Part 4: Advanced Life Support

The topics reviewed by the International Liaison Committee on Resuscitation (ILCOR) Advanced Life Support Task Force are grouped as follows: (1) causes and prevention, (2) airway and ventilation, (3) drugs and fluids given during cardiac arrest, (4) techniques and devices to monitor and assist the circulation, (5) peri-arrest arrhythmias, (6) cardiac arrest in special circumstances, (7) postresuscitation care, and (8) prognostication. Defibrillation topics are discussed in Part 3.

The most important developments in advanced life support (ALS) since the last ILCOR review in 2000 include:

- The emergence of medical emergency teams (METs) as a means of preventing in-hospital cardiac arrest
- Additional clinical data on the use of vasopressin in cardiac arrest
- Several new devices to assist circulation during CPR
- The use of therapeutic hypothermia to improve neurologic outcome after ventricular fibrillation (VF) cardiac arrest
- The potential importance of glucose control after cardiac arrest

For many topics there were insufficient data with which to make firm treatment recommendations. The following interventions in particular need further research:

- The impact of METs on the incidence of cardiac arrest
- Outcome data to define the most appropriate advanced airway adjunct
- Evidence to identify the most effective vasopressor or if any vasopressor is better than placebo for cardiac arrest
- Randomized controlled trials on several new devices to assist circulation during CPR
- Randomized controlled trial data on several postresuscitation care therapies, such as control of ventilation, sedation, and glucose
- The precise role of, and method for implementing, therapeutic hypothermia: patient selection, external versus internal cooling, optimum target temperature, and duration of therapy

Causes and Prevention

Rescuers may be able to identify some noncardiac causes of arrest and tailor the sequence of attempted resuscitation. Most patients sustaining in-hospital cardiac arrest display signs of deterioration for several hours before the arrest. Early identification of these high-risk patients and the immediate arrival of a MET (also known as Rapid Response Team in the United States) to care for them may help prevent cardiac arrest. Hospitals in many countries are introducing early warning systems such as METs.

Identification of the Etiology of Cardiac Arrest

Consensus on Science

Very few data address the etiology of cardiac arrest directly. One prospective study (LOE 3)\(^1\) and one retrospective study (LOE 4)\(^2\) suggested that rescuers can identify some noncardiac causes of some arrests.

Treatment Recommendation

The physical circumstances, history, or precipitating events may enable the rescuer to determine a noncardiac cause of the cardiorespiratory arrest. Under these circumstances the rescuer should undertake interventions based on the presumed noncardiac etiology.

Impact of Medical Emergency Teams

The METs studied were composed generally of a doctor and nurse with critical-care training who were available at all times, responded immediately when called, and had specific, well-defined calling criteria. The MET system normally includes a strategy for educating ward staff about early recognition of critical illness. Variations of the MET system include critical-care outreach teams and patient-at-risk teams; all such variants use early warning scoring (EWS) systems to indicate patients who may be critically ill or at risk of cardiac arrest.

Consensus on Science

Two supportive before-and-after single-center studies (LOE 3)\(^3,4\) documented significant reductions in cardiac arrest rates and improved outcomes following cardiac arrest (eg, survival and length of stay in the intensive care unit [ICU]) after introduction of a MET. One cluster randomized controlled trial documented no difference in the composite primary outcome (cardiac arrest, unexpected death, unplanned ICU admission) between 12 hospitals in which a MET system was introduced and 11 hospitals that continued to function as normal (LOE 2).\(^5\) In this study, however, the MET system increased significantly the rate of emergency team calling. Two neutral studies documented a trend toward reduction in the rates of adult in-hospital cardiac arrest and overall mortality (LOE 3)\(^6\) and a reduction in unplanned admissions to the ICU (LOE 3).\(^7\) A before-and-after study documented reductions in cardiac arrest and death in children after...
introduction of a MET service into a children’s hospital,8 but these did not reach statistical significance.

Two before-and-after studies (LOE 3)9,10 showed reduced mortality among unplanned ICU admissions after the introduction of an EWS system. Another before-and-after in-hospital study (LOE 3)11 failed to show any significant reduction in the incidence of cardiac arrest or unplanned ICU admissions when an EWS system was used to identify and treat adults at risk of deterioration.

Treatment Recommendation
Introduction of a MET system for adult hospital in-patients should be considered, with special attention to details of implementation (eg, composition and availability of the team, calling criteria, education and awareness of hospital staff, and method of activation of the team). Introduction of an EWS system for adult in-hospital patients may be considered.

Airway and Ventilation

Consensus conference topics related to the management of airway and ventilation are categorized as (1) basic airway devices, (2) advanced airway devices, (3) confirmation of advanced airway placement, (4) strategies to secure advanced airways, and (5) strategies for ventilation.

Basic Airway Devices

Nasopharyngeal Airway

Consensus on Science
Despite frequent successful use of nasopharyngeal airways by anesthetists, there are no published data on the use of these airway adjuncts during CPR. One study in anesthetized patients showed that nurses inserting nasopharyngeal airways were no more likely than anesthesiologists to cause nasopharyngeal trauma (LOE 7).12 One LOE 5 study13 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. In one report insertion of a nasopharyngeal airway caused some airway bleeding in 30% of cases (LOE 7).14 Two case reports involve inadvertent intracranial placement of a nasopharyngeal airway in patients with basilar skull fractures (LOE 7).15,16

Treatment Recommendation
In the presence of a known or suspected basilar skull fracture, an oral airway is preferred, but if this is not possible and the airway is obstructed, gentle insertion of a nasopharyngeal airway may be lifesaving (ie, the benefits may far outweigh the risks).

Advanced Airway Devices

The tracheal tube has generally been considered the optimal method of managing the airway during cardiac arrest. There is evidence that without adequate training and experience, the incidence of complications, such as unrecognized esophageal intubation, is unacceptably high. Alternatives to the tracheal tube that have been studied during CPR include the bag-valve mask and advanced airway devices such as the laryngeal mask airway (LMA) and esophageal-tracheal combitube (Combitube). There are no data to support the routine use of any specific approach to airway management during cardiac arrest. The best technique depends on the precise circumstances of the cardiac arrest and the competence of the rescuer.

Tracheal Intubation Versus Ventilation With Bag-Valve Mask

Consensus on Science
There were no randomized trials that assessed the effect of airway and ventilation management with bag-valve mask (BVM) alone versus airway management that includes tracheal intubation in adult victims of cardiac arrest.

The only published randomized controlled trial identified (LOE 7)17 that compared tracheal intubation with BVM ventilation was performed in children who required airway management out-of-hospital. In this study there was no difference in survival-to-discharge rates, but it is unclear how applicable this pediatric study is to adult resuscitation. The study had some important limitations, including the provision of only 6 hours of additional training for intubation, limited opportunity to perform intubations, and short transport times. Two studies compared outcomes from out-of-hospital cardiac arrest in adults treated by either emergency medical technicians or paramedics (LOE 318; LOE 419). The skills provided by the paramedics, including intubation and intravenous (IV) cannulation18,19 and drug administration19, made no difference in survival to hospital discharge.

The reported incidence of unrecognized misplaced tracheal tube is 6% (LOE 5)20–22 to 14% (LOE 5).23 An additional problem common to any advanced airway is that intubation attempts generally require interruptions in chest compressions.

Treatment Recommendation
There is insufficient evidence to support or refute the use of any specific technique to maintain an airway and provide ventilation in adults with cardiopulmonary arrest. Either bag-valve mask alone or in combination with tracheal intubation is acceptable for ventilation during CPR by prehospital providers. Rescuers must weigh the risks and benefits of intubation versus the need to provide effective chest compressions. The intubation attempt will require interruption of chest compressions, but once an advanced airway is in place, ventilation will not require interruption (or even pausing) of chest compressions. To avoid substantial interruptions in chest compressions, providers may defer an intubation attempt until return of spontaneous circulation (ROSC). To ensure competence, healthcare systems that utilize advanced airways should address factors such as adequacy of training and experience and quality assurance. Providers must confirm tube placement and ensure that the tube is adequately secured (see below).

Tracheal Intubation Versus the Combitube/Laryngeal Mask Airway

Consensus on Science
In some communities tracheal intubation is not permitted or practitioners have inadequate opportunity to maintain their
intubation skills. Under these circumstances several studies indicate a high incidence of unrecognized esophageal intubation misplacement and unrecognized dislodgment. Prolonged attempts at tracheal intubation are harmful: the cessation of chest compressions during this time will compromise coronary and cerebral perfusion. Several alternative airway devices have been considered or studied for airway management during CPR; the Combitube and the LMA are the only alternative devices to be studied specifically during CPR. None of the studies of the LMA and Combitube during CPR has been adequately powered to study survival as a primary end point; instead, most researchers have studied insertion and ventilation success rates.

**Combitube.** Five randomized controlled trials conducted on adult patients undergoing resuscitation (LOE 2)\(^24–28\) and 3 additional randomized controlled trials involving patients undergoing anesthesia (LOE 7)\(^29–31\) documented successful Combitube insertion and acceptable ventilation when compared with tracheal intubation. Benefits were documented for both experienced and inexperienced healthcare professionals with patients in hospital as well as in out-of-hospital settings.

Six additional studies support the use of the Combitube during CPR (LOE 3\(^2; \)LOE 4\(^3\); LOE 5\(^34–37\)). Successful ventilation was achieved with the Combitube during CPR in 78.9% to 98% of patients (LOE 2\(^26,27,38\); LOE 3\(^32\); LOE 4\(^33\); LOE 5\(^34,35\)).

**LMA.** Seven randomized controlled trials involving anesthetized patients (LOE 7)\(^39–45\) that compared the LMA with tracheal intubation and another 7 randomized control trials (LOE 7)\(^46–52\) that compared the LMA with other airways or ventilation techniques were reviewed. These studies suggested that experienced and inexperienced personnel can insert the device or successfully ventilate the patient’s lungs in a high proportion of cases compared with the tracheal tube or other airway management and ventilation devices.

One randomized crossover study (LOE 2)\(^38\) in adults undergoing resuscitation in the prehospital setting compared the Combitube with the LMA and showed that LMA insertion and successful ventilation could be achieved in a high proportion of patients.

Nonrandomized studies (LOE 3\(^53–55\); LOE 4\(^31\); LOE 5\(^56–61\)) have also shown high insertion success rates by inexperienced providers both in and out of the hospital. Complication rates in nonrandomized studies (LOE 3\(^58\); LOE 4\(^33\); LOE 5\(^56\)) have been extremely low.

Successful ventilation was achieved with the LMA during CPR in 71.5% to 98% of cases (LOE 2\(^38\); LOE 3\(^54\); LOE 4\(^33\); LOE 5\(^56,58–60\)).

**Additional airway devices.** Use of the laryngeal tube during CPR was described in just a few cases included in 2 LOE 5 studies\(^62,63\) and 1 LOE 8 paper.\(^64\) There were no studies comparing the laryngeal tube with the tracheal tube in any patient population, although 4 randomized controlled trials compared the laryngeal tube favorably with the LMA in anesthetized patients (LOE 7).\(^65–68\)

Other devices include the ProSeal LMA, intubating LMA, airway management device, and pharyngeal airway express.

There are no published data on the use of these devices during CPR.

**Treatment Recommendation**

It is acceptable for healthcare professionals to use the Combitube or the LMA as alternatives to the tracheal tube for airway management in cardiac arrest.

**Confirming Advanced Airway Placement**

Unrecognized esophageal intubation is the most serious complication of attempted tracheal intubation. Routine confirmation of correct placement of the tracheal tube should reduce this risk. There are inadequate data to identify the optimal method of confirming tube placement during cardiac arrest. All devices should be considered adjuncts to other confirmatory techniques. There is no data quantifying the capability of these devices to monitor tube position after initial placement.

**Exhaled CO\(_2\)**\(^W47,W50\)

**Consensus on Science**

Evidence from 1 meta-analysis in adults (LOE 1),\(^69\) 1 prospective controlled cohort study (LOE 3),\(^70\) case series (LOE 5),\(^71–79\) and animal models (LOE 6)\(^80,81\) indicate that exhaled CO\(_2\) detectors (waveform, colorimetry, or digital) may be useful as adjuncts to confirm tracheal tube placement during cardiac arrest. Of the 14 references included in this statement, 10 referred to colorimetric assessment, \(^69,71–76,79,81,82\) 4 to digital, \(^69–71,77\) and 4 to waveform.\(^69,70,78,80\) There are insufficient data from cardiac arrests to allow any firm recommendations for any particular technique. The range of results obtained from the reviewed papers is as follows:

- Percentage of tracheal placements detected: 33% to 100%
- Percentage of esophageal placements detected: 97% to 100%
- Probability of tracheal placement if test result is positive (exhaled CO\(_2\) is detected): 100%
- Probability of esophageal placement if test result is negative (exhaled CO\(_2\) is not detected): 20% to 100%

One adult case series (LOE 5)\(^82\) shows that in the presence of a perfusing rhythm, exhaled CO\(_2\) detection can be used to monitor tracheal tube position during transport.

No studies directly evaluated exhaled CO\(_2\) to confirm placement of the Combitube or LMA during cardiac arrest in humans.

**Treatment Recommendation**

Healthcare providers should recognize that evaluation of exhaled CO\(_2\) is not infallible for confirming correct placement of a tracheal tube, particularly in patients in cardiac arrest. Exhaled CO\(_2\) should be considered as just one of several independent methods for confirming tracheal tube placement. Continuous capnometry may be useful for early detection of tracheal tube dislodgement during transport.

**Esophageal Detector Device**\(^W48A,W51A,W51B\)

**Consensus on Science**

Eight studies of at least fair quality evaluated the accuracy of the syringe or self-inflating bulb type of esophageal detector
device (EDD) (LOE 321,77,83; LOE 584; LOE 7119–121) for noncardiac arrest setting85–88), but many suffer from few subjects and lack of a control group.

The EDD was highly sensitive for detection of misplaced tracheal tubes in the esophagus (LOE 584; LOE 785–88). In 2 studies (LOE 3)77,83 of patients in cardiac arrest, the EDD had poor sensitivity for confirming tracheal placement of a tracheal tube. In these studies up to 30% of correctly placed tubes may have been removed because the EDD suggested esophageal placement of a tube (LOE 3).78

The EDD had poor sensitivity and specificity in the operating room in 20 children <1 year of age (LOE 2).89

Treatment Recommendation
The use of the EDD should be considered as just one of several independent methods for tracheal tube confirmation.

Strategies to Secure Advanced Airways
Accidental dislodgment of a tracheal tube can occur at any time but may be more likely during resuscitation and during transport. The most effective method for securing the tracheal tube has yet to be determined.

Securing the Tracheal Tube84

Consensus on Science
There are no studies comparing different strategies for securing the tracheal tube during CPR. Two studies in the intensive care setting (LOE 7)90,91 indicated that commercial devices for securing tracheal tubes, backboards, cervical collars, and other strategies provide an equivalent method for preventing accidental tube displacement when compared with the traditional method of securing the tube with tape.

Treatment Recommendation
Either commercially made tracheal tube holders or conventional tapes or ties should be used to secure the tracheal tube.

Strategies for Ventilation
Very few studies address specific aspects of ventilation during ALS. Three recent observational studies report the ventilation rates delivered by healthcare personnel during cardiac arrest (LOE 5)92–94: 2 studies92,93 show ventilation rates that are much higher than those recommended by the 2000 International Guidelines for CPR and ECC. Automatic transport ventilators (ATVs) might enable delivery of appropriate ventilatory rates, but no data demonstrate clear benefit over bag-valve mask devices.

Disconnection From Ventilation During Cardiac Arrest84

Consensus on Science
Eighteen LOE 5 articles involving 31 cases95–112 reported unexpected return of circulation (and in some cases prolonged neurologically intact survival) after cessation of resuscitation attempts. One case series suggested that this occurred in patients with obstructive airway disease (LOE 5).100 Four studies reported unexpected return of circulation in 6 cases in which resuscitation had ceased and ventilation was shown on repeated occasions (or was highly likely) to result in gas trapping and consequent hemodynamic compromise (LOE 5).100–102 The authors of all these studies suggested that a period of disconnection from ventilation during resuscitation from PEA may be useful to exclude gas trapping.

Automatic Transport Ventilators

Consensus on Science
Research of simulated cardiac arrest with manikins showed a significant decrease in gastric inflation with manually triggered, flow-limited, oxygen-powered resuscitators and masks compared with bag-valve masks (LOE 6).113 Anesthetized patients with unprotected airways but not in cardiac arrest who were ventilated by firefighters had less gastric inflation with manually triggered, flow-limited, oxygen-powered resuscitators and masks than with bag-valve masks (LOE 5).114 A prospective cohort study of intubated patients, most of whom were in cardiac arrest, in an out-of-hospital urban setting showed no significant difference in arterial blood gas values between those ventilated with an ATV and those ventilated with a bag-valve device (LOE 4).115 Two laboratory studies showed that ATVs may provide safe and effective management of mask ventilation during CPR of adult patients with an unprotected airway (LOE 6).116,117

Treatment Recommendation
The use of a manually triggered, flow-limited resuscitator or an ATV by professional healthcare providers is reasonable for ventilation of adults with an advanced airway in place during cardiac arrest. The use of ATVs for adults without an advanced airway in place is discussed in Part 2: “Adult Basic Life Support.”

Drugs and Fluids for Cardiac Arrest

Questions related to the use of drugs during cardiac arrest that were discussed during the 2005 Consensus Conference are categorized as (1) vasopressors, (2) antiarrhythmics, (3) other drugs and fluids, and (4) alternative routes of delivery.

Vasopressors
Despite the widespread use of epinephrine/adrenaline during resuscitation and several studies involving vasopressin, there is no placebo-controlled study that shows that the routine use of any vasopressor at any stage during human cardiac arrest increases survival to hospital discharge. Current evidence is insufficient to support or refute the routine use of any particular drug or sequence of drugs. Despite the lack of human data, it is reasonable to continue to use vasopressors on a routine basis.

Epinephrine and Vasopressin
Treatment Recommendation
Despite the absence of placebo-controlled trials, epinephrine has been the standard vasopressor in cardiac arrest. There is insufficient evidence to support or refute the use of vasopressin as an alternative to, or in combination with, epinephrine in any cardiac arrest rhythm.

Alpha-methyl Norepinephrine

Consensus on Science
Preliminary animal studies (LOE 6)\(^{125-127}\) have suggested some potential short-term benefits with the use of alpha-methyl norepinephrine in animal models of VF. At this stage no published human studies have been identified.

Endothelin

Consensus on Science
Evidence from 5 studies of cardiac arrest in animals (LOE 6)\(^{128-132}\) documented consistent improvement in coronary perfusion pressure with endothelin-1, but this did not translate into improved myocardial blood flow. No published human studies were available.

Antiarrhythmics

There is no evidence that giving any antiarrhythmic drug routinely during human cardiac arrest increases rate of survival to hospital discharge. In comparison with placebo and lidocaine, the use of amiodarone in shock-refractory VF improves the short-term outcome of survival to hospital admission. Despite the lack of human long-term outcome data, it is reasonable to continue to use antiarrhythmic drugs on a routine basis.

Amiodarone

Consensus on Science
In 2 blinded randomized controlled clinical trials in adults (LOE 1)\(^{133,134}\), administration of amiodarone (300 mg/\(133\); 5 mg/kg/\(134\)) by paramedics to patients with refractory VF/pulseless ventricular tachycardia (VT) in the out-of-hospital setting improved survival to hospital admission when compared with administration of placebo\(^{133}\) or lidocaine (1.5 mg/kg).\(^{134}\) Additional studies (LOE 7)\(^{135-139}\) document consistent improvement in defibrillation response when amiodarone is given to humans or animals with VF or hemodynamically unstable VT.

Treatment Recommendation
In light of the short-term survival benefits, amiodarone should be considered for refractory VF/VT.

Other Drugs and Fluids

There is no evidence that routinely giving other drugs (eg, buffers, aminophylline, atropine, calcium, magnesium) during human cardiac arrest increases survival to hospital discharge. There are several reports on the successful use of fibrinolytics during cardiac arrest, particularly when the arrest was caused by pulmonary embolism.

Aminophylline

Consensus on Science
One case series (LOE 5)\(^{140}\) and 3 small randomized trials (LOE 2)\(^{141-143}\) indicate that aminophylline does not increase ROSC when given for bradyasystolic cardiac arrest. No studies have shown an effect of aminophylline on rates of survival to hospital discharge. There is no evidence of harm from giving aminophylline in bradyasystolic cardiac arrest (LOE 2\(^{144-145}\); LOE 5\(^{140}\)).

Atropine

Consensus on Science
Five prospective controlled nonrandomized cohort studies in adults (LOE 3)\(^{19,144-147}\) and 1 LOE 4 study\(^{148}\) showed that treatment with atropine was not associated with any consistent benefits after in-hospital or out-of-hospital cardiac arrest.

Buffers

Consensus on Science
There were no published LOE 1, 2, or 3 studies on the use of sodium bicarbonate during CPR. One LOE 2 study\(^{149}\) showed no advantage of Tribonate over placebo (neutral), and 5 retrospective analyses of uncontrolled clinical use of sodium bicarbonate were inconclusive (LOE 4).\(^{150-154}\) One LOE 4 study\(^{155}\) suggested that emergency medical services (EMS) systems using sodium bicarbonate earlier and more frequently had significantly higher rates of ROSC and hospital discharge and better long-term neurologic outcome.

Results of animal studies are conflicting and inconclusive. Sodium bicarbonate was effective for treating the cardiovascular toxicity (hypotension, cardiac arrhythmias) caused by tricyclic antidepressants and other fast sodium channel blockers (see “Drug Overdose and Poisoning,” below). Only 1 LOE 5 publication\(^{156}\) reported the successful treatment of VF cardiac arrest caused by tricyclic poisoning using sodium bicarbonate.

Treatment Recommendation
Giving sodium bicarbonate routinely during cardiac arrest and CPR (especially in out-of-hospital cardiac arrest) or after ROSC is not recommended. Sodium bicarbonate may be considered for life-threatening hyperkalemia or cardiac arrest associated with hyperkalemia, preexisting metabolic acidosis, or tricyclic antidepressant overdose.

Magnesium

Consensus on Science
Studies in adults in- and out-of-hospital (LOE \(^{2157-160}\); LOE 3\(^{161}\); LOE 7\(^{162}\)) and animal studies (LOE 6)\(^{163-166}\) indicated...
no increase in the rate of ROSC when magnesium was given during CPR. Results from 1 small case series of 5 patients (LOE 5)\textsuperscript{167} indicated benefit from giving magnesium in shock-resistant and epinephrine/lidocaine-resistant VF.

**Treatment Recommendation**
Magnesium should be given for hypomagnesemia and torsades de pointes, but there is insufficient data to recommend for or against its routine use in cardiac arrest.

**Fibrinolysis During CPR**\textsuperscript{W105} W96A, W96B, W96C

**Consensus on Science**
Adults have been successfully resuscitated following administration of fibrinolytics after initial failure of standard CPR techniques, particularly when the condition leading to the arrest was acute pulmonary embolism or other presumed cardiac cause (LOE 3\textsuperscript{168}; LOE 4\textsuperscript{169–171}; LOE 5\textsuperscript{172–176}). One large clinical trial (LOE 2)\textsuperscript{177} failed to show any significant treatment effect from administration of fibrinolytics to out-of-hospital patients with undifferentiated pulseless electrical activity (PEA) cardiac arrest unresponsive to initial interventions. Four clinical studies (LOE 3\textsuperscript{168}; LOE 4\textsuperscript{169–171}) and 5 case series (LOE 5)\textsuperscript{172–176} indicated that there is no increase in bleeding complications with fibrinolysis during CPR for nontraumatic cardiac arrest. Two animal studies (LOE 6)\textsuperscript{178,179} showed positive effects on cerebral reperfusion with fibrinolysis during CPR.

**Treatment Recommendation**
Fibrinolysis should be considered in adult patients with cardiac arrest with proven or suspected pulmonary embolism. There is insufficient data to support or refute the routine use of fibrinolysis in cardiac arrest from other causes.

**Fluids**\textsuperscript{W105}

**Consensus on Science**
There were no published human studies of routine fluid use compared with no fluids during normovolemic cardiac arrest. Four animal studies (LOE 6)\textsuperscript{180–183} of experimental VF and 6 other studies (LOE 4\textsuperscript{184}; LOE 5\textsuperscript{187–189}; LOE 7\textsuperscript{190,191}) documented that IO access is safe and effective for fluid resuscitation, drug delivery, and laboratory evaluation, and is attainable in all age groups.

**Drugs Given via the Tracheal Tube**\textsuperscript{W32, W108}

**Consensus on Science**
Atropine and epinephrine. In 1 historic nonrandomized cohort study (LOE 4)\textsuperscript{192} in adults, the rate of ROSC (27% vs 15%, \(P=0.01\)) and rate of survival to hospital admission (20% vs 9%, \(P=0.01\)) was significantly higher in the IV drug (atropine and adrenaline) group compared with the tracheal drug group. No patient who received tracheal drugs survived to hospital discharge compared with 5% of those who received IV drugs.

Epinephrine. During CPR the equipotent epinephrine dose given endobronchially was approximately 3 to 10 times higher than the IV dose (LOE 5\textsuperscript{193}; LOE 6\textsuperscript{194}). Endobronchial epinephrine (2 to 3 mg) diluted in 5 to 10 mL 0.9% NaCl achieved therapeutic plasma concentrations (LOE 5).\textsuperscript{196} Endobronchial epinephrine achieved higher plasma concentrations when diluted with water rather than 0.9% saline (LOE 6).\textsuperscript{195}

During CPR lung perfusion is only 10% to 30% of the normal value, resulting in a pulmonary epinephrine depot. When cardiac output is restored after a high dose of endobronchial epinephrine, prolonged reabsorption of epinephrine from the lungs into the pulmonary circulation may occur (LOE 6),\textsuperscript{194} causing arterial hypertension, malignant arrhythmias, and recurrence of VF.

Lidocaine. All studies were performed in hemodynamically stable (nonarrest) patients. Therapeutic plasma concentrations of lidocaine were achieved in these patients (LOE 5)\textsuperscript{196,197} after tracheal tube instillation but in only 40% of similar patients after instillation via an LMA (LOE 5).\textsuperscript{197,198} In anesthetized healthy adults, endobronchial delivery delayed the increase in lidocaine plasma concentrations (LOE 2).\textsuperscript{199} In some (LOE 5),\textsuperscript{198,200} but not all of these studies (LOE 2\textsuperscript{199}; LOE 5\textsuperscript{196}), deep endobronchial delivery of lidocaine via a catheter achieved lower blood concentrations than when lidocaine was injected directly into the tracheal tube. Endobronchial lidocaine achieved higher plasma concentrations and caused less reduction in PaO\textsubscript{2} when diluted with water instead of 0.9% sodium chloride (LOE 5).\textsuperscript{201}

Vasopressin. Endobronchial vasopressin was more effective in increasing diastolic blood pressure than equivalent doses of endobronchial epinephrine (LOE 6).\textsuperscript{202} In a small animal study, endobronchial vasopressin was more effective than placebo in increasing coronary perfusion pressure during CPR and improving survival rates (LOE 6).\textsuperscript{203}

**Treatment Recommendation**
If IV access is delayed or cannot be achieved, IO access should be considered. Give drugs via the tracheal tube if intravascular (IV or IO) access is delayed or cannot be achieved. There are no benefits from endobronchial injection compared with injection of the drug directly into the tracheal tube. Dilution with water instead of 0.9% saline may achieve better drug absorption.

**Monitoring and Assisting the Circulation**
Specific questions related to the use of techniques and devices to (1) monitor the performance of CPR during cardiac arrest or (2) assist the circulation (alternatives to standard...
CPR) during cardiac arrest were discussed during the 2005 Consensus Conference. They are listed below.

Monitoring CPR Performance
End-tidal CO₂ can be used as an indicator of ROSC. Arterial blood gas analysis may help to guide therapy. Measurement of coronary artery perfusion might be helpful, but because it is technically difficult to measure, it is not available routinely.

End-Tidal CO₂ Monitoring to Guide Therapy During Cardiac Arrest

Consensus on Science
No studies have addressed this topic directly. The studies published over the past 5 years were consistent with the older literature, which showed that higher end-tidal CO₂ values during CPR correlate with ROSC (LOE 5). 204–207

In experimental models, end-tidal CO₂ concentration during ongoing CPR correlated with cardiac output, coronary perfusion pressure, and successful resuscitation from cardiac arrest (LOE 6). 208–214 Eight case series have shown that patients who were successfully resuscitated from cardiac arrest had significantly higher end-tidal CO₂ levels than patients who could not be resuscitated (LOE 5). 215–217 Capnometry can also be used as an early indicator of ROSC (LOE 5). 218, 219; LOE 6. 220

In case series totaling 744 patients, intubated adults in cardiac arrest receiving CPR who had a maximum end-tidal CO₂ of <10 mm Hg had a poor prognosis even if CPR was optimal (LOE 5). 204, 205, 217, 221–223 This prognostic indicator may be unreliable immediately after starting CPR because 2 studies (LOE 5) 217, 223 showed no difference in ROSC and survival in those with an initial end-tidal CO₂ of <10 mm Hg. Two additional studies (LOE 5) 221, 222 reported that 5 patients achieved ROSC despite an initial end-tidal CO₂ of <10 mm Hg (1 patient survived).

Treatment Recommendation
End-tidal CO₂ monitoring is a safe and effective noninvasive indicator of cardiac output during CPR and may be an early indicator of ROSC in intubated patients.

Arterial Blood Gas Monitoring During Cardiac Arrest

Consensus on Science
There was evidence from 1 LOE 5 study 224 and 10 LOE 7 studies 225–234 that arterial blood gas values are an inaccurate indicator of the magnitude of tissue acidosis during cardiac arrest and CPR in both the in-hospital and out-of-hospital settings. The same studies indicate that both arterial and mixed venous blood gases are required to establish the degree of acidosis.

Arterial blood gas analysis alone can disclose the degree of hypoxemia (LOE 5) 235; LOE 6. 236, 237; LOE 7. 225, 227, 231, 238–240.

Arterial blood gas analysis can also highlight the extent of metabolic acidosis (LOE 5). 241; LOE 6. 246; LOE 7. 225, 227, 230, 231, 238, 239.

Arterial CO₂ is an indicator of adequacy of ventilation during CPR (LOE 5). 242; LOE 5. 235; LOE 6. 236; LOE 7. 292, 227, 239, 243. If ventilation is constant, an increase in Paco₂ is a potential marker of improved perfusion during CPR (LOE 5). 244; LOE 6. 209, 245; LOE 7. 246).

Treatment Recommendation
Arterial blood gas monitoring during cardiac arrest enables estimation of the degree of hypoxemia and the adequacy of ventilation during CPR but is not a reliable indicator of the extent of tissue acidosis.

Coronary Perfusion Pressure to Guide Resuscitation

Consensus on Science
Coronary perfusion pressure (CPP) (aortic relaxation [diastolic] minus the right atrial relaxation phase blood pressure during CPR) correlated with both myocardial blood flow and ROSC (LOE 3). 247, 248. A value ≥15 mm Hg is predictive of ROSC. Increased CPP correlated with improved 24-hour survival in animal studies (LOE 6) 249 and is associated with improved myocardial blood flow and ROSC in studies of epinephrine, vasopressin, and angiotensin II (LOE 6). 249–251

Treatment Recommendation
Coronary perfusion pressure can guide therapy during cardiac arrest. In an intensive care facility the availability of direct arterial and central venous pressure monitoring makes calculation of CPP potentially useful. Outside the intensive care facility the technical difficulties of invasive monitoring of central arterial and venous pressure make it difficult to calculate CPP routinely during cardiac arrest.

Techniques and Devices to Assist Circulation During Cardiac Arrest

Several techniques or adjuncts to standard CPR have been investigated, and the relevant data was reviewed extensively. One multicenter human study (LOE 2) 94 showed poor quality and frequent interruptions in chest compressions delivered during prehospital CPR. In the hands of some groups, novel techniques and adjuncts may be better than standard CPR. The success of any technique depends on the education and training of the rescuers or the resources available (including personnel). Because information about these techniques and devices is often limited, conflicting, or supportive only for short-term outcomes, no recommendations can be made to support or refute their routine use.

Transcutaneous Pacing for Asystole

Consensus on Science
Three randomized controlled trials (LOE 2) 252–254 and additional studies (LOE 3) 255–259. LOE 6. 260; LOE 7. 261 indicate no improvement in the rate of admission to hospital or survival to hospital discharge when pacing was attempted by paramedics or physicians in asystolic patients in the prehospital or the hospital (emergency department) setting.

Treatment Recommendation
Pacing is not recommended for patients in asystolic cardiac arrest.

CPR Prompt Devices

Consensus on Science
Two studies in adults (LOE 5) 293, 294 show that unprompted CPR was frequently of poor quality in the out-of-hospital and...
in-hospital settings. One study in adults (LOE 3),262 one study in children (LOE 3),263 and animal (LOE 6)264,265 and manikin studies (LOE 6)266–272 show consistent improvement in end tidal CO₂ or quality of CPR performed, or both, when feedback was provided with a variety of formats to guide CPR. In one manikin study (LOE 6),270 95% of rescuers reported discomfort in the heels of their hands and wrists when using a CPR prompt applied between their hands and the victim’s chest, but no long-term injuries were noted. A crossover study of paramedic students previously trained in CPR showed that audio feedback significantly improved the proportion of correct inflations, correct compression depth, and duration of compressions (LOE 6).266 A similar study of nursing students showed improved inflations and depth of compression (LOE 6).272

Treatment Recommendation
CPR prompt devices may improve CPR performance. See also Part 8: “Interdisciplinary Topics.”

Interposed Abdominal Compression CPR

Consensus on Science
Two randomized controlled trials (LOE 1273; LOE 2274) of in-hospital cardiac arrests showed improved ROSC and survival of event when interposed abdominal compression CPR (IAC-CPR) performed by rescuers trained in the technique was compared with standard CPR. One of these studies (LOE 1)273 also reported improved rates of survival to hospital discharge. This data and that from a crossover study (LOE 3)275 were combined in 2 meta-analyses (LOE 1).276,277 One randomized controlled trial (LOE 2)278 of out-of-hospital cardiac arrests did not show any survival advantage when IAC-CPR was undertaken by rescuers trained in the technique compared with standard CPR. Some harm was reported in 1 child (LOE 5).279 Although only a small proportion of patients had postmortem examinations, there was no evidence of significant harm.

High-Frequency CPR

Consensus on Science
One clinical trial of 9 patients (LOE 4)280 showed that high-frequency CPR (120 compressions per minute) improved hemodynamics over standard CPR. Three laboratory studies (LOE 6)281–283 showed that high-frequency CPR (120 to 150 compressions per minute) improved hemodynamics without increasing trauma. In one additional laboratory study (LOE 6),284 high-frequency CPR did not improve hemodynamics over standard CPR.

Active Compression-Decompression CPR

Consensus on Science
Despite initial promising studies suggesting short-term survival benefits (LOE 2)285,286 and even intact neurologic survival (LOE 1),287 a Cochrane meta-analysis (LOE 1)288 of 10 trials (involving 4162 patients) compared active compression-decompression (ACD) CPR with standard CPR in the out-of-hospital setting and did not show a significant increase in rates of immediate survival or hospital discharge. One meta-analysis (LOE 1)288 of 2 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. Although one small study (LOE 4)289 showed harm with an increased incidence of sternal fractures in the ACD-CPR group when compared with standard CPR alone, the large meta-analysis288 did not find any increase in complications when ACD-CPR was compared with standard CPR.

Load Distributing Band CPR

Consensus on Science
The load distributing band (LDB) is a circumferential chest compression device composed of a pneumatically actuated constricting band and backboard. A case control study of 162 adults (LOE 4)290 documented improvement in survival to the emergency department when LDB-CPR was administered by adequately trained rescue personnel to patients with cardiac arrest in the prehospital setting. The use of LDB-CPR improved hemodynamics in 1 in-hospital study of end-stage patients (LOE 3)291 and 2 laboratory studies (LOE 6).292,293

Mechanical (Piston) CPR

Consensus on Science
One prospective randomized study and 2 prospective randomized crossover studies in adults (LOE 2)294–296 indicated improvement in end-tidal CO₂ and mean arterial pressure when automatic mechanical (piston) CPR was undertaken by medical and paramedical personnel in the hospital or prehospital setting. In several studies in animals (LOE 6)297–300 mechanical (piston) CPR improved end-tidal CO₂, cardiac output, cerebral blood flow, mean arterial pressure, and short-term neurologic outcome.

Lund University Cardiac Arrest System CPR

Consensus on Science
The Lund University Cardiac Arrest System (LUCAS) is a gas-driven sternal compression device that incorporates a suction cup for active decompression. There were no published randomized human studies comparing LUCAS-CPR with standard CPR. A single study of pigs with VF showed that LUCAS-CPR improved hemodynamic and short-term survival rates compared with standard CPR (LOE 6).299 The LUCAS was also used in 20 patients, but incomplete outcome data was reported (LOE 6).299

Phased Thoracic-Abdominal Compression-Decompression CPR

Consensus on Science
Phased thoracic-abdominal compression-decompression (PTACD) CPR combines the concepts of IAC-CPR and ACD-CPR. One modeling study (LOE 7)301 and one laboratory study (LOE 6)302 showed that PTACD-CPR improved hemodynamics. One clinical, randomized study in adults (LOE 2)301 and additional experimental studies (LOE 6)303,304 documented no improvement in survival rates for patients with cardiac arrest when PTACD-CPR was used for assistance of circulation during ALS in the prehospital or in-hospital setting. PTACD-CPR did not substantially delay
starting CPR and had no significant known disadvantages nor caused harm when used correctly.

**Minimally Invasive Direct Cardiac Massage**

**Consensus on Science**

Minimally invasive direct cardiac massage (MIDCM) involves insertion of a plunger-like device through a small incision in the chest wall to enable direct compression of the heart. MIDCM improved ROSC and coronary perfusion pressure compared with standard CPR in one laboratory study (LOE 6) and generated systemic blood flow and myocardial and cerebral flow similar to that produced with open-chest cardiac massage in 2 laboratory studies (LOE 6). The MIDCM device was placed in patients in the field and generated improved blood pressure over standard CPR in one clinical study (LOE 3). But in this study, use of the MIDCM device caused cardiac rupture in 1 patient. MIDCM increased the defibrillation threshold for standard external defibrillation but reduced the defibrillation threshold if the MIDCM device was used as one of the electrodes in one laboratory study (LOE 6).

**Impedance Threshold Device**

**Consensus on Science**

The impedance threshold device (ITD) is a valve that limits air entry into the lungs during chest recoil between chest compressions. It is designed to reduce intrathoracic pressure and enhance venous return to the heart. A randomized study of 230 adults documented increased admissions to the ICU and 24-hour survival rates (LOE 2) when an ITD was used with standard CPR in patients with cardiac arrest (PEA only) in the prehospital setting. The addition of the ITD improved the hemodynamics during standard CPR in 5 laboratory studies (LOE 6) and 1 clinical study (LOE 2). A randomized study of 400 adults showed increased ROSC and 24-hour survival rates (LOE 1) when an ITD was used with ACD-CPR in patients with cardiac arrest in the prehospital setting. The addition of the ITD improved the hemodynamics during ACD-CPR in 1 laboratory study (LOE 6) and 1 clinical study (LOE 2). One laboratory study failed to show an improvement in hemodynamics with the use of the ITD during ACD-CPR (LOE 6). Compared with standard CPR, ROSC and 24-hour survival were increased when the ITD was used with ACD in a randomized study of 210 prehospital patients (LOE 1) and hemodynamics were improved in 2 laboratory studies (LOE 6).

**Extracorporeal Techniques and Invasive Perfusion Devices**

**Consensus on Science**

The only adult data comes from 3 case series (LOE 5). One of these indicated that extracorporeal CPR (ECPR) was more successful in postcardiotomy patients than those in cardiac arrest from other causes. The other 2 studies suggested that ECPR is not beneficial for patients presenting to the emergency department in cardiac arrest with the exception of cardiac arrest associated with hypothermia or drug intoxication.

**Open-Chest CPR**

**Consensus on Science**

No prospective randomized studies of open-chest CPR for resuscitation have been published. Four relevant human studies were reviewed, 2 after cardiac surgery (LOE 4), and 2 after out-of-hospital cardiac arrest (LOE 4). The observed benefits of open-chest cardiac massage included improved coronary perfusion pressure and increased ROSC. Evidence from animal studies (LOE 6) indicates that open-chest CPR produces greater survival rates, perfusion pressures, and organ blood flow than closed-chest CPR.

**Treatment Recommendation**

Open-chest CPR should be considered for patients with cardiac arrest in the early postoperative phase after cardiothoracic surgery or when the chest or abdomen is already open.

**Periarrest Arrhythmias**

**Narrow-Complex Tachycardia**

There are 4 options for the treatment of narrow-complex tachycardia in the periarrest setting: electrical conversion, physical maneuvers, pharmacologic 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.

**Drug Therapy for Atrial Fibrillation**

**Consensus on Science**

One randomized controlled trial in adults and 3 additional studies documented improvement in rate control when magnesium (LOE 3), diltiazem (LOE 2), or β-blockers (LOE 2) were given by physicians, nurses, and paramedics in both the out-of-hospital (LOE 3) and hospital settings to patients with atrial fibrillation with a rapid ventricular response. Two randomized controlled trials in adults (LOE 2) and additional studies documented improvement in rhythm when ibutilide, digoxin, clonidine, magnesium, or amiodarone were given by physicians or nurses to patients with atrial fibrillation in the hospital setting.

**Treatment Recommendation**

Magnesium, diltiazem, or β-blockers may be used for rate control in patients with atrial fibrillation with a rapid ventricular response. Amiodarone, ibutilide, propafenone, flecainide, digoxin, clonidine, or magnesium may be used for rhythm control in patients with atrial fibrillation.

**Drug Therapy for Regular Narrow-Complex Tachycardia**

**Consensus on Science**

In one randomized study in the ED, 41 of 148 (28%) patients with paroxysmal supraventricular tachycardia (PSVT) were converted to sinus rhythm with carotid sinus massage or a Valsalva maneuver (LOE 2). One study (LOE 4) showed that stable paroxysmal supraventricular tachycardia (PSVT)
in younger patients may be treated first with vagal maneuvers but will be unsuccessful 80% of the time.

Five prospective controlled nonrandomized cohort studies (LOE 2)\(^3\)-\(^5\); LOE 3\(^5\)-\(^3\)\(^8\) indicated that adenosine is safe and effective in converting PSVT in the hospital and out-of-hospital settings. Two randomized clinical trials (LOE 2)\(^3\)-\(^5\)\(^6\) documented no statistical significance in PSVT conversion rate between adenosine and calcium channel blockers, but the effect of adenosine is more rapid, and side effects are less severe than with verapamil. One randomized clinical trial in the ED (LOE 2)\(^3\)\(^0\) documented no difference in the PSVT conversion rate between infusions of verapamil (99%) and diltiazem (96%). One randomized clinical trial in the ED (LOE 1)\(^3\)\(^1\) documented significantly better PSVT conversion rates with diltiazem (100%) in comparison with esmolol (25%). One electrophysiologic study (LOE 6)\(^3\)\(^2\) documented that amiodarone achieved 100% efficacy in the inhibition of induced sustained reentrant PSVT.

**Treatment Recommendation**

Stable narrow-complex tachycardia (excluding atrial fibrillation or atrial flutter) should be treated first with vagal maneuvers (avoiding carotid sinus massage in the elderly); these will terminate about 20% of PSVTs. If vagal maneuvers are not used or if they fail, give adenosine.

A calcium channel blocker (verapamil or diltiazem) infusion or amiodarone may be used as a second-line treatment for the 10% to 15% of patients who do not respond to adenosine. In unstable PSVT electrical cardioversion is the treatment of choice; IV rapid bolus adenosine can be tried if electrical cardioversion is not immediately available.

**Broad-Complex Tachycardia**

The stability of the patient determines the choice of treatment for wide-complex (broad-complex) tachycardia. In unstable wide-complex tachycardia electrical cardioversion is the treatment of choice.

**Drug Therapy for Stable Ventricular Tachycardia**\(^3\)\(^5\),\(^3\)\(^8\)

**Consensus on Science**

Three observational studies (LOE 5)\(^3\)\(^3\)\(^-\)\(^3\)\(^6\) indicated that amiodarone is effective for the termination of shock-resistant or drug-refractory VT. One randomized parallel study (LOE 2)\(^1\)\(^3\)\(^8\) indicated that aqueous amiodarone is more effective than lidocaine in the treatment of shock-resistant VT. One randomized trial (LOE 2)\(^3\)\(^6\) indicated that procainamide is superior to lidocaine in terminating spontaneously occurring VT. Three retrospective analyses (LOE 5)\(^3\)\(^6\)-\(^3\)\(^6\)\(^7\)\(^-\)\(^3\)\(^6\)\(^9\) indicated a low rate of termination of VT with lidocaine in patients with and without acute myocardial infarction. One randomized controlled trial (LOE 1)\(^3\)\(^7\) indicated that sotalol is significantly more effective than lidocaine for terminating acute sustained VT. One meta-analysis (LOE 1)\(^3\)\(^6\)\(^7\) showed that the overall risk of torsades de pointes in patients treated with a single infusion of IV sotalol is approximately 0.1%.

**Treatment Recommendation**

Amiodarone, procainamide, and sotalol are effective in terminating stable sustained VT.

**Drug Therapy for Polymorphic Ventricular Tachycardia**\(^3\)\(^8\)

**Consensus on Science**

One observational study (LOE 5)\(^3\)\(^7\) showed that IV magnesium will not terminate polymorphic VT (excluding torsades de pointes) in patients with a normal QT interval. Lidocaine is not effective, but amiodarone may be (LOE 4).\(^3\)\(^7\)

**Treatment Recommendation**

For hemodynamically stable polymorphic VT, where electrical therapy is not desirable or is ineffective, treatment with amiodarone may be effective.

**Therapy for Torsades de Pointes**\(^3\)\(^8\)

**Consensus on Science**

Two observational studies (LOE 5)\(^3\)\(^7\),\(^3\)\(^7\) showed that IV magnesium can effectively terminate torsades de pointes in patients with prolonged QT interval. One adult case series (LOE 5)\(^3\)\(^7\) showed that isoproterenol or ventricular pacing can be effective in terminating torsades de pointes associated with bradycardia and drug-induced QT prolongation.

**Treatment Recommendation**

Magnesium, isoproterenol, and ventricular pacing can be used to treat torsades de pointes.

**Bradycardia**

In the periarrest setting the rescuer should seek and treat reversible causes of bradycardia. In the absence of reversible causes, atropine remains the first-line drug for acute symptomatic bradycardia. Failure to respond to atropine will usually necessitate transcatheter pacing, although second-line drug therapy with dopamine, epinephrine, isoproterenol, or theophylline may be successful. Fist pacing may be attempted pending the arrival of an electrical pacing unit.

**Drug Therapy for Symptomatic Bradycardia**\(^3\)\(^9\)

**Consensus on Science**

In 1 randomized clinical trial in adults (LOE 2)\(^3\)\(^7\) and 1 historic cohort study in adults and additional reports (LOE 4),\(^3\)\(^7\)-\(^3\)\(^7\) IV atropine improved heart rate, symptoms, and signs associated with bradycardia. An initial dose of 0.5 mg, repeated as needed to a total of 1.5 mg, was effective in both in-hospital and out-of-hospital treatment of symptomatic bradycardia.

In 2 prospective controlled nonrandomized cohort studies in hospitalized adults (LOE 4),\(^3\)\(^7\)-\(^3\)\(^8\) administration of IV theophylline improved heart rate, symptoms, and signs associated with bradycardia that did not respond to atropine.

One case series (LOE 5)\(^3\)\(^7\) documented improvement in heart rate, symptoms, and signs associated with bradycardia when IV glucagon (3 mg initially, followed by infusion at 3 mg/h if necessary) was given to hospital patients with drug-induced symptomatic bradycardia not responding to atropine.

One study in 10 healthy volunteers indicated that a 3-mg dose of atropine produces the maximum achievable increase in resting heart rate (LOE 7).\(^3\)\(^8\) One study indicated that atropine may paradoxically cause high-degree AV block in patients after cardiac transplantation (LOE 5).\(^3\)\(^8\)
**Fist Pacing in Cardiac Arrest**

**Consensus on Science**

Three case series indicated that fist pacing can be effective. Two of the largest studies have included 100 (LOE 5)\(^383\) and 50 (LOE 5)\(^384\) patients. One study (LOE 5)\(^385\) compared fist pacing with 2 electrical modes in the same patient and found all 3 techniques equally effective. Selected case series indicate that the most effective technique is to deliver serial rhythmic blows (fist pacing) with the closed fist over the left lower edge of the sternum to pace the heart at a physiological rate of 50 to 70 beats per minute (bpm) (LOE 5).\(^383,384\) There are no prehospital case reports of fist pacing. In virtually all published cases of fist pacing, complete heart block was the underlying bradyarrhythmia.

**Treatment Recommendation**

Fist pacing may be considered in hemodynamically unstable bradyarrhythmias until an electrical pacemaker (transcutaneous or transvenous) is available.

**Cardiac Arrest in Special Circumstances**

In some circumstances modification of the standard resuscitation technique is required to maximize the victim’s chance of survival. In many of these special circumstances recognition of the critically ill patient may enable early treatment to prevent cardiac arrest. The special circumstances reviewed during the consensus process can be categorized as environmental (hypothermia, submersion, electrocution), pregnancy, asthma, and drug overdose/poisoning.

**Environmental**

**Hypothermia**

**Consensus on Science**

Hypothermic patients with pulse. One randomized controlled trial (LOE 1)\(^386\) showed active surface heating to be more effective than metallic foil insulation in an experimental model of accidental hypothermia. Two studies (LOE 4)\(^387,388\) documented successful active rewarming with external surface, forced air, and warm infusions.

Hypothermic patients with cardiac arrest. Two studies (LOE 4)\(^389,390\) documented successful resuscitation with prolonged CPR and successful recovery using invasive rewarming (extracorporeal circulation or cardiopulmonary bypass). Successful resuscitation from hypothermic cardiac arrest was reported using active noninvasive rewarming (forced air, warm infusions) (LOE 4).\(^389\) Better outcomes were documented for nonasphyxial versus presumed asphyxial hypothermic arrest (LOE 4).\(^390\) For victims of avalanche, a small air pocket may prevent an asphyxial component of the arrest (LOE 5).\(^391\)

**Treatment Recommendation**

For hypothermic patients with a perfusing rhythm and without a preceding cardiac arrest, consider active (noninvasive) external warming (with heating blankets, forced air, and warmed infusion). Severely hypothermic patients in cardiac arrest may benefit from invasive warming (cardiopulmonary bypass or extracorporeal circulation).

**Drowning**

For additional information see “Drowning” in Part 2: “Adult Basic Life Support.”

**Consensus on Science**

One study indicated that victims of drowning are at risk for cervical spine injury only if they have clinical signs of severe injury (LOE 4).\(^392\) Three single case reports (LOE 5)\(^393–395\) documented the use of exogenous surfactant for fresh water–induced severe respiratory distress syndrome; 2 victims survived. A case report described the use of noninvasive positive-pressure ventilation in 2 victims of submersion (LOE 5).\(^396\)

There was no evidence to support or refute the use of steroids (LOE 5),\(^397\) nitric oxide (LOE 5),\(^398\) extracorporeal membrane oxygenation (ECMO) rewarming after ROSC (LOE 5),\(^389\) therapeutic hypothermia after ROSC (LOE 5),\(^399\) or vasopressin (LOE 5) after submersion. Case reports documented the use of ECMO in young children with severe hypothermia after submersion (LOE 5).\(^400,401\)

**Treatment Recommendation**

Victims of submersion should be removed from the water and resuscitated by the fastest means available. Only victims with risk factors (history of diving, water slide use, trauma, alcohol) or clinical signs of injury or focal neurologic signs should be treated as having a potential spinal cord injury, with stabilization of the cervical and thoracic spine.

**Electrocution**

**Consensus on Science**

Case reports (LOE 5)\(^403–412\) indicated that early BLS and ALS may be lifesaving and may decrease short- and long-term cardiac and neurologic sequelae for victims of electrocution and lightning injuries.

Case studies of victims of lightning and electric injuries emphasize the possible coexistence of multiple injuries and the importance of ensuring initial responder safety. Survivors may have permanent neurologic and cardiac sequelae.

**Pregnancy**

**Etiology of Cardiac Arrest in Pregnancy**

**Consensus on Science**

One large case series (LOE 5)\(^413\) suggested that systematic consideration of the reversible causes of cardiac arrest may...
enable skilled rescuers to identify the etiology of cardiac arrest in pregnancy in the hospital setting.

Evidence extrapolated from peri-arrest resuscitation scenarios (LOE 7)\textsuperscript{414,415} indicated that ultrasound assessment undertaken by trained rescuers may help to identify intraperitoneal hemorrhage as a cause of cardiac arrest in pregnancy in the hospital setting.

Treatment Recommendation
Rescuers should try to identify common and reversible causes of cardiac arrest in pregnancy during resuscitation attempts. The use of abdominal ultrasound by a skilled operator should be considered in detecting pregnancy and possible causes of cardiac arrest in pregnancy, but this should not delay other treatments.

Resuscitation Technique for Pregnancy\textsuperscript{W134}

Consensus on Science
A case series (LOE 5)\textsuperscript{416} and numerous case reports (LOE 7\textsuperscript{417,418}; LOE 8\textsuperscript{421}) documented an improvement in rates of maternal and neonatal survival to discharge when delivery of the fetus was performed within 5 minutes of cardiac arrest in pregnancy if initial resuscitative efforts by skilled rescuers in the hospital setting failed.

Extrapolation from anesthesia (LOE 7)\textsuperscript{422} and a manikin study (LOE 6\textsuperscript{423}) suggests that a left lateral tilt of 15 degrees will relieve aortocaval compression in the majority of pregnant women and enable effective chest compressions by rescuers in any setting.

A human volunteer study (LOE 7)\textsuperscript{424} showed that there was no change in transthoracic impedance during pregnancy. The standard recommended energy levels for adults should be used by rescuers when attempting defibrillation in cardiac arrest during pregnancy in any setting.

Treatment Recommendation
If initial resuscitative efforts fail, caesarean delivery of the fetus (hysterotomy) should be performed within 5 minutes of onset of cardiac arrest in pregnancy to improve maternal or fetal survival. A left lateral tilt of 15 degrees is required to relieve inferior vena caval compression in the majority of pregnant women. The energy levels used for defibrillation in adults are appropriate for use in pregnancy.

Asthma

Defibrillation in Asthma\textsuperscript{W133}

Consensus on Science
One volunteer study in healthy adults (LOE 7)\textsuperscript{425} documented an increased transthoracic impedance with increasing positive end-expiratory pressure (PEEP) and suggested that increased shock energy may be required if initial defibrillation attempts fail for patients with asthma-induced cardiac arrest in any clinical setting.

Treatment Recommendation
If initial attempts at defibrillation fail for the patient with asthma and VF, higher shock energies should be considered.

Ventilation in Asthma\textsuperscript{W119B}

Consensus on Science
Evidence extrapolated from a systematic review of patients with noncardiac arrest (LOE 7)\textsuperscript{426} suggested decreased dynamic hyperinflation (auto-PEEP) when helium/oxygen mixtures were used to ventilate the lungs of asthmatic patients during in-hospital cardiac arrest.

Evidence extrapolated from 3 noncardiac arrest case series (LOE 7)\textsuperscript{427–429} suggested that asthmatic patients were at risk of gas trapping during cardiac arrest, especially if they were ventilated with higher tidal volumes and rates than recommended. Two small case series (LOE 5\textsuperscript{430,431}) and anecdotal reports (LOE 8\textsuperscript{432}) failed to show a consistent benefit from compression of the chest wall, followed by a period of apnea to relieve gas trapping, for patients with asthma-induced cardiac arrest in any clinical setting (see also “Disconnection From Ventilation During Cardiac Arrest,” above).

Evidence extrapolated from 3 noncardiac arrest case series (LOE 7)\textsuperscript{428} suggested improved ventilation of the lungs and decreased gastric inflation if the trachea is intubated early by trained rescuers for patients with asthma-induced cardiac arrest in any setting. Evidence from 2 noncardiac arrest case reports (LOE 7\textsuperscript{433}; LOE 8\textsuperscript{434}) neither supported nor refuted the use of open-chest ventilation and cardiac compressions in asthma-induced cardiac arrest.

Treatment Recommendation
There are insufficient data to support or refute the use of helium-oxygen mixtures in asthma-related cardiac arrest. Compression of the chest wall or a period of apnea may relieve gas trapping if dynamic hyperinflation occurs. In asthma-related cardiac arrest the patient’s trachea should be intubated early to facilitate ventilation and minimize the risk of gastric inflation.

Drug Overdose and Poisoning\textsuperscript{W198}

Sodium Bicarbonate for Poisoning and Electrolyte Disturbances\textsuperscript{W197A,W197B,W197C,W197D,W197E}

Consensus on Science
Evidence from the use of bicarbonate in calcium channel blocker overdose in 2 children (LOE 5\textsuperscript{435}) with fatal overdoses of nifedipine neither supported nor refuted the value of bicarbonate in calcium channel blocker overdose.

There were no controlled human studies of sodium bicarbonate therapy for arrhythmias or hypotension related to tricyclic antidepressant overdose. However, evidence from case reports (LOE 5\textsuperscript{436,437}) animal studies (LOE 6\textsuperscript{438–447}) and in vitro studies (LOE 6\textsuperscript{445,446,449}; LOE 7\textsuperscript{450,451}) supported the use of sodium bicarbonate to treat tricyclic antidepressant–induced arrhythmias or hypotension.

Treatment Recommendation
Sodium bicarbonate is recommended for the treatment of tricyclic antidepressant–induced arrhythmia or hypotension. Although no study has investigated the optimal target pH with bicarbonate therapy, a pH of 7.45 to 7.55 has been commonly accepted and seems reasonable.
**Ventilation Before Naloxone in Opioid Overdose**

**Consensus on Science**

Evidence from case series (LOE 5)\(^{452–454}\) in adults and extrapolation from LOE 7\(^{455,456}\) and LOE 8\(^{457}\) studies indicate fewer adverse events when ventilation is provided before administration of naloxone by EMS personnel to patients with opioid-induced respiratory depression in the prehospital setting.

**Postresuscitation Care**

ROSC is just the first step toward the goal of complete recovery from cardiac arrest. Interventions in the postresuscitation period are likely to significantly influence the final outcome, yet there are relatively few data relating to this phase. In the absence of firm guidelines, approaches to postresuscitation care are heterogeneous. Postresuscitation interventions are categorized into the following areas: (1) ventilation, (2) temperature control (therapeutic hypothermia and prevention and treatment of hyperthermia), (3) seizure control and sedation, and (4) other supportive therapies (blood glucose control, coagulation control, prophylactic antiarrhythmic therapy).

Therapeutic hypothermia improves neurologic outcome in some cardiac arrest survivors, and hyperthermia appears harmful. Tight blood glucose control improves outcome in undifferentiated critically ill patients, but the effect of this therapy in the postresuscitation phase is unknown. Prediction of outcome in comatose survivors of cardiac arrest remains problematic: median nerve somatosensory-evoked potentials measured 72 hours after cardiac arrest may be helpful, but analyses of several serum markers were inconclusive.

**Ventilation**

**Control of Arterial Carbon Dioxide**\(^{W114B}\)

**Consensus on Science**

Five studies in adults (LOE 2\(^{458,459}\), LOE 3\(^{460}\), LOE 5\(^{461}\), LOE 7\(^{462}\) and numerous animal studies (LOE 6\(^{463–465}\) documented harmful effects of hypocapnia (cerebral ischemia) after cardiac arrest. Two studies provide neutral evidence (LOE 5\(^{466}\), LOE 6\(^{467}\)).

**Treatment Recommendation**

There are no data to support the targeting of a specific PaCO\(_2\) after resuscitation from cardiac arrest. Data extrapolated from patients with brain injury, however, imply that ventilation to normocarbia is appropriate. Routine hyperventilation may be detrimental and should be avoided.

**Temperature Control**

**Therapeutic Hypothermia**\(^{W109A, W109B}\)

**Consensus on Science**

Two randomized clinical trials (LOE 1\(^ {468}\); LOE 2\(^{469}\)) showed improved outcome in adults who remained comatose after initial resuscitation from out-of-hospital VF cardiac arrest and who were cooled within minutes to hours after ROSC. Patients in these studies were cooled to 33°C\(^ {468}\) or to the range of 32°C to 34°C\(^ {469}\) for 12 to 24 hours. The Hypothermia After Cardiac Arrest (HACA) study\(^ {468}\) included a small subset of patients with in-hospital cardiac arrest.

One study (LOE 2\(^ {470}\)) documented improved metabolic end points (lactate and O\(_2\) extraction) when comatose adult patients were cooled after ROSC from out-of-hospital cardiac arrest in which the initial rhythm was PE/A/asytole. A small study (LOE 4\(^ {471}\)) showed benefit after therapeutic hypothermia in comatose survivors of non-VF arrest.

External or internal cooling techniques can be used to initiate cooling within minutes to hours (LOE 1\(^ {468}\); LOE 2\(^{469,470}\); LOE 5\(^ {472–475}\)). The only studies documenting improved outcome with therapeutic hypothermia after cardiac arrest used external cooling (LOE 1\(^ {468}\); LOE 2\(^{469,470}\)). An infusion of 30 mL/kg of 4°C saline achieved a decrease in core temperature of approximately 1.5°C (LOE 5)\(^ {472,473,475}\).

One study in patients with cardiac arrest (LOE 5\(^ {474}\)) and 3 other studies (LOE 7\(^ {476–478}\)) have documented that intravascular cooling enables more precise control of core temperature than external methods.

Studies documenting improved outcome with therapeutic hypothermia after cardiac arrest used continuous temperature monitoring (LOE 1\(^ {468}\); LOE 2\(^{469,470}\)).

Multiple studies in animals (LOE 6)\(^ {479–484}\) documented the importance of initiating cooling as soon as possible and for adequate duration (eg, 12 to 24 hours). Optimal parameters, including onset, depth, and duration of cooling, are unknown.

Seizures or myoclonus occurs in survivors of cardiac arrest (LOE 5\(^ {474,485–487}\)). Shivering will necessitate sedation and intermittent or continuous neuromuscular blockade. Use of continuous neuromuscular blockade could mask seizure activity.

**Treatment Recommendation**

Unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest should be cooled to 32°C to 34°C for 12 to 24 hours when the initial rhythm was VF. Cooling to 32°C to 34°C for 12 to 24 hours may be considered for unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest from any other rhythm or cardiac arrest in hospital.

**Prevention and Treatment of Hyperthermia**\(^ {W110}\)

**Consensus on Science**

A period of postarrest hyperthermia is common in the first 48 hours after cardiac arrest (LOE 4)\(^ {488–490}\). There were no controlled prospective studies that examined the clinical impact of antipyretics (or physical cooling devices) to prevent hyperthermia after cardiac arrest.

The risk of unfavorable neurologic outcome increased for each degree of body temperature >37°C (LOE 3)\(^ {491}\). Hyperthermia was associated with increased morbidity and mortality in post-stroke patients (LOE 7)\(^ {492}\). Post-stroke pyrexia was not treated effectively by antipyretics such as acetaminophen or ibuprofen (LOE 7)\(^ {493,494}\); however, antipyretics or physical cooling methods have been associated with decreased infarct volumes in animal models of global ischemia (LOE 7)\(^ {495,496}\).

**Treatment Recommendation**

Hyperthermia should be avoided after cardiac arrest.
Seizure Control and Sedation

Prevention and Control of Seizures

Consensus on Science
There were no studies that directly addressed the use of prophylactic anticonvulsant drugs after cardiac arrest in adults. There are data indicating that seizures can precipitate cardiac arrest (LOE 4), and respiratory arrest (LOE 5).502

Treatment Recommendation
Seizures increase the oxygen requirements of the brain and can cause life-threatening arrhythmias and respiratory arrest; therefore, seizures following cardiac arrest should be treated promptly and effectively. Maintenance therapy should be started after the first event once potential precipitating causes (eg, intracranial hemorrhage, electrolyte imbalance, etc) are excluded.

Sedation and Pharmacologic Paralysis

Consensus on Science
There were no data to support or refute the use of a defined period of ventilation, sedation, and neuromuscular blockade after cardiac arrest. One observational study in adults (LOE 5)503 documents increased incidence of pneumonia when sedation is prolonged beyond 48 hours after prehospital or in-hospital cardiac arrest.

Other Supportive Therapies

Blood Glucose Control

Consensus on Science
Tight control of blood glucose (range 80 to 110 mg/dL or 4.4 to 6.1 mmol/L) with insulin reduces hospital mortality rates in critically ill adults (LOE 1504; LOE 4505), but this has not been shown in post–cardiac arrest patient. Several human studies have documented a strong association between high blood glucose after resuscitation from cardiac arrest and poor neurologic outcome (LOE 4508; LOE 5507–513). There was good evidence that persistent hyperglycemia after stroke is associated with a worse neurologic outcome (LOE 7).514–517

The optimal blood glucose target in critically ill patients has not been determined. Comatose patients were at particular risk from unrecognized hypoglycemia, and the risk of this complication occurring increases as the target blood glucose concentration is lowered (LOE 8). One study in rats has shown that glucose plus insulin improves cerebral outcome after asphyxial cardiac arrest (LOE 6).518

Therapeutic hypothermia was associated with hyperglycemia (LOE 2).469

Treatment Recommendation
Providers should monitor blood glucose frequently after cardiac arrest and should treat hyperglycemia with insulin but avoid hypoglycemia.

Coagulation Control

Consensus on Science
There are no studies evaluating the role of anticoagulation alone to improve outcome after ROSC. In three nonexperi-mental reports (LOE 4; LOE 5; LOE 6) using fibrinolysis combined with heparin (anticoagulation) after prolonged cardiac arrest in humans, ROSC, but not 24-hour survival rates, was significantly better.

Prophylactic Antiarrhythmic Therapy

Consensus on Science
No studies specifically and directly addressed the prophylactic use of antiarrhythmic therapy started immediately after resuscitation from cardiac arrest. Six studies (LOE 5)520–525 documented inconsistent improvement in long-term survival when prophylactic antiarrhythms were given to survivors of cardiac arrest from all causes. Six studies (LOE 1526–528; LOE 2529,530; LOE 3531) showed that implantable cardioverter defibrillators (ICDs) improve survival when compared with antiarrhythmics in survivors of cardiac arrest.

Treatment Recommendation
Giving prophylactic antiarrhythmics to patients who have survived cardiac arrest, irrespective of etiology, can neither be recommended nor rejected. It may be reasonable, however, to continue an infusion of an antiarrhythmic drug that successfully restored a stable rhythm during resuscitation.

Prognostication

Prognostication During Cardiac Arrest

Predictive Value of Neurologic Examination

Consensus on Science
Five studies (LOE 4532,533; LOE 5534–536) documented some ability to predict outcome in adults when neurologic examination is undertaken during cardiac arrest, but there is insufficient negative predictive value for this assessment to be used clinically.

Treatment Recommendation
Relying on the neurologic exam during cardiac arrest to predict outcome is not recommended and should not be used.

Prognostication After Resuscitation

Predictive Value of Standard Laboratory Analyses

Consensus on Science
In 8 human prospective studies (LOE 3537,538; LOE 4241,539–543) of the value of biomarkers in predicting outcome from cardiac arrest, none was clinically useful in ascertaining outcome in the acute setting. One retrospective human study suggested that creatine kinase-MB could be used as an independent predictor of survival (LOE 4),539 but delays in completing the measurement may make this clinically less helpful.

In some studies in animals (LOE 6),544–556 lactate and acid base values showed a trend correlating with unfavorable outcomes. None of these studies could conclusively formulate a predictive model identifying a biochemical marker level that gave a reasonable prediction of outcome.

Predictive Value of Neuron-Specific Enolase and Protein S-100b

Consensus on Science
One randomized controlled study (LOE 2),557 4 prospective controlled studies (LOE 3),558–561 and 11 case series/cohorte
studies (LOE 4596,539,562–564; LOE 5512,513,565–568) indicated that neuron-specific enolase (NSE) and protein S-100b may be useful in predicting the outcome of cardiac arrest. But the 95% confidence interval (CI) in these trials was wide, and in many of the trials, return to consciousness (without comment 95% confidence interval (CI) in these trials was wide, and in many of the trials, return to consciousness (without comment 95% confidence interval (CI) in these trials was wide, and in many of the trials, return to consciousness (without comment 95% confidence interval (CI) in these trials was wide, and in many of the trials, return to consciousness (without comment)

The only meta-analysis to look at this topic estimated that to obtain 95% CI with a 5% false-positive rate would require a study population of approximately 600 patients (LOE 1). 569 No study this large has been conducted.

Treatment Recommendation

No laboratory analyses (NSE, S-100b, base deficit, glucose, or soluble P-selectin) provide reliable prediction of the outcome after cardiac arrest.

Somatosensory-Evoked Potentials

Consensus on Science

Eighteen prospective studies (LOE 3)568,570–586 and 1 meta-analysis (LOE 1)587 indicated that median nerve somatosensory-evoked potentials in normothermic patients comatose for at least 72 hours after cardiac arrest predict poor outcome with 100% specificity. Bilateral absence of the N20 component of the evoked potentials in comatose patients with coma of hypoxic-anoxic origin is uniformly fatal.

Treatment Recommendation

Median nerve somatosensory-evoked potentials measured 72 hours after cardiac arrest can be used to predict a fatal outcome in patients with hypoxic-anoxic coma.

Electroencephalogram

Consensus on Science

The use of the electroencephalogram (EEG), performed at least 24 to 48 hours after arrest, has been evaluated in case series of humans (LOE 5)578,585,588–598 and animals (LOE 6).599–601. On the modified Hockaday scale, grades I (normal alpha with theta-delta activity), IV (alpha coma, spikes, sharp waves, slow waves with very little background activity), and V (very flat to isoelectric) were most useful prognostically. But the prognosis was unpredictable for those with grade II and III EEGs.

Treatment Recommendation

The use of the EEG performed a minimum of 24 to 48 hours after a cardiac arrest can help define the prognosis in patients with grade I, IV, and V EEGs.

References

28. Staudinger T, Brugger S, Roggla M, Rintelen C, Atherton GL, Johnson JC, Frass M. [Comparison of the Combitube with the endotracheal tube


epinephrine, a selective alpha2-adrenergic agonist for cardiac resusc-

128. DeBehnke DJ, Spreng D, Wickman LL, Crowe DT. The effects of endo-
thelin-1 on coronary perfusion pressure during cardiopulmonary resuscita-

129. DeBehnke DJ, Benson L. Effects of endothelin-1 on resuscitation rate

130. DeBehnke DJ, Berg RA, Kern KB, Ewy GA. Endothelin-1 vasocon-
striction during swine cardiopulmonary resuscitation improves coronary perfu-
sion pressures but worsens postresuscitation outcome. Circulation.

Kittler H, Konschitzky R, Laggner AN. Endothelin-1 elevates regional cer-
bral perfusion during prolonged ventilatory resuscitation cardiac arrest in pigs.


133. DeBehnke DJ, Spreng D, Wickman LL, Crowe DT. The effects of endo-


136. DeBehnke DJ, Benson L. Effects of endothelin-1 on resuscitation rate

137. DeBehnke DJ, Berg RA, Kern KB, Ewy GA. Endothelin-1 vasocon-
striction during swine cardiopulmonary resuscitation improves coronary perfu-
sion pressures but worsens postresuscitation outcome. Circulation.

138. Somberg JC, Bailin SJ, Haffajee CI, Paladino WP, Kerin NZ, Bridges D,

139. Skrifvars MB, Kuisma M, Boyd J, Maatta T, Repo J, Rosenberg PH,
Castren M. The use of undiluted amiodarone in the management of out-of-
582–587.

518–519.

141. Levine JH, Massumi A, Scheinman MM, Winkle RA, Platia EV,


143. Mader TJ, Smithline HA, Durkin L, Scriver G. A randomized controlled

144. Thel MC, Armstrong AL, McNulty SE, Califf RM, O’Connor CM.


149. Longstreth WT Jr, Fahrenbruch AE, Olsufka M, Walsh TR, Copass MK,


158. Janata K, Holzer M, Kurkcyian I, Losert H, Riedmuller E, Pikula B,
Laggen AN, Laczkia K. Major bleeding complications in cardiopulmo-


266. Chiang WC, Chen WJ, Chen SY, Ko PC, Lin CH, Tsai MS, Chang WT, Chen SC, Tsan CY. Ma MH. Better adherence to the guidelines during cardiopulmonary resuscitation through the provision of audio-prompts. Resuscitation. 2005;64:297–301.


280. Tucker JK, Redberg RF, Schiller NB, Cohen TJ. Active compression-decompression resuscitation: analysis of transmitial flow and left ventricular volume by transesophageal echocardiography in humans. Car-


475. 2005 International Consensus Conference


Part 4: Advanced Life Support

Circulation. 2005;112:III-25-III-54
doi: 10.1161/CIRCULATIONAHA.105.166474
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2005 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/112/22_suppl/III-25

Data Supplement (unedited) at:
http://circ.ahajournals.org/content/suppl/2005/11/28/112.22_suppl.III-25.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/