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Editorial

EtCO2 measurement during pediatric cardiac arrest: Does the Emperor have no clothes?

More than 40 years have passed since the first description of end-tidal CO2 (EtCO2) monitoring of cardiac output during CPR (cardio-pulmonary resuscitation) [1]. Soon thereafter, EtCO2 was suggested as a metric for chest compression (CC) quality [2], an early marker of return of spontaneous circulation (ROSC) [3], and by which the likelihood of successful resuscitation might be predicted [4]. Major CPR guidelines organizations now recommend capnography during resuscitation [5,6]. Recent systematic reviews suggest, however, that using specific EtCO2 values to guide patient care during adult cardiac arrest is based upon low quality evidence [7,8]. EtCO2 may vary widely due to other confounders, including cardiac arrest etiology (asphyxial vs. cardiac), the use of certain resuscitation drugs (epinephrine or sodium bicarbonate), underlying pulmonary pathology, or the minute volume delivered during ventilation by rescuers. Research into capnography's role during pediatric cardiac arrest is even more limited, and the quality of the literature universally low. Despite some preclinical evidence and case reports suggesting that EtCO2 levels correlate with CPR-quality [9,10], other bench studies [11] and now Berg's study potentially suggest otherwise. While researchers continue to debate what EtCO2 cut-offs should be in CPR guidelines, rescuers are left without reliable values with which to guide treatment.

Berg's study [12] is the first multicenter study to research capnography's uses and potential limitations during pediatric cardiac arrest care. It is a prospective Intensive Care Unit CPR multicenter cohort examination of the associations between measured EtCO2 during resuscitation with specific outcomes measures. All children aged between 37 week's gestation up to 18 years of age were eligible for inclusion; each child had chest compressions for 1 min or longer, and to have capnography prior to, and during CPR. The enrollment period was between July 2013 to June 2016 in 11 institutions, with additional measurements being recorded: central venous pressure, respiratory plethysmography, arterial BP or ECG to determine the start and stop of CPR. Other exclusions were congenital cardiac conditions e.g. hypoplastic left heart syndrome (including pre-operative patients, Post Norwood with modified Blalock-Taussig shunt or Sano modification, post bi-directional Glenn). However, other cardiac conditions in which CPR might effect pulmonary circulation were not excluded.

The primary hypothesis was that a mean EtCO2 of greater than 20 mmHg was associated with survival to hospital discharge, with secondary hypotheses that EtCO2 greater 20 mmHg was associated with ROSC, EtCO2 < 10 mmHg of CPR precludes ROSC and that a mean value of EtCO2 during CPR is associated with ROSC and survival to hospital discharge. Data was collected included patient factors, arrest characteristics and outcome data, with Pediatric Cerebral Performance Categories (PCPC) available pre-arrest being used; a hospital discharge with favorable neurological outcome was PCPC between 1 to 3. The conclusion was that children with mean EtCO2 > 20 mmHg were not more likely to be discharged from hospital or attain ROSC; the same findings for EtCO2 of < 10 mmHg or < 15 mmHg versus patients with higher mean EtCO2 were found.

The authors note significant limitations of their study, the largest being its size. That 11 large US hospitals could only recruit 43 patients over three years speaks to the challenges commonly faced in pediatric cardiac arrest research. Single institutions or EMS systems often find it difficult to gather sufficient pediatric cardiac arrest cases during which accurate patient physiologic monitoring (eg. EtCO2) is captured, leading to the need for multisite studies or registries for adequate patient numbers. Large numbers of pediatric inpatients who suffer cardiac arrests are infants, often (as in this study) with complicated congenital heart disease. These patients often have parallel as opposed to in-series pulmonary and systemic circulations, leading to the inability of measured EtCO2 levels to measure systemic cardiac output accurately [13] The small study size also precluded the ability to conclude whether the absence of association between EtCO2 measurements during CPR and patient outcomes might have stemmed from the failure of EtCO2 measured during CPR being able to predict CPR-quality. Drugs such as epinephrine or sodium bicarbonate can effect EtCO2 levels independently of increases to EtCO2 arising from increased cardiac output from CPR, impeding any EtCO2 level's ability to reflect accurately CC-quality. Looking solely at the effect of these drugs on patient outcomes including ROSC or survival (as in this study) does not answer if these drugs transiently effect EtCO2′s ability to predict CPR-quality when compared to BPd-measurement during CPR. Similar arguments apply when considering whether the high incidence of hyperventilation during CPR in this study masked any positive correlation between EtCO2 and CPR.

Should we conclude from Berg's study of 43 patients that the pediatrics guidelines-writers mis-stepped in making their 2015 pediatric treatment recommendation for EtCO2-guidance of CPR quality? Did this stem from using contradictory adult data and insufficient pediatric data? Maybe it was premature for resuscitation guidelines to specify an EtCO2 value targeting CC-quality, let alone any value from which to 'diagnose futility of on-going resuscitation efforts.' Recent observational studies suggest that due to the association between diastolic blood pressure (BPd) and coronary perfusion, chest compressions targeted to a minimum BPd may be a better CPR-performance metric (than EtCO2) and might more reliably predict patient outcomes [12,14]. BPd measurement during cardiac arrest necessitates arterial line placement, something not done in the pre-hospital setting and rarely performed during cardiac arrest in emergency departments. What does this leave pre-ICU practitioners to use as a tool by which to monitor CPR-quality? While monitor-defibrillators that measure CPR-performer metrics (i.e. CC-rate and depth) on small children do exist, they are not widely used, limiting the ability of most pre-hospital rescuers to quantitatively

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measure and target CC-rate and depth as the minimum markers of CPR quality. Or maybe, as suggested by some, EtCO2 trends as opposed to an absolute clinical value would be more predictive of outcome [15]. No adequately sized studies of capnography and out of hospital pediatric cardiac arrest exist to suggest whether EtCO2-monitoring during pre-hospital pediatric CPR demonstrates a similar lack of association between EtCO2 and patient outcomes.

Like so many pediatric cardiac arrest studies, there are more questions remaining than answers. Future multisite studies of in-hospital and out of hospital pediatric cardiac arrest should strive to gather sufficient patient numbers so that pediatric data can answer specifically pediatric questions. International cardiac arrest research networks are currently accumulating pediatric data that will hopefully answer many pertinent questions, including how best to measure CPR-quality in pre-hospital, Emergency Department and ICU settings [16]. It may be that measurement of specific CPR-performance metrics (CC-depth and rate), physiologic metrics (EtCO2) and invasive measurement of hemodynamics (BPd) all have their roles through various stages of the 'resuscitation journey'. Conversely, we may find that generic guideline targets need to be superseded by personalized resuscitation targets based upon individual patient-needs as measured metabolically/ physiologically real-time at the bedside [17]. Meanwhile, resuscitation guidelines writers should be cognisant that premature or inappropriate extrapolation of adult and animal data may inadvertently lead to pediatric recommendations that reveal guidelines-writers ("the Emperor") as "having no clothes" [18].

Conflict of interest

Allan de Caen was the first author of the American Heart Association/ Heart and Stroke Canada Pediatric Advanced Life Support Guidelines published in 2015, and co-chair of the Pediatric Task Force of the International Liaison Committee on Resuscitation between 2006–2016.

Ian Maconochie was the first author of the European Resuscitation Council Paediatric Life Support Guidelines published in 2015, and co-chair of the Pediatric Task Force of the International Liaison Committee on Resuscitation since 2011

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