New insights for adult cardiopulmonary resuscitation. 
Up-coming resuscitation guidelines 2010

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Summary. Despite advances in cardiac arrest care, the overall survival to hospital discharge remains poor. The objective of this paper was to review the innovations in cardiopulmonary resuscitation that could influence survival or change our understanding about cardiopulmonary resuscitation. We have performed a search in the MEDLINE and the Cochrane databases for randomized controlled trials, meta-analyses, expert reviews from December 2005 to March 2010 using the terms cardiac arrest, basic life support, and advanced life support. The lack of randomized trials during the last 5 years remains the main problem for crucial decisions in cardiopulmonary resuscitation. Current trends in cardiopulmonary resuscitation are toward minimizing the interruptions of chest compressions and improving the quality of cardiopulmonary resuscitation. In addition, attention should be paid to all the parts of chain of survival, which remains essential in improving survival rates.

Introduction

Despite advances in cardiac arrest care, the survival to hospital discharge remains low – around 20% after in-hospital cardiac arrests (1, 2) and up to 5–10% after out-of-hospital arrests (3, 4). There are several factors affecting the outcome of patients: the type of the arrest (cardiac or respiratory), whether the arrest was witnessed or not, duration of resuscitation (5, 6). The etiology and presentation of in-hospital arrests differ from that of out-of-hospital arrests. In hospital, around 72% of patients with cardiac arrest have asystole or pulseless electrical activity as the initial cardiac rhythm, whereas the remaining patients have ventricular tachycardia or fibrillation (1, 5). In case of the out-of-hospital cardiac arrest, ventricular fibrillation or ventricular tachycardia is recorded as initial rhythms in 30–40% of cases. This means that many more victims have ventricular fibrillation or ventricular tachycardia as the initial rhythm (2–5). According to Brindley et al. (5), among all the witnessed arrests in hospital, 1 in 2 patients were resuscitated, 1 in 3 survived to 24 hours, 1 in 4 survived to discharge, and 1 in 5 could return home. Only 1 in 5 patients with unwitnessed cardiac arrest was resuscitated despite efforts to resuscitate; however, no one of them survived to discharge. Survival rates were not associated with age, but were lower at night or in early morning (3, 5, 7).

The International Liaison Committee on Resuscitation (ILCOR) was formed in 1992 to provide scientific aspects of cardiopulmonary and cerebral resuscitation worldwide and produce statements that reflect an international consensus. The last consensus on CPR and Emergency Cardiac Care Science with Treatment Recommendations was published in 2005 (8). Five years have passed, and ILCOR, in collaboration with the American Heart Association, is coordinating an evidence-based review of resuscitation science, which will be published in October 2010. This Consensus will provide material for regional resuscitation
The goal of this article is to review the tendencies of possible changes in the new upcoming 2010 CPR guidelines. To achieve this goal, we have searched the MEDLINE and the Cochrane database for randomized controlled trials, meta-analyses, expert reviews from December 2005 to March 2010 using terms cardiac arrest, basic life support, and advanced life support.

Chain of survival

The chain of survival concept, originally proposed by the Advanced Cardiac Life Support (ACLS) Subcommittee and the Emergency Cardiac Care Committee of the American Heart Association (AHA) in 1991 (9), was updated in the 2005 guidelines with two additional concepts, such as early cardiac arrest recognition and/or prevention, and postresuscitation care. Today chain of survival consists of the four important links: 1) early recognition of the emergency and activation of the emergency medical services (EMS) system; 2) early CPR; 3) early defibrillation; and 4) early advanced life support, including postresuscitation care (8). The chain of survival must be performed well to optimize survival in cardiac arrest.

Early recognition of an emergency in hospital

Some in-hospital cardiac arrests may be prevented by better care (10). In response to that, healthcare providers have introduced “track and trigger” systems enabling early recognition of seriously ill hospital patients and, through early intervention, reducing the number of unexpected deaths, cardiac arrests, and unplanned ICU admissions (11). Within these systems, nursing and/or medical staff can call a medical emergency team (MET) based on one or combined specified vital sign abnormalities (“triggers”) or because they are genuinely worried about the patient’s clinical state (“worried” criterion). The MET differs from the cardiac arrest team, as it quickly responds to special calling criteria at an earlier stage of physiological instability. There is a wide range of “track and trigger” systems in clinical use. These systems can be categorized as single-parameter systems, such as MET calling criteria (12), multiple-parameter systems, such as the patient at risk team (PART) calling criteria (13), aggregate weighted scoring systems, such as the Modified Early Warning Score (MEWS) (14), or combination systems, such as the Early Warning Scoring System (EWSS) (15). The most often incorporated signs are breathing rate, pulse rate, systolic blood pressure, oxygen saturation, change in conscious state, urine output, temperature (16–18). Accuracy of “track and trigger” systems relates to sensitivity and specificity (19). A large cluster-randomized controlled trial involving 23 Australian hospitals revealed that the sensitivity and specificity of MET calling criteria was below 50% (12). Smith et al. observed marked differences in the performance of single-parameter systems, with variation in their sensitivities (from 7.3% to 52.8%) and specificities (from 69.1% to 98.1%) (18). Another work by Smith et al. showed that values of the area under the receiver operating characteristic (AUROC) curve varied from 0.657 to 0.782 for aggregate-weighted “track and trigger” systems, and only 12 out of 33 of these systems discriminated reasonably well between survivors and nonsurvivors, and the best scores incorporated age (17). For outcomes, such as mortality, a high sensitivity is preferred. Consequently, the main disadvantage of scoring systems is inadequate sensitivities (16–18) and the lack of randomized trials. Potentially, the sensitivity could be improved at the cost of the decreased specificity by reducing the trigger cut point and, consequently, increasing the workload (18). According to Cuthbertson, “Low cut points generate more calls, but identify more patients who need help at the cost of more false alarms (high sensitivity and low specificity)” (19). A consensus conference on the afferent limb of Rapid Response Systems published in 2010 defines what constitutes monitoring, the patients that should be monitored, and the frequency and timing of monitoring to ensure the efficiency and effectiveness of the Rapid Response System afferent limb (20).

Early cardiopulmonary resuscitation

The hemodynamics of chest compressions. The primary elements of CPR are chest compressions, defibrillation, and ventilation. Chest compressions generate the arterial pressure, which is a determinant of cerebral perfusion. The difference between the aortic “diastolic” pressure and the right atrial “diastolic” pressure is known as the coronary perfusion pressure. Chest compression phase equals the “systole,” and the release phase of chest compressions equals the “diastole” (21, 22). The brain receives blood during both the compression and decompression phases. Arrested heart is perfused only during the decompression phase (23). When the chest compressions are started, time is needed for cerebral and coronary perfusion pressures to develop. When the chest compressions are interrupted for rescue breathing or for other reasons, cerebral and coronary perfusion pressures

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drop suddenly (24). The longer the interruption, the longer chest compressions are needed to achieve adequate coronary perfusion pressure. The coronary perfusion pressures generated by chest compressions influence the return of spontaneous circulation in humans (25). When an adequate coronary pressure is produced, ventricular fibrillation can be maintained for longer period of time (21). According to the experiments with pigs by Steen et al., some blood flow continues for several minutes after the cardiac arrest. After the cardiac arrest, the blood is shifted over to the venous circulation, and the right heart becomes more distended. Simultaneously, the left heart becomes emptier over the first 3 minutes of ventricular fibrillation. After about 5 minutes, blood pressure on the arterial side becomes equal to the blood pressure on the venous side. At this moment, the coronary perfusion pressure and the carotid flow fall to zero. To achieve acceptable carotid artery flow, chest compressions should be continued for 10 seconds, but to bring a negative coronary perfusion pressure back to zero, 1 minute of chest compressions is necessary. Finally, to bring it up to an adequate level, an additional half minute of chest compressions is needed (23). This study shows that after 5 minutes of untreated ventricular fibrillation, the pressure gradient is reversed after 60 seconds, and adequate pressure level is achieved after 90 seconds of CPR. The right ventricle becomes substantially dilated during the first minute of untreated ventricular fibrillation followed by an impairment of left ventricular myocyte stretch (23, 26). Weisfeld et al. has proposed a 3-phase time-sensitive model revealing the response to treatment. During electrical phase, the heart can respond to a shock, followed by a longer hemodynamic phase when compressions may still be effective. During metabolic phase, the developed stone heart is not responsive to treatment (27). After successful delayed defibrillation, any contractions are initially very weak, and the heart will dilate again (28, 29).

During chest compressions, gasping and compressions themselves may be a possible source of ventilation. Unconscious humans generally have an obstructed airway in supine position. Despite this fact, gasping enables significant ventilation and is associated with higher survival rates. Gasping is defined as “an abrupt, sudden, transient inspiratory effort” (breaths usually with intervals rare than 10 seconds), and it is observed in 55% of patients suffering witnessed cardiac arrest (30). Gasping can enhance pulmonary gas exchange (oxygenation and ventilation) and circulation by improving venous return, which results in enhanced cardiac output, aortic pressures, coronary artery pressures, and cerebral blood flow (31). Once external chest compression has commenced, ventilation may occur passively through chest recoil resulting from external chest compression, which generates a negative intrathoracic pressure and entrains air through an airway if it is open (32, 33). Despite poorer saturation when the airway was occluded, overall oxygen delivery to the tissues may be matched by the improved flows with uninterrupted compressions (34).

Initial assessment and calling. The ILCOR 2005 recommends that rescuers should start CPR if a victim is unconscious (unresponsive), not moving, and not breathing. It is important to recognize occasional gasps as a sign of cardiac arrest and start CPR (8, 35). If cardiac arrest is confirmed, the resuscitation team should be called. It is important to diagnose cardiac arrest early, as this saves time for calling the resuscitation team and CPR. A study with 119 healthcare professionals showed that there was no difference in diagnostic accuracy between those rescuers who used the simultaneous assessment and those who used the sequential assessment of breathing and pulse. But the use of a sequential assessment (48.2%, the mean time for completing assessment was 13.4 seconds) was associated with a higher number of correct diagnoses compared to a simultaneous assessment (33.5%, mean time for completing assessment was 7.3 seconds). The Birmingham assessment of breathing study demonstrated that Basic life support (BLS)-trained medical students were unable to reliably identify normal breathing from abnormal breathing during 10 seconds (36). In other aspect, it is important for laypersons not to miss patients with cardiac or respiratory arrest. Attempting CPR on an unconscious patient who looks lifeless has not been shown to be harmful. An animal study showed that the exclusion of the interval for assessment of airway, breathing, and signs of circulation might reduce postresuscitation dysfunction (37). In addition, teaching lay citizens or helping dispatcher to assess for the presence of agonal respiration over the telephone can significantly increase the detection of cardiac arrest (38). Further investigations are needed.

Conventional CPR or compression-only CPR. According to the ILCOR 2005 recommendations, conventional CPR is carried out in cycles with compression-ventilation ratio of 30:2. Chest compressions should be provided by pushing hard at a rate of 100 per minute, allowing full chest recoil, and minimizing interruptions. After 30 chest compressions, the rescuer
Mouth-to-mouth ventilation is associated with an increased risk of regurgitation compared with compression-only CPR (39). Also, bystander CPR is a strong predictor of long-term survival (8). Laypersons or healthcare personnel have fears of infection and hold mouth-to-mouth ventilation unpleasant that causes the reluctance to perform it (40). Based on animal data and some low-level human data (41–44), ventilation may not be necessary for several minutes after primary cardiac arrest. At least 4 observational studies of out-of-hospital cardiac arrest have been published during the last 5 years. All these studies showed that patients were more likely to survive with any form of bystander CPR than without, and there was no difference in survival to discharge between compression-only CPR and conventional CPR (41–44). The AHA in an effort to increase the relatively low rate of bystander CPR in the USA in 2008 published an advisory statement on compression-only CPR for bystanders responding to out-of-hospital cardiac arrest. This statement emphasizes 2 important components, which bystanders must do at a minimum if they witness a suddenly collapsed adult. First, activate their community emergency medical response system (e.g., call 112) and second, provide high-quality chest compressions by pushing hard and fast in the center of the chest, minimizing interruptions (45). This statement did not recommend to completely avoid laypersons’ teaching how to perform mouth-to-mouth ventilation in context that some cardiac arrest victims (e.g., pediatric and asphyxial) may benefit from conventional CPR. In addition, compression-only CPR is effective when resuscitation is required for a relatively short period (43). The decision of a layperson to make compression-only CPR or conventional CPR depends on whether the collapsed victim is a child or an adult, whether the cause of collapse is cardiac or noncardiac, the time from the collapse to the first attempt of CPR (witnessed arrest or not), and ambulance response time (45, 46). Is it known that 63–70% of hospital-treated cardiac arrest patients have a primary cardiac cause (41). Victims with asphyxial cardiac arrest or where response times are long will need early ventilation (46). The rational approach is to teach BLS for lay citizens in two stages: first, to introduce compression-only CPR as the default technique, and second, to add an explanation of breathing importance in specific situations to increase the effectiveness of CPR (47).

CPR quality. The quality of CPR, which depends on depth and rate of chest compressions, interruptions in chest compressions, affects patient outcomes (48–50). A systematic review by Yeung et al. (51) concluded that there was good evidence supporting the use of CPR feedback/prompt devices during CPR training to improve CPR skill acquisition and retention. Their use in clinical practice as part of an overall strategy to improve the quality of CPR may be beneficial. Feedback can be given on chest compression rate, chest compression depth, ventilation rate, pauses in chest compression, and incomplete chest wall recoil. The accuracy of devices that measure compression depth should be calibrated taking in account the stiffness of the surface on which CPR is delivered. But still there are doubts, whether these devices actually improve patient outcomes. Other factors influencing quality of CPR include rescuer’s fatigue, switching between CPR operators, rescuer’s position, leaning, and CPR during transportation. Sugerman et al. demonstrated that decay started after 90 seconds and achieved a significant decrease in chest compression depth over 3 minutes during in-hospital CPR (52). Sutton et al. showed that during in-hospital resuscitation with CPR, quality feedback systems and allowing rescuers with good CPR skills to continue chest compressions longer than 2 minutes might be beneficial to improve CPR quality by minimizing switches and no-flow time (53). The quality of chest compressions decreased when the bed height was 20 cm higher than the knee height of the rescuer (54). Jones et al. showed that delivery of chest compressions while standing produced greater spinal compression and mechanical energy flow, but this position had more permanent effectiveness than did delivery while kneeling (55).

Defibrillation and precordial thump

Precordial thump. According to the ILCOR 2005 recommendations, one immediate precordial thump may be considered after a monitored cardiac arrest if an electrical defibrillator is not immediately available (8). At least 3 prospective studies (56–58) exploring the value of the precordial thump have been published during the last 5 years. These studies demonstrated low success rates, being 1.3% (n=2/155) in (57) and 1.9% (n=1/52) in (56), with all effects of the precordial thump on ventricular tachycardia and no effect on ventricular fibrillation. Pellis et al. studied the thump as a first maneuver of resuscitation in all out-of-hospital cardiac arrest patients, without reference to the initial rhythm. The thump had changed the rhythm.
in 6 out of 144 patients, but only in 3 of these 6 patients spontaneous circulation had been restored and two patients were discharged alive, both after witnessed asystole (58). The precordial thump is not effective for ventricular fibrillation and has limited use for ventricular tachycardia (56–58). However, it is the fastest accessible resuscitative maneuver for witnessed onset of ventricular tachycardia, if a defibrillator is not available, with good safety profile (59). Greater effectiveness is observed in witnessed asystolic cardiac arrest than suggested by current guidelines (58).

The preshock pause. The ILCOR 2005 recommendations are directed on minimizing the preshock pause. The preshock pause is the time between stopping chest compressions and delivery of the shock. The preshock pause longer than 10 seconds can reduce the chances of successful defibrillation. The tendency is that the shorter the preshock pause, the greater chance of successful defibrillation (49). The preshock pause can be reduced by using the defibrillator with a fast charge time, hands-free electrodes (60), artifact filtering technology to enable rhythm analysis during chest compressions (61), continuing chest compressions during charging and maybe during shock (62, 63). The possibilities depend on using monitors-defibrillators, technology progress, and resuscitation team debriefing (49). A study by Lloyd et al. demonstrated that volunteers wearing polyethylene medical gloves, pressed down to the patient’s sternum, did not sense a shock, and the leakage current was significantly lower than current safety standards for medical equipment (63). However, for the safety reason, more data are needed to implement this method into the practice. Thus, charging during chest compressions is safer and more realistic at this time.

Compressions before defibrillation. Bobrow et al. published data concerning the strategy of minimally interrupted cardiac resuscitation (MICR) (64). In this study, 200 chest compressions were given before the first shock, if ventricular fibrillation or ventricular tachycardia was the initial rhythm, and 200 chest compressions were given after the shock. Tracheal intubation was performed after three cycles of 200 chest compressions and rhythm analysis. Interestingly, that during this period before intubation, an oral airway is inserted and oxygen is given by a nonrebreather face mask (passive oxygen delivery). Adrenaline at a dose of 1 mg was administered intravenously as soon as possible. This study included 886 patients. Survival to hospital discharge increased from 1.8% (n=4/218) before MICR training to 5.4% (n=36/668) after MICR training (OR, 3.0; 95% confidence interval [CI], 1.1–8.9) and from 4.7% (n=2/43) before MICR training to 17.6% (n=23/131) after MICR training (OR, 8.6; 95% CI, 1.8–42.0) in subgroup of 174 patients with witnessed cardiac arrest and ventricular fibrillation. Bradley et al. published an observational study of 1638 patients treated for ventricular fibrillation or ventricular tachycardia arrests. Higher survival rates were observed in the group of patients who received CPR for 46–195 seconds before defibrillation in comparison to the group of patients receiving CPR for less than 45 seconds before defibrillation (65). Due to the lack of prospective randomized trials, this new concept about compressions before defibrillation remains open.

Defibrillation energy. The ILCOR 2005 recommended a single-shock strategy for the treatment of ventricular fibrillation or ventricular tachycardia (8). The BIPHASIC trial compared fixed versus escalating energy regimens for 221 out-of-hospital cardiac arrest patients who required at least one shock (66). This study demonstrated that conversion rates and ventricular fibrillation termination rates were significantly higher in the escalating energy group, but the success of the first shock was similar between groups, and no differences in survival outcomes or adverse effects were observed between the groups. This means that higher biphasic energy levels are beneficial for patients with ventricular fibrillation, if multiple defibrillation shocks are required and are not harmful (67).

Advanced life support

Tracheal intubation. The benefits of tracheal intubation are the possibility of ventilation without interrupting chest compressions, effective ventilation, minimal risk of regurgitation, and protection from aspiration. Disadvantages of tracheal intubation are complications, such as unrecognized esophageal intubation (2.9–16.9%) (68), unrecognized main stem bronchial intubation, unrecognized dislodgement, interruption of chest compressions during intubation (69), and need of high-skilled healthcare professionals. A meta-analysis of three randomized controlled clinical trials comparing tracheal intubation versus alternative airway managing for acutely ill and injured patients concluded that in nontraumatic cardiac arrest tracheal intubation had no overall benefit against bag-mask ventilation or use of Combitube (70). Wang et al. studied 100 adult out-of-hospital cardiopulmonary arrest patients treated by an emergency medical services agency (69). In this study, the median duration of the first endotracheal intubation-associated CPR
Supraglottic airway devices are easier to insert and can be inserted without interrupting chest compressions (71). There is a wide range of supraglottic airway devices, such as Combitube, classic laryngeal mask, Supreme laryngeal mask, I-gel mask (72), and others. Unfortunately there are no studies in which supraglottic device insertion during CPR would be a primary endpoint for the study of survival (73). A prospective nonrandomized study of the SOS-KANTO group demonstrated that there was no greater benefit of respiratory status in patients resuscitated by emergency medical personnel with a bag-valve-mask airway group than in the bag-mask group (13.4% vs. 6.1%, P=0.03) (73, 74).

**Drugs.** There are no randomized clinical studies demonstrating the benefit of drugs administered during CPR in survival, and thus no level I evidence is available for drug use in CPR. In 2009, Olasveegen et al. published a prospective randomized trial with 851 out-of-hospital cardiac arrest patients, in which they compared patients receiving the advanced cardiac life support with intravenous drug administration and without intravenous drug administration (75). Short-term survival (admitted to the intensive care unit) was significantly better in the intravenous drug group compared to the group without intravenous drug administration (30% vs. 20%, OR, 1.67; 95% CI, 1.22–2.29; P=0.002), but there was no difference in long-term survival (discharged from the hospital) (10.5% vs. 9.2%, OR, 1.16; 95% CI, 0.74–1.82; P=0.61). Considering that both the groups had similar good CPR quality and no difference in long-term survival, the most important part of CPR remains the quality of CPR (good-quality chest compressions with minimizing interruptions, early defibrillation). Prospective randomized controlled studies comparing a standard drug, epinephrine, with vasopressin alone in repeated doses (76) or vasopressin and epinephrine with epinephrine (77) for patients undergoing CPR did not show differences in outcome. In addition, there are no additional data regarding the effectiveness of amiodarone and atropine during CPR.

**Mechanical devices.** Hand-held device with a suction cup, applied to the mid-sternum to perform actively chest compressions and decompressions during CPR, belongs to an active compression-decompression device. A meta-analysis of randomized controlled clinical trials comparing active compression-decompression with standard manual chest compression concluded that active chest compression-decompression in patients with cardiac arrest was not associated with a clear benefit (78). Most known mechanical devices, used to provide mechanical chest compressions, are the Load Distributing Band (Autopulse) and the Lund University Cardiac Assist System (LUCAS). The main disadvantage of mechanical devices is the lack of clinical evidence for improved survival, also contradictory results of existing clinical trials (79). In specific circumstances, such as a small team or prolonged CPR, mechanical CPR may deliver better depth and rate of compressions, compared with manual CPR (80). Time required for application may deleteriously increase “hands-off” time. Delay in decision to apply a device may negatively influence outcomes. Chen et al. (81) published a prospective observational study on the use of extracorporeal life support in adults with witnessed in-hospital cardiac arrest of cardiac origin undergoing CPR for more than 10 minutes compared with patients receiving conventional CPR. From 975 resuscitated patients, 113 were enrolled in the conventional CPR group and 59 were enrolled in the extracorporeal CPR group. The patients in the assisted extracorporeal CPR group had a significantly better outcome of hospital survival (RR, 0.51; 95% CI, 0.35–0.74; P=0.001), 30-day mortality (RR, 0.47; 95% CI, 0.28–0.77; P=0.003), and one-year survival (RR, 0.53; 95% CI, 0.33–0.83; P=0.006) than those in the conventional CPR group. These fascinating results support the use of a portable miniature version of extracorporeal life support. Randomized trials are needed to obtain more data.

**Postresuscitation care**

A complex set of pathophysiological processes that develop after the return of spontaneous circulation (ROSC) is called the postcardiac arrest syndrome. This syndrome consists of four components: postcardiac arrest brain injury, postcardiac arrest myocardial dysfunction, systemic ischemia/reperfusion response, and persistent precipitating pathology (82). Some interventions applied after ROSC can significantly influence the chances of survival with good neurological outcome. A meta-analysis of three randomized controlled clinical trials comparing adult populations cooled with any cooling method applied within 6 hours...
after cardiac arrest versus standard postresuscitation care concluded that therapeutic hypothermia improved survival and neurological status in comatose survivors of cardiac arrest, and cooling must be induced within the first hours of the restoration of spontaneous circulation (83). The benefits of hypothermia after cardiac arrest from nonventricular fibrillation or ventricular tachycardia rhythms are being less investigated, although this does not stop from implementing the therapy in practice (84). Therapeutic hypothermia can be initiated even before hospital admission (85, 86). Animal data show that starting the cooling process during cardiac arrest may facilitate ROSC (87), and nasopharyngeal cooling, achieved by instilling perfluorocarbon via nasal prongs, is a novel way of inducing hypothermia (88).

Also, the implementation of a standardized treatment protocol for postresuscitation care (89), which includes therapeutic hypothermia (83), primary percutaneous coronary intervention for cardiac arrest associated with ST-segment elevation myocardial infarction (90) and moderate glucose control (below 10 mmol/L or 180 mg/dL) (91) improves survival and neurological outcome in cardiac arrest survivors.

Concluding remarks
The lack of randomized trials during the last 5 years remains the main problem for crucial decisions in cardiopulmonary resuscitation. Current trends in cardiopulmonary resuscitation are toward minimizing the interruptions of chest compressions and improving the quality of cardiopulmonary resuscitation. In addition, attention should be paid to all the parts of chain of survival, which remains essential in improving survival rates and emphasizing the introduction of “track and trigger” systems, education on cardiopulmonary resuscitation quality, resuscitation team debriefing, implementation of advanced defibrillation technology, and postresuscitation care with mild therapeutic hypothermia.

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