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Editorial

Resuscitation highlights in 2012

We are delighted to report that the number and quality of manuscripts submitted to *Resuscitation* continues to rise. We have summarised below some of the key papers across the full spectrum of cardiopulmonary resuscitation (CPR).

1. Epidemiology

An analysis of a nationwide registry in South Korea showed that poisonings were responsible for 4.4% of 20, 536 out-of-hospital cardiac arrest (OHCA) cases of non-cardiac aetiology.[1] Poisons included insecticides (15.5%); herbicides (13.2%); unknown pesticides (19.9%); non-pesticide drugs (16.8%); and unknown poisons (6%). The survival to admission rate was 22.5% for insecticides, 3.2% for herbicides, 16.2% for unknown pesticides, 16.7% for non-pesticides and 11.3% for the unknown poisoning cases. The survival to discharge rates was 9.9% for insecticides, 0.0% for herbicides, 2.1% for unknown pesticides, 3.3% for non-pesticides and 3.2% for the unknown group.

Cardiac arrest from a non-shockable rhythm or non-cardiac cause comprises a substantial proportion of those who survive to hospital discharge. In a study of 1001 OHCA patients who were resuscitated and discharged alive, 313/1001 (31%) had presented with a non-shockable rhythm and 210/1001 (21%) with non-cardiac aetiology.[2] Five-year survival was 43% for non-shockable rhythms compared to 73% for shockable rhythms, and 45% for non-cardiac aetiology compared to 69% for cardiac aetiology ($p < 0.001$).

It is unclear how often resuscitation is futile when applied to individuals who experience OHCA in nursing homes. Of 2350 cardiac arrests in such facilities in Melbourne, Australia from 2000 to 2009, bystander CPR had been performed in 66% and a shockable rhythm was present in 7.6% of patients on arrival of paramedics.[3] Survival was less than survival in those aged >70 years of age who had an OHCA in their own homes (1.8% vs. 4.7%, $p = 0.001$). The authors concluded that survival might be improved by basic life support (BLS) training of nursing home staff and availability of automated external defibrillators (AEDs).

Based on the theoretical protective effect of sex hormones, there is considerable interest in whether age and/or female gender are associated with survival after OHCA. An analysis of data from 29 cities in the U.S. that participate in the Cardiac Arrest Registry to Enhance Survival (CARES) program showed that although females of all ages were less likely to have a cardiac arrest in public, or one that was witnessed or treatable with defibrillation, odds of survival were higher in younger females.[4]

2. Prevention

Resuscitation continues to be a leading journal for publications related to rapid response teams (RRTs) and systems and identification of the deteriorating patient. After expansion of the medical emergency system to include a mental health facility, it was shown that the rate of Medical Emergency Team (MET) calls to this facility was similar to that of a tertiary hospital; the staff needed to manage neurological and cardiovascular problems in particular.[5]

The ANZICS-CORE MET dose Investigators studied team composition, resourcing and details of activation criteria from 39 Australian hospitals.[6] They showed significant variation in RRT composition, staff skills and activation criteria. They recommended improved resourcing of RRTs, training of the team members, and improved standardisation of calling criteria. The National Early Warning System (NEWS) was introduced into the United Kingdom (UK) in 2012. An abbreviated version of the UK-based VitalPAC EWS (ViEWS) scoring system, which is very similar to NEWS, has been validated in a Canadian hospital.[7] The abbreviated ViEWS score had comparable discrimination to the original score and had reasonable goodness of fit for most patients except for those requiring intensive care.

A retrospective study of the staffing of a RRS documented that resident-led RRS may have similar outcomes to attending intensivist-led events, prompting the suggestion of prospective studies to determine ideal team composition.[8] Optimising the different components of the RRS is critical before conclusions can be made about the efficacy of this intervention. Determining who should lead the team is one component in this.[9] It was demonstrated that medication errors are very common during medical emergencies and education and systematic changes are needed during medical emergencies to avoid harm.[10] Other authors found that observation chart design has a substantial impact on the decision accuracy and response times of health professionals and novices in recognising abnormal patient observations.[11] With increasing use of electronic systems this may become less of an issue.

The prognostic value of point-of-care measurement of biomarkers related to dyspnoea (brain natriuretic peptide (BNP), D-dimer, myoglobin, creatine kinase MB isoenzyme, and troponin I) was evaluated in patients receiving a medical emergency team (MET) review.[12] Although, BNP and D-dimer were poor discriminants of ICU admission and hospital mortality, normal BNP and D-dimer levels practically exclude subsequent need for ICU admission and hospital mortality.

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The British Thoracic Society (BTS) has published guidance for oxygen administration and recommends a target SpO_2 of 94–98% for most adult patients. Using a large dataset of routinely collected vital signs from four hospitals, SpO_2 values and mortality were analysed among 37,593 acute general medical inpatients breathing room air.[13] Mortality (95% CI) for patients with initial SpO_2 values of 97%, 96% and 95% was 3.65% (3.22–4.13); 4.47% (3.99–5.00); and 5.67% (5.03–6.38), respectively. SpO_2 ranged from 70% to 100% with a median (IQR) of 97% (95–98%). These important findings inform review of further BTS guidelines, and consideration of definitions of normal oxygen saturation, and encourage study of the impact of oxygenation on outcome. The authors have suggested that the BTS should consider changing its target saturation for actively treated patients not at risk of hypercapnic respiratory failure to 96–98%.

Applying what has been learnt from in-hospital identification of critical illness to the pre-hospital environment, it was shown that clinical judgement alone has a low sensitivity for critical illness pre-hospital, and the addition of a Modified Early Warning Score (MEWS) improved detection but at the expense of reduced specificity.[14] An optimal scoring system for identifying critical illness prehospital is awaited.

3. Defibrillation

The value of a brief period of CPR before defibrillation continues to be studied. Whether a brief period of CPR during prolonged ventricular fibrillation (VF) restores high energy phosphates in the myocardium was studied using a rat model.[15] After 4 min of untreated VF, just 2 min of CPR restored ATP levels to that of control rats not in cardiac arrest.

Using a porcine prolonged (8 min) VF model, the effect on oxygen metabolism and resuscitation outcomes of a shock-first versus strategy was compared with a CPR-first approach.[16] The shock-first strategy resulted in better oxygen metabolism and haemodynamic status, although there was no difference in the rates of ROSC or 24-h survival. These results are similar to the clinical outcomes reported in the Resuscitation Outcomes Consortium (ROC) randomised clinical trial showing no difference in survival between groups of OHCA patients treated with an early versus a late analysis of cardiac rhythm.[17]

4. Resuscitation teams

There has been a steady growth in the number of studies examining the evaluation/auditing of resuscitation team performance. Investigators have used a variety of methods to document performance ranging from direct observation[10,18] and chart review[19] downloads from CPR feedback/prompt devices,[20,21] audio recording,[22] video recording,[23,24] analysis of transthoracic impedance,[25,26] ECG signals[27] and capnography.[28] Whilst most studies that have used these data for post event debriefing have produced encouraging results, other authors recommend that given the cost of implementation, institutions should carefully consider implementation as part of a broader quality improvement programme.[29]

In addition to evaluating technical skill performance, there is growing recognition of the importance of non-technical skills such as team work, leadership, communication, co-ordination, situational awareness, leadership and decision-making.[30,31] A number of different tools have emerged that can be used to measure different domains of non-technical skills. The performance characteristics of two of the more promising tools were compared: the Observational Skill-based Clinical Assessment tool for Resuscitation (OSCAR) and the Team Emergency Assessment Measure (TEAM) both performed well with high levels of inter-observer and intra-observer agreement.[32] The TEAM score is a short, simple to use tool that measures the performance of the entire resuscitation team over 12 domains.[33] The tool is suggested as useful when a quick global perspective of resuscitation team performance is required. The OSCAR score measures individual performance in teams covering 48 assessment areas.[34] The tool is longer and more complex to use but provides information about individual team member's performance and may have a role in identifying future training needs. The Simulation Team Assessment Tool (STAT) evaluates both technical and non-technical domains.[35] Evaluation of this tool's performance characteristics found similarly good for results for overall performance, basic skills, circulation and human factors, although performed less well in the assessment of airway and breathing skills. However, as the tool has over 90 elements to assess, its use is likely to be limited to the simulation and experimental settings.

5. Quality of CPR

Important data on the quality of CPR and its relationship with outcome emerged during 2012. In a series of large, observational studies, new insights into optimal chest compression characteristics were identified. A relationship between chest compression rate and depth was identified first in a simulation study – faster chest compression rates compromised the ability to maintain adequate compression depth.[36] These findings have been verified in subsequent human studies. Among 133 patients receiving CPR for OHCA according to the European Resuscitation Council (ERC) 2005 guidelines, chest compression rates exceeding $120\,min^{-1}$ were associated with a lower compression depth (4.5 (SE 0.06) vs. 4.1 (SE 0.06), $p < 0.001$).[37] Taken together with data from the ROC study, which recruited 3098 patients in OHCA and found ROSC rates peaked at a compression rate of $125\,min^{-1}$,[38] these data reinforce the ERC basic life support guidelines that compression rate for adults should be between $100–120\,min^{-1}$.[39,40]

6. Advanced life support

6.1. Airway

The role of advanced airway techniques during CPR is controversial. Observational data from the North American ROC epistry compared tracheal intubation with one of the three supraglottic airway (SGA) devices: laryngeal tube (LT), Combitube, or laryngeal mask airway (LMA) for 10,455 OHCAs recruited to the ROC PRIMED trial.[41] Survival to hospital discharge with modified Rankin score ≤3 was: intubation 4.7%, SGA 3.9%. Successful tracheal intubation was associated with increased survival to hospital discharge (adjusted OR 1.40; 95% CI 1.04, 1.89), ROSC (adjusted OR 1.78; 95% CI 1.54, 2.04) and 24 h survival (adjusted OR 1.74; 95% CI 1.49, 2.04) when compared with successful SGA insertion. Although these results need to be interpreted with caution, they provide an impetus for a definitive study.

A study of patients in the Korean OHCA database used propensity matching to compare outcomes in patients who had tracheal intubation, bag mask ventilation or LMA insertion.[42] Overall survival to admission was 20.2% and discharge 6.9%. Adjusted outcomes using propensity-matched samples showed survival to admission and discharge were similar for tracheal intubation and bag mask. Adjusted survival to admission was similar for LMA and bag mask, but survival to discharge was significantly lower for LMA compared with bag mask.

A further question mark over the use of SGAs during CPR is whether they affect carotid blood flow. Insertion of a SGA (LTS-D, LMA Flexible, Combitube) during experimental CPR in pigs was associated with a decrease in carotid artery blood flow when compared with tracheal intubation.[43] An MRI of an anesthetised patient suggested that the AirQ SGA did not distort the carotid arteries.[44]

Skills for tracheal intubation are not available in all settings and SGAs may be a useful alternative. Intermediate level emergency medical technicians (EMTs) working in a rural prehospital setting had a 77% insertion success rate with the LTS-D.[45] In a report from the in-hospital setting, the i-gel SGA was inserted successfully by nurses and junior doctors with an 82% first attempt insertion success rate and 99% overall success rate.[46] The simplicity of i-gel use compared to other SGAs is leading to its increased use for in-hospital resuscitation whilst awaiting the arrival of an airway expert.[47]

The Japanese Emergency Airway Network recorded 1486 (502 with cardiac arrest) emergency department tracheal intubations with success rates between hospitals for first attempts of 40–83%, and with up to 3 attempts of 74–100%.[48] The overall adverse event rate was 11% and unrecognised oesophageal intubation (lapse of time and clinical deterioration such as oxygen saturation <90%) was 3.9%. A multicentre Korean registry of tracheal intubation attempts in 281 children under 10 years of age reported a first attempt success of 68%.[49] The experience of the intubator is an important determinant of successful tracheal intubation. A single-centre German study showed that experts (based on number of intubations performed and an anaesthesia background) had fewer difficult intubations, and had a far greater use of neuromuscular blocking drugs compared with 'proficient performers'.[50]

Several video laryngoscopes are now available. When compared with a Macintosh laryngoscope, the Glidescope Ranger, Storz C-MAC, Ambu Pentax AWS, Airtraq, and McGrath Series 5 video laryngoscopes were better for tracheal intubation of a manikin wearing a rigid cervical collar.[51] In a cadaver model, the Macintosh laryngoscope was superior for upper airway foreign body removal when compared with the GlideScope.[52]

6.2. Capnography

The use of waveform capnography is now recommended for identification of correct tracheal tube placement during CPR.[53] In an analysis of capnography data from 575 patients with OHCA, those with ROSC tended to have a higher end-tidal carbon dioxide ($ETCO_2$) value.[28] Patients with a respiratory cause of cardiac arrest tended to have higher $ETCO_2$ values, whereas those with pulmonary embolism tended to have lower $ETCO_2$ values. Confounders such as cause of arrest, initial rhythm, and bystander CPR affect $ETCO_2$ values and therefore limit the prognostic role of waveform capnography during CPR.

6.3. Mechanical devices

New technologies can help to elucidate pitfalls in the use of devices during resuscitation. An air-filled catheter placed inside a tracheal tube and connected to a custom-made portable device was used to measure tracheal airway pressure and calculate ventilation rate in 98 patients (57 with vs. 47 without cardiac arrest).[54] The data showed that cardiac arrest patients' lungs were ventilated at double the guideline-recommended rate. An analysis of defibrillator ECG and transthoracic impedance data in 32 patients showed that interruptions in CPR during application of a mechanical compression device are often longer than 20 s, but rescuers frequently perceive the delays to be much shorter.[25] Using continuous video and compression data on 248 patients, it was shown that a 'pit crew' protocol to application of a mechanical device reduced the application time by nearly half.[55]

6.4. Extracorporeal life support

The use of extracorporeal CPR continues to increase. During 2012, several groups of investigators documented their experience with extracorporeal CPR following in- and out-of-hospital cardiac arrest in adults and in children.[56–60]

6.5. Drugs

Several studies have questioned the role of vasopressors in cardiac arrest. An animal model showed adrenaline increased aortic pressure, cerebral and coronary perfusion pressures, while significantly decreasing carotid blood flow and $ETCO_2$.[61] A post hoc analysis of a randomised controlled trial that compared intravenous (IV) versus no IV access for OHCA assessed outcomes in 367 patients who received adrenaline and 481 who did not.[62] Although adrenaline was associated with improved survival to hospital discharge, survival with favourable neurological outcome at 1 year was worse in those receiving adrenaline. A review of 946 in- and out-of-hospital PEA and asystolic cardiac arrests from a single centre showed that a higher cumulative dose of adrenaline is independently associated with worse in-hospital survival and neurological outcome.[63] The only randomised controlled trial of adrenaline versus placebo to date showed a benefit of adrenaline in terms of ROSC but the study was underpowered to assess longer term outcomes.[64] A meta-analysis of six randomised controlled trials showed vasopressin did not differ from adrenaline in terms of improved ROSC and longer-term neurological outcomes.[65] A systematic review of 53 studies of any vasopressor in cardiac arrest also showed no differences between adrenaline and vasopressin.[66] It also suggested that adrenaline appears to have only short-term benefits. Finally a recent randomised, double-blind, multicentre trial comparing vasopressin and adrenaline (adrenaline = 353; vasopressin = 374) showed no difference between groups for survival to hospital discharge.[67] It appears that the optimal role of adrenaline in cardiac arrest will remain unknown until defined by the results of an appropriately powered, placebo-controlled trial.

Data from the North American ROC investigators showed wide variability in the use of drugs during CPR among different EMS systems.[68] A total of 16,221 OHCAs were attended by 74 EMS. Adrenaline use ranged from 57 to 98% within agencies. Use of lidocaine or amiodarone was not associated with a survival benefit, while there was an inverse relationship associated with adrenaline, atropine and sodium bicarbonate use and survival to hospital discharge.

Animal studies suggest beta-blockers may be beneficial in VF cardiac arrest as they reduce myocardial oxygen use, the number of defibrillation attempts needed, improve post resuscitation myocardial function and recurrent arrhythmias, and prolong survival, but good quality human studies are lacking.[69]

Large well designed studies that include high-quality CPR with minimal interruptions for shocks, and a standardised approach to post resuscitation care and prognostication are needed to assess whether drugs have an added benefit during CPR.[70] Another view is that those patients with little or no chance of survival should be excluded from future studies – 'in future CPR trials, inclusion and exclusion criteria need to ensure that ALS drugs get the chance that they deserve'.[71]

6.6. Intraosseous access

There is a growing interest in the use of the intraosseous route in adults during CPR as studies suggest it is a viable alternative to intravenous access. A systemic review identified low level studies which suggested battery operated insertion devices performed better than manually inserted intraosseous needles.[72] Intraosseous access was much quicker to achieve then central venous access in patients in whom peripheral venous access was not possible.[73] In a pig cardiac arrest model, intraosseous access by both tibial and sternal routes was effective, although adrenaline bioavailability was greater with sternal access.[74] Intravenous access and drugs can cause tissue necrosis. The same complication was described two days after adrenaline and thrombolysis given by the tibial intraosseous route during cardiac arrest despite early removal of the intraosseous needle.[75,76] Animal data indicate that electrolyte measurements of blood taken via intraosseous needles are similar to arterial blood values measured with a handheld cartridge analyser.[77]

6.7. Trauma

Resuscitation with haemoglobin-based oxygen carriers (HBOCs) is appealing but safety and effectiveness are still to be demonstrated. The current status of products under development and those that have completed phase three clinical trials were reviewed recently.[78] Transfusion practices are inconsistent and it is unknown if some practices improve survival. The PRospective Observational Multicenter Major Trauma Transfusion (PROMMTT) study enrolled 1245 trauma patients admitted to ten Level 1 trauma centres in the US; 297 received massive transfusions.[79] The collaboration has demonstrated the feasibility of prospective trauma transfusion studies and the observational data collected are a valuable resource for research in trauma to guide future randomised trials.

Two studies from Melbourne, Australia documented the epidemiology and outcome from traumatic cardiac arrest in adults and children.[80,81] Resuscitation for traumatic OHCA is often considered futile and, disappointingly, their data for children support that conclusion. For adults in this paramedic-based EMS system, resuscitation resulted in a survival of 5% but the quality of survival needs more study. While the role of resuscitative thoracotomy is established in adult traumatic cardiac arrest, its role in paediatric trauma is unclear. In one study, the authors concluded that emergent thoracotomy is a potentially life-saving procedure (10% survived to hospital discharge) for children following traumatic cardiac arrest from penetrating trauma to the heart; no blunt trauma patients survived.[82]

A systolic blood pressure (SBP) of 90 mmHg is often used as the threshold for prioritising penetrating trauma patients, but data from the Trauma Audit and Research Network (TARN) between 2000 and 2009 indicated that a SBP of <110 mmHg was associated with increased mortality and should be used as the triage threshold for these patients.[83]

6.8. Drowning

Drowning is the third leading cause of accidental death in the world and survival rates after cardiac arrest from drowning are particularly poor.[84] Data from 250 cardiac arrests due to drowning in Sweden showed very poor one-month survival rates despite short rescue times[85]; in contrast, much better outcomes were achieved among young individuals who had cardiac arrest from submersion accidental hypothermia and who were treated with extracorporeal circulation support, controlled temperature management and intensive neurorehabilitation.[86]

7. Post resuscitation care

7.1. Post cardiac arrest syndrome

The pathophysiology of the post cardiac arrest syndrome (PCAS) continues to be investigated. The endothelial glycocalyx is known to modulate vascular permeability and inflammation. In 25 post cardiac arrest patients, plasma levels of the glycocalyx components syndecan-1, heparan sulfate and hyaluronic acid increased compared with controls. This implies that shedding of the endothelial glycocalyx is a pathophysiological component of the PCAS.[87] Coenzyme Q_{10} (ubiquinone) is a component of the mitochondrial electron transport chain and improved survival when given to post cardiac arrest patients in a pilot study.[88] In a study of 23 post cardiac arrest patients, coenzyme Q_{10} values were lower than those in healthy controls and were associated with increased mortality.[89] A large placebo-controlled study of coenzyme Q_{10} after cardiac arrest is needed.

7.2. Hypothermia

Therapeutic hypothermia (TH) continues to be the most extensively investigated intervention in the PCAS. Cooling is easily initiated by infusing ice-cold crystalloid but the authors of a review on this topic conclude that this therapy remains poorly implemented.[90] It is thought that better outcomes can be achieved with earlier cooling but this hypothesis as yet proven in clinical studies. In an observational study of 172 post cardiac arrest patients, the adjusted odds of a poor neurological outcome at discharge follow up increased with each 5 min delay in initiating cooling (OR = 1.08, 95% CI 1.03–1.13) and with every 30 min delay in time to target temperature (OR = 1.17, 95% CI 1.01–1.36).[91] In contrast, preliminary observations from 17 Italian intensive care units showed that mortality was higher in those patients in whom cooling was started within 2 h of cardiac arrest compared with those in whom cooling was started later.[92] There were likely to be have been hidden confounders but further research is clearly required. One explanation for the difficulty in showing a consistent relationship between time to target temperature and outcome is that impaired temperature regulation may reflect post resuscitation neurological injury. In a study of 177 post cardiac arrest patients treated with TH, lower spontaneous admission body temperature and longer time of passive rewarming were associated with increased in-hospital mortality.[93]

In a retrospective cohort study of 1200 OHCA patients remaining comatose after ROSC, the beneficial effect of TH ($n = 598$) correlated with no-flow time. The maximum benefit of TH was documented in those with no-flow times longer than 8 min (OR 6.15; 95% CI 2.23–16.99).[94]

Acute kidney injury (AKI) is common after cardiac arrest but its incidence is not well documented using modern RIFLE (risk, injury, failure, loss, end stage) criteria.[95] Among 105 post cardiac arrest patients admitted to an intensive care unit (ICU) in Australia, one-third developed RIFLE I/F AKI and of those with cardiogenic shock, half developed RIFLE I/F AKI.[96] In a systematic review of 19 trials that documented kidney endpoints, TH did not prevent AKI or the requirement for dialysis, but was associated with lower mortality.[97]

The benefit of TH for comatose survivors of cardiac arrest with non-shockable initial rhythms remains uncertain. A systematic review of TH after non-shockable rhythm cardiac arrest identified two randomised and twelve non-randomised studies.[98] The authors concluded that TH is associated with reduced in-hospital mortality for adult patients resuscitated from non-shockable CA, but that most of the studies had substantial risks of bias and the quality of evidence was very low. An additional single centre observational study of non-shockable rhythm post arrest patients ($n = 100$) not included in this meta-analysis documented an adjusted odds ratio for survival to discharge from the hospital with TH compared with controls of 5.65 (CI 1.66–19.23, $p = 0.006$) respectively.[99]

Current consensus is to rewarm slowly (0.25–0.5 $^\circ$C h^{-1}) after TH and to avoid fever. In a retrospective cohort study of 128 post cardiac arrest patients, the patients who needed active rewarming did not have a worse outcome.[100] Neither the speed of rewarming nor the development of fever had an effect on outcome.

Accurate temperature control during cooling is essential to prevent cooling-related side effects. The optimal site of temperature measurement during TH remains controversial. In a prospective observational study of 12 patients assessed during intravascular cooling following cardiac arrest, both nasopharyngeal and urinary bladder temperature measurements were similar to blood temperatures measured using a pulmonary artery catheter.[101]

The mechanism by which TH improves neurological outcome continues to be investigated. A study using a rat cardiac arrest model showed that post cardiac arrest TH protects selectively vulnerable cerebellar Purkinje cells even when initiation of cooling was delayed to 8 h.[102]

Although most research on TH focuses on its neurological effects, it also has significant effects on the cardiovascular system. Other than the bradycardia that usually accompanies TH, and which is probably beneficial, there are no additional risks of arrhythmias.[103] In a pig model of VF cardiac arrest, TH attenuated histological myocardial injury.[104] In a pig myocardial infarction model, TH did not potentiate diastolic LV failure, but stabilised haemodynamics and improved systemic oxygen supply/demand imbalance by reducing demand.[105] In contrast, in a sheep model, TH was associated with decreased ventricular function, oxygen extraction and microvascular flow compared to normothermia;[106] these changes were associated with increased blood lactate values. The authors suggest that TH may impair tissue oxygen delivery through maldistribution of capillary flow.

The 2008 International Liaison Committee on Resuscitation (ILCOR)/American Heart Association (AHA) Consensus Statement for the treatment of PCAS suggests that goal-directed therapy, targeting mean arterial pressure (MAP), central venous pressure (CVP), and central venous oxygen saturation ($ScvO_2$), should be used to optimise oxygen delivery.[107] A review of 44 implementation studies showed that only one-third specified at least one haemodynamic goal. The authors conclude that an explicit description of haemodynamic goals should be provided in future studies.[108]

7.3. Hyperoxia

The effect of hyperoxia following cardiac arrest remains uncertain. In a meta-analysis of six animal studies ($n = 95$), treatment with 100% oxygen resulted in a significantly worse neurological deficit score than oxygen administered at lower concentrations, with a standardised mean difference of −0.64 (95% CI −1.06 to −0.22).[109] However, the authors conclude that the poor generalisability of animal models to human cardiac arrest makes the clinical applicability of these data uncertain. In study of 223 children who had been resuscitated after in-hospital cardiac arrest, hyperoxaemia after ROSC or 24 h later was not associated with mortality; however, hypercapnia and hypocapnia were associated with higher mortality than normocapnia.[110]

7.4. Cerebral oxygenation

Cerebral oxygenation measured using near infrared spectroscopy (NIRS) is being evaluated by several investigators during and after cardiac arrest. Regional cerebral oximetry (rSO_2) was evaluated during CPR in 19 patients; the 5 patients achieving ROSC had significantly higher mean rSO_2 values than those not achieving ROSC.[111] Cerebral oximetry may have a role in predicting ROSC in cardiac arrest and is undergoing further evaluation. This technology could provide real-time feedback on the quality of CPR – better CPR should result in higher rSO_2 values. This hypothesis was investigated in 9 patients with in-hospital cardiac arrest but unfortunately high quality CPR was not reflected significantly by an increase in rSO_2 values.[112] In another study, rSO_2 values were measured in 92 patients admitted to hospital in Japan after OHCA and were correlated with outcome.[113] Sixty-one patients with $rSO_2 \leq 25\%$ showed poor neurological outcome in the receiver operating curve analysis (optimal cut-off point 25%; sensitivity 0.772; specificity 1.000; positive predictive value 1.000; area under the curve (AUC) 0.919; $p < 0.0001$).

7.5. Coronary revascularisation

Acute coronary angiography with percutaneous coronary intervention (PCI) is becoming a standard of care for patients with ROSC after OHCA and who do not have an obvious non-cardiac cause for their cardiac arrest. A systematic review of acute coronary angiography in patients resuscitated from OHCA identified no randomised controlled trials, 10 non-randomised cohort studies and 22 case series without controls.[114] The 10 comparison studies demonstrated a pooled unadjusted odds ratio for survival of 2.78 (95% CI 1.89–4.10) favouring acute coronary angiography. However, a further small study ($n = 70$) from Australia did not show a survival advantage for out-of-hospital VF/pVT cardiac arrest patients undergoing immediate coronary angiography +/− PCI compared with those admitted directly to the ICU.[115] The PROCAT (Parisian Region Out of Hospital Cardiac Arrest) investigators have shown that among 896 OHCA patients, the use of an early diagnosis protocol with immediate coronary angiography and/or CT scan identified the cause of cardiac arrest in nearly two-third of cases.[116]

8. Prognostication

Prognostication in the comatose cardiac arrest survivor continues to be challenging and has been made potentially more difficult following widespread implementation of TH. A review of the history of prognostication in anoxic–ischaemic coma[117] provides valuable background and sets the scene for eagerly anticipated revised guidelines.

In a retrospective analysis of 38 comatose PCAS patients treated with TH and continuous EEG monitoring (cEEG), 9 (23%) had electrographic seizures and 17 (48%) had evidence of epileptiform activity (electrographic seizures or interictal epileptiform discharges).[118] Most seizures started before rewarming and evolved from prior interictal epileptiform activity. Ninety-four percent (16/17) of patients with epileptiform activity had poor neurological outcome or death at discharge. Early myoclonus in comatose survivors of cardiac arrest is considered a sign of severe global brain ischaemia and has been associated with high rates of mortality and poor neurological outcomes. In contrast, is a report on three cardiac arrest patients treated with TH who had good neurological outcomes (two patients with a CPC score = 1 and one patient with a CPC score = 2), despite showing massive myoclonus within the first 4 h after ROSC.[119] The authors conclude that early myoclonus may not imply a uniformly poor prognosis in patients treated with TH.

Prediction of the ultimate outcome of individual patients early after ROSC would be very valuable but is currently considered too unreliable. Investigators from Japan have proposed a seven-point score (5-R score: arrest-to-first CPR interval ≤ 5 min, VF/pVT, absence of re-arrest before leaving the emergency department, time to ROSC ≤ 30 min and recovery of pupillary light reflex), which can be used in the emergency department to predict ultimate outcome in patients undergoing TH.[120] A score of ≥5 predicted good neurological outcome with a sensitivity of 82.5% (95% confidence interval [CI], 67.2–92.7%) and specificity of 92.3% (95% CI, 74.9–99.1%).

In a pilot study from Japan, high concentrations of high mobility group box 1 (HMGB1) and S100B in cerebrospinal fluid (CSF), and S100B in serum were associated with neurologically poor outcome in 25 OHCA patients.[121] In another study from Japan, investigators evaluated early CT scans using the modified Alberta stroke programme early CT (m-ASPECT) score and showed it to be good predictor of poor outcome (CPC 4 or 5) with an AUC of 0.905.[122]

The APACHE III and the OHCA score were not particularly good at predicting outcome among 123 patients treated in an Australian ICU following out-of-hospital, in-hospital or ICU cardiac arrest.[123] The OHCA score performed with moderate accuracy for predicting 30-day mortality (AUC 0.77 [0.69–0.86] and was slightly better than the APACHE III score 0.71 (0.61–0.80).

9. Cardiac arrest centres

There is a trend towards treating post cardiac arrest patients in cardiac arrest centres that can provide 24/7 cardiac catheterisation and that treat large numbers of such patients. Whether this results in better outcomes is unproven. In a Korean study of 27,662 OHCA patients without prehospital ROSC, a higher rate of survival to discharge was documented among patients who were transported to high-volume (4.78%) rather than low-volume centres (1.43%).[124] The rate was still significantly higher when the transportation time was longer compared with that of low-volume centres. The relationship between receiving hospital emergency department volume of cases and survival from OHCA of non-cardiac aetiology was explored in another study from Korea.[125] There were 10,425 eligible patients (trauma 5735; drowning 98; poisoning 684; asphyxia 1413; and hanging 1605) in their national OHCA database. Overall survival to admission and hospital discharge rates in this cohort were 9.6% and 2.4%, respectively. The authors found that a greater annual volume of OHCA cases treated in a hospital emergency department was associated with higher survival to admission and hospital discharge.

In contrast to the findings from these Korean studies, an analysis of the United States CARES database showed that survival varied substantially across but hospital OHCA volume was not associated with likelihood of survival.[126]

Conflict of interest statement

JPN is Editor-in-Chief of Resuscitation. GDP, JPO, MJAP and JS are Editors of Resuscitation. JO is on the Science Advisory Board for ZOLL Circulation and serves as Cardiac Co-Chair for the National Institutes of Health-sponsored Resuscitation Outcomes Consortium (ROC). He serves as the Virginia Commonwealth University Principal Investigator for the National Institutes of Health-sponsored Neurological Emergency Treatment Trials Network (NETT). JS is Co-Chair of the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation.

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