Towards evidence based emergency medicine: Best BETs from the Manchester Royal Infirmary

Edited by Simon D Carley

BET 1: CAN THE VALUE OF END TIDAL CO_2 PROGNOSTICATE ROSC IN PATIENTS COMING INTO EMERGENCY DEPARTMENT WITH AN OUT-OF-HOSPITAL CARDIAC ARREST (OOHCA)?

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ABSTRACT

A short cut review was carried out to establish whether end tidal CO_2 can be used to prognosticate in out-of-hospital cardiac arrest. 232 papers were found of which 4 presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of these best papers are tabulated. The clinical bottom line is that a single end tidal CO_2 reading cannot be used as an indicator to terminate resuscitation attempts in out-of-hospital cardiac arrest.

THREE-PART QUESTION

Patient group—(In adults admitted to the ED with an out-of-hospital cardiac arrest)

Intervention—(does end tidal CO_2 measurement)

Outcome—(predict/prognosticate return of spontaneous circulation)?

CLINICAL SCENARIO

A 60-year-old male is brought into the ED with an out-of-hospital cardiac arrest (OOHCA). All monitoring is attached while ALS protocol is ongoing, including CO_2 monitoring. You want to assess whether the patient is going to survive and thereby achieve a return of spontaneous circulation (ROSC) and you wonder whether the patient's end tidal CO_2 ($ETCO_2$) level can prognosticate this.

SEARCH STRATEGY

Medline, Cochrane and EMBASE databases (2006 to present).

[exp HEART ARREST/ or "Heart arrest".ti,ab or "cardiac arrest".ti,ab] AND [ETCO2.ti,ab or "end tidal co2".ti,ab or exp CAPNOGRAPHY/ or capnometry.ti,ab or {exp CARBON DIOXIDE/ AND exp TIDAL VOLUME/ AND 19 AND 20}] AND [{exp SURVIVAL/ OR exp SURVIVAL ANALYSIS/} or exp TREATMENT OUTCOME/ or {(rosc OR "return of spontaneous circulation").ti,ab} or exp "OUTCOME ASSESSMENT (HEALTH CARE)"/]

Conference abstracts removed. Inpatient studies removed. Case reports, editorials and notes removed. Paediatric studies removed. Duplicate results removed. Limited to Human studies, English papers and solely papers between 2006 and 2016. Studies that did not answer research question removed manually.

SEARCH OUTCOME

232 articles obtained of which 4 were of sufficient quality (table 1). Results already reviewed in these meta-analyses were not presented below.

COMMENTS

Overall the recent paper by Hartmann *et al* is well-written and the most up to date and most pertinent study on this research topic. While the quality of the study may have been deemed low by the GRADE criteria, it is important to remember that ETCO2 in participants (with and without ROSC) can be compiled, despite the variety of interventions in the included studies, as $ETCO_2$ is a proxy measurement for cardiac output—a physiological outcome that can be achieved under many differing circumstances. In a meta-analysis such as this one where homogenous study design is not necessary to evaluate a physiological state, the level of evidence appears falsely poor. This has been clearly addressed by the authors. This paper gives a clear idea of what $ETCO_2$ level should be aimed for when resuscitating patients and thereby can prognosticate between a positive and a negative outcome. It also emphasises that current guidelines may need to be updated to acknowledge that an aim of 10–20 mm Hg may be too low. The paper by Poon *et al* is important in deciding whether a 3 min $ETCO_2$ level of ≤10 mm Hg can help clinicians decide whether to discontinue resuscitation on the basis that there is a much greater chance of morbidity and mortality. The paper by Akinci *et al*

Best Evidence Topic reports (BETs) summarise the evidence pertaining to particular clinical questions. They are not systematic reviews, but rather contain the best (highest level) evidence that can be practically obtained by busy practicsing clinicians. The search strategies used to find the best evidence are reported in detail in order to allow clinicians to update searches whenever necessary. Each BET is based on a clinical scenario and ends with a clinical bottom line which indicates, in the light of the evidence found, what the reporting clinician would do if faced with the same scenario again.

The BETs published below were first reported at the Critical Appraisal Journal Club at the Manchester Royal Infirmary[1] or placed on the BestBETs website. Each BET has been constructed in the four stages that have been described elsewhere.[2] The BETs shown here together with those published previously and those currently under construction can be seen at http://www.bestbets.org.[3] Three BETs are included in this issue of the journal.

	Title
1	Can the value of end tidal CO2 prognosticate ROSC in patients coming into EDemergency department with an out- of -hospital cardiac arrest (OOHCA)?
2	Trendelenburg Pposition helps to cardiovert patients in SVT back to sinus rhythm.
3	Peripheral Mmetaraminol Iinfusion in the Eemergency Ddepartment.

1 Carley SD, Mackway-Jones K, Jones A, et al. Moving towards evidence based emergency medicine: use of a structured critical appraisal journal club. *J Accid Emerg Med* 1998;15:220–2.

2 Hou LCMackway-Jones K, Carley SD, Morton RJ, et al. The best evidence topicreporttopic report: Aa modified CAT for summarising the available evidence inemergencyin emergency medicine. *J Accid Emerg Med* 1998;15:222–6.

3 Mackway-Jones K. Bestbets.org: odds on favourite for evidence in emergency medicine reaches the world wide web. *Emer Med J* 2000;17:235–6.

Table 1 Relevant papers

Author, year, country of publication	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Hartmann *et al*, 2015,[1] USA	7276 subjects from 27 studies used for qualitative analysis. 6565 subjects from 20 studies used for average $EtCO_2$. 6550 subjects from 19 studies for meta-analysis	Systematic review and meta-analysis	Participants with ROSC after CPR have statistically higher levels of $ETCO_2$	The overall mean $ETCO_2$ value was significantly higher among participants with ROSC than those without ROSC (25.8/−9.8 mm Hg vs 13.1/−8.2 mm Hg, p=0.001) The average $ETCO_2$ level was 25 mm Hg in participants with ROSC The mean difference in $ETCO_2$ was 12.7 mm Hg (95% CI 10.3 to 15.1) between participants with and without ROSC (p<0.001) The mean difference in $ETCO_2$ was not modified by the receipt of sodium bicarbonate, uncontrolled minute ventilation or era of resuscitation guidelines The overall quality of data by Grades of Recommendations, Assessment, Development and Evaluation criteria is very low, but there are currently no prospective data	(1) The overall level of evidence was characterised as very low by the GRADE criteria. (2) Mostly only cohort studies analysed (26/27 studies). (3) Big variance on time taken to initiate resuscitation, quality of compressions and use of different methods to deliver compressions between studies. (4) Presence of serious inconsistency, as measured by the degree of heterogeneity (p<0.001 and I^2 value of 98.5%)
Poon *et al*, 2016,[2] Hong Kong	319 patients	Prospective cohort study	A 3 min $ETCO_2 \leq 10$ mm Hg was associated with poor prognosis and low chance of ROSC	A 3 min $ETCO_2 > 10$ mm Hg was a predictor of ROSC with OR 18.16 (95% CI 4.79 to 51.32, p<0.001). In other words, when cardiac arrested, for a patient with a 3 min $ETCO_2 > 10$ mm Hg the odds of ROSC was 18 times higher than those with $ETCO_2 \leq 10$ mm Hg	Large number of patients excluded due to improper documentation of the use of $ETCO_2$ (approximately one-third). (2) Quality of chest compressions was not controlled or measured. (3) The decision to stop resuscitation may have been influenced by the $ETCO_2$ value at the time, which could have potential bias on ROSC rate
Akinci *et al*, 2014,[3] Turkey	80 patients	Prospective cohort study	$PetCO_2$ values are higher in the ROSC group	$ETCO_2$ levels of the ROSC group in the 5th, 10th, 15th and 20th min were significantly higher compared with the Exitus group (p<0.001)	(1) $ETCO_2$ levels not measured on transport to hospital. $ETCO_2$ value differences, which might be resulting from different arrest aetiologies (asphyxia and cardiac) could not be determined as a result of this. (2) Small sample size. (3) No clear indication or suggestion of what $ETCO_2$ level can be used to prognosticate ROSC—however, does give an indication of when best to assess this. (4) Published in a low impact medical journal
			During the CPR, the most reliable time for ROSC estimation according to $PetCO_2$ values is 20th min	In distinguishing ROSC and Exitus, $ETCO_2$ measurements within 5–20 min intervals showed highest performance on the 20th (area below the ROC curve was determined to be 0.850 (95% CI 0.721 to 0.980)) and lowest on the 5th minute (area below the ROC curve was determined to be 0.730 (95% CI 0.610 to 0.849))	
				None of the patients who had $ETCO_2$ levels less than 14 mm Hg survived	
Pantazopoulos *et al*, 2015,[4] Greece	42 studies included in qualitative synthesis	Narrative review		Although changes and trends in $ETCO_2$ values during CPR are more important than absolute $ETCO_2$ levels, current data suggest that certain cut-off values may be targeted; an $ETCO_2 > 10$ mm Hg is correlated with increased possibility for ROSC	No systematic review or meta-analysis done
				Rescuers should target a 20 min $ETCO_2$ of at least 20 mm Hg The value of a trend more than absolute $ETCO_2$ values may be most important in the presence of a treatable cause An abrupt increase in $ETCO_2$, under constant ventilation and CO_2 production, provides the fastest indication of ROSC	

CPR, cardiopulmonary resuscitation; $EtCO_2$, end tidal CO_2; $PetCO_2$, end tidal CO_2 tension; ROSC, return of spontaneous circulation.

highlights that a 20 min $ETCO_2$ check has a greater performance in predicting ROSC than earlier times, although the data itself may not be robust enough to go by from a resuscitation guideline perspective. Having said this, the data are important and as such more studies in this research topic would definitely help.

Clinical bottom line

Current literature suggests that: (1) Our current $ETCO_2$ aim of 10–20 mm Hg may be inadequate and should be modified to 25 mm Hg. (2) A 3–5 min $ETCO_2$ level of ≤10 mm Hg is associated with bad prognosis and as such, it may be beneficial to consider stopping patient resuscitation should this be the clinical case. (3) It is important to see the trend of $ETCO_2$ rather than making a decision solely on one specific value, as sometimes an abrupt increase in $ETCO_2$ could be a sign of impending ROSC. (4) More robust prospective data on the optimal $ETCO_2$ value that is associated with ROSC would be helpful in defining a more accurate future target for intervention.

REFERENCES

1 Hartmann SM, Farris RWD, Di Gennaro JL, *et al*. Systematic review and Meta-Analysis of End-Tidal carbon dioxide values associated with return of spontaneous circulation during cardiopulmonary resuscitation. *J Intensive Care Med* 2015;30:426–35.
2 Poon KM, Lui CT, Tsui KL. Prognostication of out-of-hospital cardiac arrest patients by 3-min end-tidal capnometry level in emergency department. *Resuscitation* 2016;102:80–4.
3 Akinci E, Ramadan H, Yuzbasioglu Y, *et al*. Comparison of end-tidal carbon dioxidelevels with cardiopulmonary resuscitation success presented to emergencydepartment with cardiopulmonary arrest. *Pak J Med Sci* 2014;30:16–21.
4 Pantazopoulos C, Xanthos T, Pantazopoulos I, *et al*. A review of carbon dioxide monitoring during adult cardiopulmonary resuscitation. *Heart Lung Circ* 2015;24:1053–61.

Emerg Med J 2017;**34**:187–189.
doi:10.1136/emermed-2017-206590.1