Improving cardiac arrest survival by providing high quality, co-ordinated care: 2010 International Liaison Committee on Resuscitation guidelines

Cardiac arrest is an important public health concern, affecting millions of people each year throughout the world [1]. Although major advances have been made, the survival rate for cardiac arrests occurring outside of the hospital has remained the same for over 30 years; fewer than one in ten people will survive an out-of-hospital cardiac arrest (OHCA) [2]. In-hospital cardiac arrest patients have fared better, with a survival of approximately only 20% [3].

In the last 15 years, more emphasis has been placed on creating consensus guidelines advising how cardiac arrest patients should be treated. Groups like the European Resuscitation Council and the American Heart Association (AHA) have combined efforts to create the International Liaison Committee on Resuscitation (ILCOR). This group, comprised of a multidisciplinary group of researchers, scientists and physicians, have created a rigorous process to assess the current state of the literature and to put forward consensus guidelines, updated every 5 years, for the treatment of cardiac arrest patients [4].

In the most recent update to these guidelines, released October 2010, major recommendations in the treatment of cardiac arrest patients are highlighted [1]:

* Creation of resuscitation centers to provide regionalized, co-ordinated care;

* Implementation of postarrest management protocols;

* Induction of therapeutic hypothermia for patients with return of spontaneous circulation (ROSC);

* Implementation of early angiography for cardiac arrest survivors.

This article will highlight the rationale, evidence base and major research gaps for each of these recommendations.

Creation of cardiac arrest resuscitation centers to provide regionalized, co-ordinated care

Regionalized, co-ordinated care of patients has been the mainstay of trauma care in the USA for over 20 years. Trauma centers are certified through the American College of Surgeons to provide a specific level of care and advanced consultative services for patients who sustain serious traumatic injuries [5–7]. This model has been further explored in the setting of stroke care, with the Joint Commission providing certifications for hospitals in the USA that are able to provide timely and specialized care for stroke victims [8]. Based on data suggesting improved outcomes for patients cared for at certified stroke and trauma centers, the idea of regionalized, co-ordinated resuscitation centers to care for postcardiac arrest patients has been proposed [9].

Currently, in all patients who have ROSC after OHCA, an average of 7% survive to hospital discharge, with variations in survival based on presenting cardiac rhythm and timing of arrest [2,10]. For patients who suffer an in-hospital cardiac arrest, the average survival to discharge rate is approximately 20% [3]. The rationale for developing resuscitation centers is twofold.
The recommendation for regionalizing the care of cardiac arrest patients has been promulgated by the AHA in their consensus statement, which further outlines the rationale for the development and designation of these centers [7]. Based on these recommendations, cities in Arizona [11] and Massachusetts [12] have begun to implement a co-ordinated care delivery system for cardiac arrest patients, which includes transport to a designated resuscitation center. Data from the Arizona system of co-ordinated care have been impressive, with survival doubling in the 5 years since this large-scale initiative has been in place [13]. Arizona has utilized a multifactorial intervention designed to increase bystander CPR, and improve emergency medical service (EMS) care and postarrest management, so no single intervention can be completely attributed to increasing survival from OHCA in this state. However, the designation of cardiac arrest receiving centers has been an integral part of this program.

Although a co-ordinated care delivery system for cardiac arrest makes sense, there are still gaps in the literature regarding which criteria should be used to designate resuscitation centers [7]. Research in other emergency medicine settings (e.g., coronary interventions) has shown a volume–outcome relationship [14,15]. However, the evidence base to date does not suggest that there is an association between high-volume hospitals (greater than 40 arrests per year) and survival-to-hospital discharge for cardiac arrest. A recent study conducted by the Resuscitation Outcomes Consortium showed an association between the number of cardiac arrest patients treated in a center and the neurological outcome at discharge, however the association disappeared in the final adjusted analysis [16]. Two additional recent studies from Australia and the Cardiac Arrest Registry to Enhance Survival (CARES) in the USA showed this hospital volume outcome relationship did not persist after adjustments for both patient and hospital characteristics [17,18]. This suggests that other hospital factors may be influential in the care of cardiac arrest patients. Further research will need to examine important factors like the level of experience a provider has in caring for cardiac arrest patients, the level of resources available at the treating facility (e.g., primary percutaneous coronary intervention (PCI), therapeutic hypothermia and placement of an automated implantable cardioverter-defibrillator) and the impact of transport times and geographic distances in the allocation of centers [19–22].

Postarrest management protocols for cardiac arrest victims

The goal of a postcardiac arrest management protocol is to optimize cardiac output and cerebral perfusion, optimize systemic hemodynamics to meet the body’s oxygen demands and metabolic needs, minimize reperfusion injury, and support cellular recovery [23,24]. Postcardiac arrest care was highlighted in the recent 2010 AHA ILCOR guidelines for cardiopulmonary resuscitation and emergency cardiac care, leading to the creation of a fifth link in the chain of survival [25]. A protocol consists of an integration of guidelines and routine clinical practices to optimize postcardiac arrest care and to minimize the inflammatory response and cell death that occur during the reperfusion period following cardiac arrest.

The use of a multidisciplinary team to manage patients following cardiac arrest has been shown to improve outcomes [26]. Postcardiac arrest care can begin at the time of EMS arrival with the initiation of Advanced Cardiac Life Support (ACLS) protocols. Each subsequent team involved in patient care (emergency medicine, pulmonary/critical care, interventional cardiology, neurology) has a specific role during postarrest management to help improve patient outcomes.

Emergency medical services

In patients presenting with OHCA to the EMS system, cardiopulmonary resuscitation and ACLS protocols should be initiated. There are two additional goals for the EMS system. The first is to initiate induction of mild therapeutic hypothermia while transporting patients in the timeliest manner to the emergency department. Induction of mild therapeutic hypothermia by EMS personnel has been found to be safe and effective in reducing core body temperature in cardiac arrest patients [27–29]. During patient transport, induction of therapeutic hypothermia may be achieved with an intravenous infusion of 4°C saline administered as a bolus of 30 ml/kg of body weight to reach a target core temperature of 33 ± 1°C [30]. While sufficient for induction of hypothermia, intravenous infusion of ice-cold saline is not suitable for maintenance of hypothermia and thus rapid transport to an emergency department with hypothermia capabilities is imperative to continue therapeutic hypothermia.

The second goal of EMS during resuscitation and transport is related to ventilatory management. Ventilatory management should provide adequate oxygenation without hyperventilation. Current guidelines recommend the maintenance
of pulse oximetry greater than 94% and the consideration of an advanced definitive airway [25]. Waveform capnography during advanced airway management is also recommended in the current guidelines. In particular, hyperventilation has been found to be detrimental to survival outcomes and should be carefully monitored [31,32].

### Emergency department

The goals of management in the emergency department are to achieve hemodynamic stability with the use of specific hemodynamic targets, to improve neurological outcomes with the continuation or initiation of therapeutic hypothermia to determine the etiology of the arrest, to continue ventilatory management, and, in conjunction with the interventional cardiology service, to determine the need for emergent cardiac catheterization.

Survivors of cardiac arrest should have an early 12-lead EKG to determine the need for emergent cardiac catheterization. Early consultation with the interventional cardiology service, especially in cases of presumed cardiac etiology, such as those with an initial presenting rhythm of ventricular fibrillation, pulseless ventricular tachycardia, or with evidence for an acute myocardial infarction on the initial 12-lead EKG, is an important determinant for survival. Some evidence suggests a benefit even in those without EKG criteria.

Following the induction of hypothermia via cold saline infusion, continued maintenance of therapeutic hypothermia should be achieved with the use of a cooling device that will maintain a targeted core body temperature of 32–34°C for a 12–24-h period [33,34]. Temperature should be monitored to prevent complications, such as dysrhythmias, infection and coagulopathy, whose incidence is more likely if core body temperature falls below 32°C [35]. All patients being cooled should be intubated and sedated for airway management and paralytics may be considered to prevent shivering.

Due to the similarities in inflammatory responses of the body postresuscitation and during septic shock, hemodynamic parameters similar to those seen in early goal-directed therapy protocols are suggested therapeutic goals, although no specific guidelines currently exist for normalized values [36]. This approach involves goal-oriented management of cardiac preload, afterload and contractility to attain a balance between oxygen delivery and oxygen demand to prevent tissue hypoxia or shock. Central venous and arterial lines for central monitoring and interventions may be placed in the emergency department or ICU as appropriate.

### Cardiology

Upon admission to the emergency department, a 12-lead EKG should be performed, and the interventional cardiology service should be consulted to determine the need for emergent cardiac catheterization, regardless of EKG findings. Early coronary artery reperfusion should be achieved, in order to optimize cardiac output and brain perfusion. Patients receiving PCI are more likely to survive than those who require PCI but do not receive it [37]. The identification of patients requiring emergent cardiac catheterization remains difficult. Patients with a presenting rhythm of ventricular fibrillation or pulseless ventricular tachycardia after arrest have a high incidence of having an identifiable culprit lesion on cardiac catheterization [38,39]. The etiology of arrest remains less certain for those who present with either pulseless electrical activity or asystole as an initial rhythm.

### Pulmonary/critical care

The goals of the pulmonary/critical care (medical intensive care unit) team are to optimize transition of care from the emergency department and to provide continued intensive monitoring of physiological parameters of surviving patients after cardiac arrest in an effort to maintain hemodynamic stability and improved neurological and cardiac outcome [24]. The medical intensive care unit team will maintain and optimize hemodynamic parameters initiated in the emergency department, continue to maintain and complete the hypothermia protocol, and monitor and optimize serum laboratory values.

While in the medical intensive care unit, hemodynamic parameters will be maintained to help prevent vital organ injury and improve chances for survival by utilizing goal-oriented management of cardiac preload, afterload and contractility as previously described. It is important to closely monitor and control physiological values because abnormalities in baseline blood glucose, electrolyte and blood gas values are associated with poorer survival and functional outcome following cardiac arrest [40]. Blood glucose should be maintained between 144–180 mg/dl. [41] Therapeutic hypothermia has been shown to cause hyperglycemia and, by contrast, the rewarming process can cause hypoglycemia. Monitoring electrolytes (e.g., sodium, potassium and magnesium) is
important as these abnormalities can lead to cardiac arrhythmias and cellular dysfunction [42]. Normal levels of oxygenation and ventilation should be maintained as oxidative stress can increase neuronal injury following cardiac arrest [43]. Pulse oximetry and blood gas analysis should be utilized to maintain adequate ventilation and to titrate oxygen use. Hyperventilation reduces cerebral perfusion and cardiac venous return and should be avoided to prevent ischemic injury [31,32]. Oxygen saturation should be maintained between 95–98% and the arterial pressure of carbon dioxide should be maintained at 35–45 mmHg. Adjustment of the fraction of inspired oxygen and positive end-expiratory pressure on the respirator should allow for maintenance of normal ventilation [24,44].

Neurology

Neurological damage owing to global cerebral ischemia after cardiac arrest is common. The duration and severity of the interrupted cerebral blood flow contributes to the extent of brain damage. Therapeutic hypothermia appears to be one of the most efficacious treatment options to reduce cerebral injury and its immediate application by the EMS and emergency department will allow for a potential improvement in neurological status [23]. The goals of the neurology service are to monitor survivors with continuous EEG and to use clinical data and prognostic values to determine functional neurological outcomes [24].

Continuous EEG is used to monitor early occurrence of seizures. This is particularly important for patients during the hypothermia protocol [45]. Additionally, the EEG can be useful in determining the predictive outcome of comatose patients following therapeutic hypothermia. Both seizures and myoclonic activity are associated with poor neurological outcome in both conscious and unconscious individuals [46]. If the EEG indicates that the patient is seizing and requires therapeutic medications, staff should provide an increase in sedation or anticonvulsive medication.

Early prediction of neurological outcome is important to comatose patients in the ICU as futile care can be terminated in patients who will not regain consciousness or have an extremely poor outcome. The neurological examination, which includes papillary, corneal, gag and cough reflex [47], should be performed in comatose patients at admission into the ICU and again in unconscious patients 72 h after rewarming from therapeutic hypothermia to predict neurological outcome and determine necessity or futility of further treatment [46]. However, a growing body of evidence questions the utility of the first neurological examination, usually conducted while the patient is hypothermic and comatose, as it may be unreliable and potentially should not be used for prognostication [48–50]. The continuation of treatment in comatose patients is a medical, ethical and financial issue and continues to be a growing area of research. In all surviving patients following OHCA, the cerebral performance category (CPC) or the Glasgow-Pittsburgh outcome categories can be utilized to measure the neurological function of the individual and aid in determining the quality of life postcardiac arrest.

Summary

Research gaps in the literature regarding therapeutic hypothermia and primary PCI postarrest will be further elucidated in the next section. Although postarrest management protocols again appear to be an important consideration in the treatment of cardiac arrest victims, there are still large gaps in the literature regarding these protocols. There are two studies [33,34] that show that postresuscitation care may be an important part of increasing survival from cardiac arrest. However, there are no standardized protocols or consensus guidelines in the length of hypothermia treatment, criteria to involve cardiology, neurology and pulmonary/critical care in the management of patients with hypothermia treatment. No randomized controlled trials exist to test the utility of a postarrest management protocol as compared with standard care. A large-scale trial will be needed to address these major questions before postarrest management protocols are widely implemented.

Therapeutic hypothermia treatment after ROSC

In all cases of cardiac arrest, cerebral oxygen deprivation occurs owing to the loss of cerebral perfusion. This oxygen deprivation leads to neurological injury that is directly responsible for approximately two-thirds of the deaths in cardiac arrest patients who initially survived the event, and leads to poor neurological outcomes in others [51]. Care and treatment directed towards improving neurological outcome is thus important for patients who suffer cardiac arrest. Therapeutic hypothermia is a promising treatment that has been shown to decrease the effect of reperfusion injury in cardiac arrest.
Review the metabolic demands of the body postarrest. Signaling pathways in the body and lessening ischemia/anoxia that result in a cascade of multiple, independently-lethal biochemical events. This mechanism of ischemia–reperfusion injury is well described in animal models 

The induction of therapeutic hypothermia is theorized to act by altering biochemical and signaling pathways in the body and lessening the metabolic demands of the body postarrest.

The 2010 ILCOR guidelines state that any patient with a witnessed OHCA with ventricular fibrillation or ventricular tachycardia as the presenting rhythm who remains unconscious after ROSC should be cooled to a temperature of 32–34°C for 12–24 h [4,54]. Two landmark, randomized controlled trials of therapeutic hypothermia conducted in patients with ventricular fibrillation or ventricular tachycardia as presenting rhythms have shown an improvement in neurological survival at discharge. The guidelines also recommend that therapeutic hypothermia should be considered for those patients with other presenting rhythms, based on observational clinical data, experimental laboratory findings, and conceptual understandings of mechanism of reperfusion injury.

There are still major research gaps regarding the mechanism and process of inducing hypothermia. Prehospital literature suggests that the administration of normal saline cooled to 4°C with a bolus of 30 ml/kg of body weight can be used to reach a target core temperature of 33 ± 1°C [30]. Although useful to induce hypothermia, the maintenance of hypothermia has been the topic of debate. Intravascular devices have been shown to be effective in inducing and maintaining a core temperature of 33°C [55,56]. However, given the amount of time, personnel and resources needed for this intervention, as well as operator experience in placing the device, there are limitations to this approach [57]. Surface cooling using cooling blankets and ice packs to maintain core temperatures [58,59]. One study has shown that both intravascular and surface cooling are equivalent in their effectiveness to reach and maintain core temperatures [60]. Further research comparing surface versus intravascular cooling will need to be conducted to independently assess the difference between these two modalities for inducing and maintaining therapeutic hypothermia.

There are also little data to suggest the timeframe in which a person should have therapeutic hypothermia induced. To date, the theory of “the sooner the better” has been employed, hence the reason that EMS providers are cooling cardiac arrest victims in the field prior to transport. The timeframe in which this intervention will be useful is still uncertain, with trials like the Hypothermia After Cardiac Arrest (HACA) and the Bernard trial suggesting that hypothermia treatment should be to a target temperature of 33°C, which should be achieved at 2–12 h postarrest [33,34]. Further research will need to be conducted to understand the implications of immediate versus delayed hypothermia treatment.

Finally, the length of time that hypothermia treatment should be maintained is also uncertain. The Bernard trial recommended 12 h of hypothermia treatment [33], while the HACA trial recommended 24 h [33]. Further research using a multicentered study design to test the difference in neurological outcome based on 12, 24, 36 and 48 h of hypothermia treatment will need to be conducted.

**Early versus delayed angiography postarrest**

Sudden cardiac arrest is predominantly triggered by an acute coronary thrombosis [61]. However, it is unclear whether these patients profit from immediate angiography followed by revascularization. Currently, there is no consensus and clinical practice is highly variable among different medical centers and among cardiologists. Recent ILCOR guidelines suggest that a 12-lead EKG be performed both in the prehospital and emergency department setting to assess for ST-elevation myocardial infarction (STEMI). The guidelines further state that, because neurological prognostication can be difficult in postcardiac arrest patients who are comatose and hypothermic, aggressive treatment of STEMI patients should begin immediately. The rationale for urgent angiography is that early revascularization may minimize myocardial death, reduce dysrhythmias...
Conclusions
The 2010 ILCOR guidelines highlight a shift in the care of cardiac arrest patients. The development of resuscitation centers, postarrest management protocols, therapeutic hypothermia, and postarrest angiography are important recommendations that may dramatically change the manner in which cardiac arrest patients are cared for. Although there is a body of evidence to support each of these recommendations, there are still large gaps in the research regarding how these major interventions will be implemented in the real-world setting. Translational research will need to be conducted to assess how the transition from guidelines to practical interventions can be achieved in both urban and rural areas, as well as within varying medical care systems. The overall impact of these interventions will also need to be systematically studied via large registries, such as Get-With-the-Guidelines, CARES and the Pan-Asian Resuscitation Outcomes Study (PAROS). These registries can complement RCTs as they evaluate the impact of interventions in more routine clinical care setting than is typical of RCTs.

It appears that we are embarking upon a new era of cardiac arrest care that is committed to providing high-quality, multidisciplinary, coordinated care to cardiac arrest victims. We are transitioning away from the perception that survival of cardiac arrest victims is futile and toward a renewed sense of hope that these four ILCOR recommendations may improve the intact neurological survival from cardiac arrest.

Future perspective
The field of resuscitation science is brimming with new areas for research, scientific discovery and therapeutic interventions. Although the survival rate from cardiac arrest has been fairly constant in the last 30 years, the areas highlighted in this article have the potential to revolutionize the field. In the next 5–10 years, the emphasis for cardiac arrest care will become more focused, based on the current models of care for trauma and stroke patients. This paradigm shift towards a co-ordinated healthcare delivery system will hopefully lead to improvements in the timeliness of appropriate interventions, such as therapeutic hypothermia, early angiography, and protocol-based postarrest management. It is probable that in the next update to the consensus guidelines by the ILCOR, expected in 2015, the four areas highlighted in this review will be both a mainstay of

and increase cerebral blood flow secondary to increased cardiac output. Seven nonrandomized pre–post studies have shown a survival benefit to be associated with early angiography postarrest [62–68]. An additional study, conducted in postcardiac arrest patients, found that there was no increased risk of cardiac or neurologic complications in those patients who receive early angiography (within 6 h) and therapeutic hypothermia concurrently [69]. However, despite guidelines for early angiography for these patients, in current practice, this is frequently not being done until the neurologic status of the patient can be determined. With patients who have therapeutic hypothermia, this ascertainment of neurological status may not occur until 24–48 h post-event due to the inability to assess neurological status while the patient is hypothermic. This is due to two prevailing thoughts: the perception that cardiac arrest survivors are futile and rarely survive neurologically intact and cardiologists and hospitals in the USA and some countries in Europe (UK) are being publicly scored for their PCI outcomes, and cardiac arrest victims will adversely affect the overall rating for the hospital and the provider [70].

There are still many unanswered questions in this debate about early versus delayed or no angiography, namely, what is considered the critical stenosis that requires intervention will also need to be determined.
cardiac arrest care and will have been adopted by the international resuscitation community at-large. Although there are still many unanswered questions about the implementation of these guidelines, the next 10 years of research will begin to answer these very important questions so that the treatment of cardiac arrest patients can become standardized and optimized across the world.

Financial & competing interests disclosure
The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Executive summary

- The 2010 International Liaison Committee on Resuscitation guidelines highlight the need for improving cardiac arrest care for those patients who have a return of spontaneous circulation in four major areas:
  - Creating resuscitation centers to provide regionalized, co-ordinated care.
  - Implementing post-arrest management protocols.
  - Inducing therapeutic hypothermia.
  - Taking cardiac arrest patients for urgent angiography.

Creation of cardiac arrest resuscitation centers to provide regionalized, co-ordinated care

- The rationale for developing resuscitation centers is twofold. First, that emergency medical services providers will be able to transport patients to those hospitals that are best suited for caring for cardiac arrest victims, and second, that hospitals that care for large numbers of patients with cardiac arrest are more likely to be experienced in caring for these patients and will have both therapeutic hypothermia and angiography readily available for patients who achieve return of spontaneous circulation.

- There are still gaps in the literature regarding which criteria should be used to designate resuscitation centers. How do the hospital volume, the level of experience a provider has in caring for cardiac arrest patients, level of resources available at the treating facility (e.g., primary percutaneous coronary intervention, therapeutic hypothermia and placement of defibrillators) and the impact of transport times and geographic distances factor into the allocation of centers?

Postarrest management protocols for cardiac arrest victims

- The goal of a postcardiac arrest management protocol is to optimize cardiac output and cerebral perfusion, optimize systemic hemodynamics to meet the body’s oxygen demands and metabolic needs, minimize reperfusion injury, and support cellular recovery by developing standardized procedures for individuals who have suffered a cardiac arrest through the collaboration of an interdisciplinary team of emergency medical services, emergency medicine, cardiology, pulmonary/critical care and neurology staff, all of whom have an important role in patient care during the postarrest period.

- There are no universal standardized protocols or consensus guidelines on how to implement a postarrest management protocol and research gaps remain. What are the criteria to involve cardiology, neurology and pulmonary/critical care in the care of the hypothermic patient? What is the best management strategy of patients with hypothermia treatment?

Therapeutic hypothermia treatment after return of spontaneous circulation

- Therapeutic hypothermia is a promising treatment that has been shown in animal models to decrease the effects of reperfusion injury in cardiac arrest victims. The 2010 International Liaison Committee on Resuscitation guidelines state that any patient with a witnessed out-of-hospital cardiac arrest with ventricular fibrillation or ventricular tachycardia as the presenting rhythm who remains unconscious after return of spontaneous circulation should be cooled to a temperature of 32–34°C for 12–24 h. The guidelines also recommend that therapeutic hypothermia should be considered for those patients with in-hospital cardiac arrest and other presenting rhythms, based on observational clinical data, experimental laboratory findings, and conceptual understandings of mechanism of reperfusion injury.

- There are still major research gaps regarding the mechanism and process of inducing hypothermia. Is surface versus intravascular cooling more efficacious? What is the timeframe in which hypothermia should be induced? What is the optimal length of time for hypothermia treatment?

Angiography postarrest

- The International Liaison Committee on Resuscitation guidelines suggest that a 12-lead EKG should be performed both in the prehospital and emergency department setting to assess for ST-elevation myocardial infarction. Early interventional cardiology involvement for urgent (within hours of presentation) angiography is advocated. The rationale for urgent angiography is that early revascularization may minimize myocardial death, reduce arrhythmias and increase brain perfusion.

- Currently, there is no consensus and clinical practice is highly variable among different medical centers and among cardiologists. There are still many unanswered questions in this debate about early versus delayed or no angiography. What is the correct time interval in which a patient should be taken to the cardiac catheterization lab? Should only ST-elevation myocardial infarction patients be taken to angiography? What is the amount of critical stenosis needed for intervention?

Conclusion

- Although there is a body of evidence to support each of these International Liaison Committee on Resuscitation recommendations, there are still large gaps in the research about how these major interventions will be implemented in the real-world setting.

- It appears that we are transitioning away from the perception that cardiac arrest victims are futile toward a renewed sense of hope that providing high quality, co-ordinated care may improve the intact neurological survival from cardiac arrest.
Improving cardiac arrest survival by providing high quality, co-ordinated care


