Chapter 2

ALS; Advanced Life Support

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1　Cardiac arrest algorithm

When a lay rescuer gives CPR, they should follow the Basic Life Support (BLS) algorithm. But healthcare providers who would treat a cardiac arrest patient in hospital or as their duty are recommended to follow the BLS algorithm for healthcare providers (Figure.1) as a preface of Advanced Life Support (ALS) algorithm (Figure.2). These algorithms are ideal when rescuer can use the devices and drugs if needed. ALS algorithm includes the managements during cardiac arrest and after return of spontaneous circulation.

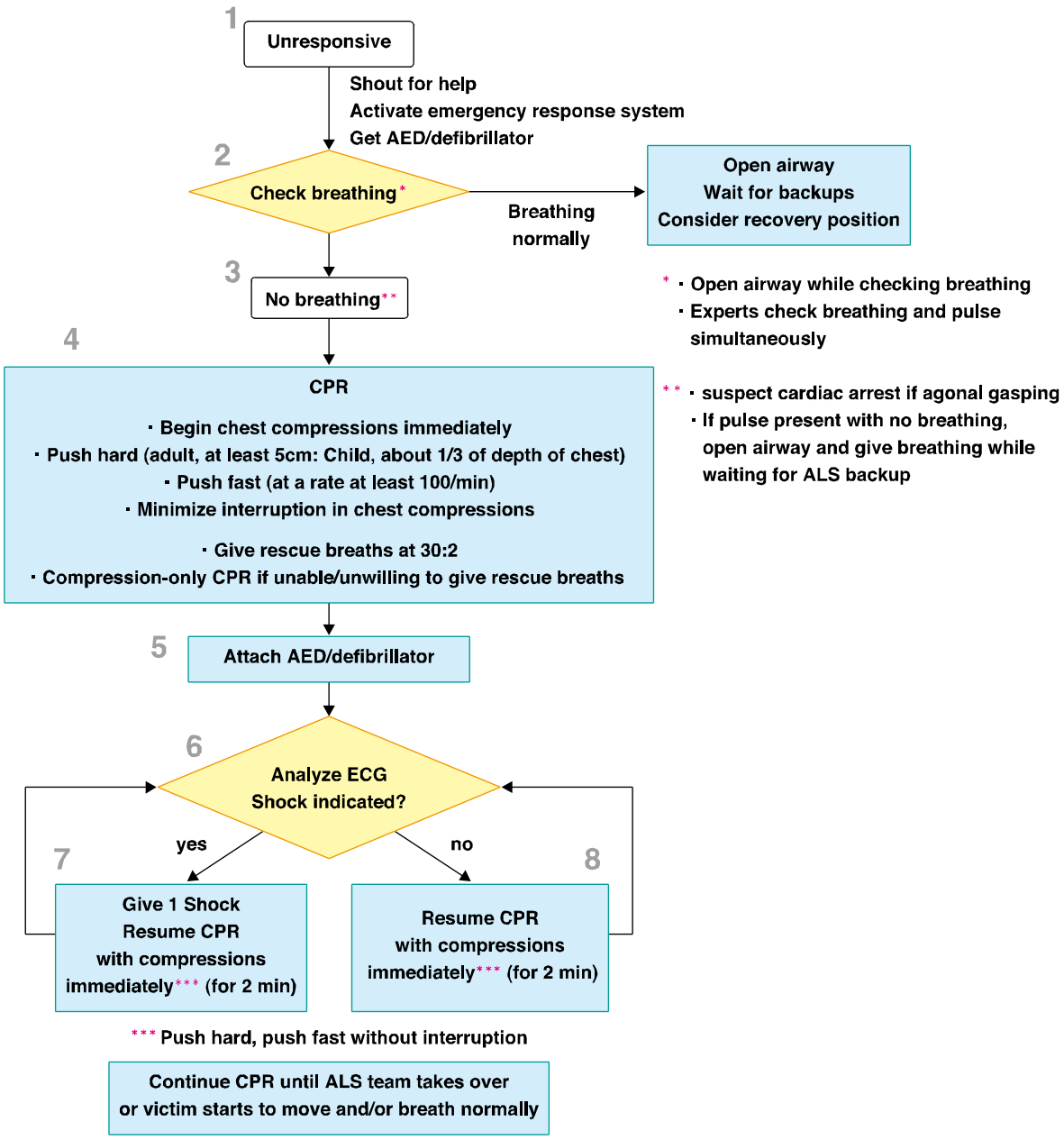

Figure 1. Basic life support for healthcare providers

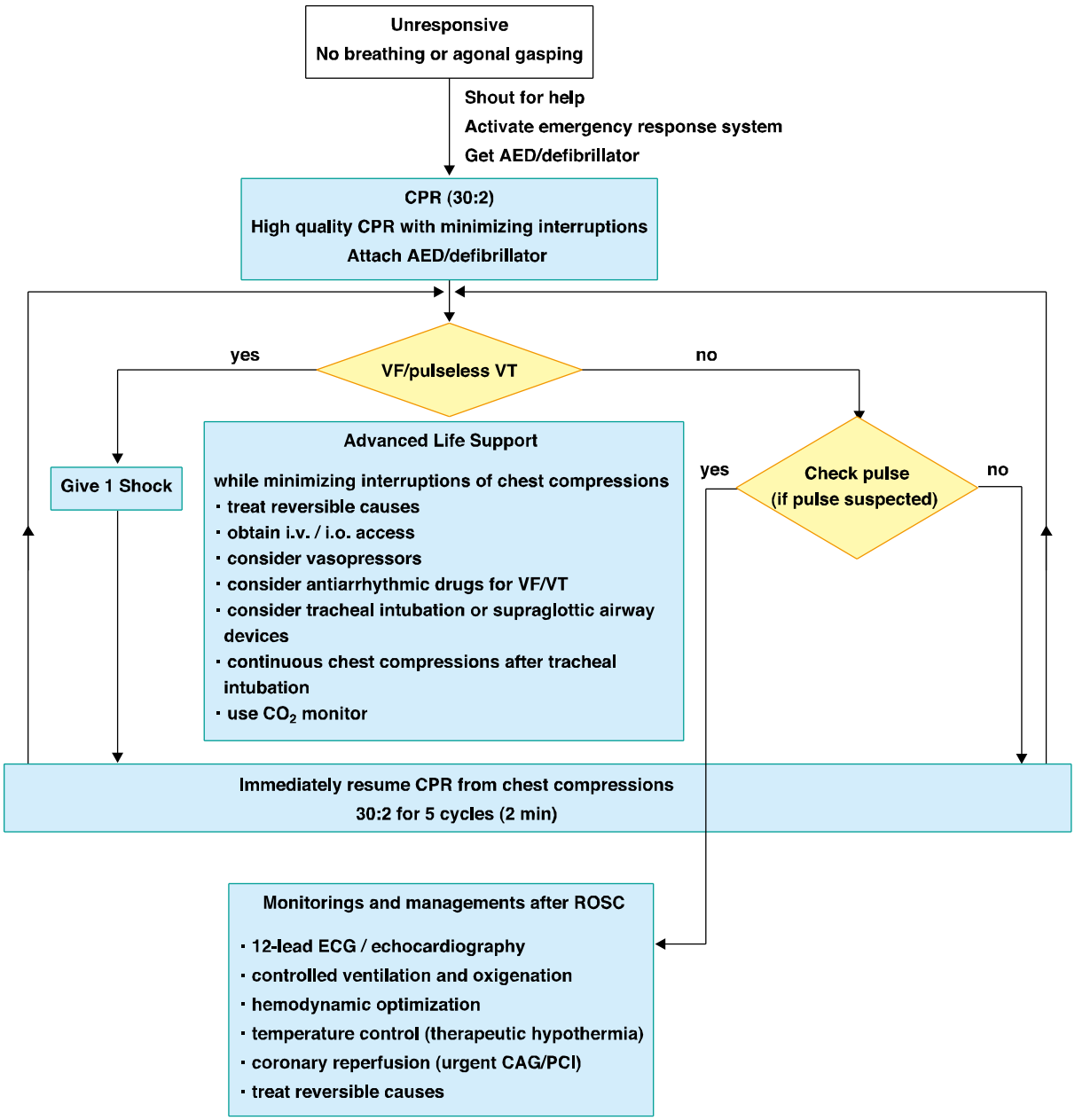

Figure 2 Advance life support

2 Airway and ventilation

■1 Basic Airway Devices

1. Oropharyngeal and Nasopharyngeal Airways

Despite frequent successful use of nasopharyngeal and oropharyngeal airways in the management of non-arrest patients, there are no published data on the use of these airway adjuncts during CPR in humans. When bag-mask ventilation was undertaken with an oral airway and compared with no oral airway, one study in anaesthetized patients demonstrated higher tidal volumes (LOE 5[1]).

In one report, insertion of a nasopharyngeal airway caused some airway bleeding in 30% of cases (LOE 5[2]). One study of nasopharyngeal airways in anesthetized patients showed that nurses inserting nasopharyngeal airways were no more likely than anesthesiologists to cause nasopharyngeal trauma (LOE 5[3]). One study showed that the traditional methods of sizing a nasopharyngeal airway (measurement against the patient's little finger or anterior nares) do not correlate with the airway anatomy and are unreliable (LOE 5[4]). Two case reports reported inadvertent intracranial placement of a nasopharyngeal airway in patients with basal skull fractures (LOE 5[5, 6]).

Oro- and nasopharyngeal airways have long been used in cardiac arrest, despite never being studied in this clinical context. It is reasonable to continue to use oro and naso-pharyngeal airways when performing bag-mask ventilation in cardiac arrest (Class IIa), but in the presence of a known or suspected basal skull fracture an oral airway is preferred (Class IIa).

2. Cricoid pressure

No studies addressing the use of cricoid pressure during cardiac arrest were identified. All the identified studies were conducted under anaesthesia or in awake volunteers, cadavers or manikins. (The descriptions of LOE 5* shown in this chapter are adopted for the studies about non cardiac arrest patients.) The effect of cricoid presssure on gastric inflation during BVM ventilation was examined by 2 adult (LOE 5* [7, 8]) and 2 pediatric studies (LOE 5* [9, 10]). All showed less gastric inflation with cricoid pressure than without, although all of the studies used ventilation volumes higher than those recommended in cardiac arrest.

Nine studies in non arrest adult subjects undergoing anaesthesia showed that cricoid pressure impairs ventilation in many patients, increases peak inspiratory pressures and causes complete obstruction in up to 50% of patients depending on the amount of cricoid pressure (in the range of recommended effective pressure) that is applied (LOE 5* [7, 8, 11-16 17]).

One study in anaesthetized patients determined that cricoid pressure prevents correct placement and ventilation with the laryngeal tube (LT) (LOE 5*[18]). Eight studies in anaesthetized adults showed that when cricoid pressure was used before insertion of a laryngeal mask airway (LMA) there was a reduced proportion of tubes correctly positioned, an increased incidence of failed insertion, and impaired ventilation once the LMA had been placed (LOE 5[19-26]). No significant impairment to

tracheal intubation was found by four studies performed in anaesthetized patients (LOE 5* [27-30]), while Seven studies (LOE 5*[19, 31-36]) did show impairment of intubation with increased time to intubation and decreased intubation success rates. One clinical study and One cadaver study demonstrated a worse laryngoscopic view with the application of cricoid pressure (LOE 5*[37, 38]).

Cricoid pressure prevented movement of liquid from the oesophagus into the pharynx in 5 cadaver studies (LOE 5* [39-43]) however, in 1 LOE 5* study[44] of 4891 obstetric patients undergoing anaesthesia, no significant difference was observed in regurgitation rates between patients who received cricoid pressure and those who did not.

The routine use of cricoid pressure to prevent aspiration in cardiac arrest is not recommended (Class III). If cricoid pressure is used during cardiac arrest, the pressure should be adjusted, relaxed or released if it impedes ventilation or placement of an advanced airway.

■2 Advanced Airway Devices

There isinsufficient evidence to support or refute the routine use of specific advanced airway devices during CPR to improve outcome from cardiac arrest. No data support the routine use of a particular device for advanced airway placement during cardiac arrest.

1. Timing of Advanced Airway Placement

One registry study evaluated the impact of timing of advanced airway placement during 25,006 in-hospital cardiac arrests (LOE 2[45]). In this study, earlier time to invasive airway (< 5 min) was associated with no improvement in ROSC but improved 24 hour survival (NNT = 48). In an urban out-of-hospital setting, intubation in <12 minutes was associated with better survival than intubation ≥13 minutes[46]. In an out-of-hospital urban and rural setting, patients intubated during resuscitation had better survival than patients not intubated[47]; whereas, in an in-hospital setting, patients requiring intubation during CPR had worse survival[48]. A recent study found that delayed tracheal intubation bundled with passive oxygen delivery and minimally interrupted chest compressions was associated with improved neurologically intact survival after out-of-hospital cardiac arrest in patients with adult, witnessed, ventricular fibrillation/ ventricular tachycardia[49]. The independent contribution of the timing of the advanced airway was not available in the study.

There is inadequate evidence to define the optimal timing of advanced airway placement during cardiac arrest. In the case of shortage of rescuers, early placement of these devices might help the rescuers focus on other effective treatment without having to deal with BVM ventilation.

The tracheal tube was once considered the optimal method of managing the airway in CPR. However, tracheal intubation is a high risk treatment because of esophageal intubation, and requires adequate training and ongoing skills maintenance for secure and prompt intubation. Because prolonged attempts of tracheal intubation are harmful if chest compressions are interrupted, it should be minimized even when performing tracheal intubation (Class I).

2. Supraglottic Airway Device Versus Ventilation With Bag-Mask

A retrospective case series (LOE 4) comparing a laryngeal mask airway with bag-mask ventilation in cardiac arrest patients demonstrated a regurgitation rate of 3.5% with use of a laryngeal mask airway and 12.4% with use of bag-mask ventilation[50]. When a variety of supraglottic airway devices were compared with bagmask ventilation in manikin models, six studies showed improved ventilation and a decrease in gastric inflation (LOE 5[51-56]). One pseudorandomized and one nonrandomized clinical trial (LOE 2) found no difference in arterial blood gas values or survival rates when a variety of supraglottic airway devices were compared to bagmask ventilation[57, 58]. Three studies performed in manikin cardiac arrest models (LOE 5[59-61]) found that compared with a bag-mask, use of a single-use, disposable laryngeal tube to provide ventilation may decrease no-flow times. Holding the mask to the victim's face with both hands can ensure a better mask seal during bag-mask ventilation(LOE 5 [62, 63]).

A supraglottic airway device may be considered by healthcare professionals trained in its use as an alternative to bag-mask ventilation during cardiopulmonary resuscitation (Class IIb). When two or more experienced rescuers preform CPR, ventilation with bag-mask is reasonable (Class IIa). It may be beneficial that one rescuer holds the mask with both hands to open the airway and maintain a tight mask-to-face seal while another rescuer compresses the ventilation bag (Class IIa).

Knowledge Gaps

Further data are needed on the adequacy of ventilation with the various supraglottic airway devices if chest compressions are not interrupted and comparison of the various supraglottic airway devices with bag-mask ventilation and with each other when used clinically by inexperienced and by experienced providers.

3. Tracheal Intubation Versus Supraglottic Airway Device

Nine studies compared a variety of supraglottic airway devices with the tracheal tube during cardiac arrest (LOE 1[64], LOE 2[65-72]) and a further six studies compared a variety of supraglottic airway devices with the tracheal tube in patients undergoing anaesthesia (LOE 5[73-78]). Overall in these studies the supraglottic airway device performed as well as, or better than, the tracheal tube with respect to successful insertion and/or time to tube insertion or to ventilation. One study retrospectively compared outcomes in cardiac arrest patients treated with esophageal-trachealcombitube or tracheal tube and found no difference in ROSC, survival to admission or survival to discharge (LOE 2[71]). One study compared survival in cardiac arrests managed with laryngeal mask airway with an historical control group of cardiac arrests managed with tracheal tube and found that ROSC was significantly higher in the study period (61% vs 36%) (LOE 3[72]).

Nine studies documented that when a supraglottic airway device is used as a rescue airway after failed tracheal intubation, most patients can be ventilated successfully with the supraglottic airway device (LOE 2[65, 66, 70], LOE 3[79-82], LOE 5[74, 83])

Two studies performed while wearing anti-chemical protective clothing, one randomized crossover trial on anaesthetized patients and a second pseudorandomized study on manikins, found increased

time to tracheal tube insertion but not to laryngeal mask airway insertion (LOE 5[75, 84]).

Three manikin studies comparing a supraglottic airway device with the tracheal tube during ongoing chest compressions demonstrated decreased time to intubation with the supraglottic airway device as well as reduced no flow time (LOE 5[85-87]). One non-randomized manikin study found that chest compressions caused only a minor increase in time to tracheal intubation but not to supraglottic airway device insertion (LOE 5[88]).

Healthcare professionals trained to use supraglottic airway devices may consider their use for airway management during cardiac arrest and as a backup or rescue airway in a difficult or failed tracheal intubation (Class IIb). These devices may be used as a backup for a difficult or failed tracheal intubation (Class IIb). Among supraglottic airway devices, there is sufficient evidence to support only for Combitube or LMA as the substitute of tracheal intubation. Although the laryngeal tube is widely used in Japan during CPR, there is insufficient evidence to show its benefit.

Knowledge Gaps

The adequacy of ventilation with supraglottic airway devices during uninterrupted chest compressions is unknown. The performance of the various supraglottic airway devices should be compared with each other and with the tracheal tube when used in cardiac arrest. Use of the supraglottic airway devices by providers of differing experience should also be studied.

■3 Confirming tracheal tube Placement

1. Exhaled carbon dioxide detection and esophageal detection devices

Two studies of waveform capnography (LOE 2) to verify tracheal tube position in victims of cardiac arrest after intubation demonstrated 100% sensitivity and 100% specificity in identifying correct tracheal tube placement[89, 90]. Grmec reported that the capnography detected 4 esophageal intubations of 246 cardiac arrests[89]. Silvestri demonstrated that the rate of unrecognized misplaced intubations in the group with continuous ETCO2 monitoring was zero, and the rate in the group without the monitoring was 23.3%, but this study included non-cardiac arrest patients and did not show the accuracy for cardiac arrest patients[90].

Three studies (LOE 1[91-93]) with a cumulative total of 194 tracheal and 22 esophageal tube placements demonstrated an overall 64% sensitivity and 100% specificity in identifying correct tracheal tube placement when using the same model capnometer (no waveform capnography) on prehospital cardiac arrest victims. The sensitivity may have been adversely affected by the prolonged resuscitation times and very prolonged transport times of many of the cardiac arrest victims studied. Intubation was performed after arrival at hospital and time to intubation averaged more than 30 minutes.

Studies of colorimetric ETCO2 detectors, (LOE 2[94, 95], LOE 4[96-98], LOE 5[99, 100]), the syringe aspiration esophageal detector device (LOE 1[92], LOE 4[101]) the self-inflating bulb esophageal detector device (LOE 1[91-93]), and non-waveform end tidal CO2 capnometers (LOE 2[89, 102], LOE 4[96], LOE 5[100])

show that the accuracy of these devices is similar to the accuracy of clinical assessment (not uniformly defined across all studies) for confirming the tracheal position of a tracheal tube in victims of cardiac arrest.

Waveform capnography is recommended to confirm and continuously monitor the position of a tracheal tube in victims of cardiac arrest and it should be used in addition to clinical assessment (auscultation and direct visualization is suggested) (Class I).

If waveform capnography is not available, a non-waveform carbon dioxide detector or esophageal detector device in addition to clinical assessment (auscultation and direct visualization is suggested) is an alternative (Class IIa).

Knowledge Gaps

If a waveform capnography shows zero ETCO2, the duration between cardiac arrest and measurement should be considered.

2. Thoracic Impedance

Two studies in adults (LOE 5[103, 104]) and one study in children (LOE 5[105]) in patients undergoing anaesthesia demonstrated high sensitivity (0.975-1.0) and specificity (0.925-1.0) of thoracic impedance in diagnosing tracheal and esophageal intubations. One non-randomized trial in immediately post-mortem patients (LOE 2[106]) demonstrated smaller changes in thoracic impedance with esophageal ventilations than with tracheal ventilations. One study (LOE 2[107]) tested impedance-based ventilation recognition during cardiac arrest with ongoing compressions and was able to detect 90.4% of ventilations with a 95.5% positive predictive value. Two case reports comprising a total of 6 cardiac arrest patients with ongoing CPR (LOE 3[108], LOE 4[109]) demonstrated disappearance of ventilation-induced changes in thoracic impedance after esophageal intubation.

The evidence evaluating the use of thoracic impedance in diagnosing adequacy of ventilation is scant. Supportive evidence from one animal study (LOE 5[110]) demonstrated that the intensity of the thoracic impedance signal was proportional to the observed tidal volumes. An exploratory study conducted in human cardiac arrest patients (LOE 2[111]) demonstrated a strong correlation between thoracic impedance changes and tidal volume changes in the absence of chest compressions, but large variations in measured impedance coefficients (Ω /kg/ml) were observed.

Thoracic impedance may be used as an adjunctive measure to diagnose tracheal tube placement in cardiac arrest patients; however, treatment decisions pertaining to accuracy of airway placement should not be based solely upon thoracic impedance measurements until further study has confirmed its utility and accuracy in this population. Thoracic impedance has not been clinically used as a measure to diagnose tracheal tube placement in Japan.

Knowledge Gaps

More research is needed to clarify the usefulness of thoracic impedance to independently confirm

placement of a tracheal tube and adequacy of ventilation during cardiopulmonary resuscitation.

■4 Oxygen

1. Supplemental oxygen: 100% versus titration

There were no adult (>8 years of age) human studies that addressed directly whether titrated oxygen compared with 100% oxygen during cardiopulmonary resuscitation affects outcome. Two animal studies (LOE 5[112, 113]) using a fibrillatory model of cardiac arrest suggested that use of 100% oxygen during CPR and for 15-60 minutes after return of spontaneous circulation results in worse neurological outcomes compared with normoxic (21% oxygen, room air) resuscitation, whereas one animal study (LOE 5[114]) using an asphyxial model documented that ventilation with either 100% oxygen or 21% oxygen during resuscitation did not affect outcome.

There is insufficient evidence to support or refute the use of a titrated oxygen concentration or constant 21% oxygen (room air) when compared with 100% oxygen during adult cardiac arrest. In the absence of any other data there is no reason to change the current treatment algorithm, which includes use of 100% oxygen during adult cardiac arrest.

Knowledge Gaps

Prospective clinical trials will be necessary to explore constant (including room air) versus titrated oxygen resuscitation approaches during human adult cardiac arrest.

2. Passive oxygen versus positive pressure oxygen during CPR

Two studies (LOE 1[115, 116]) involving ALS providers in- and out-of-hospital settings, and two animal studies (LOE 5[117, 118]) suggested that passive oxygen delivery through a Boussignac tube at a flow of 15 L/min associated with continuous chest compressions (with or without active compression-decompression CPR) generated equal or improved gas exchange and hemodynamics, but without improved outcome (ROSC, hospital discharge survival or neurological outcome), when compared with a standard tracheal tube and positive pressure ventilation.

Four animal models (LOE 5) utilising different devices or approaches (nasal cannula in the oropharynx[119], pharyngeal-tracheal lumen airway[120] and oxygen catheter tip at the level of the carina [121, 122] confirmed an equivalent or better gas exchange and/or hemodynamics, with continuous oxygen inflation compared with standard ventilation.

One swine model (LOE 5[123]) demonstrated equivalent gas exchange and 48-hour survival following 4 minutes VF arrest with passive oxygen supplied via tracheal tube compared with oxygen supplied by positive pressure ventilation.

Two studies (LOE 3[124, 125]) of a simplified minimally interrupted cardiac resuscitation (MICR) protocol (concept of cardiocerebral resuscitation), that included passive oxygen delivery via a standard oxygen mask with non-rebreather bag and continuous chest compressions, showed an improvement in neurologically intact survival in adults with bystander-witnessed cardiac arrest and an initially

shockable rhythm when controlled with historical controls using standard CPR. Another study (LOE 3[49]) demonstrated better survival with passive oxygen delivery than with bag-mask ventilation.

In the three human studies which demonstrated possibility of better neurological outcome, the effective component of the treatment bundle is unknown, because the passive oxygen delivery with continuous chest compressions was compared with the oxygen delivery via bag-mask-ventilation with interruption of chest compressions.

In the studies with a Boussignac tube and some of animal studies, the efficacy of MICR may be reduced, because the passive oxygen delivery was compared with the oxygen delivery through tracheal tube with continuous chest compressions. Arterial blood gas values and circulatory status were certainly improved but there was no difference of the outcome. In addition, these improvements may result from a specific structure of a Boussignac tube itself.

There is insufficient evidence to support or refute the use of passive oxygen delivery during CPR to improve outcomes (ROSC, hospital discharge rate and improve neurological survival) when compared with oxygen delivery by positive pressure ventilation.

Knowledge Gaps

High-quality controlled clinical trials are required to evaluate the relationship between continuous positive airway pressure and important clinical outcomes and comparison with passive oxygen delivery during cardiopulmonary resuscitation.

■5 Strategies for Ventilation

1. Monitoring ventilatory parameters during CPR

There are no studies that directly addressed the relationship between monitoring of minute ventilation and peak pressure during cardiopulmonary resuscitation and changes in outcome (other than respiratory rate). One animal study (LOE 5[126]) showed that hyperventilation was associated with decreased coronary perfusion pressure and decreased survival. The study also demonstrated that hyperventilation during cardiac arrest is common. One study (LOE 3[127]) demonstrated that real-time feedback during CPR compared with no feedback resulted in a delivered ventilation rate closer to that indicated by current guidelines.

One animal study (LOE 5[128]) showed that during CPR applying PEEP up to 10 cm H2O, in addition to intermittent positive pressure ventilation (IPPV), may improve oxygenation compared with IPPV alone. Another study demonstrated that continuous positive airway pressure with pressure support ventilation (CPAP PSV) during resuscitation also may improve oxygenation and outcome (LOE 5[129]).

There is insufficient evidence to support or refute the use of peak pressure and minute ventilation monitoring to improve outcome from cardiac arrest. There is indirect evidence that monitoring the respiratory rate with real time feedback is effective in avoiding hyperventilation and achieving ventilation rates closer to recommended values, but there is no evidence that ROSC or survival is improved.

Knowledge Gaps

Clinical trials evaluating ventilation monitoring during cardiac arrest resuscitation for all outcomes are needed. There is limited information on the accuracy of ventilation rate monitoring in the new defibrillator software that evaluates CPR process measures. This initial work would be helpful to enable controlled trials to determine the optimal ventilation rate associated with survival.

2. Monitoring physiological parameters during

None of the 17 studies that were reviewed evaluated physiological feedback (ETCO2, coronary perfusion pressure, superior vena caval central venous oxygen saturation, bispectral index monitoring) specifically as a tool to guide resuscitation intervention in real time to improve outcomes from cardiac arrest. Eleven studies showed that physiologic monitoring values (end tidal CO2, coronary perfusion pressure, venous oxygen saturation) increased when return of spontaneous circulation was achieved (LOE 4[94, 130-139]) and may be an indication of ROSC before it can be seen in vital signs[140].

Five of the studies found that ETCO2 was accurate for predicting patients who could not be resuscitated; some giving a time frame for that prediction of 20 minutes (LOE 4[95, 133, 137, 141, 142]). However, two studies documented patients who did not meet the ETCO2 range but who survived (LOE 4[133, 143]). Multiple studies by one group (LOE 4[134-136]) showed that when ETCO2 exceeded 10 mmHg, all patients achieved ROSC. In one of these studies all the survivors had an initial ETCO2

higher than 10 mmHg[135]. Similarly, two studies showed that if the ETCO2 did not exceed 10 mmHg, survival was zero (LOE 4[141, 142]).

One study showed no correlation between BIS values during cardiopulmonary resuscitation and ROSC and survival (LOE 4[144]).

Continuous capnography or capnometry monitoring may be beneficial by providing feedback on the effectiveness of chest compressions (Class IIb). The prognostic value of end tidal CO2 is further reviewed in the section on prognostication.

Knowledge Gaps

Animal and human studies evaluating the effects of modification of resuscitation based on physiologic feedback would be helpful.

■6 Automatic Transport Ventilators

1. Automatic ventilators vs manual ventilation during CPR

One pseudo-randomized study suggests that use of an automatic transport ventilator with intubated patients may enable the EMS team to perform more tasks while subjectively providing similar ventilation to that of a bag-valve device (LOE 2[145]). One study suggests that use of an automatic transport ventilator with intubated patients provides similar oxygenation and ventilation as use of a bag-valve device with no difference in survival (LOE 2[146]).

There is insufficient evidence to support or refute the use of an automatic transport ventilator over manual ventilation during resuscitation of the intubated cardiac arrest victim.

Knowledge Gaps

Studies evaluating adequacy of oxygenation, difference between volume and pressure cycled ventilation, survival and complication rates when comparing manual ventilation versus automatic transport ventilator in cardiopulmonary resuscitation with an advanced airway in place are needed to advance the science in this area.

2 Supporting the circulation during cardiac arrest

Questions related to circulatory support during cardiac arrest that were discussed during the 2010 Consensus Conference are categorized as (1) timing of drug delivery, (2) vasopressors during cardiac arrest, (3) other drugs during cardiac arrest (4) intravenous fluids and (5) extracorporeal support. It is recognised that the vast majority of studies assessing the effects of drugs on survival have not been able to control for the quality of cardiopulmonary resuscitation. Furthermore, most drug evaluations to date have been conducted before recent advances in post-cardiac arrest care including therapeutic hypothermia. Since most drug trials have, at most, demonstrated only short-term outcome advantage it may be important to evaluate long-term outcome when these drugs are combined with optimized post-cardiac arrest care. One study (LOE 1[147]) compared the use of all drugs (adrenaline, amiodarone, atropine, vasopressin), without isolating the effect of each individual drug alone, with placebo in adult out-of-hospital cardiopulmonary resuscitation and demonstrated improvement in return of spontaneous circulation and survival to hospital and intensive care unit admission, but no difference in survival to discharge or neurologic outcomes at discharge and at 1-year follow-up; however, this study 17 was not powered to detect clinically meaningful differences in long-term outcome. Similarly one study (LOE 3[148]) with a before and after design, compared various outcomes after out-of-hospital cardiac arrest, and was not able to demonstrate any improvements after introduction of advanced life support (adrenaline, atropine, lidocaine). Neither of these studies was able to isolate outcomes specifically related to individual drug administration.

■1 Timing of drug delivery

There are no studies that addressed the order of drug administration. Subgroup analyses from two clinical studies reported decreased survival for every minute drug delivery was delayed, measured from call received at EMS dispatch (LOE 4[149, 150]). This finding was likely to be biased by a concomitant delay in onset of ALS. In one study the interval from the first shock to the injection of the drug was a significant predictor of survival (LOE 4[149]). One animal study reported lower coronary perfusion pressure when delivery of vasopressor was delayed (LOE 5[151]). Time to drug administration was a predictor of return of spontaneous circulation in a retrospective analysis of swine cardiac arrest (LOE 5[152]).

There is inadequate evidence to define the optimal timing or order for drug administration. An incomplete review of animal studies suggests that timing of vasopressor administration may affect circulation and further investigations are important to help guide the timing of drug administration.

Knowledge Gaps

Advancing the science in the timing of drug administration is closely related to the need to conduct

placebo-controlled trials to determine the efficacy of some drugs in cardiopulmonary resuscitation. The timing of drug administration and route of delivery are important data points to be captured in future studies. Animal models and clinical trials addressing efficacy can also be designed to provide substantial information on how timing and delivery can impact on outcome. In future, inclusion of 18 studies on pharmacokinetics combined with dose response, as well as studies addressing the impact of timing of defibrillation on circulation and drug effect might better address the question of optimal timing of drug delivery.

■2 Vasopressors

One study retrospectively compared adrenaline with no adrenaline for sustained VF and PEA/asystole and found improved ROSC with adrenaline for both rhythms but no difference in survival (LOE 2[153]). In a large retrospective registry-based study from Sweden adrenaline was an independent predictor of poor outcome (LOE 2[154])

Three studies (LOE 1[155-157]) and a meta-analysis (LOE 1[158]) demonstrated no difference in outcomes (ROSC, survival to discharge, or neurologic outcome) with vasopressin when compared with adrenaline as a first line vasopressor in cardiac arrest. Also one study (J-LOE 1[159]) that compared outcomes in out-of-hospital cardiac arrest patients treated with vasopressin or adrenaline, shows no significant difference in ROSC, 24 hour survival or survival to discharge. Two studies (LOE 2[160, 161]) demonstrated no difference in outcomes (ROSC, survival to discharge, or neurologic) comparing adrenaline in combination with vasopressin with adrenaline alone in cardiac arrest. No study demonstrated a survival benefit with high-dose versus standard-dose adrenaline in cardiac arrest.

Two studies (LOE 1[162, 163]) reported improvement in ROSC using high-dose adrenaline. One meta-analysis (LOE 1[164]) 204 of pooled data 19 from 5 studies[162, 163, 165-167] supported improvement in ROSC with high-dose adrenaline but no change in survival outcomes.

Although there is evidence that vasopressors (adrenaline or vasopressin) may improve return of spontaneous circulation and short-term survival, there is insufficient evidence to suggest that vasopressors improve survival to discharge and neurologic outcome. There is insufficient evidence to suggest the optimal dosage of any vasopressor in the treatment of adult cardiac arrest. Given the observed benefit in short-term outcomes, the use of adrenaline or vasopressin may be considered in adult cardiac arrest (Class IIb).

Knowledge Gaps

Placebo-controlled trials to evaluate the use of any vasopressor in adult and paediatric cardiac arrest are needed.

■3 Other drugs during cardiac arrest

1. Atropine

Three studies (LOE 4[168-170]) documented improvement in survival when atropine was given to patients in asystole; Two of them are in combination with adrenaline[168, 169] and the rest one was the use of atropine for asystole following induction with succinylcholine and fentanyl[170]. One study documented improvement in ROSC (14% versus 0%) when atropine was given to adults in asystolic out-of-hospital cardiac arrest in combination with adrenaline and sodium bicarbonate, but none survived to discharge (LOE 3[171]).

Three studies suggested that the use of atropine for treatment of cardiac arrest was not associated with any change in survival (LOE 2[172], LOE 5[173, 174]). Four human studies suggested that the use of atropine was associated with poor survival (LOE 4[48, 175-177]).

One study about out-of-hospital cardiac arrest in Japan reavealed that atropine increased ROSC and survival rate to hospital admission in patients with asystole, however, it decreased 30-day survival rate in patients with PEA (J-LOE 2[178]) .

Routine use of atropine for asystole and PEA is not recommended (Class III). Atropine may be considered when adrenaline is not effective in asystole (Class IIb).

Knowledge Gaps

Randomised placebo-controlled trials are required to define the role of atropine in PEA and asystolic cardiac arrest.

2. Antiarrhythmic drug

There was little evidence to suggest the advantages in outcomes (e.g., ROSC, survival-to-discharge) with any antiarrhythmic drug (lidocaine, procainamide, amiodarone, bretylium) used during resuscitation from out-of-hospital or in-hospital cardiac arrest.

1) Amiodarone

Two randomised trials for shock refractory or recurrent VT/VF had been performed. One RCT[150] compared 300mg amiodarone with placebo and the other[149] compared amiodarone (initially 5mg/kg, followed by 2.5mg/kg as the second dose) with lidocaine (initially 1.5mg/kg, followed by 1.5mg/kg as the second dose) demonstrated the benefit of amiodarone on survival to hospital admission, however, it showed no significant difference about survival to hospital discharge.

2) Nifekalant

One randomised trial (J-LOE 2[179]) for out-of-hospital cardiac arrest due to shock refractory or recurrent VT/VF was performed. The trial compared the outcome of the patients who administered 0.3mg/kg nifekalant intravenously with 1.5mg/kg lidocaine intravenously. Nifekalant demonstrated the benefit on survival to hospital admission and 24-hour survival rate, while there was no significant difference about the neurological outcome on discharge. Also in the other two studies (J-LOE 2[180],

J-LOE 3[181]), nifekalant improved ROSC and survival to admission. Combined administration of lidocaine and nifekalant revealed advantage in 24-hour survival rate compared to only lidocaine, however, threr was no significant difference about neurological outcome at 30-day of admission (J-LOE 5[182]).

3) Lidocaine

Lidocaine (50mg intravenously, up to 4 times) improved survival to admission for out-of-hospital VF in one study (LOE 4[183]).

4) Procainamide

A retrospective review found procainamide was associated with increased survival to 1-h postarrest in patients with VF in hospital (LOE 4[174]).

5) Magnesium

Four studies comparing magnesium with placebo showed no advantages in ROSC and survival rate (LOE 1[184-187]).

Amiodarone may be considered for those who have refractory VT/VF, defined as VT/VF not terminated by defibrillation, or VT/VF recurrence in out-of-hospital cardiac arrest or in-hospital cardiac arrest (Class IIb). Nifekalant may be considered for those who have electrical shock-refractory VT/VF, or VT/VF recurrence out-of-hospital cardiac arrest or in-hospital cardiac arrest (Class IIb). Lidocaine may be considered when amiodarone or nifekalant is not available, however the efficacy is inferior (Class IIb).

Knowledge Gaps

All the studies to date were done with stacked shocks; it may be helpful to re-evaluate the efficacy of amiodarone in the setting of a single-shock defibrillation strategy.

3. Calcium

Three randomised control trials (LOE 1[188-190]) and three cohort studies (LOE 2[174, 177, 191]) and 1 case series (LOE 4[192]) demonstrated no effect on survival when calcium was given to in-hospital or outof-hospital cardiac arrest patients. Two adult studies suggest that calcium administration during cardiac arrest was associated with decreased survival to hospital discharge (LOE 2[177, 193]).

In VF, calcium did not restore a spontaneous circulation (LOE 4[192]). In one study of PEA arrests, calcium demonstrated improved ROSC, without reporting long-term survival, but only in a subgroup of patients with wide QRS (LOE 1[189]). Another study showed improved ROSC and survival to hospital arrival; however, there was no significant effect on survival (LOE 4[192]). Another study showed decreased rate of ROSC in the calcium group (LOE 2[193]). In two studies of asystole calcium administration failed to show any improvement in ROSC or survival to hospital discharge (LOE 1[188,

[190]). One study showed reduced ROSC in the calcium group (LOE 2[193]).

Routine administration of calcium for treatment of in-hospital and out-of-hospital cardiac arrest is not recommended (Class III).

Knowledge Gaps

More data are needed on the administration of calcium for specific circumstances, such as hyperkalaemia, documented hypocalcaemia, hypermagnesaemia, calcium channel blocker overdose, or wide QRS complexes.

4. Steroid and hormonal therapy

There were no human or animal studies that directly addressed the use of the estrogen, progesterone, insulin, or insulin-like growth factor in cardiac arrest. Early observational studies of the use corticosteroids during cardiac arrest suggested possible benefit (LOE 4[194, 195]). One complex randomised pilot study (LOE 1[196]) and one nonrandomised human study (LOE 2[197]) suggested benefit with corticosteroids, whereas one small, older, human prehospital controlled clinical trial suggested no benefit (LOE 1[198]). One animal study of corticosteroids suggested possible benefit (LOE 5[199]).

There is insufficient evidence to support or refute the use of corticosteroids alone or in combination with other drugs during cardiac arrest.

Knowledge Gaps

High-quality clinical trials are required to determine if there is a role in cardiopulmonary resuscitation for hormonal therapy with or without vasopressor while controlling for in-hospital use of hormonal therapy postarrest.

5. Sodium bicarbonate

Two studies evaluated buffering agents during CPR (LOE 1[200, 201]). Both had limitations but showed no improvement in outcome. Two retrospective cohort studies also showed no benefit in the use of buffering agents during CPR (LOE 2[202, 203]). Two studies demonstrated increased ROSC, hospital admission, and survival at hospital discharge with bicarbonate use (LOE 2[204], LOE 3[205]). Four cohort studies reported that bicarbonate use was associated with poor short- and long-term outcome (LOE 2[177, 206-208]).

Routine administration of sodium bicarbonate for treatment of in-hospital and out-of-hospital cardiac arrest is not recommended (Class III). For patients with cardiac arrest due to poisoning tricyclic antidepressants may consider the administration of sodium bicarbonate (Class IIb).

Knowledge Gaps

There are large differences in direction and effect between results from the laboratory and those derived from clinical trials; therefore, well-designed trials, using bicarbonate or non-CO_2 generating buffers, are necessary to clarify the role of buffers in the treatment of short or prolonged cardiac arrest.

6. Fibrinolytics

Two studies failed to show any improvement in short- or long-term outcomes with the use of fibrinolytics (LOE 1[209, 210]). One study showed an increased risk of intracranial bleeding associated with the routine use of fibrinolytics during cardiac arrest (LOE 1[210]). Seven studies showed benefit from fibrinolytic therapy in the treatment of victims of cardiopulmonary arrest unresponsive to standard therapy; however, those studies had significant limitations (LOE 1[211], LOE 2[212-215], LOE 3[216, 217]).

Routine administration of fibrinolytics for the treatment of in-hospital and out-of-hospital cardiac arrest is not recommended (Class III) . Administration of fibrinolytics may be considered for cardiac arrest caused by pulmonary embolus (Class IIb). (Pulmonary embolus is described in the section of Chapter 2 [7] Cardiac arrest in special situations.)

Knowledge Gaps

The potential role of adjuvant antithrombotic and antiplatelet drugs needs exploration.

■4 Intravenous fluids during cardiac arrest

Two animal studies reported that normothermic fluid infusion during CPR causes a decrease in coronary perfusion pressure (LOE 5[218, 219]), and another animal study showed that the coronary perfusion pressure rise with adrenaline during CPR is not improved with the addition of a fluid infusion (LOE 5[220]). Most animal studies of fluid infusion during CPR lack a control group that receives no fluids; without a control group, it is difficult to assess of benefit or harm from fluid therapy (LOE 5[221-232]).

1. Hypertonic Fluid

One small randomized clinical trial (RCT) in adults found no significant ROSC or survival benefit with hypertonic intravenous fluid infusion when compared to isotonic intravenous fluid infusion during CPR (LOE 5[221]). One animal study showed that hypertonic saline improves cerebral blood flow during CPR (LOE 5[227]). Two animal studies found neither benefit nor harm with infusion of hypertonic saline (LOE 5[225, 232]).

2. Chilled fluid vs room-temperature fluid

Two adult studies (LOE 5[223, 226]) and 2 animal studies (LOE 5[230, 231]) showed no improvement in ROSC when cold intravenous fluids (compared with room temperature intravenous fluids) were infused during CPR. One of the reported animal studies showed that the infusion of cold fluids during CPR caused a decrease in coronary perfusion pressure when compared to no fluids (LOE 5[233]).

There is insufficient evidence to recommend for or against the routine infusion of intravenous fluids during cardiac arrest resuscitation.

■5 Extracorporeal circulatory support during cardiac arrest

All the studies on this topic were small and there was a lack of consistency in the management before and after extracorporeal-CPR (ECPR). Three studies documented improvement in outcome in patients 70 years old, without significant comorbid conditions and with potential reversible/correctable conditions, when using ECMO（Extracorporeal Membrane Oxigenation）/PCPS（Percutaneous Cardiopulmonary Support） compared with traditional CPR (LOE 2[234, 235], LOE 3[236]). Two prospective studies demonstrated that 12-52% of out-of-hospital cardiac arrest patients showed improvements in neurological outcomes. These patients had been unresponsive with ordinary CPR and treated with a combination of circulatory support using PCPS and therapeutic hypothermia at 34°CC (J-LOE 4[237, 238]). One study demonstrated a 3-month survival of 22.7% for ECPR during out-of-hospital cardiac arrest unresponsive to advance life support after 20 minutes, with 10.6% having a Cerebral Performance Category (CPC) of 1 (LOE 2[235]). However, the ECPR group was more likely to have had a witnessed arrest, received bystander CPR, and be younger (with a mean age of 52 years, compared with 70 years in the standard treatment group).

ECPR (mainly PCPS) may be considered if the duration of circulatory arrest is relatively short and the cause of cardiac arrest (accidental hypothermia, drug intoxication or STEMI) is expected to treat (Class IIb).

Knowledge Gaps

Future research should define the criteria for ECPR after out-of-hospital cardiac arrest and the criteria for ECPR as a bridge to left ventricular assist device (LVAD) or transplant. In addition, the role of IABP during CPR needs to be studied.

4 CPR Techniques and Devices

■1 Introduction

The success of any technique or device depends on the education and training of the rescuers and as well as on resources (including personnel). In the hands of some groups, novel techniques and adjuncts may produce better short- or long-term outcome than standard CPR. However, a device or technique that provides good quality CPR when used by a highly trained team or in a test setting may show poor quality and create frequent interruptions in CPR when used in an uncontrolled clinical setting[239].

While no circulatory adjunct is currently recommended instead of manual CPR for routine use, some circulatory adjuncts are being routinely used in both out-of-hospital and in-hospital resuscitation. If a circulatory adjunct is used, rescuers should be well-trained and a program of continuous surveillance should be in place to ensure that use of the adjunct does not adversely affect survival.

The following CPR techniques and devices were reviewed during C2010. It should be noted that interposed abdominal compression has not been studied on humans since 1994 and active compression-decompression has not been studied in humans since 2003. Therefore, these techniques have not been evaluated against the international resuscitation guideline changes of 2000 and 2005 (for interposed abdominal compression) and 2005 (for active compression- decompression).

■2 Interposed Abdominal Compression CPR (IAC-CPR)

Two randomized controlled trials in in-hospital cardiac arrests, showed improved ROSC and survival to hospital discharge when interposed abdominal compressions (IAC)-CPR was compared with standard CPR (LOE 1[240], LOE 2[241]). However, there were no differences in neurologically intact survival.

One randomized controlled trial in out-of-hospital cardiac arrest was unable to show any consistent benefits when IAC-CPR was compared with standard CPR (LOE 2[242]).

Evidence from LOE 3[243, 244] and LOE 5[245] in-hospital studies suggests better or neutral[246, 247] hemodynamics with IAC-CPR compared with standard CPR.

There is insufficient evidence to support or refute the use of IAC-CPR.

■3 Active Compression-Decompression CPR (ACD-CPR)

Five randomized controlled trials (LOE 1[248-252]) and three controlled trials (LOE 2[253-255]) failed to show a difference in ROSC or survival with use of ACD-CPR compared with standard CPR. Six studies (LOE 2[256-261]) demonstrated improved ROSC or survival to hospital discharge although there were no statistically significant differences in neurologically intact survival. A meta-analysis[252] of two trials (826 patients) comparing ACD-CPR with standard CPR after in- hospital cardiac arrest did not

detect a significant increase in rates of immediate survival or hospital discharge.

There is insufficient evidence to support or refute the use of ACD-CPR.

■4 Open-Chest CPR

There are no published randomized controlled trials and very limited data in humans comparing open chest CPR to standard CPR in cardiac arrest. One retrospective clinical trial (LOE 3[262]) demonstrated ROSC was improved by open chest CPR in OHCA. One case series in victims of OHCA who had failed standard CPR (LOE 4[263]) reported ROSC in 13 of 33 highly selected patients of whom two survived to hospital discharge.

Multiple animals studies (LOE 5[264-282]) utilizing a variety of endpoints demonstrated benefit with open chest CPR.

There is insufficient evidence to support or refute the routine use of open-chest CPR in cardiac arrest.

■5 Load Distributing Band CPR (LDB-CPR)

One multicenter randomized control trial in over 1000 adults documented no improvement in 4-hour survival and significantly worse neurological outcome when LDB-CPR administered by EMS providers was compared with traditional CPR for primary out-of-hospital cardiac arrest (LOE 1[283]). However, a post-hoc analysis of this study revealed significant heterogeneity between study sites (LOE 1[284]).

In one LOE 3 study[285] the use of LDB-CPR was associated with lower odds of 30-day survival (OR 0.4). However, when a smaller (77 patient) subgroup of LDB-CPR treated patients was analyzed against concurrent controls, increased rate of ROSC was noted.[47]

Other non-randomized human series (LOE 3[286, 287]) have reported increased rates of sustained ROSCand increased survival to discharge[49] following out-of-hospital cardiac arrest (OHCA) and improved hemodynamics following failed resuscitation from in-hospital cardiac arrest (LOE 4[288]). In a prospective before-after study (LOE 3[289]) the mean no-flow ratio with manual CPR was 0.28 in the first 5 minutes of CPR compared to 0.40 with LDB-CPR. However between 5 and 10 minutes, no-flow time with manual CPR was 0.34 and 0.21 with LDB-CPR.

Evidence from both clinical (LOE 1[283, 284]) and simulation (LOE 5[290]) studies suggest that site-specific factors may influence resuscitation quality and device efficacy.

A case report documented successful performance of a CT scan while the LDB CPR was used (LOE 4[291]).

There are insufficient data to support or refute the routine use of the load-distributing band (LDB) instead of manual CPR. It may be reasonable to consider LDB to maintain continuous chest compression while undergoing CT scan or similar diagnostic studies, when provision of manual CPR would be difficult (Class IIb) .

■6 Mechanical (Piston) CPR

When a piston CPR device was compared with manual CPR, one randomized controlled trial documented no improvement in ROSC or survival among adults in cardiac arrest (LOE 1[292]).

Supportive data from one prospective, randomized crossover designed study (LOE 1[293]), and one paired cohort study (LOE 2[294]) documented that the use of a piston CPR device improved hemodynamics during CPR in adult cardiac arrest victims.

One prospective pseudorandomized trial documented improvement in hemodynamic variables during CPR in adult cardiac arrest victims but no improvement in ROSC or survival (LOE 2[295]).

Data from one, prospective cohort study comparing the use of a piston CPR device with manual CPR documented that the use of a piston CPR device increased interruption in CPR because time was required to set up and remove the device from patients during transportation in out-of-hospital adult cardiac arrest (LOE 2[296]).

There is insufficient evidence to support or refute the use of a piston CPR instead of manual CPR for adult victims of cardiac arrest.

■7 Lund University Cardiac Arrest System CPR (LUCAS-CPR)

There are no RCTs evaluating the LUCAS device in human cardiac arrests.

One study using concurrent controls in witnessed OHCA was unable to show any benefit (ROSC, survival to hospital or survival to hospital discharge) with the use of the LUCAS device over standard CPR (LOE 2[297]).

One postmortem study showed similar injuries with LUCAS and standard CPR (LOE 2[298]).

Six case series involving approximately 200 patients have reported variable success in use of the LUCAS device, when implemented after an unsuccessful period of manual CPR (LOE 4[299-304]).

Six adult human studies (LOE 4[300, 301, 304-307]) and one animal study (LOE 5[306]) reported that the use of a mechanical chest compression device in cardiac arrest during percutaneous coronary intervention maintained circulation and enabled the procedure to be completed. A small number of patients in the case series survived.

Two case reports demonstrated that a CT scan could be performed during CPR with the LUCAS device (LOE 4[291]).

There are insufficient data to support or refute the use of LUCAS-CPR instead of manual CPR. It may be reasonable to consider LUCAS-CPR to maintain continuous chest compression while undergoing CT scan or similar diagnostic studies, when provision of manual CPR would be difficult (Class IIb) .

■8 Impedance Threshold Device (ITD)

One meta-analysis that pooled the data from both conventional CPR and ACD-CPR randomized

controlled trials (RCTs) demonstrated improved ROSC and short-term survival but no significant improvement in either survival to discharge or neurologically intact survival to discharge associated with the use of an ITD in the management of adult OHCA patients (LOE 1[308]).

One randomized controlled trial suggested that the use of an ITD in combination with ACD-CPR improved 24 hour survival and survival to ICU admission in adult OHCA patients, compared with ACD-CPR and a sham ITD (LOE 1[309]). This contrasts with another randomized controlled trial which compared ITD plus ACD-CPR with ACD-CPR plus a sham ITD that did not show significant improvement in ROSC or 24hour survival with use of the ITD (LOE 1[310]).

One randomized controlled trial reported that the use of an ITD in combination with standard CPR (CPR) did not significantly improve ROSC, 24 hour survival or survival to ICU admission in adult OHCA patients, compared with CPR and a sham ITD (LOE 1[311]).

One randomized controlled trial comparing ACD-CPR plus ITD with CPR in adult OHCA patients showed improved ROSC and 24hour survival rates associated with ACD-CPR plus ITD, but no significant improvement in hospital discharge or intact neurologic survival to hospital discharge rates (LOE 1[312]).

One prospective cohort study (with historical control) of CPR plus ITD vs. CPR (without ITD) in OHCA reported improved survival to ED admission for OHCA patients presenting in any rhythm (LOE 3[313]).

Three cohort studies comparing CPR using 2005 Guidelines plus ITD, with historic controls of CPR using 2000 Guidelines, demonstrated improved survival to hospital discharge in out of hospital cardiac arrest (LOE 3[314-316]). It was not possible to determine the relative contribution of the ITD to the improved outcome.

In a porcine model of cardiac arrest, 8 studies demonstrated improved hemodynamic variables during CPR with use of the ITD (LOE 5[128, 317-323]). A further three animal studies (LOE 5[324-326]) showed no difference in survival or in any hemodynamic variable and two animal studies (LOE 5[325, 327]) reported evidence of a decrease in ROSC, 20minute survival and arterial oxygen saturation associated with the use of an ITD.

There is insufficient data to support or refute the use of the ITD. (ITD is unapproved per the Pharmaceutical Affairs Law in Japan.)

5 Defibrillation

■1 lntroduction

The 2010 Defibrillation Task Force considered many questions related to defibrillation. In general, the 2010 Intemational Consensus on Science with Treatment Recommendations statement contains no major differences or dramatic changes from the 2005 Intemational Consensus statement. The questions have been grouped into the following categories: (1)CPR Before Defibrillation, (2)Electrode-Patient Interface, (3)Defibrillation strategy, (4)Special Circumstances and (5)Related defibrillation topics.

Science and treatment recommendations dealing with the infant or child requiring defibrillation can be found in the "Pediatric Basic and Advanced Life Support" chapter. The only two treatment recommendations that differ for adult and pediatric patients are defibrillation dose and AED use.

There are several Knowledge Gaps created by the lack of high-quality, large clinical studies. These include: the minimal acceptable first shock success rate; the characteristics of the optimal biphasic waveform; the optimal energy levels for specific waveforms; and the best shock strategy (fixed versus escalating).

■2 Integration of CPR and defibrillation

Whether a period of CPR should be performed before defibrillation in ventricular fibrillation (VF), especilly after long response times, has recently been the subject of intense debate. The theoretical rationale for CPR before shock delivery is to improve coronary perfusion and thereby the chances of achieving sustained retum of spontaneous circulation (ROSC).

1. CPR before defibrillation

ln two randomized controlled trials (LOE 1[328, 329]), a period of l.5 to 3 minutes of CPR by EMS personnel before defibrillation did not improve retum of spontaneous circulation (ROSC) or survival to hospital discharge in patients with out-of-hospital VF or pulseless ventricular tachycardia (VT), regardless of EMS response interval. 0ne before and after study (LOE 3[330]) and another study (LOE 4[331]) failed to demonstrate significant improvements in ROSC or survival to hospital discharge when a strategy of CPR before defibrillation (CPR first) was compared to a shock first strategy. In the Hayakawa study, the CPR first group showed a higher rate of favorable neurologic outcome 30 days and one year after cardiac arrest.

One randomized controlled trial (LOE 1[332]) and one clinical trial with historic controls (LOE 3[333]) comparing CPR first versus shock first also found no overall difference in outcomes. However, in both studies, improvements in ROSC, survival to hospital discharge, neurologic outcome and one-year survival were observed in a subgroup of patients who received CPR first where the EMS response interval was greater than 4 to 5 minutes.

There is inconsistent evidence to support or refute delay in defibrillation to provide a period of CPR (90 seconds to 3 minutes) for patients in ventricular fibrillation/pulseless VT cardiac arrest.

2. Use of filtering devices for rhythm analysis during CPR

As chest compressions produce artifacts, it is difficult to analyze the ECG during CPR. Therefore once AED starts ECG analysis, chest compressions are forced to be interrupted. However, interruptions of chest compressions decrease the rate of ROSC, survival, and myocardial function after ROSC. Especially the time for ECG analysis by AED is one of the main cause of the interruption. On the other hand, there is a possibility to shorten the interruption of compression by using a filtering devices for rhythm analysis.

In six studies (LOE 5[334-339]) using human-derived ECG recordings with actual or simulated CPR artifacts and one study in a swine model of VF (LOE 5[340]) ,the use of computerized algorithms that removed compression artifacts from the ECG during CPR reduced the accuracy of rhythm analysis relative to rhythm analysis during pauses. Sensitivity was between 90% and 98%, which would cause inappropriate prolongations in chest compression for shockable rhythms in up to 1 out of 10 patients. Specificity was between 80% and 89%, which could result in inappropriate interruptions in chest compression for shock delivery in victims who actually had nonshockable rhythms.

There is insufficient evidence to support or refute the use of artifact-filtering algorithms for analysis of ECG rhythm during CPR.

■3 Electrode–patient interface

Studies on defibrillation for cardiac arrest and on cardioversion for atrial fibrillation (AF) are both included here. While few studies compared differences in outcome, many studies compared secondary end points such as effect on transthoracic impedance (TTI). In ventricular arrhythmias, however, there is no direct evidence that TTI affects shock success.

1. Self-adhesive defibrillation pads compared with paddles

Since 2005 there have been no new studies comparing selfadhesive defibrillation pads with paddles in cardiac arrest. Evidence from one small, good-quality controlled study (LOE 3[341]) in 1987 showed that self-adhesive pads were associated with a significantly improved rate of ROSC and hospital admission compared with hand-held paddles. Several studies have shown the practical benefits of pads over paddles for routine monitoring and defibrillation[342-346].

One prospective study (LOE 3[347]) found lower TTI when paddles applied at an optimal force of 8 kg were compared with pads. In a cohort study in patients with atrial fibrillation (LOE 2[348]) the use of hand-held paddles placed in the anterior–posterior position increased the success rate of monophasic cardioversion compared with similarly placed self-adhesive electrodes for monophasic defibrillation. The overall cardioversion success rate for biphasic defibrillators was high (>95%) in all groups. In the majority of other studies, self-adhesive electrodes were associated with similarly high cardioversion success rates.

For both defibrillation and AF cardioversion, when using biphasic defibrillators, self-adhesive defibrillation pads are safe and effective and are an acceptable alternative to standard defibrillation paddles (Class IIb). In AF cardioversion using monophasic defibrillators, hand-held paddles are preferable (Class IIa).

2. Placement of paddles/pads

There are no studies in patients with VF/pulseless VT directly comparing the effects of various positions of paddle/pad placement on defibrillation success and ROSC. Most studies evaluate cardioversion (e.g., AF) or secondary end points (e.g., TTI). Eleven studies (LOE 5[349-359]) found all four positions (anterior–apex, anterior–posterior, anterior–left infrascapular, anterior–right infrascapular) to be equally effective in defibrillation (for VF/pulseless VT) or elective AF cardioversion success. Four studies support the anterior–posterior position (LOE 5[360-364]), one study supports the anterior–lateral position (LOE 5[365]), and one study supports the anterior–apex position (LOE 5[366]).

Five studies (LOE 5[350, 355-358]) found no effect of electrode position on TTI. One study showed that paddles/pads should be placed under the breast tissue (LOE 5[367]) and two studies showed that hirsute males should be shaved before the application of pads (LOE 5[368, 369]). Of the 36 studies reviewed, only four examined biphasic waveforms (LOE 5[352, 359, 363, 370]) that have gained widespread use.

It is reasonable to place paddles/pads on the exposed chest in an anterior–lateral position (Class IIa). Acceptable alternative positions are anterior–posterior (for paddles/pads) and apex–posterior (for pads). In large-breasted individuals it is reasonable to place the left electrode paddle/pad lateral to or underneath the left breast, avoiding breast tissue (Class IIa). Consideration should be given to the rapid removal of excessive chest hair before the application of paddles/pads but emphasis must be on minimizing delay in shock delivery.

3. Size of paddles/pads

No new clinical study on this topic has been published since 2005. One study demonstrated that TTI decreased and shock success increased with increasing pad size (from 8 to 12 cm) (LOE 3[371]). Ten other studies showed that larger paddle/pad sizes (8- to 12-cm diameter) lowered TTI and that maximum paddle/pad size was limited by the chest wall size and anatomy (LOE 3[372], LOE 5[357, 370, 373-379]). No data related to survival outcome was included in these studies.

There is insufficient evidence to recommend a specific electrode size for optimal external defibrillation in adults. However, it is reasonable to use a paddle/pad size >8 cm (Class IIa).

4. Composition of conductive material

Fourteen studies showed that the composition of the conductive material (e.g., saline, hypertonic sodium chloride [NaCl] solution, or silver-silver chloride) may alter TTI by more than 20% (LOE 2[373,

[380, 381], LOE 3[371], LOE 4[382], LOE 5[368, 383-390]). Five studies (LOE 3[391, 392], LOE 5[393-395]) showed that TTI was not affected by electrode composition. The end point for all of these studies was TTI, and no studies involved outcomes following cardiac arrest.

The composition of the conductive material of defibrillation electrodes influences TTI. In terms of cardiac arrest outcomes, there is insufficient evidence to recommend a specific composition of the defibrillation electrode conductive material.

■4 Waveforms, energy levels, and strategies

All new defibrillators currently deliver shocks using biphasic waveforms. Although it has not been demonstrated conclusively in randomised clinical studies that biphasic defibrillators save more lives than monophasic defibrillators, biphasic defibrillators achieve higher first-shock success rates. Shock success is usually defined as termination of VF 5 seconds after the shock.

1. Biphasic compared with monophasic defibrillation waveform

In three randomised trials (LOE 1[396-398]) and four other human studies (LOE 3[399-401]) biphasic waveforms had higher shock-success rates compared with monophasic defibrillation. One randomised study comparing transthoracic incremental monophasic with biphasic defibrillation for out-of-hospital pulseless VT/VF cardiac arrest failed to demonstrate any significant differences in any outcome (LOE 1[402]). A single-cohort study (LOE 3[403]) using the 2000 International Guidelines[404] demonstrated better hospital discharge and neurological survival with biphasic than with monophasic waveforms. However, there were confounding factors in that the intervals between the first and second shocks (of three-stacked shocks) were shorter with the biphasic defibrillators.

There is no clinical evidence for superiority of any specific biphasic waveform over another.

Biphasic waveforms are more effective in terminating VF when compared with monophasic waveforms (Class IIb). There is insufficient evidence to recommend any specific biphasic waveform. In the absence of biphasic defibrillators, monophasic defibrillators are acceptable.

2. Multiphasic compared with biphasic defibrillation waveform

There are no human studies to support the use of multiphasic waveforms over biphasic waveforms for defibrillation. Animal data suggests that multiphasic waveformsmay defibrillate at lower energies and induce less postshock myocardial dysfunction[405, 406].These results are limited because in all studies duration of VF was very short (approximately 30 s) and results have not been validated in human studies.

Currently, multiphasic defibrillators are not commercially available.

3. Waveforms, energy levels, and myocardial damage

Several different biphasic waveforms are used in commercially available defibrillators, but no

human studies have directly compared these waveforms or compared them at different energy levels related to defibrillation success or survival.

1) Biphasic truncated exponential (BTE) waveform

Evidence from one well-conducted randomised trial (LOE 1[407]) and one other human study (LOE 2[408]) employing BTE waveforms suggested that higher energy levels are associated with higher shock-success rates. In the randomised trial, the first-shock success ratewassimilar with 150 J and 200 J[407].

2) Pulsed biphasic waveform

In one study using pulsed biphasic waveforms at 130 J the first-shock success rate was 90% (LOE 4[409]).

3) Rectilinear biphasic waveform

When defibrillation success was defined as ROSC (this differs from the definition in other studies), one study using a rectilinear biphasic waveform showed that an organised rhythm was restored by the first shock (120 J) in 23% of cases (LOE 1[396]). Success rate for the termination of VF at 5 s was not published for this waveform.

For the different biphasic waveforms, studies of different size and quality have been performed and are presented separately. For all waveforms, insufficient evidence exists to make clear recommendations.

4) Monophasic waveform (damped sinusoid or truncated exponential)

Evidence from three studies of monophasic defibrillation suggested equivalent outcomes with lower and higher starting energies (LOE 1[410], LOE 2[411, 412]).

5) Myocardial damage associated with higher energy level shocks

Several animal studies have suggested the potential for myocardial damage with higher energy shocks using BTE or monophasic waveforms (LOE 5[370, 413-415]). Human studies involving BTE waveforms[407, 416] with energy levels up to 360 J have not shown harm as indicated by biomarker levels, ECG findings, and ejection fractions.

It is reasonable to start at a selected energy level of 150–200 J for a BTE waveform for defibrillation of pulseless VT/VF cardiac arrest (Class I). There is insufficient evidence to determine the initial energy levels for any other biphasic waveform. Although evidence is limited, because of the lower total shock success for monophasic defibrillation, initial and subsequent shocks using this waveform should be at 360 J.

6) One-shock compared with three-stacked shock protocols

One study showed no survival benefit from a protocol that included a single-shock protocol compared to a three-shock protocol (LOE 1[417]). Evidence from three pre–post design studies suggested significant survival benefit with a single-shock defibrillation protocol compared with three-stacked shock protocols (LOE 3[285, 418, 419]). However, these studies included confounders related to pre–post design and the multiple interventions that were included as part of the defibrillation protocol. Another pre–post study, with fewer confounding factors, showed a significantly lower hands-off ratio (i.e., percentage of total CPR timewhen no compressions were provided) with the one-shock protocol but no statistical difference in survival (LOE 3[420]).

One observational study of fixed-dose biphasic defibrillation suggested higher defibrillation success with three shocks (LOE 4[421]). The same study also suggested that chest compressions immediately following a shock did not result in recurrence of VF. In contrast another study showed earlier recurrence of VF when chest compressions were resumed immediately after the shock compared with delayed resumption of compressions (LOE 1[422]). There was no significant difference in total incidence of recurrent VF or outcome. A single study demonstrated that early termination of recurrent VF was associated with increased ROSC, but quality of CPR was poor and few patients achieved ROSC (LOE 4[423]). Another study showed decreased survival when defibrillation for recurrent VF was, for a variety of reasons, delayed (LOE 4[424]).

When defibrillation is required, a single shock should be provided with immediate resumption of chest compressions after the shock (Class I). Chest compressions should not be delayed for rhythm reanalysis or pulse check immediately after a shock. CPR should not be interrupted until rhythm reanalysis is undertaken.

7) Fixed versus escalating defibrillation energy protocol

One randomised trial (LOE 1[407]) of 150-J fixed versus 200-J to 300-J to 360-J shocks and one LOE 2 study[408] of 150-J fixed versus 100-J to 150-J to 200-J shocks supported the use of an escalatingenergy biphasic defibrillation protocol compared with a fixed-dose defibrillation protocol. In one study (escalating 200-J to 200-J to 360-J shocks), the success rate of defibrillation for recurrent VF declined with the number of recurrences (LOE 4[425]). However, these studies were not designed to demonstrate an improvement in the rate of ROSC or survival to hospital discharge. One study of fixeddose biphasic defibrillation suggested that defibrillation success improved with three shocks (LOE 4[421]). All of these studies were done with the three-shock protocol (before the change in Guidelines 2005).

For second and subsequent biphasic shocks the same initial energy level is acceptable (Class IIb). It is reasonable to increase the energy level when possible (Class IIa).

8) Shock using manual versus semiautomatic mode

Modern defibrillators can be operated in both manual and semiautomatic (AED-similar) modes.

However, few studies compare these two options. One randomised controlled study showed no significant difference in survival-to-hospital-discharge rate but significant reduction in time to first shock in the AED group versus the manual group (1.1 min versus 2.0 min) (LOE 1[426]). One good concurrent controlled OHCA study in 36 rural communities showed no improvements in ROSC, survival, or neurological outcome but significantly shorter times to first shock and higher VF conversion rates when paramedics used AEDs in semiautomatic mode compared with manual mode (LOE 2[427]). One retrospective study demonstrated no improvement in survival to hospital discharge for adult IHCA when comparing AED with manual defibrillators (LOE 4[428]). In patients with initial asystole or pulseless electric activity (PEA), AEDs were associated with a significantly lower survival (15%) compared with manual defibrillators (23%, P = 0.04) [428].

In a study of three different EMS systems and one in-hospital centre, manual mode of defibrillation was associated with a lower total hands-off ratio (i.e., percentage of total CPR time when no compressions were provided) than AED mode (LOE 3[429]). However, more shocks were delivered inappropriately by rescuers using manual defibrillators (26% manual versus 6% AEDs). A randomised manikin study simulating cardiac arrest showed a lower handsoff ratio, mainly due to a shorter preshock pause, when trained paramedics used the defibrillator in manual mode compared with semiautomatic mode (LOE 5[430]). More inappropriate shocks (12% versus 0) were delivered in manual mode. All episodes of VF were detected and shocked appropriately. A shorter preshock pause and lower total hands-off ratio increased vital organ perfusion and the probability of ROSC (LOE 5[431-433]).

No significant survival differences have been demonstrated between defibrillation in semiautomatic and manual modes during out-of-hospital or in-hospital resuscitation; however, the semiautomatic mode is preferred because it is easier to use andmaydeliver fewer inappropriate shocks.

Trained personnel may deliver defibrillation in manual mode (Class IIb). Use of the manual mode enables chest compressions to be continued during charging, thereby minimizing the preshock pause. When using the defibrillator in manual mode, frequent team training and ECG recognition skills are essential.

The defibrillation mode that results in the best outcome will be influenced by the system of care and by provider skills, training, and ECG recognition.

9) Cardioversion strategy in atrial fibrillation

Twenty-two studies have compared specific cardioversion strategies (monophasic vs biphasic defibrillators, different energy levels) administered by cardiologists in the hospital setting to patients with atrial fibrillation (both acute/chronic) (LOE 1[348, 351, 360, 361, 365, 434-447], LOE 2[448, 449]). Most of these studies document that biphasic shocks were more effective than monophasic shocks for cardioversion.

Studies with varying strategies (fixed and escalating) and energy levels all resulted in high cardioversion rates for a variety of biphasic waveforms, with no clear evidence of superiority. For monophasic defibrillation, higher initial energy levels (360J) were associated with higher cardioversion rates and less total energy used than escalating from lower to higher energy levels. Body weight may affect cardioversion success, and one study suggested that initial shock should be 200J for patients < 90 kg and 360 J if > 90 kg (LOE 1[450]). In general, increased total energy use was associated

with more dermal injury and post-procedural pain (LOE 1[435, 444, 451]).

Biphasic defibrillators are preferred for cardioversion of atrial fibrillation (Class IIa). There is no evidence to recommend a specific waveform, energy level or strategy (fixed vs escalating) when using biphasic defibrillators. For monophasic defibrillators, a high initial energy (360 J) seems preferable (Class IIb).

■5 Special circumstances

Some special circumstances, such as if pacing is ever indicated during cardiac arrest, or how to respond in cardiac arrest if the patient has a pacemaker or an internal defibrillator are presented and discussed is this section.

1. Precordial thump

In five prospective case series of out-of-hospital (LOE 4[452-456]) and two series (LOE 4[453, 454]) of in-hospital VF cardiac arrest, healthcare provider administration of the precordial thump did not result in ROSC. In three prospective case series of VT in the electrophysiology laboratory (LOE 4[453, 457, 458]), administration of the precordial thump by experienced cardiologists was of limited use (1.3% ROSC). When events occurred outside of the electrophysiology laboratory, in six case series of in- and out-of-hospital VT (LOE 4[454-456, 459-461]), the precordial thump was followed by ROSC in 19% of patients. Rhythm deterioration following precordial thump occurred in 3% of patients and was observed predominantly in patients with prolonged ischaemia or digitalis-induced toxicity.

Two case series (LOE 4[456, 462]) and a case report (LOE 5[463]) documented the potential for complications from use of the precordial thump, including sternal fracture, osteomyelitis, stroke, and rhythm deterioration in adults and children.

The precordial thump is relatively ineffective for VF, and it should not be used for unwitnessed OHCA (Class III). The precordial thump may be considered for patients with monitored, unstable VT if a defibrillator is not immediately available (Class IIb). There is insufficient evidence to recommend for or against the use of the precordial thump for witnessed onset of asystole caused by atrioventricular conduction disturbance.

2. Pacing (e.g., transcutaneous [TC], transvenous [TV], needle, and fist)

Four studies addressed the efficacy of pacing in cardiac arrest (LOE 2[464-466], LOE 3[467]). These studies found no benefit from routine pacing in cardiac arrest patients. Use of pacing (transcutaneous, transvenous, needle) in cardiac arrest (in-hospital or out-of-hospital) did not improve ROSC or survival. There was no apparent benefit related to the time at which pacing was initiated (early or delayed in established asystole), location of arrest (in-hospital or out-of-hospital),or primary cardiac rhythm (asystole, PEA). Five case series (LOE 4[468-472]), a review with two additional case reports[473], and a moderate sized case series (LOE 4[474]), support percussion pacing in p-wave asystolic cardiac arrest/complete heart block or hemodynamically unstable patients with bradycardia. In these reports,

sinus rhythm with a pulse was restored using different pacing techniques.

Electrical pacing is not effective as routine treatment in patients with asystolic cardiac arrest (Class III). Percussion pacing is not recommended in cardiac arrest in general (Class III). However, fist pacing may be considered in hemodynamically unstable bradyarrhythmias until an electrical pacemaker (transcutaneous or transvenous) is available (Class IIb). The use of epicardial wires to pace the myocardium following cardiac surgery is effective and discussed elsewhere (Class I).

3. Implantable cardioverter defibrillator or pacemaker

Two case series reported pacemaker or implantable cardioverter defibrillator (ICD) malfunction after external defibrillation when the pads were placed in close proximity to the device generator (LOE 4[475, 476]). One small study on atrial cardioversion demonstrated that positioning the pads on the chest at least 8 cm from the device generator did not produce significant damage to pacing sensing and capturing (LOE 4[475]).

One case report suggested that pacemaker spikes generated by devices programmed to unipolar pacing may confuse AED software and emergency personnel andmayprevent the detection of VF (LOE 4[477]).

In patients with an ICD or a permanent pacemaker, the placement of pads/paddles should not delay defibrillation (Class I). In this case, it is reasonable to avoid placing the pads/paddles directly over the implanted device (Class IIa). Although some reports suggest that the pads/paddles should be placed on the chest wall ideally at least 8 cm from the generator position, shock delivery should not be delayed for ideal pads/paddles placement.

■6 Defibrillation-related topics

1. Predicting success of defibrillation and outcome (VF waveform analysis)

VF waveform analysis has been shown to correlate with myocardial perfusion/coronary perfusion pressure. In theory waveform analysis could be a tool for predicting outcome of defibrillation and therefore indicate the optimal time for shock delivery.

Retrospective analysis of the VF waveform in multiple clinical (LOE 1[478, 479], LOE 4[480, 481] , LOE 5[482, 483]) and animal studies (LOE 5[484-486]) and theoretical models suggested that it is possible to predict the success of defibrillation from the fibrillation waveform with varying reliability. One animal study was neutral (LOE 5[487]). No human studies have specifically evaluated whether treatment altered by predicting success of defibrillation can improve successful defibrillation, ROSC, or survival from cardiac arrest. Multiple waveform parameters have been examined without consensus on the most important parameters to predict outcome.

There is insufficient evidence to support routine use of VF waveform analysis to guide defibrillation

management in adult cardiac arrest in- or out-of-hospital.

2. Defibrillation in the immediate vicinity of supplementary oxygen

Four case reports involving adults (LOE 4[488-491]) and one case report involving a neonate (LOE 4[492]) described fires caused by sparks generated during defibrillation attempts when paddles were used in the vicinity of high-flow (>10 L/min) oxygen. There are no case reports of fires caused by sparking when shocks were delivered using adhesive pads. In two manikin studies the oxygen concentration in the zone of defibrillation was not increased when ventilation devices (self-inflating bag, and more) were left attached to a tracheal tube or when the oxygen source was vented at least one metre behind the patient's mouth (LOE 5[493, 494]). One study described higher oxygen concentrations and longer washout periods when oxygen was administered in confined spaces without adequate ventilation (LOE 5[495]).

Rescuers should take precautions to minimise sparking (by paying attention to pad/paddle placement, contact, etc.) during attempted defibrillation (Class I). Rescuers should try to ensure that defibrillation is not attempted in an oxygen-enriched atmosphere (e.g., when high-flow oxygen is directed across the chest) (Class I).

6 Antiarrhythmic therapies during periarrest

■1 Overview

When you recognize arrhythmias of the patients as healthcare providers, you should check airway, breathing and pulse immediately. CPR should be started promptly in cardiac arrest. You should attach the ECG monitor and pulse oxymeter in non-cardiac arrest case. Oxygen may be given if needed. Then you have to evaluate the patient's symptoms and clinical sings whether the patient's condition is stable or unstable. When an arrhythmia causes a patient unstable, you should establish any venous access for possible emergent medicines. Then you have to assess whether or not decreasing cardiac output by the arrhythmia is a direct cause for the signs and symptoms of the patients. Treat the arrhythmias first in the former cases but the treatment is not necessary in the latter.

For references; Signs and symptoms suggesting the unstable status are as follows:

- symptoms: altered mental status, syncope, ongoing chest pain, dyspnea, etc.
- signs:hypotention, other signs of shock (perspiration, cold clammy skin, oliguria, disturbance of consciousness), etc.

■2 Bradycardia

1. Algorithm for the management of bradyarrhythmias

Bradycardia is defined as a heart rate of below 60 beats per minute.

1) The key principles of bradyarrhythmias management in adult (Fig.3)

A provider should start the treatment of bradycardia emergently when a patient's condition is unstable and bradycardia is the cause of the signs and symptoms [comment 1)]. As is described later, third-degree (complete) atrioventricular block (AVB) and high-degree AVB [comment 2)] are the exceptions and these heart blocks should always be treated as emergency regardless of the signs and symptoms. The provider will contact the specialist of the cardiovascular diseases and begin treatment immediately according to the algorithm. Well-trained athletes often show their heart rate around 40/min. The heart rates of healthy normal persons are often below 50/min during the sleep. But it is obvious the treatment is not necessary for them. On the other hand, when the patient with AMI becomes hypotensive due to the bradycardia, the patient should be received immediate treatment of the bradycardia because it may trigger the next myocardial ischemic attack. The emergent treatment for the symptomatic bradycardia is indicated when the condition of the patient is unstable. The bradycardia algorithm shows that both the third-degree (complete) AVB and sinus bradycardia can be dealt with the same way. Third-degree (complete) AVB and high-degree AVB need the transvenous pacing regardless of the signs and symptoms. For this reason it is important to identified these heart

blocks. The figure shows the ECG identification of bradyarrhythmias and their therapies.

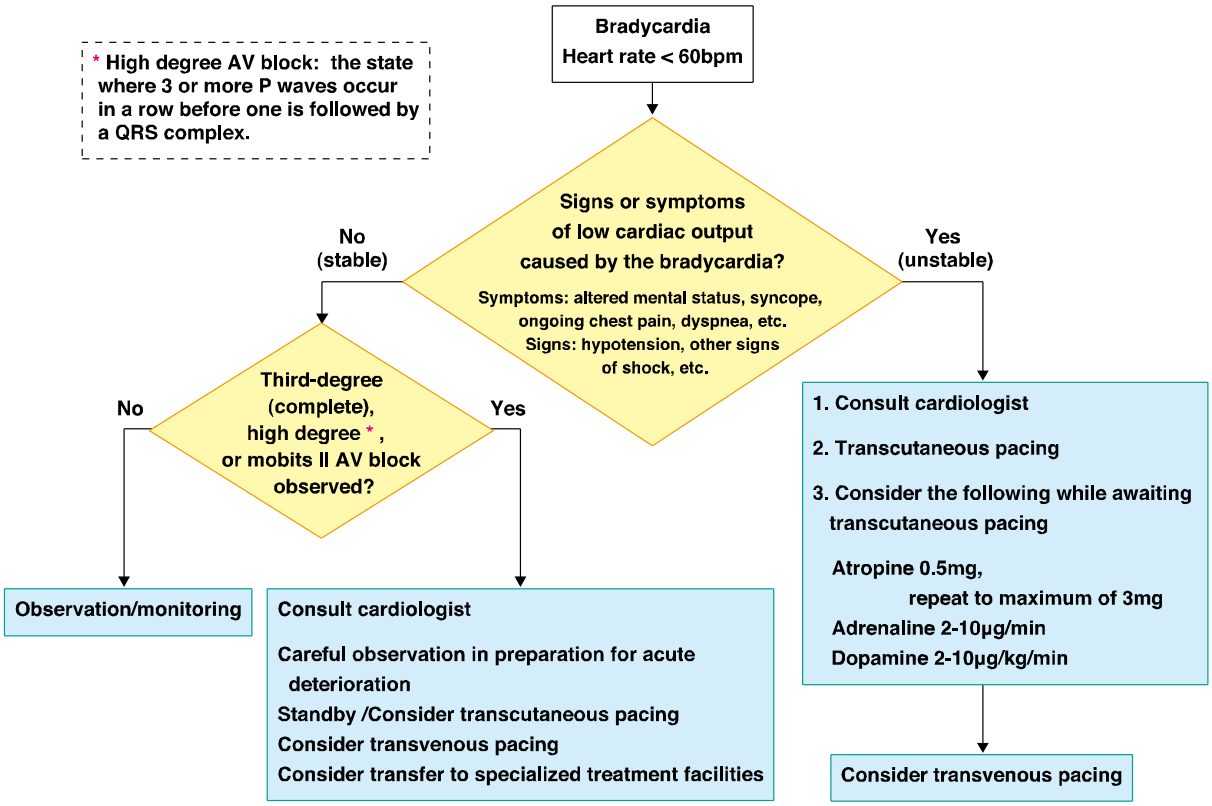

Figure 3 Bradycardia

Comment 1) Relationship between the signs and symptoms with bradycardia: If the patient's condition is unstable while the bradycardia is not the primary cause of instability, you cannot stabilize the condition by the treatment for the bradycardia itself. As the underlying cause of the patient's symptoms are various, such as hypoxemia and electrolytes abnormalities, you should treat these causes for the first which may lead the patient to brady PEA .

Comment 2) Definition of the high degree AV block: Transient atrioventricular block, QRS without P occurs in at least two consecutive waves (that is, three or more P waves occur in a row before one is followed by a QRS complex). High degree AV block does not include three degree (complete) AV block.

2. Bradycardia

1) Transcutaneous pacing

Four case series (LOE 4) demonstrated that in-hospital transcutaneous pacing had slightly higher success rates for rhythm capture[496] and survival to discharge (18–75%)[497-499] compared with survival-to-discharge rates (69%) when transcutaneous pacing was given for out-of-hospital bradycardia (LOE 1[500]). A systematic review supported this survival-to-discharge rate of 15–70% in the prehospital setting (LOE 3[501]).

Few studies have compared drugs with transcutaneous pacing for the treatment of bradycardia. One feasibility study (LOE 1[500]) compared dopamine with transcutaneous pacing in patients with bradycardia refractory to atropine. There were no differences in outcomes of survival to discharge (70% versus 69%).

2) Atropine

One randomized clinical trial (LOE 1[502]), 2 retrospective cohort studies (LOE 4[503, 504]), and 2 additional observational studies (LOE 4[505, 506]) documented that intravenous atropine improved heart rate and symptoms and signs associated with bradycardia. An initial dose of 0.5 to 1 mg, repeated as needed to a total of 1.5 to 3 mg, was effective in both in-hospital and out-of-hospital treatment of symptomatic bradycardia. One study (LOE 4[506]) reported that a ≥0.8 mg dose increased the incidence of tachycardia. One other study in 10 healthy volunteers (LOE 5[507]) indicated that a 3-mg dose of atropine produces the maximum achievable increase in resting heart rate. Two studies indicated that atropine may paradoxically cause high-degree atrioventricular (AV) block in patients after cardiac transplantation (LOE 5[508], LOE 4[509]).

3) Other drugs

Second-line drug therapy with dopamine (LOE 1[500]) and adrenaline for undifferentiated hemodynamically unstable bradycardia may be successful; it should be tailored according to potential causes in individual patients. For the treatment of bradycardia unresponsive to atropine in post inferior–myocardial infarction, post–cardiac transplant, or post–spinal cord injury, theophylline may be administered (LOE 2[510], LOE 4[511, 512], J-LOE 4[513]).

First-line drug treatment for symptomatic bradycardia is atropine 0.5 to 1 mg intravenous (IV) repeated every 3 to 5 minutes as needed up to 1.5 to 3 mg total (Class I). If not effective, then consider adrenaline (2 to 10 μg/min) or dopamine (2 to 10 μg/kg/min) (Class IIb). Transcutaneous pacing may be considered when full-dose atropine fails, although it may not be any more effective then second-line drug therapy (Class IIb). Avoid relying on atropine in patients with third-degree AV block accompanied by a wide-QRS escape rhythm. These bradyarrhythmias are not likely to be responsive to atropine and are preferably treated with transcutaneous pacing or second-line drug therapy.

Other second-line choices for symptomatic bradycardia should be tailored according to potential causes. After inferior myocardial infarction, cardiac transplant, or spinal cord injury, theophylline 100 to 200 mg slow injection IV (maximum 250 mg) may be given (Class IIb). Atropine should be used with caution in patients with bradycardia after heart transplant as it may cause paradoxical AV block.

4) Transvenous pacing

Transcutaneous pacing or antropine is, at best, a temporizing or emergency measure. If the bradycardia continues, the patient should be prepared for transvenous pacing (Class IIa).

■3 Tachycardia

1. Algorithm for the management of tachyarrhythmias

Definition of tachycardia: The heart rate is more than or equal to 100/min.

1) The key principles of tachyarrhythmias management in adult

As provider, you should identify the patient's condition whether it is stable or unstable by the signs and symptoms (hemodynamic parameter, etc.) and whether these signs and symptoms is related to a suspected arrhythmia or not.

(1) Determination of whether stable or unstable

The patient's symptoms suggesting unstable are acute altered mental status, syncope, ongoing chest pain, dyspnea and the signs for unstable conditions are the hypotension, or other signs of shock (perspiration, cold clammy skin , oliguria, disturbance of consciousness). However it cannot be definitively stated that it is unstable even if one of these signs and symptoms can be found in the patient. These signs and symptoms determine whether the condition of the patient is stable or unstable comprehensively. The heart rate of the patient in an unstable condition is generally over 150 beats per minute. In addition, it is important to identify whether the signs and symptoms of instability are caused primarily by the tachycardia or secondary to the underling diseases.

(2) Identification of tachycardia causing other signs or symptoms

If the signs and symptoms are related to a suspected tachyarrhythmia and the patient is unstable, immediate electrical shock should be performed (synchronized or unsynchronized). But the therapy for the tachycardia is not recommended if the signs and symptoms are caused secondary to the underling diseases. For example, a patient in shock caused by sepsis or bleeding may present sinus tachycardia as a physiologic compensation for maintaining the cardiac output. Treatment for this sinus tachycardia is not favorable. Lowering the heart rate may result in suppression of physiological compensative response and may aggravate the patient's condition to the state of cardiac arrest.

2) Management for unstable tachyarrhythmias in adult (Fig.4)

(1) key principles

If a patient is unstable with signs and symptoms related to a suspected tachyarrhythmia, give intervention quickly to this tachyarrhythmia is critically important. The primary intervention to unstable tachycardia is immediate synchronized electrical shock. If no pulse is detected, you should start CPR and switch to the cardiac arrest algorithm.

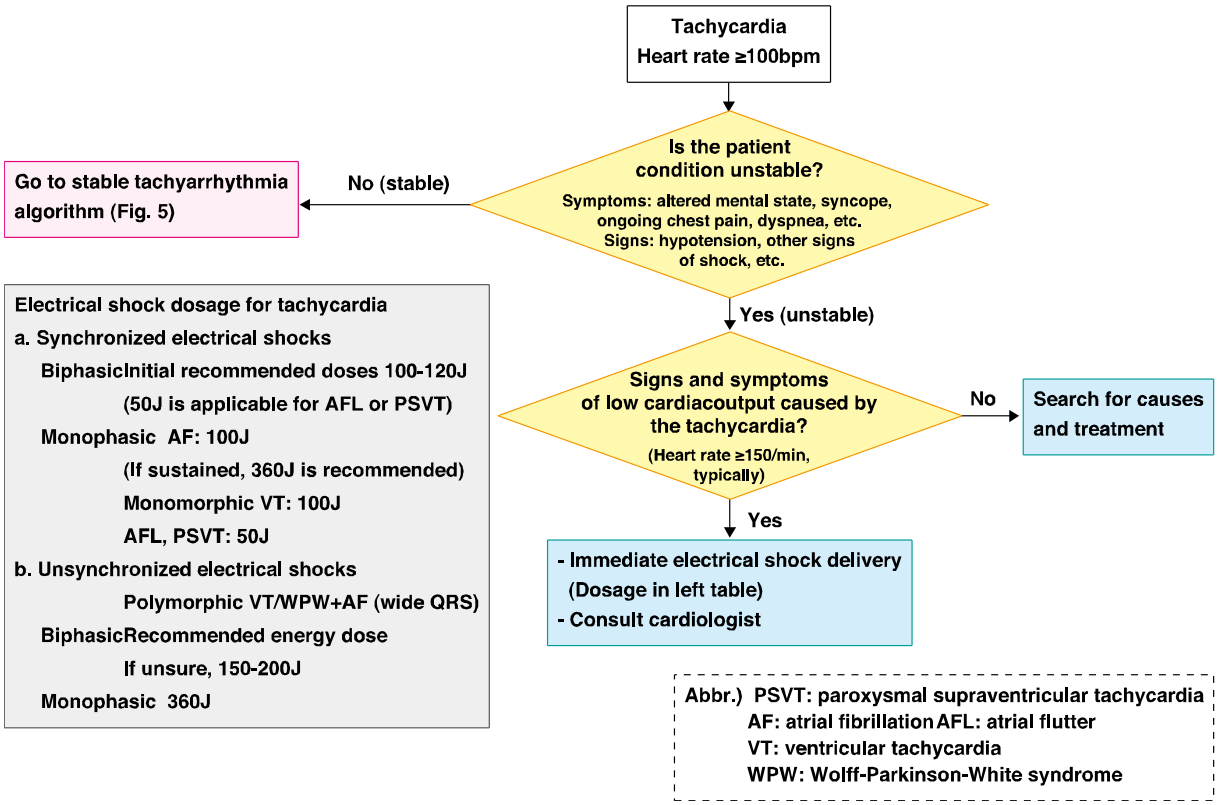

Figure 4 unstable tachyarrhythmia

(2) Electrical shock

For patients in unstable conditions with tachycardia, perform immediate synchronized shock. The specific practices of electrical shock are described in the paragraph"Defibrillation". Expert consultation may be considered also in unstable patients, however, do not delay the synchronized shock on the excuse of it. We should always remind that the delay in response to a patient with unstable condition might lead to cardiac arrest. Synchronized shocks sometimes take time to implement. So, use unsynchronized shock at the recommended energy doses (defibrillation doses) if the patient's condition is getting aggravated (e.g. increase in heart rate or appearance of the state of the shock) abruptly or the condition has been critically serious. Because unsynchronized electrical shocks may induce cardiac arrest, you should prepare for it. Specific shock energies for each tachyarrhythmias are shown in table 1.

3) Management for stable tachyarrhythmias in adult (Fig. 5)

(1) Key principles

If the patient with tachycardia is judged stable, you can obtain a 12-lead ECG and evaluate the rhythm before treatment. You may consider the expert consultation immediately. When it takes time to prepare a 12-lead ECG, you may print out the monitor recordings to analyze the specific rhythm. As the patient's condition can be aggravated at any time, you should observe the patient continuously while you are waiting for the experts. If the patient became unstable, such as hypotension, follow the algorithm for unstable tachycardia. If the patient loses the consciousness, respiration, and pulseyou should proceed to the algorithm to the cardiac arrest. In case no experts are available, follows the

algorithm for the stable tachycardia (Fig 3).

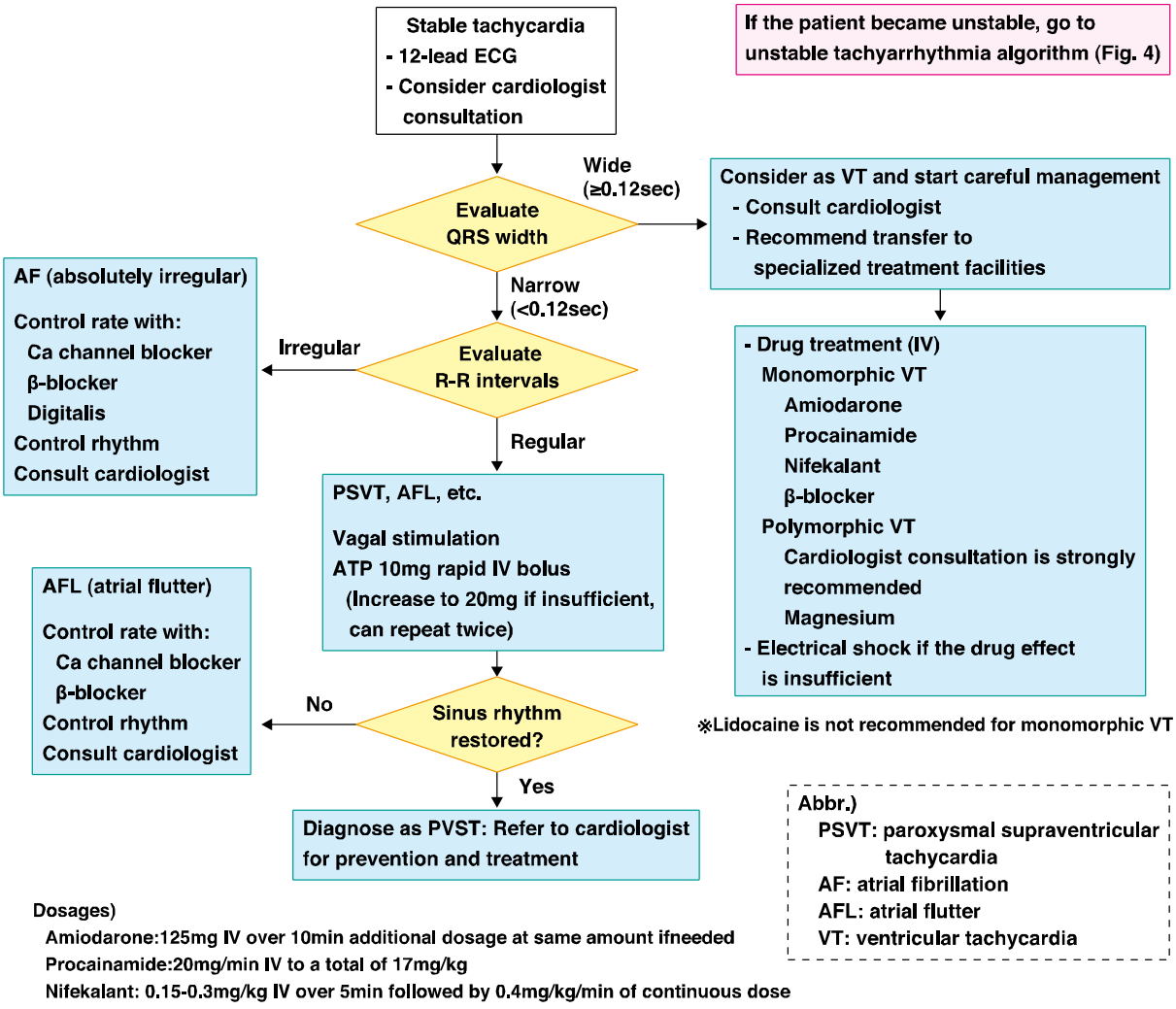

Figure 5 stable tachyarrhythmia

(2) Narrow-complex tachycardia

①Narrow-complex tachycardia excluding atrial fibrillation

There are four options for the treatment of narrow-complex tachycardia in the periarrest setting: electrical conversion, physical maneuver, pharmacological conversion, or rate control. The choice depends on the stability of the patient and the rhythm. In a hemodynamically unstable patient, narrow complex tachycardia is best treated with electrical cardioversion.

Five trials supported the use of adenosine in the treatment of narrow-complex tachycardia (LOE 1[514-518]).Six trials demonstrated the effectiveness of verapamil in conversion to sinus rhythm (LOE 1[514-517, 519, 520]). The effectiveness of diltiazem in conversion to sinus rhythm is supported by four trials (LOE 1[515, 519, 521, 522]). The evidence to support the use of other drugs for conversion to sinus rhythm is limited to a few trials for each drug, including sotalol (LOE 1[523]), amiodarone (LOE 4[524]), propafenone (LOE 1[525]), and nadolol (LOE 1[526]). The study on nadolol suggested treatment effect on rate as well. Cibenzoline terminated narrow-QRS complex tachycardia appeared after surgery (LOE 1[527]). There was no evidence of benefit with magnesium for narrow-comlex tachycardia (LOE 1[528], LOE 4[529], LOE

5[530]). Two studies demonstrated conversion effectiveness of vagal maneuvres (carotid massage and Valsalva) (LOE 2[531], LOE 4[532]).

Vagal maneuvres, IV adenosine, verapamil, and diltiazem are recommended as first-line treatment strategies in the termination of narrow-complex tachycardias (Class I). Nadolol, sotalol, propafenone, and amiodarone may be considered (Class IIb).

□ atrial fibrillation

For the treatment of AF, non-cardiologists are expected to choose rate-control therapy (optimizing heart rate with medication) by suppression of atrioventricular nodal conduction, while rhythm-control therapy (returning to sinus rhythm by medications or electrical shock) needs expert consultation. After the successful rate control, it is recommended to consult a cardiologist about rhythm control and prevention of thrombus formation.

In adult patients in atrial fibrillation either in the prehospital or in-hospital setting, whether or not the use of any drug or combination of drugs improves outcomes compared with not using, has been comprehensively reviewed by the European Society of Cardiology, the American Heart Association, and the American College of Cardiology[533].

③Rate control in atrial fibrillation

A systematic review (LOE 1[534]) demonstrated superiority for β-blockers (esmolol, metroprolol, and propranolol) with 70% success in meeting target heart rate or verapamil and diltiazem with 54% success[535] as first-line therapy for rate control in atrial fibrillation without a known accessory pathway and amiodarone when an accessory pathway was known and amiodarone or digoxin when fast atrial fibrillation occurred with heart failure (LOE 1[534]).

Four studies showed benefit for diltiazem in controlling rate in hospital (LOE 1[536-538], LOE 2[539]), and one study for out of hospital (LOE 3[540]).Two studies showed that verapamil is equally effective in rate control for atrial fibrillation (LOE 1[541, 542]). Adverse event rates with calcium channel blockers were reported as 18% [542].

Amiodarone may control rate and rhythm (LOE 1[543]),but significant complications were described in placebo-controlled trials: the risk of adverse events was 26.8% as a pooled estimate, and the most common side effects encountered were phlebitis, bradycardia, and hypotension (LOE 1[543]).

Digoxin is not effective for cardioversion (LOE 1[544-546]), but in some studies it has been shown to have moderate rate controlling properties (LOE 1[539, 545, 546]).

④Rhythm control in atrial fibrillation

Ibutilide has consistently been more effective in converting atrial fibrillation to sinus rhythm when compared with placebo (LOE 1[547-549]), or other antiarrhythmic drugs (LOE 1: sotalol[550], procainamide[551], and amiodarone[552]) and equal to other drugs (LOE 1: flecainide[553]).

Propafenone has been consistently more effective than placebo in converting AF to sinus rhythm (LOE 1[554-556]), but inferior to other drugs (LOE 1: amiodarone[543], procainamide[557], and flecainide[558]).

There are also data supporting flecainide (LOE 1[559-562]) and dofetilide (LOE 1[563, 564]) for conversion in patients without coronary artery disease.

Data supporting amiodarone for cardioversion are relatively weak (LOE 1[552, 565-567]); however, amiodarone does have ratecontrolling properties (LOE 1[565, 568]).

Sotalol has consistently been shown to be inferior in conversion compared to other drugs (LOE 1: flecainide[553] and ibutalide[550]), but equal to amiodarone in one study (LOE 1[567]).

Most studies showed no conversion benefit for magnesium (LOE 1[569, 570]), although 1 meta-analysis showed conversion benefit (LOE 1[571]). Most studies showed a benefit for magnesium in rate control (LOE 1[537, 571, 572]), although one study was neutral for magnesium for rate control (LOE 1[570]).

Quinidine has been shown to have greater conversion than sotalol in two studies (LOE 1[573, 574]), although this was with greater toxicity. Clonidine has rate-controlling properties compared with placebo (LOE 1[575, 576]).

Procainamide has shown increased efficacy in conversion of AF to sinus rhythm when compared with placebo[577] and to propafenone[557], but appears to be as effective as amiodarone[578].

Patients who are haemodynamically unstable with atrial fibrillation should receive prompt electrical cardioversion (Class I).

In the rate control in atrial fibrillation, Beta-blockers and diltiazem are the drugs of choice for acute rate control in most individuals with atrial fibrillation and rapid ventricular response (Class IIa) . Digoxin and amiodarone may be used in patients with congestive heart failure, and amiodarone may also result in cardioversion to normal sinus rhythm (Class IIb) . As magnesium and clonidine have rate controlling effects, though there are fewer data supporting their use, they can be used in some cases (Class IIb) .

In the rhythm control and maintenance of artial fibrillation, chemical cardioversion can be achieved with ibutilide, dofetilide, and flecainide (Class IIb) . Amiodarone can also be used for chemical cardioversion, but it is less effective (Class IIb) . Quinidine, procainamide and propafenone may be useful for cardioversion (Class IIb) . There is no role for digoxin in chemical cardioversion.

(3) Wide-complex tachycardia

There are two options for the treatment of wide-complex tachycardia in the periarrest setting: electrical conversion and chemical conversion. Most wide QRS tachycardias are VT. Wide QRS tachycardias should be treated as VT, beacause even though the patient seems stable, VT may rapidly deteriorate the hemodynamic condition to unstable, inducing pulseless VT or VF (cardiac arrest). The choice depends on the stability of the patient and the rhythm. In a hemodynamically unstable patient, wide complex tachycardia is best treated with electrical synchronized shock (cardioversion).

①Monomorphic VT

In wide QRS tachycardia with uniform QRS morphology (monomorphic VT), the following drugs may be used if the patient's conditions are sufficiently stable. It always should be kept in mind the possibility of sudden change and the defibrillator should be prepared in advance.

i) Conversion of acute onset of monomorphic (wide-complex) hemodynamically stable VT

- Procainamide: One unblinded study comparing lidocaine with procainamide (LOE 1[579]) documented an improved reversion rate over lidocaine (1.5mg/kg) when procainamide

(10mg/kg) was given to adult patients with haemodynamically stable monomorphic ventricular tachycardia (mVT), but without severe congestive heart failure or acute myocardial infarction in the hospital setting. One retrospective study in Japan also revealed that procainamide (358 ± 50 mg) was more effective than lidocaine (81 ± 30 mg) in terminating stable mVT (J-LOE 5[580]). Additional evidence from a case series suggested that procainamide was effective in terminating stable mVT in the hospital setting (LOE 4[581]).

- Sotalol: A double-blind study comparing lidocaine with sotalol documented an improved reversion rate over lidocaine (100 mg) when sotalol (100 mg) was given to patients with spontaneous onset haemodynamically stable sustained mVT in the hospital setting (LOE 1[582]).
- Amiodarone: The evidence on the effectiveness of amiodarone (150–300 mg) in terminating VT is conflicting with reported conversion rates between 20% and 40% based on one controlled trial (LOE 1[583]) and three case series (LOE 4[584-586])in patients with coronary artery disease with a low left ventricular ejection fraction in the hospital setting. The use of amiodarone (300 mg) was associated with side effects (primarily hypotension) [584, 586], but the effect of these on outcome remains unclear.
- Lidocaine: Lidocaine was less effective than sotalol (LOE 1[582]), procainamide (LOE 2[579]), and amiodarone (LOE 2[583]) in terminating VT. Three retrospective analyses showed lidocaine was poorly effective when given to patients with or without a history of myocardial infarction with spontaneous sustained stable VT in the hospital setting (LOE 4[587-589]). In one randomised controlled study (LOE 5[590]) lidocaine was injected by paramedics intramuscularly in patients with acute myocardial infarction and VT in the prehospital setting. Lidocaine terminated VT in six of nine patients with an average of 10 minutes after administration while VT was not terminated in none of five patients in control group. Efficacy of intramuscular lidocaine for VT unassociated with acute myocardial infarction in the prehospital setting was 36% (LOE 5[591]). In addition one retrospective study in Japan revealed the efficacy of terminating stable monomorphic VT by lidocaine was 35%, which was not superior to 76% of that of procainamide (J-LOE 5[580]).
- Cibenzoline: One case series suggested cibenzoline (70±12 mg) may be effective in terminating VT (LOE 4[592]).
- Magnesium: One study suggested magnesium was effective in terminating VT (LOE 5[593]).
- Adenosine: Adenosine may aid in diagnosing VT, but it will not terminate it (LOE 4[594, 595]).
- Calcium channel blockers: The evidence for the use of calcium channel blockers in VT is conflicting, with most studies opposing their use (LOE 4[596-598]), but one study supported the use as long as coronary disease was not present (LOE 5[599]). Calcium channel blockers may terminate some VT (J-LOE 5[600]).
- Nifekalant: There is insufficient evidence about the efficacy of nifekalant for stable mVT, See other sections for the patients with shock refractory VF/VT.

ii) Preventing recurrence and late conversion in refractory ventricular tachyarrhythmias including mVT

- Synchronized electric shock (cardioversion): Electric cardioversion at an early stage or as first-line treatment was reasonable based on a prospective case series (LOE 4[601]). Indirect evidence

was also provided by 3 case studies (LOE 4[587, 602, 603]).

- Amiodarone: Two RCTs (LOE 1) comparing amiodarone with lidocaine[583] or bretylium[604],two double-blind randomised dose-range studies (LOE 4[605, 606]), and five case series (LOE 4[607-611]) suggested that amiodarone reduced the number of life-threatening arrhythmias (event rate), required shocks, and episodes of symptomatic sustained VT that occurred in patients with recurrent refractory ventricular arrhythmias in hospital. One study in Japan showed amiodarone was suggested to be effective in preventing recurrence of VT (J-LOE 5[612]).
- β-blockers: A single prospective case series (LOE 4[613]) suggested that recurrent and refractory ventricular arrhythmias were reduced while long- and short-term survival were improved in patients treated with sympathetic blockade (including β-blockers) during electrical storm. One study in Japan suggested the effectiveness of landiolol (short-acting β-blockers) for the electrical storm (J-LOE 5[614]).
- Nifekalant: Two retrospective control study (LOE 3[615, 616]), one case series (LOE 4[617]), and one other study (LOE 5[618]) suggested that nifekalant showed the improved outcome in patients with shock refractory VF/VT. However, it did not seem to be effective in immediately terminating the arrhythmia (LOE 4[617]).

Procainamide is recommended for patients with hemodynamically stable monomorphic ventricular tachycardia (mVT) who do not have severe congestive heart failure or acute myocardial infarction (Class I) . Amiodarone is recommended for patients with hemodynamically stable mVT with or without either severe congestive heart failure or acute myocardial infarction (Class IIa). Nifekalant may be useful in improving outcomes in shock refractory VF/VT even though it did not seem to be effective in immediately terminating the arrhythmia (Class IIb).

Sotalol may be considered for patients with haemodynamically stable sustained mVT, including patients with acute myocardial infarction (Class IIb).

iii) Undifferentiated regular stable wide-complex tachycardia

Five studies involving more than 300 patients (LOE 4[594, 595, 619-621]) demonstrated that adenosine could safely be administered in regular wide-complex tachycardia: it converted wide-complex tachycardia secondary to supraventricular tachycardia to normal sinus rhythm, but rarely terminated VT. One small study showed poor rates of conversion to sinus rhythm in patients known to have VT (LOE 4[587]). No patient in these trials had serious adverse events; however, there are case reports in patients with irregular wide-complex tachycardia (generally pre-excited atrial fibrillation) in whom VF was precipitated by adenosine (LOE 4[622-625]).

Other studies that included lidocaine showed poor rates of conversion to sinus rhythm with lidocaine in patients known to have VT (LOE 4[587]). In one study, 11 of 25 patients known to have VT and treated with verapamil developed profound hypotension (LOE 4[626]).

In undifferentiated regular stable wide-complex tachycardia, IV adenosine may be considered relatively safe, may convert the rhythm to sinus, and may help diagnose the underlying rhythm (Class IIb).

Polymorphic wide-complex tachycardia

In case QRS morphologies of VT are not uniform (polymorphic VT), consultation to cardiologist or transfer to the facilities where specific treatment can be available is strongly recommended. Evidence for benefit from these therapies is limited, mainly anecdotal, extrapolated, or from small, observational studies and based on the presumed mechanism for polymorphic wide-complex tachycardia, which may not always be clinically evident. There are three subtypes of polymorphic VT:

i) Polymorphic VT with delayed abnormal repolarization

Torsade de pointes (TdP) is a specific form of polymorphic VT. TdP is characterized by a gradual change in the amplitude and twisting of R wave polarity around the baseline on the ECG. Prolonged QT intervals on 12-lead ECG during sinus rhythm reveal congenital (such as heritable) or acquired (such as drug-induced, resulting from electrolyte disturbances, etc.) long QT syndrome. Therefore, QT measurement on 12-lead ECG is important. There are 2 subtypes of TdP with long QT, as well as "pause-dependent" initiating sequence, and coexisting factors associated with delayed repolarization with 2 subtypes:

- Familial (congenital) long QT (torsades de pointes): Recurrences of polymorphic wide-complex tachycardia associated with congenital long QT may be reduced with IV magnesium, based on extrapolation from a small case series of children (LOE 5[627]); overdrive pacing (atrial or ventricular); or β-blockers derived from extrapolation from two registry case series of secondary prevention in patients with congenital long QT (LOE 5[628, 629]). There is virtually no published experience regarding the acute use of these therapies in such patients.
- Acquired long QT (torsades de pointes): Recurrences of polymorphic wide-complex tachycardia associated with acquired or drug-precipitated Long QT may be reduced with IV magnesium, based on five studies (LOE 3[630]; LOE 4[631]; LOE 5 (paediatrics) [627]; LOE 5 (animals)[632, 633]); overdrive pacing (atrial or ventricular) based on seven studies (LOE 4[631, 634-637]; LOE 5 [extrapolation from secondary prevention in patients with congenital LQTS] [628, 629]); and IV isoprenaline (when not contraindicated by presence of ischaemia or hypertension) is supported by four studies (LOE 4[631, 635]; LOE 5 (animal) [633, 638]) but opposed by one study (LOE 4[635]).

Polymorphic wide-complex tachycardia associated with familial long QT may be treated with IV magnesium, pacing and/or β-blockers (Class IIb); however, isoprenaline should be avoided (Class III). Polymorphic wide-complex tachycardia associated with acquired long QT may be treated with IV magnesium (Class IIa). Addition of pacing or IV isoprenaline may be considered when polymorphic wide-complex tachycardia is accompanied by bradycardia or appears to be precipitated by pauses in rhythm (Class IIb).

ii) Polymorphic wide-complex tachycardia associated with acute myocardial ischemia

This tachycardia usually accompanies short QT intervals. The patients presents the feature of acute myocardial ischemia such as the history, signs and symptoms, and electrocardiographic findings. When polymorphic wide-complex tachycardia is caused by acute myocardial ischemia, it may respond

to IV β-blockers in a modestly sized study (LOE 3[613]); however, there was no benefit from IV magnesium in a small study (LOE 3[630]).

iii) Polymorphic VT secondary to other mechanisms

The science on the management of polymorphic wide-complex tachycardia caused by short QT syndrome is limited to case reports involving amiodarone, β-blockers, and quinidine (LOE 4[639, 640]).

A LOE-4 study[641] and extrapolation from a small case series suggested that isoprenaline attenuated the ST elevation associated with Brugada syndrome (LOE 5[642]). Extrapolation from one case series suggested worsened Brugada ST elevation with class IA antiarrhythmics (LOE 5[642]).

A pediatric case report (LOE 5[643]) and extrapolation from a small case series of secondary prevention using oral β-blockers alone (LOE 5[644]) or in combination with verapamil (LOE 5[645, 646])) suggested IV propranolol successfully terminated catecholamineinduced polymorphic wide-complex tachycardia.

Among patients with impaired ventricular function due to structural heart disease (ischaemic, valvular, or cardiomyopathy), in the absence of QT prolongation or drug provocation, treatment of hemodynamically unstable VT with intravenous amiodarone reduced the frequency of recurrent arrhythmias. This evidence rests on extrapolation from three prospective RCTs (LOE 5[604-606]) performed in the in-hospital setting but in which VT morphology was not addressed specifically.

Nifekalant is reported effective for both termination and prevention with hemodynamically unstable VT (LOE 4[615], J-LOE 4[180, 617, 647, 648], J-LOE 5[179, 649]) and the effectiveness was same as that of amiodarone.

Polymorphic wide-complex tachycardia without long QT may be responsive to IV β-blockers (for ischaemic VT and catecholaminergic VT) or isoprenaline (for Brugada syndrome) (Class IIb). Amiodarone and nifekalant may be considered for polymorphic wide-complex tachycardia without QT prolongation (Class IIb).

7 Cardiac arrest in special situations

■1 Cardiac arrest caused by avalanche

1. Time of burial and patent airway

Four studies (LOE P3[650-653]) demonstrated a progressive nonlinear reduction in survival as time of burial lengthened. In eight studies (LOE P3[651, 652, 654-657], LOE P4[658, 659]) victims who were buried beyond 35 min did not survive if they had an obstructed airway (defined as obstructed by avalanche debris or by other means) on uncovering the head. One study (LOE P5[660]) demonstrated that when breathing in simulated air pockets of different volumes, hypoxia and hypercapnia achieved a steady state after 10 min. This finding suggested that long-term survival was possible as long as an air pocket, even as small as 1 L, was present. One study (LOE P5[661]) indicated that deflection of expired air away from an air pocket may slow the development of hypoxia and hypercapnia.

2. Core temperature

Two relevant LOE P3-studies in the general hypothermia literature found that survival decreased with core temperatures less than 32 ℃ and reported the use of extracorporeal rewarming only when core temperatures were less than 32 ℃[662, 663]. One relevant LOE P3-study reported amaximum cooling rate of 8 ℃/h in buried victims[664]. An avalanche case report described a maximum cooling rate of 9 ℃/h (LOE P4[658]). Those cooling rates suggested that, at 35 min of burial, the core temperature may drop as low as 32 ℃. Three relevant studies (LOE P3[655, 664, 665]) and four case series or reports (LOE P4[658, 663, 666, 667]) recorded ROSC in 22, and survival to hospital discharge in 7 of those 22, buried avalanche victims in cardiac arrest with a core temperature less than 32 ℃ with aggressive rewarming using extracorporeal circulation.

3. Serum potassium

A serum potassium of less than 8 mmol/L on hospital admission was found to be predictive of increased ROSC in avalanche burial victims in one study (LOE P3[655]) and for increased survival to hospital discharge in two studies (LOE P3[654, 664]). Five studies found an inverse correlation between admission potassium concentration and survival to discharge in all-cause hypothermic patients (LOE P3[654, 662, 665, 668, 669]). Four studies (LOE 3[654, 664, 670, 671]) found that high potassium values were associated with asphyxia in all hypothermic patients. The highest reported serum potassium value in an avalanche survivor was 6.4 mmol/L[664], although survival to hospital discharge from all-cause hypothermia with a potassium concentration as high as 11.8 mmol/L has been documented[672].

Avalanches occur in areas that are difficult for rescuers to access in a timely manner, and burials frequently involve multiple victims. The decision to initiate full resuscitative measures should be determined by the number of victims and the resources available, and it should be informed by the

likelihood of survival.

Avalanche victims are not likely to survive when they are

- Buried >35 min and in cardiac arrest with an obstructed airway on extrication.
- Buried initially and in cardiac arrest with an obstructed airway on extrication, and an initial core temperature of <32 ℃.
- Buried initially and in cardiac arrest on extrication with an initial serum potassium of >8 mmol/L or more.

Full resuscitative measures, including extracorporeal rewarming, when available, are indicated for all other avalanche victims without evidence of an unsurvivable injury (Class I).

Knowledge Gaps

Prospective validation studies of patient airway, core temperature, and serum potassium as prognostic factors among patients in cardiac arrest on extrication, measurement of core temperature of avalanche victims in cardiac arrest at the time of rescue and prospective studies on effectiveness of prehospital treatment of nonarrested hypothermic avalanche victims would advance the science of avalanche resuscitation.

■2 Pregnancy

There are no RCTs evaluating the effect of specialised obstetric resuscitation versus standard care in postarrest pregnant women. Many studies of women not in cardiac arrest document the important physiological changes that occur in pregnancy that may influence treatment recommendations and guidelines for resuscitation of cardiac arrest in pregnancy.

1. Aortocaval decompression to improve maternal haemodynamics and fetal well-being

In the nonarrest literature, left lateral tilt improved maternal blood pressure, cardiac output, and stroke volume (LOE 5[673-675]) and improved fetal parameters of oxygenation, nonstress test, and fetal heart rate5[676-678]. While chest compressions in the left lateral tilt position were shown to be feasible in a manikin study[679], they have been shown to result in less forceful chest compressions than in the supine position[680]. Two studies found no improvement in maternal haemodynamic or fetal parameters in nonarrest patients with 10–20° left lateral tilt[681, 682]. One study found more aortic compression at 15° left lateral tilt when compared to a full left lateral tilt[677]. In addition, aortic compression has been found to persist at over 30° of tilt[683]; however, the majority of these patients were in labor. Two nonarrest studies found that manual left uterine displacement (which is done with the patient supine) was as good as, or better than, left lateral tilt in relieving aortocaval compression, as assessed by the incidence of hypotension and ephedrine use[684, 685].

2. Respiratory considerations

One study documented that the upper airways in the third trimester of pregnancy are smaller (supine mean difference 0.20; 95% confidence interval [CI] 0.06–0.35) compared with their postpartum state and to nonpregnant controls (LOE 5[686]). One study found increased intrapulmonary shunting in normal pregnancy at 12.8–15.3% compared with the nonpregnant state normal value of 2–5% (LOE 5[687]), suggesting a change in the approach to oxygenation demands and in the size of the advanced airway may be physiologically justifiable in maternal cardiac arrest.

3. Perimortem Caesarean section

One retrospective cohort study of 55 maternal cardiac arrests evaluated the incidence of perimortem Caesarean section after the introduction of a targeted training course (Managing Obstetric Emergencies and Trauma; MOET) and compared it with a historical rate (LOE 4[688]). There are no cases where the caesarean section was conducted within 5 minutes of cardiac arrest as recommended in the MOET course. With caesarean sections in cardiac arrest, maternal ROSC rate was 67%, maternal mortality rate was 83%, and infant mortality rate was 58%. One systematic review of perimortem caesarean sections documented 38 cases, with 34 surviving infants and 13 maternal survivors at discharge, suggesting that perimortem caesarean section may have improved maternal and neonatal outcomes (LOE 5[689]). At older gestational ages (30–38 weeks), infant survival was possible even when delivery was after 5min from the onset of maternal cardiac arrest (LOE 5[689]). One retrospective study concluded that for delivery of infants between 22 and 25 weeks gestational age, neonatal outcome is best at 25 weeks, and there was no infant survival when delivery occurred at 22 weeks (LOE 5[690]).

4. Changes in pharmacokinetics

One study documented an increase in glomerular filtration rate, cardiac output, and plasma volume early in the first trimester that starts to return to normal in the end of the third trimester, suggesting that known physiological vascular and fluid changes of pregnancy may respond to fluid resuscitation during maternal cardiac arrest (LOE 5[691]).

5. Defibrillation

One underpowered case control study reported no difference in transthoracic impedance during pregnancy compared with postpartum, suggesting current energy requirements for adult defibrillation were appropriate (LOE 5[692]).

6. Positioning

One study indicated that the human wedge technique can provide left lateral tilt and effective external chest compressions and mouth-to-mouth rescue breathing in a manikin (LOE 5[679]). However, another study found that the estimation of the degree of table tilt is unreliable and often overestimated, suggesting rescuers are more likely to employ an insufficient amount of tilt to achieve the required

haemodynamic benefit (LOE 5[693]). A small study assessed the efficacy of resuscitation at various angles of inclination using a calibrated force transducer (LOE 5[680]). This study found that the maximum possible resuscitative force decreased as the angle of inclination of the plane increased, from 67% of body weight in the supine position to 36% in the full lateral position. Therefore at an inclination of 27° the maximum resuscitative force for chest compressions was only 80% of the force generated at 0° of inclination (supine). Also at an incline of >30° the patient/manikin tended to roll off the incline plane (LOE 5[680]).

7. Therapeutic hypothermia postarrest

A single case report suggested that post–cardiac arrest hypothermia was used safely and effectively in early pregnancy with fetal heart monitoring and resulted in favorable maternal and fetal outcome after a term delivery (LOE 5[694]).

There is insufficient evidence to support or refute the use of specialised obstetric resuscitation techniques in maternal cardiac arrest and the use of therapeutic hypothermia in the postarrest period. Treatment may be guided by understanding the physiology of pregnancy, the importance of releasing aortocaval compression, the increased risk for hypovolaemia, the compression advantage through positioning, and the value of perimortem caesarean section early in maternal cardiac arrest.

Knowledge Gaps

Research in the area of maternal resuscitation is lacking, and most of the science is extrapolated from nonpregnant women, manikin studies, or case reports. Epidemiological studies are needed to document the incidence of cardiac arrest in pregnancy as there as is a perception that it is increasing because of increased numbers of women with congenital heart conditions who are now having children.

■3 Cardiac arrest in morbid obesity

Evidence from two studies did not find a survival difference associated with obesity following out-of-hospital cardiac arrest (LOE 2[695-697]).

There is insufficient evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for obese patients.

Knowledge Gaps

There is a paucity of research in this area, and studies looking at epidemiology, current variations from the standard protocol, and associated outcomes, as well as simple experimental studies, would be helpful.

■4 Cardiac arrest caused by asthma

There are no RCTs that specifically evaluate or compare adjuvant treatment with standard treatment for cardiac arrest in asthmatic patients. Most of the literature comprises case reports and case series.

When ventilation is difficult due to bronchial asthma, it is effective to decrease ventilation by lowering the tidal volume and respiratory rate, and prolonging the expiration time (J-LOE 5[698]). Evidence from three non-cardiac arrest case series involving 35 patients suggests that asthmatic patients are at risk for gas trapping during cardiac arrest, especially if their lungs are ventilated with high tidal volumes and/or rapid rates (LOE 5[699-701]). One volunteer adult study demonstrated that increasing PEEP caused increased transthoracic impedance (LOE 5[702]).

Seven case series involving 37 patients suggested increased ease of ventilation and ROSC with lateral chest compressions at the base of the ribs (LOE 4[703-709]). In a single case report, lateral chest compressions were associated with cardiac arrest and poor cardiac output (LOE 4[710]).

Brief interruptions of ventilation were effective in the case of difficulty of ventilation (J-LOE 4[711-714]). Three single case reports (two intraoperative and one ED) involving cardiac arrest caused by asthma suggested improvement in ease of ventilation and ROSC with thoracotomy and manual lung compression (LOE 4[704, 708, 709]).

There is insufficient evidence to suggest any routine change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by asthma. However, it is reasonable to perform resuscitation, understanding that the fatal bronchial asthma is characterized by distal airway closure and lung hyperinflation, which can cause respiratory arrest resulting in cardiac arrest.

When ventilation for a victim in cardiac arrest caused by asthma is difficult or impossible to perform due to lung hyperinflation from air trapping, interruption of ventilation for 30-60 seconds may be applied (to let the air escape) (Class IIb). Since lung hyperinflation increases transthoracic impedance, if initial defibrillation attempts fail then delivering higher shock energies for defibrillation may be considered (Class IIb). In addition, there is a possibility of pneumothorax with lung hyperinflation, which should be remembered all the time, and releasing air if needed should be considered (Class IIb).

Knowledge Gaps

Several key areas for research include: the role of disconnecting from positive pressure ventilation and the ideal duration of this disconnection; the role of lateral external compression and the timing with respect to chest compressions; the comparison of these techniques and their cumulative advantage; and the role of magnesium infusions and ECMO in cardiac arrest caused by asthma.

■5 Cardiac arrest caused by anaphylaxis

There are no RCTs evaluating conventional versus alternative therapies for the treatment of cardiac

arrest caused by anaphylaxis. Evidence is limited to case reports, extrapolations from nonfatal cases, interpretation of pathophysiology, and animal studies.

One human study of a randomised venom immunotherapy trial where 19 of 21 patients became symptomatic and required emergency treatment suggests that carefully titrated continuous infusion of IV adrenaline in addition to volume infusion may be effective for the treatment of anaphylactic shock (not in cardiac arrest) (LOE 5[715]). One randomised controlled crossover study of animals preshock, but symptomatic with ragweed sensitivity, showed that a continuous IV infusion of 0.01mg/kg adrenaline maintained a mean arterial pressure at 70% of preshock levels better than no treatment or bolus treatment (LOE 5[716]).

A small case series of patients with anaphylactic shock with or without cardiac arrest suggested that patients who did not respond to standard therapy may benefit from vasopressin (LOE 4[717, 718]). A few small case series (LOE 4) have described promising initial findings with α-agonists such as noradrenaline[719], methoxamine[720], terlipressin[721], and metaraminol[722-724]. A few small case reports (LOE 4) of cardiac arrest suggest cardiopulmonary bypass[725, 726] or mechanical support of circulation （LUCAS） [727] may be helpful in the setting of anaphylaxis. One patient was reported who suffered a cardiac arrest due to drug anaphylaxis despite administration of steroid and antihistamine was successfully resuscitated with prolonged advanced cardiac life support (LOE 5[728]).

There is insufficient evidence to suggest any routine change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by anaphylaxis.

Anaphylaxis accompanied by rapid circulatory collapse and airway obstruction can lead to cardiac arrest. It is important to recognize symptoms in the early stage and start adrenaline administration and fluids treatment (Class I).

Knowledge Gaps

Future research should consider a comparison between the different IV α-agonists and a comparison of infusion versus bolus doses for cardiac arrest caused by anaphylaxis. The value of secondary therapies such as glucagon, antihistamines, volume infusions, and steroids should be explored.

■6 Drug overdose and poisoning

The majority of questions addressing cardiac arrest caused by drug toxicity remain unanswered. Epidemiological studies are required to document the incidence of cardiac arrests caused by drugs, current treatment strategies, and the safety and efficacy of existing treatments. Animal models, controlled clinical trials, and pharmacodynamic studies are needed to advance the treatment of cardiac arrest caused by drugs. Most of the evidence is limited to case reports, extrapolations from nonfatal cases (including severe cardiovascular toxicity cases), and animal studies.

1. Cardiac arrest caused by local anaesthetic

Local anaesthetic toxicity typically occurs in the setting of regional anaesthesia, when a bolus of local anaesthetic inadvertently enters the arterial or venous system, leading to refractory seizures and/or rapid cardiovascular collapse. There are no RCTs evaluating conventional versus alternative therapies for the treatment of cardiac arrest caused by local anaesthetics (lidocaine). Evidence is limited to case reports involving cardiac arrest and severe cardiovascular toxicity and animal studies.

Five single-case reports describe patients in cardiac arrest attributed to local anaesthetic intoxication, who were refractory to advanced life support conventional treatment, but who obtained ROSC soon after treatment with IV lipid emulsion (LOE 5[729-733]). Five single-case reports (LOE 5) describe patients with acute, life-threatening cardiovascular toxicity from local anaesthetic intoxication, but who were not pulseless at the time of lipid administration. In three cases[734-736] severe cardiovascular toxicity resolved rapidly following IV lipid, but in two other cases[737, 738] the patient's condition deteriorated to cardiac arrest after IV lipid, although the patients were resuscitated and survived to hospital discharge.

Five controlled animal studies demonstrated that a variety of dosages of IV lipid emulsion were more effective than placebo in models of local anaesthetic intoxication with ROSC as the primary outcome (LOE 5[739-743]).

Two controlled animal studies suggested that, in combination with basic life support (BLS), IV lipid emulsion improved the rate of ROSC when compared with vasopressor therapy (vasopressin and adrenaline) (LOE 5[740, 743]). Contrasting results were published in one controlled animal study that demonstrated a survival advantage with vasopressin and adrenaline over lipid emulsion therapy in a model of asystole induced by low-dose bupivacaine and asphyxia (LOE 5[744]). Two controlled animal studies reported no additional benefit from lipid emulsion infusions when combined with highdose adrenaline 0.1mg/kg (LOE 5[745]) and 0.01 and 0.025mg/kg (LOE 5[746]). Lipid emulsion bolus doses and infusion rates vary across case reports and animal studies. Typical bolus doses were 1–3mL/kg. When infusions were used the typical doses were 0.1–0.3mL/kg/h. A 20% solution of long-chain fatty acid emulsion was used in almost all reports.

Two controlled animal studies showed a survival advantage when cardiac arrest from local anaesthetic toxicity was treated with high-dose insulin (1–2U/kg IV bolus) accompanied by glucose and sometimes potassium, compared with basic life support resuscitation alone (LOE 5[747, 748]). There were no animal studies comparing this intervention with advanced life support resuscitation.

The use of clonidine (150 μ g boluses, repeated as needed) to treat cardiac arrest caused by local anaesthetic was described in one human case report (LOE 4[749]) while a second case report (LOE 4[750]) was neutral. An animal study demonstrated partial improvement in bupivacaine-induced intracardiac conduction delays following clonidine administration (0.01mg/kg IV), but nonperfusing rhythms were not studied (LOE 5[751]).

There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by local anaesthetics. Animal studies and case reports suggest severe cardiovascular toxicity or cardiac arrest attributable to local anaesthetic intoxication may respond to treatment with IV lipid emulsion (Class IIb).

2. Benzodiazepine toxicity

No human studies or reports of any patients who had cardiac arrest solely resulting from benzodiazepine toxicity alone were identified.

Five reports of cardiac arrests resulting from exposure to combinations of medication that included one of the benzodiazepines were identified (LOE 4[752-756]). One case report indicated that standard care alone was sufficient to reverse the severe cardiovascular toxicity attributed to an anaphylactic reaction to a benzodiazepine (LOE 5[757]).

One case report described improved outcome when minor cardiovascular toxicity caused by benzodiazepines was treated with flumazenil (LOE 5[758]). Four studies indicated that flumazenil is unlikely to improve haemodynamic function in the setting of benzodiazepine overdose and may complicate other therapy (LOE 5[755, 759-761]). Two studies described serious adverse effects such as seizure, arrhythmia, hypotension, and withdrawal syndrome after flumazenil was given to patients presenting with decreased level of consciousness attributed to either benzodiazepine toxicity or an unknown cause (LOE 5[755, 762]). These side effects were more common with coingestants (such as tricyclic antidepressant and opioids), chronic benzodiazepine use or abuse, and known seizure disorder.

There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by benzodiazepines. Routine use of flumazenil for a victim with impaired consciousness by unknown cause is not recommended (Class III).

3. β-blocker toxicity

There are no RCTs evaluating conventional versus alternative treatment of cardiac arrest caused by β-blockers. Evidence is limited to case reports, extrapolations from nonfatal cases, severe cardiovascular toxicity cases, and animal studies. The wide variety of β-blockers with differing pharmacological and physiochemical profiles makes it difficult to generalise from the limited data available.

In 13 case studies (n = 16) of human patients with severe cardiovascular toxicity caused by β-blockers refractory to standard treatment, including vasopressors, the administration of glucagon (50–150 μg/kg) was followed by haemodynamic improvement and survival (LOE 5[763-775]).

In two animal studies, high-dose insulin infusions (1U/kg/h) given with glucose supplementation and electrolyte monitoring appeared effective (as measured by rates of improved haemodynamic stability and survival) in the setting of cardiovascular toxicity associated with β-blockers (LOE 5[776, 777]). A single human case report documented that high-dose insulin (10U/kg/h IV), given with glucose supplementation and electrolyte monitoring, was followed by improved haemodynamic stability and survival to hospital discharge in the setting of severe cardiovascular toxicity associated with β-blocker toxicity (LOE 5[778]).

Case reports described the use of phosphodiesterase inhibitors (LOE 5[779, 780]), calcium salts (LOE 4[781, 782]), extracorporeal support (LOE 5[783]), intraaortic balloon pumps (LOE 4[784]), and ECMO (Extracorporeal Membrane Oxigenation) (LOE 4[785]).

Animal studies supported the use of the phosphodiesterase inhibitor amrinone (LOE 5[786]). Animal studies suggested that dopamine (LOE 5[787]), a combination of dopamine and isoprenaline (LOE 5[788]), and milrinone (LOE 5[789]) may decrease the effectiveness of glucagon as an antidote for β-blocker toxicity.

There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by β-blockers. Animal studies and case reports suggest severe cardiovascular toxicity caused by β-blockers may respond to treatment with intravenous glucagon, high-dose insulin (with glucose supplementation and electrolyte monitoring), or IV calcium salts or extracorporeal-CPR (ECPR) using ECMO/PCPS（Percutaneous Cardiopulmonary Support）in addition to conventional treatment (Class IIb).

4. Calcium channel blocker toxicity

There are no RCTs evaluating conventional versus alternative therapies for the treatment of cardiac arrest caused by calcium channel blockers. Evidence is limited to extrapolations from nonfatal case reports of severe cardiovascular toxicity.

In 16 human case series (n=28) high-dose insulin (bolus 0.5 to 2 U/kg followed by 0.5 U/kg/h infusion) given with glucose supplementation and electrolyte monitoring appeared effective (as measured by improved hemodynamic stability [25/28] and survival [26/28]) in the setting of severe cardiovascular toxicity associated with calcium channel blockers (LOE 5[790-805])

There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by calcium channel blockers. Case reports suggest severe cardiovascular toxicity caused by calcium channel blockers may respond to treatment with high-dose insulin given with glucose supplementation and electrolyte monitoring in addition to conventional treatment (Class IIb).

Knowledge Gaps

Controlled clinical trials are needed to advance the treatment of cardiac arrest caused by calcium channel blockers. While case reports focus on verapamil toxicity, the different properties of other calcium channel blockers may affect the response to the proposed treatment. Other special interest topics include the use of vasopressin to treat severe cardiovascular toxicity caused by dihydroropyridines, the use of combination therapy, sequencing of interventions, and the evaluation of new and emerging therapies, namely intravenous lipid infusion and calcium sensitizers and nonpharmacological interventions.

5. Carbon Monoxide Toxicity

Three studies suggested that most patients who develop cardiac arrest from carbon monoxide poisoning will not survive to hospital discharge, regardless of whether hyperbaric oxygen therapy is administered following ROSC (LOE 4[806-808]).

Two studies (LOE 5) suggested that neurological outcomes were improved in patients (all severity excluding cardiac arrest[809]; and mild-to-moderate, excluding loss of consciousness and cardiac instability[810]) who received hyperbaric oxygen therapy for carbon monoxide poisoning. However, 2 studies found no difference in neurologically intact survival (LOE 5[811, 812]). Two systematic reviews concluded that improvement in neurologically intact survival following the administration of hyperbaric oxygen to carbon monoxide poisoning patients was possible but unproven (LOE 5[813, 814]).

Two studies demonstrated that patients with carbon monoxide toxicity treated with hyperbaric oxygen who developed myocardial infarction have an increased risk of cardiovascular and all-cause mortality lasting at least 7 years after the event (LOE 5[815, 816]).

Patients who develop cardiac arrest caused by carbon monoxide rarely survive to hospital discharge, even if ROSC is achieved; however, 100% oxygen ventilationafter ROSC as early as possible is recommended (Class I) and hyperbaric oxygen therapy may be considered (Class IIb) in these patients because it may reduce the risk of developing persistent or delayed neurological injury. The risks inherent in transporting critically ill post arrest patients to a hyperbaric facility may be significant; it must be weighed against the possibility of benefit on a case-by-case basis. Patients who develop myocardial injury caused by carbon monoxide have an increased risk of cardiac and all-cause mortality lasting at least 7 years after the event; it is reasonable to recommend cardiology follow-up for these patients (Class IIa).

Knowledge Gaps

The epidemiology of cardiac arrest and severe cardiotoxicity caused by carbon monoxide needs further documentation. More precise estimates of the proportion of patients who survive to hospital discharge and who have full neurological recovery following severe carbon monoxide poisoning treated with various interventions are needed. Though challenging, further prospective treatment studies are important and necessary.

6. Cocaine Toxicity

There are no RCTs evaluating conventional versus alternative therapies for the treatment of cardiac arrest caused by cocaine. Evidence is limited to a small case series that demonstrated excellent overall and neurologically intact survival (12/22, 55%) in patients with cocaine-associated cardiac arrest treated with standard therapy (LOE 4[817]).

No studies were found that addressed the treatment of severe cardiotoxicity caused by cocaine; however, human studies have evaluated the treatment of cocaine-associated wide-complex tachycardia and ischemic acute coronary syndrome, as well as coronary artery vasospasm caused by cocaine. Thus the benefit or harm of specific agents in cocaine-associated peri-arrest states (defined as severe hypertension, tachycardia, cocaine-induced arrhythmias) is informed by LOE 5-studies (extrapolation for nonarrest patients and, in some cases, cocaine naive patients).

A single study demonstrated reversal of cocaine-induced coronary artery vasospasm in the coronary catheterization laboratory with phentolamine (LOE 5[818]).

A single study (LOE 5[819]) of patients with cocaine-associated chest pain demonstrated improved

autonomic findings and resolution of chest pain when treated with diazepam. An additional study reported no additional benefit associated with benzodiazepine administration in patients already receiving nitroglycerin (LOE 5[820]).

A retrospective case series of patients hospitalized for acute coronary syndrome associated with cocaine use suggested that there was a decrease in the incidence of death and nonfatal myocardial infarction with the use of β-blockers (LOE 5[821]). A prospective clinical trial in cocaine-naive volunteers suggested that propanolol reduced cocaine-induced tachycardia (LOE 5[822]). A prospective clinical trial demonstrated worsening of cocaine-induced coronary artery vasoconstriction following the administration of propanolol to cocaine-naive research subjects (LOE 5[823]). A retrospective case series of 7 ED and hospitalized patients with cocaine-associated cardiovascular toxicity demonstrated no consistent improvement in hypertension or tachycardia following treatment with esmolol (LOE 5[824]). Three of 7 patients developed apparent adverse effects (hypertension, hypotension, and CNS depression with vomiting).

In a pair of double-blind, crossover studies (LOE 5) of volunteers with a history of crack cocaine use, pretreatment with oral carvedilol[825] or labetolol[826] attenuated the cocaine-induced increases in heart rate and blood pressure compared with placebo, without apparent adverse effect. A prospective clinical trial demonstrated no change in cocaine-induced coronary artery vasoconstriction following the administration of labetolol to cocaine-naive research subjects (LOE 5[827]).

One study of cocaine-naive human volunteers demonstrated resolution of cocaine-induced coronary artery vasospasm with verapamil (LOE 5[828]).

A retrospective case series of 29 patients who received lidocaine in the setting of cocaine-associated myocardial infarction included 8 patients with wide-complex tachycardia (2 sustained, 6 nonsustained) (LOE 5[829]). No patient developed complications and all survived the event.

One study of cocaine-naive human volunteers demonstrated that morphine partially reversed cocaine-induced coronary artery vasospasm (LOE 5[830]).

In a clinical trial of cocaine-naive volunteers administration of nitroglycerin reversed cocaine-induced coronary artery vasospasm (LOE 5[831]). In a prospective observational study of patients presenting with cocaine-associated acute coronary syndrome, 37/83 (45%) of patients treated with nitroglycerin reported reduction in the severity of chest pain, while 5 patients had other forms of clinical improvement (resolution of ischemia based on ECG, 2; hypertension, 2; or congestive heart failure, 1) (LOE 5[832]).

There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest or cardiotoxicity caused by cocaine. In patients with severe cardiovascular toxicity (defined as severe hypertension, tachycardia, and/or cocaine-induced arrhythmias) it may be reasonable to try drugs known to be effective in acute coronary syndromes: α-blockers (phentolamine), benzodiazepines (lorazepam, diazepam), calcium channel blockers (verapamil), morphine, and sublingual nitroglycerin (Class IIb). The available data do not support the use of 1 drug over another.

Knowledge Gaps

Controlled clinical trials are needed to advance the treatment of cardiac arrest and cardiotoxicity due to cocaine. Future studies should evaluate the role of sodium bicarbonate and lidocaine and the safety and effectiveness of other antiarrhythmic drugs, such as amiodarone, in the treatment of cocaine-associated VT.

7. Cyanide Toxicity

There are no randomized controlled trials evaluating conventional versus alternative therapies for the treatment of cardiac arrest caused by cyanide. The use of hydroxocobalamin (alone or with sodium thiosulfate) for cardiac arrest caused by cyanide was suggested by three LOE 4 studies[833-835]. The use of hydroxocobalamin (alone or with sodium thiosulfate) in life-threatening cardiovascular toxicity was supported by seven studies (LOE 5[833-839]).

The use of nitrites plus sodium thiosulfate was suggested by three studies, none of which enrolled cardiac arrest patients (LOE 5[837, 840, 841]); however, one additional study found no benefit to this strategy (LOE 5[842]).

Patients with severe cardiotoxicity (cardiac arrest, cardiovascular instability, metabolic acidosis, or altered mental status) caused by known or suspected cyanide poisoning should receive administration of 100% oxygen as early as possible, and cyanide antidote therapy. In addition to standard resuscitation, initial therapy should include a cyanide scavenger (either intravenous hydroxocobalamin [Cyanokit injection 5g/ normal saline 200ml] or a nitrite – i.e. intravenous sodium nitrite and/or inhaled amylnitrite [inhalation of amyl nitrite 0.25ml or slow intravenous injection of 3% sodium nitrite 10ml]), followed as soon as possible by intravenous sodium thiosulfate [sodium thiosulfate 2g/20mlx6A](Class I). Hydroxocobalamin and nitrites are equally effective but hydroxocobalamin may be safer because it does not cause methemoglobin formation or hypotension. Mouth-to-mouth rescue breathing should not be conducted to avoid secondary cyanide poisoning damage to the rescuer (Class III).

Knowledge Gaps

Controlled clinical trials are needed to advance the treatment of cardiac arrest and cardiotoxicity caused by cyanide. Comparative studies on antidote therapy and health outcomes including neurological outcomes are required to address the question of which combination of drugs is most effective.

8. Tricyclic antidepressant toxicity

There are no randomized controlled trials evaluating conventional versus alternative treatments for cardiac arrest caused by tricyclic antidepressant toxicity. Evidence was limited to a one small case series of cardiac arrest patients, which demonstrated improvement with the use of sodium bicarbonate and adrenaline (LOE 4[843]). Notably, in this case series the pre-arrest use of physostigmine (unavailable

in Japan) was a significant potential confounder.

The evidence for the management of cardiotoxicity caused by tricyclic antidepressant was limited to case reports, case series and animal studies. The use of sodium bicarbonate has been described in two case series (LOE 5[844, 845]) and 6 animal studies (LOE 5[846-851]). The use of hyperventilation was described in one small case series (LOE 5[852]) and one animal study (LOE 5[849]). The evidence for the efficacy of specific antidysrhythmics (lidocaine, magnesium, amiodarone, phenytoin) was limited to negative case reports (LOE 5[849, 853-859]). Specific vasopressors that have been associated with improvement in the treatment of tricyclic-induced hypotension include noradrenaline (LOE 5[855, 860-862]), adrenaline (LOE 5[848, 855, 863]), dopamine (LOE 5[862, 864, 865]), and dobutamine (LOE 5[864]). Diazepam improved seizure control and survival in one animal study (LOE 5[864]). The use of physostigmine (unavailable in Japan) for tricyclic-induced anticholinergic symptoms was not supported by the current literature given the conflicting associations suggested by several case series (LOE 4[850], LOE 5[845, 866, 867]). Limited animal research demonstrates a benefit for intravenous lipid infusions in models of tricyclic toxicity (LOE 5[868, 869]). Anti-tricyclic Fab (unavailable in Japan) has been beneficial in animal models of varying degrees of tricyclic cardiotoxicity (LOE 5[870-875]), and one small human study (LOE 5[876]) provided evidence of safety and pharmacokinetic advantage; however, clinical benefit has yet to be demonstrated clearly.

There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest or cardiotoxicity caused by tricyclic antidepressants.

If patients with cardiotoxicity caused by tricyclic antidepressants (or after resuscitation from cardiac arrest caused by tricyclic antidepressants) show a wide QRS complex (≥0.12sec) administer 1-2mEq/kg of sodium bicarbonate intravenously, and maintain blood pH between 7.45 and 7.55 against tricyclic-induced cardiac conduction abnormalities (Class IIb).

When mechanical ventilation is required respiratory acidosis should be avoided (Class I).

Knowledge Gaps

Controlled clinical trials are needed to advance the treatment of cardiac arrest and cardiotoxicity caused by tricyclic antidepressants. Future trials exploring novel therapies (FAB, intravenous lipid infusions) and the use of sodium bicarbonate for hypotension in the absence of cardiac conductions abnormalities would be helpful.

9. Digoxin Toxicity

There are no randomized controlled trials evaluating conventional versus alternative treatments for cardiac arrest caused by digoxin. Evidence is limited to fourteen studies demonstrating the usefulness of antidigoxin Fab fragments (unavailable in Japan) for severe cardiac glycoside toxicity (LOE 5[877-890]).

There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by digoxin.

Knowledge Gaps

Animal models and controlled clinical trials are needed to advance the treatment of cardiac arrest caused by digoxin. Pharmacokinetic and clinical studies would be helpful to help establish the dosing of anti-digoxin Fab fragment for digoxin cardiotoxicity.

10. Opioid Toxicity

Opioids used in Japan are morphine, fentanyl and others. There are no randomized controlled trials evaluating conventional versus alternative treatments for cardiac arrest caused by opioids. Evidence is limited to studies of mild, moderate, and severe cardiovascular toxicity (LOE 5 for cardiac arrest). Evidence from studies assessing other endpoints (efficacy of naloxone), as well as animal studies, support the use of assisted ventilation before giving naloxone in opioid-poisoned patients with severe cardiopulmonary toxicity (LOE 1[891, 892], LOE 3[893], LOE 4[894-896] , LOE 5[897]).

The use and safety of naloxone is supported by human studies (LOE 4[894-896, 898-901]), as well as those assessing other endpoints (alternate routes of administration) (LOE 1[891], LOE 3[893], LOE 4[902, 903]). Naloxone can be given intravenously (LOE 4[894, 895, 899, 902]), intramuscularly (LOE 1[891], LOE 4[894, 895]), intranasally (LOE 1[891], LOE 4[902]), and into the trachea (LOE 5[904]).

There is insufficient clinical evidence to suggest any change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by opioids. In adults with severe cardiovascular toxicity caused by opioids, ventilation should be assisted using a bag-mask, followed by naloxone, and tracheal intubation if there is no response to naloxone (Class I). Naloxone should be given intravenously or intramuscularly (Class I). Intranasal or tracheal routes may be used if conditions preclude intravenous or intramuscular administration (Class IIb) .

Knowledge Gaps

Animal models and controlled clinical trials are needed to advance the treatment of cardiac arrest caused by opioids. In particular such studies should determine if naloxone has a role in the resuscitation of the cardiac arrest patient pre- or post-ROSC.

■7 Cardiac Arrest during Coronary Catheterization

There are no randomized controlled trials evaluating alternative treatment strategies as opposed to standard care for cardiac arrest during PCI. Evidence is limited to case studies for all interventions.

Three adult human case reports (LOE 4[300, 305, 905]), 2 adult human case series (LOE 4[301, 304, 307]), and 1 animal study (LOE 5[306]) reported that the use of a mechanical chest compression device in cardiac arrest during PCI maintained circulation and enabled the procedure to be completed. Although a small proportion of patients in the case series (13/60) survived to hospital discharge, no randomized controlled or comparison study of this intervention has been performed.

One case study suggested that the use of emergency cardiopulmonary bypass to stabilize and

facilitate emergency coronary angioplasty improved the survival of patients who had cardiac arrest during PCI that was unresponsive to advanced life support (LOE 4[906]).

Five studies (LOE 4[907-909], LOE 5[910, 911]) supported the use of cough CPR as a temporary intervention to maintain adequate blood pressure and level of consciousness in patients who developed ventricular arrhythmias during coronary angiography (CAG) and PCI while definite therapy for malignant arrhythmias was instituted.

There are insufficient data to support or refute the use of mechanical chest compression, cough CPR, or emergency cardiopulmonary bypass to improve outcome of cardiac arrest during PCI. The use of cough CPR may be considered as a temporary intervention in patients who developed ventricular arrhythmias during CAG and PCI while definite therapy was instituted (Class IIb) . The use of emergency cardiopulmonary bypass may be considered in patients who had cardiac arrest during PCI that was unresponsive to ALS (Class IIb) .

Knowledge Gaps

Clinical trials, perhaps initially with historical controls, are needed to advance the treatment of cardiac arrest during PCI.

■8 Cardiac Arrest after Open or Closed Heart Surgery

Eleven studies documented improvement in outcome in patients with cardiac arrest following cardiac surgery who were treated with resternotomy and internal cardiac compression compared with standard protocol, when administered by experienced personnel in intensive care units (LOE 2[912, 913], LOE 4[914-922]). Five studies neither supported nor opposed this finding (LOE 4[923-926] LOE 5[927]). One study documented that the risk of infection was not significant after resternotomies conducted appropriately outside of the operating room (LOE 4[921]) where as 3 studies demonstrated very poor outcomes when resternotomy was performed outside an intensive care unit (ICU) (LOE 2 [912], LOE 4[918], LOE 5[927]).

Six studies supported the use of mechanical circulatory support devices during cardiac arrest following cardiac surgery (LOE 3[922], LOE 4[928-930], LOE 5[931, 932]). Three studies reported equivocal findings (LOE 5[933-935]). No studies opposed use of mechanical circulatory support. Mechanical circulatory support devices in these studies included extra-corporeal membrane oxygenation or cardiopulmonary bypass.

Two case reports described damage to the heart caused possibly by external chest compressions before resternotomy (LOE 5[936, 937]).

One study reported 2 cases that responded to escalating doses of adrenaline (LOE 4[938]). One study reported 18 cases with VF/VT after cardiac surgery (LOE 4[939]).

Resternotomy for patients with cardiac arrest following cardiac surgery should be considered in an appropriately staffed and equipped ICU (Class IIa). Resternotomy performed outside these specialized

environments has poor results. Chest compressions should not be withheld while preparing for emergency resternotomy (Class IIa). Mechanical circulatory support may be considered in the setting of cardiac arrest following cardiac surgery (Class IIb).

There is insufficient evidence to make any recommendations about adrenaline dose, antiarrhythmic use, or any other intervention separate from those recommended in standard protocols.

Knowledge Gaps

Clinical trials are needed to determine the safety and efficacy of mechanical circulatory support devices, chest compressions, and pharmacological adjuncts for the treatment of cardiac arrest after cardiac surgery.

■9 Cardiac arrest caused by cardiac tamponade

Five studies (LOE 5[940-944]) indicate that echocardiographically guided pericardiocentesis is a safe and effective method of relieving tamponade, especially when used in conjunction with a pericardial drain.

One study (LOE 4[945]) documented 39 patients who received prehospital emergency thoracotomy by physicians to treat cardiac arrest from penetrating trauma. Eighteen patients had cardiac tamponade and 4 (22%) survived. Two additional studies (LOE 4[946, 947]) indicated that emergency department thoracotomy may be beneficial in patients who have cardiac arrest associated with cardiac tamponade and may have improved results over standard needle pericardiocentesis. One study (LOE 2[948]) indicated that emergency department thoracotomy may be especially beneficial if gross blood causes clotting and blocking of a pericardiocentesis needle, and two studies (LOE 4[914, 949]) indicated that emergency thoracotomy may also be beneficial in patients who have post procedure complications. But one study (LOE 5[950]) indicated that a more definitive sternotomy or thoracotomy in an operating room may also be beneficial if transportation to the operating room does not introduce significant delay.

Pericardiocentesis guided by echocardiography should be considered for treatment of cardiac arrest associated with cardiac tamponade (Class IIa) while non-image guided pericardiocentesis is an acceptable alternative if echocardiography is not available (Class IIb). Placement of a pericardial drain may be beneficial (Class IIa) and may obviate the need for subsequent operating room treatment. Emergency department thoracotomy and pericardiotomy should be considered as an acceptable alternative to operating room thoracotomy and pericardiotomy for treatment of traumatic cardiac arrest associated with cardiac tamponade (Class IIb), and can be considered for use in the treatment of nontraumatic cardiac arrest when pericardiocentesis is unsuccessful in relieving cardiac tamponade (Class IIb).

Knowledge Gaps

Clinical trials should include patients with pericardial tamponade secondary to nontraumatic arrest and compare safety and efficacy of needle drainage versus thoracotomy and prehospital versus emergency department versus operating room thoracotomy

■10 Cardiac arrest caused by pulmonary embolus

One double-blind randomized control trial (LOE 1[209]) showed no improvement in survival to discharge with the use of tissue plasminogen activator following cardiac arrest with pulseless electrical activity. One randomized controlled trial of fibrinolytics (LOE 1[210]) showed no difference in short- or long-term (30 days) survival or bleeding in patients randomized to receive tenecteplase or placebo during cardiopulmonary resuscitation. Patients with suspected pulmonary embolism were excluded from the study if open thrombolysis was possible in the prehospital setting. Thirty-seven cases with suspected pulmonary embolism were randomized in the trial. Of these, 2 of 15 patients survived when treated with tenecteplase compared with no survivors in the 22 patients in the placebo treated group[210].

One meta-analysis (LOE 2[951]) of eight restrospective cohort studies with a variety of causes of cardiac arrest (pulmonary embolism (2 studies), myocardial infarctions (4 studies), cardiology diseases (1 study) and non-traumatic etiologies (1 study)) demonstrated an increased rate of return to spontaneous circulation, survival to discharge and long-term neurologic function with fibrinolytic but also increased the risk of severe bleeding.

Nine studies of patients with presumed pulmonary embolism or all patients with cardiopulmonary arrests (LOE 1[211], LOE 2[213, 215], LOE 3[216], LOE 4[212, 952-955]), showed improvement with fibrinolysis in return of spontaneous circulation and admission to the hospital or intensive care unit, but no improvement in survival to discharge. Three studies (LOE 2[951], LOE 3[954], LOE 4[953]) showed good neurological function of those that survived after successful fibrinolysis during cardiopulmonary resuscitation.

Fibrinolytic therapy may be considered when pulmonary embolism is suspected as the cause of the cardiac arrest (Class IIb).

Knowledge Gaps

The true incidence of pulmonary embolus as a cause of cardiac arrest is not well documented. Surveillance studies of cardiac arrest noting contributing factors and pathological reports may be helpful to define the impact on public health of this cause of cardiac arrest.

■11 Cardiac arrest caused by electrolyte disorders

1. Magnesium

No studies were identified that addressed specifically the correction of low magnesium concentrations. The presence of a low plasma magnesium concentration was associated with poor prognosis in cardiac arrest patients in three studies (LOE 5[956-958]). The use of magnesium in cardiac arrest was supported by five case series (LOE 4[959-963]), however, five randomised controlled trials (LOE 1[184-187, 964]), and a systematic review (LOE 1[965]) found no benefit from the use of magnesium in cardiac arrest.

2. Calcium

No studies were identified that specifically addressed the treatment of cardiac arrest caused by hypocalcemia or hypercalcemia.

3. Potassium

There are no randomized trials on the treatment of potassium abnormalities in the setting of cardiac arrest. The management of hypokalemia and hyperkalemia in the setting of cardiac arrest is based on case reports and animal studies. One case series of 2 patients reported the resolution of torsades de pointes with potassium replacement in patients with hypokalemia (LOE 4[966]). Several clinical studies (LOE 5[956, 967-969]) report an association between hypokalemia and the development of VF, and an animal study (LOE 5[970]) reported that hypokalemia lowers the VF threshold. In an animal model of cardiac arrest (LOE 5[971]), it was reported that hyperkalemic animals had a higher rate of survival.

Knowledge Gaps

Epidemiological studies are required to document the incidence of cardiac arrests secondary to electrolyte disturbance. Studies are needed to determine the safety and efficacy of current treatments electrolyte replacement strategies during cardiac arrest.

8 Intensive Care after ROSC

In the ILCOR statement of Post Cardiac Arrest Syndrome (PCAS) [972], which was published in 2008, the concept for PCAS included the pathological conditions both before and after ROSC. Since this COSTR 2010 addressed mainly the therapy after ROSC, we have used the term of "Intensive Care After ROSC" rather than "Postresuscitation Care".

■1 Comprehensive Treatment Protocol for Post-Cardiac Arrest Syndrome

RCTs addressing the use of comprehensive treatment protocols after sustained ROSC have not been performed. Several retrospective studies documented increases in survival of comatose patients with sustained ROSC after out-of-hospital cardiac arrest with implementation of a comprehensive treatment protocol (LOE 2[973], LOE 3[905, 974]). Protocols included multiple elements such as therapeutic hypothermia, glucose control, goal-directed hemodynamic optimization, ventilation, and PCI. The independent effect of each element of the bundle treatment could not be established.

A retrospective study showed that if high quality advanced life support in each region is followed by intensive care after ROSC, outcomes in patients with cardiogenic witnessed VF and VT were improved (J-LOE 3[975]).

Knowledge Gaps

Studies are needed to determine whether a comprehensive treatment protocol after cardiac arrest with a sustained ROSC improves short- and long-term outcomes. Future studies should define what interventions other than hypothermia are important inclusions in an effective comprehensive treatment protocol.

■2 Ventilation control

1. Ventilation

There were limited studies that addressed alternative ventilation strategies after ROSC. A human study (LOE 2[976]) and studies in animals (LOE 5[977-980]) indicated that hyperventilation reduced cerebral blood flow after ROSC. But, after prolonged cerebral ischemia, the cerebral blood flow response to hyperventilation and to hypoventilation may be absent (LOE 5[981, 982]). Avoiding hyperventilation, as part of a bundle of care, improved long-term outcome in humans (LOE 3[905]) and in dogs (LOE 5[983]), but the independent effect of ventilation could not be determined. A single animal study suggested that hyperventilation reduced degenerating neurons (LOE 5[984, 985]).

Ventilation with tidal volumes ≤9 mL/kg after ROSC is associated with increased incidence of

atelectasis (LOE 3[986]). In cohort studies, manipulation of tidal volume and PEEP are not associated independently with improved survival in critical patients including those after ROSC (LOE 2[987], LOE 3[986]).

After ROSC , routine hyperventilation leading to hypocapnia should be avoided in order to prevent additional cerebral ischemia (Class III).

2. Controlled Oxygenation

A randomized clinical trial compared ventilation with 30% oxygen or 100% oxygen for the first 60 minutes after ROSC (LOE 1[988]). Mean partial pressure of oxygen in arterial blood (PaO_2) at 60 minutes after ROSC was 110±25 mm Hg in the 30% oxygen group and 343±174 mm Hg in the 100% oxygen group. No statistical difference was detected in serum biomarkers reflecting acute brain injury, survival, or the percentages of good neurological outcome (cerebral performance category 1 or 2) at hospital discharge. A significant subset of patients in this study (30%) who were ventilated with 30% oxygen after ROSC required increased FiO_2 to maintain a pulse oximetry reading of >95%. The study was underpowered to determine efficacy or harm.

A multi-ceter chohort study examining the effects of hyperoxia in hypoxic brain damage after ROSC showed that hyperoxia of more than 300 mmHg was associated with an increase in mortality rate in hospital as compared with that in hypoxia less than 60 mmHg and normoxic state (J-LOE 3[989]).

An animal study demonstrated that ventilation with 100% oxygen (generating PaO_2 >450 mmHg) during the first 15 to 60 minutes after ROSC caused neurodegeneration and worse neurological outcome when compared with FiO_2 titrated to an arterial pulse oximetry reading between 94% and 96% (LOE 5[990]).

Six animal studies demonstrated that ventilation with 100% oxygen (generating PaO_2 >250 to 350 mmHg) during the first 10 to 60 minutes after ROSC causes increased brain lipid peroxidation, increased metabolic dysfunction (glucose utilization and mitochondrial dysfunction), increased neurodegeneration, and worse neurological outcome when compared to ventilation with room air (LOE 5[112, 113, 991-994]). But, these studies addressed only short-term evaluation of outcomes (≤24 hours).

An animal study did not detect any difference in outcome at 72 hours when animals were ventilated with 100% oxygen or room air during CPR and for the first hour after ROSC (LOE 5[114]). Another animal study failed to show any difference in outcome when comparing 2 levels of hypoxic FiO_2 (0.085 and 0.12) with normoxic ventilation when given for the intra- and early (15 minutes) period after ROSC (LOE 5[995]). The study did not demonstrate a significant difference in neurological assessment scores at 72 hours or in survival. The study also failed to show a significant difference in the serum biomarkers of oxidative injury.

An animal study reported that a PaO_2 of 250 to 350 mm Hg during the first 10 minutes of cardiopulmonary bypass reperfusion after cardiac arrest resulted in worse cardiac function compared to a PaO_2 40 to 90 mm Hg during the same time period (LOE 5[996]). A second animal study found no difference in myocardial function or injury when PaO_2 was gradually increased from 40 to 110 mm Hg over the first 15 minutes of cardiopulmonary bypass reperfusion compared to initiating reperfusion at normoxia (LOE 5[997]).

The control of arterial blood oxygen saturation or tension in the early care for patients after ROSC is reasonable (Class IIa).

Knowledge Gaps

Prospective randomized controlled clinical trials are needed to compare ventilation with 100% oxygen versus ventilation with inspired oxygen titrated to an arterial blood oxygen saturation goal (possibly 94% to 96%) for the first hour after sustained ROSC.

■3 Support of the Circulation

1. Hemodynamic Optimization

There are no RCTs addressing early hemodynamic optimization after cardiac arrest. A study suggested that hemodynamic optimization (fluids, s, catecholamines, intra-aortic balloon pump, and PCI) as part of a bundle of interventions improved outcome in comparison with historical controls (LOE 3[905]). The independent effect of early hemodynamic optimization was not assessed in this study. A recent study that included early hemodynamic optimization as part of a post–cardiac arrest treatment bundle was not powered to measure a survival benefit (LOE 3[974]).

Despite limited data, the hemodynamic stabilization according to the pathophysiology of post–cardiac arrest syndrome has a rationale in titrating hemodynamics to optimize organ perfusion.

2. Fluid Therapy

There are no human studies that compare intravenous fluids after ROSC in patients with cardiac dysfunction compared with no intravenous fluids. A small sample human study used intravenous fluid (0.9% saline or lactated Ringer's) as part of early goal-directed therapy in post–cardiac arrest syndrome and found no significant improvements in survival (LOE 5[974]). In an additional before-and-after study (LOE 5), intravenous fluids (0.9% saline, lactated Ringer's, or colloids) were administered as part of a package of care (including PCI and therapeutic hypothermia) that improved survival with favorable neurological outcome in adult patients after ROSC in prehospital or in-hospital settings[905]. The intervention period had a significantly increased positive fluid balance (345 versus 2300 mL). Six human studies showed that rapid infusion of fluids (500 to 3000 mL of 0.9% saline or lactated Ringer's) to induce therapeutic hypothermia after ROSC produced little harm (LOE 5[998-1003]). A human study showed that the deterioration in oxygenation after ROSC was not significantly affected by the infusion of cold 0.9% saline (3427 ±210 mL) (LOE 5[1004]). Three animal studies reported neurological and cardiac protection with the administration of hypertonic fluid compared to normal saline (LOE 5[1005-1007]). An animal study showed an increase in cerebral blood flow with fluid for hemodilution combined with induced hypertension (LOE 5[1008]).

Rapid infusion of cold 0.9% saline or lactated Ringer's appears to be well tolerated when induced therapeutic hypothermia. Based on the pathophysiology of post–cardiac arrest syndrome, it is reasonable to use intravenous fluids as part of a package of post–cardiac arrest care (Class IIa).

3. Cardioactive Drugs

There are no clinical trials that have determined the independent effect of vasopressors and/or inotropes after ROSC on cardiovascular dysfunction and/ or survival to discharge. Four clinical trials have suggested improved survival to discharge with vasopressors or inotropes, but they are underpowered for achiving (LOE 3[905, 974, 1009], LOE 4[1010]). Six experimental studies showed improvement in postresuscitation cardiac dysfunction (left ventricular function) with the administration of cardioactive drugs, such as dobutamine or levosimendan, but none have shown that such improvement in function translates into improved survival (LOE 5[1011-1016]).

There is insufficient evidence to support the routine use of vasopressors and/ or inotropes for improving survival in adult patients with cardiovascular dysfunction after ROSC .

Knowledge Gaps

Specific clinical research is required to investigate whether treatment of post–cardiac arrest cardiovascular dysfunction with vasopressors and/or inotropes will yield incremental beneficial impact on long-term outcomes beyond those achieved with therapeutic hypothermia alone.

4. Antiarrhythmic Drugs

No controlled studies addressed specifically the use of amiodarone, lidocaine, or β-blockers soon after ROSC . One uncontrolled retrospective study did not demonstrate an improvement in 6-month survival when amiodarone or lidocaine was given to patients resuscitated from VF or tachycardia during early (first 72 hours) in-hospital postresuscitation care (LOE 4[1017]). One single prospective nonrandomized study suggested that recurrent VF was reduced and long- and short-term survival were improved in patients treated with β-blockers during electrical storm (LOE 5[613]). One study reported an incidence of approximately 5% for VF or VT in hospitalized post–cardiac arrest patients (LOE 4[1018]). Five RCTs documented consistent improvement in all-cause mortality and sudden death when implantable cardioverter defibrillators were inserted as late, secondary prophylaxis compared with amiodarone or β-blocker administration to patients that survived VF or VT cardiac arrest (LOE 5[1019-1023]).

There are insufficient evidence to support or refute continued administration of amiodarone or lidocaine after ROSC.

Knowledge Gaps

The incidence of recurrent ventricular arrhythmias after hospital admission following survival of cardiac arrest and the effect of therapeutic hypothermia on their incidence during the early phase of the postresuscitation period should be further investigated.

5. Mechanical circulatory support

There are no studies addressing the use of mechanical circulatory support in patients with ROSC but who have cardiovascular dysfunction. A swine study showed worse left ventricular function when an intra-aortic balloon pump was compared with standard treatment including dobutamine after ROSC (LOE 5[1015]). Five studies of nonarrested patients in cardiogenic shock or severe heart failure showed that left ventricular assist device or continuous aortic flow augmentation improved hemodynamics but not survival (LOE 5[1024-1028]). Two case series reported the use of the intraaortic balloon pump in patients with severe myocardial dysfunction after ROSC, but the effect was impossible to isolate from other interventions (LOE 4[905, 1029]).

There is insufficient evidence to support the use of mechanical circulatory support in post–cardiac arrest patients who have cardiovascular dysfunction.

■4 Temperature control

1. Prevention and treatment of hyperthermia

There are no RCTs evaluating the effect of treatment of pyrexia (defined as ≥37.6°C) compared with no temperature control in patients after cardiac arrest. There were eleven studies suggesting an association between pyrexia and poor outcomes (LOE 4[1030-1034], LOE 5[1035-1040]). Patients with cerebrovascular events who developed pyrexia had worsened short- and long-term outcomes (LOE 5[1035-1040]).

Patients who develop hyperthermia after cardiac arrest have a worse prognosis. Despite the lack of evidence, it is reasonable to treat hyperthermia in the post cardiac arrest period (Class IIa).

2. Therapeutic Hypothermia

1) Who to Cool?

All studies of post–cardiac arrest therapeutic hypothermia have included only patients in coma. One trial defined coma as “not responding to verbal commands” (LOE 1[1041]). The other trials defined coma similarly, used the Glasgow Coma Score (GCS) ≤8, or did not provide a clear definition.

A randomized trial (LOE 1[1041]) and a pseudorandomized trial (LOE 2[1042]) demonstrated improved neurological outcome at hospital discharge or at 6 months after hospital discharge in comatose patients after out-of-hospital VF cardiac arrest. Cooling was initiated within minutes to hours after ROSC, and a temperature range of 32 to 34°C was maintained for 12 to 24 hours. Two studies with historical control groups (LOE 3[1043, 1044]) showed improvement in neurological outcome after therapeutic

hypothermia for comatose survivors of VF cardiac arrest. One systematic review demonstrated that conventional cooling methods were more likely to reach a best cerebral performance category score of 1 or 2 (5-point scale where 1 is good recovery and 5 is brain death) with a relative risk of 1.55 (99.5% CI 1.22 to 1.96) and more likely to survive to hospital discharge (relative risk of 1.35 95% CI 1.1 to 1.65) compared with standard postresuscitation care (LOE 1[1045]).

One small (n=30) randomized trial showed reduced plasma lactate values and oxygen extraction ratios in a group (n=16) of comatose survivors after cardiac arrest with asystole or PEA who were cooled with a cooling cap (LOE 1[1046]).

Six studies with historical control groups showed benefit using therapeutic hypothermia in comatose survivors of out-of-hospital cardiac arrest after all-rhythm arrests (LOE 3[905, 1047-1051]). One study with historical controls showed better neurological outcome after VF cardiac arrest but no difference after cardiac arrest from other rhythms (LOE 3[1052]).

Two nonrandomized studies with concurrent controls indicated possible benefit of hypothermia following cardiac arrest from other initial rhythms in- and out-of-hospital (LOE 2[1053, 1054]). One registry study, which included almost 1000 cooled comatose patients following cardiac arrest from all rhythms, showed that survival with good outcome at 6 months was 56% after initial VT/VF, 21% after initial asystole, and 23% after initial PEA (LOE 4[1055]).

A preliminary prospective study about therapeutic hypothermia was performed for 23 patients whose systolic blood pressure more than 90 mmHg and GCS 3 to 5 among 50 patients who did not obtain ROSC after oridinary CPR treated with PCPS and IABP. As a result, 12 patients recovered to good neurological state (J-LOE 4[237]).

Another prospective study about therapeutic hypothermia with PCPS (34 °C for 72 hours, which included patients of starting hypothermia during CPR, with PCI or IABP if necessary) was performed. As a result, the numbers of good neurological outcome decreased when the achieving time to 34 °C from cardiac arrest was delayed (cut-off time of arrest to PCPS: 55.5 minutes in accuracy of 85.4%; PCPS to 34 °C: 21.5 minutes in accuracy of 89.5%) (J-LOE 4[238]).

2) How to Cool?

Nineteen studies indicated that cooling could be initiated safely with intravenous ice-cold fluids (30 mL/kg of saline 0.9% or Ringer's lactate) (LOE 3[905, 974, 1044, 1050, 1052, 1056], LOE 4[998, 999, 1001-1004, 1029, 1055, 1057-1062]). Six studies indicated that cooling with IV cold saline can be initiated in the prehospital phase (LOE 1[1000, 1063], LOE 2[1064], LOE 3[226, 1065]). Thirteen studies documented the use of an intravascular heat exchanger to induce and maintain hypothermia (LOE 2[1053, 1054], LOE 3[905, 974], LOE 4[1001, 1058, 1060, 1066-1071]). Twelve studies documented the use of ice packs and either water- or air-circulating blankets to induce and maintain hypothermia (LOE 2[1053], LOE 3[974, 1044, 1048, 1051, 1052], LOE 4[974, 1060, 1069, 1072-1074]). Seven studies documented the use of ice packs (sometimes combined with wet towels) alone to induce and maintain hypothermia (LOE 2[1042], LOE 3[1043, 1047, 1049], LOE 4[1066, 1068, 1075]). Four studies documented the use of ice packs alone to maintain hypothermia (LOE 3[1056], LOE 4[1029, 1059, 1062]). Seven studies documented the use of cooling blankets or pads alone to induce and maintain hypothermia (LOE 2[1076], LOE 3[1077], LOE 4[1060, 1078-1081]). Eight studies documented the use of water-circulating, gel-coated pads to induce and maintain, or just maintain, hypothermia (LOE 3[905, 1050], LOE 4[1057, 1060,

[1061, 1073, 1079, 1082]). One RCT (LOE 1) used a cold-air tent[1041] and another used a cooling helmet[1046] to induce and maintain hypothermia. In a registry study, cooling was maintained with ice packs (17%), air cooling (8%), circulating water blankets (63%), an intravascular cooling device (16%), and other methods (8%) (LOE 4[1055]).

3) When to Cool?

One registry-based case series of 986 comatose post–cardiac arrest patients suggested that time to initiation of cooling (median 90 minutes; interquartile range IQR 60 to 165 minutes) was not associated with improved neurological outcome postdischarge (LOE 4[1055]). A case series of 49 consecutive comatose post–cardiac arrest patients who were intravascularly cooled after out-of-hospital cardiac arrest also documented that time to target temperature (median 6.8 hours; IQR 4.5 to 9.2 hours) was not an independent predictor of neurological outcome (LOE 4[1071]).

4) The combination of therapeutic hypothermia and primary percutaneous intervention

Five studies indicated that the combination of therapeutic hypothermia and PCI is feasible and safe after cardiac arrest caused by acute myocardial infarction (LOE 3[905, 1056, 1083], LOE 4[1029, 1055]).

Comatose adult patients (not responding in a meaningful way to verbal commands) with spontaneous circulation after out-of-hospital VF cardiac arrest should be cooled to 32 to 34°C for 12 to 24 hours (Class I). Induced hypothermia might also benefit comatose adult patients with spontaneous circulation after out-of-hospital cardiac arrest from a nonshockable rhythm, or cardiac arrest in hospital (Class IIb). Rapid infusion of ice-cold intravenous fluid 30 mL/kg or ice packs are feasible, safe, and simple methods for initially lowering core temperature up to 1.5°C. When intravenous fluids are used to induce hypothermia, additional cooling strategies will be required to maintain hypothermia. Limited available evidence suggests that PCI during therapeutic hypothermia is feasible and safe and may be associated with improved outcome (Class IIb).

Knowledge Gaps

Although the data support cooling to 32°C to 34°C, the optimal temperature has not been determined. Furthermore the optimal method, onset, duration and rewarming rate, and therapeutic window remain unknown. Further investigation is also needed to determine the benefit of post–cardiac arrest therapeutic hypothermia after nonshockable cardiac arrest, in-hospital cardiac arrest, and in children. Clinical and cost comparisons are required of the methods used for inducing and maintaining therapeutic hypothermia in- and out-of-hospital. The safety and efficacy of therapeutic hypothermia during cardiac arrest resuscitation needs to be explored through controlled clinical trials.

■5 Seizure control

No controlled clinical trials directly addressed prophylactic treatment for seizures after cardiac arrest. Five studies documented a 3–44% incidence of seizures after sustained ROSC (LOE 4[306, 1033, 1084-1086]). Two studies reported no difference in neurological outcome after use of single-dose diazepam or magnesium or both; or thiopental given after sustained ROSC (LOE 5[963, 1084]). There are no studies addressing prompt and aggressive treatment after the first seizure occurring after circulation was restored. Seizures in the postarrest period may be refractory to multiple medications (LOE 4[1085, 1087]). There was no reported difference in the occurrence of seizures after sustained ROSC in patients treated with therapeutic hypothermia or with normothermia care (LOE 5[974, 1041]).

There are insufficient data to support or refute the use of specific antiseizure medication in the prevention or treatment of seizures after ROSC.

Knowledge Gaps

Studies need to determine the true incidence of clinical and electrographic seizures in patients after cardiac arrest, particularly in those treated with therapeutic hypothermia.

Clinical trials are required to assess interventions and drugs for the prevention and treatment of seizures. Studies should evaluate whether continuous electroencephalograph (EEG) monitoring to diagnose and treat seizures after cardiac arrest is feasible, interpretable, of prognostic value, and beneficial for patients.

■6 Other Supportive Therapies

1. Blood Glucose Control

One human randomized interventional study that prospectively evaluated strict glucose control ((4–6mmol/L, [72–108mg/dL]) compared with moderate glucose control (6–8mmol/L, [108–144mg/dL]) in patients resuscitated from prehospital cardiac arrest with VF found no survival benefit with strict glucose control (LOE 1[1088]). Five retrospective studies in post–cardiac arrest patients suggested an association of higher glucose levels with increased mortality and worse neurological outcomes, but those findings may be related to other factors (LOE 4[1017, 1033, 1089-1091]). Based on those studies, the suggested target ranges for glucose values have been variable. A good randomized trial of intensive glucose control versus conventional glucose control in the largest number of ICU patients to date reported increased mortality in patients treated with intensive glucose control (LOE 5[1092]). Two meta-analyses of studies of tight glucose control versus conventional glucose control in critically ill patients showed no significant difference in mortality but found tight glucose control was associated with a significantly increased risk of hypoglycemia (LOE 5[1093, 1094]).

Strategies to treat hyperglycemia >10mmol/L (>180mg/dL) should be considered in adult patients with ROSC after cardiac arrest (Class IIb). Hypoglycemia resulting from exceed strict blood glucose control should be avoided.

2. Steroid Therapy

Two observational studies (LOE 2[1095, 1096]). and 2 animal studies (LOE 5[1097, 1098]). failed to demonstrate any benefit or harm from the use of steroids after ROSC . One small, single-center randomized placebo-controlled trial showed benefit from the use of a package of care consisting of vasopressin and dexamethasone in addition to adrenaline during cardiopulmonary resuscitation, combined with the treatment of post–cardiac arrest shock with hydrocortisone in the study group (LOE 1[196]). The complex design of this study makes it impossible to determine the independent effect of any interventions on outcome.

There is insufficient evidence to support the use of corticosteroids for patients after ROSC.

Knowledge Gaps

It is important to determine the incidence of adrenal insufficiency after ROSC. Clinical trials are needed to determine the effect of exogenous steroids administered after cardiac arrest.

3. Hemofiltration

One RCT demonstrated no difference in survival or neurological outcome between groups treated with high-volume hemofiltration (200mL/kg/h for 8h) irrespective of inducing mild hypothermia, and control group without hemofiltration (LOE 1[1099]). The combined hemofiltration-only and hemofiltration-plus-hypothermia groups had increased survival at 6 months after cardiac arrest when compared to controls. One study suggested improved survival and neurological outcome in patients treated with high-volume hemofiltration after ROSC (LOE 2[1100]).

There is insufficient evidence to support the use of hemofiltration in patients after ROSC .

4. Neuroprotective Therapy

One small pilot study in witnessed, out-of-hospital cardiac arrests of presumed cardiac etiology showed improved survival at 3 months when therapeutic hypothermia (35°C) and the oral administration of coenzyme Q10 (250 mg followed by 150 mg TID for 5 days) was compared with therapeutic hypothermia alone; however, there was no difference in neurologically intact survival (LOE 1[1078]).

Four RCTs (LOE 1) using nimodipine[1101, 1102], lidoflazine[1103], or diazepam[964] in out-of-hospital cardiac arrest showed no benefits from any of the drugs when compared with standard care. Two RCTs (LOE 1) using thiopental[1103] or nimodipine[1104] in out-of-hospital cardiac arrest were unable to show any benefits when compared with standard care. A retrospective analysis using glucocorticoids in out-of-hospital cardiac arrest was unable to show any benefits when compared with standard care (LOE 2[1096]).

There are insufficient data to recommend for or against the use of neuroprotective drugs (coenzyme Q10, thiopental, glucocorticoids, nimodipine, lidoflazine, or diazepam) alone or as an adjunct to therapeutic hypothermia in comatose cardiac arrest after ROSC.

Knowledge Gaps

Specific research and larger clinical trials are required on the use of coenzyme Q10 in patients with therapeutic hypothermia of 33°C on neurologically intact survival.

■7 Treatment of Precipitating Causes of Cardiac Arrest

There is insufficient evidence about the benefit offibrinolysis following cardiac arrest in patients with suspected pulmonary embolism is beneficial. Several studies (LOE 5 [212, 213, 216, 1105, 1106]) and a case series (LOE 4[1107]) showed no significant increase in survival to hospital discharge. There was an increase in bleeding complications following fibrinolysis in most of those studies. One study suggested that the risk of major hemorrhage is further increased in patients who have undergone CPR (LOE 5[212]).

Five reviews demonstrated that pulmonary embolectomy after cardiac arrest caused a high mortality rate (LOE 4[1108-1112]). One study showed that percuteneous cardiopulmonary support (PCPS) may be beneficial in the management of shock caused by massive pulmonary embolism (J-LOE 5[1113]). One case series reported outcomes of 7 patients after cardiac arrest caused by pulmonary embolism and they were treated with percutaneous mechanical thrombectomy (LOE 4[952]); 3 patients also received recombinant tissue plasminogen activator. Only 1 of the 7 patients died and pulmonary perfusion was restored in the majority (85.7%).

In patients with diagnosed or suspected pulmonary embolism after ROSC, there is inadequate evidence to recommend for fibrinolytic therapy in addition to heparin. The mortality with surgical embolectomy for suspected or diagnosed pulmonary embolism in cardiac arrest patients is high , so that it should be avoided in patients who have received CPR (Class III), especially with fibrinolytic therapy. There are few data on percutaneous mechanical thromboembolectomy, but it may be beneficial and may be considered in patients sustaining cardiac arrest from a pulmonary embolism who are not candidates for fibrinolytic therapy (Class IIb).

9 Prognostication

■1 Prognostication During Cardiac Arrest

1. End-Tidal CO_2 and Prediction of Outcome

Thirteen studies (LOE P2[135-137, 141, 142, 1114, 1115], LOE P3[1116], LOE P5[99, 139, 1117-1119]) indicated that higher maximal end-tidal CO_2 levels can predict ROSC. Seven studies demonstrate that end-tidal CO_2 values <1.33kPa (10mmHg) obtained after intubation and during CPR efforts are associated with a low probability of survival from cardiac arrest (LOE P2[135-137, 141, 142, 1114, 1115]). Two prospective human studies demonstrated a significant increase in end-tidal CO_2 when ROSC occurs (LOE 5[99, 139]).

Quantitative measurement of end tidal CO_2 may be a safe and effective noninvasive indicator of cardiac output during CPR and may be an early indicator of ROSC in intubated patients (Class IIa). Although low values of end tidal CO_2 are associated with a low probability of survival, there are insufficient data to support a specific cutoff of end tidal CO_2 at different time intervals as a prognostic indicator of outcome during adult cardiac arrest.

Knowledge Gaps

More well-designed prognostic studies of end tidal CO_2 monitoring designed to measure long-term morbidity, mortality, and neurological survivability are recommended.

In future studies the cause of cardiac arrest should be documented. Use of vasopressors and ventilation rates may lower end-tidal CO_2; and this effect should be controlled in future studies. Evaluation of end-tidal CO_2 for prognosis should be repeated with supraglottic airway devices.

2. Ultrasound During Cardiac Arrest

No studies examined the impact of ultrasound or echocardiography on patient outcomes in cardiac arrest specifically. Three studies examined the prognostic value of the presence or absence of sonographic cardiac motion in cardiac arrest (LOE 4[143, 1120, 1121]). One retrospective chart review (LOE 4[1122]) and 1 prospective comparison (LOE 4[1123]) documented the diagnostic accuracy of transesophageal ultrasound in detecting the cause of circulatory collapse. One study documented the frequency of pulmonary embolism in PEA arrest as detected with transesophageal ultrasound (LOE 4[1124]). An additional 2 prospective observational studies examined the use of transthoracic ultrasound by “nonexpert” sonographers to detect pericardial effusion and other causes of PEA (LOE 4[1125], LOE 5[1126]).

Three prospective studies examined ultrasound determination of cardiac standstill as a predictor of clinical outcomes and ROSC in patients in cardiac arrest (LOE 4[143, 1120, 1121]). Absence of cardiac

motion on sonography during resuscitation of patients in cardiac arrest was highly predictive of death: of the 341 patients from the 3 studies, 218 had no detectable cardiac activity and only 2 of those had ROSC (no data on survival to hospital discharge).

There is insufficient evidence to support or refute the routine use of ultrasound or echocardiography to guide cardiac arrest resuscitation.

Knowledge Gaps

Future research should address the role ultrasound (both transesophageal and transtracheal) can perform as a targeted intervention (detection of potential causes, guidance of key procedures) during cardiac arrest resuscitation. With increasing emphasis on uninterrupted chest compressions, there is the potential for harm with the use of transthoracic ultrasound because it often requires interruption of compressions and ventilation to acquire adequate images. This is less of a concern with transesophageal or intracardiac echocardiography.

■2 Prognostication after resuscitation

1. Clinical Examination

In adult patients comatose after cardiac arrest who had not been treated with therapeutic hypothermia, the following parameters predicted poor outcome (CPC 4 or 5) with a false-positive rate (FPR) of 0%: absent vestibulo-ocular reflexes at ≥24 hours [(95% CI 0% to 14%)] (LOE P1[1127, 1128]); absence of pupillary light *and* corneal reflex at 72 hours [(95% CI 0% to 9%)](LOE P1[1129]); GCS <5 at 48 hours (95% CI 0% to 13%) (LOE P1[1130]) and on day 3 (95% CI 0% to 6%) (LOE P2[1131]) and a clinical examination score <15 on day 4 [(95% CI 0% to 18%)](LOE P1[1132]). However, in 1 study an absent motor response (GCS motor=1) at 72 hours after cardiac arrest predicted poor outcome with a FPR of 5% [(95%CI 2% to 9%)](LOE P1[1129]). The presence of myoclonus status in adults was strongly associated with poor outcome (LOE P1[1085, 1129], LOE P3[1087, 1133], LOE P4[1134]), but rare cases of good neurological recovery have been described and accurate diagnosis was problematic[1135-1139].

There are no clinical neurologic signs that reliably predict poor outcome <24 hours after ROSC. In adult patients who are comatose after cardiac arrest, have *not been treated with hypothermia* and have no confounding factors (eg, hypotension, sedatives or neuromuscular blockers), the absence of both pupillary light and corneal reflex at ≥72 hours reliably predicts poor outcome. Absence of vestibulo-ocular reflexes at ≥24 hours and a GCS motor score of 2 or less at ≥72 hours are less reliable. Other clinical signs, including myoclonus, are not recommended for predicting poor outcome (Class III).

2. Biochemical Markers

Serum neuronal-specific enolase (NSE) elevations are associated with poor outcome for comatose patients after cardiac arrest (LOE P1[1140, 1141], LOE P2[1071, 1129, 1132, 1142-1155], LOE P3[1156, 1157]). Although specific cutoff values with a FPR of 0% have been reported, clinical application is limited due to variability in the 0% FPR cutoff values reported among various studies.

Serum S100 elevations are associated with poor outcome for comatose patients after cardiac arrest (LOE P1[1140, 1141], LOE P2[1129, 1132, 1142, 1148, 1150, 1152, 1153, 1158-1163], LOE P3[1156]).

Many other serum markers measured after sustained ROSC have been associated with poor outcome after cardiac arrest, including brain natriuretic peptide (BNP) (LOE P3[1164]), vWF (LOE P3[1165]), ICAM-1 (LOE P3[1165]), procalcitonin (LOE P2[1159]), IL-1ra, RANTES, sTNFRII, IL-6, IL-8 and IL-10 (LOE P3[1166]). However, other studies found no relationship between outcome and serum IL-8 (LOE P1[1158]), and procalcitonin and sTREM-1 (LOE P3[1167]).

Worse outcomes for comatose survivors of cardiac arrest are also associated with increased levels of cerebrospinal fluid (CSF)-CK (LOE P2[1168, 1169]) and cerebrospinal fluid-CKBB (LOE P1[1140, 1141], LOE P2[1143, 1154, 1169, 1170], LOE P3[1171-1173]). However, A study found no relationship between cerebrospinal fluid-CKBB and prognosis (LOE P2[1174]).

Outcomes are also associated with increased cerebrospinal fluid levels of other markers including NSE (LOE P1[1141], LOE P2[1150, 1154]); S100 (LOE P2[1150]), LDH, GOT(LOE P2[1143, 1169]) neurofilament (LOE P3[1175]); and acid phosphatase and lactate (LOE P2[1169]). Cerebrospinal fluid levels of β-D-N-acetylglucosaminidase and pyruvate were not associated with the prognosis of cardiac arrest (LOE P2[1169]).

Evidence does not support the use of serum or cerebrosphinal fluid biomarkers alone as predictors of poor outcomes in comatose patients after cardiac arrest with or without treatment with therapeutic hypothermia. Limitations included small numbers of patients and/or inconsistency in cutoff values for predicting poor outcome.

Knowledge Gaps

Future studies should identify and resolve the heterogeneity of cutoff values used to predict poor outcome with a FPR of zero. Studies also must account for confounders that may alter levels or predictive performance of various markers (eg, hypothermia, underlying disease, pregnancy, intra-aortic balloon pump, brain instrumentation, hemodialyisis, or other organ failure). Studies examining whether biomarkers can be used to monitor ongoing injury and response to therapy may be useful.

3. Electrophysiological Studies (Comatose adult patients after ROSC)

1) Somatosensory evoked potentials

Somatosensory evoked potentials measured between 4 hours and 2 weeks after cardiac arrest were associated with poor outcome in 14 studies (LOE P1[1128, 1129, 1140, 1176-1181], LOE P2[1132], LOE P3[1171,

[1182-1184]). In a meta-analysis of patients not treated with therapeutic hypothermia, the absence of cortical N20 response to median nerve stimulation at 24 to 72 hours after cardiac arrest predicted poor outcome (death or Cerebral Performance Category 3 to 4) with a FPR of 0.7% (95% CI 0.1 to 3.7) (LOE P1[1140]).

2) Abnormal Brain Stem Auditory Evoked Potentials

Abnormal brain stem auditory evoked potentials recorded 1 to 56 days after cardiac arrest in patients not treated with hypothermia predicted poor outcome with a FPR of 0% (95% CI 0 to 14) in 1 LOE P1-study[1177]. Abnormal brainstem auditory evoked potentials recorded 55 to 235 minutes after cardiac arrest before initiation of therapeutic hypothermia predicted poor outcome with a FPR of 0% (95% CI 0 to 32) (LOE P1[1185]). One study found no predictive value with brainstem auditory evoked potentials (LOE P1[1181]). In patients not treated with therapeutic hypothermia, medium-latency auditory evoked potentials predicted poor outcome after cardiac arrest in 1 LOE P1-study with a FPR of 0% (95% CI 0 to14[1177]) and in 1 LOE P3-study[1183]. Auditory N100 and mismatch negativity was also associated with poor outcome in 1 LOE P1-study[1177].

3) Electroencephalography

Electroencephalography predicted poor outcome in comatose survivors of cardiac arrest within 1 week after cardiac arrest in 12 studies (LOE P1[1128, 1129, 1140, 1176, 1186-1188], LOE P3[1189, 1190], LOE P4[1191, 1192], LOE P5[1193]). In a meta-analysis, EEG showing generalized suppression to less than 20μV, burst-suppression pattern associated with generalized epileptic activity, or diffuse periodic complexes on a flat background 12 to 72 hours after sustained ROSC predicted a poor outcome (FPR of 3%, 95% CI 0.9% to 11%) in patients not receiving therapeutic hypothermia (LOE P1[1140]).

No electrophysiological study reliably predicts outcome of comatose patient after cardiac arrest in the first 24 hours treated without therapeutic hypothermia. After 24 hours, bilateral absence of the N20 cortical response to median nerve stimulation predicts poor outcome in comatose cardiac arrest survivors not treated with therapeutic hypothermia. In the absence of confounding circumstances, such as sedatives, hypotension, hypothermia, or hypoxemia, it is reasonable to use unprocessed electroencephalography interpretation (specifically identifying generalized suppression to less than 20 μV, burst suppression pattern with generalized epileptic activity, or diffuse periodic complexes on a flat background) observed between 24 and 72 hours after sustained ROSC to assist the prediction of a poor outcome in comatose survivors of cardiac arrest not treated with hypothermia (Class IIa).

4. Imaging studies

1) Computerized Tomography

There are no LOE P1 or LOE P2 studies that support the use of computerized tomography imaging to predict outcome of comatose cardiac arrest survivors. Use of computerized tomography imaging is supported by twenty-two studies (LOE P3[1194], LOE P4[1195-1205], LOE P5[1206-1213], The timing of

computerized tomography in these studies ranged from 1 hour to 20 days after sustained return of spontaneous circulation. Computerized tomography parameters associated with poor outcome included grey matter to white matter Hounsfield unit ratio <1.22, cerebral atrophy (chronic), low cerebral blood flow, low acetazolamide reactivity, bicaudate ratio, low Hounsfield number in putamen and cortex, low density in basal ganglia and thalamus, diffuse mass effect, and global cortical gray matter density. Overall, these studies were limited by small sample sizes, variable time of imaging (many very late in the course of the event), lack of comparison with a standardized method of prognostication, and early withdrawal of care. Two LOE P3 studies found computerized tomography did not predict outcome[1189, 1214], and one LOE P4 study was neutral in its findings [1215]. The timing of computerized tomography in these studies ranged from <72 hours to 96 hours after return of spontaneous circulation. Computerized tomography parameters not associated with poor outcome included normal scans. Overall, these studies were limited by small sample sizes, imaging performed too early in the clinical course, non-modern computerized tomography imaging, and early withdrawal of care.

2) Magnetic Resonance Imaging

There are no LOE P1 or LOE P2 studies that support the use of magnetic resonance imaging to predict outcome of comatose cardiac arrest survivors. Use of magnetic resonance imaging to predict outcome is supported by thirty-two studies (LOE P3[1216-1220], LOE P4[1195, 1221-1232], LOE P5 [1196, 1206-1208, 1233-1242]). The timing of magnetic resonance imaging in these studies ranged from 1 day to 10 months after sustained return of spontaneous circulation. Magnetic resonance imaging parameters associated with poor outcome included lower gray matter volume, lower hippocampal volume, global cerebral atrophy, higher number of neuroradiologic findings, extensive abnormalities on digital weight imaging, increased lactate on magnetic resonance spectroscopy, hyperintense lesions in basal ganglia, extensive digital weight imaging abnormalities, global apparent diffusion coefficient depression, extensive white matter abnormalities, and cortical laminar enhancement. Overall these studies were limited by small sample sizes, variable time of imaging (many very late in the course of the event), lack of comparison with a standardized method of prognostication, often non-modern magnetic resonance imaging techniques, and early withdrawal of care. One study found that magnetic resonance imaging performed on comatose cardiac arrest survivors 1-47 days after sustained return of spontaneous circulation did not correlate with outcome (LOE P2 [1243]). Magnetic resonance imaging parameters used in this study were leukoaraiosis, cerebral infarcts, and edema. Modern magnetic resonance imaging techniques (i.e. diffusion-weighted imaging) were not used in this study.

3) Single photon emission CT (SPECT)

Single Photon Emission Computed Tomography is supported by three LOE P5 studies[1213, 1242, 1244] and is opposed by one LOE P2 study[1245]. 1219 The timing of single photon emission computed tomography in these studies ranged from 1-23 days after sustain return of spontaneous circulation. Single photon emission computed tomography parameters associated with poor outcome included diminished cerebral blood flow, particularly frontal and temporal, particularly when persistent on repeated imaging. Single photon emission computed tomography parameters not associated with

outcome included the anterior:posterior perfusion ratio. These studies were limited by small samples sizes, variable imaging times, early withdrawal of care, and lack of comparison with a standardized method of prognostication.

4) Cerebral angiography

Cerebral angiography has been reported by one case report (LOE P5[1206]). The timing of cerebral angiography was 1 day after sustained return of spontaneous circulation. Cerebral angiography parameters associated with poor outcome included delayed cerebral circulation time.

5) Transcranial Doppler (TCD)

Transcranial Doppler was evaluated in one study (LOE P4[1232]). The timing of transcranial Doppler in this study ranged from 4 to 120 hours after return of spontaneous circulation. Transcranial Doppler parameters associated with poor outcome included delayed hyperemia. This study was limited by a small sample size, early withdrawal of care, and lack of comparison with a standardized method of prognostication.

6) Nuclear medicine

One case report was supportive of nuclear medicine studies (LOE P5[1208]), but the timing of the images after sustained return of spontaneous circulation was not described. Nuclear medicine parameters associated with poor outcome included abnormal tracer uptake in the cerebral cortices. This case report included only a limited description of the findings and and was further limited lack of comparison with a standardized method of prognostication.

7) Near infra-red spectroscopy:

One study of near infra-red spectroscopy was not supportive (LOE P3[1246]). The timing of near infra-red spectroscopy in this study ranged from 6-24 hours after sustained return of spontaneous circulation. This study was limited by a small sample size, early withdrawal of care, inclusion of non-cardiac arrest patients, and lack of comparison with a standardized method of prognostication.

There is insufficient evidence to recommend the routine use of neuroimaging to predict outcome of adult cardiac arrest survivors.

5. Impact of Therapeutic Hypothermia on Accuracy of Post–Cardiac Arrest Prognostication

Two studies (LOE P1[1133, 1181]) provided evidence that status myoclonus (FPR 0%, 95% CI 0% to 40%), absence of corneal and pupillary reflexes at 3 days postsustained ROSC (FPR 0%, 95% CI 0% to 48%), and bilateral absence of N20 peak on somotosensory evoked potentials at 24 hours postsustained ROSC (FPR 0%, 95% CI 0% to 69%) in patients treated with therapeutic hypothermia

predict poor outcome. One study evaluated somatosensory evoked potential responses in 112 postarrest patients more then 24 hours after cardiac arrest who were treated with hypothermia and found that 35 of 36 patients with bilateral absent N20 cortical response had a poor outcome (FPR 3%, 95% CI 0% to 14%[1247]). One patient with bilaterally absent N20 and another with a barely detectable N20 had a good recovery; both were evaluated at 3 days post–cardiac arrest (LOE P1[1247]). One LOE P1-study[1133] provided evidence that a Glasgow Coma Motor Score of 2 or less at 3 days after sustained ROSC in patients treated with therapeutic hypothermia has a FPR of 14% (95% CI 3% to 44%) for poor outcome. Two studies provided evidence that status epilepticus in postarrest patients treated with hypothermia has a FPR of 7% (95% CI 1% to 25%) to 11.5% (95% CI 3% to 31%) for predicting poor outcome (LOE P2[1248], LOE P3[1190]). One study (LOE P3[1249]) suggested that glial fibrillary acidic protein level >1.0 ng/dL drawn 12 to 48 hours after sustained ROSC predicts poor outcome (defined as CPC score 3 to 5 at 6 months) both in post–cardiac arrest patients treated with normothermia (FPR 0% 95% CI 0% to 27%) or hypothermia (FPR 0% 95% CI 0% to 48%). One study provided evidence that NSE and S-100b protein cutoff values that reliably predict poor outcome are significantly higher in post–cardiac arrest patients treated with hypothermia compared with those not treated with hypothermia (LOE P2[1152]). Two studies prospectively measured NSE in cohorts of patients treated with post–cardiac arrest hypothermia and reported cutoff values for 0% FPR (LOE P2[1250, 1251]): 1 study[1250] reported that all patients with a 48-hour NSE value >33 μg/L had a poor outcome (FPR 0%, 95% CI 0% to 23%); the other study[1251] reported that all patients with a 48-hour NSE >28 μg/L had a poor outcome (FPR 0%, 95% CI 0% to 18%). Variability in 0% FPR cutoff values from these derivation cohorts potentially results from variability among assays and performance sites. In one study of patients treated with therapeutic hypothermia, the BNP cutoff value for a poor neurological outcome was 80 pg/ml (accuracy of 87.2%)(J-LOE 4 [1252]). Two studies examined the utility of bispectral index monitoring in prognosticating poor outcome in post–cardiac arrest patients treated with hypothermia who were under neuromuscular blockade (LOE P1[1188, 1253]). One study reported that an initial bispectral index monitoring score of ≥22 predicted poor outcome with a FPR of 6% (19 patients having a positive test), and a suppression ratio ≥48 predicted poor outcome with a FPR of 7% [(95% CI 1% to 26%)][1254]. The other study reported that a bispectral index monitoring level of 0 at any time in the first 72 hours after cardiac arrest predicted poor outcome with a FPR of 0% [0% to 27%][1188]. Finally, 1 study (LOE P1[1255]) of 111 post–cardiac arrest patients treated with therapeutic hypothermia attempted to validate prognostic criteria proposed by the American Academy of Neurology[1140]. That study demonstrated that clinical examination findings at 36 to 72 hours were unreliable predictors of poor neurological outcome [motor response less than flexion (FPR 16%, 95% CI 6% to 35%); ≥ 1 brainstem reflexes absent (FPR 8%, 95% CI 2% to 25%); early myoclonus (FPR 4%, 95% CI 1% to 19%), while bilaterally absent N20 peak on somatosensory evoked potentials (FPR 0%, 95% CI 0% to 13%) and unreactive electroencephalogram background (FPR 0%, 95% CI 0% to 13%) were the most reliable. A decision rule derived using that dataset demonstrated that the presence of 2 independent predictors of poor neurological outcome (incomplete recovery brainstem reflexes, early myoclonus, unreactive electroencephalogram, and bilaterally absent cortical somatosensory evoked potentials) predicted poor neurological outcome with a FPR of 0% (95% CI 0% to 14%).

There is inadequate evidence to recommend a specific approach to prognosticating poor outcome in

post–cardiac arrest patients treated with therapeutic hypothermia. There are no clinical neurological signs, electrophysiological studies, biomarkers, or imaging modalities that can reliably predict neurological outcome in the first 24 hours after cardiac arrest. Beyond 24 hours, no single parameter for predicting poor neurological outcome in post–cardiac arrest patients treated with hypothermia is without reported false-positives. Based on limited available evidence, potentially reliable prognosticators of poor outcome in patients treated with therapeutic hypothermia after cardiac arrest include bilateral absence of N20 peak on somatosensory evoked potential ≥24 hours after cardiac arrest or unreactive electroencephalogram background at 36 to 72 hours; and the absence of both corneal and pupillary reflexes >72 hours after cardiac arrest. Limited available evidence also suggests that a Glasgow Coma Motor Score of 2 or less at 3 days after sustained ROSC and the presence of status epilepticus are potentially unreliable prognosticators of poor outcome in post–cardiac arrest patients treated with therapeutic hypothermia. Serum biomarkers such as NSE are potentially valuable as adjunctive studies in prognostication of poor outcome in patients treated with hypothermia, but their reliability is limited by the relatively few patients who have been studied and lack of assay standardization. Given the limited available evidence, prognostication for poor outcome should be done at least 72 hours after ROSC (Class IIa), and decisions to limit care should not be made based on the results of a single prognostication tool (Class III).

Knowledge Gaps

Further research is needed to elucidate the impact of therapeutic hypothermia on the accuracy and timing of post–cardiac arrest prognostication tools. Prospective derivation and validation of a clinical decision rule for early prediction of poor outcome in post–cardiac arrest patients treated with or without hypothermia are urgently needed.

■3 Organ Donation

Three studies suggested no difference in functional outcomes of organs transplanted from patients who were determined to be brain dead as a consequence of cardiac arrest when compared with donors who were brain dead from other causes (LOE 2[1256-1258]).

Adult patients who progress to brain death after resuscitation from out-of-hospital cardiac arrest should be considered for organ donation (Class IIa).

1. Koga K, Sata T, Kaku M, Takamoto K, Shigematsu A. Comparison of no airway device, the Guedel-type airway and the Cuffed Oropharyngeal Airway with mask ventilation during manual in-line stabilization. *J Clin Anesth.* 2001;13(1):6-10.
2. Stoneham MD. The nasopharyngeal airway. Assessment of position by fibreoptic laryngoscopy. *Anaesthesia.* 1993;48(7):575-580.
3. Chung CH, Sum CW, Li HL, Cheng KS, Tan PC. Comparison of nasal trauma associated with nasopharyngeal airway applied by nurses and experienced anesthesiologists. *Changgeng Yi Xue Za*

Zhi. 1999;22(4):593-597.

4. Roberts K, Porter K. How do you size a nasopharyngeal airway. *Resuscitation.* 2003;56(1):19-23.
5. Schade K, Borzotta A, Michaels A. Intracranial malposition of nasopharyngeal airway. *J Trauma.* 2000;49(5):967-968.
6. Muzzi DA, Losasso TJ, Cucchiara RF. Complication from a nasopharyngeal airway in a patient with a basilar skull fracture. *Anesthesiology.* 1991;74(2):366-368.
7. Petito SP, Russell WJ. The prevention of gastric inflation--a neglected benefit of cricoid pressure. *Anaesth Intensive Care.* 1988;16(2):139-143.
8. Lawes EG, Campbell I, Mercer D. Inflation pressure, gastric insufflation and rapid sequence induction. *Br J Anaesth.* 1987;59(3):315-318.
9. Salem MR, Wong AY, Mani M, Sellick BA. Efficacy of cricoid pressure in preventing gastric inflation during bag-mask ventilation in pediatric patients. *Anesthesiology.* 1974;40(1):96-98.
10. Moynihan RJ, Brock-Utne JG, Archer JH, Feld LH, Kreitzman TR. The effect of cricoid pressure on preventing gastric insufflation in infants and children. *Anesthesiology.* 1993;78(4):652-656.
11. Allman KG. The effect of cricoid pressure application on airway patency. *J Clin Anesth.* 1995;7(3):197-199.
12. Hocking G, Roberts FL, Thew ME. Airway obstruction with cricoid pressure and lateral tilt. *Anaesthesia.* 2001;56(9):825-828.
13. Mac GPJH, Ball DR. The effect of cricoid pressure on the cricoid cartilage and vocal cords: an endoscopic study in anaesthetised patients. *Anaesthesia.* 2000;55(3):263-268.
14. Georgescu A, Miller JN, Lecklitner ML. The Sellick maneuver causing complete airway obstruction. *Anesth Analg.* 1992;74(3):457-459.
15. Ho AM, Wong W, Ling E, Chung DC, Tay BA. Airway difficulties caused by improperly applied cricoid pressure. *J Emerg Med.* 2001;20(1):29-31.
16. Shorten GD, Alfille PH, Gliklich RE. Airway obstruction following application of cricoid pressure. *J Clin Anesth.* 1991;3(5):403-405.
17. Hartsilver EL, Vanner RG. Airway obstruction with cricoid pressure. *Anaesthesia.* 2000;55(3):208-211.
18. Asai T, Goy RW, Liu EH. Cricoid pressure prevents placement of the laryngeal tube and laryngeal tube-suction II. *Br J Anaesth.* 2007;99(2):282-285.
19. Asai T, Barclay K, Power I, Vaughan RS. Cricoid pressure impedes placement of the laryngeal mask airway and subsequent tracheal intubation through the mask. *Br J Anaesth.* 1994;72(1):47-51.
20. Asai T, Barclay K, Power I, Vaughan RS. Cricoid pressure impedes placement of the laryngeal mask airway. *Br J Anaesth.* 1995;74(5):521-525.
21. Ansermino JM, Blogg CE. Cricoid pressure may prevent insertion of the laryngeal mask airway. *Br J Anaesth.* 1992;69(5):465-467.
22. Aoyama K, Takenaka I, Sata T, Shigematsu A. Cricoid pressure impedes positioning and ventilation through the laryngeal mask airway. *Can J Anaesth.* 1996;43(10):1035-1040.
23. Brimacombe J, White A, Berry A. Effect of cricoid pressure on ease of insertion of the laryngeal mask airway. *Br J Anaesth.* 1993;71(6):800-802.
24. Gabbott DA, Sasada MP. Laryngeal mask airway insertion using cricoid pressure and manual in-line neck stabilisation. *Anaesthesia.* 1995;50(8):674-676.

25. Xue FS, Mao P, Li CW, Xu YC, Yang QY, Liu Y, Liu KP, Sun HT. [Influence of pressure on cricoid on insertion ProSeal laryngeal mask airway and ventilation function]. *Zhongguo Wei Zhong Bing Ji Jiu Yi Xue.* 2007;19(9):532-535.
26. Li CW, Xue FS, Xu YC, Liu Y, Mao P, Liu KP, Yang QY, Zhang GH, Sun HT. Cricoid pressure impedes insertion of, and ventilation through, the ProSeal laryngeal mask airway in anesthetized, paralyzed patients. *Anesth Analg.* 2007;104(5):1195-1198, tables of contents.
27. Turgeon AF, Nicole PC, Trepanier CA, Marcoux S, Lessard MR. Cricoid pressure does not increase the rate of failed intubation by direct laryngoscopy in adults. *Anesthesiology.* 2005;102(2):315-319.
28. McCaul CL, Harney D, Ryan M, Moran C, Kavanagh BP, Boylan JF. Airway management in the lateral position: a randomized controlled trial. *Anesth Analg.* 2005;101(4):1221-1225, table of contents.
29. Vanner RG, Clarke P, Moore WJ, Raftery S. The effect of cricoid pressure and neck support on the view at laryngoscopy. *Anaesthesia.* 1997;52(9):896-900.
30. Asai T, Murao K, Johmura S, Shingu K. Effect of cricoid pressure on the ease of fibrescope-aided tracheal intubation. *Anaesthesia.* 2002;57(9):909-913.
31. McNelis U, Syndercombe A, Harper I, Duggan J. The effect of cricoid pressure on intubation facilitated by the gum elastic bougie. *Anaesthesia.* 2007;62(5):456-459.
32. Harry RM, Nolan JP. The use of cricoid pressure with the intubating laryngeal mask. *Anaesthesia.* 1999;54(7):656-659.
33. Noguchi T, Koga K, Shiga Y, Shigematsu A. The gum elastic bougie eases tracheal intubation while applying cricoid pressure compared to a stylet. *Can J Anaesth.* 2003;50(7):712-717.
34. Asai T, Murao K, Shingu K. Cricoid pressure applied after placement of laryngeal mask impedes subsequent fibreoptic tracheal intubation through mask. *Br J Anaesth.* 2000;85(2):256-261.
35. Smith CE, Boyer D. Cricoid pressure decreases ease of tracheal intubation using fibreoptic laryngoscopy (WuScope System. *Can J Anaesth.* 2002;49(6):614-619.
36. Heath ML, Allagain J. Intubation through the laryngeal mask. A technique for unexpected difficult intubation. *Anaesthesia.* 1991;46(7):545-548.
37. Levitan RM, Kinkle WC, Levin WJ, Everett WW. Laryngeal view during laryngoscopy: a randomized trial comparing cricoid pressure, backward-upward-rightward pressure, and bimanual laryngoscopy. *Ann Emerg Med.* 2006;47(6):548-555.
38. Snider DD, Clarke D, Finucane BT. The "BURP" maneuver worsens the glottic view when applied in combination with cricoid pressure. *Can J Anaesth.* 2005;52(1):100-104.
39. Fanning GL. The efficacy of cricoid pressure in preventing regurgitation of gastric contents. *Anesthesiology.* 1970;32(6):553-555.
40. Salem MR, Wong AY, Fizzotti GF. Efficacy of cricoid pressure in preventing aspiration of gastric contents in paediatric patients. *Br J Anaesth.* 1972;44(4):401-404.
41. Vanner RG, Pryle BJ. Regurgitation and oesophageal rupture with cricoid pressure: a cadaver study. *Anaesthesia.* 1992;47(9):732-735.
42. Strang TI. Does the laryngeal mask airway compromise cricoid pressure? *Anaesthesia.* 1992;47(10):829-831.
43. Salem MR, Joseph NJ, Heyman HJ, Belani B, Paulissian R, Ferrara TP. Cricoid compression is effective in obliterating the esophageal lumen in the presence of a nasogastric tube. *Anesthesiology.*

1985;63(4):443-446.

44. Fenton PM, Reynolds F. Life-saving or ineffective? An observational study of the use of cricoid pressure and maternal outcome in an African setting. *Int J Obstet Anesth.* 2009;18(2):106-110.

45. Wong ML, Carey S, Mader TJ, Wang HE. Time to invasive airway placement and resuscitation outcomes after inhospital cardiopulmonary arrest. *Resuscitation.* 2010;81(2):182-186.

46. Shy BD, Rea TD, Becker LJ, Eisenberg MS. Time to intubation and survival in prehospital cardiac arrest. *Prehosp Emerg Care.* 2004;8(4):394-399.

47. Jennings PA, Cameron P, Walker T, Bernard S, Smith K. Out-of-hospital cardiac arrest in Victoria: rural and urban outcomes. *Med J Aust.* 2006;185(3):135-139.

48. Dumot JA, Burval DJ, Sprung J, Waters JH, Mraovic B, Karafa MT, Mascha EJ, Bourke DL. Outcome of adult cardiopulmonary resuscitations at a tertiary referral center including results of "limited" resuscitations. *Arch Intern Med.* 2001;161(14):1751-1758.

49. Bobrow BJ, Ewy GA, Clark L, Chikani V, Berg RA, Sanders AB, Vadeboncoeur TF, Hilwig RW, Kern KB. Passive oxygen insufflation is superior to bag-valve-mask ventilation for witnessed ventricular fibrillation out-of-hospital cardiac arrest. *Ann Emerg Med.* 2009;54(5):656-662 e651.

50. Stone BJ, Chantler PJ, Baskett PJ. The incidence of regurgitation during cardiopulmonary resuscitation: a comparison between the bag valve mask and laryngeal mask airway. *Resuscitation.* 1998;38(1):3-6.

51. Doerges V, Sauer C, Ocker H, Wenzel V, Schmucker P. Smaller tidal volumes during cardiopulmonary resuscitation: comparison of adult and paediatric self-inflatable bags with three different ventilatory devices. *Resuscitation.* 1999;43(1):31-37.

52. Doerges V, Sauer C, Ocker H, Wenzel V, Schmucker P. Airway management during cardiopulmonary resuscitation--a comparative study of bag-valve-mask, laryngeal mask airway and combitube in a bench model. *Resuscitation.* 1999;41(1):63-69.

53. Dorges V, Ocker H, Wenzel V, Sauer C, Schmucker P. Emergency airway management by non-anaesthesia house officers--a comparison of three strategies. *Emerg Med J.* 2001;18(2):90-94.

54. Genzwuerker HV, Finteis T, Slabschi D, Groeschel J, Ellinger K. Assessment of the use of the laryngeal tube for cardiopulmonary resuscitation in a manikin. *Resuscitation.* 2001;51(3):291-296.

55. Kurola J, Harve H, Kettunen T, Laakso JP, Gorski J, Paakkonen H, Silfvast T. Airway management in cardiac arrest--comparison of the laryngeal tube, tracheal intubation and bag-valve mask ventilation in emergency medical training. *Resuscitation.* 2004;61(2):149-153.

56. Ocker H, Wenzel V, Schmucker P, Dorges V. Effectiveness of various airway management techniques in a bench model simulating a cardiac arrest patient. *J Emerg Med.* 2001;20(1):7-12.

57. Rumball CJ, MacDonald D. The PTL, Combitube, laryngeal mask, and oral airway: a randomized prehospital comparative study of ventilatory device effectiveness and cost-effectiveness in 470 cases of cardiorespiratory arrest. *Prehosp Emerg Care.* 1997;1(1):1-10.

58. Comparison of arterial blood gases of laryngeal mask airway and bag-valve-mask ventilation in out-of-hospital cardiac arrests. *Circ J.* 2009;73(3):490-496.

59. Wiese CH, Bahr J, Bergmann A, Bergmann I, Bartels U, Graf BM. [Reduction in no flow time using a laryngeal tube: comparison to bag-mask ventilation]. *Anaesthesist.* 2008;57(6):589-596.

60. Wiese CH, Bartels U, Schultens A, Steffen T, Torney A, Bahr J, Graf BM. Influence of airway management strategy on "no-flow-time" during an "advanced life support course" for intensive care

nurses - a single rescuer resuscitation manikin study. *BMC Emerg Med.* 2008;8:4.

61. Wiese CH, Bartels U, Schultens A, Steffen T, Torney A, Bahr J, Graf BM. Using a Laryngeal Tube Suction-Device (LTS-D) Reduces the "No Flow Time" in a Single Rescuer Manikin Study. *J Emerg Med.* 2009.
62. Elam JO. Bag-valve-mask O2 ventilation. In: Safar P, Elam JO, eds, eds. *Advances in Cardiopulmonary Resuscitation: The Wolf Creek Conference on Cardiopulmonary Resuscitation*. New York: Springer-Verlag; 1977:73-79.
63. Elling R, Politis J. An evaluation of emergency medical technicians' ability to use manual ventilation devices. *Ann Emerg Med.* 1983;12(12):765-768.
64. Frass M, Frenzer R, Rauscha F, Schuster E, Glogar D. Ventilation with the esophageal tracheal combitube in cardiopulmonary resuscitation. Promptness and effectiveness. *Chest.* 1988;93(4):781-784.
65. Atherton GL, Johnson JC. Ability of paramedics to use the Combitube in prehospital cardiac arrest. *Ann Emerg Med.* 1993;22(8):1263-1268.
66. Rabitsch W, Schellongowski P, Staudinger T, Hofbauer R, Dufek V, Eder B, Raab H, Thell R, Schuster E, Frass M. Comparison of a conventional tracheal airway with the Combitube in an urban emergency medical services system run by physicians. *Resuscitation.* 2003;57(1):27-32.
67. Rumball C, Macdonald D, Barber P, Wong H, Smecher C. Endotracheal intubation and esophageal tracheal Combitube insertion by regular ambulance attendants: a comparative trial. *Prehosp Emerg Care.* 2004;8(1):15-22.
68. Samarkandi AH, Seraj MA, el Dawlatly A, Mastan M, Bakhamees HB. The role of laryngeal mask airway in cardiopulmonary resuscitation. *Resuscitation.* 1994;28(2):103-106.
69. Staudinger T, Brugger S, Watschinger B, Roggla M, Dielacher C, Lobl T, Fink D, Klauser R, Frass M. Emergency intubation with the Combitube: comparison with the endotracheal airway. *Ann Emerg Med.* 1993;22(10):1573-1575.
70. Staudinger T, Brugger S, Roggla M, Rintelen C, Atherton GL, Johnson JC, Frass M. [Comparison of the Combitube with the endotracheal tube in cardiopulmonary resuscitation in the prehospital phase]. *Wien Klin Wochenschr.* 1994;106(13):412-415.
71. Cady CE, Weaver MD, Pirrallo RG, Wang HE. Effect of emergency medical technician-placed Combitubes on outcomes after out-of-hospital cardiopulmonary arrest. *Prehosp Emerg Care.* 2009;13(4):495-499.
72. Verghese C, Prior-Willeard PF, Baskett PJ. Immediate management of the airway during cardiopulmonary resuscitation in a hospital without a resident anaesthesiologist. *Eur J Emerg Med.* 1994;1(3):123-125.
73. Davies PR, Tighe SQ, Greenslade GL, Evans GH. Laryngeal mask airway and tracheal tube insertion by unskilled personnel. *Lancet.* 1990;336(8721):977-979.
74. Deakin CD, Peters R, Tomlinson P, Cassidy M. Securing the prehospital airway: a comparison of laryngeal mask insertion and endotracheal intubation by UK paramedics. *Emerg Med J.* 2005;22(1):64-67.
75. Flaishon R, Sotman A, Ben-Abraham R, Rudick V, Varssano D, Weinbroum AA. Antichemical protective gear prolongs time to successful airway management: a randomized, crossover study in humans. *Anesthesiology.* 2004;100(2):260-266.

76. Pennant JH, Walker MB. Comparison of the endotracheal tube and laryngeal mask in airway management by paramedical personnel. *Anesth Analg.* 1992;74(4):531-534.

77. Reinhart DJ, Simmons G. Comparison of placement of the laryngeal mask airway with endotracheal tube by paramedics and respiratory therapists. *Ann Emerg Med.* 1994;24(2):260-263.

78. Timmermann A, Russo SG, Crozier TA, Eich C, Mundt B, Albrecht B, Graf BM. Novices ventilate and intubate quicker and safer via intubating laryngeal mask than by conventional bag-mask ventilation and laryngoscopy. *Anesthesiology.* 2007;107(4):570-576.

79. Calkins TR, Miller K, Langdorf MI. Success and complication rates with prehospital placement of an esophageal-tracheal combitube as a rescue airway. *Prehosp Disaster Med.* 2006;21(2):97-100.

80. Guyette FX, Wang H, Cole JS. King airway use by air medical providers. *Prehosp Emerg Care.* 2007;11(4):473-476.

81. Tentillier E, Heydenreich C, Cros AM, Schmitt V, Dindart JM, Thicoipe M. Use of the intubating laryngeal mask airway in emergency pre-hospital difficult intubation. *Resuscitation.* 2008;77(1):30-34.

82. Timmermann A, Russo SG, Rosenblatt WH, Eich C, Barwing J, Roessler M, Graf BM. Intubating laryngeal mask airway for difficult out-of-hospital airway management: a prospective evaluation. *Br J Anaesth.* 2007;99(2):286-291.

83. Martin SE, Ochsner MG, Jarman RH, Agudelo WE, Davis FE. Use of the laryngeal mask airway in air transport when intubation fails. *J Trauma.* 1999;47(2):352-357.

84. Ben-Abraham R, Weinbroum AA. Laryngeal mask airway control versus endotracheal intubation by medical personnel wearing protective gear. *Am J Emerg Med.* 2004;22(1):24-26.

85. Wiese CH, Bahr J, Popov AF, Hinz JM, Graf BM. Influence of airway management strategy on "no-flow-time" in a standardized single rescuer manikin scenario (a comparison between LTS-D and I-gel). *Resuscitation.* 2009;80(1):100-103.

86. Abo BN, Hostler D, Wang HE. Does the type of out-of-hospital airway interfere with other cardiopulmonary resuscitation tasks? *Resuscitation.* 2007;72(2):234-239.

87. Wiese CH, Bartels U, Bergmann A, Bergmann I, Bahr J, Graf BM. Using a laryngeal tube during cardiac arrest reduces "no flow time" in a manikin study: a comparison between laryngeal tube and endotracheal tube. *Wien Klin Wochenschr.* 2008;120(7-8):217-223.

88. Gatward JJ, Thomas MJ, Nolan JP, Cook TM. Effect of chest compressions on the time taken to insert airway devices in a manikin. *Br J Anaesth.* 2008;100(3):351-356.

89. Grmec S. Comparison of three different methods to confirm tracheal tube placement in emergency intubation. *Intensive Care Med.* 2002;28(6):701-704.

90. Silvestri S, Ralls GA, Krauss B, Thundiyil J, Rothrock SG, Senn A, Carter E, Falk J. The effectiveness of out-of-hospital use of continuous end-tidal carbon dioxide monitoring on the rate of unrecognized misplaced intubation within a regional emergency medical services system. *Ann Emerg Med.* 2005;45(5):497-503.

91. Takeda T, Tanigawa K, Tanaka H, Hayashi Y, Goto E, Tanaka K. The assessment of three methods to verify tracheal tube placement in the emergency setting. *Resuscitation.* 2003;56(2):153-157.

92. Tanigawa K, Takeda T, Goto E, Tanaka K. The efficacy of esophageal detector devices in verifying tracheal tube placement: a randomized cross-over study of out-of-hospital cardiac arrest patients. *Anesth Analg.* 2001;92(2):375-378.

93. Tanigawa K, Takeda T, Goto E, Tanaka K. Accuracy and reliability of the self-inflating bulb to verify tracheal intubation in out-of-hospital cardiac arrest patients. *Anesthesiology.* 2000;93(6):1432-1436.

94. Ornato JP, Shipley JB, Racht EM, Slovis CM, Wrenn KD, Pepe PE, Almeida SL, Ginger VF, Fotre TV. Multicenter study of a portable, hand-size, colorimetric end-tidal carbon dioxide detection device. *Ann Emerg Med.* 1992;21(5):518-523.

95. Varon AJ, Morrina J, Civetta JM. Clinical utility of a colorimetric end-tidal CO2 detector in cardiopulmonary resuscitation and emergency intubation. *J Clin Monit.* 1991;7(4):289-293.

96. Anton WR, Gordon RW, Jordan TM, Posner KL, Cheney FW. A disposable end-tidal CO2 detector to verify endotracheal intubation. *Ann Emerg Med.* 1991;20(3):271-275.

97. MacLeod BA, Heller MB, Gerard J, Yealy DM, Menegazzi JJ. Verification of endotracheal tube placement with colorimetric end-tidal CO2 detection. *Ann Emerg Med.* 1991;20(3):267-270.

98. Schaller RJ, Huff JS, Zahn A. Comparison of a colorimetric end-tidal CO2 detector and an esophageal aspiration device for verifying endotracheal tube placement in the prehospital setting: a six-month experience. *Prehosp Disaster Med.* 1997;12(1):57-63.

99. Bhende MS, Thompson AE. Evaluation of an end-tidal CO2 detector during pediatric cardiopulmonary resuscitation. *Pediatrics.* 1995;95(3):395-399.

100. Li J. Capnography alone is imperfect for endotracheal tube placement confirmation during emergency intubation. *J Emerg Med.* 2001;20(3):223-229.

101. Pelucio M, Halligan L, Dhindsa H. Out-of-hospital experience with the syringe esophageal detector device. *Acad Emerg Med.* 1997;4(6):563-568.

102. Bozeman WP, Hexter D, Liang HK, Kelen GD. Esophageal detector device versus detection of end-tidal carbon dioxide level in emergency intubation. *Ann Emerg Med.* 1996;27(5):595-599.

103. Mehta KH, Turley A, Peyrasse P, Janes J, Hall JE. An assessment of the ability of impedance respirometry distinguish oesophageal from tracheal intubation. *Anaesthesia.* 2002;57(11):1090-1093.

104. Yong-xing Y, Zhen J, Xia-hui L, et al. A clinical study of impedenance graph in verigying trachea intubation. *Natl Med Journal China.* 2007;87(13):898-901.

105. Absolom M, Roberts R, Bahlmann UB, Hall JE, Armstrong T, Turley A. The use of impedance respirometry to confirm tracheal intubation in children. *Anaesthesia.* 2006;61(12):1145-1148.

106. Kramer-Johansen J, Eilevstjonn J, Olasveengen TM, Tomlinson AE, Dorph E, Steen PA. Transthoracic impedance changes as a tool to detect malpositioned tracheal tubes. *Resuscitation.* 2008;76(1):11-16.

107. Risdal M, Aase SO, Stavland M, Eftestol T. Impedance-based ventilation detection during cardiopulmonary resuscitation. *IEEE Trans Biomed Eng.* 2007;54(12):2237-2245.

108. Pytte M, Olasveengen TM, Steen PA, Sunde K. Misplaced and dislodged endotracheal tubes may be detected by the defibrillator during cardiopulmonary resuscitation. *Acta Anaesthesiol Scand.* 2007;51(6):770-772.

109. Kramer-Johansen J, Wik L, Steen PA. Advanced cardiac life support before and after tracheal intubation--direct measurements of quality. *Resuscitation.* 2006;68(1):61-69.

110. Pellis T, Bisera J, Tang W, Weil MH. Expanding automatic external defibrillators to include automated detection of cardiac, respiratory, and cardiorespiratory arrest. *Crit Care Med.* 2002;30(4 Suppl):S176-178.

111. Losert H, Risdal M, Sterz F, Nysaether J, Kohler K, Eftestol T, Wandaller C, Myklebust H, Uray T, Sodeck G, Laggner AN. Thoracic impedance changes measured via defibrillator pads can monitor ventilation in critically ill patients and during cardiopulmonary resuscitation. *Crit Care Med.* 2006;34(9):2399-2405.

112. Liu Y, Rosenthal RE, Haywood Y, Miljkovic-Lolic M, Vanderhoek JY, Fiskum G. Normoxic ventilation after cardiac arrest reduces oxidation of brain lipids and improves neurological outcome. *Stroke.* 1998;29(8):1679-1686.

113. Zwemer CF, Whitesall SE, D'Alecy LG. Cardiopulmonary-cerebral resuscitation with 100% oxygen exacerbates neurological dysfunction following nine minutes of normothermic cardiac arrest in dogs. *Resuscitation.* 1994;27(2):159-170.

114. Lipinski CA, Hicks SD, Callaway CW. Normoxic ventilation during resuscitation and outcome from asphyxial cardiac arrest in rats. *Resuscitation.* 1999;42(3):221-229.

115. Saissy JM, Boussignac G, Cheptel E, Rouvin B, Fontaine D, Bargues L, Levecque JP, Michel A, Brochard L. Efficacy of continuous insufflation of oxygen combined with active cardiac compression-decompression during out-of-hospital cardiorespiratory arrest. *Anesthesiology.* 2000;92(6):1523-1530.

116. Bertrand C, Hemery F, Carli P, Goldstein P, Espesson C, Ruttimann M, Macher JM, Raffy B, Fuster P, Dolveck F, Rozenberg A, Lecarpentier E, Duvaldestin P, Saissy JM, Boussignac G, Brochard L. Constant flow insufflation of oxygen as the sole mode of ventilation during out-of-hospital cardiac arrest. *Intensive Care Med.* 2006;32(6):843-851.

117. Brochard L, Boussignac G, Adnot S, Bertrand C, Isabey D, Harf A. Efficacy of cardiopulmonary resuscitation using intratracheal insufflation. *Am J Respir Crit Care Med.* 1996;154(5):1323-1329.

118. Steen S, Liao Q, Pierre L, Paskevicius A, Sjoberg T. Continuous intratracheal insufflation of oxygen improves the efficacy of mechanical chest compression-active decompression CPR. *Resuscitation.* 2004;62(2):219-227.

119. Hayes MM, Ewy GA, Anavy ND, Hilwig RW, Sanders AB, Berg RA, Otto CW, Kern KB. Continuous passive oxygen insufflation results in a similar outcome to positive pressure ventilation in a swine model of out-of-hospital ventricular fibrillation. *Resuscitation.* 2007;74(2):357-365.

120. Kern KB, Nelson JR, Norman SA, Milander MM, Hilwig RW. Oxygenation and ventilation during cardiopulmonary resuscitation utilizing continuous oxygen delivery via a modified pharyngeal-tracheal lumened airway. *Chest.* 1992;101(2):522-529.

121. Okamoto K, Morioka T. Transtracheal O2 insufflation (TOI) as an alternative method of ventilation during cardiopulmonary resuscitation. *Resuscitation.* 1990;20(3):253-262.

122. Okamoto K, Kishi H, Choi H, Morioka T. Cardiopulmonary resuscitation without intermittent positive pressure ventilation. *Resuscitation.* 1993;26(3):251-260.

123. Noc M, Weil MH, Tang W, Turner T, Fukui M. Mechanical ventilation may not be essential for initial cardiopulmonary resuscitation. *Chest.* 1995;108(3):821-827.

124. Kellum MJ, Kennedy KW, Ewy GA. Cardiocerebral resuscitation improves survival of patients with out-of-hospital cardiac arrest. *Am J Med.* 2006;119(4):335-340.

125. Kellum MJ, Kennedy KW, Barney R, Keilhauer FA, Bellino M, Zuercher M, Ewy GA. Cardiocerebral resuscitation improves neurologically intact survival of patients with out-of-hospital cardiac arrest. *Ann Emerg Med.* 2008;52(3):244-252.

126. Aufderheide TP, Sigurdsson G, Pirrallo RG, Yannopoulos D, McKnite S, von Briesen C, Sparks CW, Conrad CJ, Provo TA, Lurie KG. Hyperventilation-induced hypotension during cardiopulmonary resuscitation. *Circulation.* 2004;109(16):1960-1965.

127. Abella BS, Edelson DP, Kim S, Retzer E, Myklebust H, Barry AM, O'Hearn N, Hoek TL, Becker LB. CPR quality improvement during in-hospital cardiac arrest using a real-time audiovisual feedback system. *Resuscitation.* 2007;73(1):54-61.

128. Voelckel WG, Lurie KG, Zielinski T, McKnite S, Plaisance P, Wenzel V, Lindner KH. The effects of positive end-expiratory pressure during active compression decompression cardiopulmonary resuscitation with the inspiratory threshold valve. *Anesth Analg.* 2001;92(4):967-974.

129. Kleinsasser A, Lindner KH, Schaefer A, Loeckinger A. Decompression-triggered positive-pressure ventilation during cardiopulmonary resuscitation improves pulmonary gas exchange and oxygen uptake. *Circulation.* 2002;106(3):373-378.

130. Callaham M, Barton C. Prediction of outcome of cardiopulmonary resuscitation from end-tidal carbon dioxide concentration. *Crit Care Med.* 1990;18(4):358-362.

131. Paradis NA, Martin GB, Rivers EP, Goetting MG, Appleton TJ, Feingold M, Nowak RM. Coronary perfusion pressure and the return of spontaneous circulation in human cardiopulmonary resuscitation. *JAMA.* 1990;263(8):1106-1113.

132. Rivers EP, Martin GB, Smithline H, Rady MY, Schultz CH, Goetting MG, Appleton TJ, Nowak RM. The clinical implications of continuous central venous oxygen saturation during human CPR. *Ann Emerg Med.* 1992;21(9):1094-1101.

133. Cantineau JP, Lambert Y, Merckx P, Reynaud P, Porte F, Bertrand C, Duvaldestin P. End-tidal carbon dioxide during cardiopulmonary resuscitation in humans presenting mostly with asystole: a predictor of outcome. *Crit Care Med.* 1996;24(5):791-796.

134. Grmec S, Lah K, Tusek-Bunc K. Difference in end-tidal CO2 between asphyxia cardiac arrest and ventricular fibrillation/pulseless ventricular tachycardia cardiac arrest in the prehospital setting. *Crit Care.* 2003;7(6):R139-144.

135. Grmec S, Kupnik D. Does the Mainz Emergency Evaluation Scoring (MEES) in combination with capnometry (MEESc) help in the prognosis of outcome from cardiopulmonary resuscitation in a prehospital setting? *Resuscitation.* 2003;58(1):89-96.

136. Grmec S, Klemen P. Does the end-tidal carbon dioxide (EtCO2) concentration have prognostic value during out-of-hospital cardiac arrest? *Eur J Emerg Med.* 2001;8(4):263-269.

137. Kolar M, Krizmaric M, Klemen P, Grmec S. Partial pressure of end-tidal carbon dioxide successful predicts cardiopulmonary resuscitation in the field: a prospective observational study. *Crit Care.* 2008;12(5):R115.

138. Steedman DJ, Robertson CE. Measurement of end-tidal carbon dioxide concentration during cardiopulmonary resuscitation. *Arch Emerg Med.* 1990;7(3):129-134.

139. Sehra R, Underwood K, Checchia P. End tidal CO2 is a quantitative measure of cardiac arrest. *Pacing Clin Electrophysiol.* 2003;26(1 Pt 2):515-517.

140. Grmec S, Krizmaric M, Mally S, Kozelj A, Spindler M, Lesnik B. Utstein style analysis of out-of-hospital cardiac arrest--bystander CPR and end expired carbon dioxide. *Resuscitation.* 2007;72(3):404-414.

141. Levine RL, Wayne MA, Miller CC. End-tidal carbon dioxide and outcome of out-of-hospital cardiac

arrest. *N Engl J Med.* 1997;337(5):301-306.

142. Wayne MA, Levine RL, Miller CC. Use of end-tidal carbon dioxide to predict outcome in prehospital cardiac arrest. *Ann Emerg Med.* 1995;25(6):762-767.

143. Salen P, O'Connor R, Sierzenski P, Passarello B, Pancu D, Melanson S, Arcona S, Reed J, Heller M. Can cardiac sonography and capnography be used independently and in combination to predict resuscitation outcomes? *Acad Emerg Med.* 2001;8(6):610-615.

144. Chollet-Xemard C, Combes X, Soupizet F, Jabre P, Penet C, Bertrand C, Margenet A, Marty J. Bispectral index monitoring is useless during cardiac arrest patients' resuscitation. *Resuscitation.* 2009;80(2):213-216.

145. Weiss SJ, Ernst AA, Jones R, Ong M, Filbrun T, Augustin C, Barnum M, Nick TG. Automatic transport ventilator versus bag valve in the EMS setting: a prospective, randomized trial. *South Med J.* 2005;98(10):970-976.

146. Johannigman JA, Branson RD, Johnson DJ, Davis K, Jr., Hurst JM. Out-of-hospital ventilation: bag--valve device vs transport ventilator. *Acad Emerg Med.* 1995;2(8):719-724.

147. Olasveengen TM, Sunde K, Brunborg C, Thowsen J, Steen PA, Wik L. Intravenous drug administration during out-of-hospital cardiac arrest: a randomized trial. *JAMA.* 2009;302(20):2222-2229.

148. Stiell IG, Wells GA, Field B, Spaite DW, Nesbitt LP, De Maio VJ, Nichol G, Cousineau D, Blackburn J, Munkley D, Luinstra-Toohey L, Campeau T, Dagnone E, Lyver M. Advanced cardiac life support in out-of-hospital cardiac arrest. *N Engl J Med.* 2004;351(7):647-656.

149. Dorian P, Cass D, Schwartz B, Cooper R, Gelaznikas R, Barr A. Amiodarone as compared with lidocaine for shock-resistant ventricular fibrillation. *N Engl J Med.* 2002;346(12):884-890.

150. Kudenchuk PJ, Cobb LA, Copass MK, Cummins RO, Doherty AM, Fahrenbruch CE, Hallstrom AP, Murray WA, Olsufka M, Walsh T. Amiodarone for resuscitation after out-of-hospital cardiac arrest due to ventricular fibrillation. *N Engl J Med.* 1999;341(12):871-878.

151. Wenzel V, Lindner KH, Krismer AC, Miller EA, Voelckel WG, Lingnau W. Repeated administration of vasopressin but not epinephrine maintains coronary perfusion pressure after early and late administration during prolonged cardiopulmonary resuscitation in pigs. *Circulation.* 1999;99(10):1379-1384.

152. Rittenberger JC, Menegazzi JJ, Callaway CW. Association of delay to first intervention with return of spontaneous circulation in a swine model of cardiac arrest. *Resuscitation.* 2007;73(1):154-160.

153. Herlitz J, Ekstrom L, Wennerblom B, Axelsson A, Bang A, Holmberg S. Adrenaline in out-of-hospital ventricular fibrillation. Does it make any difference? *Resuscitation.* 1995;29(3):195-201.

154. Holmberg M, Holmberg S, Herlitz J. Low chance of survival among patients requiring adrenaline (epinephrine) or intubation after out-of-hospital cardiac arrest in Sweden. *Resuscitation.* 2002;54(1):37-45.

155. Lindner A, Zierz S. [Differential sciatica pain diagnosis from the neurologic viewpoint]. *Med Klin (Munich).* 1997;92(6):335-343.

156. Wenzel V, Krismer AC, Arntz HR, Sitter H, Stadlbauer KH, Lindner KH. A comparison of vasopressin and epinephrine for out-of-hospital cardiopulmonary resuscitation. *N Engl J Med.* 2004;350(2):105-113.

157. Stiell IG, Hebert PC, Wells GA, Vandemheen KL, Tang AS, Higginson LA, Dreyer JF, Clement C,

Battram E, Watpool I, Mason S, Klassen T, Weitzman BN. Vasopressin versus epinephrine for inhospital cardiac arrest: a randomised controlled trial. *Lancet.* 2001;358(9276):105-109.

158. Aung K, Htay T. Vasopressin for cardiac arrest: a systematic review and meta-analysis. *Arch Intern Med.* 2005;165(1):17-24.

159. Mukoyama T, Kinoshita K, Nagao K, Tanjoh K. Reduced effectiveness of vasopressin in repeated doses for patients undergoing prolonged cardiopulmonary resuscitation. *Resuscitation.* 2009;80(7):755-761.

160. Callaway CW, Hostler D, Doshi AA, Pinchalk M, Roth RN, Lubin J, Newman DH, Kelly LJ. Usefulness of vasopressin administered with epinephrine during out-of-hospital cardiac arrest. *Am J Cardiol.* 2006;98(10):1316-1321.

161. Gueugniaud PY, David JS, Chanzy E, Hubert H, Dubien PY, Mauriaucourt P, Braganca C, Billeres X, Clotteau-Lambert MP, Fuster P, Thiercelin D, Debaty G, Ricard-Hibon A, Roux P, Espesson C, Querellou E, Ducros L, Ecollan P, Halbout L, Savary D, Guillaumee F, Maupoint R, Capelle P, Bracq C, Dreyfus P, Nouguier P, Gache A, Meurisse C, Boulanger B, Lae C, Metzger J, Raphael V, Beruben A, Wenzel V, Guinhouya C, Vilhelm C, Marret E. Vasopressin and epinephrine vs. epinephrine alone in cardiopulmonary resuscitation. *N Engl J Med.* 2008;359(1):21-30.

162. Callaham M, Madsen CD, Barton CW, Saunders CE, Pointer J. A randomized clinical trial of high-dose epinephrine and norepinephrine vs standard-dose epinephrine in prehospital cardiac arrest. *JAMA.* 1992;268(19):2667-2672.

163. Gueugniaud PY, Mols P, Goldstein P, Pham E, Dubien PY, Deweerdt C, Vergnion M, Petit P, Carli P. A comparison of repeated high doses and repeated standard doses of epinephrine for cardiac arrest outside the hospital. European Epinephrine Study Group. *N Engl J Med.* 1998;339(22):1595-1601.

164. Vandycke C, Martens P. High dose versus standard dose epinephrine in cardiac arrest - a meta-analysis. *Resuscitation.* 2000;45(3):161-166.

165. Choux C, Gueugniaud PY, Barbieux A, Pham E, Lae C, Dubien PY, Petit P. Standard doses versus repeated high doses of epinephrine in cardiac arrest outside the hospital. *Resuscitation.* 1995;29(1):3-9.

166. Brown CG, Martin DR, Pepe PE, Stueven H, Cummins RO, Gonzalez E, Jastremski M. A comparison of standard-dose and high-dose epinephrine in cardiac arrest outside the hospital. The Multicenter High-Dose Epinephrine Study Group. *N Engl J Med.* 1992;327(15):1051-1055.

167. Stiell IG, Hebert PC, Weitzman BN, Wells GA, Raman S, Stark RM, Higginson LA, Ahuja J, Dickinson GE. High-dose epinephrine in adult cardiac arrest. *N Engl J Med.* 1992;327(15):1045-1050.

168. Brown DC, Lewis AJ, Criley JM. Asystole and its treatment: the possible role of the parasympathetic nervous system in cardiac arrest. *JACEP.* 1979;8(11):448-452.

169. Lovstad RZ, Granhus G, Hetland S. Bradycardia and asystolic cardiac arrest during spinal anaesthesia: a report of five cases. *Acta Anaesthesiol Scand.* 2000;44(1):48-52.

170. Sorensen M, Engbaek J, Viby-Mogensen J, Guldager H, Molke Jensen F. Bradycardia and cardiac asystole following a single injection of suxamethonium. *Acta Anaesthesiol Scand.* 1984;28(2):232-235.

171. Stueven HA, Tonsfeldt DJ, Thompson BM, Whitcomb J, Kastenson E, Aprahamian C. Atropine in asystole: human studies. *Ann Emerg Med.* 1984;13(9 Pt 2):815-817.

172. Coon GA, Clinton JE, Ruiz E. Use of atropine for brady-asystolic prehospital cardiac arrest. *Ann Emerg Med.* 1981;10(9):462-467.

173. Tortolani AJ, Risucci DA, Powell SR, Dixon R. In-hospital cardiopulmonary resuscitation during asystole. Therapeutic factors associated with 24-hour survival. *Chest.* 1989;96(3):622-626.

174. Stiell IG, Wells GA, Hebert PC, Laupacis A, Weitzman BN. Association of drug therapy with survival in cardiac arrest: limited role of advanced cardiac life support drugs. *Acad Emerg Med.* 1995;2(4):264-273.

175. Engdahl J, Bang A, Lindqvist J, Herlitz J. Can we define patients with no and those with some chance of survival when found in asystole out of hospital? *Am J Cardiol.* 2000;86(6):610-614.

176. Engdahl J, Bang A, Lindqvist J, Herlitz J. Factors affecting short- and long-term prognosis among 1069 patients with out-of-hospital cardiac arrest and pulseless electrical activity. *Resuscitation.* 2001;51(1):17-25.

177. van Walraven C, Stiell IG, Wells GA, Hebert PC, Vandemheen K. Do advanced cardiac life support drugs increase resuscitation rates from in-hospital cardiac arrest? The OTAC Study Group. *Ann Emerg Med.* 1998;32(5):544-553.

178. Japan (SOS-KANTO) Study Group. Atropine Sulfate for Patients With Out-of-Hospital Cardiac Arrest due to Asystole and Pulseless Electrical Activity. *Circ J.* 2011;75(3):580-588.

179. Tahara Y, Kimura K, Kosuge M, Ebina T, Sumita S, Hibi K, Toyama H, Kosuge T, Moriwaki Y, Suzuki N, Sugiyama M, Umemura S. Comparison of nifekalant and lidocaine for the treatment of shock-refractory ventricular fibrillation. *Circ J.* 2006;70(4):442-446.

180. Yoshioka K, Amino M, Morita S, Nakagawa Y, Usui K, Sugimoto A, Matsuzaki A, Deguchi Y, Yamamoto I, Inokuchi S, Ikari Y, Kodama I, Tanabe T. Can nifekalant hydrochloride be used as a first-line drug for cardiopulmonary arrest (CPA)? : comparative study of out-of-hospital CPA with acidosis and in-hospital CPA without acidosis. *Circ J.* 2006;70(1):21-27.

181. Yasuda S, Sawano H, Hazui H, Ukai I, Yokoyama H, Ohashi J, Sase K, Kada A, Nonogi H. Report from J-PULSE multicenter registry of patients with shock-resistant out-of-hospital cardiac arrest treated with nifekalant hydrochloride. *Circ J.* 2010;74(11):2308-2313.

182. Nagao K. Nifekalant hydrochloride for patients with cardiac arrest caused by shockable rhythm. *Circ J.* 2010;74(11):2285-2287.

183. Herlitz J, Ekstrom L, Wennerblom B, Axelsson A, Bang A, Lindkvist J, Persson NG, Holmberg S. Lidocaine in out-of-hospital ventricular fibrillation. Does it improve survival? *Resuscitation.* 1997;33(3):199-205.

184. Allegra J, Lavery R, Cody R, Birnbaum G, Brennan J, Hartman A, Horowitz M, Nashed A, Yablonski M. Magnesium sulfate in the treatment of refractory ventricular fibrillation in the prehospital setting. *Resuscitation.* 2001;49(3):245-249.

185. Thel MC, Armstrong AL, McNulty SE, Califf RM, O'Connor CM. Randomised trial of magnesium in in-hospital cardiac arrest. Duke Internal Medicine Housestaff. *Lancet.* 1997;350(9087):1272-1276.

186. Fatovich DM, Prentice DA, Dobb GJ. Magnesium in cardiac arrest (the magic trial). *Resuscitation.* 1997;35(3):237-241.

187. Hassan TB, Jagger C, Barnett DB. A randomised trial to investigate the efficacy of magnesium sulphate for refractory ventricular fibrillation. *Emerg Med J.* 2002;19(1):57-62.

188. Stueven HA, Thompson BM, Aprahamian C, Tonsfeldt DJ. Calcium chloride: reassessment of use in

asystole. *Ann Emerg Med.* 1984;13(9 Pt 2):820-822.

189. Stueven HA, Thompson B, Aprahamian C, Tonsfeldt DJ, Kastenson EH. The effectiveness of calcium chloride in refractory electromechanical dissociation. *Ann Emerg Med.* 1985;14(7):626-629.

190. Stueven HA, Thompson B, Aprahamian C, Tonsfeldt DJ, Kastenson EH. Lack of effectiveness of calcium chloride in refractory asystole. *Ann Emerg Med.* 1985;14(7):630-632.

191. Gando S, Tedo I, Tujinaga H, Kubota M. Variation in serum ionized calcium on cardiopulmonary resuscitation. *J Anesth.* 1988;2(2):154-160.

192. Harrison EE, Amey BD. The use of calcium in cardiac resuscitation. *Am J Emerg Med.* 1983;1(3):267-273.

193. Stueven H, Thompson BM, Aprahamian C, Darin JC. Use of calcium in prehospital cardiac arrest. *Ann Emerg Med.* 1983;12(3):136-139.

194. White BC. Pulseless idioventricular rhythm during CPR: an indication for massive intravenous bolus glucocorticoids. *JACEP.* 1976;5(6):449-454.

195. White BC, Petinga TJ, Hoehner PJ, Wilson RF. Incidence, etiology, and outcome of pulseless idioventricular rhythm treated with dexamethasone during advanced CPR. *JACEP.* 1979;8(5):188-193.

196. Mentzelopoulos SD, Zakynthinos SG, Tzoufi M, Katsios N, Papastylianou A, Gkisioti S, Stathopoulos A, Kollintza A, Stamataki E, Roussos C. Vasopressin, epinephrine, and corticosteroids for in-hospital cardiac arrest. *Arch Intern Med.* 2009;169(1):15-24.

197. Tsai MS, Huang CH, Chang WT, Chen WJ, Hsu CY, Hsieh CC, Yang CW, Chiang WC, Ma MH, Chen SC. The effect of hydrocortisone on the outcome of out-of-hospital cardiac arrest patients: a pilot study. *Am J Emerg Med.* 2007;25(3):318-325.

198. Paris PM, Stewart RD, Deggler F. Prehospital use of dexamethasone in pulseless idioventricular rhythm. *Ann Emerg Med.* 1984;13(11):1008-1010.

199. Smithline H, Rivers E, Appleton T, Nowak R. Corticosteroid supplementation during cardiac arrest in rats. *Resuscitation.* 1993;25(3):257-264.

200. Dybvik T, Strand T, Steen PA. Buffer therapy during out-of-hospital cardiopulmonary resuscitation. *Resuscitation.* 1995;29(2):89-95.

201. Vukmir RB, Katz L. Sodium bicarbonate improves outcome in prolonged prehospital cardiac arrest. *Am J Emerg Med.* 2006;24(2):156-161.

202. Aufderheide TP, Martin DR, Olson DW, Aprahamian C, Woo JW, Hendley GE, Hargarten KM, Thompson B. Prehospital bicarbonate use in cardiac arrest: a 3-year experience. *Am J Emerg Med.* 1992;10(1):4-7.

203. Suljaga-Pechtel K, Goldberg E, Strickon P, Berger M, Skovron ML. Cardiopulmonary resuscitation in a hospitalized population: prospective study of factors associated with outcome. *Resuscitation.* 1984;12(2):77-95.

204. Bar-Joseph G, Abramson NS, Kelsey SF, Mashiach T, Craig MT, Safar P. Improved resuscitation outcome in emergency medical systems with increased usage of sodium bicarbonate during cardiopulmonary resuscitation. *Acta Anaesthesiol Scand.* 2005;49(1):6-15.

205. Weaver WD, Fahrenbruch CE, Johnson DD, Hallstrom AP, Cobb LA, Copass MK. Effect of epinephrine and lidocaine therapy on outcome after cardiac arrest due to ventricular fibrillation. *Circulation.* 1990;82(6):2027-2034.

206. Skovron ML, Goldberg E, Suljaga-Petchel K. Factors predicting survival for six months after cardiopulmonary resuscitation: multivariate analysis of a prospective study. *Mt Sinai J Med.* 1985;52(4):271-275.

207. Delooz HH, Lewi PJ. Are inter-center differences in EMS-management and sodium-bicarbonate administration important for the outcome of CPR? The Cerebral Resuscitation Study Group. *Resuscitation.* 1989;17 Suppl:S161-172; discussion S199-206.

208. Roberts D, Landolfo K, Light RB, Dobson K. Early predictors of mortality for hospitalized patients suffering cardiopulmonary arrest. *Chest.* 1990;97(2):413-419.

209. Abu-Laban RB, Christenson JM, Innes GD, van Beek CA, Wanger KP, McKnight RD, MacPhail IA, Puskaric J, Sadowski RP, Singer J, Schechter MT, Wood VM. Tissue plasminogen activator in cardiac arrest with pulseless electrical activity. *N Engl J Med.* 2002;346(20):1522-1528.

210. Bottiger BW, Arntz HR, Chamberlain DA, Bluhmki E, Belmans A, Danays T, Carli PA, Adgey JA, Bode C, Wenzel V. Thrombolysis during resuscitation for out-of-hospital cardiac arrest. *N Engl J Med.* 2008;359(25):2651-2662.

211. Fatovich DM, Dobb GJ, Clugston RA. A pilot randomised trial of thrombolysis in cardiac arrest (The TICA trial). *Resuscitation.* 2004;61(3):309-313.

212. Janata K, Holzer M, Kurkciyan I, Losert H, Riedmuller E, Pikula B, Laggner AN, Laczika K. Major bleeding complications in cardiopulmonary resuscitation: the place of thrombolytic therapy in cardiac arrest due to massive pulmonary embolism. *Resuscitation.* 2003;57(1):49-55.

213. Lederer W, Lichtenberger C, Pechlaner C, Kroesen G, Baubin M. Recombinant tissue plasminogen activator during cardiopulmonary resuscitation in 108 patients with out-of-hospital cardiac arrest. *Resuscitation.* 2001;50(1):71-76.

214. Bozeman WP, Kleiner DM, Ferguson KL. Empiric tenecteplase is associated with increased return of spontaneous circulation and short term survival in cardiac arrest patients unresponsive to standard interventions. *Resuscitation.* 2006;69(3):399-406.

215. Stadlbauer KH, Krismer AC, Arntz HR, Mayr VD, Lienhart HG, Bottiger BW, Jahn B, Lindner KH, Wenzel V. Effects of thrombolysis during out-of-hospital cardiopulmonary resuscitation. *Am J Cardiol.* 2006;97(3):305-308.

216. Bottiger BW, Bode C, Kern S, Gries A, Gust R, Glatzer R, Bauer H, Motsch J, Martin E. Efficacy and safety of thrombolytic therapy after initially unsuccessful cardiopulmonary resuscitation: a prospective clinical trial. *Lancet.* 2001;357(9268):1583-1585.

217. Kurkciyan I, Meron G, Sterz F, Janata K, Domanovits H, Holzer M, Berzlanovich A, Bankl HC, Laggner AN. Pulmonary embolism as a cause of cardiac arrest: presentation and outcome. *Arch Intern Med.* 2000;160(10):1529-1535.

218. Ditchey RV, Lindenfeld J. Potential adverse effects of volume loading on perfusion of vital organs during closed-chest resuscitation. *Circulation.* 1984;69(1):181-189.

219. Voorhees WD, 3rd, Ralston SH, Kougias C, Schmitz PM. Fluid loading with whole blood or Ringer's lactate solution during CPR in dogs. *Resuscitation.* 1987;15(2):113-123.

220. Gentile NT, Martin GB, Appleton TJ, Moeggenberg J, Paradis NA, Nowak RM. Effects of arterial and venous volume infusion on coronary perfusion pressures during canine CPR. *Resuscitation.* 1991;22(1):55-63.

221. Bender R, Breil M, Heister U, Dahmen A, Hoeft A, Krep H, Fischer M. Hypertonic saline during

CPR: Feasibility and safety of a new protocol of fluid management during resuscitation. *Resuscitation.* 2007;72(1):74-81.

222. Breil M, Krep H, Sinn D, Hagendorff A, Dahmen A, Eichelkraut W, Hoeft A, Fischer M. Hypertonic saline improves myocardial blood flow during CPR, but is not enhanced further by the addition of hydroxy ethyl starch. *Resuscitation.* 2003;56(3):307-317.

223. Bruel C, Parienti JJ, Marie W, Arrot X, Daubin C, Du Cheyron D, Massetti M, Charbonneau P. Mild hypothermia during advanced life support: a preliminary study in out-of-hospital cardiac arrest. *Crit Care.* 2008;12(1):R31.

224. D'Alecy LG, Lundy EF, Barton KJ, Zelenock GB. Dextrose containing intravenous fluid impairs outcome and increases death after eight minutes of cardiac arrest and resuscitation in dogs. *Surgery.* 1986;100(3):505-511.

225. Fischer M, Dahmen A, Standop J, Hagendorff A, Hoeft A, Krep H. Effects of hypertonic saline on myocardial blood flow in a porcine model of prolonged cardiac arrest. *Resuscitation.* 2002;54(3):269-280.

226. Kamarainen A, Virkkunen I, Tenhunen J, Yli-Hankala A, Silfvast T. Prehospital induction of therapeutic hypothermia during CPR: a pilot study. *Resuscitation.* 2008;76(3):360-363.

227. Krep H, Breil M, Sinn D, Hagendorff A, Hoeft A, Fischer M. Effects of hypertonic versus isotonic infusion therapy on regional cerebral blood flow after experimental cardiac arrest cardiopulmonary resuscitation in pigs. *Resuscitation.* 2004;63(1):73-83.

228. Longstreth WT, Jr., Copass MK, Dennis LK, Rauch-Matthews ME, Stark MS, Cobb LA. Intravenous glucose after out-of-hospital cardiopulmonary arrest: a community-based randomized trial. *Neurology.* 1993;43(12):2534-2541.

229. Miclescu A, Basu S, Wiklund L. Methylene blue added to a hypertonic-hyperoncotic solution increases short-term survival in experimental cardiac arrest. *Crit Care Med.* 2006;34(11):2806-2813.

230. Nordmark J, Rubertsson S. Induction of mild hypothermia with infusion of cold (4 degrees C) fluid during ongoing experimental CPR. *Resuscitation.* 2005;66(3):357-365.

231. Nozari A, Safar P, Stezoski SW, Wu X, Kostelnik S, Radovsky A, Tisherman S, Kochanek PM. Critical time window for intra-arrest cooling with cold saline flush in a dog model of cardiopulmonary resuscitation. *Circulation.* 2006;113(23):2690-2696.

232. Ujhelyi MR, Winecoff AP, Schur M, Frede T, Bottorff MB, Gabel M, Markel ML. Influence of hypertonic saline solution infusion on defibrillation efficacy. *Chest.* 1996;110(3):784-790.

233. Riter HG, Brooks LA, Pretorius AM, Ackermann LW, Kerber RE. Intra-arrest hypothermia: both cold liquid ventilation with perfluorocarbons and cold intravenous saline rapidly achieve hypothermia, but only cold liquid ventilation improves resumption of spontaneous circulation. *Resuscitation.* 2009;80(5):561-566.

234. Chen YS, Lin JW, Yu HY, Ko WJ, Jerng JS, Chang WT, Chen WJ, Huang SC, Chi NH, Wang CH, Chen LC, Tsai PR, Wang SS, Hwang JJ, Lin FY. Cardiopulmonary resuscitation with assisted extracorporeal life-support versus conventional cardiopulmonary resuscitation in adults with in-hospital cardiac arrest: an observational study and propensity analysis. *Lancet.* 2008;372(9638):554-561.

235. Tanno K, Itoh Y, Takeyama Y, Nara S, Mori K, Asai Y. Utstein style study of cardiopulmonary bypass after cardiac arrest. *Am J Emerg Med.* 2008;26(6):649-654.

236. Chen YS, Yu HY, Huang SC, Lin JW, Chi NH, Wang CH, Wang SS, Lin FY, Ko WJ. Extracorporeal membrane oxygenation support can extend the duration of cardiopulmonary resuscitation. *Crit Care Med.* 2008;36(9):2529-2535.

237. Nagao K, Hayashi N, Kanmatsuse K, Arima K, Ohtsuki J, Kikushima K, Watanabe I. Cardiopulmonary cerebral resuscitation using emergency cardiopulmonary bypass, coronary reperfusion therapy and mild hypothermia in patients with cardiac arrest outside the hospital. *J Am Coll Cardiol.* 2000;36(3):776-783.

238. Nagao K, Kikushima K, Watanabe K, Tachibana E, Tominaga Y, Tada K, Ishii M, Chiba N, Kasai A, Soga T, Matsuzaki M, Nishikawa K, Tateda Y, Ikeda H, Yagi T. Early induction of hypothermia during cardiac arrest improves neurological outcomes in patients with out-of-hospital cardiac arrest who undergo emergency cardiopulmonary bypass and percutaneous coronary intervention. *Circ J.* 2010;74(1):77-85.

239. Wik L, Kramer-Johansen J, Myklebust H, Sorebo H, Svensson L, Fellows B, Steen PA. Quality of cardiopulmonary resuscitation during out-of-hospital cardiac arrest. *JAMA.* 2005;293(3):299-304.

240. Sack JB, Kesselbrenner MB, Bregman D. Survival from in-hospital cardiac arrest with interposed abdominal counterpulsation during cardiopulmonary resuscitation. *JAMA.* 1992;267(3):379-385.

241. Sack JB, Kesselbrenner MB, Jarrad A. Interposed abdominal compression-cardiopulmonary resuscitation and resuscitation outcome during asystole and electromechanical dissociation. *Circulation.* 1992;86(6):1692-1700.

242. Mateer JR, Stueven HA, Thompson BM, Aprahamian C, Darin JC. Pre-hospital IAC-CPR versus standard CPR: paramedic resuscitation of cardiac arrests. *Am J Emerg Med.* 1985;3(2):143-146.

243. Barranco F, Lesmes A, Irles JA, Blasco J, Leal J, Rodriguez J, Leon C. Cardiopulmonary resuscitation with simultaneous chest and abdominal compression: comparative study in humans. *Resuscitation.* 1990;20(1):67-77.

244. Ward KR, Sullivan RJ, Zelenak RR, Summer WR. A comparison of interposed abdominal compression CPR and standard CPR by monitoring end-tidal PCO2. *Ann Emerg Med.* 1989;18(8):831-837.

245. Berryman CR, Phillips GM. Interposed abdominal compression-CPR in human subjects. *Ann Emerg Med.* 1984;13(4):226-229.

246. Adams CP, Martin GB, Rivers EP, Ward KR, Smithline HA, Rady MY. Hemodynamics of interposed abdominal compression during human cardiopulmonary resuscitation. *Acad Emerg Med.* 1994;1(5):498-502.

247. McDonald JL. Effect of interposed abdominal compression during CPR on central arterial and venous pressures. *Am J Emerg Med.* 1985;3(2):156-159.

248. Stiell IG, Hebert PC, Wells GA, Laupacis A, Vandemheen K, Dreyer JF, Eisenhauer MA, Gibson J, Higginson LA, Kirby AS, Mahon JL, Maloney JP, Weitzman BN. The Ontario trial of active compression-decompression cardiopulmonary resuscitation for in-hospital and prehospital cardiac arrest. *JAMA.* 1996;275(18):1417-1423.

249. Mauer D, Schneider T, Dick W, Withelm A, Elich D, Mauer M. Active compression-decompression resuscitation: a prospective, randomized study in a two-tiered EMS system with physicians in the field. *Resuscitation.* 1996;33(2):125-134.

250. Goralski M, Villeger JL, Cami G, Linassier P, Guilles-Des-Buttes P, Fabbri P, Venot P, Tazarourte K,

Cami M. Evaluation of active compression-decompression cardiopulmonary resuscitation in out-of-hospital cardiac arrest. *Reanimation Urgences.* 1998;7(5):543-550.

251. Skogvoll E, Wik L. Active compression-decompression cardiopulmonary resuscitation: a population-based, prospective randomised clinical trial in out-of-hospital cardiac arrest. *Resuscitation.* 1999;42(3):163-172.

252. Lafuente-Lafuente C, Melero-Bascones M. Active chest compression-decompression for cardiopulmonary resuscitation. *Cochrane Database Syst Rev.* 2004(2):CD002751.

253. Nolan J, Smith G, Evans R, McCusker K, Lubas P, Parr M, Baskett P. The United Kingdom pre-hospital study of active compression-decompression resuscitation. *Resuscitation.* 1998;37(2):119-125.

254. Schwab TM, Callaham ML, Madsen CD, Utecht TA. A randomized clinical trial of active compression-decompression CPR vs standard CPR in out-of-hospital cardiac arrest in two cities. *JAMA.* 1995;273(16):1261-1268.

255. Luiz T, Ellinger K, Denz C. Active compression-decompression cardiopulmonary resuscitation does not improve survival in patients with prehospital cardiac arrest in a physician-manned emergency medical system. *J Cardiothorac Vasc Anesth.* 1996;10(2):178-186.

256. Plaisance P, Adnet F, Vicaut E, Hennequin B, Magne P, Prudhomme C, Lambert Y, Cantineau JP, Leopold C, Ferracci C, Gizzi M, Payen D. Benefit of active compression-decompression cardiopulmonary resuscitation as a prehospital advanced cardiac life support. A randomized multicenter study. *Circulation.* 1997;95(4):955-961.

257. Plaisance P, Lurie KG, Vicaut E, Adnet F, Petit JL, Epain D, Ecollan P, Gruat R, Cavagna P, Biens J, Payen D. A comparison of standard cardiopulmonary resuscitation and active compression-decompression resuscitation for out-of-hospital cardiac arrest. French Active Compression-Decompression Cardiopulmonary Resuscitation Study Group. *N Engl J Med.* 1999;341(8):569-575.

258. Cohen TJ, Goldner BG, Maccaro PC, Ardito AP, Trazzera S, Cohen MB, Dibs SR. A comparison of active compression-decompression cardiopulmonary resuscitation with standard cardiopulmonary resuscitation for cardiac arrests occurring in the hospital. *N Engl J Med.* 1993;329(26):1918-1921.

259. Lurie KG, Shultz JJ, Callaham ML, Schwab TM, Gisch T, Rector T, Frascone RJ, Long L. Evaluation of active compression-decompression CPR in victims of out-of-hospital cardiac arrest. *JAMA.* 1994;271(18):1405-1411.

260. Tucker KJ, Galli F, Savitt MA, Kahsai D, Bresnahan L, Redberg RF. Active compression-decompression resuscitation: effect on resuscitation success after in-hospital cardiac arrest. *J Am Coll Cardiol.* 1994;24(1):201-209.

261. He Q, Wan Z, Wang L. [Random control trial of the efficacy of cardiopump on pre-hospital cardiac arrest]. *Zhongguo Wei Zhong Bing Ji Jiu Yi Xue.* 2003;15(5):292-294.

262. Takino M, Okada Y. The optimum timing of resuscitative thoracotomy for non-traumatic out-of-hospital cardiac arrest. *Resuscitation.* 1993;26(1):69-74.

263. Hachimi-Idrissi S, Leeman J, Hubloue Y, Huyghens L, Corne L. Open chest cardiopulmonary resuscitation in out-of-hospital cardiac arrest. *Resuscitation.* 1997;35(2):151-156.

264. Angelos MG, DeBehnke DJ, Leasure JE. Arterial pH and carbon dioxide tension as indicators of tissue perfusion during cardiac arrest in a canine model. *Crit Care Med.* 1992;20(9):1302-1308.

265. Arai T, Dote K, Tsukahara I, Nitta K, Nagaro T. Cerebral blood flow during conventional, new and open-chest cardio-pulmonary resuscitation in dogs. *Resuscitation.* 1984;12(2):147-154.

266. Barnett WM, Alifimoff JK, Paris PM, Stewart RD, Safar P. Comparison of open-chest cardiac massage techniques in dogs. *Ann Emerg Med.* 1986;15(4):408-411.

267. Bartlett RL, Stewart NJ, Jr., Raymond J, Anstadt GL, Martin SD. Comparative study of three methods of resuscitation: closed-chest, open-chest manual, and direct mechanical ventricular assistance. *Ann Emerg Med.* 1984;13(9 Pt 2):773-777.

268. Benson DM, O'Neil B, Kakish E, Erpelding J, Alousi S, Mason R, Piper D, Rafols J. Open-chest CPR improves survival and neurologic outcome following cardiac arrest. *Resuscitation.* 2005;64(2):209-217.

269. Bircher N, Safar P. Cerebral preservation during cardiopulmonary resuscitation. *Crit Care Med.* 1985;13(3):185-190.

270. DeBehnke DJ, Angelos MG, Leasure JE. Comparison of standard external CPR, open-chest CPR, and cardiopulmonary bypass in a canine myocardial infarct model. *Ann Emerg Med.* 1991;20(7):754-760.

271. Emerman CL, Pinchak AC, Hancock D, Hagen JF. Effect of injection site on circulation times during cardiac arrest. *Crit Care Med.* 1988;16(11):1138-1141.

272. Fleisher G, Sagy M, Swedlow DB, Belani K. Open- versus closed-chest cardiac compressions in a canine model of pediatric cardiopulmonary resuscitation. *Am J Emerg Med.* 1985;3(4):305-310.

273. Jackson RE, Joyce K, Danosi SF, White BC, Vigor D, Hoehner TJ. Blood flow in the cerebral cortex during cardiac resuscitation in dogs. *Ann Emerg Med.* 1984;13(9 Pt 1):657-659.

274. Kern KB, Sanders AB, Badylak SF, Janas W, Carter AB, Tacker WA, Ewy GA. Long-term survival with open-chest cardiac massage after ineffective closed-chest compression in a canine preparation. *Circulation.* 1987;75(2):498-503.

275. Kern KB, Sanders AB, Janas W, Nelson JR, Badylak SF, Babbs CF, Tacker WA, Ewy GA. Limitations of open-chest cardiac massage after prolonged, untreated cardiac arrest in dogs. *Ann Emerg Med.* 1991;20(7):761-767.

276. Raessler KL, Kern KB, Sanders AB, Tacker WA, Jr., Ewy GA. Aortic and right atrial systolic pressures during cardiopulmonary resuscitation: a potential indicator of the mechanism of blood flow. *Am Heart J.* 1988;115(5):1021-1029.

277. Redding JS, Cozine RA. A comparison of open-chest and closed-chest cardiac massage in dogs. *Anesthesiology.* 1961;22:280-285.

278. Rubertsson S, Grenvik A, Wiklund L. Blood flow and perfusion pressure during open-chest versus closed-chest cardiopulmonary resuscitation in pigs. *Crit Care Med.* 1995;23(4):715-725.

279. Rubertsson S, Grenvik A, Zemgulis V, Wiklund L. Systemic perfusion pressure and blood flow before and after administration of epinephrine during experimental cardiopulmonary resuscitation. *Crit Care Med.* 1995;23(12):1984-1996.

280. Sanders AB, Kern KB, Ewy GA, Atlas M, Bailey L. Improved resuscitation from cardiac arrest with open-chest massage. *Ann Emerg Med.* 1984;13(9 Pt 1):672-675.

281. Sanders AB, Kern KB, Atlas M, Bragg S, Ewy GA. Importance of the duration of inadequate coronary perfusion pressure on resuscitation from cardiac arrest. *J Am Coll Cardiol.* 1985;6(1):113-118.

282. Weiser FM, Adler LN, Kuhn LA. Hemodynamic effects of closed and open chest cardiac resuscitation in normal dogs and those with acute myocardial infarction. *Am J Cardiol.* 1962;10:555-561.

283. Hallstrom A, Rea TD, Sayre MR, Christenson J, Anton AR, Mosesso VN, Jr., Van Ottingham L, Olsufka M, Pennington S, White LJ, Yahn S, Husar J, Morris MF, Cobb LA. Manual chest compression vs use of an automated chest compression device during resuscitation following out-of-hospital cardiac arrest: a randomized trial. *JAMA.* 2006;295(22):2620-2628.

284. Paradis NA, Young G, Lemeshow S, Brewer JE, Halperin HR. Inhomogeneity and temporal effects in AutoPulse Assisted Prehospital International Resuscitation--an exception from consent trial terminated early. *Am J Emerg Med.* 2010;28(4):391-398.

285. Steinmetz J, Barnung S, Nielsen SL, Risom M, Rasmussen LS. Improved survival after an out-of-hospital cardiac arrest using new guidelines. *Acta Anaesthesiol Scand.* 2008;52(7):908-913.

286. Casner M, Andersen D, Isaacs SM. The impact of a new CPR assist device on rate of return of spontaneous circulation in out-of-hospital cardiac arrest. *Prehosp Emerg Care.* 2005;9(1):61-67.

287. Ong ME, Ornato JP, Edwards DP, Dhindsa HS, Best AM, Ines CS, Hickey S, Clark B, Williams DC, Powell RG, Overton JL, Peberdy MA. Use of an automated, load-distributing band chest compression device for out-of-hospital cardiac arrest resuscitation. *JAMA.* 2006;295(22):2629-2637.

288. Timerman S, Cardoso LF, Ramires JA, Halperin H. Improved hemodynamic performance with a novel chest compression device during treatment of in-hospital cardiac arrest. *Resuscitation.* 2004;61(3):273-280.

289. Ong ME, Annathurai A, Shahidah A, Leong BS, Ong VY, Tiah L, Ang SH, Yong KL, Sultana P. Cardiopulmonary resuscitation interruptions with use of a load-distributing band device during emergency department cardiac arrest. *Ann Emerg Med.* 2010;56(3):233-241.

290. Tomte O, Sunde K, Lorem T, Auestad B, Souders C, Jensen J, Wik L. Advanced life support performance with manual and mechanical chest compressions in a randomized, multicentre manikin study. *Resuscitation.* 2009;80(10):1152-1157.

291. Wirth S, Korner M, Treitl M, Linsenmaier U, Leidel BA, Jaschkowitz T, Reiser MF, Kanz KG. Computed tomography during cardiopulmonary resuscitation using automated chest compression devices--an initial study. *Eur Radiol.* 2009;19(8):1857-1866.

292. Taylor GJ, Rubin R, Tucker M, Greene HL, Rudikoff MT, Weisfeldt ML. External cardiac compression. A randomized comparison of mechanical and manual techniques. *JAMA.* 1978;240(7):644-646.

293. Ward KR, Menegazzi JJ, Zelenak RR, Sullivan RJ, McSwain NE, Jr. A comparison of chest compressions between mechanical and manual CPR by monitoring end-tidal PCO2 during human cardiac arrest. *Ann Emerg Med.* 1993;22(4):669-674.

294. McDonald JL. Systolic and mean arterial pressures during manual and mechanical CPR in humans. *Ann Emerg Med.* 1982;11(6):292-295.

295. Dickinson ET, Verdile VP, Schneider RM, Salluzzo RF. Effectiveness of mechanical versus manual chest compressions in out-of-hospital cardiac arrest resuscitation: a pilot study. *Am J Emerg Med.* 1998;16(3):289-292.

296. Wang HC, Chiang WC, Chen SY, Ke YL, Chi CL, Yang CW, Lin PC, Ko PC, Wang YC, Tsai TC, Huang CH, Hsiung KH, Ma MH, Chen SC, Chen WJ, Lin FY. Video-recording and time-motion analyses of manual versus mechanical cardiopulmonary resuscitation during ambulance transport.

Resuscitation. 2007;74(3):453-460.

297. Axelsson C, Nestin J, Svensson L, Axelsson AB, Herlitz J. Clinical consequences of the introduction of mechanical chest compression in the EMS system for treatment of out-of-hospital cardiac arrest-a pilot study. *Resuscitation.* 2006;71(1):47-55.

298. Smekal D, Johansson J, Huzevka T, Rubertsson S. No difference in autopsy detected injuries in cardiac arrest patients treated with manual chest compressions compared with mechanical compressions with the LUCAS device--a pilot study. *Resuscitation.* 2009;80(10):1104-1107.

299. Steen S, Liao Q, Pierre L, Paskevicius A, Sjoberg T. Evaluation of LUCAS, a new device for automatic mechanical compression and active decompression resuscitation. *Resuscitation.* 2002;55(3):285-299.

300. Steen S, Sjoberg T, Olsson P, Young M. Treatment of out-of-hospital cardiac arrest with LUCAS, a new device for automatic mechanical compression and active decompression resuscitation. *Resuscitation.* 2005;67(1):25-30.

301. Larsen AI, Hjornevik AS, Ellingsen CL, Nilsen DW. Cardiac arrest with continuous mechanical chest compression during percutaneous coronary intervention. A report on the use of the LUCAS device. *Resuscitation.* 2007;75(3):454-459.

302. Deakin CD, O'Neill JF, Tabor T. Does compression-only cardiopulmonary resuscitation generate adequate passive ventilation during cardiac arrest? *Resuscitation.* 2007;75(1):53-59.

303. Bonnemeier H, Olivecrona G, Simonis G, Gotberg M, Weitz G, Iblher P, Gerling I, Schunkert H. Automated continuous chest compression for in-hospital cardiopulmonary resuscitation of patients with pulseless electrical activity: a report of five cases. *Int J Cardiol.* 2009;136(2):e39-50.

304. Wagner H, Terkelsen CJ, Friberg H, Harnek J, Kern K, Lassen JF, Olivecrona GK. Cardiac arrest in the catheterisation laboratory: a 5-year experience of using mechanical chest compressions to facilitate PCI during prolonged resuscitation efforts. *Resuscitation.* 2010;81(4):383-387.

305. Agostoni P, Cornelis K, Vermeersch P. Successful percutaneous treatment of an intraprocedural left main stent thrombosis with the support of an automatic mechanical chest compression device. *Int J Cardiol.* 2008;124(2):e19-21.

306. Grogaard HK, Wik L, Eriksen M, Brekke M, Sunde K. Continuous mechanical chest compressions during cardiac arrest to facilitate restoration of coronary circulation with percutaneous coronary intervention. *J Am Coll Cardiol.* 2007;50(11):1093-1094.

307. Larsen AI, Hjornevik A, Bonarjee V, Barvik S, Melberg T, Nilsen DW. Coronary blood flow and perfusion pressure during coronary angiography in patients with ongoing mechanical chest compression: a report on 6 cases. *Resuscitation.* 2010;81(4):493-497.

308. Cabrini L, Beccaria P, Landoni G, Biondi-Zoccai GG, Sheiban I, Cristofolini M, Fochi O, Maj G, Zangrillo A. Impact of impedance threshold devices on cardiopulmonary resuscitation: a systematic review and meta-analysis of randomized controlled studies. *Crit Care Med.* 2008;36(5):1625-1632.

309. Plaisance P, Lurie KG, Vicaut E, Martin D, Gueugniaud PY, Petit JL, Payen D. Evaluation of an impedance threshold device in patients receiving active compression-decompression cardiopulmonary resuscitation for out of hospital cardiac arrest. *Resuscitation.* 2004;61(3):265-271.

310. Plaisance P, Lurie KG, Payen D. Inspiratory impedance during active compression-decompression cardiopulmonary resuscitation: a randomized evaluation in patients in cardiac arrest. *Circulation.* 2000;101(9):989-994.

311. Aufderheide TP, Pirrallo RG, Provo TA, Lurie KG. Clinical evaluation of an inspiratory impedance threshold device during standard cardiopulmonary resuscitation in patients with out-of-hospital cardiac arrest. *Crit Care Med.* 2005;33(4):734-740.

312. Wolcke BB, Mauer DK, Schoefmann MF, Teichmann H, Provo TA, Lindner KH, Dick WF, Aeppli D, Lurie KG. Comparison of standard cardiopulmonary resuscitation versus the combination of active compression-decompression cardiopulmonary resuscitation and an inspiratory impedance threshold device for out-of-hospital cardiac arrest. *Circulation.* 2003;108(18):2201-2205.

313. Thayne RC, Thomas DC, Neville JD, Van Dellen A. Use of an impedance threshold device improves short-term outcomes following out-of-hospital cardiac arrest. *Resuscitation.* 2005;67(1):103-108.

314. Aufderheide TP, Alexander C, Lick C, Myers B, Romig L, Vartanian L, Stothert J, McKnite S, Matsuura T, Yannopoulos D, Lurie K. From laboratory science to six emergency medical services systems: New understanding of the physiology of cardiopulmonary resuscitation increases survival rates after cardiac arrest. *Crit Care Med.* 2008;36(11 Suppl):S397-404.

315. Aufderheide TP, Yannopoulos D, Lick CJ, Myers B, Romig LA, Stothert JC, Barnard J, Vartanian L, Pilgrim AJ, Benditt DG. Implementing the 2005 American Heart Association Guidelines improves outcomes after out-of-hospital cardiac arrest. *Heart Rhythm.* 2010;7(10):1357-1362.

316. Hinchey PR, Myers JB, Lewis R, De Maio VJ, Reyer E, Licatese D, Zalkin J, Snyder G. Improved out-of-hospital cardiac arrest survival after the sequential implementation of 2005 AHA guidelines for compressions, ventilations, and induced hypothermia: the Wake County experience. *Ann Emerg Med.* 2010;56(4):348-357.

317. Lurie KG, Coffeen P, Shultz J, McKnite S, Detloff B, Mulligan K. Improving active compression-decompression cardiopulmonary resuscitation with an inspiratory impedance valve. *Circulation.* 1995;91(6):1629-1632.

318. Lurie KG, Mulligan KA, McKnite S, Detloff B, Lindstrom P, Lindner KH. Optimizing standard cardiopulmonary resuscitation with an inspiratory impedance threshold valve. *Chest.* 1998;113(4):1084-1090.

319. Lurie KG, Voelckel WG, Zielinski T, McKnite S, Lindstrom P, Peterson C, Wenzel V, Lindner KH, Samniah N, Benditt D. Improving standard cardiopulmonary resuscitation with an inspiratory impedance threshold valve in a porcine model of cardiac arrest. *Anesth Analg.* 2001;93(3):649-655.

320. Lurie KG, Zielinski T, McKnite S, Aufderheide T, Voelckel W. Use of an inspiratory impedance valve improves neurologically intact survival in a porcine model of ventricular fibrillation. *Circulation.* 2002;105(1):124-129.

321. Lurie KG, Barnes TA, Zielinski TM, McKnite SH. Evaluation of a prototypic inspiratory impedance threshold valve designed to enhance the efficiency of cardiopulmonary resuscitation. *Respir Care.* 2003;48(1):52-57.

322. Raedler C, Voelckel WG, Wenzel V, Bahlmann L, Baumeier W, Schmittinger CA, Herff H, Krismer AC, Lindner KH, Lurie KG. Vasopressor response in a porcine model of hypothermic cardiac arrest is improved with active compression-decompression cardiopulmonary resuscitation using the inspiratory impedance threshold valve. *Anesth Analg.* 2002;95(6):1496-1502, table of contents.

323. Yannopoulos D, Aufderheide TP, Gabrielli A, Beiser DG, McKnite SH, Pirrallo RG, Wigginton J, Becker L, Vanden Hoek T, Tang W, Nadkarni VM, Klein JP, Idris AH, Lurie KG. Clinical and hemodynamic comparison of 15:2 and 30:2 compression-to-ventilation ratios for cardiopulmonary

resuscitation. *Crit Care Med.* 2006;34(5):1444-1449.

324. Mader TJ, Kellogg AR, Smith J, Hynds-Decoteau R, Gaudet C, Caron J, Murphy B, Paquette A, Sherman LD. A blinded, randomized controlled evaluation of an impedance threshold device during cardiopulmonary resuscitation in swine. *Resuscitation.* 2008;77(3):387-394.

325. Menegazzi JJ, Salcido DD, Menegazzi MT, Rittenberger JC, Suffoletto BP, Logue ES, Mader TJ. Effects of an impedance threshold device on hemodynamics and restoration of spontaneous circulation in prolonged porcine ventricular fibrillation. *Prehosp Emerg Care.* 2007;11(2):179-185.

326. Langhelle A, Stromme T, Sunde K, Wik L, Nicolaysen G, Steen PA. Inspiratory impedance threshold valve during CPR. *Resuscitation.* 2002;52(1):39-48.

327. Herff H, Raedler C, Zander R, Wenzel V, Schmittinger CA, Brenner E, Rieger M, Lindner KH. Use of an inspiratory impedance threshold valve during chest compressions without assisted ventilation may result in hypoxaemia. *Resuscitation.* 2007;72(3):466-476.

328. Baker PW, Conway J, Cotton C, Ashby DT, Smyth J, Woodman RJ, Grantham H. Defibrillation or cardiopulmonary resuscitation first for patients with out-of-hospital cardiac arrests found by paramedics to be in ventricular fibrillation? A randomised control trial. *Resuscitation.* 2008;79(3):424-431.

329. Jacobs IG, Finn JC, Oxer HF, Jelinek GA. CPR before defibrillation in out-of-hospital cardiac arrest: a randomized trial. *Emerg Med Australas.* 2005;17(1):39-45.

330. Hayakawa M, Gando S, Okamoto H, Asai Y, Uegaki S, Makise H. Shortening of cardiopulmonary resuscitation time before the defibrillation worsens the outcome in out-of-hospital VF patients. *Am J Emerg Med.* 2009;27(4):470-474.

331. Bradley SM, Gabriel EE, Aufderheide TP, Barnes R, Christenson J, Davis DP, Stiell IG, Nichol G. Survival increases with CPR by Emergency Medical Services before defibrillation of out-of-hospital ventricular fibrillation or ventricular tachycardia: observations from the Resuscitation Outcomes Consortium. *Resuscitation.* 2010;81(2):155-162.

332. Wik L, Hansen TB, Fylling F, Steen T, Vaagenes P, Auestad BH, Steen PA. Delaying defibrillation to give basic cardiopulmonary resuscitation to patients with out-of-hospital ventricular fibrillation: a randomized trial. *JAMA.* 2003;289(11):1389-1395.

333. Cobb LA, Fahrenbruch CE, Walsh TR, Copass MK, Olsufka M, Breskin M, Hallstrom AP. Influence of cardiopulmonary resuscitation prior to defibrillation in patients with out-of-hospital ventricular fibrillation. *JAMA.* 1999;281(13):1182-1188.

334. Eilevstjonn J, Eftestol T, Aase SO, Myklebust H, Husoy JH, Steen PA. Feasibility of shock advice analysis during CPR through removal of CPR artefacts from the human ECG. *Resuscitation.* 2004;61(2):131-141.

335. Aramendi E, de Gauna SR, Irusta U, Ruiz J, Arcocha MF, Ormaetxe JM. Detection of ventricular fibrillation in the presence of cardiopulmonary resuscitation artefacts. *Resuscitation.* 2007;72(1):115-123.

336. Li Y, Bisera J, Tang W, Weil MH. Automated detection of ventricular fibrillation to guide cardiopulmonary resuscitation. *Crit Pathw Cardiol.* 2007;6(3):131-134.

337. Li Y, Bisera J, Geheb F, Tang W, Weil MH. Identifying potentially shockable rhythms without interrupting cardiopulmonary resuscitation. *Crit Care Med.* 2008;36(1):198-203.

338. Ruiz de Gauna S, Ruiz J, Irusta U, Aramendi E, Eftestol T, Kramer-Johansen J. A method to remove

CPR artefacts from human ECG using only the recorded ECG. *Resuscitation.* 2008;76(2):271-278.

339. Irusta U, Ruiz J, de Gauna SR, Eftestol T, Kramer-Johansen J. A least mean-square filter for the estimation of the cardiopulmonary resuscitation artifact based on the frequency of the compressions. *IEEE Trans Biomed Eng.* 2009;56(4):1052-1062.

340. Berger RD, Palazzolo J, Halperin H. Rhythm discrimination during uninterrupted CPR using motion artifact reduction system. *Resuscitation.* 2007;75(1):145-152.

341. Stults KR, Brown DD, Cooley F, Kerber RE. Self-adhesive monitor/defibrillation pads improve prehospital defibrillation success. *Ann Emerg Med.* 1987;16(8):872-877.

342. Bojar RM, Payne DD, Rastegar H, Diehl JT, Cleveland RJ. Use of self-adhesive external defibrillator pads for complex cardiac surgical procedures. *Ann Thorac Surg.* 1988;46(5):587-588.

343. Brown J, Rogers J, Soar J. Cardiac arrest during surgery and ventilation in the prone position: a case report and systematic review. *Resuscitation.* 2001;50(2):233-238.

344. Wilson RF, Sirna S, White CW, Kerber RE. Defibrillation of high-risk patients during coronary angiography using self-adhesive, preapplied electrode pads. *Am J Cardiol.* 1987;60(4):380-382.

345. Bradbury N, Hyde D, Nolan J. Reliability of ECG monitoring with a gel pad/paddle combination after defibrillation. *Resuscitation.* 2000;44(3):203-206.

346. Perkins GD, Davies RP, Soar J, Thickett DR. The impact of manual defibrillation technique on no-flow time during simulated cardiopulmonary resuscitation. *Resuscitation.* 2007;73(1):109-114.

347. Deakin CD. Paddle size in defibrillation. *Br J Anaesth.* 1998;81(4):657-658.

348. Kirchhof P, Monnig G, Wasmer K, Heinecke A, Breithardt G, Eckardt L, Bocker D. A trial of self-adhesive patch electrodes and hand-held paddle electrodes for external cardioversion of atrial fibrillation (MOBIPAPA). *Eur Heart J.* 2005;26(13):1292-1297.

349. Kerber RE, Martins JB, Ferguson DW, Jensen SR, Parke JD, Kieso R, Melton J. Experimental evaluation and initial clinical application of new self-adhesive defibrillation electrodes. *Int J Cardiol.* 1985;8(1):57-66.

350. Garcia LA, Kerber RE. Transthoracic defibrillation: does electrode adhesive pad position alter transthoracic impedance? *Resuscitation.* 1998;37(3):139-143.

351. Boodhoo L, Mitchell AR, Bordoli G, Lloyd G, Patel N, Sulke N. DC cardioversion of persistent atrial fibrillation: a comparison of two protocols. *Int J Cardiol.* 2007;114(1):16-21.

352. Brazdzionyte J, Babarskiene RM, Stanaitiene G. Anterior-posterior versus anterior-lateral electrode position for biphasic cardioversion of atrial fibrillation. *Medicina (Kaunas).* 2006;42(12):994-998.

353. Chen CJ, Guo GB. External cardioversion in patients with persistent atrial fibrillation: a reappraisal of the effects of electrode pad position and transthoracic impedance on cardioversion success. *Jpn Heart J.* 2003;44(6):921-932.

354. Dodd TE, Deakin CD, Petley GW, Clewlow F. External defibrillation in the left lateral position--a comparison of manual paddles with self-adhesive pads. *Resuscitation.* 2004;63(3):283-286.

355. Kerber RE, Jensen SR, Grayzel J, Kennedy J, Hoyt R. Elective cardioversion: influence of paddle-electrode location and size on success rates and energy requirements. *N Engl J Med.* 1981;305(12):658-662.

356. Mathew TP, Moore A, McIntyre M, Harbinson MT, Campbell NP, Adgey AA, Dalzell GW. Randomised comparison of electrode positions for cardioversion of atrial fibrillation. *Heart.* 1999;81(6):576-579.

357. Camacho MA, Lehr JL, Eisenberg SR. A three-dimensional finite element model of human transthoracic defibrillation: paddle placement and size. *IEEE Trans Biomed Eng.* 1995;42(6):572-578.

358. Lateef F, Lim SH, Anantharaman V, Lim CS. Changes in chest electrode impedance. *Am J Emerg Med.* 2000;18(4):381-384.

359. Stanaitiene G, Babarskiene RM. [Impact of electrical shock waveform and paddle positions on efficacy of direct current cardioversion for atrial fibrillation]. *Medicina (Kaunas).* 2008;44(9):665-672.

360. Botto GL, Politi A, Bonini W, Broffoni T, Bonatti R. External cardioversion of atrial fibrillation: role of paddle position on technical efficacy and energy requirements. *Heart.* 1999;82(6):726-730.

361. Kirchhof P, Eckardt L, Loh P, Weber K, Fischer RJ, Seidl KH, Bocker D, Breithardt G, Haverkamp W, Borggrefe M. Anterior-posterior versus anterior-lateral electrode positions for external cardioversion of atrial fibrillation: a randomised trial. *Lancet.* 2002;360(9342):1275-1279.

362. Krasteva V, Matveev M, Mudrov N, Prokopova R. Transthoracic impedance study with large self-adhesive electrodes in two conventional positions for defibrillation. *Physiol Meas.* 2006;27(10):1009-1022.

363. Karlsson G, Zhang Y, Davies LR, Coddington W, Kerber RE. Does electrode polarity alter the energy requirements for transthoracic biphasic waveform defibrillation? Experimental studies. *Resuscitation.* 2001;51(1):77-81.

364. Panescu D, Webster JG, Tompkins WJ, Stratbucker RA. Optimization of cardiac defibrillation by three-dimensional finite element modeling of the human thorax. *IEEE Trans Biomed Eng.* 1995;42(2):185-192.

365. Alp NJ, Rahman S, Bell JA, Shahi M. Randomised comparison of antero-lateral versus antero-posterior paddle positions for DC cardioversion of persistent atrial fibrillation. *Int J Cardiol.* 2000;75(2-3):211-216.

366. Caterine MR, Yoerger DM, Spencer KT, Miller SG, Kerber RE. Effect of electrode position and gel-application technique on predicted transcardiac current during transthoracic defibrillation. *Ann Emerg Med.* 1997;29(5):588-595.

367. Pagan-Carlo LA, Spencer KT, Robertson CE, Dengler A, Birkett C, Kerber RE. Transthoracic defibrillation: importance of avoiding electrode placement directly on the female breast. *J Am Coll Cardiol.* 1996;27(2):449-452.

368. Bissing JW, Kerber RE. Effect of shaving the chest of hirsute subjects on transthoracic impedance to self-adhesive defibrillation electrode pads. *Am J Cardiol.* 2000;86(5):587-589, A510.

369. Sado DM, Deakin CD, Petley GW, Clewlow F. Comparison of the effects of removal of chest hair with not doing so before external defibrillation on transthoracic impedance. *Am J Cardiol.* 2004;93(1):98-100.

370. Killingsworth CR, Melnick SB, Chapman FW, Walker RG, Smith WM, Ideker RE, Walcott GP. Defibrillation threshold and cardiac responses using an external biphasic defibrillator with pediatric and adult adhesive patches in pediatric-sized piglets. *Resuscitation.* 2002;55(2):177-185.

371. Dalzell GW, Cunningham SR, Anderson J, Adgey AA. Electrode pad size, transthoracic impedance and success of external ventricular defibrillation. *Am J Cardiol.* 1989;64(12):741-744.

372. Kerber RE, Grayzel J, Hoyt R, Marcus M, Kennedy J. Transthoracic resistance in human

defibrillation. Influence of body weight, chest size, serial shocks, paddle size and paddle contact pressure. *Circulation.* 1981;63(3):676-682.

373. Connell PN, Ewy GA, Dahl CF, Ewy MD. Transthoracic impedance to defibrillator discharge. Effect of electrode size and electrode-chest wall interface. *J Electrocardiol.* 1973;6(4):313-317.

374. Dahl CF, Ewy GA, Warner ED, Thomas ED. Myocardial necrosis from direct current countershock. Effect of paddle electrode size and time interval between discharges. *Circulation.* 1974;50(5):956-961.

375. Hoyt R, Grayzel J, Kerber RE. Determinants of intracardiac current in defibrillation. Experimental studies in dogs. *Circulation.* 1981;64(4):818-823.

376. Thomas ED, Ewy GA, Dahl CF, Ewy MD. Effectiveness of direct current defibrillation: role of paddle electrode size. *Am Heart J.* 1977;93(4):463-467.

377. Atkins DL, Kerber RE. Pediatric defibrillation: current flow is improved by using "adult" electrode paddles. *Pediatrics.* 1994;94(1):90-93.

378. Atkins DL, Sirna S, Kieso R, Charbonnier F, Kerber RE. Pediatric defibrillation: importance of paddle size in determining transthoracic impedance. *Pediatrics.* 1988;82(6):914-918.

379. Samson RA, Atkins DL, Kerber RE. Optimal size of self-adhesive preapplied electrode pads in pediatric defibrillation. *Am J Cardiol.* 1995;75(7):544-545.

380. Sirna SJ, Ferguson DW, Charbonnier F, Kerber RE. Factors affecting transthoracic impedance during electrical cardioversion. *Am J Cardiol.* 1988;62(16):1048-1052.

381. Razumov KV, Vostrikov VA, Kholin PV. [Optimisation of electroimpulse therapy of life threatening arrhythmia in patients with ischemic heart disease]. *Anesteziol Reanimatol.* 2003(6):45-47.

382. Drury NE, Petley GW, Clewlow F, Deakin CD. Evidence-based guidelines for the use of defibrillation pads. *Resuscitation.* 2001;51(3):283-286.

383. Das DP, Webster JG. Defibrillation recovery curves for different electrode materials. *IEEE Trans Biomed Eng.* 1980;27(4):230-233.

384. Deakin CD, Petley GW, Drury NE, Clewlow F. How often should defibrillation pads be changed?: the effect of evaporative drying. *Resuscitation.* 2001;48(2):157-162.

385. Lloyd MS, Heeke B, Walter PF, Langberg JJ. Hands-on defibrillation: an analysis of electrical current flow through rescuers in direct contact with patients during biphasic external defibrillation. *Circulation.* 2008;117(19):2510-2514.

386. Ewy GA, Horan WJ, Ewy MD. Disposable defibrillator electrodes. *Heart Lung.* 1977;6(1):127-130.

387. Ewy GA, Taren D. Impedance to transthoracic direct current discharge: a model for testing interface material. *Med Instrum.* 1978;12(1):47-48.

388. Deakin CD, McLaren RM, Petley GW, Clewlow F, Dalrymple-Hay MJ. A comparison of transthoracic impedance using standard defibrillation paddles and self-adhesive defibrillation pads. *Resuscitation.* 1998;39(1-2):43-46.

389. Meyer PF, Gadsby PD, Van Sickle D, Schoenlein WE, Foster KS, Graber GP. Impedance-gradient electrode reduces skin irritation induced by transthoracic defibrillation. *Med Biol Eng Comput.* 2005;43(2):225-229.

390. Aylward PE, Kieso R, Hite P, Charbonnier F, Kerber RE. Defibrillator electrode-chest wall coupling agents: influence on transthoracic impedance and shock success. *J Am Coll Cardiol.* 1985;6(3):682-686.

391. Kerber RE, Martins JB, Kelly KJ, Ferguson DW, Kouba C, Jensen SR, Newman B, Parke JD, Kieso R, Melton J. Self-adhesive preapplied electrode pads for defibrillation and cardioversion. *J Am Coll Cardiol.* 1984;3(3):815-820.

392. Andersen C, Larsen B. [A comparative study of contact media for defibrillation]. *Ugeskr Laeger.* 1989;151(31):1987-1988.

393. Atkins DL, Jorgenson DB. Attenuated pediatric electrode pads for automated external defibrillator use in children. *Resuscitation.* 2005;66(1):31-37.

394. Berg RA, Chapman FW, Berg MD, Hilwig RW, Banville I, Walker RG, Nova RC, Sherrill D, Kern KB. Attenuated adult biphasic shocks compared with weight-based monophasic shocks in a swine model of prolonged pediatric ventricular fibrillation. *Resuscitation.* 2004;61(2):189-197.

395. Krasteva VT, Papazov SP. Estimation of current density distribution under electrodes for external defibrillation. *Biomed Eng Online.* 2002;1:7.

396. Morrison LJ, Dorian P, Long J, Vermeulen M, Schwartz B, Sawadsky B, Frank J, Cameron B, Burgess R, Shield J, Bagley P, Mausz V, Brewer JE, Lerman BB. Out-of-hospital cardiac arrest rectilinear biphasic to monophasic damped sine defibrillation waveforms with advanced life support intervention trial (ORBIT). *Resuscitation.* 2005;66(2):149-157.

397. Schneider T, Martens PR, Paschen H, Kuisma M, Wolcke B, Gliner BE, Russell JK, Weaver WD, Bossaert L, Chamberlain D. Multicenter, randomized, controlled trial of 150-J biphasic shocks compared with 200- to 360-J monophasic shocks in the resuscitation of out-of-hospital cardiac arrest victims. Optimized Response to Cardiac Arrest (ORCA) Investigators. *Circulation.* 2000;102(15):1780-1787.

398. van Alem AP, Chapman FW, Lank P, Hart AA, Koster RW. A prospective, randomised and blinded comparison of first shock success of monophasic and biphasic waveforms in out-of-hospital cardiac arrest. *Resuscitation.* 2003;58(1):17-24.

399. Carpenter J, Rea TD, Murray JA, Kudenchuk PJ, Eisenberg MS. Defibrillation waveform and post-shock rhythm in out-of-hospital ventricular fibrillation cardiac arrest. *Resuscitation.* 2003;59(2):189-196.

400. Freeman K, Hendey GW, Shalit M, Stroh G. Biphasic defibrillation does not improve outcomes compared to monophasic defibrillation in out-of-hospital cardiac arrest. *Prehosp Emerg Care.* 2008;12(2):152-156.

401. Hess EP, Atkinson EJ, White RD. Increased prevalence of sustained return of spontaneous circulation following transition to biphasic waveform defibrillation. *Resuscitation.* 2008;77(1):39-45.

402. Kudenchuk PJ, Cobb LA, Copass MK, Olsufka M, Maynard C, Nichol G. Transthoracic incremental monophasic versus biphasic defibrillation by emergency responders (TIMBER): a randomized comparison of monophasic with biphasic waveform ascending energy defibrillation for the resuscitation of out-of-hospital cardiac arrest due to ventricular fibrillation. *Circulation.* 2006;114(19):2010-2018.

403. Kajino K, Iwami T, Berg RA, Hiraide A, Hayashi Y, Yukioka H, Tanaka H, Shimazu T, Sugimoto H. Comparison of neurological outcomes following witnessed out-of-hospital ventricular fibrillation defibrillated with either biphasic or monophasic automated external defibrillators. *Emerg Med J.* 2009;26(7):492-496.

404. American Heart Association in collaboration with International Liaison Committee on Resuscitation.

Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care: International Consensus on Science, Part 3: Adult Basic Life Support. *Circulation.* 2000;102(suppl I)(8):I22-I59.

405. Pagan-Carlo LA, Allan JJ, Spencer KT, Birkett CL, Myers R, Kerber RE. Encircling overlapping multipulse shock waveforms for transthoracic defibrillation. *J Am Coll Cardiol.* 1998;32(7):2065-2071.

406. Zhang Y, Ramabadran RS, Boddicker KA, Bawaney I, Davies LR, Zimmerman MB, Wuthrich S, Jones JL, Kerber RE. Triphasic waveforms are superior to biphasic waveforms for transthoracic defibrillation: experimental studies. *J Am Coll Cardiol.* 2003;42(3):568-575.

407. Stiell IG, Walker RG, Nesbitt LP, Chapman FW, Cousineau D, Christenson J, Bradford P, Sookram S, Berringer R, Lank P, Wells GA. BIPHASIC Trial: a randomized comparison of fixed lower versus escalating higher energy levels for defibrillation in out-of-hospital cardiac arrest. *Circulation.* 2007;115(12):1511-1517.

408. Walsh SJ, McClelland AJ, Owens CG, Allen J, Anderson JM, Turner C, Adgey AA. Efficacy of distinct energy delivery protocols comparing two biphasic defibrillators for cardiac arrest. *Am J Cardiol.* 2004;94(3):378-380.

409. Didon JP, Fontaine G, White RD, Jekova I, Schmid JJ, Cansell A. Clinical experience with a low-energy pulsed biphasic waveform in out-of-hospital cardiac arrest. *Resuscitation.* 2008;76(3):350-353.

410. Weaver WD, Cobb LA, Copass MK, Hallstrom AP. Ventricular defibrillation -- a comparative trial using 175-J and 320-J shocks. *N Engl J Med.* 1982;307(18):1101-1106.

411. Gascho JA, Crampton RS, Cherwek ML, Sipes JN, Hunter FP, O'Brien WM. Determinants of ventricular defibrillation in adults. *Circulation.* 1979;60(2):231-240.

412. Kerber RE, Jensen SR, Gascho JA, Grayzel J, Hoyt R, Kennedy J. Determinants of defibrillation: prospective analysis of 183 patients. *Am J Cardiol.* 1983;52(7):739-745.

413. Tang W, Weil MH, Sun S, Jorgenson D, Morgan C, Klouche K, Snyder D. The effects of biphasic waveform design on post-resuscitation myocardial function. *J Am Coll Cardiol.* 2004;43(7):1228-1235.

414. Xie J, Weil MH, Sun S, Tang W, Sato Y, Jin X, Bisera J. High-energy defibrillation increases the severity of postresuscitation myocardial dysfunction. *Circulation.* 1997;96(2):683-688.

415. Walcott GP, Melnick SB, Killingsworth CR, Ideker RE. Comparison of low-energy versus high-energy biphasic defibrillation shocks following prolonged ventricular fibrillation. *Prehosp Emerg Care.* 2010;14(1):62-70.

416. Higgins SL, Herre JM, Epstein AE, Greer GS, Friedman PL, Gleva ML, Porterfield JG, Chapman FW, Finkel ES, Schmitt PW, Nova RC, Greene HL. A comparison of biphasic and monophasic shocks for external defibrillation. Physio-Control Biphasic Investigators. *Prehosp Emerg Care.* 2000;4(4):305-313.

417. Jost D, Degrange H, Verret C, Hersan O, Banville IL, Chapman FW, Lank P, Petit JL, Fuilla C, Migliani R, Carpentier JP. DEFI 2005: a randomized controlled trial of the effect of automated external defibrillator cardiopulmonary resuscitation protocol on outcome from out-of-hospital cardiac arrest. *Circulation.* 2010;121(14):1614-1622.

418. Bobrow BJ, Clark LL, Ewy GA, Chikani V, Sanders AB, Berg RA, Richman PB, Kern KB. Minimally

interrupted cardiac resuscitation by emergency medical services for out-of-hospital cardiac arrest. *JAMA.* 2008;299(10):1158-1165.

419. Rea TD, Helbock M, Perry S, Garcia M, Cloyd D, Becker L, Eisenberg M. Increasing use of cardiopulmonary resuscitation during out-of-hospital ventricular fibrillation arrest: survival implications of guideline changes. *Circulation.* 2006;114(25):2760-2765.

420. Olasveengen TM, Vik E, Kuzovlev A, Sunde K. Effect of implementation of new resuscitation guidelines on quality of cardiopulmonary resuscitation and survival. *Resuscitation.* 2009;80(4):407-411.

421. Hess EP, Russell JK, Liu PY, White RD. A high peak current 150-J fixed-energy defibrillation protocol treats recurrent ventricular fibrillation (VF) as effectively as initial VF. *Resuscitation.* 2008;79(1):28-33.

422. Berdowski J, Tijssen JG, Koster RW. Chest compressions cause recurrence of ventricular fibrillation after the first successful conversion by defibrillation in out-of-hospital cardiac arrest. *Circ Arrhythm Electrophysiol.* 2010;3(1):72-78.

423. Eilevstjonn J, Kramer-Johansen J, Sunde K. Shock outcome is related to prior rhythm and duration of ventricular fibrillation. *Resuscitation.* 2007;75(1):60-67.

424. Berdowski J, Schulten RJ, Tijssen JG, van Alem AP, Koster RW. Delaying a shock after takeover from the automated external defibrillator by paramedics is associated with decreased survival. *Resuscitation.* 2010;81(3):287-292.

425. Koster RW, Walker RG, Chapman FW. Recurrent ventricular fibrillation during advanced life support care of patients with prehospital cardiac arrest. *Resuscitation.* 2008;78(3):252-257.

426. Cummins RO, Eisenberg MS, Litwin PE, Graves JR, Hearne TR, Hallstrom AP. Automatic external defibrillators used by emergency medical technicians. A controlled clinical trial. *JAMA.* 1987;257(12):1605-1610.

427. Stults KR, Brown DD, Kerber RE. Efficacy of an automated external defibrillator in the management of out-of-hospital cardiac arrest: validation of the diagnostic algorithm and initial clinical experience in a rural environment. *Circulation.* 1986;73(4):701-709.

428. Forcina MS, Farhat AY, O'Neil WW, Haines DE. Cardiac arrest survival after implementation of automated external defibrillator technology in the in-hospital setting. *Crit Care Med.* 2009;37(4):1229-1236.

429. Kramer-Johansen J, Edelson DP, Abella BS, Becker LB, Wik L, Steen PA. Pauses in chest compression and inappropriate shocks: a comparison of manual and semi-automatic defibrillation attempts. *Resuscitation.* 2007;73(2):212-220.

430. Pytte M, Pedersen TE, Ottem J, Rokvam AS, Sunde K. Comparison of hands-off time during CPR with manual and semi-automatic defibrillation in a manikin model. *Resuscitation.* 2007;73(1):131-136.

431. Yu T, Weil MH, Tang W, Sun S, Klouche K, Povoas H, Bisera J. Adverse outcomes of interrupted precordial compression during automated defibrillation. *Circulation.* 2002;106(3):368-372.

432. Eftestol T, Sunde K, Steen PA. Effects of interrupting precordial compressions on the calculated probability of defibrillation success during out-of-hospital cardiac arrest. *Circulation.* 2002;105(19):2270-2273.

433. Edelson DP, Abella BS, Kramer-Johansen J, Wik L, Myklebust H, Barry AM, Merchant RM, Hoek

TL, Steen PA, Becker LB. Effects of compression depth and pre-shock pauses predict defibrillation failure during cardiac arrest. *Resuscitation.* 2006;71(2):137-145.

434. Deakin CD, Ambler JJ. Post-shock myocardial stunning: a prospective randomised double-blind comparison of monophasic and biphasic waveforms. *Resuscitation.* 2006;68(3):329-333.

435. Page RL, Kerber RE, Russell JK, Trouton T, Waktare J, Gallik D, Olgin JE, Ricard P, Dalzell GW, Reddy R, Lazzara R, Lee K, Carlson M, Halperin B, Bardy GH. Biphasic versus monophasic shock waveform for conversion of atrial fibrillation: the results of an international randomized, double-blind multicenter trial. *J Am Coll Cardiol.* 2002;39(12):1956-1963.

436. Alatawi F, Gurevitz O, White RD, Ammash NM, Malouf JF, Bruce CJ, Moon BS, Rosales AG, Hodge D, Hammill SC, Gersh BJ, Friedman PA. Prospective, randomized comparison of two biphasic waveforms for the efficacy and safety of transthoracic biphasic cardioversion of atrial fibrillation. *Heart Rhythm.* 2005;2(4):382-387.

437. Ambler JJ, Deakin CD. A randomized controlled trial of efficacy and ST change following use of the Welch-Allyn MRL PIC biphasic waveform versus damped sine monophasic waveform for external DC cardioversion. *Resuscitation.* 2006;71(2):146-151.

438. Boos C, Thomas MD, Jones A, Clarke E, Wilbourne G, More RS. Higher energy monophasic DC cardioversion for persistent atrial fibrillation: is it time to start at 360 joules? *Ann Noninvasive Electrocardiol.* 2003;8(2):121-126.

439. Glover BM, Walsh SJ, McCann CJ, Moore MJ, Manoharan G, Dalzell GW, McAllister A, McClements B, McEneaney DJ, Trouton TG, Mathew TP, Adgey AA. Biphasic energy selection for transthoracic cardioversion of atrial fibrillation. The BEST AF Trial. *Heart.* 2008;94(7):884-887.

440. Joglar JA, Hamdan MH, Ramaswamy K, Zagrodzky JD, Sheehan CJ, Nelson LL, Andrews TC, Page RL. Initial energy for elective external cardioversion of persistent atrial fibrillation. *Am J Cardiol.* 2000;86(3):348-350.

441. Kawabata VS, Vianna CB, Moretti MA, Gonzalez MM, Ferreira JF, Timerman S, Cesar LA. Monophasic versus biphasic waveform shocks for atrial fibrillation cardioversion in patients with concomitant amiodarone therapy. *Europace.* 2007;9(2):143-146.

442. Khaykin Y, Newman D, Kowalewski M, Korley V, Dorian P. Biphasic versus monophasic cardioversion in shock-resistant atrial fibrillation. *J Cardiovasc Electrophysiol.* 2003;14(8):868-872.

443. Kmec J. Comparison the effectiveness of damped sine wave monophasic and rectilinear biphasic shocks in patients with persistent atrial fibrillation. *Kardiologia.* 2006;15:265-278.

444. Koster RW, Dorian P, Chapman FW, Schmitt PW, O'Grady SG, Walker RG. A randomized trial comparing monophasic and biphasic waveform shocks for external cardioversion of atrial fibrillation. *Am Heart J.* 2004;147(5):e20.

445. Marinsek M, Larkin GL, Zohar P, Bervar M, Pekolj-Bicanic M, Mocnik FS, Noc M, Podbregar M. Efficacy and impact of monophasic versus biphasic countershocks for transthoracic cardioversion of persistent atrial fibrillation. *Am J Cardiol.* 2003;92(8):988-991.

446. Mittal S, Ayati S, Stein KM, Schwartzman D, Cavlovich D, Tchou PJ, Markowitz SM, Slotwiner DJ, Scheiner MA, Lerman BB. Transthoracic cardioversion of atrial fibrillation: comparison of rectilinear biphasic versus damped sine wave monophasic shocks. *Circulation.* 2000;101(11):1282-1287.

447. Mortensen K, Risius T, Schwemer TF, Aydin MA, Koster R, Klemm HU, Lutomsky B, Meinertz T,

Ventura R, Willems S. Biphasic versus monophasic shock for external cardioversion of atrial flutter: a prospective, randomized trial. *Cardiology.* 2008;111(1):57-62.

448. Pinski SL, Sgarbossa EB, Ching E, Trohman RG. A comparison of 50-J versus 100-J shocks for direct-current cardioversion of atrial flutter. *Am Heart J.* 1999;137(3):439-442.

449. Ermis C, Zhu AX, Sinha S, Iskos D, Sakaguchi S, Lurie KG, Benditt DG. Efficacy of biphasic waveform cardioversion for atrial fibrillation and atrial flutter compared with conventional monophasic waveforms. *Am J Cardiol.* 2002;90(8):891-892.

450. Rashba EJ, Gold MR, Crawford FA, Leman RB, Peters RW, Shorofsky SR. Efficacy of transthoracic cardioversion of atrial fibrillation using a biphasic, truncated exponential shock waveform at variable initial shock energies. *Am J Cardiol.* 2004;94(12):1572-1574.

451. Ambler JJ, Deakin CD. A randomised controlled trial of the effect of biphasic or monophasic waveform on the incidence and severity of cutaneous burns following external direct current cardioversion. *Resuscitation.* 2006;71(3):293-300.

452. Pellis T, Kette F, Lovisa D, Franceschino E, Magagnin L, Mercante WP, Kohl P. Utility of pre-cordial thump for treatment of out of hospital cardiac arrest: a prospective study. *Resuscitation.* 2009;80(1):17-23.

453. Amir O, Schliamser JE, Nemer S, Arie M. Ineffectiveness of precordial thump for cardioversion of malignant ventricular tachyarrhythmias. *Pacing Clin Electrophysiol.* 2007;30(2):153-156.

454. Volkmann H, Klumbies A, Kuhnert H, Paliege R, Dannberg G, Siegert K. [Terminating ventricular tachycardias by mechanical heart stimulation with precordial thumps]. *Z Kardiol.* 1990;79(10):717-724.

455. Caldwell G, Millar G, Quinn E, Vincent R, Chamberlain DA. Simple mechanical methods for cardioversion: defence of the precordial thump and cough version. *Br Med J (Clin Res Ed).* 1985;291(6496):627-630.

456. Miller J, Tresch D, Horwitz L, Thompson BM, Aprahamian C, Darin JC. The precordial thump. *Ann Emerg Med.* 1984;13(9 Pt 2):791-794.

457. Haman L, Parizek P, Vojacek J. Precordial thump efficacy in termination of induced ventricular arrhythmias. *Resuscitation.* 2009;80(1):14-16.

458. Miller J, Addas A, Akhtar M. Electrophysiology studies: precordial thumping patients paced into ventricular tachycardia. *J Emerg Med.* 1985;3(3):175-179.

459. Morgera T, Baldi N, Chersevani D, Medugno G, Camerini F. Chest thump and ventricular tachycardia. *Pacing Clin Electrophysiol.* 1979;2(1):69-75.

460. Nejima J. [Clinical features and treatment of ventricular tachycardia associated with acute myocardial infarction]. *Nippon Ika Daigaku Zasshi.* 1991;58(4):40-49.

461. Befeler B. Mechanical stimulation of the heart: its therapeutic value in tachyarrhythmias. *Chest.* 1978;73(6):832-838.

462. Muller GI, Ulmer HE, Bauer JA. Complications of chest thump for termination of supraventricular tachycardia in children. *Eur J Pediatr.* 1992;151(1):12-14.

463. Ahmar W, Morley P, Marasco S, Chan W, Aggarwal A. Sternal fracture and osteomyelitis: an unusual complication of a precordial thump. *Resuscitation.* 2007;75(3):540-542.

464. Barthell E, Troiano P, Olson D, Stueven HA, Hendley G. Prehospital external cardiac pacing: a prospective, controlled clinical trial. *Ann Emerg Med.* 1988;17(11):1221-1226.

465. Cummins RO, Graves JR, Larsen MP, Hallstrom AP, Hearne TR, Ciliberti J, Nicola RM, Horan S. Out-of-hospital transcutaneous pacing by emergency medical technicians in patients with asystolic cardiac arrest. *N Engl J Med.* 1993;328(19):1377-1382.

466. Hedges JR, Syverud SA, Dalsey WC, Feero S, Easter R, Shultz B. Prehospital trial of emergency transcutaneous cardiac pacing. *Circulation.* 1987;76(6):1337-1343.

467. White JD, Brown CG. Immediate transthoracic pacing for cardiac asystole in an emergency department setting. *Am J Emerg Med.* 1985;3(2):125-128.

468. Chan L, Reid C, Taylor B. Effect of three emergency pacing modalities on cardiac output in cardiac arrest due to ventricular asystole. *Resuscitation.* 2002;52(1):117-119.

469. Dowdle JR. Ventricular standstill and cardiac percussion. *Resuscitation.* 1996;32(1):31-32.

470. Eich C, Bleckmann A, Paul T. Percussion pacing in a three-year-old girl with complete heart block during cardiac catheterization. *Br J Anaesth.* 2005;95(4):465-467.

471. Iseri LT, Allen BJ, Baron K, Brodsky MA. Fist pacing, a forgotten procedure in bradyasystolic cardiac arrest. *Am Heart J.* 1987;113(6):1545-1550.

472. Tucker KJ, Shaburihvili TS, Gedevanishvili AT. Manual external (fist) pacing during high-degree atrioventricular block: a lifesaving intervention. *Am J Emerg Med.* 1995;13(1):53-54.

473. Eich C, Bleckmann A, Schwarz SK. Percussion pacing--an almost forgotten procedure for haemodynamically unstable bradycardias? A report of three case studies and review of the literature. *Br J Anaesth.* 2007;98(4):429-433.

474. Zeh E, Rahner E. [The manual extrathoracal stimulation of the heart. Technique and effect of the precordial thump (author's transl)]. *Z Kardiol.* 1978;67(4):299-304.

475. Manegold JC, Israel CW, Ehrlich JR, Duray G, Pajitnev D, Wegener FT, Hohnloser SH. External cardioversion of atrial fibrillation in patients with implanted pacemaker or cardioverter-defibrillator systems: a randomized comparison of monophasic and biphasic shock energy application. *Eur Heart J.* 2007;28(14):1731-1738.

476. Alferness CA. Pacemaker damage due to external countershock in patients with implanted cardiac pacemakers. *Pacing Clin Electrophysiol.* 1982;5(3):457-458.

477. Monsieurs KG, Conraads VM, Goethals MP, Snoeck JP, Bossaert LL. Semi-automatic external defibrillation and implanted cardiac pacemakers: understanding the interactions during resuscitation. *Resuscitation.* 1995;30(2):127-131.

478. Weaver WD, Cobb LA, Dennis D, Ray R, Hallstrom AP, Copass MK. Amplitude of ventricular fibrillation waveform and outcome after cardiac arrest. *Ann Intern Med.* 1985;102(1):53-55.

479. Yang Z, Lu W, Harrison RG, Eftestol T, Steen PA. A probabilistic neural network as the predictive classifier of out-of-hospital defibrillation outcomes. *Resuscitation.* 2005;64(1):31-36.

480. Box MS, Watson JN, Addison PS, Clegg GR, Robertson CE. Shock outcome prediction before and after CPR: a comparative study of manual and automated active compression-decompression CPR. *Resuscitation.* 2008;78(3):265-274.

481. Watson JN, Addison PS, Clegg GR, Steen PA, Robertson CE. Practical issues in the evaluation of methods for the prediction of shock outcome success in out-of-hospital cardiac arrest patients. *Resuscitation.* 2006;68(1):51-59.

482. Jagric T, Marhl M, Stajer D, Kocjancic ST, Podbregar M, Perc M. Irregularity test for very short electrocardiogram (ECG) signals as a method for predicting a successful defibrillation in patients

with ventricular fibrillation. *Transl Res.* 2007;149(3):145-151.

483. Strohmenger HU, Lindner KH, Brown CG. Analysis of the ventricular fibrillation ECG signal amplitude and frequency parameters as predictors of countershock success in humans. *Chest.* 1997;111(3):584-589.

484. Li Y, Ristagno G, Bisera J, Tang W, Deng Q, Weil MH. Electrocardiogram waveforms for monitoring effectiveness of chest compression during cardiopulmonary resuscitation. *Crit Care Med.* 2008;36(1):211-215.

485. Menegazzi JJ, Wang HE, Lightfoot CB, Fertig KC, Chengelis NL, Sherman LD, Callaway CW. Immediate defibrillation versus interventions first in a swine model of prolonged ventricular fibrillation. *Resuscitation.* 2003;59(2):261-270.

486. Young S, Wolff M, Lucey P, Maurana CA. The Milwaukee General Assistance Medical Program: patient perspectives on primary care in an urban safety net. *WMJ.* 2004;103(7):56-60.

487. Holzer M, Behringer W, Sterz F, Kofler J, Oschatz E, Schuster E, Laggner AN. Ventricular fibrillation median frequency may not be useful for monitoring during cardiac arrest treated with endothelin-1 or epinephrine. *Anesth Analg.* 2004;99(6):1787-1793, table of contents.

488. Miller PH. Potential fire hazard in defibrillation. *JAMA.* 1972;221(2):192.

489. ECRI. Defibrillation in oxygen-enriched environments [hazard]. *Health Devices.* 1987;16(3-4):113-114.

490. Hummel RS, 3rd, Ornato JP, Weinberg SM, Clarke AM. Spark-generating properties of electrode gels used during defibrillation. A potential fire hazard. *JAMA.* 1988;260(20):3021-3024.

491. Lefever J, Smith A. Risk of fire when using defibrillation in an oxygen enriched atmosphere. *Medical Devices Agency Safety Notices.* 1995;3:1-3.

492. Theodorou AA, Gutierrez JA, Berg RA. Fire attributable to a defibrillation attempt in a neonate. *Pediatrics.* 2003;112(3 Pt 1):677-679.

493. Robertshaw H, McAnulty G. Ambient oxygen concentrations during simulated cardiopulmonary resuscitation. *Anaesthesia.* 1998;53(7):634-637.

494. Cantello E, Davy TE, Koenig KL. The question of removing a ventilation bag before defibrillation. *J Accid Emerg Med.* 1998;15(4):286.

495. Deakin CD, Paul V, Fall E, Petley GW, Thompson F. Ambient oxygen concentrations resulting from use of the Lund University Cardiopulmonary Assist System (LUCAS) device during simulated cardiopulmonary resuscitation. *Resuscitation.* 2007;74(2):303-309.

496. Sodeck GH, Domanovits H, Meron G, Rauscha F, Losert H, Thalmann M, Vlcek M, Laggner AN. Compromising bradycardia: management in the emergency department. *Resuscitation.* 2007;73(1):96-102.

497. Clinton JE, Zoll PM, Zoll R, Ruiz E. Emergency noninvasive external cardiac pacing. *J Emerg Med.* 1985;2(3):155-162.

498. Vukov LF, Johnson DQ. External transcutaneous pacemakers in interhospital transport of cardiac patients. *Ann Emerg Med.* 1989;18(7):738-740.

499. Rosenthal E, Thomas N, Quinn E, Chamberlain D, Vincent R. Transcutaneous pacing for cardiac emergencies. *Pacing Clin Electrophysiol.* 1988;11(12):2160-2167.

500. Morrison LJ, Long J, Vermeulen M, Schwartz B, Sawadsky B, Frank J, Cameron B, Burgess R, Shield J, Bagley P, Mausz V, Brewer JE, Dorian P. A randomized controlled feasibility trial

comparing safety and effectiveness of prehospital pacing versus conventional treatment: 'PrePACE'. *Resuscitation.* 2008;76(3):341-349.

501. Sherbino J, Verbeek PR, MacDonald RD, Sawadsky BV, McDonald AC, Morrison LJ. Prehospital transcutaneous cardiac pacing for symptomatic bradycardia or bradyasystolic cardiac arrest: a systematic review. *Resuscitation.* 2006;70(2):193-200.
502. Smith I, Monk TG, White PF. Comparison of transesophageal atrial pacing with anticholinergic drugs for the treatment of intraoperative bradycardia. *Anesth Analg.* 1994;78(2):245-252.
503. Brady WJ, Swart G, DeBehnke DJ, Ma OJ, Aufderheide TP. The efficacy of atropine in the treatment of hemodynamically unstable bradycardia and atrioventricular block: prehospital and emergency department considerations. *Resuscitation.* 1999;41(1):47-55.
504. Swart G, Brady WJ, Jr., DeBehnke DJ, Ma OJ, Aufderheide TP. Acute myocardial infarction complicated by hemodynamically unstable bradyarrhythmia: prehospital and ED treatment with atropine. *Am J Emerg Med.* 1999;17(7):647-652.
505. Chadda KD, Lichstein E, Gupta PK, Choy R. Bradycardia-hypotension syndrome in acute myocardial infarction. Reappraisal of the overdrive effects of atropine. *Am J Med.* 1975;59(2):158-164.
506. Chadda KD, Lichstein E, Gupta PK, Kourtesis P. Effects of atropine in patients with bradyarrhythmia complicating myocardial infarction. Usefulness of an optimum dose for overdrive. *Am J Med.* 1977;63(4):503-510.
507. Chamberlain DA, Turner P, Sneddon JM. Effects of atropine on heart-rate in healthy man. *Lancet.* 1967;2(7505):12-15.
508. Bernheim A, Fatio R, Kiowski W, Weilenmann D, Rickli H, Brunner-La Rocca HP. Atropine often results in complete atrioventricular block or sinus arrest after cardiac transplantation: an unpredictable and dose-independent phenomenon. *Transplantation.* 2004;77(8):1181-1185.
509. Brunner-La Rocca HP, Kiowski W, Bracht C, Weilenmann D, Follath F. Atrioventricular block after administration of atropine in patients following cardiac transplantation. *Transplantation.* 1997;63(12):1838-1839.
510. Bertolet BD, Eagle DA, Conti JB, Mills RM, Belardinelli L. Bradycardia after heart transplantation: reversal with theophylline. *J Am Coll Cardiol.* 1996;28(2):396-399.
511. Strasberg B, Bassevich R, Mager A, Kusniec J, Sagie A, Sclarovsky S. Effects of aminophylline on atrioventricular conduction in patients with late atrioventricular block during inferior wall acute myocardial infarction. *Am J Cardiol.* 1991;67(6):527-528.
512. Goodfellow J, Walker PR. Reversal of atropine-resistant atrioventricular block with intravenous aminophylline in the early phase of inferior wall acute myocardial infarction following treatment with streptokinase. *Eur Heart J.* 1995;16(6):862-865.
513. Schulz-Stubner S. The use of small-dose theophylline for the treatment of bradycardia in patients with spinal cord injury. *Anesth Analg.* 2005;101(6):1809-1811.
514. DiMarco JP, Miles W, Akhtar M, Milstein S, Sharma AD, Platia E, McGovern B, Scheinman MM, Govier WC. Adenosine for paroxysmal supraventricular tachycardia: dose ranging and comparison with verapamil. Assessment in placebo-controlled, multicenter trials. The Adenosine for PSVT Study Group. *Ann Intern Med.* 1990;113(2):104-110.
515. Lim SH, Anantharaman V, Teo WS, Chan YH. Slow infusion of calcium channel blockers compared

with intravenous adenosine in the emergency treatment of supraventricular tachycardia. *Resuscitation.* 2009;80(5):523-528.

516. Cheng KA. [A randomized, multicenter trial to compare the safety and efficacy of adenosine versus verapamil for termination of paroxysmal supraventricular tachycardia]. *Zhonghua Nei Ke Za Zhi.* 2003;42(11):773-776.

517. Hood MA, Smith WM. Adenosine versus verapamil in the treatment of supraventricular tachycardia: a randomized double-crossover trial. *Am Heart J.* 1992;123(6):1543-1549.

518. Rankin AC, Oldroyd KG, Chong E, Dow JW, Rae AP, Cobbe SM. Adenosine or adenosine triphosphate for supraventricular tachycardias? Comparative double-blind randomized study in patients with spontaneous or inducible arrhythmias. *Am Heart J.* 1990;119(2 Pt 1):316-323.

519. Lim SH, Anantharaman V, Teo WS. Slow-infusion of calcium channel blockers in the emergency management of supraventricular tachycardia. *Resuscitation.* 2002;52(2):167-174.

520. Ferreira JF, Pamplona D, Cesar LA, Leite PF, Sosa EA, da Luz PL, Bellotti G. [Comparative study between verapamil and adenosine triphosphate in the treatment of paroxysmal supraventricular tachycardia]. *Arq Bras Cardiol.* 1996;66(2):55-57.

521. Gupta A, Naik A, Vora A, Lokhandwala Y. Comparison of efficacy of intravenous diltiazem and esmolol in terminating supraventricular tachycardia. *J Assoc Physicians India.* 1999;47(10):969-972.

522. Boudonas G, Lefkos N, Efthymiadis AP, Styliadis IG, Tsapas G. Intravenous administration of diltiazem in the treatment of supraventricular tachyarrhythmias. *Acta Cardiol.* 1995;50(2):125-134.

523. Sung RJ, Tan HL, Karagounis L, Hanyok JJ, Falk R, Platia E, Das G, Hardy SA. Intravenous sotalol for the termination of supraventricular tachycardia and atrial fibrillation and flutter: a multicenter, randomized, double-blind, placebo-controlled study. Sotalol Multicenter Study Group. *Am Heart J.* 1995;129(4):739-748.

524. Cybulski J, Kulakowski P, Makowska E, Czepiel A, Sikora-Frac M, Ceremuzynski L. Intravenous amiodarone is safe and seems to be effective in termination of paroxysmal supraventricular tachyarrhythmias. *Clin Cardiol.* 1996;19(7):563-566.

525. Shen EN, Keung E, Huycke E, Dohrmann ML, Nguyen N, Morady F, Sung RJ. Intravenous propafenone for termination of reentrant supraventricular tachycardia. A placebo-controlled, randomized, double-blind, crossover study. *Ann Intern Med.* 1986;105(5):655-661.

526. Olukotun AY, Klein GJ. Efficacy and safety of intravenous nadolol for supraventricular tachycardia. *Am J Cardiol.* 1987;60(6):59D-62D.

527. Ollitrault J, Quilliet L, Scheck F, Lelong B, Richard A, Jarry G, Guize L. Single infusion of intravenous cibenzoline in the treatment of supraventricular tachyarrhythmias following heart surgery. A double-blind placebo-controlled parallel study. *Eur Heart J.* 1994;15(9):1274-1278.

528. Joshi PP, Deshmukh PK, Salkar RG. Efficacy of intravenous magnesium sulphate in supraventricular tachyarrhythmias. *J Assoc Physicians India.* 1995;43(8):529-531.

529. Wesley RC, Jr., Haines DE, Lerman BB, DiMarco JP, Crampton RS. Effect of intravenous magnesium sulfate on supraventricular tachycardia. *Am J Cardiol.* 1989;63(15):1129-1131.

530. Stiles MK, Sanders P, Disney P, Brooks A, John B, Lau DH, Shashidhar, Wilson L, Mackenzie L, Young GD. Differential effects of intravenous magnesium on atrioventricular node conduction in supraventricular tachycardia. *Am J Cardiol.* 2007;100(8):1249-1253.

531. Lim SH, Anantharaman V, Teo WS, Goh PP, Tan AT. Comparison of treatment of supraventricular tachycardia by Valsalva maneuver and carotid sinus massage. *Ann Emerg Med.* 1998;31(1):30-35.

532. Wen ZC, Chen SA, Tai CT, Chiang CE, Chiou CW, Chang MS. Electrophysiological mechanisms and determinants of vagal maneuvers for termination of paroxysmal supraventricular tachycardia. *Circulation.* 1998;98(24):2716-2723.

533. Fuster V, Ryden LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, Halperin JL, Le Heuzey JY, Kay GN, Lowe JE, Olsson SB, Prystowsky EN, Tamargo JL, Wann S, Smith SC, Jr., Jacobs AK, Adams CD, Anderson JL, Antman EM, Hunt SA, Nishimura R, Ornato JP, Page RL, Riegel B, Priori SG, Blanc JJ, Budaj A, Camm AJ, Dean V, Deckers JW, Despres C, Dickstein K, Lekakis J, McGregor K, Metra M, Morais J, Osterspey A, Zamorano JL. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Circulation.* 2006;114(7):e257-354.

534. Segal JB, McNamara RL, Miller MR, Kim N, Goodman SN, Powe NR, Robinson K, Yu D, Bass EB. The evidence regarding the drugs used for ventricular rate control. *J Fam Pract.* 2000;49(1):47-59.

535. Olshansky B, Rosenfeld LE, Warner AL, Solomon AJ, O'Neill G, Sharma A, Platia E, Feld GK, Akiyama T, Brodsky MA, Greene HL. The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study: approaches to control rate in atrial fibrillation. *J Am Coll Cardiol.* 2004;43(7):1201-1208.

536. Sticherling C, Tada H, Hsu W, Bares AC, Oral H, Pelosi F, Knight BP, Strickberger SA, Morady F. Effects of diltiazem and esmolol on cycle length and spontaneous conversion of atrial fibrillation. *J Cardiovasc Pharmacol Ther.* 2002;7(2):81-88.

537. Chiladakis JA, Stathopoulos C, Davlouros P, Manolis AS. Intravenous magnesium sulfate versus diltiazem in paroxysmal atrial fibrillation. *Int J Cardiol.* 2001;79(2-3):287-291.

538. Siu CW, Lau CP, Lee WL, Lam KF, Tse HF. Intravenous diltiazem is superior to intravenous amiodarone or digoxin for achieving ventricular rate control in patients with acute uncomplicated atrial fibrillation. *Crit Care Med.* 2009;37(7):2174-2179; quiz 2180.

539. Wattanasuwan N, Khan IA, Mehta NJ, Arora P, Singh N, Vasavada BC, Sacchi TJ. Acute ventricular rate control in atrial fibrillation: IV combination of diltiazem and digoxin vs. IV diltiazem alone. *Chest.* 2001;119(2):502-506.

540. Wang HE, O'Connor R E, Megargel RE, Schnyder ME, Morrison DM, Barnes TA, Fitzkee A. The use of diltiazem for treating rapid atrial fibrillation in the out-of-hospital setting. *Ann Emerg Med.* 2001;37(1):38-45.

541. Waxman HL, Myerburg RJ, Appel R, Sung RJ. Verapamil for control of ventricular rate in paroxysmal supraventricular tachycardia and atrial fibrillation or flutter: a double-blind randomized cross-over study. *Ann Intern Med.* 1981;94(1):1-6.

542. Phillips BG, Gandhi AJ, Sanoski CA, Just VL, Bauman JL. Comparison of intravenous diltiazem and verapamil for the acute treatment of atrial fibrillation and atrial flutter. *Pharmacotherapy.* 1997;17(6):1238-1245.

543. Hilleman DE, Spinler SA. Conversion of recent-onset atrial fibrillation with intravenous amiodarone: a meta-analysis of randomized controlled trials. *Pharmacotherapy.* 2002;22(1):66-74.

544. Falk RH, Knowlton AA, Bernard SA, Gotlieb NE, Battinelli NJ. Digoxin for converting recent-onset atrial fibrillation to sinus rhythm. A randomized, double-blinded trial. *Ann Intern Med.* 1987;106(4):503-506.

545. Intravenous digoxin in acute atrial fibrillation. Results of a randomized, placebo-controlled multicentre trial in 239 patients. The Digitalis in Acute Atrial Fibrillation (DAAF) Trial Group. *Eur Heart J.* 1997;18(4):649-654.

546. Jordaens L, Trouerbach J, Calle P, Tavernier R, Derycke E, Vertongen P, Bergez B, Vandekerckhove Y. Conversion of atrial fibrillation to sinus rhythm and rate control by digoxin in comparison to placebo. *Eur Heart J.* 1997;18(4):643-648.

547. Abi-Mansour P, Carberry PA, McCowan RJ, Henthorn RW, Dunn GH, Perry KT. Conversion efficacy and safety of repeated doses of ibutilide in patients with atrial flutter and atrial fibrillation. Study Investigators. *Am Heart J.* 1998;136(4 Pt 1):632-642.

548. Ellenbogen KA, Stambler BS, Wood MA, Sager PT, Wesley RC, Jr., Meissner MC, Zoble RG, Wakefield LK, Perry KT, Vanderlugt JT. Efficacy of intravenous ibutilide for rapid termination of atrial fibrillation and atrial flutter: a dose-response study. *J Am Coll Cardiol.* 1996;28(1):130-136.

549. Soucier R, Silverman D, Abordo M, Jaagosild P, Abiose A, Madhusoodanan KP, Therrien M, Lippman N, Dalamagas H, Berns E. Propafenone versus ibutilide for post operative atrial fibrillation following cardiac surgery: neither strategy improves outcomes compared to rate control alone (the PIPAF study). *Med Sci Monit.* 2003;9(3):PI19-23.

550. Vos MA, Golitsyn SR, Stangl K, Ruda MY, Van Wijk LV, Harry JD, Perry KT, Touboul P, Steinbeck G, Wellens HJ. Superiority of ibutilide (a new class III agent) over DL-sotalol in converting atrial flutter and atrial fibrillation. The Ibutilide/Sotalol Comparator Study Group. *Heart.* 1998;79(6):568-575.

551. Volgman AS, Carberry PA, Stambler B, Lewis WR, Dunn GH, Perry KT, Vanderlugt JT, Kowey PR. Conversion efficacy and safety of intravenous ibutilide compared with intravenous procainamide in patients with atrial flutter or fibrillation. *J Am Coll Cardiol.* 1998;31(6):1414-1419.

552. Kafkas NV, Patsilinakos SP, Mertzanos GA, Papageorgiou KI, Chaveles JI, Dagadaki OK, Kelesidis KM. Conversion efficacy of intravenous ibutilide compared with intravenous amiodarone in patients with recent-onset atrial fibrillation and atrial flutter. *Int J Cardiol.* 2007;118(3):321-325.

553. Reisinger J, Gatterer E, Lang W, Vanicek T, Eisserer G, Bachleitner T, Niemeth C, Aicher F, Grander W, Heinze G, Kuhn P, Siostrzonek P. Flecainide versus ibutilide for immediate cardioversion of atrial fibrillation of recent onset. *Eur Heart J.* 2004;25(15):1318-1324.

554. Fak AS, Tezcan H, Caymaz O, Tokay S, Oktay S, Oktay A. Intravenous Propafenone for Conversion of Atrial Fibrillation or Flutter to Sinus Rhythm: A Randomized, Placebo-controlled, Crossover Study. *J Cardiovasc Pharmacol Ther.* 1997;2(4):251-258.

555. Bianconi L, Mennuni M. Comparison between propafenone and digoxin administered intravenously to patients with acute atrial fibrillation. PAFIT-3 Investigators. The Propafenone in Atrial Fibrillation Italian Trial. *Am J Cardiol.* 1998;82(5):584-588.

556. Ganau G, Lenzi T. Intravenous propafenone for converting recent onset atrial fibrillation in emergency departments: a randomized placebo-controlled multicenter trial. FAPS Investigators

Study Group. *J Emerg Med.* 1998;16(3):383-387.

557. Mattioli AV, Lucchi GR, Vivoli D, Mattioli G. Propafenone versus procainamide for conversion of atrial fibrillation to sinus rhythm. *Clin Cardiol.* 1998;21(10):763-766.

558. Martinez-Marcos FJ, Garcia-Garmendia JL, Ortega-Carpio A, Fernandez-Gomez JM, Santos JM, Camacho C. Comparison of intravenous flecainide, propafenone, and amiodarone for conversion of acute atrial fibrillation to sinus rhythm. *Am J Cardiol.* 2000;86(9):950-953.

559. Donovan KD, Power BM, Hockings BE, Dobb GJ, Lee KY. Intravenous flecainide versus amiodarone for recent-onset atrial fibrillation. *Am J Cardiol.* 1995;75(10):693-697.

560. Reisinger J, Gatterer E, Heinze G, Wiesinger K, Zeindlhofer E, Gattermeier M, Poelzl G, Kratzer H, Ebner A, Hohenwallner W, Lenz K, Slany J, Kuhn P. Prospective comparison of flecainide versus sotalol for immediate cardioversion of atrial fibrillation. *Am J Cardiol.* 1998;81(12):1450-1454.

561. Alp NJ, Bell JA, Shahi M. Randomised double blind trial of oral versus intravenous flecainide for the cardioversion of acute atrial fibrillation. *Heart.* 2000;84(1):37-40.

562. Crijns HJ, van Wijk LM, van Gilst WH, Kingma JH, van Gelder IC, Lie KI. Acute conversion of atrial fibrillation to sinus rhythm: clinical efficacy of flecainide acetate. Comparison of two regimens. *Eur Heart J.* 1988;9(6):634-638.

563. Falk RH, Pollak A, Singh SN, Friedrich T. Intravenous dofetilide, a class III antiarrhythmic agent, for the termination of sustained atrial fibrillation or flutter. Intravenous Dofetilide Investigators. *J Am Coll Cardiol.* 1997;29(2):385-390.

564. Norgaard BL, Wachtell K, Christensen PD, Madsen B, Johansen JB, Christiansen EH, Graff O, Simonsen EH. Efficacy and safety of intravenously administered dofetilide in acute termination of atrial fibrillation and flutter: a multicenter, randomized, double-blind, placebo-controlled trial. Danish Dofetilide in Atrial Fibrillation and Flutter Study Group. *Am Heart J.* 1999;137(6):1062-1069.

565. Galve E, Rius T, Ballester R, Artaza MA, Arnau JM, Garcia-Dorado D, Soler-Soler J. Intravenous amiodarone in treatment of recent-onset atrial fibrillation: results of a randomized, controlled study. *J Am Coll Cardiol.* 1996;27(5):1079-1082.

566. Cotter G, Blatt A, Kaluski E, Metzkor-Cotter E, Koren M, Litinski I, Simantov R, Moshkovitz Y, Zaidenstein R, Peleg E, Vered Z, Golik A. Conversion of recent onset paroxysmal atrial fibrillation to normal sinus rhythm: the effect of no treatment and high-dose amiodarone. A randomized, placebo-controlled study. *Eur Heart J.* 1999;20(24):1833-1842.

567. Joseph AP, Ward MR. A prospective, randomized controlled trial comparing the efficacy and safety of sotalol, amiodarone, and digoxin for the reversion of new-onset atrial fibrillation. *Ann Emerg Med.* 2000;36(1):1-9.

568. Thomas SP, Guy D, Wallace E, Crampton R, Kijvanit P, Eipper V, Ross DL, Cooper MJ. Rapid loading of sotalol or amiodarone for management of recent onset symptomatic atrial fibrillation: a randomized, digoxin-controlled trial. *Am Heart J.* 2004;147(1):E3.

569. Ho KM, Sheridan DJ, Paterson T. Use of intravenous magnesium to treat acute onset atrial fibrillation: a meta-analysis. *Heart.* 2007;93(11):1433-1440.

570. Chu K, Evans R, Emerson G, Greenslade J, Brown A. Magnesium sulfate versus placebo for paroxysmal atrial fibrillation: a randomized clinical trial. *Acad Emerg Med.* 2009;16(4):295-300.

571. Onalan O, Crystal E, Daoulah A, Lau C, Crystal A, Lashevsky I. Meta-analysis of magnesium

therapy for the acute management of rapid atrial fibrillation. *Am J Cardiol.* 2007;99(12):1726-1732.

572. Davey MJ, Teubner D. A randomized controlled trial of magnesium sulfate, in addition to usual care, for rate control in atrial fibrillation. *Ann Emerg Med.* 2005;45(4):347-353.

573. Halinen MO, Huttunen M, Paakkinen S, Tarssanen L. Comparison of sotalol with digoxin-quinidine for conversion of acute atrial fibrillation to sinus rhythm (the Sotalol-Digoxin-Quinidine Trial). *Am J Cardiol.* 1995;76(7):495-498.

574. Hohnloser SH, van de Loo A, Baedeker F. Efficacy and proarrhythmic hazards of pharmacologic cardioversion of atrial fibrillation: prospective comparison of sotalol versus quinidine. *J Am Coll Cardiol.* 1995;26(4):852-858.

575. Simpson CS, Ghali WA, Sanfilippo AJ, Moritz S, Abdollah H. Clinical assessment of clonidine in the treatment of new-onset rapid atrial fibrillation: a prospective, randomized clinical trial. *Am Heart J.* 2001;142(2):E3.

576. Roth A, Kaluski E, Felner S, Heller K, Laniado S. Clonidine for patients with rapid atrial fibrillation. *Ann Intern Med.* 1992;116(5):388-390.

577. Kochiadakis GE, Igoumenidis NE, Solomou MC, Parthenakis FI, Christakis-Hampsas MG, Chlouverakis GI, Tsatsakis AM, Vardas PE. Conversion of atrial fibrillation to sinus rhythm using acute intravenous procainamide infusion. *Cardiovasc Drugs Ther.* 1998;12(1):75-81.

578. Xanthos T, Prapa V, Papadimitriou D, Papadimitriou L. Comparative study of intravenous amiodarone and procainamide in the treatment of atrial fibrillation of recent onset. *Minerva Cardioangiol.* 2007;55(4):433-441.

579. Gorgels AP, van den Dool A, Hofs A, Mulleneers R, Smeets JL, Vos MA, Wellens HJ. Comparison of procainamide and lidocaine in terminating sustained monomorphic ventricular tachycardia. *Am J Cardiol.* 1996;78(1):43-46.

580. Komura S, Chinushi M, Furushima H, Hosaka Y, Izumi D, Iijima K, Watanabe H, Yagihara N, Aizawa Y. Efficacy of procainamide and lidocaine in terminating sustained monomorphic ventricular tachycardia. *Circ J.* 2010;74(5):864-869.

581. Berry K, Garlett EL, Bellet S, Gefter WI. Use of pronestyl in the treatment of ectopic rhythms; treatment of 98 episodes in 78 patients. *Am J Med.* 1951;11(4):431-441.

582. Ho DS, Zecchin RP, Richards DA, Uther JB, Ross DL. Double-blind trial of lignocaine versus sotalol for acute termination of spontaneous sustained ventricular tachycardia. *Lancet.* 1994;344(8914):18-23.

583. Somberg JC, Bailin SJ, Haffajee CI, Paladino WP, Kerin NZ, Bridges D, Timar S, Molnar J. Intravenous lidocaine versus intravenous amiodarone (in a new aqueous formulation) for incessant ventricular tachycardia. *Am J Cardiol.* 2002;90(8):853-859.

584. Marill KA, deSouza IS, Nishijima DK, Stair TO, Setnik GS, Ruskin JN. Amiodarone is poorly effective for the acute termination of ventricular tachycardia. *Ann Emerg Med.* 2006;47(3):217-224.

585. Schutzenberger W, Leisch F, Kerschner K, Harringer W, Herbinger W. Clinical efficacy of intravenous amiodarone in the short term treatment of recurrent sustained ventricular tachycardia and ventricular fibrillation. *Br Heart J.* 1989;62(5):367-371.

586. Tomlinson DR, Cherian P, Betts TR, Bashir Y. Intravenous amiodarone for the pharmacological termination of haemodynamically-tolerated sustained ventricular tachycardia: is bolus dose amiodarone an appropriate first-line treatment? *Emerg Med J.* 2008;25(1):15-18.

587. Armengol RE, Graff J, Baerman JM, Swiryn S. Lack of effectiveness of lidocaine for sustained, wide QRS complex tachycardia. *Ann Emerg Med.* 1989;18(3):254-257.

588. Nasir N, Jr., Taylor A, Doyle TK, Pacifico A. Evaluation of intravenous lidocaine for the termination of sustained monomorphic ventricular tachycardia in patients with coronary artery disease with or without healed myocardial infarction. *Am J Cardiol.* 1994;74(12):1183-1186.

589. Marill KA, Greenberg GM, Kay D, Nelson BK. Analysis of the treatment of spontaneous sustained stable ventricular tachycardia. *Acad Emerg Med.* 1997;4(12):1122-1128.

590. Koster RW, Dunning AJ. Intramuscular lidocaine for prevention of lethal arrhythmias in the prehospitalization phase of acute myocardial infarction. *N Engl J Med.* 1985;313(18):1105-1110.

591. Roth A, Malov N, Bloch Y, Schlesinger Z, Laniado S, Kaplinski E. Usefulness of self-administration of intramuscular lidocaine in the prehospital setting for ventricular tachyarrhythmias unassociated with acute myocardial infarction (the "Shahal" experience in Israel). *Am J Cardiol.* 1997;79(5):611-614.

592. Chevalier P, Dacosta A, Chalvidan T, Bonnefoy E, Kirkorian G, Isaaz K, Touboul P. Safety and tolerability of intravenous cibenzoline for acute termination of spontaneous sustained ventricular tachycardia. Cibenzoline and spontaneous VT. *Int J Cardiol.* 1998;64(3):265-270.

593. Manz M, Pfeiffer D, Jung W, Lueritz B. Intravenous treatment with magnesium in recurrent persistent ventricular tachycardia. *New Trends in Arrhythmias.* 1991;7(4):437-442.

594. Marill KA, Wolfram S, Desouza IS, Nishijima DK, Kay D, Setnik GS, Stair TO, Ellinor PT. Adenosine for wide-complex tachycardia: efficacy and safety. *Crit Care Med.* 2009;37(9):2512-2518.

595. Rankin AC, Oldroyd KG, Chong E, Rae AP, Cobbe SM. Value and limitations of adenosine in the diagnosis and treatment of narrow and broad complex tachycardias. *Br Heart J.* 1989;62(3):195-203.

596. Heng MK, Singh BN, Roche AH, Norris RM, Mercer CJ. Effects of intravenous verapamil on cardiac arrhythmias and on the electrocardiogram. *Am Heart J.* 1975;90(4):487-498.

597. Rankin AC, Rae AP, Cobbe SM. Misuse of intravenous verapamil in patients with ventricular tachycardia. *Lancet.* 1987;2(8557):472-474.

598. Stewart RB, Bardy GH, Greene HL. Wide complex tachycardia: misdiagnosis and outcome after emergent therapy. *Ann Intern Med.* 1986;104(6):766-771.

599. Wang JC, Lim SH, Teo WS, Anantharaman V. Calcium channel blockers as first line treatment for broad complex tachycardia with right bundle branch block: ingenuity or folly? *Resuscitation.* 2002;52(2):175-182.

600. Kasanuki H, Ohnishi S, Tanaka E, Hirosawa K. Idiopathic sustained ventricular tachycardia responsive to verapamil: clinical electrocardiographic and electrophysiologic considerations. *Jpn Circ J.* 1986;50(1):109-118.

601. van der Watt MJ, Aboo AA, Millar RN. A prospective study of electrical cardioversion for sustained tachycardias by emergency unit personnel. *S Afr Med J.* 1995;85(6):508-511.

602. Desanctis RW. Electrical Conversion of Ventricualar Tachycardia. *JAMA.* 1965;191:632-636.

603. Domanovits H, Paulis M, Nikfardjam M, Holzer M, Stuhlinger HG, Hirschl MM, Laggner AN. Sustained ventricular tachycardia in the emergency department. *Resuscitation.* 1999;42(1):19-25.

604. Kowey PR, Levine JH, Herre JM, Pacifico A, Lindsay BD, Plumb VJ, Janosik DL, Kopelman HA, Scheinman MM. Randomized, double-blind comparison of intravenous amiodarone and bretylium in the treatment of patients with recurrent, hemodynamically destabilizing ventricular tachycardia or

fibrillation. The Intravenous Amiodarone Multicenter Investigators Group. *Circulation.* 1995;92(11):3255-3263.

605. Levine JH, Massumi A, Scheinman MM, Winkle RA, Platia EV, Chilson DA, Gomes A, Woosley RL. Intravenous amiodarone for recurrent sustained hypotensive ventricular tachyarrhythmias. Intravenous Amiodarone Multicenter Trial Group. *J Am Coll Cardiol.* 1996;27(1):67-75.

606. Scheinman MM, Levine JH, Cannom DS, Friehling T, Kopelman HA, Chilson DA, Platia EV, Wilber DJ, Kowey PR. Dose-ranging study of intravenous amiodarone in patients with life-threatening ventricular tachyarrhythmias. The Intravenous Amiodarone Multicenter Investigators Group. *Circulation.* 1995;92(11):3264-3272.

607. Helmy I, Herre JM, Gee G, Sharkey H, Malone P, Sauve MJ, Griffin JC, Scheinman MM. Use of intravenous amiodarone for emergency treatment of life-threatening ventricular arrhythmias. *J Am Coll Cardiol.* 1988;12(4):1015-1022.

608. Klein RC, Machell C, Rushforth N, Standefur J. Efficacy of intravenous amiodarone as short-term treatment for refractory ventricular tachycardia. *Am Heart J.* 1988;115(1 Pt 1):96-101.

609. Mooss AN, Mohiuddin SM, Hee TT, Esterbrooks DJ, Hilleman DE, Rovang KS, Sketch MH, Sr. Efficacy and tolerance of high-dose intravenous amiodarone for recurrent, refractory ventricular tachycardia. *Am J Cardiol.* 1990;65(9):609-614.

610. Morady F, Scheinman MM, Shen E, Shapiro W, Sung RJ, DiCarlo L. Intravenous amiodarone in the acute treatment of recurrent symptomatic ventricular tachycardia. *Am J Cardiol.* 1983;51(1):156-159.

611. Ochi RP, Goldenberg IF, Almquist A, Pritzker M, Milstein S, Pedersen W, Gobel FL, Benditt DG. Intravenous amiodarone for the rapid treatment of life-threatening ventricular arrhythmias in critically ill patients with coronary artery disease. *Am J Cardiol.* 1989;64(10):599-603.

612. Aiba T, Yamagata K, Shimizu W, Taguchi A, Satomi K, Noda T, Okamura H, Suyama K, Aihara N, Kamakura S, Kurita T. Electrophysiologic study-guided amiodarone for sustained ventricular tachyarrhythmias associated with structural heart diseases. *Circ J.* 2008;72(1):88-93.

613. Nademanee K, Taylor R, Bailey WE, Rieders DE, Kosar EM. Treating electrical storm : sympathetic blockade versus advanced cardiac life support-guided therapy. *Circulation.* 2000;102(7):742-747.

614. Miwa Y, Ikeda T, Mera H, Miyakoshi M, Hoshida K, Yanagisawa R, Ishiguro H, Tsukada T, Abe A, Yusu S, Yoshino H. Effects of landiolol, an ultra-short-acting beta1-selective blocker, on electrical storm refractory to class III antiarrhythmic drugs. *Circ J.* 2010;74(5):856-863.

615. Ando J, Kakishita M, Sakai K, Komura Y, Nishiyama K, Iwabuchi M, Yokoi H, Yasumoto H, Nosaka H, Nobuyoshi M. Efficacy of nifekalant hydrochloride in the treatment of fatal ventricular arrhythmia in patients with ischemic heart disease. *Int Heart J.* 2005;46(4):647-656.

616. Yusu S, Ikeda T, Mera H, Miyakoshi M, Miwa Y, Abe A, Tsukada T, Ishiguro H, Shimizu H, Yoshino H. Effects of intravenous nifekalant as a lifesaving drug for severe ventricular tachyarrhythmias complicating acute coronary syndrome. *Circ J.* 2009;73(11):2021-2028.

617. Katoh T, Mitamura H, Matsuda N, Takano T, Ogawa S, Kasanuki H. Emergency treatment with nifekalant, a novel class III anti-arrhythmic agent, for life-threatening refractory ventricular tachyarrhythmias: post-marketing special investigation. *Circ J.* 2005;69(10):1237-1243.

618. Shiga T, Tanaka K, Kato R, Amino M, Matsudo Y, Honda T, Sagara K, Takahashi A, Katoh T, Urashima M, Ogawa S, Takano T, Kasanuki H. Nifekalant versus lidocaine for in-hospital

shock-resistant ventricular fibrillation or tachycardia. *Resuscitation.* 2010;81(1):47-52.

619. Domanovits H, Laske H, Stark G, Sterz F, Schmidinger H, Schreiber W, Mullner M, Laggner AN. Adenosine for the management of patients with tachycardias--a new protocol. *Eur Heart J.* 1994;15(5):589-593.

620. Ilkhanipour K, Berrol R, Yealy DM. Therapeutic and diagnostic efficacy of adenosine in wide-complex tachycardia. *Ann Emerg Med.* 1993;22(8):1360-1364.

621. Wilber DJ, Baerman J, Olshansky B, Kall J, Kopp D. Adenosine-sensitive ventricular tachycardia. Clinical characteristics and response to catheter ablation. *Circulation.* 1993;87(1):126-134.

622. Parham WA, Mehdirad AA, Biermann KM, Fredman CS. Case report: adenosine induced ventricular fibrillation in a patient with stable ventricular tachycardia. *J Interv Card Electrophysiol.* 2001;5(1):71-74.

623. Exner DV, Muzyka T, Gillis AM. Proarrhythmia in patients with the Wolff-Parkinson-White syndrome after standard doses of intravenous adenosine. *Ann Intern Med.* 1995;122(5):351-352.

624. Gupta AK, Shah CP, Maheshwari A, Thakur RK, Hayes OW, Lokhandwala YY. Adenosine induced ventricular fibrillation in Wolff-Parkinson-White syndrome. *Pacing Clin Electrophysiol.* 2002;25(4 Pt 1):477-480.

625. Shah CP, Gupta AK, Thakur RK, Hayes OW, Mehrotra A, Lokhandwala YY. Adenosine-induced ventricular fibrillation. *Indian Heart J.* 2001;53(2):208-210.

626. Buxton AE, Marchlinski FE, Doherty JU, Flores B, Josephson ME. Hazards of intravenous verapamil for sustained ventricular tachycardia. *Am J Cardiol.* 1987;59(12):1107-1110.

627. Hoshino K, Ogawa K, Hishitani T, Isobe T, Etoh Y. Successful uses of magnesium sulfate for torsades de pointes in children with long QT syndrome. *Pediatr Int.* 2006;48(2):112-117.

628. Moss AJ, Liu JE, Gottlieb S, Locati EH, Schwartz PJ, Robinson JL. Efficacy of permanent pacing in the management of high-risk patients with long QT syndrome. *Circulation.* 1991;84(4):1524-1529.

629. Moss AJ, Zareba W, Hall WJ, Schwartz PJ, Crampton RS, Benhorin J, Vincent GM, Locati EH, Priori SG, Napolitano C, Medina A, Zhang L, Robinson JL, Timothy K, Towbin JA, Andrews ML. Effectiveness and limitations of beta-blocker therapy in congenital long-QT syndrome. *Circulation.* 2000;101(6):616-623.

630. Tzivoni D, Banai S, Schuger C, Benhorin J, Keren A, Gottlieb S, Stern S. Treatment of torsade de pointes with magnesium sulfate. *Circulation.* 1988;77(2):392-397.

631. Stern S, Keren A, Tzivoni D. Torsade de pointes: definitions, causative factors, and therapy: experience with sixteen patients. *Ann N Y Acad Sci.* 1984;427:234-240.

632. Bando S, Yamamoto H, Nishikado A, Hamai K, Fujino K, Nakaya Y, Shinohara A. Effect of magnesium sulfate on ventricular refractoriness and its efficacy for torsade de pointes. *Tokushima J Exp Med.* 1990;37(3-4):69-73.

633. Yamamoto H, Bando S, Nishikado A, Hamai K, Yamamoto K, Shinohara A. [Efficacy of isoproterenol, magnesium sulfate and verapamil for torsade de pointes]. *Kokyu To Junkan.* 1991;39(3):261-265.

634. Keren A, Tzivoni D, Gavish D, Levi J, Gottlieb S, Benhorin J, Stern S. Etiology, warning signs and therapy of torsade de pointes. A study of 10 patients. *Circulation.* 1981;64(6):1167-1174.

635. Keren A, Tzivoni D, Golhman JM, Corcos P, Benhorin J, Stern S. Ventricular pacing in atypical ventricular tachycardia. *J Electrocardiol.* 1981;14(2):201-205.

636. Nguyen PT, Scheinman MM, Seger J. Polymorphous ventricular tachycardia: clinical

characterization, therapy, and the QT interval. *Circulation.* 1986;74(2):340-349.

637. Khan MM, Logan KR, McComb JM, Adgey AA. Management of recurrent ventricular tachyarrhythmias associated with Q-T prolongation. *Am J Cardiol.* 1981;47(6):1301-1308.

638. Yamamoto H, Bando S, Nishikado A, Shinohara A, Hamai K, Yamamoto K, Ikefuji H, Ito S. The efficacy of isoproterenol on quinidine induced torsade de pointes. *Tokushima J Exp Med.* 1991;38(1-2):1-4.

639. Lu LX, Zhou W, Zhang X, Cao Q, Yu K, Zhu C. Short QT syndrome: a case report and review of literature. *Resuscitation.* 2006;71(1):115-121.

640. Schimpf R, Wolpert C, Gaita F, Giustetto C, Borggrefe M. Short QT syndrome. *Cardiovasc Res.* 2005;67(3):357-366.

641. Ohgo T, Okamura H, Noda T, Satomi K, Suyama K, Kurita T, Aihara N, Kamakura S, Ohe T, Shimizu W. Acute and chronic management in patients with Brugada syndrome associated with electrical storm of ventricular fibrillation. *Heart Rhythm.* 2007;4(6):695-700.

642. Miyazaki T, Mitamura H, Miyoshi S, Soejima K, Aizawa Y, Ogawa S. Autonomic and antiarrhythmic drug modulation of ST segment elevation in patients with Brugada syndrome. *J Am Coll Cardiol.* 1996;27(5):1061-1070.

643. De Rosa G, Delogu AB, Piastra M, Chiaretti A, Bloise R, Priori SG. Catecholaminergic polymorphic ventricular tachycardia: successful emergency treatment with intravenous propranolol. *Pediatr Emerg Care.* 2004;20(3):175-177.

644. Leenhardt A, Lucet V, Denjoy I, Grau F, Ngoc DD, Coumel P. Catecholaminergic polymorphic ventricular tachycardia in children. A 7-year follow-up of 21 patients. *Circulation.* 1995;91(5):1512-1519.

645. Rosso R, Kalman JM, Rogowski O, Diamant S, Birger A, Biner S, Belhassen B, Viskin S. Calcium channel blockers and beta-blockers versus beta-blockers alone for preventing exercise-induced arrhythmias in catecholaminergic polymorphic ventricular tachycardia. *Heart Rhythm.* 2007;4(9):1149-1154.

646. Sumitomo N, Harada K, Nagashima M, Yasuda T, Nakamura Y, Aragaki Y, Saito A, Kurosaki K, Jouo K, Koujiro M, Konishi S, Matsuoka S, Oono T, Hayakawa S, Miura M, Ushinohama H, Shibata T, Niimura I. Catecholaminergic polymorphic ventricular tachycardia: electrocardiographic characteristics and optimal therapeutic strategies to prevent sudden death. *Heart.* 2003;89(1):66-70.

647. Ohashi J, Yasuda S, Miyazaki S, Shimizu W, Morii I, Kurita T, Kawamura A, Kamakura S, Nonogi H. Prevention of life-threatening ventricular tachyarrhythmia by a novel and pure class-III agent, nifekalant hydrochloride. *J Cardiovasc Pharmacol.* 2006;48(6):274-279.

648. Hirasawa S, Niwano S, Kishihara J, Kiryu M, Imaki R, Izumi T. Effect of nifekalant on life-threatening ventricular arrhythmias in patients with cardiopulmonary resuscitation or during the perioperative state *J Arrhythmia.* 2008;24(3):141-148.

649. Washizuka T, Chinushi M, Watanabe H, Hosaka Y, Komura S, Sugiura H, Hirono T, Furushima H, Tanabe Y, Aizawa Y. Nifekalant hydrochloride suppresses severe electrical storm in patients with malignant ventricular tachyarrhythmias. *Circ J.* 2005;69(12):1508-1513.

650. Falk M, Brugger H, Adler-Kastner L. Avalanche survival chances. *Nature.* 1994;368(6466):21.

651. Buser O, Etter HJ, Jaccard C. [Probability of dying in an avalanche]. *Z Unfallchir Versicherungsmed.* 1993;Suppl 1:263-271.

652. Brugger H, Falk M. [New perspectives of avalanche disasters. Phase classification using pathophysiologic considerations]. *Wien Klin Wochenschr.* 1992;104(6):167-173.

653. Brugger H, Durrer B, Adler-Kastner L, Falk M, Tschirky F. Field management of avalanche victims. *Resuscitation.* 2001;51(1):7-15.

654. Locher T, Walpoth B, Pfluger D, Althaus U. [Accidental hypothermia in Switzerland (1980-1987)--case reports and prognostic factors]. *Schweiz Med Wochenschr.* 1991;121(27-28):1020-1028.

655. Mair P, Kornberger E, Furtwaengler W, Balogh D, Antretter H. Prognostic markers in patients with severe accidental hypothermia and cardiocirculatory arrest. *Resuscitation.* 1994;27(1):47-54.

656. Grosse AB, Grosse CA, Steinbach LS, Zimmermann H, Anderson S. Imaging findings of avalanche victims. *Skeletal Radiol.* 2007;36(6):515-521.

657. Stalsberg H, Albretsen C, Gilbert M, Kearney M, Moestue E, Nordrum I, Rostrup M, Orbo A. Mechanism of death in avalanche victims. *Virchows Arch A Pathol Anat Histopathol.* 1989;414(5):415-422.

658. Oberhammer R, Beikircher W, Hormann C, Lorenz I, Pycha R, Adler-Kastner L, Brugger H. Full recovery of an avalanche victim with profound hypothermia and prolonged cardiac arrest treated by extracorporeal re-warming. *Resuscitation.* 2008;76(3):474-480.

659. Radwin MI, Grissom CK. Technological advances in avalanche survival. *Wilderness Environ Med.* 2002;13(2):143-152.

660. Brugger H, Sumann G, Meister R, Adler-Kastner L, Mair P, Gunga HC, Schobersberger W, Falk M. Hypoxia and hypercapnia during respiration into an artificial air pocket in snow: implications for avalanche survival. *Resuscitation.* 2003;58(1):81-88.

661. Grissom CK, Radwin MI, Harmston CH, Hirshberg EL, Crowley TJ. Respiration during snow burial using an artificial air pocket. *JAMA.* 2000;283(17):2266-2271.

662. Danzl DF, Pozos RS, Auerbach PS, Glazer S, Goetz W, Johnson E, Jui J, Lilja P, Marx JA, Miller J, et al. Multicenter hypothermia survey. *Ann Emerg Med.* 1987;16(9):1042-1055.

663. Walpoth BH, Walpoth-Aslan BN, Mattle HP, Radanov BP, Schroth G, Schaeffler L, Fischer AP, von Segesser L, Althaus U. Outcome of survivors of accidental deep hypothermia and circulatory arrest treated with extracorporeal blood warming. *N Engl J Med.* 1997;337(21):1500-1505.

664. Locher T, Walpoth BH. [Differential diagnosis of circulatory failure in hypothermic avalanche victims: retrospective analysis of 32 avalanche accidents]. *Praxis (Bern 1994).* 1996;85(41):1275-1282.

665. Ruttmann E, Weissenbacher A, Ulmer H, Muller L, Hofer D, Kilo J, Rabl W, Schwarz B, Laufer G, Antretter H, Mair P. Prolonged extracorporeal membrane oxygenation-assisted support provides improved survival in hypothermic patients with cardiocirculatory arrest. *J Thorac Cardiovasc Surg.* 2007;134(3):594-600.

666. Althaus U, Aeberhard P, Schupbach P, Nachbur BH, Muhlemann W. Management of profound accidental hypothermia with cardiorespiratory arrest. *Ann Surg.* 1982;195(4):492-495.

667. Kornberger E, Mair P. Important aspects in the treatment of severe accidental hypothermia: the Innsbruck experience. *J Neurosurg Anesthesiol.* 1996;8(1):83-87.

668. Silfvast T, Pettila V. Outcome from severe accidental hypothermia in Southern Finland--a 10-year review. *Resuscitation.* 2003;59(3):285-290.

669. Hauty MG, Esrig BC, Hill JG, Long WB. Prognostic factors in severe accidental hypothermia: experience from the Mt. Hood tragedy. *J Trauma.* 1987;27(10):1107-1112.

670. Farstad M, Andersen KS, Koller ME, Grong K, Segadal L, Husby P. Rewarming from accidental hypothermia by extracorporeal circulation. A retrospective study. *Eur J Cardiothorac Surg.* 2001;20(1):58-64.

671. Schaller MD, Fischer AP, Perret CH. Hyperkalemia. A prognostic factor during acute severe hypothermia. *JAMA.* 1990;264(14):1842-1845.

672. Dobson JA, Burgess JJ. Resuscitation of severe hypothermia by extracorporeal rewarming in a child. *J Trauma.* 1996;40(3):483-485.

673. Carbonne B, Benachi A, Leveque ML, Cabrol D, Papiernik E. Maternal position during labor: effects on fetal oxygen saturation measured by pulse oximetry. *Obstet Gynecol.* 1996;88(5):797-800.

674. Tamas P, Szilagyi A, Jeges S, Vizer M, Csermely T, Ifi Z, Balint A, Szabo I. Effects of maternal central hemodynamics on fetal heart rate patterns. *Acta Obstet Gynecol Scand.* 2007;86(6):711-714.

675. Abitbol MM. Supine position in labor and associated fetal heart rate changes. *Obstet Gynecol.* 1985;65(4):481-486.

676. Mendonca C, Griffiths J, Ateleanu B, Collis RE. Hypotension following combined spinal-epidural anaesthesia for Caesarean section. Left lateral position vs. tilted supine position. *Anaesthesia.* 2003;58(5):428-431.

677. Rees SG, Thurlow JA, Gardner IC, Scrutton MJ, Kinsella SM. Maternal cardiovascular consequences of positioning after spinal anaesthesia for Caesarean section: left 15 degree table tilt vs. left lateral. *Anaesthesia.* 2002;57(1):15-20.

678. Bamber JH, Dresner M. Aortocaval compression in pregnancy: the effect of changing the degree and direction of lateral tilt on maternal cardiac output. *Anesth Analg.* 2003;97(1):256-258, table of contents.

679. Goodwin AP, Pearce AJ. The human wedge. A manoeuvre to relieve aortocaval compression during resuscitation in late pregnancy. *Anaesthesia.* 1992;47(5):433-434.

680. Rees GA, Willis BA. Resuscitation in late pregnancy. *Anaesthesia.* 1988;43(5):347-349.

681. Ellington C, Katz VL, Watson WJ, Spielman FJ. The effect of lateral tilt on maternal and fetal hemodynamic variables. *Obstet Gynecol.* 1991;77(2):201-203.

682. Matorras R, Tacuri C, Nieto A, Gutierrez de Teran G, Cortes J. Lack of benefits of left tilt in emergent cesarean sections: a randomized study of cardiotocography, cord acid-base status and other parameters of the mother and the fetus. *J Perinat Med.* 1998;26(4):284-292.

683. Kinsella SM, Whitwam JG, Spencer JA. Aortic compression by the uterus: identification with the Finapres digital arterial pressure instrument. *Br J Obstet Gynaecol.* 1990;97(8):700-705.

684. Kundra P, Khanna S, Habeebullah S, Ravishankar M. Manual displacement of the uterus during Caesarean section. *Anaesthesia.* 2007;62(5):460-465.

685. Amaro A, Capelli E, Cardoso M, Rosa M, Carvalho J. Manual left uterine displacement or modified Crawford's edge. A comparative study in spinal anesthesia for cesarean delivery. *Revista Brasileira de Anestesiologia.* 1998;48:99-104.

686. Izci B, Vennelle M, Liston WA, Dundas KC, Calder AA, Douglas NJ. Sleep-disordered breathing and upper airway size in pregnancy and post-partum. *Eur Respir J.* 2006;27(2):321-327.

687. Hankins GD, Harvey CJ, Clark SL, Uckan EM, Van Hook JW. The effects of maternal position and

cardiac output on intrapulmonary shunt in normal third-trimester pregnancy. *Obstet Gynecol.* 1996;88(3):327-330.

688. Dijkman A, Huisman CM, Smit M, Schutte JM, Zwart JJ, van Roosmalen JJ, Oepkes D. Cardiac arrest in pregnancy: increasing use of perimortem caesarean section due to emergency skills training? *BJOG.* 2010;117(3):282-287.

689. Katz V, Balderston K, DeFreest M. Perimortem cesarean delivery: were our assumptions correct? *Am J Obstet Gynecol.* 2005;192(6):1916-1920; discussion 1920-1911.

690. Allen MC, Donohue PK, Dusman AE. The limit of viability--neonatal outcome of infants born at 22 to 25 weeks' gestation. *N Engl J Med.* 1993;329(22):1597-1601.

691. Varga I, Rigo J, Jr., Somos P, Joo JG, Nagy B. Analysis of maternal circulation and renal function in physiologic pregnancies; parallel examinations of the changes in the cardiac output and the glomerular filtration rate. *J Matern Fetal Med.* 2000;9(2):97-104.

692. Nanson J, Elcock D, Williams M, Deakin CD. Do physiological changes in pregnancy change defibrillation energy requirements? *Br J Anaesth.* 2001;87(2):237-239.

693. Jones SJ, Kinsella SM, Donald FA. Comparison of measured and estimated angles of table tilt at Caesarean section. *Br J Anaesth.* 2003;90(1):86-87.

694. Rittenberger JC, Kelly E, Jang D, Greer K, Heffner A. Successful outcome utilizing hypothermia after cardiac arrest in pregnancy: a case report. *Crit Care Med.* 2008;36(4):1354-1356.

695. Bunch TJ, White RD, Lopez-Jimenez F, Thomas RJ. Association of body weight with total mortality and with ICD shocks among survivors of ventricular fibrillation in out-of-hospital cardiac arrest. *Resuscitation.* 2008;77(3):351-355.

696. White RD, Blackwell TH, Russell JK, Jorgenson DB. Body weight does not affect defibrillation, resuscitation, or survival in patients with out-of-hospital cardiac arrest treated with a nonescalating biphasic waveform defibrillator. *Crit Care Med.* 2004;32(9 Suppl):S387-392.

697. White RD, Blackwell TH, Russell JK, Snyder DE, Jorgenson DB. Transthoracic impedance does not affect defibrillation, resuscitation or survival in patients with out-of-hospital cardiac arrest treated with a non-escalating biphasic waveform defibrillator. *Resuscitation.* 2005;64(1):63-69.

698. Brenner B, Corbridge T, Kazzi A. Intubation and mechanical ventilation of the asthmatic patient in respiratory failure. *Proc Am Thorac Soc.* 2009;6(4):371-379.

699. Williams TJ, Tuxen DV, Scheinkestel CD, Czarny D, Bowes G. Risk factors for morbidity in mechanically ventilated patients with acute severe asthma. *Am Rev Respir Dis.* 1992;146(3):607-615.

700. Woda RP, Dzwonczyk R, Bernacki BL, Cannon M, Lynn L. The ventilatory effects of auto-positive end-expiratory pressure development during cardiopulmonary resuscitation. *Crit Care Med.* 1999;27(10):2212-2217.

701. Leatherman JW, McArthur C, Shapiro RS. Effect of prolongation of expiratory time on dynamic hyperinflation in mechanically ventilated patients with severe asthma. *Crit Care Med.* 2004;32(7):1542-1545.

702. Deakin CD, McLaren RM, Petley GW, Clewlow F, Dalrymple-Hay MJ. Effects of positive end-expiratory pressure on transthoracic impedance--implications for defibrillation. *Resuscitation.* 1998;37(1):9-12.

703. Barker P. Resuscitation in status asthmaticus. *Med J Aust.* 1985;142(3):238.

704. Diament RH, Sloan JP. Failed resuscitation in acute severe asthma: a medical indication for emergency thoracotomy? *Arch Emerg Med.* 1987;4(4):233-235.

705. Eason J, Tayler D, Cottam S, Edwards R, Beard C, Peachey T, Lanigan C, Knibb A, Dimond J. Manual chest compression for total bronchospasm. *Lancet.* 1991;337(8737):366.

706. Fisher MM, Bowey CJ, Ladd-Hudson K. External chest compression in acute asthma: a preliminary study. *Crit Care Med.* 1989;17(7):686-687.

707. Fisher MM, Whaley AP, Pye RR. External chest compression in the management of acute severe asthma--a technique in search of evidence. *Prehosp Disaster Med.* 2001;16(3):124-127.

708. Mostert JW. Lung massage for total bronchospasm: a case report. *S Afr Med J.* 1960;34:703-704.

709. Smolnikoff VP. Total bronchospasm and lung massage. *Anaesthesia.* 1960;15:40-44.

710. Narimatsu E, Nara S, Kita A, Kurimoto Y, Asai Y, Ishikawa A. Serious circulatory deficiency during external chest compression for asthma attack. *Am J Emerg Med.* 2001;19(2):169-171.

711. Lapinsky SE, Leung RS. Auto-PEEP and electromechanical dissociation. *N Engl J Med.* 1996;335(9):674.

712. Rogers PL, Schlichtig R, Miro A, Pinsky M. Auto-PEEP during CPR. An "occult" cause of electromechanical dissociation? *Chest.* 1991;99(2):492-493.

713. Rosengarten PL, Tuxen DV, Dziukas L, Scheinkestel C, Merrett K, Bowes G. Circulatory arrest induced by intermittent positive pressure ventilation in a patient with severe asthma. *Anaesth Intensive Care.* 1991;19(1):118-121.

714. Sprung J, Hunter K, Barnas GM, Bourke DL. Abdominal distention is not always a sign of esophageal intubation: cardiac arrest due to "auto-PEEP". *Anesth Analg.* 1994;78(4):801-804.

715. Brown SG. Cardiovascular aspects of anaphylaxis: implications for treatment and diagnosis. *Curr Opin Allergy Clin Immunol.* 2005;5(4):359-364.

716. Mink SN, Simons FE, Simons KJ, Becker AB, Duke K. Constant infusion of epinephrine, but not bolus treatment, improves haemodynamic recovery in anaphylactic shock in dogs. *Clin Exp Allergy.* 2004;34(11):1776-1783.

717. Schummer C, Wirsing M, Schummer W. The pivotal role of vasopressin in refractory anaphylactic shock. *Anesth Analg.* 2008;107(2):620-624.

718. Kill C, Wranze E, Wulf H. Successful treatment of severe anaphylactic shock with vasopressin. Two case reports. *Int Arch Allergy Immunol.* 2004;134(3):260-261.

719. Kluger MT. The bispectral index during an anaphylactic circulatory arrest. *Anaesth Intensive Care.* 2001;29(5):544-547.

720. McBrien ME, Breslin DS, Atkinson S, Johnston JR. Use of methoxamine in the resuscitation of epinephrine-resistant electromechanical dissociation. *Anaesthesia.* 2001;56(11):1085-1089.

721. Rocq N, Favier JC, Plancade D, Steiner T, Mertes PM. Successful use of terlipressin in post-cardiac arrest resuscitation after an epinephrine-resistant anaphylactic shock to suxamethonium. *Anesthesiology.* 2007;107(1):166-167.

722. Green R, Ball A. Alpha-agonists for the treatment of anaphylactic shock. *Anaesthesia.* 2005;60(6):621-622.

723. Heytman M, Rainbird A. Use of alpha-agonists for management of anaphylaxis occurring under anaesthesia: case studies and review. *Anaesthesia.* 2004;59(12):1210-1215.

724. Higgins DJ, Gayatri P. Methoxamine in the management of severe anaphylaxis. *Anaesthesia.*

1999;54(11):1126.

725. Allen SJ, Gallagher A, Paxton LD. Anaphylaxis to rocuronium. *Anaesthesia.* 2000;55(12):1223-1224.

726. Lafforgue E, Sleth JC, Pluskwa F, Saizy C. [Successful extracorporeal resuscitation of a probable perioperative anaphylactic shock due to atracurium]. *Ann Fr Anesth Reanim.* 2005;24(5):551-555.

727. Vatsgar TT, Ingebrigtsen O, Fjose LO, Wikstrom B, Nilsen JE, Wik L. Cardiac arrest and resuscitation with an automatic mechanical chest compression device (LUCAS) due to anaphylaxis of a woman receiving caesarean section because of pre-eclampsia. *Resuscitation.* 2006;68(1):155-159.

728. Gibbs MW, Kuczkowski KM, Benumof JL. Complete recovery from prolonged cardio-pulmonary resuscitation following anaphylactic reaction to readministered intravenous cefazolin. *Acta Anaesthesiol Scand.* 2003;47(2):230-232.

729. Litz RJ, Popp M, Stehr SN, Koch T. Successful resuscitation of a patient with ropivacaine-induced asystole after axillary plexus block using lipid infusion. *Anaesthesia.* 2006;61(8):800-801.

730. Rosenblatt MA, Abel M, Fischer GW, Itzkovich CJ, Eisenkraft JB. Successful use of a 20% lipid emulsion to resuscitate a patient after a presumed bupivacaine-related cardiac arrest. *Anesthesiology.* 2006;105(1):217-218.

731. Marwick PC, Levin AI, Coetzee AR. Recurrence of cardiotoxicity after lipid rescue from bupivacaine-induced cardiac arrest. *Anesth Analg.* 2009;108(4):1344-1346.

732. Smith HM, Jacob AK, Segura LG, Dilger JA, Torsher LC. Simulation education in anesthesia training: a case report of successful resuscitation of bupivacaine-induced cardiac arrest linked to recent simulation training. *Anesth Analg.* 2008;106(5):1581-1584, table of contents.

733. Warren JA, Thoma RB, Georgescu A, Shah SJ. Intravenous lipid infusion in the successful resuscitation of local anesthetic-induced cardiovascular collapse after supraclavicular brachial plexus block. *Anesth Analg.* 2008;106(5):1578-1580, table of contents.

734. Foxall GL, Hardman JG, Bedforth NM. Three-dimensional, multiplanar, ultrasound-guided, radial nerve block. *Reg Anesth Pain Med.* 2007;32(6):516-521.

735. Shah S, Gopalakrishnan S, Apuya J, Martin T. Use of Intralipid in an infant with impending cardiovascular collapse due to local anesthetic toxicity. *J Anesth.* 2009;23(3):439-441.

736. Zimmer C, Piepenbrink K, Riest G, Peters J. [Cardiotoxic and neurotoxic effects after accidental intravascular bupivacaine administration. Therapy with lidocaine propofol and lipid emulsion]. *Anaesthesist.* 2007;56(5):449-453.

737. Litz RJ, Roessel T, Heller AR, Stehr SN. Reversal of central nervous system and cardiac toxicity after local anesthetic intoxication by lipid emulsion injection. *Anesth Analg.* 2008;106(5):1575-1577, table of contents.

738. Ludot H, Tharin JY, Belouadah M, Mazoit JX, Malinovsky JM. Successful resuscitation after ropivacaine and lidocaine-induced ventricular arrhythmia following posterior lumbar plexus block in a child. *Anesth Analg.* 2008;106(5):1572-1574, table of contents.

739. Cave G, Harvey MG, Winterbottom T. Evaluation of the Association of Anaesthetists of Great Britain and Ireland lipid infusion protocol in bupivacaine induced cardiac arrest in rabbits. *Anaesthesia.* 2009;64(7):732-737.

740. Di Gregorio G, Schwartz D, Ripper R, Kelly K, Feinstein DL, Minshall RD, Massad M, Ori C, Weinberg GL. Lipid emulsion is superior to vasopressin in a rodent model of resuscitation from toxin-induced cardiac arrest. *Crit Care Med.* 2009;37(3):993-999.

741. Weinberg GL, VadeBoncouer T, Ramaraju GA, Garcia-Amaro MF, Cwik MJ. Pretreatment or resuscitation with a lipid infusion shifts the dose-response to bupivacaine-induced asystole in rats. *Anesthesiology.* 1998;88(4):1071-1075.

742. Weinberg G, Ripper R, Feinstein DL, Hoffman W. Lipid emulsion infusion rescues dogs from bupivacaine-induced cardiac toxicity. *Reg Anesth Pain Med.* 2003;28(3):198-202.

743. Weinberg GL, Di Gregorio G, Ripper R, Kelly K, Massad M, Edelman L, Schwartz D, Shah N, Zheng S, Feinstein DL. Resuscitation with lipid versus epinephrine in a rat model of bupivacaine overdose. *Anesthesiology.* 2008;108(5):907-913.

744. Mayr VD, Mitterschiffthaler L, Neurauter A, Gritsch C, Wenzel V, Muller T, Luckner G, Lindner KH, Strohmenger HU. A comparison of the combination of epinephrine and vasopressin with lipid emulsion in a porcine model of asphyxial cardiac arrest after intravenous injection of bupivacaine. *Anesth Analg.* 2008;106(5):1566-1571, table of contents.

745. Hicks SD, Salcido DD, Logue ES, Suffoletto BP, Empey PE, Poloyac SM, Miller DR, Callaway CW, Menegazzi JJ. Lipid emulsion combined with epinephrine and vasopressin does not improve survival in a swine model of bupivacaine-induced cardiac arrest. *Anesthesiology.* 2009;111(1):138-146.

746. Hiller DB, Gregorio GD, Ripper R, Kelly K, Massad M, Edelman L, Edelman G, Feinstein DL, Weinberg GL. Epinephrine impairs lipid resuscitation from bupivacaine overdose: a threshold effect. *Anesthesiology.* 2009;111(3):498-505.

747. Cho HS, Lee JJ, Chung IS, Shin BS, Kim JA, Lee KH. Insulin reverses bupivacaine-induced cardiac depression in dogs. *Anesth Analg.* 2000;91(5):1096-1102.

748. Kim JT, Jung CW, Lee KH. The effect of insulin on the resuscitation of bupivacaine-induced severe cardiovascular toxicity in dogs. *Anesth Analg.* 2004;99(3):728-733, table of contents.

749. Pham-Dang C, Beaumont S, Floch H, Bodin J, Winer A, Pinaud M. [Acute toxic accident following lumbar plexus block with bupivacaine]. *Ann Fr Anesth Reanim.* 2000;19(5):356-359.

750. Braque S, Bernard-Bertrand F, Guillou N, Guezennec D, Canciani JP, Gentili ME. Successful but prolonged resuscitation after local anesthetic-induced cardiac arrest: is clonidine effective? *Acta Anaesthesiol Belg.* 2008;59(2):91-94.

751. de La Coussaye JE, Eledjam JJ, Bassoul B, Bruelle P, Lefrant JY, Peray PA, Saissi G, Desch G, Sassine A. Receptor mechanisms for clonidine reversal of bupivacaine-induced impairment of ventricular conduction in pentobarbital-anesthetized dogs. *Anesth Analg.* 1994;78(4):624-637.

752. Beauvoir C, Passeron D, du Cailar G, Millet E. [Diltiazem poisoning: hemodynamic aspects]. *Ann Fr Anesth Reanim.* 1991;10(2):154-157.

753. Gillart T, Loiseau S, Azarnoush K, Gonzalez D, Guelon D. [Resuscitation after three hours of cardiac arrest with severe hypothermia following a toxic coma]. *Ann Fr Anesth Reanim.* 2008;27(6):510-513.

754. Nordt SP, Clark RF. Midazolam: a review of therapeutic uses and toxicity. *J Emerg Med.* 1997;15(3):357-365.

755. Lheureux P, Vranckx M, Leduc D, Askenasi R. Flumazenil in mixed benzodiazepine/tricyclic antidepressant overdose: a placebo-controlled study in the dog. *Am J Emerg Med.* 1992;10(3):184-188.

756. Machin KL, Caulkett NA. Cardiopulmonary effects of propofol and a medetomidine-midazolam-ketamine combination in mallard ducks. *Am J Vet Res.*

1998;59(5):598-602.

757. Fujita Y, Ishikawa H, Yokota K. Anaphylactoid reaction to midazolam. *Anesth Analg.* 1994;79(4):811-812.

758. Mullins ME. First-degree atrioventricular block in alprazolam overdose reversed by flumazenil. *J Pharm Pharmacol.* 1999;51(3):367-370.

759. Spivey WH, Roberts JR, Derlet RW. A clinical trial of escalating doses of flumazenil for reversal of suspected benzodiazepine overdose in the emergency department. *Ann Emerg Med.* 1993;22(12):1813-1821.

760. Geller E, Halpern P, Chernilas J, Niv D, Miller HB. Cardiorespiratory effects of antagonism of diazepam sedation with flumazenil in patients with cardiac disease. *Anesth Analg.* 1991;72(2):207-211.

761. Hara Y, Kobayashi H, Ooshiro S, Futamura K, Nishino T, Chugun A, Temma K, Kondo H. Negative inotropic effect of diazepam in isolated guinea pig heart. *J Vet Med Sci.* 2001;63(2):135-143.

762. Treatment of benzodiazepine overdose with flumazenil. The Flumazenil in Benzodiazepine Intoxication Multicenter Study Group. *Clin Ther.* 1992;14(6):978-995.

763. Fahed S, Grum DF, Papadimos TJ. Labetalol infusion for refractory hypertension causing severe hypotension and bradycardia: an issue of patient safety. *Patient Saf Surg.* 2008;2:13.

764. Fernandes CM, Daya MR. Sotalol-induced bradycardia reversed by glucagon. *Can Fam Physician.* 1995;41:659-660, 663-655.

765. Frishman W, Jacob H, Eisenberg E, Ribner H. Clinical pharmacology of the new beta-adrenergic blocking drugs. Part 8. Self-poisoning with beta-adrenoceptor blocking agents: recognition and management. *Am Heart J.* 1979;98(6):798-811.

766. Gabry AL, Pourriat JL, Hoang TD, Lapandry C. [Cardiogenic shock caused by metoprolol poisoning. Reversibility with high doses of glucagon and isoproterenol]. *Presse Med.* 1985;14(4):229.

767. Hazouard E, Ferrandiere M, Lesire V, Joye F, Perrotin D, de Toffol B. Peduncular hallucinosis related to propranolol self-poisoning: efficacy of intravenous glucagon. *Intensive Care Med.* 1999;25(3):336-337.

768. Khan MI, Miller MT. Beta-blocker toxicity--the role of glucagon. Report of 2 cases. *S Afr Med J.* 1985;67(26):1062-1063.

769. Moller BH. Letter: Massive intoxication with metoprolol. *Br Med J.* 1976;1(6003):222.

770. O'Mahony D, O'Leary P, Molloy MG. Severe oxprenolol poisoning: the importance of glucagon infusion. *Hum Exp Toxicol.* 1990;9(2):101-103.

771. Wallin CJ, Hulting J. Massive metoprolol poisoning treated with prenalterol. *Acta Med Scand.* 1983;214(3):253-255.

772. Weinstein RS, Cole S, Knaster HB, Dahlbert T. Beta blocker overdose with propranolol and with atenolol. *Ann Emerg Med.* 1985;14(2):161-163.

773. Alderfliegel F, Leeman M, Demaeyer P, Kahn RJ. Sotalol poisoning associated with asystole. *Intensive Care Med.* 1993;19(1):57-58.

774. Kenyon CJ, Aldinger GE, Joshipura P, Zaid GJ. Successful resuscitation using external cardiac pacing in beta adrenergic antagonist-induced bradyasystolic arrest. *Ann Emerg Med.* 1988;17(7):711-713.

775. Freestone S, Thomas HM, Bhamra RK, Dyson EH. Severe atenolol poisoning: treatment with

prenalterol. *Hum Toxicol.* 1986;5(5):343-345.

776. Kerns W, 2nd, Schroeder D, Williams C, Tomaszewski C, Raymond R. Insulin improves survival in a canine model of acute beta-blocker toxicity. *Ann Emerg Med.* 1997;29(6):748-757.

777. Holger JS, Engebretsen KM, Fritzlar SJ, Patten LC, Harris CR, Flottemesch TJ. Insulin versus vasopressin and epinephrine to treat beta-blocker toxicity. *Clin Toxicol (Phila).* 2007;45(4):396-401.

778. Page C, Hacket LP, Isbister GK. The use of high-dose insulin-glucose euglycemia in beta-blocker overdose: a case report. *J Med Toxicol.* 2009;5(3):139-143.

779. Kollef MH. Labetalol overdose successfully treated with amrinone and alpha-adrenergic receptor agonists. *Chest.* 1994;105(2):626-627.

780. O'Grady J, Anderson S, Pringle D. Successful treatment of severe atenolol overdose with calcium chloride. *CJEM.* 2001;3(3):224-227.

781. Pertoldi F, D'Orlando L, Mercante WP. Electromechanical dissociation 48 hours after atenolol overdose: usefulness of calcium chloride. *Ann Emerg Med.* 1998;31(6):777-781.

782. Brimacombe JR, Scully M, Swainston R. Propranolol overdose--a dramatic response to calcium chloride. *Med J Aust.* 1991;155(4):267-268.

783. McVey FK, Corke CF. Extracorporeal circulation in the management of massive propranolol overdose. *Anaesthesia.* 1991;46(9):744-746.

784. Lane AS, Woodward AC, Goldman MR. Massive propranolol overdose poorly responsive to pharmacologic therapy: use of the intra-aortic balloon pump. *Ann Emerg Med.* 1987;16(12):1381-1383.

785. Rooney M, Massey KL, Jamali F, Rosin M, Thomson D, Johnson DH. Acebutolol overdose treated with hemodialysis and extracorporeal membrane oxygenation. *J Clin Pharmacol.* 1996;36(8):760-763.

786. Love JN, Leasure JA, Mundt DJ, Janz TG. A comparison of amrinone and glucagon therapy for cardiovascular depression associated with propranolol toxicity in a canine model. *J Toxicol Clin Toxicol.* 1992;30(3):399-412.

787. Toet AE, Wemer J, Vleeming W, te Biesebeek JD, Meulenbelt J, de Wildt DJ. Experimental study of the detrimental effect of dopamine/glucagon combination in d,l-propranolol intoxication. *Hum Exp Toxicol.* 1996;15(5):411-421.

788. Toet AE, te Biesebeek JD, Vleeming W, Wemer J, Meulenbelt J, de Wildt DJ. Reduced survival after isoprenaline/dopamine in d,l-propranolol intoxicated rats. *Hum Exp Toxicol.* 1996;15(2):120-128.

789. Sato S, Tsuji MH, Okubo N, Nishimoto C, Naito H. Combined use of glucagon and milrinone may not be preferable for severe propranolol poisoning in the canine model. *J Toxicol Clin Toxicol.* 1995;33(4):337-342.

790. Boyer EW, Duic PA, Evans A. Hyperinsulinemia/euglycemia therapy for calcium channel blocker poisoning. *Pediatr Emerg Care.* 2002;18(1):36-37.

791. Cohen V, Jellinek SP, Fancher L, Sangwan G, Wakslak M, Marquart E, Farahani C. Tarka(R) (Trandolapril/Verapamil Hydrochloride Extended-Release) overdose. *J Emerg Med.* 2011;40(3):291-295.

792. Greene SL, Gawarammana I, Wood DM, Jones AL, Dargan PI. Relative safety of hyperinsulinaemia/euglycaemia therapy in the management of calcium channel blocker overdose: a prospective observational study. *Intensive Care Med.* 2007;33(11):2019-2024.

793. Harris NS. Case records of the Massachusetts General Hospital. Case 24-2006. A 40-year-old woman with hypotension after an overdose of amlodipine. *N Engl J Med.* 2006;355(6):602-611.

794. Herbert J, O'Malley C, Tracey J, Dwyer R, Power M. Verapamil overdosage unresponsive to dextrose/insulin therapy. *J Toxicol Clin Toxicol.* 2001;39:293-294.

795. Johansen KK, Belhage B. [A 48-year-old woman's survival from a massive verapamil overdose]. *Ugeskr Laeger.* 2007;169(47):4074-4075.

796. Kanagarajan K, Marraffa JM, Bouchard NC, Krishnan P, Hoffman RS, Stork CM. The use of vasopressin in the setting of recalcitrant hypotension due to calcium channel blocker overdose. *Clin Toxicol (Phila).* 2007;45(1):56-59.

797. Marques M, Gomes E, de Oliveira J. Treatment of calcium channel blocker intoxication with insulin infusion: case report and literature review. *Resuscitation.* 2003;57(2):211-213.

798. Meyer M, Stremski E, Scanlon M. Successful resuscitation of a verapamil intoxicated child with a dextrose-insulin infusion. *Clin Intensive Care.* 2003;14:109-113.

799. Morris-Kukoski C, Biswas A, Para M. Insulin "euglycemia" therapy for accidental nifedipine overdose. *J Toxicol Clin Toxicol.* 2000;38:557.

800. Ortiz-Munoz L, Rodriguez-Ospina LF, Figueroa-Gonzalez M. Hyperinsulinemic-euglycemic therapy for intoxication with calcium channel blockers. *Bol Asoc Med P R.* 2005;97(3 Pt 2):182-189.

801. Patel NP, Pugh ME, Goldberg S, Eiger G. Hyperinsulinemic euglycemia therapy for verapamil poisoning: case report. *Am J Crit Care.* 2007;16(5):520, 518-529.

802. Place R, Carlson A, Leikin J, Hanashiro P. Hyperinsulin therapy in the treatment of verapamil overdose. *J Toxicol Clin Toxicol.* 2000:576-577.

803. Rasmussen L, Husted SE, Johnsen SP. Severe intoxication after an intentional overdose of amlodipine. *Acta Anaesthesiol Scand.* 2003;47(8):1038-1040.

804. Smith SW, Ferguson KL, Hoffman RS, Nelson LS, Greller HA. Prolonged severe hypotension following combined amlodipine and valsartan ingestion. *Clin Toxicol (Phila).* 2008;46(5):470-474.

805. Yuan TH, Kerns WP, 2nd, Tomaszewski CA, Ford MD, Kline JA. Insulin-glucose as adjunctive therapy for severe calcium channel antagonist poisoning. *J Toxicol Clin Toxicol.* 1999;37(4):463-474.

806. Hampson NB, Zmaeff JL. Outcome of patients experiencing cardiac arrest with carbon monoxide poisoning treated with hyperbaric oxygen. *Ann Emerg Med.* 2001;38(1):36-41.

807. Sloan EP, Murphy DG, Hart R, Cooper MA, Turnbull T, Barreca RS, Ellerson B. Complications and protocol considerations in carbon monoxide-poisoned patients who require hyperbaric oxygen therapy: report from a ten-year experience. *Ann Emerg Med.* 1989;18(6):629-634.

808. Chou KJ, Fisher JL, Silver EJ. Characteristics and outcome of children with carbon monoxide poisoning with and without smoke exposure referred for hyperbaric oxygen therapy. *Pediatr Emerg Care.* 2000;16(3):151-155.

809. Weaver LK, Hopkins RO, Chan KJ, Churchill S, Elliott CG, Clemmer TP, Orme JF, Jr., Thomas FO, Morris AH. Hyperbaric oxygen for acute carbon monoxide poisoning. *N Engl J Med.* 2002;347(14):1057-1067.

810. Thom SR, Taber RL, Mendiguren, II, Clark JM, Hardy KR, Fisher AB. Delayed neuropsychologic sequelae after carbon monoxide poisoning: prevention by treatment with hyperbaric oxygen. *Ann Emerg Med.* 1995;25(4):474-480.

811. Scheinkestel CD, Bailey M, Myles PS, Jones K, Cooper DJ, Millar IL, Tuxen DV. Hyperbaric or

normobaric oxygen for acute carbon monoxide poisoning: a randomised controlled clinical trial. *Med J Aust.* 1999;170(5):203-210.

812. Raphael JC, Elkharrat D, Jars-Guincestre MC, Chastang C, Chasles V, Vercken JB, Gajdos P. Trial of normobaric and hyperbaric oxygen for acute carbon monoxide intoxication. *Lancet.* 1989;2(8660):414-419.

813. Juurlink DN, Buckley NA, Stanbrook MB, Isbister GK, Bennett M, McGuigan MA. Hyperbaric oxygen for carbon monoxide poisoning. *Cochrane Database Syst Rev.* 2005(1):CD002041.

814. Buckley NA, Isbister GK, Stokes B, Juurlink DN. Hyperbaric oxygen for carbon monoxide poisoning : a systematic review and critical analysis of the evidence. *Toxicol Rev.* 2005;24(2):75-92.

815. Satran D, Henry CR, Adkinson C, Nicholson CI, Bracha Y, Henry TD. Cardiovascular manifestations of moderate to severe carbon monoxide poisoning. *J Am Coll Cardiol.* 2005;45(9):1513-1516.

816. Henry CR, Satran D, Lindgren B, Adkinson C, Nicholson CI, Henry TD. Myocardial injury and long-term mortality following moderate to severe carbon monoxide poisoning. *JAMA.* 2006;295(4):398-402.

817. Hsue PY, McManus D, Selby V, Ren X, Pillutla P, Younes N, Goldschlager N, Waters DD. Cardiac arrest in patients who smoke crack cocaine. *Am J Cardiol.* 2007;99(6):822-824.

818. Lange RA, Cigarroa RG, Yancy CW, Jr., Willard JE, Popma JJ, Sills MN, McBride W, Kim AS, Hillis LD. Cocaine-induced coronary-artery vasoconstriction. *N Engl J Med.* 1989;321(23):1557-1562.

819. Baumann BM, Perrone J, Hornig SE, Shofer FS, Hollander JE. Randomized, double-blind, placebo-controlled trial of diazepam, nitroglycerin, or both for treatment of patients with potential cocaine-associated acute coronary syndromes. *Acad Emerg Med.* 2000;7(8):878-885.

820. Honderick T, Williams D, Seaberg D, Wears R. A prospective, randomized, controlled trial of benzodiazepines and nitroglycerine or nitroglycerine alone in the treatment of cocaine-associated acute coronary syndromes. *Am J Emerg Med.* 2003;21(1):39-42.

821. Dattilo PB, Hailpern SM, Fearon K, Sohal D, Nordin C. Beta-blockers are associated with reduced risk of myocardial infarction after cocaine use. *Ann Emerg Med.* 2008;51(2):117-125.

822. Vongpatanasin W, Mansour Y, Chavoshan B, Arbique D, Victor RG. Cocaine stimulates the human cardiovascular system via a central mechanism of action. *Circulation.* 1999;100(5):497-502.

823. Lange RA, Cigarroa RG, Flores ED, McBride W, Kim AS, Wells PJ, Bedotto JB, Danziger RS, Hillis LD. Potentiation of cocaine-induced coronary vasoconstriction by beta-adrenergic blockade. *Ann Intern Med.* 1990;112(12):897-903.

824. Sand IC, Brody SL, Wrenn KD, Slovis CM. Experience with esmolol for the treatment of cocaine-associated cardiovascular complications. *Am J Emerg Med.* 1991;9(2):161-163.

825. Sofuoglu M, Brown S, Babb DA, Pentel PR, Hatsukami DK. Carvedilol affects the physiological and behavioral response to smoked cocaine in humans. *Drug Alcohol Depend.* 2000;60(1):69-76.

826. Sofuoglu M, Brown S, Babb DA, Pentel PR, Hatsukami DK. Effects of labetalol treatment on the physiological and subjective response to smoked cocaine. *Pharmacol Biochem Behav.* 2000;65(2):255-259.

827. Boehrer JD, Moliterno DJ, Willard JE, Hillis LD, Lange RA. Influence of labetalol on cocaine-induced coronary vasoconstriction in humans. *Am J Med.* 1993;94(6):608-610.

828. Negus BH, Willard JE, Hillis LD, Glamann DB, Landau C, Snyder RW, Lange RA. Alleviation of

cocaine-induced coronary vasoconstriction with intravenous verapamil. *Am J Cardiol.* 1994;73(7):510-513.

829. Shih RD, Hollander JE, Burstein JL, Nelson LS, Hoffman RS, Quick AM. Clinical safety of lidocaine in patients with cocaine-associated myocardial infarction. *Ann Emerg Med.* 1995;26(6):702-706.

830. Saland KE, Hillis LD, Lange RA, Cigarroa JE. Influence of morphine sulfate on cocaine-induced coronary vasoconstriction. *Am J Cardiol.* 2002;90(7):810-811.

831. Brogan WC, 3rd, Lange RA, Kim AS, Moliterno DJ, Hillis LD. Alleviation of cocaine-induced coronary vasoconstriction by nitroglycerin. *J Am Coll Cardiol.* 1991;18(2):581-586.

832. Hollander JE, Hoffman RS, Gennis P, Fairweather P, DiSano MJ, Schumb DA, Feldman JA, Fish SS, Dyer S, Wax P, et al. Nitroglycerin in the treatment of cocaine associated chest pain--clinical safety and efficacy. *J Toxicol Clin Toxicol.* 1994;32(3):243-256.

833. Borron SW, Baud FJ, Barriot P, Imbert M, Bismuth C. Prospective study of hydroxocobalamin for acute cyanide poisoning in smoke inhalation. *Ann Emerg Med.* 2007;49(6):794-801, 801 e791-792.

834. Fortin JL, Giocanti JP, Ruttimann M, Kowalski JJ. Prehospital administration of hydroxocobalamin for smoke inhalation-associated cyanide poisoning: 8 years of experience in the Paris Fire Brigade. *Clin Toxicol (Phila).* 2006;44 Suppl 1:37-44.

835. Baud FJ, Barriot P, Toffis V, Riou B, Vicaut E, Lecarpentier Y, Bourdon R, Astier A, Bismuth C. Elevated blood cyanide concentrations in victims of smoke inhalation. *N Engl J Med.* 1991;325(25):1761-1766.

836. Borron SW, Baud FJ, Megarbane B, Bismuth C. Hydroxocobalamin for severe acute cyanide poisoning by ingestion or inhalation. *Am J Emerg Med.* 2007;25(5):551-558.

837. Espinoza OB, Perez M, Ramirez MS. Bitter cassava poisoning in eight children: a case report. *Vet Hum Toxicol.* 1992;34(1):65.

838. Houeto P, Hoffman JR, Imbert M, Levillain P, Baud FJ. Relation of blood cyanide to plasma cyanocobalamin concentration after a fixed dose of hydroxocobalamin in cyanide poisoning. *Lancet.* 1995;346(8975):605-608.

839. Pontal P, Bismuth C, Garnier R. Therapeutic attitude in cyanide poisoning: Retrospective study of 24 non-lethal cases. *Veterinary and Human Toxicology.* 1982;24(4):286-287.

840. Kirk MA, Gerace R, Kulig KW. Cyanide and methemoglobin kinetics in smoke inhalation victims treated with the cyanide antidote kit. *Ann Emerg Med.* 1993;22(9):1413-1418.

841. Chen KK, Rose CL. Nitrite and thiosulfate therapy in cyanide poisoning. *J Am Med Assoc.* 1952;149(2):113-119.

842. Yen D, Tsai J, Wang LM, Kao WF, Hu SC, Lee CH, Deng JF. The clinical experience of acute cyanide poisoning. *Am J Emerg Med.* 1995;13(5):524-528.

843. Pentel P, Peterson CD. Asystole complicating physostigmine treatment of tricyclic antidepressant overdose. *Ann Emerg Med.* 1980;9(11):588-590.

844. Hoffman JR, Votey SR, Bayer M, Silver L. Effect of hypertonic sodium bicarbonate in the treatment of moderate-to-severe cyclic antidepressant overdose. *Am J Emerg Med.* 1993;11(4):336-341.

845. Koppel C, Wiegreffe A, Tenczer J. Clinical course, therapy, outcome and analytical data in amitriptyline and combined amitriptyline/chlordiazepoxide overdose. *Hum Exp Toxicol.* 1992;11(6):458-465.

846. Brown TC. Tricyclic antidepressant overdosage: experimental studies on the management of

circulatory complications. *Clin Toxicol.* 1976;9(2):255-272.

847. Hedges JR, Baker PB, Tasset JJ, Otten EJ, Dalsey WC, Syverud SA. Bicarbonate therapy for the cardiovascular toxicity of amitriptyline in an animal model. *J Emerg Med.* 1985;3(4):253-260.

848. Knudsen K, Abrahamsson J. Epinephrine and sodium bicarbonate independently and additively increase survival in experimental amitriptyline poisoning. *Crit Care Med.* 1997;25(4):669-674.

849. Nattel S, Mittleman M. Treatment of ventricular tachyarrhythmias resulting from amitriptyline toxicity in dogs. *J Pharmacol Exp Ther.* 1984;231(2):430-435.

850. Pentel P, Benowitz N. Efficacy and mechanism of action of sodium bicarbonate in the treatment of desipramine toxicity in rats. *J Pharmacol Exp Ther.* 1984;230(1):12-19.

851. Sasyniuk BI, Jhamandas V, Valois M. Experimental amitriptyline intoxication: treatment of cardiac toxicity with sodium bicarbonate. *Ann Emerg Med.* 1986;15(9):1052-1059.

852. Bessen HA, Niemann JT. Improvement of cardiac conduction after hyperventilation in tricyclic antidepressant overdose. *J Toxicol Clin Toxicol.* 1985;23(7-8):537-546.

853. Hagerman GA, Hanashiro PK. Reversal of tricyclic-antidepressant-induced cardiac conduction abnormalities by phenytoin. *Ann Emerg Med.* 1981;10(2):82-86.

854. Knudsen K, Abrahamsson J. Effects of magnesium sulfate and lidocaine in the treatment of ventricular arrhythmias in experimental amitriptyline poisoning in the rat. *Crit Care Med.* 1994;22(3):494-498.

855. Knudsen K, Abrahamsson J. Effects of epinephrine, norepinephrine, magnesium sulfate, and milrinone on survival and the occurrence of arrhythmias in amitriptyline poisoning in the rat. *Crit Care Med.* 1994;22(11):1851-1855.

856. Kline JA, DeStefano AA, Schroeder JD, Raymond RM. Magnesium potentiates imipramine toxicity in the isolated rat heart. *Ann Emerg Med.* 1994;24(2):224-232.

857. Barrueto F, Jr., Chuang A, Cotter BW, Hoffman RS, Nelson LS. Amiodarone fails to improve survival in amitriptyline-poisoned mice. *Clin Toxicol (Phila).* 2005;43(3):147-149.

858. Callaham M, Schumaker H, Pentel P. Phenytoin prophylaxis of cardiotoxicity in experimental amitriptyline poisoning. *J Pharmacol Exp Ther.* 1988;245(1):216-220.

859. Mayron R, Ruiz E. Phenytoin: does it reverse tricyclic-antidepressant-induced cardiac conduction abnormalities? *Ann Emerg Med.* 1986;15(8):876-880.

860. Tran TP, Panacek EA, Rhee KJ, Foulke GE. Response to dopamine vs norepinephrine in tricyclic antidepressant-induced hypotension. *Acad Emerg Med.* 1997;4(9):864-868.

861. Tobis JM, Aronow WS. Effect of amitriptyline antidotes on repetitive extrasystole threshold. *Clin Pharmacol Ther.* 1980;27(5):602-606.

862. Vernon DD, Banner W, Jr., Garrett JS, Dean JM. Efficacy of dopamine and norepinephrine for treatment of hemodynamic compromise in amitriptyline intoxication. *Crit Care Med.* 1991;19(4):544-549.

863. Knudsen K, Abrahamsson J. Effects of epinephrine and norepinephrine on hemodynamic parameters and arrhythmias during a continuous infusion of amitriptyline in rats. *J Toxicol Clin Toxicol.* 1993;31(3):461-471.

864. Follmer CH, Lum BK. Protective action of diazepam and of sympathomimetic amines against amitryptyline-induced toxicity. *J Pharmacol Exp Ther.* 1982;222(2):424-429.

865. Sangster B, de Groot G, Borst C, de Wildt D. Dopamine and isoproterenol in imipramine

intoxication in the dog. *J Toxicol Clin Toxicol.* 1985;23(4-6):407-420.

866. Johnson PB. Physostigmine in tricyclic antidepressant overdose. *JACEP.* 1976;5(6):443-445.

867. Newton RW. Physostigmine salicylate in the treatment of tricyclic antidepressant overdosage. *JAMA.* 1975;231(9):941-943.

868. Yoav G, Odelia G, Shaltiel C. A lipid emulsion reduces mortality from clomipramine overdose in rats. *Vet Hum Toxicol.* 2002;44(1):30.

869. Harvey M, Cave G. Intralipid outperforms sodium bicarbonate in a rabbit model of clomipramine toxicity. *Ann Emerg Med.* 2007;49(2):178-185, 185 e171-174.

870. Brunn GJ, Keyler DE, Pond SM, Pentel PR. Reversal of desipramine toxicity in rats using drug-specific antibody Fab' fragment: effects on hypotension and interaction with sodium bicarbonate. *J Pharmacol Exp Ther.* 1992;260(3):1392-1399.

871. Brunn GJ, Keyler DE, Ross CA, Pond SM, Pentel PR. Drug-specific F(ab')2 fragment reduces desipramine cardiotoxicity in rats. *Int J Immunopharmacol.* 1991;13(7):841-851.

872. Hursting MJ, Opheim KE, Raisys VA, Kenny MA, Metzger G. Tricyclic antidepressant-specific Fab fragments alter the distribution and elimination of desipramine in the rabbit: a model for overdose treatment. *J Toxicol Clin Toxicol.* 1989;27(1-2):53-66.

873. Pentel PR, Scarlett W, Ross CA, Landon J, Sidki A, Keyler DE. Reduction of desipramine cardiotoxicity and prolongation of survival in rats with the use of polyclonal drug-specific antibody Fab fragments. *Ann Emerg Med.* 1995;26(3):334-341.

874. Pentel PR, Ross CA, Landon J, Sidki A, Shelver WL, Keyler DE. Reversal of desipramine toxicity in rats with polyclonal drug-specific antibody Fab fragments. *J Lab Clin Med.* 1994;123(3):387-393.

875. Dart RC, Sidki A, Sullivan JB, Jr., Egen NB, Garcia RA. Ovine desipramine antibody fragments reverse desipramine cardiovascular toxicity in the rat. *Ann Emerg Med.* 1996;27(3):309-315.

876. Heard K, Dart RC, Bogdan G, O'Malley GF, Burkhart KK, Donovan JW, Ward SB. A preliminary study of tricyclic antidepressant (TCA) ovine FAB for TCA toxicity. *Clin Toxicol (Phila).* 2006;44(3):275-281.

877. Eddleston M, Rajapakse S, Rajakanthan, Jayalath S, Sjostrom L, Santharaj W, Thenabadu PN, Sheriff MH, Warrell DA. Anti-digoxin Fab fragments in cardiotoxicity induced by ingestion of yellow oleander: a randomised controlled trial. *Lancet.* 2000;355(9208):967-972.

878. Smith TW, Butler VP, Jr., Haber E, Fozzard H, Marcus FI, Bremner WF, Schulman IC, Phillips A. Treatment of life-threatening digitalis intoxication with digoxin-specific Fab antibody fragments: experience in 26 cases. *N Engl J Med.* 1982;307(22):1357-1362.

879. Wenger TL, Butler VP, Jr., Haber E, Smith TW. Treatment of 63 severely digitalis-toxic patients with digoxin-specific antibody fragments. *J Am Coll Cardiol.* 1985;5(5 Suppl A):118A-123A.

880. Antman EM, Wenger TL, Butler VP, Jr., Haber E, Smith TW. Treatment of 150 cases of life-threatening digitalis intoxication with digoxin-specific Fab antibody fragments. Final report of a multicenter study. *Circulation.* 1990;81(6):1744-1752.

881. Woolf AD, Wenger T, Smith TW, Lovejoy FH, Jr. The use of digoxin-specific Fab fragments for severe digitalis intoxication in children. *N Engl J Med.* 1992;326(26):1739-1744.

882. Hickey AR, Wenger TL, Carpenter VP, Tilson HH, Hlatky MA, Furberg CD, Kirkpatrick CH, Strauss HC, Smith TW. Digoxin Immune Fab therapy in the management of digitalis intoxication: safety and efficacy results of an observational surveillance study. *J Am Coll Cardiol.*

1991;17(3):590-598.

883. Wenger TL. Experience with digoxin immune Fab (ovine) in patients with renal impairment. *Am J Emerg Med.* 1991;9(2 Suppl 1):21-23; discussion 33-24.

884. Wolf U, Bauer D, Traub WH. Metalloproteases of Serratia liquefaciens: degradation of purified human serum proteins. *Zentralbl Bakteriol.* 1991;276(1):16-26.

885. Taboulet P, Baud FJ, Bismuth C, Vicaut E. Acute digitalis intoxication--is pacing still appropriate? *J Toxicol Clin Toxicol.* 1993;31(2):261-273.

886. Lapostolle F, Borron SW, Verdier C, Taboulet P, Guerrier G, Adnet F, Clemessy JL, Bismuth C, Baud FJ. Digoxin-specific Fab fragments as single first-line therapy in digitalis poisoning. *Crit Care Med.* 2008;36(11):3014-3018.

887. Hougen TJ, Lloyd BL, Smith TW. Effects of inotropic and arrhythmogenic digoxin doses and of digoxin-specific antibody on myocardial monovalent cation transport in the dog. *Circ Res.* 1979;44(1):23-31.

888. Clark RF, Selden BS, Curry SC. Digoxin-specific Fab fragments in the treatment of oleander toxicity in a canine model. *Ann Emerg Med.* 1991;20(10):1073-1077.

889. Brubacher JR, Lachmanen D, Ravikumar PR, Hoffman RS. Efficacy of digoxin specific Fab fragments (Digibind) in the treatment of toad venom poisoning. *Toxicon.* 1999;37(6):931-942.

890. Lechat P, Mudgett-Hunter M, Margolies MN, Haber E, Smith TW. Reversal of lethal digoxin toxicity in guinea pigs using monoclonal antibodies and Fab fragments. *J Pharmacol Exp Ther.* 1984;229(1):210-213.

891. Kelly AM, Kerr D, Dietze P, Patrick I, Walker T, Koutsogiannis Z. Randomised trial of intranasal versus intramuscular naloxone in prehospital treatment for suspected opioid overdose. *Med J Aust.* 2005;182(1):24-27.

892. Rupreht J, Dworacek B, Oosthoek H, Dzoljic MR, Valkenburg M. Physostigmine versus naloxone in heroin-overdose. *J Toxicol Clin Toxicol.* 1983;21(3):387-397.

893. Wanger K, Brough L, Macmillan I, Goulding J, MacPhail I, Christenson JM. Intravenous vs subcutaneous naloxone for out-of-hospital management of presumed opioid overdose. *Acad Emerg Med.* 1998;5(4):293-299.

894. Leach M. Naloxone: A New Therapeutic and Diagnostic Agent for Emergency Use. *JACEP.* 1973;2:21-23.

895. Sporer KA, Firestone J, Isaacs SM. Out-of-hospital treatment of opioid overdoses in an urban setting. *Acad Emerg Med.* 1996;3(7):660-667.

896. Yealy DM, Paris PM, Kaplan RM, Heller MB, Marini SE. The safety of prehospital naloxone administration by paramedics. *Ann Emerg Med.* 1990;19(8):902-905.

897. Mills CA, Flacke JW, Flacke WE, Bloor BC, Liu MD. Narcotic reversal in hypercapnic dogs: comparison of naloxone and nalbuphine. *Can J Anaesth.* 1990;37(2):238-244.

898. Buajordet I, Naess AC, Jacobsen D, Brors O. Adverse events after naloxone treatment of episodes of suspected acute opioid overdose. *Eur J Emerg Med.* 2004;11(1):19-23.

899. Evans LE, Swainson CP, Roscoe P, Prescott LF. Treatment of drug overdosage with naloxone, a specific narcotic antagonist. *Lancet.* 1973;1(7801):452-455.

900. Kaplan JL, Marx JA, Calabro JJ, Gin-Shaw SL, Spiller JD, Spivey WL, Gaddis GM, Zhao N, Harchelroad FP, Jr. Double-blind, randomized study of nalmefene and naloxone in emergency

department patients with suspected narcotic overdose. *Ann Emerg Med.* 1999;34(1):42-50.

901. Osterwalder JJ. Naloxone--for intoxications with intravenous heroin and heroin mixtures--harmless or hazardous? A prospective clinical study. *J Toxicol Clin Toxicol.* 1996;34(4):409-416.

902. Robertson TM, Hendey GW, Stroh G, Shalit M. Intranasal naloxone is a viable alternative to intravenous naloxone for prehospital narcotic overdose. *Prehosp Emerg Care.* 2009;13(4):512-515.

903. Barton ED, Colwell CB, Wolfe T, Fosnocht D, Gravitz C, Bryan T, Dunn W, Benson J, Bailey J. Efficacy of intranasal naloxone as a needleless alternative for treatment of opioid overdose in the prehospital setting. *J Emerg Med.* 2005;29(3):265-271.

904. Greenberg MI, Roberts JR, Baskin SI. Endotracheal naloxone reversal of morphine-induced respiratory depression in rabbits. *Ann Emerg Med.* 1980;9(6):289-292.

905. Sunde K, Pytte M, Jacobsen D, Mangschau A, Jensen LP, Smedsrud C, Draegni T, Steen PA. Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. *Resuscitation.* 2007;73(1):29-39.

906. Shawl FA, Domanski MJ, Wish MH, Davis M, Punja S, Hernandez TJ. Emergency cardiopulmonary bypass support in patients with cardiac arrest in the catheterization laboratory. *Cathet Cardiovasc Diagn.* 1990;19(1):8-12.

907. Criley JM, Blaufuss AH, Kissel GL. Cough-induced cardiac compression. Self-administered from of cardiopulmonary resuscitation. *JAMA.* 1976;236(11):1246-1250.

908. Criley JM, Blaufuss AH, Kissel GL. Self-administered cardiopulmonary resuscitation by cough-induced cardiac compression. *Trans Am Clin Climatol Assoc.* 1976;87:138-146.

909. Miller B, Lesnefsky E, Heyborne T, Schmidt B, Freeman K, Breckinridge S, Kelley K, Mann D, Reiter M. Cough-cardiopulmonary resuscitation in the cardiac catheterization laboratory: hemodynamics during an episode of prolonged hypotensive ventricular tachycardia. *Cathet Cardiovasc Diagn.* 1989;18(3):168-171.

910. Keeble W, Tymchak WJ. Triggering of the Bezold Jarisch Reflex by reperfusion during primary PCI with maintenance of consciousness by cough CPR: a case report and review of pathophysiology. *J Invasive Cardiol.* 2008;20(8):E239-242.

911. Saba SE, David SW. Sustained consciousness during ventricular fibrillation: case report of cough cardiopulmonary resuscitation. *Cathet Cardiovasc Diagn.* 1996;37(1):47-48.

912. Mackay JH, Powell SJ, Charman SC, Rozario C. Resuscitation after cardiac surgery: are we ageist? *Eur J Anaesthesiol.* 2004;21(1):66-71.

913. Raman J, Saldanha RF, Branch JM, Esmore DS, Spratt PM, Farnsworth AE, Harrison GA, Chang VP, Shanahan MX. Open cardiac compression in the postoperative cardiac intensive care unit. *Anaesth Intensive Care.* 1989;17(2):129-135.

914. Anthi A, Tzelepis GE, Alivizatos P, Michalis A, Palatianos GM, Geroulanos S. Unexpected cardiac arrest after cardiac surgery: incidence, predisposing causes, and outcome of open chest cardiopulmonary resuscitation. *Chest.* 1998;113(1):15-19.

915. Dimopoulou I, Anthi A, Michalis A, Tzelepis GE. Functional status and quality of life in long-term survivors of cardiac arrest after cardiac surgery. *Crit Care Med.* 2001;29(7):1408-1411.

916. el-Banayosy A, Brehm C, Kizner L, Hartmann D, Kortke H, Korner MM, Minami K, Reichelt W, Korfer R. Cardiopulmonary resuscitation after cardiac surgery: a two-year study. *J Cardiothorac Vasc Anesth.* 1998;12(4):390-392.

917. Fairman RM, Edmunds LH, Jr. Emergency thoracotomy in the surgical intensive care unit after open cardiac operation. *Ann Thorac Surg.* 1981;32(4):386-391.

918. Mackay JH, Powell SJ, Osgathorp J, Rozario CJ. Six-year prospective audit of chest reopening after cardiac arrest. *Eur J Cardiothorac Surg.* 2002;22(3):421-425.

919. Ngaage DL, Cowen ME. Survival of cardiorespiratory arrest after coronary artery bypass grafting or aortic valve surgery. *Ann Thorac Surg.* 2009;88(1):64-68.

920. Karhunen JP, Sihvo EI, Suojaranta-Ylinen RT, Ramo OJ, Salminen US. Predictive factors of hemodynamic collapse after coronary artery bypass grafting: a case-control study. *J Cardiothorac Vasc Anesth.* 2006;20(2):143-148.

921. Kriaras I, Anthi A, Michelopoulos A, Karakatsani A, Tzelepis G, Papadimitriou L, Geroulanos S. Antimicrobial protection in cardiac surgery patients undergoing open chest CPR. *Resuscitation.* 1996;31:10-11.

922. Rousou JA, Engelman RM, Flack JE, 3rd, Deaton DW, Owen SG. Emergency cardiopulmonary bypass in the cardiac surgical unit can be a lifesaving measure in postoperative cardiac arrest. *Circulation.* 1994;90(5 Pt 2):II280-284.

923. Beyersdorf F, Kirsh M, Buckberg GD, Allen BS. Warm glutamate/aspartate-enriched blood cardioplegic solution for perioperative sudden death. *J Thorac Cardiovasc Surg.* 1992;104(4):1141-1147.

924. Feng WC, Bert AA, Browning RA, Singh AK. Open cardiac massage and periresuscitative cardiopulmonary bypass for cardiac arrest following cardiac surgery. *J Cardiovasc Surg (Torino).* 1995;36(4):319-321.

925. Wahba A, Gotz W, Birnbaum DE. Outcome of cardiopulmonary resuscitation following open heart surgery. *Scand Cardiovasc J.* 1997;31(3):147-149.

926. Kaiser GC, Naunheim KS, Fiore AC, Harris HH, McBride LR, Pennington DG, Barner HB, Willman VL. Reoperation in the intensive care unit. *Ann Thorac Surg.* 1990;49(6):903-907; discussion 908.

927. Pottle A, Bullock I, Thomas J, Scott L. Survival to discharge following open chest cardiac compression (OCCC). A 4-year retrospective audit in a cardiothoracic specialist centre--Royal Brompton and Harefield NHS Trust, United Kingdom. *Resuscitation.* 2002;52(3):269-272.

928. Chen YS, Chao A, Yu HY, Ko WJ, Wu IH, Chen RJ, Huang SC, Lin FY, Wang SS. Analysis and results of prolonged resuscitation in cardiac arrest patients rescued by extracorporeal membrane oxygenation. *J Am Coll Cardiol.* 2003;41(2):197-203.

929. Overlie PA. Emergency use of cardiopulmonary bypass. *J Interv Cardiol.* 1995;8(3):239-247.

930. Newsome LR, Ponganis P, Reichman R, Nakaji N, Jaski B, Hartley M. Portable percutaneous cardiopulmonary bypass: use in supported coronary angioplasty, aortic valvuloplasty, and cardiac arrest. *J Cardiothorac Vasc Anesth.* 1992;6(3):328-331.

931. Dalton HJ, Siewers RD, Fuhrman BP, Del Nido P, Thompson AE, Shaver MG, Dowhy M. Extracorporeal membrane oxygenation for cardiac rescue in children with severe myocardial dysfunction. *Crit Care Med.* 1993;21(7):1020-1028.

932. Parra DA, Totapally BR, Zahn E, Jacobs J, Aldousany A, Burke RP, Chang AC. Outcome of cardiopulmonary resuscitation in a pediatric cardiac intensive care unit. *Crit Care Med.* 2000;28(9):3296-3300.

933. Ghez O, Feier H, Ughetto F, Fraisse A, Kreitmann B, Metras D. Postoperative extracorporeal life

support in pediatric cardiac surgery: recent results. *ASAIO J.* 2005;51(5):513-516.

934. del Nido PJ, Dalton HJ, Thompson AE, Siewers RD. Extracorporeal membrane oxygenator rescue in children during cardiac arrest after cardiac surgery. *Circulation.* 1992;86(5 Suppl):II300-304.

935. Duncan BW, Ibrahim AE, Hraska V, del Nido PJ, Laussen PC, Wessel DL, Mayer JE, Jr., Bower LK, Jonas RA. Use of rapid-deployment extracorporeal membrane oxygenation for the resuscitation of pediatric patients with heart disease after cardiac arrest. *J Thorac Cardiovasc Surg.* 1998;116(2):305-311.

936. Bohrer H, Gust R, Bottiger BW. Cardiopulmonary resuscitation after cardiac surgery. *J Cardiothorac Vasc Anesth.* 1995;9(3):352.

937. Ricci M, Karamanoukian HL, D'Ancona G, Jajkowski MR, Bergsland J, Salerno TA. Avulsion of an H graft during closed-chest cardiopulmonary resuscitation after minimally invasive coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth.* 2000;14(5):586-587.

938. Cipolotti G, Paccagnella A, Simini G. Successful cardiopulmonary resuscitation using high doses of epinephrine. *Int J Cardiol.* 1991;33(3):430-431.

939. Kron IL, DiMarco JP, Harman PK, Crosby IK, Mentzer RM, Jr., Nolan SP, Wellons HA, Jr. Unanticipated postoperative ventricular tachyarrhythmias. *Ann Thorac Surg.* 1984;38(4):317-322.

940. Maggiolini S, Bozzano A, Russo P, Vitale G, Osculati G, Cantu E, Achilli F, Valagussa F. Echocardiography-guided pericardiocentesis with probe-mounted needle: report of 53 cases. *J Am Soc Echocardiogr.* 2001;14(8):821-824.

941. Salem K, Mulji A, Lonn E. Echocardiographically guided pericardiocentesis - the gold standard for the management of pericardial effusion and cardiac tamponade. *Can J Cardiol.* 1999;15(11):1251-1255.

942. Susini G, Pepi M, Sisillo E, Bortone F, Salvi L, Barbier P, Fiorentini C. Percutaneous pericardiocentesis versus subxiphoid pericardiotomy in cardiac tamponade due to postoperative pericardial effusion. *J Cardiothorac Vasc Anesth.* 1993;7(2):178-183.

943. Tsang TS, Barnes ME, Gersh BJ, Bailey KR, Seward JB. Outcomes of clinically significant idiopathic pericardial effusion requiring intervention. *Am J Cardiol.* 2003;91(6):704-707.

944. Tsang TS, Enriquez-Sarano M, Freeman WK, Barnes ME, Sinak LJ, Gersh BJ, Bailey KR, Seward JB. Consecutive 1127 therapeutic echocardiographically guided pericardiocenteses: clinical profile, practice patterns, and outcomes spanning 21 years. *Mayo Clin Proc.* 2002;77(5):429-436.

945. Coats TJ, Keogh S, Clark H, Neal M. Prehospital resuscitative thoracotomy for cardiac arrest after penetrating trauma: rationale and case series. *J Trauma.* 2001;50(4):670-673.

946. Powell DW, Moore EE, Cothren CC, Ciesla DJ, Burch JM, Moore JB, Johnson JL. Is emergency department resuscitative thoracotomy futile care for the critically injured patient requiring prehospital cardiopulmonary resuscitation? *J Am Coll Surg.* 2004;199(2):211-215.

947. Lewis G, Knottenbelt JD. Should emergency room thoracotomy be reserved for cases of cardiac tamponade? *Injury.* 1991;22(1):5-6.

948. Wang JC, Jiang P, Huang J, Qian GS. [The protective effects and mechanisms of peroxisome proliferator-activated receptor-gamma agonist in rats with acute lung injury]. *Zhonghua Jie He He Hu Xi Za Zhi.* 2008;31(6):425-430.

949. Bernard SA, Rosalion A. Therapeutic hypothermia induced during cardiopulmonary resuscitation using large-volume, ice-cold intravenous fluid. *Resuscitation.* 2008;76(2):311-313.

950. Degiannis E, Loogna P, Doll D, Bonanno F, Bowley DM, Smith MD. Penetrating cardiac injuries: recent experience in South Africa. *World J Surg.* 2006;30(7):1258-1264.

951. Li X, Fu QL, Jing XL, Li YJ, Zhan H, Ma ZF, Liao XX. A meta-analysis of cardiopulmonary resuscitation with and without the administration of thrombolytic agents. *Resuscitation.* 2006;70(1):31-36.

952. Fava M, Loyola S, Bertoni H, Dougnac A. Massive pulmonary embolism: percutaneous mechanical thrombectomy during cardiopulmonary resuscitation. *J Vasc Interv Radiol.* 2005;16(1):119-123.

953. Lederer W, Lichtenberger C, Pechlaner C, Kinzl J, Kroesen G, Baubin M. Long-term survival and neurological outcome of patients who received recombinant tissue plasminogen activator during out-of-hospital cardiac arrest. *Resuscitation.* 2004;61(2):123-129.

954. Zahorec R. Rescue systemic thrombolysis during cardiopulmonary resuscitation. *Bratisl Lek Listy.* 2002;103(7-8):266-269.

955. Konstantinov IE, Saxena P, Koniuszko MD, Alvarez J, Newman MA. Acute massive pulmonary embolism with cardiopulmonary resuscitation: management and results. *Tex Heart Inst J.* 2007;34(1):41-45; discussion 45-46.

956. Higham PD, Adams PC, Murray A, Campbell RW. Plasma potassium, serum magnesium and ventricular fibrillation: a prospective study. *Q J Med.* 1993;86(9):609-617.

957. Buylaert WA, Calle PA, Houbrechts HN. Serum electrolyte disturbances in the post-resuscitation period. The Cerebral Resuscitation Study Group. *Resuscitation.* 1989;17 Suppl:S189-196; discussion S199-206.

958. Cannon LA, Heiselman DE, Dougherty JM, Jones J. Magnesium levels in cardiac arrest victims: relationship between magnesium levels and successful resuscitation. *Ann Emerg Med.* 1987;16(11):1195-1199.

959. Allen BJ, Brodsky MA, Capparelli EV, Luckett CR, Iseri LT. Magnesium sulfate therapy for sustained monomorphic ventricular tachycardia. *Am J Cardiol.* 1989;64(18):1202-1204.

960. Baraka A, Ayoub C, Kawkabani N. Magnesium therapy for refractory ventricular fibrillation. *J Cardiothorac Vasc Anesth.* 2000;14(2):196-199.

961. Craddock L, Miller B, Clifton G, Krumbach B, Pluss W. Resuscitation from prolonged cardiac arrest with high-dose intravenous magnesium sulfate. *J Emerg Med.* 1991;9(6):469-476.

962. Jensen PK, Hansen SL, Lyngborg K. [Recurrent ventricular fibrillation treated with magnesium]. *Ugeskr Laeger.* 1987;149(10):663-664.

963. Tobey RC, Birnbaum GA, Allegra JR, Horowitz MS, Plosay JJ, 3rd. Successful resuscitation and neurologic recovery from refractory ventricular fibrillation after magnesium sulfate administration. *Ann Emerg Med.* 1992;21(1):92-96.

964. Longstreth WT, Jr., Fahrenbruch CE, Olsufka M, Walsh TR, Copass MK, Cobb LA. Randomized clinical trial of magnesium, diazepam, or both after out-of-hospital cardiac arrest. *Neurology.* 2002;59(4):506-514.

965. Reis AG, Ferreira de Paiva E, Schvartsman C, Zaritsky AL. Magnesium in cardiopulmonary resuscitation: critical review. *Resuscitation.* 2008;77(1):21-25.

966. Curry P, Fitchett D, Stubbs W, Krikler D. Ventricular arrhythmias and hypokalaemia. *Lancet.* 1976;2(7979):231-233.

967. Clausen TG, Brocks K, Ibsen H. Hypokalemia and ventricular arrhythmias in acute myocardial

infarction. *Acta Med Scand.* 1988;224(6):531-537.

968. Nordrehaug JE. Malignant arrhythmia in relation to serum potassium in acute myocardial infarction. *Am J Cardiol.* 1985;56(6):20D-23D.

969. Nordrehaug JE, von der Lippe G. Hypokalaemia and ventricular fibrillation in acute myocardial infarction. *Br Heart J.* 1983;50(6):525-529.

970. Obeid AI, Verrier RL, Lown B. Influence of glucose, insulin, and potassium on vulnerability to ventricular fibrillation in the canine heart. *Circ Res.* 1978;43(4):601-608.

971. Gay WA, Jr., Ebert PA, Kass RM. The protective effects of induced hyperkalemia during total circulatory arrest. *Surgery.* 1975;78(1):22-26.

972. Nolan JP, Neumar RW, Adrie C, Aibiki M, Berg RA, Bottiger BW, Callaway C, Clark RS, Geocadin RG, Jauch EC, Kern KB, Laurent I, Longstreth WT, Merchant RM, Morley P, Morrison LJ, Nadkarni V, Peberdy MA, Rivers EP, Rodriguez-Nunez A, Sellke FW, Spaulding C, Sunde K, Hoek TV. Post-cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication. A Scientific Statement from the International Liaison Committee on Resuscitation; the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Clinical Cardiology; the Council on Stroke. *Resuscitation.* 2008;79(3):350-379.

973. Kirves H, Skrifvars MB, Vahakuopus M, Ekstrom K, Martikainen M, Castren M. Adherence to resuscitation guidelines during prehospital care of cardiac arrest patients. *Eur J Emerg Med.* 2007;14(2):75-81.

974. Gaieski DF, Band RA, Abella BS, Neumar RW, Fuchs BD, Kolansky DM, Merchant RM, Carr BG, Becker LB, Maguire C, Klair A, Hylton J, Goyal M. Early goal-directed hemodynamic optimization combined with therapeutic hypothermia in comatose survivors of out-of-hospital cardiac arrest. *Resuscitation.* 2009;80(4):418-424.

975. Lund-Kordahl I, Olasveengen TM, Lorem T, Samdal M, Wik L, Sunde K. Improving outcome after out-of-hospital cardiac arrest by strengthening weak links of the local Chain of Survival; quality of advanced life support and post-resuscitation care. *Resuscitation.* 2010;81(4):422-426.

976. Buunk G, van der Hoeven JG, Meinders AE. Cerebrovascular reactivity in comatose patients resuscitated from a cardiac arrest. *Stroke.* 1997;28(8):1569-1573.

977. Kagstrom E, Smith ML, Siesjo BK. Cerebral circulatory responses to hypercapnia and hypoxia in the recovery period following complete and incomplete cerebral ischemia in the rat. *Acta Physiol Scand.* 1983;118(3):281-291.

978. Krep H, Brinker G, Pillekamp F, Hossmann KA. Treatment with an endothelin type A receptor-antagonist after cardiac arrest and resuscitation improves cerebral hemodynamic and functional recovery in rats. *Crit Care Med.* 2000;28(8):2866-2872.

979. Krep H, Brinker G, Schwindt W, Hossmann KA. Endothelin type A-antagonist improves long-term neurological recovery after cardiac arrest in rats. *Crit Care Med.* 2000;28(8):2873-2880.

980. Schmitz B, Bottiger BW, Hossmann KA. Functional activation of cerebral blood flow after cardiac arrest in rat. *J Cereb Blood Flow Metab.* 1997;17(11):1202-1209.

981. Nemoto EM, Snyder JV, Carroll RG, Morita H. Global ischemia in dogs: cerebrovascular CO2 reactivity and autoregulation. *Stroke.* 1975;6(4):425-431.

982. Hossmann KA, Lechtape-Gruter H, Hossmann V. The role of cerebral blood flow for the recovery of

the brain after prolonged ischemia. *Z Neurol.* 1973;204(4):281-299.

983. Safar P, Xiao F, Radovsky A, Tanigawa K, Ebmeyer U, Bircher N, Alexander H, Stezoski SW. Improved cerebral resuscitation from cardiac arrest in dogs with mild hypothermia plus blood flow promotion. *Stroke.* 1996;27(1):105-113.

984. Vanicky I, Marsala M, Orendacova J, Marsala J. Silver impregnability of ischemia-sensitive neocortical neurons after 15 minutes of cardiac arrest in the dog. *Anat Embryol (Berl).* 1992;186(2):167-173.

985. Fercakova A, Vanicky I, Marsala M, Marsala J. Effect of prolonged hyperventilation on ischemic injury of neurons after global brain ischemia in the dog. *J Hirnforsch.* 1995;36(3):297-304.

986. Wongsurakiat P, Pierson DJ, Rubenfeld GD. Changing pattern of ventilator settings in patients without acute lung injury: changes over 11 years in a single institution. *Chest.* 2004;126(4):1281-1291.

987. Esteban A, Anzueto A, Frutos F, Alia I, Brochard L, Stewart TE, Benito S, Epstein SK, Apezteguia C, Nightingale P, Arroliga AC, Tobin MJ. Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. *JAMA.* 2002;287(3):345-355.

988. Kuisma M, Boyd J, Voipio V, Alaspaa A, Roine RO, Rosenberg P. Comparison of 30 and the 100% inspired oxygen concentrations during early post-resuscitation period: a randomised controlled pilot study. *Resuscitation.* 2006;69(2):199-206.

989. Kilgannon JH, Jones AE, Shapiro NI, Angelos MG, Milcarek B, Hunter K, Parrillo JE, Trzeciak S. Association between arterial hyperoxia following resuscitation from cardiac arrest and in-hospital mortality. *JAMA.* 2010;303(21):2165-2171.

990. Balan IS, Fiskum G, Hazelton J, Cotto-Cumba C, Rosenthal RE. Oximetry-guided reoxygenation improves neurological outcome after experimental cardiac arrest. *Stroke.* 2006;37(12):3008-3013.

991. Marsala J, Marsala M, Vanicky I, Galik J, Orendacova J. Post cardiac arrest hyperoxic resuscitation enhances neuronal vulnerability of the respiratory rhythm generator and some brainstem and spinal cord neuronal pools in the dog. *Neurosci Lett.* 1992;146(2):121-124.

992. Vereczki V, Martin E, Rosenthal RE, Hof PR, Hoffman GE, Fiskum G. Normoxic resuscitation after cardiac arrest protects against hippocampal oxidative stress, metabolic dysfunction, and neuronal death. *J Cereb Blood Flow Metab.* 2006;26(6):821-835.

993. Richards EM, Rosenthal RE, Kristian T, Fiskum G. Postischemic hyperoxia reduces hippocampal pyruvate dehydrogenase activity. *Free Radic Biol Med.* 2006;40(11):1960-1970.

994. Richards EM, Fiskum G, Rosenthal RE, Hopkins I, McKenna MC. Hyperoxic reperfusion after global ischemia decreases hippocampal energy metabolism. *Stroke.* 2007;38(5):1578-1584.

995. Zwemer CF, Whitesall SE, D'Alecy LG. Hypoxic cardiopulmonary-cerebral resuscitation fails to improve neurological outcome following cardiac arrest in dogs. *Resuscitation.* 1995;29(3):225-236.

996. Abdel-Rahman U, Risteski P, Tizi K, Kerscher S, Behjati S, Zwicker K, Scholz M, Brandt U, Moritz A. Hypoxic reoxygenation during initial reperfusion attenuates cardiac dysfunction and limits ischemia-reperfusion injury after cardioplegic arrest in a porcine model. *J Thorac Cardiovasc Surg.* 2009;137(4):978-982.

997. Michael Smith J, Roberts WH, Miller JD, Hasselfeld KA, Pat Hendy M. Controlled cardiac reoxygenation does not improve myocardial function following global myocardial ischemia. *Int J Surg.* 2006;4(3):153-159.

998. Bernard S, Buist M, Monteiro O, Smith K. Induced hypothermia using large volume, ice-cold intravenous fluid in comatose survivors of out-of-hospital cardiac arrest: a preliminary report. *Resuscitation.* 2003;56(1):9-13.

999. Kim F, Olsufka M, Carlbom D, Deem S, Longstreth WT, Jr., Hanrahan M, Maynard C, Copass MK, Cobb LA. Pilot study of rapid infusion of 2 L of 4 degrees C normal saline for induction of mild hypothermia in hospitalized, comatose survivors of out-of-hospital cardiac arrest. *Circulation.* 2005;112(5):715-719.

1000. Kim F, Olsufka M, Longstreth WT, Jr., Maynard C, Carlbom D, Deem S, Kudenchuk P, Copass MK, Cobb LA. Pilot randomized clinical trial of prehospital induction of mild hypothermia in out-of-hospital cardiac arrest patients with a rapid infusion of 4 degrees C normal saline. *Circulation.* 2007;115(24):3064-3070.

1001. Kliegel A, Losert H, Sterz F, Kliegel M, Holzer M, Uray T, Domanovits H. Cold simple intravenous infusions preceding special endovascular cooling for faster induction of mild hypothermia after cardiac arrest--a feasibility study. *Resuscitation.* 2005;64(3):347-351.

1002. Kliegel A, Janata A, Wandaller C, Uray T, Spiel A, Losert H, Kliegel M, Holzer M, Haugk M, Sterz F, Laggner AN. Cold infusions alone are effective for induction of therapeutic hypothermia but do not keep patients cool after cardiac arrest. *Resuscitation.* 2007;73(1):46-53.

1003. Virkkunen I, Yli-Hankala A, Silfvast T. Induction of therapeutic hypothermia after cardiac arrest in prehospital patients using ice-cold Ringer's solution: a pilot study. *Resuscitation.* 2004;62(3):299-302.

1004. Jacobshagen C, Pax A, Unsold BW, Seidler T, Schmidt-Schweda S, Hasenfuss G, Maier LS. Effects of large volume, ice-cold intravenous fluid infusion on respiratory function in cardiac arrest survivors. *Resuscitation.* 2009;80(11):1223-1228.

1005. Bertsch T, Denz C, Janke C, Weiss M, Fassbender K, Luiz T, Ellinger K, Krieter H. Hypertonic-hyperoncotic solutions decrease cardiac troponin I concentrations in peripheral blood in a porcine ischemia-reperfusion model. *Exp Toxicol Pathol.* 2001;53(2-3):153-156.

1006. Kaakinen T, Alaoja H, Heikkinen J, Dahlbacka S, Laurila P, Kiviluoma K, Salomaki T, Tuominen H, Ohtonen P, Biancari F, Juvonen T. Hypertonic saline dextran improves outcome after hypothermic circulatory arrest: a study in a surviving porcine model. *Ann Thorac Surg.* 2006;81(1):183-190.

1007. Krieter H, Denz C, Janke C, Bertsch T, Luiz T, Ellinger K, Van Ackern K. Hypertonic-hyperoncotic solutions reduce the release of cardiac troponin I and s-100 after successful cardiopulmonary resuscitation in pigs. *Anesth Analg.* 2002;95(4):1031-1036, table of contents.

1008. Leonov Y, Sterz F, Safar P, Johnson DW, Tisherman SA, Oku K. Hypertension with hemodilution prevents multifocal cerebral hypoperfusion after cardiac arrest in dogs. *Stroke.* 1992;23(1):45-53.

1009. Laurent I, Monchi M, Chiche JD, Joly LM, Spaulding C, Bourgeois B, Cariou A, Rozenberg A, Carli P, Weber S, Dhainaut JF. Reversible myocardial dysfunction in survivors of out-of-hospital cardiac arrest. *J Am Coll Cardiol.* 2002;40(12):2110-2116.

1010. Mayr V, Luckner G, Jochberger S, Wenzel V, Ulmer H, Pajk W, Knotzer H, Friesenecker B, Lindner K, Hasibeder W, Dunser M. Arginine vasopressin in advanced cardiovascular failure during the post-resuscitation phase after cardiac arrest. *Resuscitation.* 2007;72(1):35-44.

1011. Wang J, Weil MH, Tang W, Sun S, Huang L. Levosimendan improves postresuscitation myocardial dysfunction after beta-adrenergic blockade. *J Lab Clin Med.* 2005;146(3):179-183.

1012. Meyer RJ, Kern KB, Berg RA, Hilwig RW, Ewy GA. Post-resuscitation right ventricular dysfunction: delineation and treatment with dobutamine. *Resuscitation.* 2002;55(2):187-191.

1013. Vasquez A, Kern KB, Hilwig RW, Heidenreich J, Berg RA, Ewy GA. Optimal dosing of dobutamine for treating post-resuscitation left ventricular dysfunction. *Resuscitation.* 2004;61(2):199-207.

1014. Huang L, Weil MH, Tang W, Sun S, Wang J. Comparison between dobutamine and levosimendan for management of postresuscitation myocardial dysfunction. *Crit Care Med.* 2005;33(3):487-491.

1015. Tennyson H, Kern KB, Hilwig RW, Berg RA, Ewy GA. Treatment of post resuscitation myocardial dysfunction: aortic counterpulsation versus dobutamine. *Resuscitation.* 2002;54(1):69-75.

1016. Kern KB, Hilwig RW, Berg RA, Rhee KH, Sanders AB, Otto CW, Ewy GA. Postresuscitation left ventricular systolic and diastolic dysfunction. Treatment with dobutamine. *Circulation.* 1997;95(12):2610-2613.

1017. Skrifvars MB, Pettila V, Rosenberg PH, Castren M. A multiple logistic regression analysis of in-hospital factors related to survival at six months in patients resuscitated from out-of-hospital ventricular fibrillation. *Resuscitation.* 2003;59(3):319-328.

1018. Engdahl J, Abrahamsson P, Bang A, Lindqvist J, Karlsson T, Herlitz J. Is hospital care of major importance for outcome after out-of-hospital cardiac arrest? Experience acquired from patients with out-of-hospital cardiac arrest resuscitated by the same Emergency Medical Service and admitted to one of two hospitals over a 16-year period in the municipality of Goteborg. *Resuscitation.* 2000;43(3):201-211.

1019. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. The Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. *N Engl J Med.* 1997;337(22):1576-1583.

1020. Buxton AE, Lee KL, Fisher JD, Josephson ME, Prystowsky EN, Hafley G. A randomized study of the prevention of sudden death in patients with coronary artery disease. Multicenter Unsustained Tachycardia Trial Investigators. *N Engl J Med.* 1999;341(25):1882-1890.

1021. Connolly SJ, Gent M, Roberts RS, Dorian P, Roy D, Sheldon RS, Mitchell LB, Green MS, Klein GJ, O'Brien B. Canadian implantable defibrillator study (CIDS) : a randomized trial of the implantable cardioverter defibrillator against amiodarone. *Circulation.* 2000;101(11):1297-1302.

1022. Kuck KH, Cappato R, Siebels J, Ruppel R. Randomized comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from cardiac arrest : the Cardiac Arrest Study Hamburg (CASH). *Circulation.* 2000;102(7):748-754.

1023. Wever EF, Hauer RN, van Capelle FL, Tijssen JG, Crijns HJ, Algra A, Wiesfeld AC, Bakker PF, Robles de Medina EO. Randomized study of implantable defibrillator as first-choice therapy versus conventional strategy in postinfarct sudden death survivors. *Circulation.* 1995;91(8):2195-2203.

1024. Stevenson LW, Miller LW, Desvigne-Nickens P, Ascheim DD, Parides MK, Renlund DG, Oren RM, Krueger SK, Costanzo MR, Wann LS, Levitan RG, Mancini D. Left ventricular assist device as destination for patients undergoing intravenous inotropic therapy: a subset analysis from REMATCH (Randomized Evaluation of Mechanical Assistance in Treatment of Chronic Heart Failure). *Circulation.* 2004;110(8):975-981.

1025. Thiele H, Sick P, Boudriot E, Diederich KW, Hambrecht R, Niebauer J, Schuler G. Randomized comparison of intra-aortic balloon support with a percutaneous left ventricular assist device in patients with revascularized acute myocardial infarction complicated by cardiogenic shock. *Eur*

Heart J. 2005;26(13):1276-1283.

1026. Burkhoff D, Cohen H, Brunckhorst C, O'Neill WW. A randomized multicenter clinical study to evaluate the safety and efficacy of the TandemHeart percutaneous ventricular assist device versus conventional therapy with intraaortic balloon pumping for treatment of cardiogenic shock. *Am Heart J.* 2006;152(3):469 e461-468.

1027. Greenberg B, Czerska B, Delgado RM, Bourge R, Zile MR, Silver M, Klapholz M, Haeusslein E, Mehra MR, Mather P, Abraham WT, Neaton JD, Brown BS, Parker IC, Konstam MA. Effects of continuous aortic flow augmentation in patients with exacerbation of heart failure inadequately responsive to medical therapy: results of the Multicenter Trial of the Orqis Medical Cancion System for the Enhanced Treatment of Heart Failure Unresponsive to Medical Therapy (MOMENTUM). *Circulation.* 2008;118(12):1241-1249.

1028. Seyfarth M, Sibbing D, Bauer I, Frohlich G, Bott-Flugel L, Byrne R, Dirschinger J, Kastrati A, Schomig A. A randomized clinical trial to evaluate the safety and efficacy of a percutaneous left ventricular assist device versus intra-aortic balloon pumping for treatment of cardiogenic shock caused by myocardial infarction. *J Am Coll Cardiol.* 2008;52(19):1584-1588.

1029. Hovdenes J, Laake JH, Aaberge L, Haugaa H, Bugge JF. Therapeutic hypothermia after out-of-hospital cardiac arrest: experiences with patients treated with percutaneous coronary intervention and cardiogenic shock. *Acta Anaesthesiol Scand.* 2007;51(2):137-142.

1030. Takino M, Okada Y. Hyperthermia following cardiopulmonary resuscitation. *Intensive Care Med.* 1991;17(7):419-420.

1031. Zeiner A, Holzer M, Sterz F, Schorkhuber W, Eisenburger P, Havel C, Kliegel A, Laggner AN. Hyperthermia after cardiac arrest is associated with an unfavorable neurologic outcome. *Arch Intern Med.* 2001;161(16):2007-2012.

1032. Hickey RW, Kochanek PM, Ferimer H, Graham SH, Safar P. Hypothermia and hyperthermia in children after resuscitation from cardiac arrest. *Pediatrics.* 2000;106(1 Pt 1):118-122.

1033. Langhelle A, Tyvold SS, Lexow K, Hapnes SA, Sunde K, Steen PA. In-hospital factors associated with improved outcome after out-of-hospital cardiac arrest. A comparison between four regions in Norway. *Resuscitation.* 2003;56(3):247-263.

1034. Takasu A, Saitoh D, Kaneko N, Sakamoto T, Okada Y. Hyperthermia: is it an ominous sign after cardiac arrest? *Resuscitation.* 2001;49(3):273-277.

1035. Wang Y, Lim LL, Levi C, Heller RF, Fisher J. Influence of admission body temperature on stroke mortality. *Stroke.* 2000;31(2):404-409.

1036. Diringer MN. Treatment of fever in the neurologic intensive care unit with a catheter-based heat exchange system. *Crit Care Med.* 2004;32(2):559-564.

1037. Diringer MN, Reaven NL, Funk SE, Uman GC. Elevated body temperature independently contributes to increased length of stay in neurologic intensive care unit patients. *Crit Care Med.* 2004;32(7):1489-1495.

1038. Reith J, Jorgensen HS, Pedersen PM, Nakayama H, Raaschou HO, Jeppesen LL, Olsen TS. Body temperature in acute stroke: relation to stroke severity, infarct size, mortality, and outcome. *Lancet.* 1996;347(8999):422-425.

1039. Hanchaiphiboolkul S. Body temperature and mortality in acute cerebral infarction. *J Med Assoc Thai.* 2005;88(1):26-31.

1040. Kammersgaard LP, Jorgensen HS, Rungby JA, Reith J, Nakayama H, Weber UJ, Houth J, Olsen TS. Admission body temperature predicts long-term mortality after acute stroke: the Copenhagen Stroke Study. *Stroke.* 2002;33(7):1759-1762.

1041. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *N Engl J Med.* 2002;346(8):549-556.

1042. Bernard SA, Gray TW, Buist MD, Jones BM, Silvester W, Gutteridge G, Smith K. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med.* 2002;346(8):557-563.

1043. Belliard G, Catez E, Charron C, Caille V, Aegerter P, Dubourg O, Jardin F, Vieillard-Baron A. Efficacy of therapeutic hypothermia after out-of-hospital cardiac arrest due to ventricular fibrillation. *Resuscitation.* 2007;75(2):252-259.

1044. Castrejon S, Cortes M, Salto ML, Benittez LC, Rubio R, Juarez M, Lopez de Sa E, Bueno H, Sanchez PL, Fernandez Aviles F. Improved prognosis after using mild hypothermia to treat cardiorespiratory arrest due to a cardiac cause: comparison with a control group. *Rev Esp Cardiol.* 2009;62(7):733-741.

1045. Arrich J, Holzer M, Herkner H, Mullner M. Cochrane corner: hypothermia for neuroprotection in adults after cardiopulmonary resuscitation. *Anesth Analg.* 2010;110(4):1239.

1046. Hachimi-Idrissi S, Corne L, Ebinger G, Michotte Y, Huyghens L. Mild hypothermia induced by a helmet device: a clinical feasibility study. *Resuscitation.* 2001;51(3):275-281.

1047. Bernard SA, Jones BM, Horne MK. Clinical trial of induced hypothermia in comatose survivors of out-of-hospital cardiac arrest. *Ann Emerg Med.* 1997;30(2):146-153.

1048. Oddo M, Schaller MD, Feihl F, Ribordy V, Liaudet L. From evidence to clinical practice: effective implementation of therapeutic hypothermia to improve patient outcome after cardiac arrest. *Crit Care Med.* 2006;34(7):1865-1873.

1049. Busch M, Soreide E, Lossius HM, Lexow K, Dickstein K. Rapid implementation of therapeutic hypothermia in comatose out-of-hospital cardiac arrest survivors. *Acta Anaesthesiol Scand.* 2006;50(10):1277-1283.

1050. Storm C, Steffen I, Schefold JC, Krueger A, Oppert M, Jorres A, Hasper D. Mild therapeutic hypothermia shortens intensive care unit stay of survivors after out-of-hospital cardiac arrest compared to historical controls. *Crit Care.* 2008;12(3):R78.

1051. Don CW, Longstreth WT, Jr., Maynard C, Olsufka M, Nichol G, Ray T, Kupchik N, Deem S, Copass MK, Cobb LA, Kim F. Active surface cooling protocol to induce mild therapeutic hypothermia after out-of-hospital cardiac arrest: a retrospective before-and-after comparison in a single hospital. *Crit Care Med.* 2009;37(12):3062-3069.

1052. Bro-Jeppesen J, Kjaergaard J, Horsted TI, Wanscher MC, Nielsen SL, Rasmussen LS, Hassager C. The impact of therapeutic hypothermia on neurological function and quality of life after cardiac arrest. *Resuscitation.* 2009;80(2):171-176.

1053. Arrich J. Clinical application of mild therapeutic hypothermia after cardiac arrest. *Crit Care Med.* 2007;35(4):1041-1047.

1054. Holzer M, Mullner M, Sterz F, Robak O, Kliegel A, Losert H, Sodeck G, Uray T, Zeiner A, Laggner AN. Efficacy and safety of endovascular cooling after cardiac arrest: cohort study and Bayesian approach. *Stroke.* 2006;37(7):1792-1797.

1055. Nielsen N, Hovdenes J, Nilsson F, Rubertsson S, Stammet P, Sunde K, Valsson F, Wanscher M,

Friberg H. Outcome, timing and adverse events in therapeutic hypothermia after out-of-hospital cardiac arrest. *Acta Anaesthesiol Scand.* 2009;53(7):926-934.

1056. Knafelj R, Radsel P, Ploj T, Noc M. Primary percutaneous coronary intervention and mild induced hypothermia in comatose survivors of ventricular fibrillation with ST-elevation acute myocardial infarction. *Resuscitation.* 2007;74(2):227-234.

1057. Kilgannon JH, Roberts BW, Stauss M, Cimino MJ, Ferchau L, Chansky ME, Dellinger RP, Parrillo JE, Trzeciak S. Use of a standardized order set for achieving target temperature in the implementation of therapeutic hypothermia after cardiac arrest: a feasibility study. *Acad Emerg Med.* 2008;15(6):499-505.

1058. Spiel AO, Kliegel A, Janata A, Uray T, Mayr FB, Laggner AN, Jilma B, Sterz F. Hemostasis in cardiac arrest patients treated with mild hypothermia initiated by cold fluids. *Resuscitation.* 2009;80(7):762-765.

1059. Larsson IM, Wallin E, Rubertsson S. Cold saline infusion and ice packs alone are effective in inducing and maintaining therapeutic hypothermia after cardiac arrest. *Resuscitation.* 2010;81(1):15-19.

1060. Hoedemaekers CW, Ezzahti M, Gerritsen A, van der Hoeven JG. Comparison of cooling methods to induce and maintain normo- and hypothermia in intensive care unit patients: a prospective intervention study. *Crit Care.* 2007;11(4):R91.

1061. Scott BD, Hogue T, Fixley MS, Adamson PB. Induced hypothermia following out-of-hospital cardiac arrest; initial experience in a community hospital. *Clin Cardiol.* 2006;29(12):525-529.

1062. Skulec R, Kovarnik T, Dostalova G, Kolar J, Linhart A. Induction of mild hypothermia in cardiac arrest survivors presenting with cardiogenic shock syndrome. *Acta Anaesthesiol Scand.* 2008;52(2):188-194.

1063. Kamarainen A, Virkkunen I, Tenhunen J, Yli-Hankala A, Silfvast T. Prehospital therapeutic hypothermia for comatose survivors of cardiac arrest: a randomized controlled trial. *Acta Anaesthesiol Scand.* 2009;53(7):900-907.

1064. Hammer L, Vitrat F, Savary D, Debaty G, Santre C, Durand M, Dessertaine G, Timsit JF. Immediate prehospital hypothermia protocol in comatose survivors of out-of-hospital cardiac arrest. *Am J Emerg Med.* 2009;27(5):570-573.

1065. Kamarainen A, Virkkunen I, Tenhunen J, Yli-Hankala A, Silfvast T. Induction of therapeutic hypothermia during prehospital CPR using ice-cold intravenous fluid. *Resuscitation.* 2008;79(2):205-211.

1066. Aberle J, Kluge S, Prohl J, al. e. Hypothermia after CPR through conduction and convection - Initial experience on an ICU. *Intensivmedizin und Notfallmedizin.* 2006;43:37-43.

1067. Al-Senani FM, Graffagnino C, Grotta JC, Saiki R, Wood D, Chung W, Palmer G, Collins KA. A prospective, multicenter pilot study to evaluate the feasibility and safety of using the CoolGard System and Icy catheter following cardiac arrest. *Resuscitation.* 2004;62(2):143-150.

1068. Feuchtl A, al. e. Endovascular cooling improves neurological short-term outcome after prehospital cardiac arrest. *Intensivmed.* 2007;44:37-42.

1069. Flint AC, Hemphill JC, Bonovich DC. Therapeutic hypothermia after cardiac arrest: performance characteristics and safety of surface cooling with or without endovascular cooling. *Neurocrit Care.* 2007;7(2):109-118.

1070. Pichon N, Amiel JB, Francois B, Dugard A, Etchecopar C, Vignon P. Efficacy of and tolerance to mild induced hypothermia after out-of-hospital cardiac arrest using an endovascular cooling system. *Crit Care.* 2007;11(3):R71.

1071. Wolff B, Machill K, Schumacher D, Schulzki I, Werner D. Early achievement of mild therapeutic hypothermia and the neurologic outcome after cardiac arrest. *Int J Cardiol.* 2009;133(2):223-228.

1072. Felberg RA, Krieger DW, Chuang R, Persse DE, Burgin WS, Hickenbottom SL, Morgenstern LB, Rosales O, Grotta JC. Hypothermia after cardiac arrest: feasibility and safety of an external cooling protocol. *Circulation.* 2001;104(15):1799-1804.

1073. Heard KJ, Peberdy MA, Sayre MR, Sanders A, Geocadin RG, Dixon SR, Larabee TM, Hiller K, Fiorello A, Paradis NA, O'Neil BJ. A randomized controlled trial comparing the Arctic Sun to standard cooling for induction of hypothermia after cardiac arrest. *Resuscitation.* 2010;81(1):9-14.

1074. Merchant RM, Abella BS, Peberdy MA, Soar J, Ong ME, Schmidt GA, Becker LB, Vanden Hoek TL. Therapeutic hypothermia after cardiac arrest: unintentional overcooling is common using ice packs and conventional cooling blankets. *Crit Care Med.* 2006;34(12 Suppl):S490-494.

1075. Fries M, Stoppe C, Brucken D, Rossaint R, Kuhlen R. Influence of mild therapeutic hypothermia on the inflammatory response after successful resuscitation from cardiac arrest. *J Crit Care.* 2009;24(3):453-457.

1076. Benson DW, Williams GR, Jr., Spencer FC, Yates AJ. The use of hypothermia after cardiac arrest. *Anesth Analg.* 1959;38:423-428.

1077. Yanagawa Y, Ishihara S, Norio H, Takino M, Kawakami M, Takasu A, Okamoto K, Kaneko N, Terai C, Okada Y. Preliminary clinical outcome study of mild resuscitative hypothermia after out-of-hospital cardiopulmonary arrest. *Resuscitation.* 1998;39(1-2):61-66.

1078. Damian MS, Ellenberg D, Gildemeister R, Lauermann J, Simonis G, Sauter W, Georgi C. Coenzyme Q10 combined with mild hypothermia after cardiac arrest: a preliminary study. *Circulation.* 2004;110(19):3011-3016.

1079. Hay AW, Swann DG, Bell K, Walsh TS, Cook B. Therapeutic hypothermia in comatose patients after out-of-hospital cardiac arrest. *Anaesthesia.* 2008;63(1):15-19.

1080. Uray T, Malzer R. Out-of-hospital surface cooling to induce mild hypothermia in human cardiac arrest: a feasibility trial. *Resuscitation.* 2008;77(3):331-338.

1081. Zeiner A, Holzer M, Sterz F, Behringer W, Schorkhuber W, Mullner M, Frass M, Siostrzonek P, Ratheiser K, Kaff A, Laggner AN. Mild resuscitative hypothermia to improve neurological outcome after cardiac arrest. A clinical feasibility trial. Hypothermia After Cardiac Arrest (HACA) Study Group. *Stroke.* 2000;31(1):86-94.

1082. Haugk M, Sterz F, Grassberger M, Uray T, Kliegel A, Janata A, Richling N, Herkner H, Laggner AN. Feasibility and efficacy of a new non-invasive surface cooling device in post-resuscitation intensive care medicine. *Resuscitation.* 2007;75(1):76-81.

1083. Wolfrum S, Pierau C, Radke PW, Schunkert H, Kurowski V. Mild therapeutic hypothermia in patients after out-of-hospital cardiac arrest due to acute ST-segment elevation myocardial infarction undergoing immediate percutaneous coronary intervention. *Crit Care Med.* 2008;36(6):1780-1786.

1084. Randomized clinical study of thiopental loading in comatose survivors of cardiac arrest. Brain Resuscitation Clinical Trial I Study Group. *N Engl J Med.* 1986;314(7):397-403.

1085. Krumholz A, Stern BJ, Weiss HD. Outcome from coma after cardiopulmonary resuscitation: relation

to seizures and myoclonus. *Neurology.* 1988;38(3):401-405.

1086. Gustafson I, Edgren E, Hulting J. Brain-oriented intensive care after resuscitation from cardiac arrest. *Resuscitation.* 1992;24(3):245-261.

1087. Wijdicks EF, Parisi JE, Sharbrough FW. Prognostic value of myoclonus status in comatose survivors of cardiac arrest. *Ann Neurol.* 1994;35(2):239-243.

1088. Oksanen T, Skrifvars MB, Varpula T, Kuitunen A, Pettila V, Nurmi J, Castren M. Strict versus moderate glucose control after resuscitation from ventricular fibrillation. *Intensive Care Med.* 2007;33(12):2093-2100.

1089. Nolan JP, Laver SR, Welch CA, Harrison DA, Gupta V, Rowan K. Outcome following admission to UK intensive care units after cardiac arrest: a secondary analysis of the ICNARC Case Mix Programme Database. *Anaesthesia.* 2007;62(12):1207-1216.

1090. Losert H, Sterz F, Roine RO, Holzer M, Martens P, Cerchiari E, Tiainen M, Mullner M, Laggner AN, Herkner H, Bischof MG. Strict normoglycaemic blood glucose levels in the therapeutic management of patients within 12h after cardiac arrest might not be necessary. *Resuscitation.* 2008;76(2):214-220.

1091. Mullner M, Sterz F, Binder M, Schreiber W, Deimel A, Laggner AN. Blood glucose concentration after cardiopulmonary resuscitation influences functional neurological recovery in human cardiac arrest survivors. *J Cereb Blood Flow Metab.* 1997;17(4):430-436.

1092. Finfer S, Chittock DR, Su SY, Blair D, Foster D, Dhingra V, Bellomo R, Cook D, Dodek P, Henderson WR, Hebert PC, Heritier S, Heyland DK, McArthur C, McDonald E, Mitchell I, Myburgh JA, Norton R, Potter J, Robinson BG, Ronco JJ. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med.* 2009;360(13):1283-1297.

1093. Griesdale DE, de Souza RJ, van Dam RM, Heyland DK, Cook DJ, Malhotra A, Dhaliwal R, Henderson WR, Chittock DR, Finfer S, Talmor D. Intensive insulin therapy and mortality among critically ill patients: a meta-analysis including NICE-SUGAR study data. *CMAJ.* 2009;180(8):821-827.

1094. Wiener RS, Wiener DC, Larson RJ. Benefits and risks of tight glucose control in critically ill adults: a meta-analysis. *JAMA.* 2008;300(8):933-944.

1095. Grafton ST, Longstreth WT, Jr. Steroids after cardiac arrest: a retrospective study with concurrent, nonrandomized controls. *Neurology.* 1988;38(8):1315-1316.

1096. Jastremski M, Sutton-Tyrrell K, Vaagenes P, Abramson N, Heiselman D, Safar P. Glucocorticoid treatment does not improve neurological recovery following cardiac arrest. Brain Resuscitation Clinical Trial I Study Group. *JAMA.* 1989;262(24):3427-3430.

1097. Ebmeyer U, Safar P, Radovsky A, Xiao F, Capone A, Tanigawa K, Stezoski SW. Thiopental combination treatments for cerebral resuscitation after prolonged cardiac arrest in dogs. Exploratory outcome study. *Resuscitation.* 2000;45(2):119-131.

1098. Katz L, Vaagenes P, Safar P, Diven W. Brain enzyme changes as markers of brain damage in rat cardiac arrest model. Effects of corticosteroid therapy. *Resuscitation.* 1989;17(1):39-53.

1099. Laurent I, Adrie C, Vinsonneau C, Cariou A, Chiche JD, Ohanessian A, Spaulding C, Carli P, Dhainaut JF, Monchi M. High-volume hemofiltration after out-of-hospital cardiac arrest: a randomized study. *J Am Coll Cardiol.* 2005;46(3):432-437.

1100. Huang D, Xu R, al. e. Effect of high volume hemofiltration on outcome of cerebral edema following

cerebral reperfusion injury. [Chinese]. *Chinese Journal of Clinical Rehabilitation.* 2004;8:3796-3797.

1101. Roine RO, Kaste M, Kinnunen A, Nikki P, Sarna S, Kajaste S. Nimodipine after resuscitation from out-of-hospital ventricular fibrillation. A placebo-controlled, double-blind, randomized trial. *JAMA.* 1990;264(24):3171-3177.

1102. Roine RO, Kajaste S, Kaste M. Neuropsychological sequelae of cardiac arrest. *JAMA.* 1993;269(2):237-242.

1103. A randomized clinical study of a calcium-entry blocker (lidoflazine) in the treatment of comatose survivors of cardiac arrest. Brain Resuscitation Clinical Trial II Study Group. *N Engl J Med.* 1991;324(18):1225-1231.

1104. Gueugniaud PY, Gaussorgues P, Garcia-Darennes F, Bancalari G, Roux H, Robert D, Petit P. Early effects of nimodipine on intracranial and cerebral perfusion pressures in cerebral anoxia after out-of-hospital cardiac arrest. *Resuscitation.* 1990;20(3):203-212.

1105. Thabut G, Thabut D, Myers RP, Bernard-Chabert B, Marrash-Chahla R, Mal H, Fournier M. Thrombolytic therapy of pulmonary embolism: a meta-analysis. *J Am Coll Cardiol.* 2002;40(9):1660-1667.

1106. Wan S, Quinlan DJ, Agnelli G, Eikelboom JW. Thrombolysis compared with heparin for the initial treatment of pulmonary embolism: a meta-analysis of the randomized controlled trials. *Circulation.* 2004;110(6):744-749.

1107. Spohr F, Bottiger BW. Thrombolytic therapy during or after cardiopulmonary resuscitation. Efficacy and safety of a new therapeutic approach. *Minerva Anestesiol.* 2003;69(5):357-364.

1108. Clarke DB, Abrams LD. Pulmonary embolectomy: a 25 year experience. *J Thorac Cardiovasc Surg.* 1986;92(3 Pt 1):442-445.

1109. Dauphine C, Omari B. Pulmonary embolectomy for acute massive pulmonary embolism. *Ann Thorac Surg.* 2005;79(4):1240-1244.

1110. Doerge HC, Schoendube FA, Loeser H, Walter M, Messmer BJ. Pulmonary embolectomy: review of a 15-year experience and role in the age of thrombolytic therapy. *Eur J Cardiothorac Surg.* 1996;10(11):952-957.

1111. Ullmann M, Hemmer W, Hannekum A. The urgent pulmonary embolectomy: mechanical resuscitation in the operating theatre determines the outcome. *Thorac Cardiovasc Surg.* 1999;47(1):5-8.

1112. Schmid C, Zietlow S, Wagner TO, Laas J, Borst HG. Fulminant pulmonary embolism: symptoms, diagnostics, operative technique, and results. *Ann Thorac Surg.* 1991;52(5):1102-1105; discussion 1105-1107.

1113. Tayama E, Ouchida M, Teshima H, Takaseya T, Hiratsuka R, Akasu K, Hayashida N, Fukunaga S, Akashi H, Kawara T, Aoyagi S. Treatment of acute massive/submassive pulmonary embolism. *Circ J.* 2002;66(5):479-483.

1114. Ahrens T, Schallom L, Bettorf K, Ellner S, Hurt G, O'Mara V, Ludwig J, George W, Marino T, Shannon W. End-tidal carbon dioxide measurements as a prognostic indicator of outcome in cardiac arrest. *Am J Crit Care.* 2001;10(6):391-398.

1115. Sanders AB, Kern KB, Otto CW, Milander MM, Ewy GA. End-tidal carbon dioxide monitoring during cardiopulmonary resuscitation. A prognostic indicator for survival. *JAMA.* 1989;262(10):1347-1351.

1116. Asplin BR, White RD. Prognostic value of end-tidal carbon dioxide pressures during out-of-hospital cardiac arrest. *Ann Emerg Med.* 1995;25(6):756-761.

1117. Nakatani K, Yukioka H, Fujimori M, Maeda C, Noguchi H, Ishihara S, Yamanaka I, Tase C. Utility of colorimetric end-tidal carbon dioxide detector for monitoring during prehospital cardiopulmonary resuscitation. *Am J Emerg Med.* 1999;17(2):203-206.

1118. Mauer D, Schneider T, Elich D, Dick W. Carbon dioxide levels during pre-hospital active compression--decompression versus standard cardiopulmonary resuscitation. *Resuscitation.* 1998;39(1-2):67-74.

1119. White JG. Platelets and atherosclerosis. *Eur J Clin Invest.* 1994;24 Suppl 1:25-29.

1120. Blaivas M, Fox JC. Outcome in cardiac arrest patients found to have cardiac standstill on the bedside emergency department echocardiogram. *Acad Emerg Med.* 2001;8(6):616-621.

1121. Salen P, Melniker L, Chooljian C, Rose JS, Alteveer J, Reed J, Heller M. Does the presence or absence of sonographically identified cardiac activity predict resuscitation outcomes of cardiac arrest patients? *Am J Emerg Med.* 2005;23(4):459-462.

1122. Memtsoudis SG, Rosenberger P, Loffler M, Eltzschig HK, Mizuguchi A, Shernan SK, Fox JA. The usefulness of transesophageal echocardiography during intraoperative cardiac arrest in noncardiac surgery. *Anesth Analg.* 2006;102(6):1653-1657.

1123. van der Wouw PA, Koster RW, Delemarre BJ, de Vos R, Lampe-Schoenmaeckers AJ, Lie KI. Diagnostic accuracy of transesophageal echocardiography during cardiopulmonary resuscitation. *J Am Coll Cardiol.* 1997;30(3):780-783.

1124. Comess KA, DeRook FA, Russell ML, Tognazzi-Evans TA, Beach KW. The incidence of pulmonary embolism in unexplained sudden cardiac arrest with pulseless electrical activity. *Am J Med.* 2000;109(5):351-356.

1125. Niendorff DF, Rassias AJ, Palac R, Beach ML, Costa S, Greenberg M. Rapid cardiac ultrasound of inpatients suffering PEA arrest performed by nonexpert sonographers. *Resuscitation.* 2005;67(1):81-87.

1126. Tayal VS, Kline JA. Emergency echocardiography to detect pericardial effusion in patients in PEA and near-PEA states. *Resuscitation.* 2003;59(3):315-318.

1127. Edgren E, Hedstrand U, Nordin M, Rydin E, Ronquist G. Prediction of outcome after cardiac arrest. *Crit Care Med.* 1987;15(9):820-825.

1128. Young GB, Doig G, Ragazzoni A. Anoxic-ischemic encephalopathy: clinical and electrophysiological associations with outcome. *Neurocrit Care.* 2005;2(2):159-164.

1129. Zandbergen EG, Hijdra A, Koelman JH, Hart AA, Vos PE, Verbeek MM, de Haan RJ. Prediction of poor outcome within the first 3 days of postanoxic coma. *Neurology.* 2006;66(1):62-68.

1130. Bassetti C, Bomio F, Mathis J, Hess CW. Early prognosis in coma after cardiac arrest: a prospective clinical, electrophysiological, and biochemical study of 60 patients. *J Neurol Neurosurg Psychiatry.* 1996;61(6):610-615.

1131. Edgren E, Hedstrand U, Kelsey S, Sutton-Tyrrell K, Safar P. Assessment of neurological prognosis in comatose survivors of cardiac arrest. BRCT I Study Group. *Lancet.* 1994;343(8905):1055-1059.

1132. Prohl J, Rother J, Kluge S, de Heer G, Liepert J, Bodenburg S, Pawlik K, Kreymann G. Prediction of short-term and long-term outcomes after cardiac arrest: a prospective multivariate approach combining biochemical, clinical, electrophysiological, and neuropsychological investigations. *Crit*

Care Med. 2007;35(5):1230-1237.

1133. Al Thenayan E, Savard M, Sharpe M, Norton L, Young B. Predictors of poor neurologic outcome after induced mild hypothermia following cardiac arrest. *Neurology.* 2008;71(19):1535-1537.

1134. Thomke F, Marx JJ, Sauer O, Hundsberger T, Hagele S, Wiechelt J, Weilemann SL. Observations on comatose survivors of cardiopulmonary resuscitation with generalized myoclonus. *BMC Neurol.* 2005;5:14.

1135. Arnoldus EP, Lammers GJ. Postanoxic coma: good recovery despite myoclonus status. *Ann Neurol.* 1995;38(4):697-698.

1136. Celesia GG, Grigg MM, Ross E. Generalized status myoclonicus in acute anoxic and toxic-metabolic encephalopathies. *Arch Neurol.* 1988;45(7):781-784.

1137. Datta S, Hart GK, Opdam H, Gutteridge G, Archer J. Post-hypoxic myoclonic status: the prognosis is not always hopeless. *Crit Care Resusc.* 2009;11(1):39-41.

1138. English WA, Giffin NJ, Nolan JP. Myoclonus after cardiac arrest: pitfalls in diagnosis and prognosis. *Anaesthesia.* 2009;64(8):908-911.

1139. Morris HR, Howard RS, Brown P. Early myoclonic status and outcome after cardiorespiratory arrest. *J Neurol Neurosurg Psychiatry.* 1998;64(2):267-268.

1140. Wijdicks EF, Hijdra A, Young GB, Bassetti CL, Wiebe S. Practice parameter: prediction of outcome in comatose survivors after cardiopulmonary resuscitation (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 2006;67(2):203-210.

1141. Zandbergen EG, de Haan RJ, Hijdra A. Systematic review of prediction of poor outcome in anoxic-ischaemic coma with biochemical markers of brain damage. *Intensive Care Med.* 2001;27(10):1661-1667.

1142. Grubb NR, Simpson C, Sherwood RA, Abraha HD, Cobbe SM, O'Carroll RE, Deary I, Fox KA. Prediction of cognitive dysfunction after resuscitation from out-of-hospital cardiac arrest using serum neuron-specific enolase and protein S-100. *Heart.* 2007;93(10):1268-1273.

1143. Martens P. Serum neuron-specific enolase as a prognostic marker for irreversible brain damage in comatose cardiac arrest survivors. *Acad Emerg Med.* 1996;3(2):126-131.

1144. Meynaar IA, Oudemans-van Straaten HM, van der Wetering J, Verlooy P, Slaats EH, Bosman RJ, van der Spoel JI, Zandstra DF. Serum neuron-specific enolase predicts outcome in post-anoxic coma: a prospective cohort study. *Intensive Care Med.* 2003;29(2):189-195.

1145. Rech TH, Vieira SR, Nagel F, Brauner JS, Scalco R. Serum neuron-specific enolase as early predictor of outcome after in-hospital cardiac arrest: a cohort study. *Crit Care.* 2006;10(5):R133.

1146. Reisinger J, Hollinger K, Lang W, Steiner C, Winter T, Zeindlhofer E, Mori M, Schiller A, Lindorfer A, Wiesinger K, Siostrzonek P. Prediction of neurological outcome after cardiopulmonary resuscitation by serial determination of serum neuron-specific enolase. *Eur Heart J.* 2007;28(1):52-58.

1147. Schoerkhuber W, Kittler H, Sterz F, Behringer W, Holzer M, Frossard M, Spitzauer S, Laggner AN. Time course of serum neuron-specific enolase. A predictor of neurological outcome in patients resuscitated from cardiac arrest. *Stroke.* 1999;30(8):1598-1603.

1148. Bottiger BW, Mobes S, Glatzer R, Bauer H, Gries A, Bartsch P, Motsch J, Martin E. Astroglial protein S-100 is an early and sensitive marker of hypoxic brain damage and outcome after cardiac

arrest in humans. *Circulation.* 2001;103(22):2694-2698.

1149. Fogel W, Krieger D, Veith M, Adams HP, Hund E, Storch-Hagenlocher B, Buggle F, Mathias D, Hacke W. Serum neuron-specific enolase as early predictor of outcome after cardiac arrest. *Crit Care Med.* 1997;25(7):1133-1138.

1150. Martens P, Raabe A, Johnsson P. Serum S-100 and neuron-specific enolase for prediction of regaining consciousness after global cerebral ischemia. *Stroke.* 1998;29(11):2363-2366.

1151. Stelzl T, von Bose MJ, Hogl B, Fuchs HH, Flugel KA. A comparison of the prognostic value of neuron-specific enolase serum levels and somatosensory evoked potentials in 13 reanimated patients. *Eur J Emerg Med.* 1995;2(1):24-27.

1152. Tiainen M, Roine RO, Pettila V, Takkunen O. Serum neuron-specific enolase and S-100B protein in cardiac arrest patients treated with hypothermia. *Stroke.* 2003;34(12):2881-2886.

1153. Pfeifer R, Borner A, Krack A, Sigusch HH, Surber R, Figulla HR. Outcome after cardiac arrest: predictive values and limitations of the neuroproteins neuron-specific enolase and protein S-100 and the Glasgow Coma Scale. *Resuscitation.* 2005;65(1):49-55.

1154. Roine RO, Somer H, Kaste M, Viinikka L, Karonen SL. Neurological outcome after out-of-hospital cardiac arrest. Prediction by cerebrospinal fluid enzyme analysis. *Arch Neurol.* 1989;46(7):753-756.

1155. Zingler VC, Krumm B, Bertsch T, Fassbender K, Pohlmann-Eden B. Early prediction of neurological outcome after cardiopulmonary resuscitation: a multimodal approach combining neurobiochemical and electrophysiological investigations may provide high prognostic certainty in patients after cardiac arrest. *Eur Neurol.* 2003;49(2):79-84.

1156. Rosen H, Sunnerhagen KS, Herlitz J, Blomstrand C, Rosengren L. Serum levels of the brain-derived proteins S-100 and NSE predict long-term outcome after cardiac arrest. *Resuscitation.* 2001;49(2):183-191.

1157. Dauberschmidt R, Zinsmeyer J, Mrochen H, Meyer M. Changes of neuron-specific enolase concentration in plasma after cardiac arrest and resuscitation. *Mol Chem Neuropathol.* 1991;14(3):237-245.

1158. Mussack T, Biberthaler P, Kanz KG, Wiedemann E, Gippner-Steppert C, Mutschler W, Jochum M. Serum S-100B and interleukin-8 as predictive markers for comparative neurologic outcome analysis of patients after cardiac arrest and severe traumatic brain injury. *Crit Care Med.* 2002;30(12):2669-2674.

1159. Fries M, Kunz D, Gressner AM, Rossaint R, Kuhlen R. Procalcitonin serum levels after out-of-hospital cardiac arrest. *Resuscitation.* 2003;59(1):105-109.

1160. Hachimi-Idrissi S, Van der Auwera M, Schiettecatte J, Ebinger G, Michotte Y, Huyghens L. S-100 protein as early predictor of regaining consciousness after out of hospital cardiac arrest. *Resuscitation.* 2002;53(3):251-257.

1161. Piazza O, Cotena S, Esposito G, De Robertis E, Tufano R. S100B is a sensitive but not specific prognostic index in comatose patients after cardiac arrest. *Minerva Chir.* 2005;60(6):477-480.

1162. Rosen H, Rosengren L, Herlitz J, Blomstrand C. Increased serum levels of the S-100 protein are associated with hypoxic brain damage after cardiac arrest. *Stroke.* 1998;29(2):473-477.

1163. Mussack T, Biberthaler P, Kanz KG, Wiedemann E, Gippner-Steppert C, Jochum M. S-100b, sE-selectin, and sP-selectin for evaluation of hypoxic brain damage in patients after cardiopulmonary resuscitation: pilot study. *World J Surg.* 2001;25(5):539-543; discussion 544.

1164. Sodeck GH, Domanovits H, Sterz F, Schillinger M, Losert H, Havel C, Kliegel A, Vlcek M, Frossard M, Laggner AN. Can brain natriuretic peptide predict outcome after cardiac arrest? An observational study. *Resuscitation.* 2007;74(3):439-445.

1165. Geppert A, Zorn G, Delle-Karth G, Koreny M, Siostrzonek P, Heinz G, Huber K. Plasma concentrations of von Willebrand factor and intracellular adhesion molecule-1 for prediction of outcome after successful cardiopulmonary resuscitation. *Crit Care Med.* 2003;31(3):805-811.

1166. Adrie C, Adib-Conquy M, Laurent I, Monchi M, Vinsonneau C, Fitting C, Fraisse F, Dinh-Xuan AT, Carli P, Spaulding C, Dhainaut JF, Cavaillon JM. Successful cardiopulmonary resuscitation after cardiac arrest as a "sepsis-like" syndrome. *Circulation.* 2002;106(5):562-568.

1167. Adib-Conquy M, Monchi M, Goulenok C, Laurent I, Thuong M, Cavaillon JM, Adrie C. Increased plasma levels of soluble triggering receptor expressed on myeloid cells 1 and procalcitonin after cardiac surgery and cardiac arrest without infection. *Shock.* 2007;28(4):406-410.

1168. Longstreth WT, Jr., Clayson KJ, Chandler WL, Sumi SM. Cerebrospinal fluid creatine kinase activity and neurologic recovery after cardiac arrest. *Neurology.* 1984;34(6):834-837.

1169. Karkela J, Pasanen M, Kaukinen S, Morsky P, Harmoinen A. Evaluation of hypoxic brain injury with spinal fluid enzymes, lactate, and pyruvate. *Crit Care Med.* 1992;20(3):378-386.

1170. Rothstein TL, Thomas EM, Sumi SM. Predicting outcome in hypoxic-ischemic coma. A prospective clinical and electrophysiologic study. *Electroencephalogr Clin Neurophysiol.* 1991;79(2):101-107.

1171. Sherman AL, Tirschwell DL, Micklesen PJ, Longstreth WT, Jr., Robinson LR. Somatosensory potentials, CSF creatine kinase BB activity, and awakening after cardiac arrest. *Neurology.* 2000;54(4):889-894.

1172. Longstreth WT, Jr., Clayson KJ, Sumi SM. Cerebrospinal fluid and serum creatine kinase BB activity after out-of-hospital cardiac arrest. *Neurology.* 1981;31(4):455-458.

1173. Tirschwell DL, Longstreth WT, Jr., Rauch-Matthews ME, Chandler WL, Rothstein T, Wray L, Eng LJ, Fine J, Copass MK. Cerebrospinal fluid creatine kinase BB isoenzyme activity and neurologic prognosis after cardiac arrest. *Neurology.* 1997;48(2):352-357.

1174. Clemmensen P, Strandgaard S, Rasmussen S, Grande P. Cerebrospinal fluid creatine kinase isoenzyme BB levels do not predict the clinical outcome in patients unconscious following cardiac resuscitation. *Clin Cardiol.* 1987;10(4):235-236.

1175. Rosen H, Karlsson JE, Rosengren L. CSF levels of neurofilament is a valuable predictor of long-term outcome after cardiac arrest. *J Neurol Sci.* 2004;221(1-2):19-24.

1176. Zandbergen EG, de Haan RJ, Stoutenbeek CP, Koelman JH, Hijdra A. Systematic review of early prediction of poor outcome in anoxic-ischaemic coma. *Lancet.* 1998;352(9143):1808-1812.

1177. Fischer C, Luaute J, Nemoz C, Morlet D, Kirkorian G, Mauguiere F. Improved prediction of awakening or nonawakening from severe anoxic coma using tree-based classification analysis. *Crit Care Med.* 2006;34(5):1520-1524.

1178. Gendo A, Kramer L, Hafner M, Funk GC, Zauner C, Sterz F, Holzer M, Bauer E, Madl C. Time-dependency of sensory evoked potentials in comatose cardiac arrest survivors. *Intensive Care Med.* 2001;27(8):1305-1311.

1179. Madl C, Kramer L, Domanovits H, Woolard RH, Gervais H, Gendo A, Eisenhuber E, Grimm G, Sterz F. Improved outcome prediction in unconscious cardiac arrest survivors with sensory evoked potentials compared with clinical assessment. *Crit Care Med.* 2000;28(3):721-726.

1180. Nakabayashi M, Kurokawa A, Yamamoto Y. Immediate prediction of recovery of consciousness after cardiac arrest. *Intensive Care Med.* 2001;27(7):1210-1214.

1181. Tiainen M, Kovala TT, Takkunen OS, Roine RO. Somatosensory and brainstem auditory evoked potentials in cardiac arrest patients treated with hypothermia. *Crit Care Med.* 2005;33(8):1736-1740.

1182. Bauer EM, Donzello MP, Ercolani C, Masetti E, Panero S, Ricciardi G, Rosa A, Chiesi-Villa A, Rizzoli C. "Stapled" bis(phthalocyaninato)niobium(IV), Pc2Nb: X-ray crystal structure, chemical and electrochemical behavior, and theoretical studies. Perspectives for the use of Pc2Nb (thin films) as an "optically passive electrode" in electrochromic devices. *Inorg Chem.* 2003;42(2):283-293.

1183. Logi F, Fischer C, Murri L, Mauguiere F. The prognostic value of evoked responses from primary somatosensory and auditory cortex in comatose patients. *Clin Neurophysiol.* 2003;114(9):1615-1627.

1184. Rothstein TL. The role of evoked potentials in anoxic-ischemic coma and severe brain trauma. *J Clin Neurophysiol.* 2000;17(5):486-497.

1185. Sakurai A, Kinoshita K, Moriya T, Utagawa A, Ebihara T, Furukawa M, Tanjoh K. Reduced effectiveness of hypothermia in patients lacking the wave V in auditory brainstem responses immediately following resuscitation from cardiac arrest. *Resuscitation.* 2006;70(1):52-58.

1186. Rundgren M, Rosen I, Friberg H. Amplitude-integrated EEG (aEEG) predicts outcome after cardiac arrest and induced hypothermia. *Intensive Care Med.* 2006;32(6):836-842.

1187. Shibata S, Imota T, Shigeomi S, Sato W, Enzan K. Use of the bispectral index during the early postresuscitative phase after out-of-hospital cardiac arrest. *J Anesth.* 2005;19(3):243-246.

1188. Stammet P, Werer C, Mertens L, Lorang C, Hemmer M. Bispectral index (BIS) helps predicting bad neurological outcome in comatose survivors after cardiac arrest and induced therapeutic hypothermia. *Resuscitation.* 2009;80(4):437-442.

1189. Ajisaka H. Early electroencephalographic findings in patients with anoxic encephalopathy after cardiopulmonary arrest and successful resusitation. *J Clin Neurosci.* 2004;11(6):616-618.

1190. Rossetti AO, Logroscino G, Liaudet L, Ruffieux C, Ribordy V, Schaller MD, Despland PA, Oddo M. Status epilepticus: an independent outcome predictor after cerebral anoxia. *Neurology.* 2007;69(3):255-260.

1191. Berkhoff M, Donati F, Bassetti C. Postanoxic alpha (theta) coma: a reappraisal of its prognostic significance. *Clin Neurophysiol.* 2000;111(2):297-304.

1192. Thomke F, Brand A, Weilemann SL. The temporal dynamics of postanoxic burst-suppression EEG. *J Clin Neurophysiol.* 2002;19(1):24-31.

1193. Fatovich DM, Jacobs IG, Celenza A, Paech MJ. An observational study of bispectral index monitoring for out of hospital cardiac arrest. *Resuscitation.* 2006;69(2):207-212.

1194. Choi SP, Park HK, Park KN, Kim YM, Ahn KJ, Choi KH, Lee WJ, Jeong SK. The density ratio of grey to white matter on computed tomography as an early predictor of vegetative state or death after cardiac arrest. *Emerg Med J.* 2008;25(10):666-669.

1195. Nogami K, Fujii M, Kato S, Nishizaki T, Suzuki M, Yamashita S, Oda Y, Sadamitsu D, Maekawa T. Analysis of magnetic resonance imaging (MRI) morphometry and cerebral blood flow in patients with hypoxic-ischemic encephalopathy. *J Clin Neurosci.* 2004;11(4):376-380.

1196. Fujioka M, Okuchi K, Sakaki T, Hiramatsu K, Miyamoto S, Iwasaki S. Specific changes in human brain following reperfusion after cardiac arrest. *Stroke.* 1994;25(10):2091-2095.

1197. De Reuck J, Decoo D, Vienne J, Strijckmans K, Lemahieu I. Significance of white matter lucencies in posthypoxic-ischemic encephalopathy: comparison of clinical status and of computed and positron emission tomographic findings. *Eur Neurol.* 1992;32(6):334-339.

1198. Inoue Y, Shiozaki T, Irisawa T, Mohri T, Yoshiya K, Ikegawa H, Tasaki O, Tanaka H, Shimazu T, Sugimoto H. Acute cerebral blood flow variations after human cardiac arrest assessed by stable xenon enhanced computed tomography. *Curr Neurovasc Res.* 2007;4(1):49-54.

1199. Nunes B, Pais J, Garcia R, Magalhaes Z, Granja C, Silva MC. Cardiac arrest: long-term cognitive and imaging analysis. *Resuscitation.* 2003;57(3):287-297.

1200. Yanagawa Y, Un-no Y, Sakamoto T, Okada Y. Cerebral density on CT immediately after a successful resuscitation of cardiopulmonary arrest correlates with outcome. *Resuscitation.* 2005;64(1):97-101.

1201. Della Corte F, Barelli A, Giordano A, Iacobucci T, Valente MR, Pennisi MA. CBF determination in post-ischemic-anoxic comatose patients. *Minerva Anestesiol.* 1993;59(11):637-641.

1202. Kjos BO, Brant-Zawadzki M, Young RG. Early CT findings of global central nervous system hypoperfusion. *AJR Am J Roentgenol.* 1983;141(6):1227-1232.

1203. Morimoto Y, Kemmotsu O, Kitami K, Matsubara I, Tedo I. Acute brain swelling after out-of-hospital cardiac arrest: pathogenesis and outcome. *Crit Care Med.* 1993;21(1):104-110.

1204. Torbey MT, Geocadin R, Bhardwaj A. Brain arrest neurological outcome scale (BrANOS): predicting mortality and severe disability following cardiac arrest. *Resuscitation.* 2004;63(1):55-63.

1205. Torbey MT, Selim M, Knorr J, Bigelow C, Recht L. Quantitative analysis of the loss of distinction between gray and white matter in comatose patients after cardiac arrest. *Stroke.* 2000;31(9):2163-2167.

1206. Arishima H, Ishii H, Kubota T, Maeda H, Shigemori K. [Angiographic features of anoxic encephalopathy in the acute phase: a case report]. *No To Shinkei.* 2003;55(11):977-982.

1207. Verslegers W, Crols R, van den Kerchove M, de Potter W, Appel B, Lowenthal A. Parkinsonian syndrome after cardiac arrest: radiological and neurochemical changes. *Clin Neurol Neurosurg.* 1988;90(2):177-179.

1208. Hung GU, Lee JD, Lee JK. Bilateral cranial Tc-99m MDP uptake due to hypoxic-ischemic encephalopathy. *Clin Nucl Med.* 2007;32(4):328-329.

1209. Imaizumi H, Tsuruoka K, Ujike Y, Kaneko M, Namiki A. [Hypoxic brain damage after prolonged cardiac arrest during anesthesia--changes in CT and serum NSE concentration]. *Masui.* 1994;43(8):1256-1260.

1210. Fujioka M, Okuchi K, Miyamoto S, Sakaki T, Hiramatsu K, Tominaga M, Kamada Y, Iwasaki S. Changes in the basal ganglia and thalamus following reperfusion after complete cerebral ischaemia. *Neuroradiology.* 1994;36(8):605-607.

1211. Kelsen J, Obel A. Images in clinical medicine. Fatal cerebral hypoxemia after cardiac arrest. *N Engl J Med.* 2003;348(9):817.

1212. Schwab SA, Richter G, Bautz WA, Uder M, Alibek S. [Hypoxic injury of all deep nuclei of the brain--a case report from computed tomography]. *Rontgenpraxis.* 2008;56(6):245-248.

1213. Tanaka H, Masugata H, Fukunaga R, Mandai K, Sueyoshi K, Abe H. Sequential change of heterogeneous cerebral blood blow patterns after diffuse brain ischemia. *Resuscitation.* 1992;24(3):273-281.

1214. Ross RT. Brain swelling and ventricle size. *Can J Neurol Sci.* 1983;10(2):110-113.

1215. Hollerbach S, Kullmann F, Bartsch H, al. e. Prediction of outcome in resuscitated patients by clinical course and early somatosensory-evoked potentials. A comparison with the Glasgow Coma Scale (GCS) and cranial-computed tomography (CCT). *Clin Int Care.* 1995;6:219-227.

1216. Allen JS, Tranel D, Bruss J, Damasio H. Correlations between regional brain volumes and memory performance in anoxia. *J Clin Exp Neuropsychol.* 2006;28(4):457-476.

1217. De Volder AG, Michel C, Guerit JM, Bol A, Georges B, de Barsy T, Laterre C. Brain glucose metabolism in postanoxic syndrome due to cardiac arrest. *Acta Neurol Belg.* 1994;94(3):183-189.

1218. Fujioka M, Nishio K, Miyamoto S, Hiramatsu KI, Sakaki T, Okuchi K, Taoka T, Fujioka S. Hippocampal damage in the human brain after cardiac arrest. *Cerebrovasc Dis.* 2000;10(1):2-7.

1219. Tommasino C, Grana C, Lucignani G, Torri G, Fazio F. Regional cerebral metabolism of glucose in comatose and vegetative state patients. *J Neurosurg Anesthesiol.* 1995;7(2):109-116.

1220. Lovblad K, Senn P, Walpoth B, al. e. Increased brain tolerance for ischemia in accidental deep hypothermia and circulatory arrest. *Riv Neuroradiol* 1998;11(SUPPL 2):224-226.

1221. Edgren E, Enblad P, Grenvik A, Lilja A, Valind S, Wiklund L, Hedstrand U, Stjernstrom H, Persson L, Ponten U, Langstrom B. Cerebral blood flow and metabolism after cardiopulmonary resuscitation. A pathophysiologic and prognostic positron emission tomography pilot study. *Resuscitation.* 2003;57(2):161-170.

1222. Grubb NR, Fox KA, Smith K, Best J, Blane A, Ebmeier KP, Glabus MF, O'Carroll RE. Memory impairment in out-of-hospital cardiac arrest survivors is associated with global reduction in brain volume, not focal hippocampal injury. *Stroke.* 2000;31(7):1509-1514.

1223. Gut E, Fritz R, Leyhe T, al. e. MRT after cerebral hypoxia. Correlation of imaging findings with clinical outcome and functional rehabilitation. *Klin Neuroradiol.* 1999;9:147-152.

1224. Els T, Kassubek J, Kubalek R, Klisch J. Diffusion-weighted MRI during early global cerebral hypoxia: a predictor for clinical outcome? *Acta Neurol Scand.* 2004;110(6):361-367.

1225. Kano H, Houkin K, Harada K, Koyanagi I, Nara S, Itou Y, Imaizumi H, Asai Y, Saitou M. Neuronal cell injury in patients after cardiopulmonary resuscitation: evaluation by diffusion-weighted imaging and magnetic resonance spectroscopy. *Neurosurg Rev.* 2006;29(1):88-92.

1226. Wijdicks EF, Campeau NG, Miller GM. MR imaging in comatose survivors of cardiac resuscitation. *AJNR Am J Neuroradiol.* 2001;22(8):1561-1565.

1227. Wijman CA, Mlynash M, Caulfield AF, Hsia AW, Eyngorn I, Bammer R, Fischbein N, Albers GW, Moseley M. Prognostic value of brain diffusion-weighted imaging after cardiac arrest. *Ann Neurol.* 2009;65(4):394-402.

1228. Wu WF, Wu JR, Dai ZK, Tsai CW, Tsai TC, Chen CC, Yang CY. Montelukast as monotherapy in children with mild persistent asthma. *Asian Pac J Allergy Immunol.* 2009;27(4):173-180.

1229. Arbelaez A, Castillo M, Mukherji SK. Diffusion-weighted MR imaging of global cerebral anoxia. *AJNR Am J Neuroradiol.* 1999;20(6):999-1007.

1230. Barrett KM, Freeman WD, Weindling SM, Brott TG, Broderick DF, Heckman MG, Crook JE, Divertie GD, Meschia JF. Brain injury after cardiopulmonary arrest and its assessment with diffusion-weighted magnetic resonance imaging. *Mayo Clin Proc.* 2007;82(7):828-835.

1231. Berek K, Lechleitner P, Luef G, Felber S, Saltuari L, Schinnerl A, Traweger C, Dienstl F, Aichner F. Early determination of neurological outcome after prehospital cardiopulmonary resuscitation. *Stroke.* 1995;26(4):543-549.

1232. Iida K, Satoh H, Arita K, Nakahara T, Kurisu K, Ohtani M. Delayed hyperemia causing intracranial hypertension after cardiopulmonary resuscitation. *Crit Care Med.* 1997;25(6):971-976.

1233. Ettl A, Felber S, Birbamer G, Daxer A. Corticol blindness following cerebral hypoxia. Proton nuclear magnetic resonance imaging and spectroscopy observations. *Neuro-ophthalmology.* 1994;14:259-263.

1234. Greer DM. MRI in anoxic brain injury. *Neurocrit Care.* 2004;1(2):213-215.

1235. Kuoppamaki M, Bhatia KP, Quinn N. Progressive delayed-onset dystonia after cerebral anoxic insult in adults. *Mov Disord.* 2002;17(6):1345-1349.

1236. Ali OA, Aggarwal A, Thanakrishnan G, Lowe HC. Thoracic spinal cord ischemia following acute myocardial infarction and cardiac arrest in a young male. *Heart Lung Circ.* 2006;15(1):53-55.

1237. Bolouri MR, Small GA. Neuroimaging of hypoxia and cocaine-induced hippocampal stroke. *J Neuroimaging.* 2004;14(3):290-291.

1238. Johkura K, Naito M. Wernicke's encephalopathy-like lesions in global cerebral hypoxia. *J Clin Neurosci.* 2008;15(3):318-319.

1239. Konaka K, Miyashita K, Naritomi H. Changes in diffusion-weighted magnetic resonance imaging findings in the acute and subacute phases of anoxic encephalopathy. *J Stroke Cerebrovasc Dis.* 2007;16(2):82-83.

1240. Singhal AB, Topcuoglu MA, Koroshetz WJ. Diffusion MRI in three types of anoxic encephalopathy. *J Neurol Sci.* 2002;196(1-2):37-40.

1241. Wartenberg KE, Patsalides A, Yepes MS. Is magnetic resonance spectroscopy superior to conventional diagnostic tools in hypoxic-ischemic encephalopathy? *J Neuroimaging.* 2004;14(2):180-186.

1242. Zhang YX, Liu JR, Jiang B, Liu HQ, Ding MP, Song SJ, Zhang BR, Zhang H, Xu B, Chen HH, Wang ZJ, Huang JZ. Lance-Adams syndrome: a report of two cases. *J Zhejiang Univ Sci B.* 2007;8(10):715-720.

1243. Roine RO, Raininko R, Erkinjuntti T, Ylikoski A, Kaste M. Magnetic resonance imaging findings associated with cardiac arrest. *Stroke.* 1993;24(7):1005-1014.

1244. Heckmann JG, Lang CJ, Pfau M, Neundorfer B. Electrocerebral silence with preserved but reduced cortical brain perfusion. *Eur J Emerg Med.* 2003;10(3):241-243.

1245. Roine RO, Launes J, Nikkinen P, Lindroth L, Kaste M. Regional cerebral blood flow after human cardiac arrest. A hexamethylpropyleneamine oxime single photon emission computed tomographic study. *Arch Neurol.* 1991;48(6):625-629.

1246. Buunk G, van der Hoeven JG, Meinders AE. A comparison of near-infrared spectroscopy and jugular bulb oximetry in comatose patients resuscitated from a cardiac arrest. *Anaesthesia.* 1998;53(1):13-19.

1247. Leithner C, Ploner CJ, Hasper D, Storm C. Does hypothermia influence the predictive value of bilateral absent N20 after cardiac arrest? *Neurology.* 2010;74(12):965-969.

1248. Rossetti AO, Oddo M, Liaudet L, Kaplan PW. Predictors of awakening from postanoxic status epilepticus after therapeutic hypothermia. *Neurology.* 2009;72(8):744-749.

1249. Kaneko T, Kasaoka S, Miyauchi T, Fujita M, Oda Y, Tsuruta R, Maekawa T. Serum glial fibrillary acidic protein as a predictive biomarker of neurological outcome after cardiac arrest. *Resuscitation.* 2009;80(7):790-794.

1250. Oksanen T, Tiainen M, Skrifvars MB, Varpula T, Kuitunen A, Castren M, Pettila V. Predictive power

of serum NSE and OHCA score regarding 6-month neurologic outcome after out-of-hospital ventricular fibrillation and therapeutic hypothermia. *Resuscitation.* 2009;80(2):165-170.

1251. Rundgren M, Karlsson T, Nielsen N, Cronberg T, Johnsson P, Friberg H. Neuron specific enolase and S-100B as predictors of outcome after cardiac arrest and induced hypothermia. *Resuscitation.* 2009;80(7):784-789.

1252. Nagao K, Mukoyama T, Kikushima K, Watanabe K, Tachibana E, Iida K, Tani S, Watanabe I, Hayashi N, Kanmatsuse K. Resuscitative value of B-type natriuretic peptide in comatose survivors treated with hypothermia after out-of-hospital cardiac arrest due to cardiac causes. *Circ J.* 2007;71(3):370-376.

1253. Seder DB, Jarrah S. Therapeutic hypothermia for cardiac arrest: a practical approach. *Curr Treat Options Neurol.* 2009;11(2):137-149.

1254. Seder DB, Fraser GL, Robbins T, Libby L, Riker RR. The bispectral index and suppression ratio are very early predictors of neurological outcome during therapeutic hypothermia after cardiac arrest. *Intensive Care Med.* 2010;36(2):281-288.

1255. Rossetti AO, Oddo M, Logroscino G, Kaplan PW. Prognostication after cardiac arrest and hypothermia: a prospective study. *Ann Neurol.* 2010;67(3):301-307.

1256. Adrie C, Haouache H, Saleh M, Memain N, Laurent I, Thuong M, Darques L, Guerrini P, Monchi M. An underrecognized source of organ donors: patients with brain death after successfully resuscitated cardiac arrest. *Intensive Care Med.* 2008;34(1):132-137.

1257. Ali AA, Lim E, Thanikachalam M, Sudarshan C, White P, Parameshwar J, Dhital K, Large SR. Cardiac arrest in the organ donor does not negatively influence recipient survival after heart transplantation. *Eur J Cardiothorac Surg.* 2007;31(5):929-933.

1258. Matsumoto CS, Kaufman SS, Girlanda R, Little CM, Rekhtman Y, Raofi V, Laurin JM, Shetty K, Fennelly EM, Johnson LB, Fishbein TM. Utilization of donors who have suffered cardiopulmonary arrest and resuscitation in intestinal transplantation. *Transplantation.* 2008;86(7):941-946.