United States Food and Drug Administration 2005c). Data from the temperature monitor is integrated into the system via software that controls the temperature of the sterile saline to be circulated through the catheter to maintain the desired body temperature. The Icy™ catheter (Figure 2) is a triple lumen intravascular catheter. The shaft of the catheter has three cooling membranes. Two of the catheter's lumens are used to circulate cooled sterile saline to exchange heat with the central venous blood supply. The third lumen of the Icy™ catheter is a standard guidewire lumen that can be used as an infusion lumen. The catheter is placed in the inferior vena cava via the femoral vein. Chilled sterile saline is pumped from the CoolGard™ unit through the Icy™ intravascular heat exchange catheter. The catheter has a closed loop system, such that the cooled saline flows

from the CoolGard™ unit into the Icy™ catheter, then back to the CoolGard™ System. The cooled saline does not enter into the patient's circulation; rather, it flows through the indwelling Icy™ catheter, which in turn, exposes the venous circulation to the cooler temperature (Al-Senani et al 2003). The device induces cooling at a rate of 0.05–1.5°C per hour.

Figure 1 CoolGard™ 3000 system (printed with permission, Alsius)

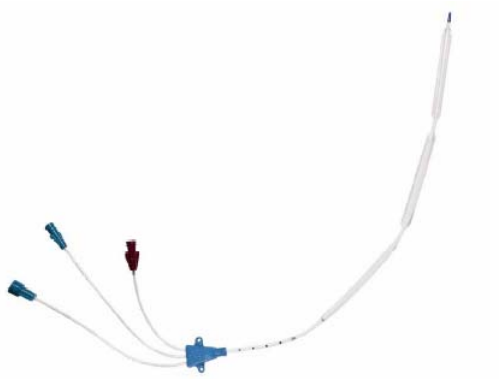

Figure 2 Icy™ catheter (printed with permission, Alsius)

CLINICAL NEED AND BURDEN OF DISEASE

The underlying cause of cardiac arrest is coronary heart disease, the most common cause of heart disease in Australia. In 2002 – 03 there were a total of 43,767 hospital separations for the principal diagnosis I21, Acute Myocardial Infarction (AIHW 2005).

The 1998 Disability, Ageing and Carers Survey reported that 1.2% of survey respondents had one or more disabling conditions associated with coronary heart disease, which corresponds to 224,400 Australians affected. Of these respondents with disabling conditions, 59% needed assistance or had difficulties with self-care, mobility or communication, and 31% had no difficulty with these activities but used aids or equipment because of their disability (AIHW 2004).

DIFFUSION

The use of hypothermia for clinical applications is growing, encompassing more patient groups. Hypothermia (using other techniques as described below) is now used in approximately half of Intensive Care Units in Australia after cardiac arrest (personal communication, The Alfred Hospital). Given that induced hypothermia is commonly used to prevent neurological injury and provide neuro-protection for other indications (traumatic brain injury and neurosurgery) and has been used in cardiac patients with favourable outcomes (Holzer et al 2005, Bernard et al 2002,

Bernard et al 1997, Hypothermia after Cardiac Arrest Study Group 2002, Nolan et al 2003), there is potential for rapid uptake.

COMPARATOR

Prior to the introduction of hypothermia therapy the standard treatment of cardiac arrest survivors has been pharmacological support until neurological outcome could be determined approximately three days later (Bernard 2004).

Hypothermia may be induced either externally or internally. There are reported problems with using external, surface cooling methods for inducing, maintaining and reversing hypothermia. External methods are time-consuming and may be imprecise (Felberg et al 2001). Using large plastic bags filled with ice is unsafe, delivers inconsistent temperature control, presents dangers associated with a wet environment and electrical equipment and impeding access to the critically ill patient (United States Food and Drug Administration, 2005a and El-Senani 2004).

An alternative (investigational) to external, surface cooling is the use of an internal infusion of large volume of ice-cold intravenous crystalloid fluid (Bernard et al 2003 and Kliegel et al 2005). A randomised controlled trial of this technique is due to commence in August 2005 in Australia (personal communication, The Alfred Hospital)

EFFECTIVENESS AND SAFETY ISSUES

A study in 13 patients (level IV intervention evidence) with a follow-up period of 30 days assessed the safety and feasibility of using the CoolGard™ for endovascular cooling after cardiac arrest (Al-Senani et al 2004). Time from cardiac arrest to return of spontaneous circulation was 14.3 minutes (range 5–32.5 minutes). All patients received sedation and pharmacological paralysis for prevention of shivering. Therapeutic hypothermia was induced, maintained, and reversed using CoolGard™ with the Icy™ catheter. During the induction phase bladder and coolant bath temperatures were recorded every 15 minutes until the patient reached the target temperature of 33°C. Patients were maintained at this temperature for 24 hours after which a slow rewarming phase was initiated with the aim of returning the patient to a temperature of 36.5°C. This was performed by re-setting the CoolGard™ unit by 0.2°C incrementally every hour until 36.5°C was reached. Temperatures were measured via bladder-temperature probes.

It took an average of three hours and 39 minutes (median 210 minutes, IQ 80-315) to reach 33°C and cooling averaged 0.8 ± 0.3°C/hour (range 0.22-1.12°C/hour). Rewarming lasted 18.3 ± 5.9hours. Twelve of the 13 patients completed 24 hours in hypothermia. Four patients died during the study, all classified as non-treatment related. One patient died of cardiac causes and three patients died after withdrawal of life support. There were two cases of sepsis possibly related to the hypothermia procedure. At 30 days, the mean Glasgow Coma Score[1] in all patients was 9.0 ± 4.9, an increase from 3.7 ± 1.2 at baseline. Two patients were in a persistent vegetative state and two patients were severely disabled. The remaining five patients (38.5%) experienced good neurological recovery.

In a separate feasibility study (level IV intervention evidence) the CoolGard™ was used in 26 cardiac arrest patients (Kliegel et al 2005). The target temperature was 33 ± 1°C. Hypothermia was maintained for 24 hours and patients were then rewarmed within eight hours to >36°C. The study outcomes were time from return of spontaneous circulation to target temperature, survival

[1] A Coma Score of ≥13 correlates with a mild brain injury, 9-12 a moderate injury and ≤8 a severe brain injury (Teasdale and Jennet, 1974).

to discharge and best cerebral function within six months. In this study hypothermia induction with the CoolGard™ was preceded by an infusion of 2000ml of ice-cold (4°C) fluid (Ringers' lactate) via peripheral venous catheters.

The study reports that treatment with the CoolGard™ began 115 ± 49 minutes after return of spontaneous circulation. Five patients (19%) had reached target temperature before treatment with CoolGard™ was initiated. Target temperature was achieved 185 ± 119minutes after return of spontaneous circulation, 135 ± 112minutes after start of Ringers' lactate infusion and 83 ± 85 minutes after starting CoolGard™ treatment. Two patients (7%) showed radiographic signs of mild pulmonary oedema attributed to the liquid infusions. Fourteen patients (54%) survived to hospital discharge and 13 patients (50%) survived with favourable neurological outcome (cerebral performance category 1 or 2)[2].

It is difficult to make meaningful clinical interpretations from this study as the CoolGard™ was used after the initial application of cold fluids, making it impossible to determine which treatment was effective or to quantify how effective the CoolGard™ was in inducing hypothermia. In addition, the study results can not be compared with other studies that use intravenous cold fluids only or the CoolGard™ only.

COST IMPACT

The cost of the CoolGard™ system is approximately $AUD 46,500 with catheters ranging in price from $AUD 400– 1600 (personal communication, Aurora BioScience).

There were no economic evaluation/cost impact data available at the time of writing this summary.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified/raised in the sources examined.

OTHER ISSUES

The El-Senani et al 2004 study was funded by the Alsius Corporation.

CONCLUSION:

There is currently insufficient high level evidence to assess the effectiveness of hypothermia induction with the CoolGard™. However, there is recognition of the benefits of hypothermia for improved neurological outcomes.

HEALTHPACT ACTION:

In the absence of randomised studies assessing its safety and effectiveness and comparing it to external, surface cooling it is recommended that this technology be monitored.

LIST OF STUDIES INCLUDED	TOTAL
Total number of studies	
Level IV intervention evidence	2

[2] The Glasgow-Pittsburgh Cerebral Performance Category 1 correlates with good recovery or 2, moderate disability (Jennett and Bond, 1975).

SOURCES OF FURTHER INFORMATION:

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SEARCH CRITERIA TO BE USED:

Advanced Cardiac Life Support/methods/standards
Body Temperature
Brain Ischemia/diagnosis/etiology/ prevention & control
Cardiopulmonary Resuscitation/methods/ standards
Heart Arrest/ therapy
Hypothermia, Induced