Management following resuscitation from cardiac arrest: recommendations from the 2003 Rocky Mountain Critical Care Conference

[Conduite à tenir après la réanimation post-arrêt cardiaque : recommandations de la conférence du Rocky Mountain Critical Care 2003]

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Purpose: To propose a strategy for the management of patients admitted to critical care units after resuscitation from cardiac arrest.

Source: Prior to the conference relevant studies were identified via literature searches and brief reviews circulated on the following topics: glucose and blood pressure management; therapeutic hypothermia; prearrest outcome prediction; post-arrest outcome prediction; and management of myocardial ischemia. Two days were devoted to assessing evidence and developing a management strategy at the conference. Consensus opinion of conference participants [intensive care unit (ICU) physicians] was used when high grade evidence was unavailable. Additional literature searches and data grading were performed post-conference.

Principal findings: High grade evidence was lacking in most areas. Specific goals of treatment were proposed for: general care; neurologic care; respiratory care; cardiac care; and gastrointestinal care. There was adequate evidence to recommend therapeutic hypothermia for comatose patients who had witnessed ventricular fibrillation or ventricular tachycardia arrests. Conference participants supported extending therapeutic hypothermia to other presenting rhythms in selected circumstances. Additional goals included mean arterial pressure 80 to 100 mmHg, glucose 5 to 8 $mmol \cdot L^{-1}$ using insulin infusions, and PaO_2 > 100 mmHg for the first 24 hr. Absent withdrawal to pain 72 hr after resuscitation should prompt consideration of palliative care. The level of evidence for other recommendations was low.

Conclusions: The proposed management strategy represents an approach to manage patients in the ICU following resuscitation from cardiac arrest. Most of the recommendations are based on low grade evidence. Additional research is needed to improve the evidence base. A standard post-arrest management strategy could help facilitate future research.

Objectif : *Proposer une stratégie de traitement à adopter avec les patients admis aux unités de soins intensifs (USI) après la réanimation post-arrêt cardiaque.*

Source : *Avant la conférence, les études utiles ont été repérées dans les publications et de brèves revues ont circulé sur : le glucose et le traitement de la tension artérielle ; l'hypothermie thérapeutique ; la prédiction de l'évolution pré-arrêt ; la prédiction des suites de l'arrêt cardiaque et le traitement de l'ischémie myocardique. Deux jours ont été alloués à l'évaluation de la preuve et au développement d'une approche thérapeutique à la conférence. L'opinion générale des participants, médecins intensivistes, a prévalu quand une preuve de haut niveau n'était pas assurée. Des recherches de documents et une classification de données supplémentaires ont été faites après la conférence.*

Constatations principales : *Une preuve de haut niveau manquait dans la majorité des domaines. On a proposé des objectifs spécifiques de traitement pour : les soins généraux, neurologiques, respiratoires, cardiaques et gastro-intestinaux. Des preuves suffisantes ont permis de recommander l'hypothermie thérapeutique chez les patients comateux victimes d'arrêts cardiaques causés par une fibrillation ou une tachycardie ventriculaire. Les participants à la conférence ont appuyé l'extension de l'hypothermie thérapeutique aux rythmes présentés dans des circonstances choisies. D'autres objectifs incluent une tension artérielle moyenne de 80 à 100 mmHg, le glucose à 5 à*

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8 mmol·L^{-1} pour des perfusions d'insuline et une PaO_2 > 100 mmHg pour les 24 premières heures. L'absence d'un mouvement de retrait à la douleur, 72 h après la réanimation, devrait suggérer les soins palliatifs. Le niveau de preuve des autres recommandations était bas.

Conclusion : *La conduite à tenir proposée représente une approche thérapeutique des patients de l'USI à la suite de la réanimation postarrêt cardiaque. La plupart des recommandations sont fondées sur des preuves de bas niveau. D'autres recherches sont nécessaires pour améliorer le fondement de la preuve. Une approche thérapeutique normalisée post-arrêt cardiaque pourrait faciliter la recherche à venir.*

THERE are clinical practice guidelines for management during cardiac resuscitation, but little has been written about post-resuscitation management. While proposals for brain-oriented extracerebral life support were developed by Safar and used in a randomized controlled trial of barbiturates in post-arrest patients,[1,2] the evidence for these recommendations was not well described. Safar's recommendations included suggestions for routine use of corticosteroids, hyperventilation, and neuromuscular blockers. New ACLS 2000 guidelines have updated the section on post-arrest management but have less detail.[3] In the current document the immediate goals of post-resuscitation care are: to optimize brain and other tissue perfusion; to transport the patient to an appropriately equipped critical care unit; to attempt to identify the precipitating causes of the arrest; and to institute therapy to prevent recurrence. The ACLS 2000 guidelines specifically recommend monitoring temperature and treating fever aggressively; avoiding hypoxemia and hypotension; avoiding sustained hypocapnia and ventilating to achieve normocarbia; and taking measures to optimize cerebral perfusion pressure.[3] There are not many other specific aspects of care singled out. Recently, randomized controlled trials in cardiac arrest patients have documented improved outcome with induced hypothermia post-arrest.[4,5] Additional controlled trials are needed to improve care and outcome in this patient population. Additional trials will require development of a more detailed standardized post-arrest management protocol.

The topic of post-arrest management in critical care units was discussed at the 2003 Rocky Mountain Critical Care Conference in Vernon, British Columbia. The meeting was designed to focus upon three topics (post-arrest management, sepsis management, and improving safety and reducing harm in critical care) with an view towards development of management plans or future research. The post-arrest section was focused towards proposing an approach to post-arrest management based upon evidence or best clinical practice. It was apparent to the organizers of this section that high grade evidence was lacking for most aspects of management. To proceed, the organizing group divided the subject into the following areas prior to the meeting: glucose and blood pressure management (D.Z.); therapeutic hypothermia (O.A.M.); pre-arrest outcome prediction (P.G.B.); post-arrest outcome prediction (D.D.B.); and management of myocardial ischemia (D.F.). If a structured review or meta-analysis had been conducted on a topic they were included. One member (D.D.B.) functioned as coordinator. Group members conducted literature searches to find relevant material (randomized controlled trials, clinical trials, and meta-analyses or structured reviews), and reference lists of relevant papers were examined. At the end of this process each member of the organizing group produced a summary document that was circulated to other core members for review. The organizing group provided comments and included their reviews in the conference syllabus distributed at the meeting. When the meeting convened in Vernon, the reviews and studies were considered by the organizing group and other critical care physicians attending the conference. Intense discussion and review occurred over two days under the direction of a moderator who came from outside of the core group. The input of participants at the conference was used to generate a document outlining specific goals of treatment for: general care; neurologic care; respiratory care; cardiac care; and gastrointestinal (GI) care. These recommendations were presented and discussed at a final session of the conference by all attendees, including those who had been working in sepsis and error prevention workshops. Approximately 35 critical care physicians participated in the conference, and the consensus was that the findings should be submitted for publication. After the conference adjourned the recommendations were reviewed by the core group to help with grading the evidence. Additional literature searches were conducted at this stage to clarify evidence grades. Grading was done using a system modified from Sackett.[6] The grading system employed is shown in Table I. There were issues deciding how to handle important positive randomized controlled trials outside of the post-arrest population. These studies were considered, but were not granted A or B grades unless they included post-arrest patients, or unless post-arrest patients were probable to accrue the same benefit as the general intensive care unit (ICU) population. Conference participants believed that data from these trials must be considered in developing their recommendations, despite low numbers of post-arrest

TABLE I Grading system used

Grading of recommendations
A. Supported by at least two level I investigations
B. Supported by one level I investigation
C. Supported by level II investigations only
D. Supported by at least one level III investigation
E. Supported by level IV or V evidence
Grading of evidence
I. Large, randomized trials with clear-cut results; low risk of false-positive (alpha) error or false-negative (beta) error
II. Small, randomized trials with uncertain results; moderate-to-high risk of false positive (alpha) and/or false-negative (beta) error
III. Nonrandomized, contemporaneous controls
IV. Nonrandomized, historical controls, and expert opinion
V. Case series, uncontrolled studies, and expert opinion

TABLE II General care recommendations

1. Induce hypothermia [bladder or esophageal temperature 32 to 34°C within four hours of return of spontaneous circulation (ROSC)] and maintain for 24 hr if the patient fulfills the following criteria after a witnessed ventricular fibrillation or witnessed ventricular tachycardia arrest: - Interval < 15 min from collapse to resuscitation attempt - ROSC achieved within 60 min of arrest Exclusions to this approach include hypotension (mean arterial pressure < 60 mmHg for more than 30 min after ROSC), response to voice after ROSC, and Glasgow coma score > 9. OVERALL EVIDENCE GRADE: B Induction of hypothermia COULD be extended to patients with pulseless electrical activity or asystolic arrests if they have witnessed arrests with collapse-resuscitation attempt intervals < 15 min and they achieve ROSC within 60 min. This is an extrapolation and has NOT been studied in randomized controlled trials. OVERALL EVIDENCE GRADE: E
2. Hyperthermia should not be tolerated. Temperatures over 38°C should be reduced. OVERALL EVIDENCE GRADE: B
3. Consider treatment of temperatures over 37°C during the first 72 hr after ROSC with active cooling and/or pharmacologic means such as acetaminophen and/or non-steroidal anti-inflammatory drugs (NSAID). OVERALL EVIDENCE GRADE: D
4. If the patient is hypothermic on presentation rewarming should be gradual and final temperature should not exceed 37°C. OVERALL EVIDENCE GRADE: B
5. Serum magnesium level and potassium levels should be normalized. OVERALL EVIDENCE GRADE: E
6. Replace peripheral or central lines placed without proper sterile techniques during the cardiac resuscitation. OVERALL EVIDENCE GRADE: E
7. Identify and manage complications resulting from cardiopulmonary resuscitation. OVERALL EVIDENCE GRADE: E
8. Administer deep vein thrombosis prophylaxis if systemic anticoagulation is not required. OVERALL EVIDENCE GRADE: A

patients. The final evidence grade and supporting data for treatment goals of post-arrest patients are outlined below.

General recommendations (Table II)

Induced hypothermia is the only intervention post-resuscitation that has been shown to improve neurologic outcome in patients.[4,5] The positive results came from a highly selected patient population, and it is reasonable to induce hypothermia in patients who meet the criteria outlined. To date, trials of hypothermia have only enrolled patients with witnessed ventricular fibrillation or ventricular tachycardia (Grade B). Conference participants believed hypothermia induction could be considered for patients presenting with other initial rhythms as long as the other entry criteria were present (Grade E). Accordingly, hypothermia may be an option in patients who present with witnessed pulseless electric activity or asystolic arrests. Additional trials are needed to validate this approach for these patients.

Hyperthermia is common following cardiac arrest and head injury.[4,5,7–9] Some benefits of hypothermia may result from avoidance of hyperthermia as temperatures over 37°C are common in post-arrest patients and are associated with increased risk of unfavourable neurologic recovery.[7] In fact, in post-arrest patients each degree Celsius over 37 is associated with increased risk of severe disability, coma, or persistent vegetative state.[7] These data are the basis for the recommendation to avoid hyperthermia[10] (temperatures over 38°C; Grade B), and to institute treatment to avoid temperatures over 37°C (Grade D). Gradual rewarming was practiced in the post-arrest hypothermia randomized controlled trials,[4,5] and is supported by data from hypothermic head injured patients[11] (Grade B). Treatment of temperatures over 37°C can be difficult in brain injured patients. Antipyretic treatment with non-steroidal anti-inflammatory drugs (NSAIDS) in head injured patients was ineffective in a multicentre Italian study, and did not reduce temperature to < 37°C even when combined with physical cooling measures.[9] Comparable data in post-arrest patients are lacking. Additional studies should be conducted to evaluate strategies to prevent hyperthermia in this population

Acetaminophen has been used as an antipyretic for many years, and has greater antipyretic efficacy than aspirin in volunteers receiving *iv* endotoxin.[12] No evaluation of acetaminophen *vs* NSAIDs for treatment of pyrexia has been performed in critically ill patients. Indeed, the entire concept of treating fever in ICU patients without cerebral injury has been questioned.[13,14] NSAID administration produces greater temperature decrements and longer duration of antipyresis than acetaminophen in studies in febrile children,[15] and was also associated with faster resolution of fever in patients with malaria.[16] In a nonrandomized open label trial in febrile cancer patients *iv* propacetamol (acetaminophen) had lower antipyretic efficacy than an NSAID (*iv* diclofenac).[17] Two randomized trials have evaluated acetaminophen in stroke patients and reported small decreases in core body temperature even in normothermic patients.[18,19] Acetaminophen may modestly promote hypothermia < 36.5°C or prevent hyperthermia > 37.5°C.[15] Unfortunately, the clinical significance of this effect appears small. Pharmacologic antipyresis with acetaminophen and/or NSAID in post-cardiac arrest patients requires more study, however, ongoing use of these medications was recommended until additional data are available (Grade E).

Additional information is also needed regarding the technique, rapidity, and duration of inducing hypothermia after resuscitation. Recent trials have administered sedative and neuromuscular blocking agents during the hypothermia interval.[14,15,20,21] Neuromuscular blockade is given to prevent shivering during hypothermia. Modest hypothermia has been induced in un-intubated stroke patients without resorting to the use of neuromuscular blockade or sedation.[22] Hypothermia has also been induced with endovascular cooling during primary percutaneous coronary interventions in acute myocardial infarction without requiring neuromuscular blockade.[23] Shivering was prevented in these studies by administration of *iv* meperidine alone or in combination with oral buspirone. Meperidine and buspirone administration was studied in human volunteers made hypothermic with an infusion of 4°C *iv* fluid, and significantly reduced the shivering threshold while causing little sedation or respiratory toxicity.[24] Intravenous meperidine administration inhibits shivering and decreases the rewarming rate in hypothermic human volunteers.[25] The administration of sedative infusions and neuromuscular blockers during hypothermia can complicate neurologic assessment in post-arrest patients, and may not be necessary if meperidine administration successfully inhibits shivering. Studies need to be conducted to determine if neuromuscular blockade is essential during therapeutic hypothermia following cardiac arrest.

Multiple techniques of hypothermia induction have been published including: application of ice packs;[5] surface cooling with cooled forced-air,[4,20] or circulating water blankets;[18,19] infusion of 4°C *iv* fluids;[26–28] immersion in cold water;[29] specialized endovascular cooling devices;[21,30,31] and cardiopulmonary bypass.[32] No trials comparing hypothermia techniques in cardiac arrest patients have been published. A small trial comparing forced-air *vs* circulating water cooling blankets in febrile critically ill adults recommended forced air cooling.[33] A small trial in anesthetized volunteers found that bladder and gastric lavage were ineffective, forced-air and circulating water cooling resulted in cooling rates around $1.6°C \cdot hr^{-1}$, and greatest cooling occurred with ice-water immersion ($9.7°C \cdot hr^{-1}$).[27] A retrospective review found endovascular cooling was superior to cooling blankets for rapid induction of hypothermia in subarachnoid hemorrhage patients.[28] At present, there is insufficient evidence to make definitive recommendations among techniques to induce therapeutic hypothermia after cardiac arrest. Comparative studies of techniques or combinations of techniques are required. Given the costs of equipment being marketed for therapeutic hypothermia, cost effectiveness and cost utility studies are also needed.

The ACLS 2000 guidelines recommend normalization of magnesium and potassium levels in the post-arrest period[34] (Grade E). It is clear that routine magnesium administration is not indicated in patients presenting with ST-elevation myocardial infarction.[35] Magnesium ions act as cerebral vasodilators and noncompetitive antagonists of the N-methyl-D-aspartate receptor and have been studied as a neuroprotective agent in human stroke.[36,37] At present, evidence is insufficient to support routine magnesium administration for neuroprotection in post-arrest patients.

The recommendation to replace lines that may have been placed when adherence to aseptic technique cannot be ensured comes from the ACLS 2000 guidelines and Centers for Disease Control guidelines[3,38] (Grade E). ACLS 2000 guidelines also suggest searching for complications of cardiopulmonary resuscitation such as rib fractures, pneumothorax, and pericardial tamponade in resuscitated post-arrest patients[3] (Grade E).

The final recommendation in this section advocates routine administration of prophylaxis to prevent venous thromboembolism in ICU patients. Venous thromboembolism prevention has been extensively reviewed, and guidelines were published by the

American College of Chest Physicians (ACP) in 2001.[39] ACP guidelines support routine prophylaxis in patients admitted to ICU following cardiac arrest. (Grade A for general ICU patients, no specific data for post-arrest patients, but benefit should be applicable to post-arrest patients).

Neurologic recommendations (Table III)

Many of these recommendations are generalized from other types of cerebral injury. It is well accepted that hypoxia, hypotension, and ongoing seizures are bad for the injured brain.[40] Some post-arrest patients will develop cerebral edema and raised intracranial pressure.[41] The recommendation to elevate the head of the bed and maintain central position reflects the standard approach in head injured patients and is advocated in the ACLS 2000 guidelines[3] (Grade C). Head elevation has not been prospectively studied in cardiac arrest patients, but is a reasonable extrapolation from head injury studies. It may also help with patients intubated for long periods as head of bed elevation has been recommended to decrease ventilator-associated pneumonia in intubated patients.[42]

There is no agreed upon standard for intervals of neurologic examination in the post-arrest population. Regular standardized neurologic examinations at predetermined post-resuscitation intervals must be documented to allow the possibility of research to assess earlier outcome prediction. Recommendations from conference participants regarding frequency of documentation of neurologic assessment were developed by consensus (Grade E). Frequent documentation was desirable to allow the possibility of post-hoc analysis for the development of clinical outcome prediction rules.

Sedation use in post-arrest patients has not been studied. The European hypothermia study employed sedation with infusions of fentanyl and midazolam and used neuromuscular blockers during the hypothermia period.[4] There are no human data to suggest that post-resuscitation administration of sedative agents improves outcome from anoxic or traumatic brain injury. A large trial of barbiturate therapy in cardiac arrest survivors was negative.[2] Routine administration of neuromuscular blockers complicates clinical neurologic examination and is not universal practice. Propofol has seen increasing use in neuroanesthesia for head injured patients and is frequently used to sedate ICU patients. It has been studied in the treatment of head injured intubated patients and shown to be safe, although not associated with better outcomes than morphine.[43] Its inclusion acknowledges the increasingly common use of propofol in intensive care units for short-term sedation of critically ill adults, but

TABLE III Neurologic care recommendations

1. Elevate head of bed at least 30° and maintain in the midline position for first 24 to 48 hr
   OVERALL EVIDENCE GRADE: C
2. Document neurologic evaluation shortly after return of spontaneous circulation (ROSC) and at 6 hr, 12 hr, 24 hr, 36 hr, 48 hr, and 72 hr after ROSC. This assessment cannot be done in patients who are anesthetized/paralyzed or hypothermic and should not be attempted if these are ongoing. The following minimum findings should be documented at each assessment:
   i. Motor response to pain (central and peripheral);
   ii. Pupillary eye signs (light response; corneal; occulocephalic);
   iii. Glasgow coma scale
   iv. Ability to breathe or trigger ventilator.
   OVERALL EVIDENCE GRADE: E
3. If sedation is needed short lasting agents are preferred. Sedation should be with fentanyl/midazolam or with propofol. Sedation should be interrupted daily unless the patient is paralyzed for hypothermia treatment.
   OVERALL EVIDENCE GRADE: B
4. Benzodiazepines (lorazepam, midazolam, diazepam) should be administered acutely to treat seizure activity if it occurs. Phenytoin (or its prodrug fosphenytoin) is indicated to prevent the recurrence of seizures (20 $mg \cdot kg^{-1}$ loading dose). Pentobarbital, midazolam, or propofol infusions may be required if seizure activity continues despite additional doses of phenytoin or lorazepam.
   OVERALL EVIDENCE GRADE: A
5. Frequent myoclonus should be treated with oral clonazepam or *iv* midazolam. If this is not successful valproic acid, propofol or newer anticonvulsant drugs can be tried.
   OVERALL EVIDENCE GRADE: E
6. If best neurologic response 72 hr after ROSC is not better than withdrawal to painful stimuli, the prognosis is dismal. Intensive medical support should be withdrawn and palliative care provided. This assumes that barbiturates, neuromuscular blockers and/or other potent sedative agents have not been administered and that there is no other reason except anoxic brain damage from the arrest to explain the neurologic findings.
   OVERALL EVIDENCE GRADE: D
7. Routine computed tomography (CT) scan of the head is not indicated. Head CT scan should be done if there are definite indications. These include signs of raised intracranial pressure or lateralizing signs. Magnetic resonance imaging of the brain can be considered as part of a research protocol to assess the contribution of this technique to outcome prediction.
   OVERALL EVIDENCE GRADE: E
8. The use of somatosensory evoked potentials should be considered as part of a protocol to assess its contribution to prognostication. Routine electroencephalogram (EEG) is not indicated but EEG should be used if there are concerns about ongoing seizure activity.
   OVERALL EVIDENCE GRADE: C
9. Glasgow outcome scores must be recorded to evaluate outcome at appropriate intervals.
   OVERALL EVIDENCE GRADE: E

also acknowledges a paucity of data. Daily interruption of sedation has been studied in critically ill patients and was associated with decreased time of mechanical ventilation and time in the ICU.[44] This intervention has not been studied in post-arrest patients, however the principle of minimizing sedation to allow assessment of neurologic status and ability to breathe should apply to this population (Grade B).

The management protocol for post-arrest patients who are seizing follows evidence-based recommendations for therapy in standard sources.[45] There are no specific studies in post-arrest patients to consider, but no reason to deviate from standard seizure treatment recommendations (Grade A). There are no evidence based recommendations for treatment of myoclonus in post-arrest survivors. There are data suggesting that myoclonic status epilepticus in post-anoxic coma arises from lethal damage to neurons.[46] Wijdicks *et al.* studied 40 patients with myoclonus status after cardiac resuscitation and concluded that it should be considered an agonal phenomenon indicating devastating neocortical damage.[47] There is a syndrome of post-hypoxic myoclonus (Lance-Adams syndrome) where myoclonus can be initiated by action or auditory or painful stimuli. This has a much better prognosis and has been treated with clonazepam.[48–50] Animal data suggest the pathogenesis of post-hypoxic myoclonus may involve activation of glutamate neurotransmission,[51] and serotonin receptors have also been implicated.[52] Animal models have tested new anticonvulsants (riluzole and lamotrigine) and reported antimyoclonic and neuroprotective effects.[52,53] Propofol has also been recommended based on anecdotal evidence.[54] The recommendations made for clonazepam or valproic acid are clearly not based on high grade evidence (Grade E). Treatment of myoclonus after cardiac arrest is an area where trials are needed. Treatment with any agent is difficult and often unsuccessful.

There are two published structured reviews on post-arrest prognostication using clinical criteria.[55,56] Both concur that accurate prediction can only occur after 72 hr have elapsed from return of spontaneous circulation (ROSC). Motor response to pain at the 72-hr interval predicted poor outcome if the patient did not move or exhibited extensor or flexor posturing. Recently a structured review of clinical examination in comatose patients following cardiac arrest found useful likelihood ratios (LR) for four clinical signs 24 hr after ROSC.[57] The four signs at 24 hr were absent corneal reflexes [LR 12.9; 95% confidence interval (CI) 2.0–68.7], absent pupillary response (LR 10.2; 95% CI 1.8–48.6), absent withdrawal response to pain (LR 4.7; 95% CI 2.2–9.8), no motor response (LR 4.9; 95% CI 1.6–13.0). Absent motor response to pain 72 hr after ROSC was also found to predict death or poor outcome (LR 9.2; 95% CI 2.1–49.4) The review by Booth and colleagues estimated 77% pretest probability of poor neurologic outcome in comatose post-arrest survivors.[57]

At the conference, participants determined that motor response to pain at 72 hr was the best supported clinical predictor. Therapeutic hypothermia can complicate using motor response to pain for prediction, especially if sedation and neuromuscular blockade are employed. These concerns resulted in recommendations for short-acting sedatives and neuromuscular blockers, and consideration of inducing therapeutic hypothermia without sedation/paralysis if possible (Grade E). If physicians are confident that sedatives and neuromuscular blockers are not confounding the neurologic examination, lack of motor response to pain 72 hr after ROSC should prompt consideration of withdrawal of life support and institution of palliative care (Grade D). The usual caveats of medications, temperature, and other disease processes beside central nervous system damage must be considered before applying this prediction rule. The best original studies on the topic were published between 1985-1995.[58,59] The age of the data suggests additional studies would be useful, given changes in practice and technology since that time.

Routine computed tomography (CT) scanning cannot be supported in post-arrest patients with anoxic cerebral damage (Grade E). There are no trials indicating that CT imaging adds to clinical assessment unless stroke, bleeding or trauma is suspected on the basis of history or clinical examination. There are preliminary reports that magnetic resonance imaging (MRI) can be used to determine the prognosis of patients with diffuse cerebral anoxia.[60,61] The role of MRI in post-arrest patients is an exciting approach which should be integrated into future research.

Systematic reviews of outcome prediction in comatose patients post-arrest have concluded that somatosensory evoked potentials (SSEP) are the best diagnostic method for predicting outcome[55,56] (Grade C). New research should evaluate SSEP in larger samples to determine the utility and value of the technique. Routine electroencephalograms were not supported by the results of the published reviews, but should be used if ongoing seizure activity is suspected.[55]

Outcome measurements beyond mortality are important for resuscitation research. Guidelines for reporting data from both out-of-hospital and in-hospital resuscitation attempts (Utstein style) have been developed by an international process.[62,63] The use of

TABLE IV Respiratory care recommendations

1. FIO_2 adjusted to give PaO_2 over 100 mmHg for the first 24 hr (SaO_2 of 99–100%). OVERALL EVIDENCE GRADE: E
2. If mechanically ventilated use positive end-expiratory pressure (PEEP) of 5 cm H_2O. More PEEP may be applied to maintain PaO_2 over 100 mmHg if FIO_2 is over 0.6 OVERALL EVIDENCE GRADE: E
3. If mechanically ventilated pCO_2 should be 35 to 40 mmHg for the first 24 hr. Hyperventilation should not be used routinely. Patients may be hyperventilated if there are objective signs of acutely increasing intracranial pressure. Hyperventilation below 35 mmHg should not be used to compensate for metabolic acidosis. OVERALL EVIDENCE GRADE: C
4. pH on arterial blood gases should be between 7.30 to 7.45 and buffer infusion can be used if the presence of metabolic acidosis results in sustained pH below 7.30. In this instance attempts should be made to ensure that filling pressures and cardiac output are assessed and augmented if inadequate. OVERALL EVIDENCE GRADE: E

the Glasgow outcome scoring system is recommended for reporting results of resuscitation research[64,65] (Grade E). This system records cerebral performance category (CPC) and overall performance category (OPC) at intervals to determine degree of impairment after cardiac arrest. Additional, more sensitive, instruments should also be employed, but CPC and OPC represent the minimum outcome dataset for resuscitation research.

Respiratory recommendations (Table IV)

In 1986 Safar proposed maintaining PaO_2 over 100 mmHg and using minimal positive end-expiratory pressure (PEEP) after ROSC.[1,2] The evidence for this recommendation is not clear, and recent ACLS 2000 revisions have not specified PaO_2 goals.[3] There are data from animal studies showing worse central nervous system outcomes and higher levels of oxidized cerebral lipids in dogs resuscitated and maintained at FIO_2 1.0 for at least one hour post-resuscitation.[66,67] There do not appear to be any human data to consider on the topic. The proposal to maintain PaO_2 over 100 mmHg for the first 24 hr reflects common practice in ICU and physician comfort (Grade E). Studies are needed to determine if this approach is harmful. The PEEP recommendation also reflects common practice and animal data that repeated opening and closing of alveoli and normal tidal volumes may be harmful in the setting of acute lung injury[68] (Grade E).

There are human data linking hyperventilation and hypocapnia to harm in head injury.[69] The recommendation to maintain normocapnia mirrors recommendations in guidelines for management of severe head injury[6] (Grade C). The ACLS 2000 guidelines also advocate ventilation to achieve normocarbia, avoidance of routine hyperventilation, and avoidance of hyperventilation for correction of metabolic acidosis.[3]

There is controversy about the efficacy of buffers in the management of lactic acidosis.[70] ACLS 200 guidelines have de-emphasized the use of buffers during resuscitation except in the setting of known or suspected hyperkalemia.[34] Buffer infusion has been shown to treat non-anion gap metabolic acidosis produced by infusion of normal saline solutions.[71] Buffer infusion was also employed for pH correction during a recent trial of low tidal volumes in the management of Acute Respiratory Distress Syndrome.[72] Given these ongoing uses of buffering agents in intensive care patients, it appears reasonable to suggest their use for specific indications in post-arrest management (Grade E). Physicians and nurses must ensure that improvement of oxygen delivery takes precedence over infusion of buffers when facing unresolving lactic acidosis post-resuscitation.

Cardiac recommendations (Table V)

Blood pressure goals after resuscitation were set by Safar in 1986.[1] Routine insertion of an arterial line in patients with brain injury post-resuscitation is recommended to measure blood pressure, facilitate arterial blood gas sampling, follow glucose levels when using insulin infusions, and to closely monitor patients receiving therapeutic hypothermia (Grade E). In the early post-arrest period, cerebral blood flow may be significantly decreased[73–75] and the cerebral autoregulatory curve right-shifted.[76,77] Therefore, hypotension (mean arterial pressure < 80 mmHg) should be scrupulously avoided. A mean arterial pressure range of 80 to 100 mmHg is recommended in post-arrest patients, with higher pressures targeted in chronically hypertensive patients with shifted autoregulatory curves (Grade D).

Four clinical studies have shown that higher blood pressures early post-resuscitation from cardiac arrest are independently associated with good cerebral outcome, whereas lower blood pressures correlated with poor cerebral outcomes.[78–81] Only published in abstract form, the largest study reviewed the database from the multicentre Brain Resuscitation Clinical Trial III and included data from almost 3,000 cases.[78] Higher systolic arterial pressure early post-resuscitation was associated with better neurological function-

TABLE V Cardiac care recommendations

1. Rapidly measure and monitor mean arterial pressure (MAP) by inserting an arterial line.
   OVERALL EVIDENCE GRADE: E
2. Maintain normotension (MAP 80–100 mmHg; or normal for the patient) after the cardiac arrest for the first 24 hr.
   OVERALL EVIDENCE GRADE: D
3. Hypotension should be managed with vasopressors and inotropes if volume infusion is ineffective or pulmonary edema limits further administration of volume.
   OVERALL EVIDENCE GRADE: E
4. Consideration should be given to obtaining cardiac index over 2.5 $L \cdot min^{-1} \cdot m^2$ before large doses of alpha adrenergic agents are used. A pulmonary artery catheter or alternate cardiac output measurement device should be considered if large doses of vasopressors or inotropes are in use.
   OVERALL EVIDENCE GRADE: E
5. Assessment of central pressures and cardiac output should be considered if metabolic acidosis is persistent or increasing after the return of spontaneous circulation or if vasopressors or inotropes are required for more than two or three hours.
   OVERALL EVIDENCE GRADE: E
6. If there is evidence of acute coronary syndrome then anticoagulation, platelet inhibition, beta blockers, and angiography/angioplasty should be used according to the American Heart Association guidelines.
   OVERALL EVIDENCE GRADE: A
7. After the correction of electrolyte deficiencies and active ischemia, amiodarone should be used if there is recurrent non-sustained ventricular tachycardia or sustained ventricular tachycardia/fibrillation.
   OVERALL EVIDENCE GRADE: B

ing at six months even after adjusting for factors such as age, insult severity, and prior morbidity. The only fully published study concluded that good functional neurological recovery was independently and positively associated with mean arterial blood pressure over 100 mmHg during the first two hours after human cardiac arrest but not with hypertensive reperfusion within the first minutes after ROSC.[81] The management of blood pressure after resuscitation is an area where randomized controlled trials of induced hypertension in the first four hours after ROSC may help clarify appropriate blood pressure goals.

In 1992 the American Heart Association ACLS guidelines included the concept of a "cardiovascular triad" of conducting system, myocardium, and vascular system to conceptualize treatment of hypotension and shock during the first hour of resuscitation.[82] Using this approach hypotension mechanisms are: rate problems, pump problems, or volume problems. The use of repeated titrated volume infusion (250–500 mL aliquots of normal saline) followed by sympathomimetic therapy (norepinephrine, dopamine) if volume infusion is unsuccessful, is suggested for restoration of systolic blood pressure[82] (Grade E). The use of pulmonary artery catheters in ICU patients has generated controversy.[83–85] Despite this, the 2000 ACLS guidelines target systolic blood pressure over 100 mmHg and cardiac index > 2.5 $L \cdot min^{-1} \cdot m^2$ using dobutamine as the first line agent for low cardiac index once systolic blood pressure exceeds 100 mmHg.[3] Poor left ventricular (LV) function has been found during the post-resuscitation period in humans surviving out-of-hospital cardiac arrest.[86] Animal studies support the use of dobutamine to manage post-resuscitation LV systolic and diastolic dysfunction.[87] Human outcome data in post-arrest patients are lacking, but maintenance of adequate forward cardiac output with inotropic support is recommended over emphasis on blood pressure goals only (Grade E). Given positive results reported from early goal-directed hemodynamic resuscitation in septic shock,[88] similar strategies should be studied during resuscitation of patients following cardiac arrest.

Acute coronary syndrome has been studied extensively and practice guidelines established by the American College of Cardiology (ACC) and the American Heart Association (AHA) for unstable angina and non-ST segment elevation myocardial infarction were updated in 2002.[89] The ACC/AHA also published guidelines in 1999 for the management of patients with acute ST elevation myocardial infarction.[90] In addition the ACLS 2000 guidelines outline management plans for resuscitated patients with acute coronary syndromes.[91] These existing guidelines are the basis for recommendations to administer aspirin, beta blockers, and anticoagulants or other antiplatelet agents when acute coronary syndrome or myocardial infarction are diagnosed. The working group felt ACC/AHA guidelines should be followed when post-arrest patients have evidence of an acute coronary syndrome (Grade A). There is evidence supporting an immediate aggressive invasive strategy in patients resuscitated from out-of-hospital cardiac arrest.[92] Application of a standardized protocol of revascularization and electrophysiologic testing in survivors of cardiac arrest has been reported to be associated with excellent long-term outcomes.[93] One group has reported a small trial where a clinical prediction rule was evaluated to aid triage decisions about use of an invasive strategy in post-arrest patients.[94] This approach requires further validation.

Amiodarone is effective treatment of hemodynamically unstable ventricular tachycardia and ventricular fibrillation and has been recommended in the ACLS

2000 guidelines because of its broad antiarrhythmic spectrum and lesser negative inotropic effects compared to lidocaine[95] (Grade B). Implantable defibrillator insertion should be considered according to guidelines published by the ACC/AHA.[96]

GI recommendations (Table VI)

Hyperglycemia is common following resuscitation from cardiac arrest and several studies have addressed the association of blood glucose concentration and neurologic outcome in humans following cardiac arrest.[97–102] Animal studies have demonstrated that insulin treatment can reduce ischemic necrosis and modify the structural and neurobehavioural consequences of cerebral ischemia in rats.[103,104] A recent study in critically ill patients admitted to surgical ICU demonstrated significant mortality benefit when glucose levels were clamped between 4.4 to 6.1 mmol·L^{-1} using insulin infusion with administration of calories via *iv* glucose infusion or enteral/parenteral nutrition.[105] These findings suggest that hyperglycemia should be treated with insulin infusions following cardiac arrest (Grade D).

Despite the data cited above, and the common practice of treating hyperglycemia with insulin following cardiac arrest, there are no prospective randomized human trials after cardiac arrest to support this practice. The biologic plausibility of benefit from controlling hyperglycemia with insulin infusion is strong, but attempts to clamp glucose levels in the normal range (4.4–6.1 mmol·L^{-1}) with insulin infusions cannot be recommended in post-arrest patients because of the risk of hypoglycemia with this approach. A glucose target of 5 to 8 mmol·L^{-1} in post-arrest patients was accepted by conference participants, but solid data to support this range are lacking (Grade D). Recently data were published suggesting an upper glucose limit of 8 mmol·L^{-1} for mortality benefits in critically ill patients.[106] More study is needed to determine the best range for serum glucose following cardiac arrest.

Infusion of glucose containing solutions or the provision of enteral or parenteral feeding was felt to be critical to prevent hypoglycemia in post-arrest patients, particularly when insulin infusions are used (Grade E). Caution must be exercised with infusion of hypotonic solutions as animal data suggest this can worsen cerebral edema and raise intracranial pressure.[107] Indeed, hypertonic resuscitation fluids have been reviewed in trauma, head injury, and sepsis and may offer outcome advantages over isotonic solutions.[108,109]

Canadian clinical practice guidelines for nutrition support in mechanically ventilated ICU patients have been published recently.[110] These guidelines favour enteral nutrition over parenteral nutrition and suggest initiation within 24 to 48 hr after ICU admission. There are no data to suggest the Canadian guidelines should not be adhered to in the management of post-cardiac arrest patients (Grade E).

Guidelines on stress ulcer prophylaxis have been published,[111] and a large randomized controlled trial in mechanically ventilated ICU patients was completed in Canada.[112] The recommendation for H_2 blocker or sucralfate administration comes from these sources. These studies have included small numbers of post-arrest patients, but the population has multiple known risk factors for stress ulceration. Despite the lack of specific trials in post-arrest populations this recommendation was assigned evidence Grade A. Proton pump inhibitors safely and efficaciously increase gastric pH in critically ill patients, but have not demonstrated superiority over H_2 blockers or sucralfate for prophylaxis in ICU patients. Their use is suggested only as an alternate to the other agents until additional data are obtained.

TABLE VI Gastrointestinal care recommendations

1. Blood glucose levels should be controlled for the duration of the intensive care unit (ICU) stay. Blood glucose should be measured at least every four hours initially. Serum glucose should be 5 to 8 mmol·L^{-1} and insulin infusions used to rapidly achieve this range. Hyperglycemia (glucose > 8 mmol·L^{-1}) should not be tolerated.
   OVERALL EVIDENCE GRADE: D
2. Consideration should be given to administration of non-hypotonic *iv* glucose solutions (D_5NS) over the first 24 hr if insulin infusions are used unless enteral/parenteral nutrition is being delivered.
   OVERALL EVIDENCE GRADE: E
3. Enteral (preferred) or parenteral feeding should be started within 48 hr of return of spontaneous circulation.
   OVERALL EVIDENCE GRADE: E
4. Pharmacologic gastrointestinal prophylaxis should be initiated (H_2 blocker, sucralfate, or proton pump inhibitor) in ICU patients who have a coagulopathy, or who are expected to be intubated for over 48 hr. Prophylaxis may be discontinued after gastric feeds are established.
   OVERALL EVIDENCE GRADE: A

Conclusion

Each day patients are resuscitated from cardiac arrest and admitted to critical care units. Recent research has demonstrated improved outcomes with pre-arrest interventions (access to automated defibrillators),[113] intra-arrest interventions (vasopressin for asystole),[114] and

post-arrest interventions (therapeutic hypothermia).[4,5] Only time will determine if these advances result in improved outcome outside of study populations. To date studies indicate that less than 20% of patients experiencing cardiac arrest are discharged from hospital.[115]

It is possible outcomes will improve if interventions from recent studies are adopted into clinical practice. Participants at the 2003 Rocky Mountain Critical Care Conference believe post-arrest management requires examination and standardization. This was felt to be particularly important to facilitate future research in cardiac arrest patients. It is apparent that many of the basic aspects of post-arrest care have never been tested in well-designed trials. There are exciting opportunities to test interventions and management strategies in post-arrest patients, which has the potential to improve care and outcome in the future.

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