The impact of prehospital resuscitation research on in-hospital care

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ABSTRACT
Since their introduction over 40 years ago, paramedics have been trained to deliver select advanced life support interventions in the community with the goal of reducing morbidity and mortality from cardiovascular disease and trauma. The ensuing decades witnessed a great deal of interest in paramedic care, with an exponential growth in prehospital resuscitation research. As part of the CJEM series on emergency medical services (EMS), we review recent prehospital research in out-of-hospital cardiac arrest and discuss how, in a novel departure from the origins of EMS, prehospital research is beginning to influence in-hospital care. We discuss emerging areas of study related to cardiopulmonary resuscitation (CPR) quality, therapeutic hypothermia, termination of resuscitation, and the use of end-tidal carbon dioxide measurement, as well as the subtle ripple effects that prehospital research is having on the broader understanding of the management of these critically ill patients.

RÉSUMÉ
Depuis leur arrivée il y a plus d’une quarantaine d’années, les ambulanciers paramédicaux sont formés pour pratiquer certaines interventions de réanimation cardior-espiratoire (RCR) médicalisée dans la collectivité dans le but de réduire la morbidité et la mortalité liées aux maladies cardiovasculaires et aux traumatismes. Au cours des décennies suivantes, les soins paramédicaux ont suscité un vif intérêt, qui s’est accompagné d’une forte croissance de la recherche en réanimation prémédicalisée. Dans le cadre de la série d’articles portant sur les services médicaux d’urgence (SMU) dans le JCMU, il sera question de la recherche récente sur la prise en charge prémédicalière des arrêts cardiaques qui surviennent dans la collectivité ainsi que de l’influence que commence à avoir la recherche dans le domaine prémédicalier sur les soins hospitaliers, influence qui signe une nouvelle orientation par rapport au point de départ des SMU. L’article portera sur de nouveaux champs d’étude liés à la qualité de la RCR, à l’hypothermie thérapeutique, à l’arrêt des manœuvres de réanimation et à l’utilisation de la mesure du gaz carbonique en fin d’expiration ainsi que sur les effets d’entraînement discrets que la recherche dans le domaine prémédicalier a sur la compréhension élargie du traitement des personnes gravement malades ou blessées.

Keywords: Emergency Medical Services, Paramedic, Cardiac Arrest, Resuscitation, CPR

INTRODUCTION
The provision of out-of-hospital care by paramedics first began in North America over 40 years ago with emergency medical technicians (EMTs) trained to deliver selected advanced life support (ALS) interventions in the community. The interventions selected for use in the prehospital environment were chosen based on their efficacy in the in-hospital setting with the assumption that the extension of select skills (e.g., endotracheal intubation, defibrillation, intravenous medication administration) in the prehospital setting would reduce mortality from cardiovascular disease and trauma. Currently, the effectiveness and safety of these interventions are subject to increasing scrutiny because there is a growing demand in emergency medical services (EMS) for interventions that have a measurable impact on survival. Medical directors and

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© Canadian Association of Emergency Physicians CJEM 2015;17(5):551-557 DOI 10.1017/cem.2015.84
EMS stakeholders have become more circumspect regarding the therapies currently employed by paramedics. Furthermore, as prehospital resuscitation science continues to evolve, several time-critical medical conditions (e.g., out-of-hospital cardiac arrest [OHCA], ST elevation myocardial infarction [STEMI], stroke and multisystem trauma) are increasingly being re-conceptualized to allow for assessment, stabilization, and treatment in the prehospital domain. This shift in thinking—conceptualizing critical components of care during the prehospital phase of a patient’s illness as part of a comprehensive care model—represents a substantial departure from the origins of EMS. Nowhere has this shift been more apparent than the prehospital management of OHCA. As part of the CJEM series on EMS, we review recent sentinel prehospital research in OHCA and discuss how, in a novel departure from the origins of EMS, prehospital research is beginning to influence in-hospital care.

CPR QUALITY

The 2010 American Heart Association (AHA) guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiac care (ECC) emphasize the importance of high quality CPR for victims of sudden cardiac arrest. Previous work has demonstrated that victims of OHCA may be sensitive to changes in CPR techniques. A recent consensus statement by the AHA stressed the importance of improving CPR quality and measuring key CPR metrics as part of a continuous quality improvement methodology to reduce preventable deaths from cardiac arrest. The following highlights the key components of the consensus statement.

Compression rate and depth

The 2010 AHA guidelines recommend a chest compression rate between 100 and 120 compressions per minute at a depth of at least 5 cm. Several studies have examined the relationship between chest compression rate, compression depth, and survival. A meta-analysis by Wallace et al. found that survival was improved with chest compression depths of at least 51 mm and compression rates between 85 and 100 compressions per minute. Vadeboncoeur et al. conducted an observational study examining the influence of an educational intervention on high quality CPR and its impact on neurologically intact survival from OHCA and found that chest compressions with a depth of at least 51 mm were independently associated with survival from cardiac arrest with a favourable neurologic outcome.

Chest compression fraction

Chest compression fraction (CCF), defined as the proportion of time that chest compressions are being delivered during resuscitation, has been shown to influence outcomes from cardiac arrest. The 2013 consensus statement by the AHA recommends a CCF of at least 80%. Previous work by Christenson et al. provided evidence to suggest that patients with an initial rhythm of ventricular fibrillation or ventricular tachycardia who had higher CCF (>61%) were more likely to achieve return of spontaneous circulation (ROSC) and survive to hospital discharge. Vaillancourt et al. conducted a similar investigation on the effects of CCF on patients with a presenting rhythm of asystole or pulseless electrical activity and found that patients with CCFs greater than 81% had the highest probability of obtaining ROSC.

Peri-shock pause

Maximizing CCF requires careful coordination to minimize interruptions in CPR. Airway management, insertion of intravenous lines, patient movement and defibrillation are notorious (albeit sometimes necessary) culprits of interrupted CPR. Although the organization of resources and teamwork may eliminate some sources of interrupted CPR, chest compressions must be paused to allow for safe defibrillation; these interruptions have been the subject of recent study. Pre-shock pause (the time from the last chest compression to the application of defibrillation energy), post-shock pause (the time from defibrillation until the resumption of chest compressions), and peri-shock pause (the sum of pre- and post-shock pauses) represent modifiable metrics with important influences on survival from cardiac arrest.

Kramer-Johansen described the influence of defibrillator mode (e.g., automated or manual) on peri-shock pause in both out-of-hospital and in-hospital cardiac arrest patients and found that using defibrillators in automatic mode resulted in significantly longer peri-shock pauses (13.5 seconds v. 8.0 seconds). The authors reported that manual defibrillation attempts were more likely to successfully convert ventricular fibrillation than those occurring in automatic mode. Research by Cheskes et al. found that among patients in the Resuscitation Outcomes Consortium (ROC), pre-shock and peri-shock
pauses were independently associated with survival from cardiac arrest. With every 5-second increase in pre- and peri-shock pause, the probability of survival was reduced by 18% and 14%, respectively.\textsuperscript{18,19}

These components of CPR quality are not only highlighted as benchmarks for prehospital resuscitation, but also are increasingly becoming standards to which in-hospital resuscitation should strive. In an attempt to improve adherence to evidence-based care of patients who sustain cardiac arrest, the AHA developed a quality improvement program known as Get with the Guidelines—Resuscitation.\textsuperscript{20} This program collects data on cardiac arrest performance for hospitals across the United States and provides feedback on resuscitation practice and performance with the aim of providing a robust registry, real-time benchmarking and performance improvement methodologies that ultimately will enhance patient outcomes. Many Canadian EMS systems regularly collect data on out-of-hospital CPR quality, but no system currently exists in Canada to consistently measure in-hospital CPR quality, missing a golden opportunity to improve resuscitation practices and patient outcomes.

These distinct components of CPR represent amendable factors that can be targeted to improve survival from cardiac arrest. Owing in part to the logistical challenges of the prehospital environment, emphasizing high quality CPR has led to novel strategies for optimizing the consistency and effectiveness of chest compressions, including mechanical CPR devices and the use of defibrillators that provide real-time feedback on CPR quality.

**Mechanical CPR**

Rescuer fatigue due to prolonged CPR has a deleterious effect on CPR quality.\textsuperscript{5} It is intuitive that mechanical devices should provide superior CPR quality compared to human rescuers as length of resuscitation increases, particularly when the number of available rescuers is limited. Recent randomized controlled trials regarding the effectiveness of different mechanical CPR devices on neurologically intact survival after cardiac arrest have shown similar CPR quality metrics when compared to manual CPR\textsuperscript{21–23} but no improvements in clinical outcomes. Some EMS systems have adopted the view that mechanical CPR devices improve paramedic safety while transporting victims of cardiac arrest to the hospital. Mechanical CPR devices are seen as a means to relieve EMS providers of the hazardous duty of performing CPR in a moving ambulance, allowing them to remain restrained during transportation. In the in-hospital setting, mechanical CPR devices are being studied as a means of providing high quality CPR as well as continuous chest compressions for prolonged or refractory cardiac arrests. It would seem intuitive that mechanical CPR may be employed on arrival to the emergency department, freeing up staff to manage the variety of challenges of airway management and drug therapy during cardiac arrest while ensuring ongoing high quality CPR. As survival from OHCA improves, subsets of patients who do not respond to traditional therapies (but have characteristics predictive of a favourable neurologic course) are candidates for increasingly complex resuscitation regimens. Such therapies include percutaneous coronary intervention for patients with STEMI prior to cardiac arrest and the use of extracorporeal membrane oxygenation\textsuperscript{24,25}; both treatments require continuous chest compressions as a bridge to definitive therapy. In these situations, prolonged high quality CPR may be optimally delivered using mechanical CPR devices.

**CPR feedback**

Given the importance of CPR quality in improving outcomes from cardiac arrest, a logical solution is to integrate real-time CPR feedback to guide provider performance during resuscitation. A meta-analysis by Kirkbright et al. was the first to examine the relationship between the use of real-time CPR feedback on survival from cardiac arrest.\textsuperscript{26} The authors noted that, although there was evidence to suggest that CPR metrics (compression rate, depth, CCF, etc.) improved with the use of real-time CPR feedback, a causal relationship between CPR feedback and survival could not be established. Of the studies included in the systematic review, only one randomized trial was powered to detect neurologically intact survival to discharge,\textsuperscript{27} while one study reported observational evidence suggesting improved outcomes with real-time CPR feedback.\textsuperscript{28} The highlighted research would seem to suggest that CPR feedback may not be sufficient in and of itself to overcome system (EMS response time, bystander CPR, bystander witnessed status, public v. private location of arrest) and patient characteristics (i.e., presenting rhythm, age gender) in determining patient survival. Can real-time CPR feedback improve manual CPR quality in the emergency department setting? Crowe et al. were...
able to demonstrate improvements in CPR quality (i.e., compression depth and recoil) as well as improved adherence to CPR quality benchmarks after implementing staff training complemented by real-time CPR feedback in a large urban emergency department. Although it may not be a panacea, preliminary findings suggest that CPR feedback technology may improve CPR rescuer performance.

**Choreography of cardiac arrest resuscitation**

High quality CPR within a comprehensive resuscitation strategy hinges on the ability of the team to incorporate several therapies simultaneously. High performing EMS systems that consistently meet CPR quality benchmarks do so by minimizing interruptions in CPR through the carefully timed integration of manual (as opposed to automated) defibrillation, minimizing patient movement, deferring airway management and intravenous cannulation, rotating chest compressors frequently, and using real-time CPR feedback to guide resuscitative efforts. Interestingly, survival appears to be sensitive to changes in resuscitation practice beyond simply optimizing technical skill (e.g., CPR) performance. Non-technical skills (e.g., leadership, scene organization, communication) appear to play a role in overall team performance. Meaney et al. highlighted the importance of resuscitation team composition, feedback, and leadership during cardiac arrest resuscitation.9 Research on leadership training and team behaviour illustrates the influential role of team performance not only on CPR quality, but also on the overall quality of the resuscitation.30-33 The TOPCAT series of trials hinted at the potentially important role that non-technical skills play during cardiac arrest resuscitations. TOPCAT2 was able to demonstrate that increasing the number of responders to cardiac arrests, having a second-tier expert (resuscitationist) (a paramedic specifically trained in cardiac resuscitation techniques and oversight) attend, and providing team members with feedback following cardiac arrest cases showed a trend toward increased ROSC rates and survival. This “pit crew” approach to resuscitation has gained traction as awareness of the importance of team dynamics and coordination increases.

**TERMINATION OF RESUSCITATION**

Termination of resuscitation is perhaps the most challenging decision faced by those in the prehospital setting. Morrison et al. were able to develop a decision rule wherein patients who had sustained an unwitnessed cardiac arrest could be predicted to have 100% mortality. This decision rule provided the first scientifically validated evidence to guide prehospital providers as to when it is safe to terminate resuscitation. Similar rules to terminate in-hospital resuscitation do not exist, yet these prehospital derived rules may serve as a guideline for termination of the unwitnessed in-hospital cardiac arrest resuscitation. Although validated in many jurisdictions, termination of resuscitation rules are now coming under increased scrutiny as a result of improvements in CPR quality since the publication of the 2010 AHA/International Liaison Committee on Resuscitation (ILCOR) guidelines. Further studies validating the decision rules in patients receiving high quality CPR and newer resuscitative strategies may be extremely informative.

**THERAPEUTIC HYPOTHERMIA**

The Hypothermia After Cardiac Arrest (HACA) group and Bernard et al. published the first randomized trials of therapeutic hypothermia for comatose survivors of cardiac arrest. The promising results sparked an explosion of interest in the use of therapeutic hypothermia over the following decade as researchers attempted to better define the target populations, ideal temperatures, and most effective cooling strategies. Despite the unknowns, therapeutic hypothermia was swiftly adopted as a class 1 recommendation for post-arrest care in the AHA guidelines. Several challenges were identified with therapeutic hypothermia, including the implementation of the therapy in-hospital. Despite the AHA guideline recommendation, only a fraction of eligible patients were being cooled in hospital emergency departments and intensive care units. Directly or indirectly, this led to an increased emphasis on EMS initiation of cooling in the field immediately following ROSC. Recently, the conversation around the optimal use of therapeutic hypothermia has intensified with two large randomized trials failing to show a survival advantage for cooled patients. Nielsen et al. examined the influence of cooling post-arrest patients to 36°C (96.8°F) instead of 33°C (91.4°F) and noted that survival was similar between groups. Kim et al. examined the influence of immediate cooling after ROSC by EMS providers. Although patients cooled in the field achieved a target temperature of 34°C (93.2°F) faster, prehospital...
cooling failed to confer a survival benefit, and cooled patients were more likely to experience a subsequent cardiac arrest with EMS.\textsuperscript{57} The results of these two studies have further magnified the confusion and controversy surrounding therapeutic hypothermia. \textit{Whom should we cool? To what temperature should we cool? How long should we cool? When should we terminate resuscitation after an adequate trial of cooling?} It appears that the findings of these prehospital research trials have sparked more confusion than clarity around the in-hospital care of this subset of patients. Further study on the novel technique of intra-arrest cooling and the optimal use of targeted temperature management is required to better understand the impact of therapeutic hypothermia on neurologically intact survival from OHCA.

END-TIDAL CARBON DIOXIDE

The routine monitoring of end-tidal carbon dioxide (ETCo2) was driven primarily by the concerning rates of unrecognized esophageal intubation reported in studies of prehospital endotracheal intubation.\textsuperscript{58-61} Carbon dioxide measurement was seen as a viable method to definitively confirm correct endotracheal tube placement after intubation and is now a mainstay of prehospital airway management. However, its usefulness has extended beyond a simple dichotomous check of endotracheal tube placement.

ETCo2 has been found to be positively correlated with arterial concentrations of carbon dioxide and is increasingly being used as a surrogate of cardiovascular perfusion in critically ill patients. During cardiac arrest, ETCo2 is recommended as an adjunct to detect ROSC, guide CPR quality, and prognosticate the probability of survival of cardiac arrest victims.\textsuperscript{4,8,62} OHCA management now employs ETCo2 as part of a provider CPR feedback bundle on many commonly used defibrillators so that both CPR quality metrics and “real-time” ETCo2 can be monitored simultaneously during the resuscitation. ETCo2, when employed with recently developed CPR filtering software (which allows for the removal of CPR artifact during ongoing chest compressions),\textsuperscript{63} provides paramedics with the earliest signal to a successful resuscitation, often prior to the actual finding of palpable pulses. Little is known regarding the use of ETCo2 and advanced CPR software during in-hospital resuscitations, but, certainly, the prehospital experience would suggest their use may evolve in the near future.

CONCLUSION

Prehospital research in CPR has driven a great deal of change in resuscitation management and has led to improvements in patient outcomes. The translation of this change in practice to the in-hospital setting remains a goal for many. The terms \textit{in-hospital} and \textit{out-of-hospital cardiac arrest} are ubiquitous within resuscitation research. This nomenclature is not divisive; rather, it recognizes the specialized nature of each setting with a goal of improving outcomes from cardiac arrest through high quality CPR in either practice setting.

Competing interests: Within the last two years, Dr. Cheskes has received speaker honoraria from Zoll Medical and has participated as a member of the advisory board for Astra Zeneca.

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