**Clinical question.**

Note: The question changed from the fall 2007 to the spring 2008. The question for the ILCOR meeting in May 2008 is as follows:

In pediatric patients with cardiac arrest (prehospital [OHCA] or in-hospital [IHCA]) (P), does the use of end-tidal CO\(_2\) (I), compared with clinical assessment (C), improve accuracy of diagnosis of a perfusing rhythm (O)?

*I thought this question was quite narrow and there would be little data available. Thus, I also updated the search and data analysis on the two questions that I originally searched for the fall 2007 ILCOR meeting. These questions are as follows:* During CPR in children (P), monitoring end-tidal CO\(_2\) (I) is useful to estimate the quality of CPR (outcome 1) and there is a threshold value of end-tidal CO\(_2\) that may be used to reliably predict failure to achieve a return of spontaneous circulation (outcome 2).

Is this question addressing an intervention/therapy, prognosis or diagnosis?  Diagnosis for first question and Prognosis for second

State if this is a proposed new topic or revision of existing worksheet: New topic for pediatrics

**Conflict of interest specific to this question**

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? No

**Search strategy (including electronic databases searched).**

PubMed Search using textwords: (capnograph* OR end-tidal OR expired OR exhaled) AND (heart arrest OR resuscitation) (search updated April 2008 and October 11, 2009). This strategy yielded 1478 citations. The titles were reviewed and 188 potentially relevant citations were identified.

Also searched using Clinical Queries focused on “prognosis” for “capnograph* OR capnometry using a sensitive strategy. This produced the following search strategy: Search (capnograph* OR capnometry OR end-tidal) AND (incidence[MeSH:noexp] OR mortality[MeSH Terms] OR follow up studies[MeSH:noexp] OR prognosis*[Text Word] OR predict*[Text Word] OR course*[Text Word]). This search identified 878 studies of which 13 additional potentially relevant articles not identified by the initial search strategy from April 2008 were found.

EndNote library search (March 24, 2008 version): used “capnography OR end-tidal OR capnometry” as search terms. This yielded 222 references of which 78 were considered potentially relevant, however only 39 were actually relevant and all of these were previously identified by other search methodologies.

To search for papers addressing the use of capnography to detect cardiac arrest or a pulse I used the following clinical query “diagnosis” sensitive search strategy:

Search ((capnograph* OR capnometry OR end-tidal) AND (heart arrest or cardiac arrest)) AND (sensitiv*[Title/Abstract] OR sensitivity and specificity[MeSH Terms] OR diagnos*[Title/Abstract] OR diagnosis[MeSH:noexp] OR diagnostic *[MeSH:noexp] OR diagnosis, differential[MeSH:noexp] OR diagnosis[Subheading:noexp]). This yielded 57 citations of which only 3 were relevant. Of these, only one paper (Salen et al. Acad Emerg Med 2001) was relevant.

I looked for related articles using the PubMed link and did not identify any other relevant papers. I also conducted another clinical query “diagnosis” search using the following search strategy: ((capnograph* OR capnometry OR end-tidal) AND (pulse)) AND (sensitiv*[Title/Abstract] OR sensitivity and specificity[MeSH Terms] OR diagnos*[Title/Abstract] OR diagnosis[MeSH:noexp] OR diagnostic *[MeSH:noexp] OR diagnosis, differential[MeSH:noexp] OR diagnosis[Subheading:noexp]). This yielded 313 citations, of which 4 were not previously identified, but none of these were relevant.

Cochrane Database (Database of systematic reviews, controlled trial registry and database of abstracts of reviews of effectiveness): Searched “capnography OR capnometry” yielding 126 citations. Of these, most dealt with ventilator management or monitoring during transport or sedation. Also searched using “end-tidal” AND (cardiac arrest OR resuscitation). This yielded 25 clinical trials. No references were identified in any Cochrane search that were not found by the other searches noted above.

Embase search performed by Anne-Marie Guerguerian MD, PhD, who did not find any additional relevant citations.
I also reviewed the following 2005 adult evidence evaluation worksheets to assure that the above search strategy did not miss any relevant study that had previously been identified: a.Capno.ABS.7Sep04Final.doc & a.ETCO2.BW.26Jan05Final.doc
There was no relevant pediatric worksheet on this topic. The closest pediatric worksheet addressed the use of end-tidal CO2 detection to confirm proper endotracheal tube placement: p.ETCO2.mek.25Sep04.final.doc
No studies were identified from the worksheets that were not identified by the search methodology listed above.

* State inclusion and exclusion criteria

All papers not dealing specifically with resuscitation or cardiac arrest were excluded from the final data analysis (see data table), but some studies that were relevant to the background physiology relating capnography to cardiac output are included in the discussion of the evidence.
Review articles and all selected relevant papers were reviewed to search their citation list, but review articles were not included in the list of relevant citations.
Since there was little data specifically in children, I reviewed adult and animal data relevant to the utility of monitoring end-tidal CO2 (capnography) as a predictor of outcome during cardiac arrest. I particularly emphasized new science since the last Guideline rather than rehashing the previously identified data.

* Number of articles/sources meeting criteria for further review: 201 citations

Initial search strategy identified 1478 potentially relevant articles based on their titles. The abstracts were then reviewed and 201 articles were selected for more detailed review.

Of the articles selected for more detailed review, 47 were included in final table. Several other studies are cited in the accompanying summary that are not included in the grid since they are not directly relevant to the evidence evaluation questions.

## Summary of evidence

### Evidence Supporting Clinical Question

In pediatric patients with cardiac arrest (prehospital [OHCA] or in-hospital [IHCA]) (P), does the use of end-tidal CO2 (I), compared with clinical assessment (C), improve accuracy of diagnosis of a perfusing rhythm (O)?

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<td>Salen,2001,610ABE</td>
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*Level of evidence*

*A = Return of spontaneous circulation  B = Survival of event  C = Survival to hospital discharge  D = Intact neurological survival  E = Other endpoint

*Key study*

*Italics = Animal studies*

Note: I will fill this in once I finish the evidence review. I don’t think this grid is particularly helpful for a prognosis or diagnosis question since the outcomes are focused on treatment effects (ie, A through E).
### Evidence Neutral to Clinical question

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<td>Grmec, 2009, 7ABC (drowning)</td>
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*A = Return of spontaneous circulation*  
*B = Survival of event*  
*C = Survival to hospital discharge*  
*D = Intact neurological survival*  
*E = Other endpoint*  
*Italicics = Animal studies*

### Evidence Opposing Clinical Question

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| **Good**          |   |   |   |   | *Berg, 1996, 245E*  
*Grmec, 1996, 349AE*  
*Grmec, 2003, R139ABC* (asphyxial arrest)* |
| **Fair**          |   |   |   |   |   |
| **Poor**          |   |   |   |   |   |

*A = Return of spontaneous circulation*  
*B = Survival of event*  
*C = Survival to hospital discharge*  
*D = Intact neurological survival*  
*E = Other endpoint*  
*Italicics = Animal studies*
Evidence Supporting Clinical Question

During CPR in children (P), monitoring end-tidal CO\textsubscript{2} (I) is useful to estimate the quality of CPR (outcome 1)

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| Good              |                                       |
| Fair              | Ornato,1988,241E                       |

A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint

Italics = Animal studies

Note: I will fill this in once I finish the evidence review. I don’t think this grid is particularly helpful for a prognosis or diagnosis question since the outcomes are focused on treatment effects (ie, A through E).

Evidence Neutral to Clinical question

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| Fair              | Ornato,1988,241E                       |
### Evidence Opposing Clinical Question

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A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint  

*italics = Animal studies*

### Evidence Supporting Clinical Question

During CPR in children (P), monitoring end-tidal CO$_2$ there is a threshold value of end-tidal CO$_2$ that may be used to reliably predict failure to achieve a return of spontaneous circulation (outcome 2).

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Falk,1988,607A  
Garnett,1987,512A  
Grmec,2003,89ABC  
Grmec,2003,R139ABC  
Grmec,2007,404AB  
Grmec,2009,7ABC  
Kolar,2008,R115ABC*  
Krep,2007,86A  
Levine,1997,301C  
Mally,2007,R39AB  
Mauer,1998,67AB  
Bhende,1995,395AB  
Grmec,2001,263A  
Li,2008,211A  
Nakatani,1999,203AB  
Salen,2001,610AB
Level of evidence

A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint

*Italicics* = Animal studies

Note: I will fill this in once I finish the evidence review. I don’t think this grid is particularly helpful for a prognosis or diagnosis question since the outcomes are focused on treatment effects (ie, A through E).

### Evidence Neutral to Clinical question

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<th><strong>Lindberg, 2000, 129E</strong></th>
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| Fair | | | | **Callaham, 1992, 337AE**
| Poor | | | | **Moon, 2007, 219A**
| | | | | **Pokorna, 2009**

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### Evidence Opposing Clinical Question

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| Fair | | | |
| Poor | | | |

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*Italicics* = Animal studies
There were two questions examined in this review with the second question having two endpoints or hypotheses.

The first question was designed to examine whether end-tidal CO₂ would be useful to identify a perfusing rhythm compared with the clinical examination.

The second question had 2 hypotheses: Hypothesis 1 is that during CPR in children, monitoring end-tidal CO₂ is useful to estimate the quality of CPR.

Hypothesis 2 states that in the same population (ie, children undergoing CPR), there is a threshold end-tidal CO₂ that may be used to reliably predict failure to have a return of spontaneous circulation and thus could be used to guide termination of resuscitation.

As reviewed in the previous worksheets and from this updated search, there is ample animal data showing a correlation between end-tidal CO₂ and cardiac output in various low-flow states and in shock (see (Gazmuri, 1989, 237; Gazmuri, 1991, 984; Idris, 1994, 568; Ornato, 1990, 1104; Pernat, 2003, 1819; Shibutani, 1994, 829; Weil, 1985, 907)). Moreover, in humans, CPR methods that produce a higher cardiac output (eg, ACD-CPR(Guly, 1995, 372; Orliaguet, 1995, 48; Rubertsson, 2005, 357; Wenzel, 2000, 1107) and use of a metronome to sequence the compression rate of CPR and thus improve the quality of CPR(Berg, 1994, 35; Kern, 1992, 145)) are associated with higher end-tidal CO₂ concentrations compared with standard CPR.

The clinical rationale for monitoring end-tidal CO₂ is based on understanding the physiologic determinants of end-tidal CO₂. In normal individuals with normal respiratory physiology, the end-tidal CO₂ concentration is closely related to the PaCO₂ (arterial pCO₂); end-tidal CO₂ is usually 2-5 mmHg lower than PaCO₂. If minute ventilation increases, end-tidal CO₂ and PaCO₂ will decrease; if minute ventilation (really alveolar ventilation) decreases, then end-tidal CO₂ will increase. Other factors that affect end-tidal CO₂ are the rate of CO₂ production and the rate of delivery of CO₂ to the alveolus. The latter is directly dependent on pulmonary blood flow. When pulmonary blood flow is low, the ratio of ventilation to pulmonary blood flow typically becomes quite large resulting in a washout of alveolar CO₂ so that end-tidal CO₂ falls. If pulmonary blood flow increases without a change in minute ventilation, more CO₂ is delivered to the alveolus and end-tidal CO₂ increases, at least initially until a new steady state is achieved. Clearly, interpretation of end-tidal CO₂ in low flow states is highly dependent on maintaining a constant minute ventilation. If ventilation increases at a given pulmonary blood flow rate, the end-tidal CO₂ will fall without any change in effective pulmonary blood flow. (Idris, 1994, 1827)

Changes in pulmonary blood flow typically reflect global changes in cardiac output, but in children with right to left shunts, an increase in right to left shunting that bypasses the lungs, as occurs in some infants and children with congenital cardiac disease or pulmonary hypertension, decreases the proportion of blood flowing through the pulmonary circulation and end-tidal CO₂ will fall. (Burrows, 1989, 219) Similarly, increasing pulmonary blood flow in children with right→left blood flow, such as following central shunt insertion in cyanotic children, increases the end-tidal CO₂ and reduces the difference between the arterial PaCO₂ minus end-tidal CO₂ (Matthews, 2009, 60; Tugrul, 2004, 152) Likewise, if there are intrapulmonary shunts that bypasses the alveoli, there will be an increased difference between the arterial pCO₂ and end-tidal CO₂ (Chuang, 2006, 117)

End-tidal CO₂ is affected also by the presence of parenchymal lung disease that increases the alveolar dead space; indeed the difference between PaCO₂ and end-tidal CO₂ has been used to quantify the severity of parenchymal lung disease. (Anderson, 2000, 207; Burrows, 1989, 219) Recently, the post-arrest gradient was found to predict survival in post-arrest patients who survived to hospital admission. (Moon, 2007, 219) although in this setting, it is likely that the gradient may also reflect ongoing low cardiac output in the post-arrest phase leading to increased physiologic dead space.

**Question 1:** In pediatric patients with cardiac arrest (prehospital [OHCA] or in-hospital [IHCA]) (P), does the use of end-tidal CO₂ (I), compared with clinical assessment (C), improve accuracy of diagnosis of a perfusing rhythm (O)?

I could only identify three papers related to using end-tidal CO₂ monitoring for detecting cardiac arrest, none of them in children. (Falk, 1988, 607; Salen, 2001, 610; Sehra, 2003, 515) None of these specifically compared end-tidal CO₂ to the clinical exam, but both showed that end-tidal CO₂ can be used to identify cardiac arrest. All studies were in adults so the evidence is extrapolated to children. In the absence of relevant evidence, this question cannot be answered. In the study by Salen et al. (Salen, 2001, 610) (LOE 4P for adults, 5P for peds), they used subxiphoid echocardiography and end-tidal CO₂ detectors to assess cardiac output in patients undergoing CPR to determine...
they could identify patients who would survive or die. Only 53/102 patients had capnography recorded. They found that the end-tidal CO$_2$ was better than detection of cardiac activity by echocardiography in predicting survival with the median end-tidal CO$_2$ being 35 mmHg in survivors versus 13.7 mmHg in nonsurvivors. An end-tidal CO$_2$ < 16 mmHg was predictive of not surviving to hospital admission (study endpoint). No patient with end-tidal CO$_2$ < 16 mmHg survived to hospital admission (0/29) but only 6/24 > 16 mmHg survived (25%).

The study by Sehra et al.(Sehra, 2003, 515) (LOE 5D, adult and peds) was conducted in the cath lab in 8 patients undergoing ICD placement in whom they studied 31 episodes of VF arrest induced while testing the ICD. Significant differences (P < 0.001) were noted between ETCO$_2$ values prior (mean 37.2 +/- 6.8 mmHg) versus during VF (mean 27.1 +/- 5.9 mmHg), and during VF versus return of spontaneous circulation (mean 36.6 +/- 6.6 mmHg). ETCO$_2$ decreased by 23% +/- 8% from pre-VF to the level during VF. It increased by 37% +/- 16% during the transition from VF to return of spontaneous circulation. Thus, the study confirmed that end-tidal CO$_2$ falls rapidly with onset of arrest, but does not show that it is a useful method to diagnose arrest and does not compare this method to the clinical exam. The data certainly are consistent with animal studies and strongly suggest that if there is a sudden fall in end-tidal CO$_2$ that is not explained by a ventilator-patient malfunction, the clinician should rapidly assess the patient for the onset of cardiac arrest or at least a very low blood flow state. Similar to this study, a report of 13 patients in the ICU on mechanical ventilation that was not adjusted reported that ETCO$_2$ decreased rapidly when cardiac arrest occurred from a mean of 1.4% (~10 mmHg) to 0.4% (3 mmHg) with onset of arrest (LOE 4P adults, 5P peds).(Falk, 1988, 607) No patient who failed to achieve an ETCO$_2$ of at least 1% (~7.1 mmHg) during CPR had ROSC.

**Question 2:** During CPR in children (P), monitoring end-tidal CO$_2$ (I) is useful to estimate the quality of CPR (outcome 1) and there is a threshold value of end-tidal CO$_2$ that may be used to reliably predict failure to achieve a return of spontaneous circulation (outcome 2)

**Outcome 1:** Although using end-tidal CO$_2$ to guide CPR is rationale, there is little objective data in children to confirm that using end-tidal CO$_2$ to guide resuscitation efforts is associated with an improved return of spontaneous circulation. The only pediatric data regarding outcome 1 is a small case series (6 children) in the Pediatric ICU (LOE 5P). (Berg, 1994, 35) The authors reported that using a metronome to achieve a compression rate of 140/min significantly improved end-tidal CO$_2$ concentration (12 +/- 7 torr versus 4 +/- 3 torr with standard CPR, p <0.05); a metronome rate of 100/min improved end-tidal CO$_2$ concentration from the pre-audio prompting CPR, but the improvement did not reach statistical significance.

There are ample data in animal models and adults, however, which shows that actions that improve cardiac output, such as increasing compression depth,(Li, 2008, 211; Ristagno, 2007, 70) compression rate,(Berg, 1994, 35; Kern, 1992, 145; Ornato, 1988, 241) and use of ACD-CPR(Guly, 1995, 372; Rubertsson, 2005, 357; Wik, 1996, 45) are associated with increased end-tidal CO$_2$. Similarly, animal models that markedly reduce cardiac output result in a fall in end-tidal CO$_2$ that is correlated with the decrease in cardiac output,(Idris, 1994, 568; Jin, 2000, 2415; Ornato, 1990, 1104) which provides strong physiologic evidence for following end-tidal CO$_2$ as a marker of improved blood flow during CPR. Provided that minute ventilation remains constant, a fall in cardiac output in patients undergoing abdominal aortic aneurysm repair also showed a tight correlation (r$^2$=0.82) between the percent decrease in end-tidal CO$_2$ and the fall in cardiac output.(Shibutani, 1994, 829) Similarly, the gradient between end-tidal CO$_2$ and arterial CO$_2$ is higher in multitrauma patients with increased metabolic acidosis and higher injury severity scores, supporting the relationship of a high PaCO$_2$ minus end-tidal CO$_2$ gradient to low cardiac output.(Warner, 2009, 26)

A recent animal study documents that the quality of chest compressions determines the likelihood of responding to defibrillation shock attempts and the likelihood of response to shocks was well correlated to differences in end-tidal CO$_2$ as a marker of cardiac output during CPR.(Ristagno, 2007, 70) The same group also showed in an animal model that end-tidal CO$_2$ is associated with changes in cortical brain blood flow in a VF arrest model.(Ristagno, 2008, 229) In summary, based on animal and adult data it is logical to recommend following end-tidal CO$_2$ as a guide to resuscitation, but there is no evidence in children to document that this recommendation will improve outcome.

**Outcome 2:** There are substantial data in adults and limited data in children, as reviewed below, that failure to achieve a threshold value of end-tidal CO$_2$ is associated with death. Furthermore, an increase in end-tidal CO$_2$ is consistently observed in adults and children who have ROSC; the increase in end-tidal CO$_2$ is often the first indicator of ROSC.
Although both animal and human studies show that a low end-tidal CO$_2$ concentration (partial pressure) is associated with failure to achieve ROSC, there is a good bit of variation among the studies regarding the time at which end-tidal CO$_2$ was measured and what was specifically measured (eg, initial, peak or average end-tidal CO$_2$). For example, some trials just measured the initial end-tidal CO$_2$, or the average or peak concentration. Other trials just evaluated the relationship between the end-tidal CO$_2$ concentration and failure to achieve ROSC following 20 minutes of CPR but not earlier than 20 minutes.(Levine, 1997, 301) One large prospective out-of-hospital study provides data over the entire resuscitation time course as reviewed below.(Kolar, 2008, R115)

There is very limited pediatric data and most of this was obtained using a semi-quantitative (colorimetric) technique.(Bhende, 1995, 395) The only pediatric CPR study (LOE 4P, fair) enrolled 40 children <40 kg; 37 of whom had out-of-hospital cardiac arrest and were intubated in the field. Only the initial (after 6 breaths) and final (with ROSC or termination of CPR efforts) end-tidal CO$_2$ value was recorded. No child with an initial end-tidal CO$_2$ <0.5% (~3.5 torr) had ROSC, but this only represented 6 children and all of these had CPR for at least 25 minutes in the out-of-hospital setting before endotracheal intubation and end-tidal CO$_2$ was recorded. All 13 children with ROSC had a second end-tidal CO$_2$ in the yellow (>2.0%, ~>15 mmHg) range, but only 2/40 patients survived hospitalization; both of these children had an initial end-tidal CO$_2$ in the yellow range. Since the initial end-tidal CO$_2$ reading occurred up to 25 minutes after the onset of advanced life support, it limits our ability to make a recommendation regarding the utility of the initial end-tidal CO$_2$ in predicting outcome in children, especially in the in-hospital setting. The authors recorded the “final” end-tidal CO$_2$ in 25 children when the child either had ROSC or was declared dead. All 12 children with failure of ROSC had a final concentration less than 0.5%, but we do not know if they achieved a concentration higher than that during CPR. In one relevant (ie, pediatric) animal model (LOE 5P; fair), 11 puppies with asphyxial cardiac arrest had an initially high end-tidal CO$_2$ when CPR was started that rapidly fell during CPR and then consistently rose to a mean of 27 torr at or just before ROSC in all animals.(Bhende, 1996, 349) This is consistent with observations in adults and emphasizes the point that the initial end-tidal CO$_2$ may be high following asphyxial arrest(Grmec, 2003, R139; Kolar, 2008, R115; Kolar, 2008, R115) and therefore should not be used to predict outcome until after at least one minute of effective CPR.

The latter observation of high initial end-tidal CO$_2$ in asphyxial arrest was also observed in a piglet model by Berg et al (LOE 5P, good).(Berg, 1996, 245) They compared the initial end-tidal CO$_2$ in 20 piglets with asphyxial arrest versus 20 with VF arrest. The initial end-tidal CO$_2$ was 91 +/- 20 mmHg in the asphyxial group versus 34 +/- 14 mmHg in the VF group and rapidly equalized between both groups of animals with CPR and ventilation. They did not report the changes in end-tidal CO$_2$ during resuscitation.

Several recent adult trials since 2005 provide additional data on the association between end-tidal CO$_2$ and survival that is relevant and may be extrapolated to children. Most of these studies were performed in the Center of Emergency Medicine, Prehospital Unit Maribor, Maribor, Slovenia, which used a physician-based prehospital ALS system. The overall results from 9 years of collecting prehospital end-tidal CO$_2$ during CPR from this group was recently published.(Kolar, 2008, R115) In one large trial,(Grmec, 2007, 404) (LOE 3P in adults; LOE 5P for children) CPR was attempted in 389 out-of-hospital cardiac arrest cases. A sidestream ETCO$_2$ monitor attached to the monitor/defibrillator was used and results were recorded every minute during resuscitation. Of these 389 arrests, 277 (72%) were classified as cardiac etiology and 112 (28%) as non-cardiac. There was ROSC in the field in 61% (237/389) and 50% still had ROSC on hospital admission (195/389). Overall, 82/389 (21.1%) survived to hospital admission. The initial rhythm was VF/VT in 156 (40%) and was asystole or PEA in 233 (60%). The initial end-tidal CO$_2$ was 0.94±0.66kPa (~7.1 mmHg) in those who died vs. 2.42±0.74kPa (~18.2 mmHg) for those who survived to hospitalization (p<.001). Final end-tidal CO$_2$ was 1.0±0.35kPa (~7.5 mmHg) vs 3.63±0.97kPa (~27.2 mmHg; p<.001); of note, final end-tidal CO$_2$ included patients who had ROSC so it is not surprising that the value was much higher. The initial end-tidal CO$_2$ associated with death in the field was 1.4±0.9kPa vs. 2.6±0.9kPa (p<.001), and final end-tidal CO$_2$ was 1.9±1.3kPa (14.3 mmHg) vs 3.9±1.2kPa (29.3 mmHg; p<.001). Multivariate analysis showed that the initial end-tidal CO$_2$ was highly associated with outcome (odds ratio for ROSC and admission to hospital was 22.0 [11.4 to 42.6; 95% CI], which was much higher than any other factor associated with outcome (ie, witnessed arrest, bystander CPR, initial rhythm, time to EMS arrival and patient sex). None of these other factors had an odds ratio for survival to hospital admission >3.1. In 158/195 (81%) of all patients with ROSC on hospital admission, a rise in end-tidal CO$_2$ was the first sign of ROSC before pulses were noted. Average rise was 1.8±0.6kPa (13.5±4.5 mmHg). Of note, all patients with ROSC had an initial end-tidal CO$_2$ over 1.33 kPa (>10 torr). Unfortunately, they do not state how many patients with subsequent end-tidal CO$_2$ <10 torr had ROSC eventually and it is not clear how many patients did not have an initial end-tidal CO$_2$ over 10 torr. In addition, the
authors do not indicate at what time interval of resuscitation the final end-tidal CO$_2$ was obtained. Of note, most of the patients (71%) had a cardiac etiology for their arrest, which was associated with better survival compared with the non-cardiac etiology (24% vs. 15%).

The observation that the initial end-tidal CO$_2$ was always <10 torr in patients without ROSC is somewhat surprising since this same group observed high initial end-tidal CO$_2$ concentrations in 44 patients with out-of-hospital asphyxial arrest (LOE 5P). (Grmec, 2003, R139) Over 4.5 years (2/1998 to 10/2002) they had 141 primary VF/VT arrests and 44 non-VF/VT arrests (initial rhythm PEA or asystole). The latter group was younger (49 vs 66 years old). ROSC was more common in the VF/VT population (yes/no: 101/40 versus 18/26 in non-VF/VT group) as was being discharged alive from the ICU; yes/no: 38/103 versus 7/37. Initial values of end-tidal CO$_2$ were much higher in the asphyxial group and did not differ between those with and without ROSC (70.1±15.3 mmHg versus 62.8±16.2 mmHg, p=0.64). At one minute the end-tidal CO$_2$ was significantly higher in patients with eventual ROSC vs. those without ROSC (35.8±8.6 vs. 19.4±8.7 torr). As in their more recent trial, they noted that ROSC only occurred in patients with an initial end-tidal CO$_2$ >10 mmHg, but they do not state how many patients exceeded that threshold, so the sensitivity, specificity and positive and negative predictive value of this threshold cannot be calculated. As seen in pediatric asphyxial animal models noted previously, (Berg, 1996, 245; Bhende, 1996, 349) a high initial end-tidal CO$_2$ is common and not prognostic, but one would expect the value after one minute of CPR to better reflect the cardiac output achieved with CPR. Their data show that even at one minute the mean end-tidal CO$_2$ was higher than 10 mmHg in the asphyxial arrest group, suggesting that this threshold may not be appropriate early after asphyxial arrest in children.

In another study from the same group reported in 2007, (Mally, 2007, R39) they analyzed out-of-hospital arrest data from Jan 2000 to April 2006 to examine the effects of vasopressin on outcome (LOE 5P). It appears likely this analysis represents many of the patients reported in previous studies. The purpose of this trial was to retrospectively analyze the outcome in patients who received vasopressin with or without epinephrine compared with epinephrine alone.

They used vasopressin routinely for VF arrests requiring medications since 11/2003 and in asystole it was the first drug used since 1/2006. All end-tidal CO$_2$ measurements used a sidestream monitor; they recorded the initial value than q minute until arrival at hospital or discontinuation of CPR efforts. Again, they note that ALL patients with ROSC had an initial end-tidal CO$_2$ over 1.33 kPa (10 torr), but they do not state how many patients had an initial value above this threshold value. There were 452 patients in the epinephrine group and 146 patients in the vasopressin±epi group. They do not state how many of these patients received only vasopressin.

It is interesting that the initial end-tidal CO$_2$ was not different between the epinephrine and vasopressin groups, but the average and final end-tidal CO$_2$ were significantly higher in the vasopressin group as was the occurrence of any ROSC (67% vs. 58%; p=0.04), and ROSC with admission to the hospital (62% vs 46%; p=0.01). Of note, the odds ratio of survival was 20.35 for each 10 mmHg increase in the initial end-tidal CO$_2$; the average and final end-tidal CO$_2$ odds ratio for survival to admission was 6.36 and 2.85 respectively for each 10 mmHg increase. This suggests that the higher average and final end-tidal CO$_2$ in the vasopressin group represented better global blood flow and thus better outcome as observed. Furthermore, having a high initial end-tidal CO$_2$ suggests better cardiac output from resuscitation as expected with bystander CPR and shorter time to ALS team arrival.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Epinephrine group</th>
<th>Vasopressin group</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median of petCO2 reading</td>
<td>16</td>
<td>15</td>
<td>0.86</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>5–26</td>
<td>6–23</td>
<td></td>
</tr>
<tr>
<td>Average petCO2 (patients with ROSC)</td>
<td>2.12 ± 0.51</td>
<td>3.6 ± 0.86</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Average petCO2 (patients without ROSC)</td>
<td>0.92 ± 0.29</td>
<td>1.78 ± 0.56</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Initial petCO2 (patients with ROSC)</td>
<td>2.24 ± 0.61</td>
<td>2.18 ± 0.72</td>
<td>0.87</td>
</tr>
<tr>
<td>Initial petCO2 (patients without ROSC)</td>
<td>0.85 ± 0.64</td>
<td>1.05 ± 0.64</td>
<td>0.48</td>
</tr>
<tr>
<td>Final petCO2 (patients with ROSC)</td>
<td>2.95 ± 0.42</td>
<td>4.68 ± 1.1</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Final petCO2 (patients without ROSC)</td>
<td>0.78 ± 0.52</td>
<td>0.88 ± 0.38</td>
<td>0.84</td>
</tr>
</tbody>
</table>

It is interesting that the initial end-tidal CO$_2$ was not different between the epinephrine and vasopressin groups, but the average and final end-tidal CO$_2$ were significantly higher in the vasopressin group as was the occurrence of any ROSC (67% vs. 58%; p=0.04), and ROSC with admission to the hospital (62% vs 46%; p=0.01). Of note, the odds ratio of survival was 20.35 for each 10 mmHg increase in the initial end-tidal CO$_2$; the average and final end-tidal CO$_2$ odds ratio for survival to admission was 6.36 and 2.85 respectively for each 10 mmHg increase. This suggests that the higher average and final end-tidal CO$_2$ in the vasopressin group represented better global blood flow and thus better outcome as observed. Furthermore, having a high initial end-tidal CO$_2$ suggests better cardiac output from resuscitation as expected with bystander CPR and shorter time to ALS team arrival.
A 2007 study from Bonn, Germany included data on end-tidal CO₂ as part of the evaluation of the AutoPulse™ system (LOE 5P, poor quality due to missing data). (Krep, 2007, 86) This case series is relatively small (46 patients) and the end-tidal CO₂ data was missing in 44% of the patients. Despite that, as seen in the figure to the left, their data is consistent with previous studies demonstrating that end-tidal CO₂ is a good indicator of ROSC. Of note, many of the patients without ROSC had end-tidal CO₂ concentrations above 15 mmHg showing that this threshold value is not a good indicator of survival with this mode of CPR, but instead this threshold is probably better for indicating which patients will not have ROSC.

The emergency medicine group from Slovenia compiled their data collected prospectively over 9 years (January 1998 through December 2006) of nontraumatic, out-of-hospital cardiac arrests in patients who received ALS including sidestream monitoring of end-tidal CO₂ (either a LifePak 12 monitor or BCI CapnoCheck model 20600A1). Of note, this is a two-tiered response system with field advanced life support provided by emergency medicine physicians. Resuscitation was attempted in 737 patients, 438 (59.9%) achieved ROSC and 402 patients (55%) survived to hospital admission; 170 (23%) were discharged alive. Univariate analysis showed that the initial ETCO₂, VF or pulseless VT as initial rhythm, witnessed arrest, female sex and response time were associated with ROSC. They defined ROSC as admission to hospital with a stable blood pressure when the prehospital team was dismissed by the ICU team. The trial documented that initial ETCO₂ is different in patients with shockable arrest rhythms versus those without shockable rhythms, suggesting that this difference is because there is more retention of CO₂ in the lungs with an asphyxial arrest than seen in the patient with an acute arrhythmia-mediated arrest. The initial PetCO₂ was higher in patients who survived and in those who achieved ROSC (values expressed as kPa [mmHg]; surviving patients: 3.17 [23.8] ± 1.42 [10.7] versus 2.34 [17.6] ± 1.95 [14.7]; ROSC patients 3.13 [23.5] ± 1.65 [12.4] versus 2.54 [19.1] ± 2.43 [18.3]; P < 0.001). The final PetCO₂ (kPa [mmHg]); surviving patients: 3.89 [29.3] ± 1.12 [8.4] versus 1.99 [15.0 mmHg] ± 1.33 [10.0]; ROSC patients: 3.64 [27.4] ± 0.94 [7.1] versus 0.97 [7.3] ± 0.33 [2.5]; P < 0.001) was also considerably higher in the surviving and ROSC patients.

In this large retrospective analysis of prospectively collected data during OOH arrest they noted the following key points:

- An ETCO₂ of 1.9 kPa (14.3 mmHg) or less measured at 20 mins after the initiation of ALS for cardiac arrest accurately predicts death in patients with a nonshockable rhythm. For ROSC, the sensitivity, specificity, PPV and NPV were all 100% using this threshold. The 20 min ETCO₂ threshold of 1.9 kPa discriminated between the 402 patients who achieved ROSC and the 335 patients without ROSC.

- A 15 minute ETCO₂ of more than 1.8 kPa (13.5 mmHg) has a sensitivity and NPV of 100% for ROSC with specificity and PPV of 98% (328 patients ≤ 1.8 kPa (13.6) versus 409 patients > 1.8 kPa (13.6 mmHg)).

- A 20 min ETCO₂ value greater than 1.5 kPa (11.3 mmHg) predicted ROSC in patients with a shockable cause of cardiac arrest; the sensitivity, specificity, PPV and NPV were all 100% for this outcome (based on 304 patients, 211 of whom had ROSC). This same threshold had a sensitivity of 100% and NPV of 100% for survival to discharge, but a specificity of 44% and PPV of 45% for survival (95/211 with ETCO₂ > 1.5 kPa survived).

- ETCO₂ > 2.1 kPa (15.8 mmHg) at 20 min in patients with nonshockable rhythm had sensitivity and NPV of 100% in predicting survival to hospital discharge (76/190 survived). Note, none of 242 patients with nonshockable rhythm survived if ETCO₂ was < 2.1 kPa at 20 minutes.

- ETCO₂ less than 1.5 kPa (11.3 mmHg) after 20 mins of CPR (or < 1.8 kPa (< 13.5 mmHg) after 15 mins of CPR) are incompatible with ROSC.
• The data are not intuitively obvious from the tables in their manuscript, but evaluation of the end-tidal CO\textsubscript{2} from 0-10 min of resuscitation found that 400 of 431 patients with an ETCO\textsubscript{2} >1.6 kPa (12.1 mmHg) had ROSC; the other 31 were false positives with respect to the outcome of ROSC. No patient with ROSC had an ETCO\textsubscript{2} \leq 1.6 kPa in the first 10 mins; 306 patients were in this low ETCO\textsubscript{2} group and all failed to have ROSC. From 11-15 mins using a threshold of >1.7 kPa (12.8 mmHg), there were 404 patients with >1.7 kPa. Of these, the sensitivity and NPV for ROSC was 100% and specificity and PPV was 99%; the area under the ROC curve was 1.0 (95% CI: 0.99-1.0).

• No patient with initial, average and maximum ETCO\textsubscript{2} <10 mmHg (1.33 kPa) had ROSC (they do not state how many patients fit this criteria; it is likely less than 97 out of 737 patients).

• Initial ETCO\textsubscript{2} was significantly higher in patients with non-shockable vs. shockable rhythm (3.4± 2.4 vs 2.2±1.2 kPa), but by 1 min, ETCO\textsubscript{2} was lower in the nonshockable vs. shockable group (2.8±1.5 vs 3.3±1.4 kPa). This is consistent with higher likelihood of asphyxial arrest in nonshockable group.

They conclude that ETCO\textsubscript{2} should be monitored during CPR since it has prognostic value in identifying non-survivors and can help in the decision-making for termination of resuscitation.

**Use of end-tidal CO\textsubscript{2} to recognize ROSC**

Several studies report that ETCO\textsubscript{2} increases often before other signs of ROSC. (Berg, 1996, 245; Garnett, 1987, 512; Grmec, 2001, 263; Grmec, 2003, 89; Pokorná, 2009) In the most recent study from Prague in the Czech Republic where they documented changes in ETCO\textsubscript{2} by every 1 second sampling from a mainstream monitor, (Pokorná, 2009) 59 adults with out-of-hospital cardiac arrest who achieved stable ROSC had a mean 9.95 mmHg increase (95% CI for difference was 6.5 to 13.5 mmHg) in ETCO\textsubscript{2} with ROSC. This is graphically seen below with the 0 vertical line indicating when ROSC was clinically recognized. Note that some patients had a very high ETCO\textsubscript{2} reflecting asphyxial arrest, chronic lung disease or both. Of note, they used a mechanical ventilator to deliver constant ventilation and their study included children (youngest was 6 months) and adults. The authors do not state how many of the arrest patients were children.

Of the patients (n=49) who did not achieve ROSC; the mean ETCO\textsubscript{2} during chest compression was 16.7±9.1 mmHg (2.24±1.2 kPa). Of note, 6/59 with ROSC had an initial ETCO\textsubscript{2} <9.4 mmHg (1.25 kPa); 4/49 without ROSC had initial ETCO\textsubscript{2} >41.25 mmHg (>5.5 kPa). These data again suggest that the initial ETCO\textsubscript{2} during resuscitation is not highly predictive of outcome. As seen in the second figure below, all 49 non-ROSC patients had little change in the value for ETCO\textsubscript{2} during CPR but there was a good bit of variation.

Like the studies from Slovenia, this was a two-tiered EMS response system with 12 anesthesiologists or emergency medicine physicians in the second tier. In their study, they excluded patients who did not achieve a stable ROSC and patients who received sodium bicarbonate.

**Figure 1. 59 patients who developed stable ROSC**
This study does not support the same threshold values for predicting death as described in the large study from Slovenia (Kolar, 2008, R115) since some patients with ROSC had initial ETCO2 <10 mmHg and others with ETCO2 higher than 20 mmHg failed to have ROSC.

Even when using face mask ventilation or an LMA, end-tidal CO$_2$ appears to identify patients who will survive to hospital admission following out-of-hospital cardiac arrest (Nakatani, 1999, 203). In this prospective study in Japan, 121 patients (most with asystole) underwent CPR with face mask (40%) or laryngeal airways (60%) using a colorimetric detector (LOE 4P, fair). Unlike the earlier pediatric study by Bhende, they observed ROSC in 17% of patients with end-tidal CO$_2$ <0.5% (~3.5 mmHg), but none of these patients survived to hospital admission. The latter outcome was associated with having an end-tidal CO$_2$ >2% (~15 mmHg). Readings were made 7 to 15 minutes into resuscitation. It is possible that the presence of ROSC in patients with very low end-tidal CO$_2$ may reflect mask leak or ineffective ventilation in patients without a secure airway suggesting that a decision to stop CPR should be made cautiously when using this form of ventilation.

**Data Summary**

The available data show that end-tidal CO$_2$ often increases as a sign of ROSC. Furthermore, there are substantial data supporting the use of ETCO2 values at 15 or 20 minutes of CPR to predict failure of ROSC, but it seems unlikely that a single value will suffice in all patients. The data suggest that maintaining an ETCO2 of at least 15 to 20 mmHg improves the likelihood of ROSC and survival, but the data do not support using a specific value of end-tidal CO$_2$ to predict which patient will survive. This is particularly true in children for whom there is very little data. The available data also do not identify a specific time interval for when this determination may be made. It is clear that if ROSC fails to occur by 20 minutes and the end-tidal CO$_2$ is <10 mmHg (1.33 kPa) in patients with PEA there is virtually no likelihood of survival (Levine, 1997, 301). In the out-of-hospital arrest experience from Slovenia (Kolar, 2008, R115) an ETCO2 of 1.9 kPa (14.3 mmHg) or less after 20 minutes of ALS was uniformly associated with death, but higher levels were seen in patients without ROSC in the study from Prague (Pokorná, 2009). Unfortunately, the sensitivity, specificity, positive and negative predictive values of a threshold end-tidal CO$_2$ cannot be calculated from most of the available studies and are difficult to combine because often only the initial and final end-tidal CO$_2$ is stated in the publication. All clinical studies show 100% sensitivity for predicting ROSC when the end-tidal CO$_2$ is >10 mmHg, but this certainly does not assure that ROSC will occur. Furthermore, as seen in the above figures (Pokorná, 2009) the end-tidal CO$_2$ may initially rise in excess of 20 mmHg in patients without ROSC but then generally declines over 20 minutes. The large prehospital data set from Slovenia also show that failure to achieve an ETCO$_2$ >10 mmHg throughout resuscitation is associated with death (Kolar, 2008, R115).

In conclusion there is substantial data in animals and humans that shows there is an association between the end-tidal CO$_2$ concentrations and outcome, but the variation in clinical study design with different measurement time...
points makes it difficult to combine the studies together to develop a reliable predictive value. All of the studies consistently show that failure to achieve an end-tidal CO\(_2\) concentration above 10 or 15 mmHg is highly associated with death. It is logical to assume that interventions that increase the end-tidal CO\(_2\) concentration during resuscitation will improve the likelihood of survival, but there is no data to recommend a specific end-tidal CO\(_2\) treatment endpoint to guide resuscitation.

There is insufficient data in children to make any evidence-based recommendation to use end-tidal CO\(_2\) to guide or stop resuscitation. In addition, there is very little data on end-tidal CO\(_2\) monitoring in hospitalized adults and no data in hospitalized children. It is likely that the initial end-tidal CO\(_2\) concentrations will be different in these populations so that observations in the out-of-hospital setting may not be generalizable to the hospitalized population. There is clearly a need for additional data. In acquiring this data, the following points are important to consider:

- In view of the higher initial end-tidal CO\(_2\) concentrations in asphyxial arrest and in patients with a non-shockable initial rhythm, these patients should be analyzed separately from cardiac-related causes of arrest in children, particularly with respect to the initial and one minute end-tidal CO\(_2\) concentrations. The end-tidal CO\(_2\) concentrations after one or more minutes of resuscitation following asphyxial arrest are likely to be more predictive.

- It is likely that end-tidal CO\(_2\) concentration will be a better predictor of death rather than a predictor of ROSC or survival. Thus, it is important to report the number of patients who never exceed specific threshold values, such as 10 and 15 mmHg to permit calculation of the positive and negative predictive value of these threshold limits. Ideally, these data should be reported on a minute-by-minute basis to determine at what time point the threshold becomes valid. It is important to note that many of the older adult trials were performed in the emergency department after a variable period of out-of-hospital resuscitation, so the period of low blood flow was likely to be highly variable within the study population.

- There are likely to be patient subgroups requiring cautious interpretation of end-tidal CO\(_2\) concentration. This includes children with severe lower airway obstruction (eg, asthma and bronchiolitis) and children with shunt dependent pulmonary blood flow (eg, single ventricle physiology) or children with cyanotic congenital heart disease (eg, Tetralogy of Fallot). (Chuang, 2006, 117; Matthews, 2009, 60; Tugrul, 2004, 152)

- Since sodium bicarbonate transiently increases end-tidal CO\(_2\) concentration (Falk, 1988, 607) and epinephrine (or other vasoconstrictive agents) (Callaham, 1992, 337; Cantineau, 1994, 267; Chase, 1993, 413; Gonzalez, 1989, 920; Lindberg, 2000, 129) sometimes transiently decreases end-tidal CO\(_2\) concentration, data obtained within a few minutes of administration of these agents generally should not be included in analyzing the prognostic significance of end-tidal CO\(_2\) concentration. The effect of vasoconstrictors such as epinephrine appears to be dose-dependent and likely also depends on the duration of arrest with a shorter arrest period resulting in more intense vasoconstriction and thus global reduction in total cardiac output and pulmonary blood flow.

- There are no clinical data on the potential effect of newer CPR guidelines (i.e., giving more compressions and fewer or no breaths during BLS and emphasis on continuous chest compression and relatively few breaths during ALS) on the initial and subsequent end-tidal CO\(_2\) concentration. Since minute ventilation is one determinant of end-tidal CO\(_2\) concentration, it seems likely that giving fewer breaths will result in a higher end-tidal CO\(_2\) concentration than studies conducted in the past, particularly since we know that often too many ventilations are given during CPR. (Aufderheide, 2004, 1960) Once the airway is secured, it is important to assure that an appropriate ventilation rate and tidal volume are used since high ventilation rates, as observed in actual resuscitations may result in lower end-tidal CO\(_2\) concentration. In support, a well conducted animal study of VF arrest (LOE 5P, good quality) showed that a 30:2 compression:ventilation produced a 35% increase in cardiac output and common carotid blood flow compared with a 15:2 compression:ventilation ratio that was reflected by an increase in end-tidal CO\(_2\) and a decrease in the gradient between arterial and end-tidal CO\(_2\). (Yannopoulos, 2006, 1444)

- If used as a predictor of ROSC, survival to admission, survival to hospital discharge or some combination of these outcomes, ideally the results of end-tidal CO\(_2\) monitoring should be blinded to the rescuers so that it does not bias the rate or depth of compressions based on the observed data. Conversely, if the study goal is to use end-tidal CO\(_2\) as part of goal-directed resuscitation, then the data must be prominently displayed and readily available to the resuscitation team to guide resuscitation efforts.

- As an extrapolation of this data review, a sudden fall in end-tidal CO\(_2\) in mechanically ventilated children with continuous capnography monitoring should prompt a rapid assessment of the child’s ventilation looking for problems such as airway obstruction or ventilator malfunction. If the child is otherwise stable, than the CO\(_2\) detector may be contaminated. Conversely, if the child has signs of poor perfusion or falling blood pressure, the decline in
end-tidal CO$_2$ likely represents a fall in cardiac output. In this setting, the end-tidal CO$_2$ may be used as one parameter to guide resuscitation.

**Acknowledgements:**

Note: the following table includes all of the citations identified in my search. The actual citations for the review follow this table.

**Citation List**


Review article, not in evidence grid


This citation is not directly related to the worksheet and was included as a background citation.


5P - animal piglet model, so physiology may be close to infant; good study methodology.
Descriptive study documenting higher initial ETCO2 in asphyxial compared with VF arrest.
Study relates to using ETCO2 to diagnose presence of cardiac arrest--a high initial ETCO2 may be seen in asphyxial arrest, so it does not support using initial ETCO2 to diagnose arrest in infants and children.


I cannot figure out why this reference was duplicated by Endnote.


P2, good methodology. Prospective cohort with small sample size limiting interpretation of data.
The purpose of this study was to evaluate the effect of audio prompting. The improved PetCO2 certainly suggests that audio-prompted CPR was effective in improving the quality of CPR but they cannot confirm that the improvement was related to an actual improvement in cardiac output.

They evaluated the effect of audio-prompted CPR in 6 children in asystolic or PEA arrest in the PICU. Mean arrest was **14±9 mins prior to audio tape use**. Success of CPR was quantified by PETCO2. Rate of 100/min was compared with 140/min. Standard CPR PETCO2 was 4±3 torr; at 140/min it was 12±7 torr. It was not significantly higher (p=.08) at 100/min.

They note that the most junior person is often relegated to doing the basic CPR. Performance appears to be poor, however, suggesting that either compression rate or technique is inadequate. The tape may help everyone sequence properly and could improve outcome. None of the 6 children in this study had ROSC.

Study supports use of ETCO2 to guide quality of CPR


Duplicated by endnote


5P, fair quality. Data obtained as side point of original study.

Animal study in dogs of size relevant to infants. *Data were obtained from a previous, unpublished study examining epinephrine in asphyxial arrest. 8 animals had 5 minutes of arrest before CPR; 3 animals had 10 minutes of arrest before CPR. ROSC in mean of 4.2±2.2 mins in first group and 6.5±2.3 mins in group 2.

Study does not support using initial ETCO2 to identify arrest when arrest is due to asphyxia.

Study does support using ETCO2 to recognize ROSC with the sudden increase in ETCO2 seen at or just before ROSC is clinically recognized.


This is a case series (LOE 4P); evaluation of prognosis was not part of the primary goal of the study.

**Key pediatric paper--one of the few available**

They evaluated the use of a disposable, colorimetric ETCO2 monitor in determining accurate tube position during pediatric CPR. Study included all pediatric CPR patients < 40 kg, including prehospital arrests intubated in the field. Detector attached and 6 breaths given per manufacturer's directions before the reading was obtained, to wash out any residual gas that may have been in the esophagus from BVM ventilation. When CPR was discontinued, recorded readings again to see if they were predictive of outcome.
There were 40 children, mostly infants, and 37 intubated in the field by paramedics. 25 < 1 yr; 31/40 weighed < 15 kg. No data on the number of arrests during this time that were not included in this study, so may have ascertainment bias. The 40 children underwent 48 intubations; one patient had 3 esophageal intubations. 39 intubations were judged to be tracheal based on clinical examination, and 9 were thought to be esophageal (18.5% of attempts, but if exclude one patient with 3 intubations = 6/45 or 13.3% of attempts). Lack of color change correctly identified all 9 esophageal intubations and color change identified all 33 ET intubations. The 6 false negatives (no color change with tracheal tube) had been in arrest for at least 25 minutes; most were SIDS with one severe trauma case. The detector had a sensitivity of 84.6%, specificity of 100%, PPV of 100% and NPV of 60%. They note that the dead space is 38 ml, so may not want to leave it in place.

Outcome was related to color change; only 2/40 survived to discharge, and both had initial colors in the yellow range (>2.0% CO2). Last color before stopping CPR also correlated with ROSC. Because they only recorded the last value this study was not very helpful in determining the utility of following ETCO2 over time, but does show that if the child in arrest does not increase their ETCO2 above a low level, they will not survive.

Supports prognostic utility of ETCO2 to predict outcome.


This study does not specifically address the evidence evaluation question, but it is relevant because it illustrates a potential factor affecting the interpretation of ETCO2. Specifically, in children with cyanotic heart disease, the right to left shunt and resulting lower effective pulmonary blood flow increases the gradient between ETCO2 and PaCO2.

Study is not on the evidence evaluation grid.


Duplicated by EndNote-no obvious reason


4P for adults; of fair quality with probable bias from missing some patients who presented to the ED

This is a prospective study of 64 adults (70±12 yrs) who presented to an ED with out-of-hospital cardiac arrest. They determined the value of ETCO2 monitoring on predicting outcome, and the change in response to epinephrine. Epi doses were determined by MD; 16 received HDE. Of note, only 64 enrolled from 1/1987 to 5/1990, so significant risk of bias. Also, most patients had prolonged arrest.

ROSC defined as pulse detectable for at least 5 mins. First ETCO2 obtained after 1 min of manual ventilation, which introduces another potential bias since minute ventilation may have
been variable. Initial values were excluded from 14 patients who received bicarbonate before study inclusion and had a baseline ETCO2 higher than the others. Overall, mean ETCO2 was 9±6 in 15 responders and 6±4 in the 49 non-ROSC patients. Even when they excluded the 23 patients with ETCO2 < 5 torr, there was still no relationship between epinephrine administration and response.

**Patients with a return of pulse had a -2 torr decrease with a PPV of 56% and NPV of 92%**. An ETCO2 of 10 torr prior to epinephrine, but not on first arrival, was a good predictor of ROSC. The response to epi was quite variable. Other studies report that the PPV of ETCO2 was eliminated by epi administration. Of note, they **only analyzed the change 4 mins after epi given, which may be too late**; and these patients had prolonged arrest prior to study. None survived to hospital discharge and only 15/64 had ROSC. **Conclude the change in ETCO2 in response to epinephrine does not provide clinically useful information.** It is not clear how applicable their results are to a real world situation with earlier ETCO2 measurements.


5P-case series, unselected.

It is interesting to note that the initial pETCO2 was higher in this study than some of the other studies; this may be because they used controlled mechanical ventilation rather than the usual manual over-ventilation by rescuers. It appears that if there is a reasonable cardiac output (CO), an effective dose of epinephrine will likely decrease the ETCO2. If the CO is poor, however, than it will be difficult to detect an effect. Similar to Gonzales and Weil data showing that epinephrine reduces cardiac output.

Data are not relevant to the evidence evaluation directly, but instead illustrate a caveat related to the interpretation of ETCO2 following administration of epinephrine.


5P, good study design. Shows that high-dose epinephrine improves coronary perfusion pressure but reduces global cardiac output as reflected by the fall in ETCO2. This was a relatively short arrest period yet the CPP was low and there was little effect from standard dose epinephrine, which is somewhat surprising. The study design gave high-dose epinephrine always last. The study supports the relationship between ETCO2 and cardiac output during cardiac arrest, so it supports using ETCO2 to guide CPR but does not directly test that outcome.


This is a small case series report that does not directly address the evidence evaluation question. It is included because it describes a caveat to the interpretation of ETCO2—specifically the
presence of a right to left shunt, which will reduce effective pulmonary blood flow and thus ETCO2.


Case series, 4P for adults, good quality. Evaluated ROSC; study supports using ETCO2 as prognostic indicator, but small study. They found a significant increase in ETCO2 heralded ROSC, so supports its utility to identify ROSC. The rapid decline in
They studied 10 adult patients in the ICU with endotracheal tubes in place and PA catheters in 8/10 patients. These patients experienced 13 cardiac arrests. **Ventilation and Vt was maintained constant during CPR.** Monitored ETCO2 before and during CPR. They found that the ETCO2 decreased from 1.4+0.9% (~10 mmHg) before arrest to 0.4+0.4% (3 mmHg) after arrest and only returned >1% in those patients who survived. Overall 7/13 arrest episodes led to ROSC. After ROSC there was an initial overshoot to 3.7+2.1% then returned to lower value. Most of the patients were in a low flow state before arrest at 1.8+0.8 L/min/m$^2$.

*After the injection of NaHCO3 into the central venous circulation, the ETCO2 transiently increased from 0.8+0.5 to 2.1+1.4% and returned to baseline levels after 2 minutes. This illustrates the importance of knowing that NaHCO2 will affect the interpretation of ETCO2 for up to 2 minutes.*

They also documented correlation between ETCO2 and the cardiac output, although thermodilution CO may not be as accurate in low CO states.

ETCO2 serves as a predictor of outcome in adult cardiac arrest victims. During the arrest, plateau ETCO2 was 0.7+0.2%. Unless ETCO2 was increased to levels of >1.0% during CPR, resuscitation is not likely.

Basically, during constant ventilation, ETCO2 correlates with the cardiac output during CPR.


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Case series, P4, fair.
This is a small study and is neutral with respect to the utility of ETCO2 to identify patients who will have ROSC. One strength of study is that ventilation was held constant.

In this selected population, the overall ETCO2 was relatively high with a mean value of 12.8 mmHg without ROSC versus 12.1 mmHg in those with ROSC. It is important that ventilation was held constant, but the ventilation rate was high by today's standards.


5P animal study
By extrapolation, this study supports using ETCO2 to guide resuscitation therapy based on the correlation between ETCO2 and cardiac output. This study also shows the marked rise in ETCO2 with ROSC.


5P, good model design. This porcine study is not directly related to the evidence question since it uses extracorporeal circulation to adjust cardiac output. The model shows a good correlation between directly determined cardiac output from extracorporeal circulation and the ETCO2. This study documented the close correlation between blood flow and ETCO2 in a cardiac arrest model and thus supports using ETCO2 as a monitor of cardiac output during CPR.


Letter to the editor. The authors of the paper (Levine et al, 2007 in NEJM) note that the patients with high ETCO2 and ROSC had return of ROSC prior to the 20 min time period when they reported the second value.


5P, fair. They studied 10 patients with out-of-hospital cardiac arrest who arrived in the ED with ongoing VF. Inserted radial artery line by cutdown and measured ETCO2. Time to ED arrival was 40±9.5 mins. Gave 1, 3 and 5 mg of epinephrine. Found that systolic and diastolic BP both increased with increased epi doses from baseline of 47±5 and 18±2 to high of 85±8 and 36±6 after the 5 mg dose. *ET-CO2 decreased progressively* from 1.9±0.2% with each dose. This data suggests that cardiac output decreased even though perfusion pressure increased. Suggests that fall in ETCO2 reflects decrease in cardiac output due to epinephrine. See study by Weil's group. Total CO does decrease-cardiac output is redirected to heart and brain with improved perfusion pressure.


4P for adults, fair quality because they do not provide the raw values to allow you to estimate the failure to achieve ROSC based on a threshold ETCO2 value. This is strictly an out-of-hospital adult arrest population. Overall 53/139 had ROSC (38%) and 23 (17%) survived to discharge. They report the statistical outcomes, but there appear to be missing values at different times because I cannot back calculate the same values based on the total number of ROSC and non-ROSC patients. Also cannot calculate the confidence intervals for the estimates. They note that no patient with a maximal, final or average <10 survived. Initial ETCO2 was 15.8±5.9 in pts with ROSC vs. 9+6.8 without ROSC. Thus, this reports supports using this threshold to predict
outcome in cardiac arrest. There was significant variation in the ETCO2 value over time with a mean difference of 14+6.4 mmHg. See Kolar for a more extensive evaluation of ETCO2 from this same group.


3P, observational prospective study, good quality
No industry support.
From prehospital unit Maribor Slovenia. Enrolled patients from 01/2001 to 12/2004, so there was some overlap with 2003 study, but not that much. Included all OHCA calls. Used mainstream monitor integrated into Lifepack 12. Data lumped all patients together even though their earlier data showed that asphyxial group initially had higher ETCO2. Data would likely even be more striking if you eliminated the asphyxial group. Recorded initial end-tidal CO2 and then every minute thereafter. During the time period, there were 592 OHCA for which CPR was attempted in 389. Of these, 277 (72%) were classified as cardiac etiology and 112 (28%) as non-cardiac. There was ROSC in the field in 61% (237/389) and 50% ROSC to hospital admission (195/389). There were 82/389 survival to hospital discharge. The initial rhythm was VF/VT in 156 (40%) and was asystole or PEA in 233 (60%). The *initial* end-tidal CO2 was 0.94±0.66kPa in those who died vs. 2.42±0.74 for those who survived to hospitalization (p<0.001). Note, 1 kPa = 7.5 torr. Final end-tidal CO2 was 1.0±0.35kPa vs 3.63±0.97 (p<.001). The initial end-tidal CO2 for death in field was 1.4±0.9kPa vs. 2.6±0.9 (p<.001) and final end-tidal CO2 was 1.9±1.3kPa vs 3.9±1.2 (p<.001). **Multivariate analysis shows that initial petco2 was highly associated with outcome (odds ratio for ROSC and admission to hospital was 22.0 [11.4 to 42.6; 95% CI], which was much higher than any other factor associated with outcome (ie, witnessed arrest, bystander CPR, initial rhythm, time to EMS arrival and patient sex). None of these factors had an odds ratio for hospital admission >3.1. In 158/195 (81%) of all patients with ROSC, a rise in end-tidal CO2 was the first sign of ROSC before pulses were noted. Average rise was 1.8±0.6% (12.6±4.2 torr). Of note, **all patients with ROSC had an initial end-tidal CO2 over 1.33 kPa (>10 torr)**. Unfortunately, they do not state how many patients with initial or subsequent end-tidal CO2 <10 had ROSC eventually.

They recommend stratifying reports of CA patients by initial ETCO2 > or < 1.33 kPa. This study provides strong support for the prognostic implications of initial ETCO2. They also document that the rise in ETCO2 was the first sign of ROSC before detectable pulses were present.


5P, good, adult (≥18) with non-traumatic, normothermic CA in Maribor Slovenia from 2/98 to 2/01. Recorded initial ETCO2 after intubation and final (with ROSC or when resuscitation efforts were stopped). Used standard BLS/ALS. Used the ETCO2 added to the Mainz Emergency Evaluation Score (MEES). They added a score of 1 or 2 to the MEES based on the initial and subsequent pETCO2. This increased maximal score to 28. 246 patients; 52% male. Most patients with ROSC had witnessed arrest. Using a cutoff of 10 mmHg, the sensitivity of
initial value for predicting ROSC was 1.0 and specificity was 0.74 (ie, 26% were incorrectly classified). Similarly, sensitivity for predicting survival was 1.0 and specificity was 0.8 (20% misclassified) for a cutoff of 10 mmHg.

For the final ETCO2 values, the sensitivity for predicting ROSC was 1.0 and specificity was 0.9 while sensitivity/specificity for survival was 1.0 and 0.92 respectively. Thus, 8% of patients who subsequently did not have ROSC had a final ETCO2 > 10 mmHg. Conversely, no patient had ROSC without ETCO2>10.

With a cutoff of initial pETCO2 of 2.13 kPa (16 torr) the sensitivity for predicting survival was 1.0 and specificity was 0.94. The final value pETCO2 at the same threshold was sensitivity of 1.0 and specificity of 0.95 for predicting survival.

MEES is based on GCS, HR, frequency of breathing, ECG rhythm, presence of pain, systolic BP and O₂ sat. The score ranged from low of 10 to 28, so all CA patients had score of 10. This study group appears to overlap with the 2001 study group.

The study does not present the raw data to determine the distribution of patients in a 2X2 table. They calculated the sensitivity, specificity, PPV and NPV for the threshold pETCO2 as follows:

- sensitivity = # of pts with ROSC and ≥ threshold pETCO2/# with ROSC
- specificity = # of pts without ROSC and pETCO2 < threshold/total # without ROSC
- PPV = # of pts with ROSC and ≥ threshold pETCO2/total # of pts with pECTO2 > threshold
- NPV = # of pts without ROSC and pETCO2 < threshold/ # of patients with pETCO2 < threshold.

This study supports the relationship between ETCO2 and outcome.


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3P for adults, observational prospective cohort study treated in the ED using sidestream ETCO2 monitor. Good quality. Consistent with animal model studies by Berg and Bhende, showed that initial PetCO2 was higher in asphyxial arrest than VF arrest. Prehospital ALS-physician-based team recorded initial value, than q minute thereafter. 411 consecutive resuscitation attempts; 66 non-cardiac and 335 cardiac. Of the 66 non-cardiac, there were 11 VF and 4 VT so 41 non-VF/VT available for analysis. ROSC represents a sufficiently long return of circulation to permit hospitalization. Over 4.5 years (2/98 to 10/02) they had 141 primary VF/VT arrests and 44 non-VF/VT arrests (initial rhythm PEA or asystole). The latter group was younger (49 vs 66 years old). ROSC was more common in the VF/VT population (yes/no: 101/40 versus 18/26), as was being discharged alive from the ICU; yes/no: 38/103 versus 7/37 asphyxial arrest. Initial values of end-tidal CO2 were much higher in the asphyxial group and did not differ between those with and without ROSC (70.1±15.3 mmHg versus 62.8±16.2 mmHg, p+0.64). At one minute the end-tidal CO2 was significantly higher in patients with ROSC
vs. those without ROSC (35.8±8.6 vs. 19.4±8.7 torr). As in their more recent trial, they noted that ROSC only occurred in patients with an initial end-tidal CO2 >10 mmHg, but they do not state how many patients exceeded that threshold, so the sensitivity, specificity and positive and negative predictive value of this threshold cannot be calculated.

Table 3. The mean values for all patients of the initial, final, average and after 1 min of cardiopulmonary resuscitation (CPR) partial pressures of end-tidal carbon dioxide (PetCO2) for arrest due to asphyxia and for ventricular fibrillation/pulseless ventricular tachycardia (VF/VT) cardiac arrest

<table>
<thead>
<tr>
<th>Asphyxial cardiac arrest</th>
<th>PetCO2 after 1 min</th>
<th>Average PetCO2</th>
<th>Final PetCO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial PetCO2</td>
<td>66.4±17.3</td>
<td>29.1±4.9</td>
<td>48.2±10.1</td>
</tr>
<tr>
<td>VT/VT cardiac arrest</td>
<td>16.5±9.2</td>
<td>24.2±5.1</td>
<td>17.3±7.1</td>
</tr>
</tbody>
</table>

P value (Student t test) < 0.01 0.73 < 0.05 0.78

1 mmHg = 0.133 kPa.

Initial PetCO2 in asphyxial group: ROSC/no ROSC – 70.1±15.3 / 62.8 ± 16.2 (NS)
At one minute there was a significant difference: 35.8±8.6 vs 19.4 ± 8.7 and final – 31.2±8.4 v 7.2 ± 3.3
Similarly in VF/VT group: 20.3±6.2 v. 8.2 ± 4.3 (p=0.04) 1 minute: 30.2 ± 8.3 v 14.2 ± 5.2
Final: 28.1 ± 4.8 vs. 6.2 ± 2.8. (all others, p<0.05)

Conclude that initial PetCO2 is not prognostic in asphyxial arrest, but becomes prognostic at 1 minute; however threshold level is not clear. One should expect the PetCO2 to fall with ventilation in asphyxia arrest and then rise up again if effective CPR is being delivered. It is also possible that if you see a very low PetCO2 you should slow your ventilation significantly and work on improving chest compressions and perfusion until you see the PetCO2 start to rise again. Conversely, if the PetCO2 is high, than perhaps a more rapid (within reason) respiratory rate would be appropriate.

This study supports the use of ETCO2 to predict outcome.


4P for adults, good quality
This study documents the higher initial ETCO2 in asphyxial arrest (in this case drowning) than seen with primary cardiac arrest. This observation is an important caveat to consider when evaluating the ETCO2 as a predictor of outcome. They also show that after a minute of CPR with ventilation, the ETCO2 becomes predictive of subsequent survival. Additional caveats are that the drowning victims were about 20 years younger on average; survivors were cooler in the drowning victims and overall, drowning arrest victims were cooler than the primary cardiac arrest group. Finally, they again observed the sudden rise in ETCO2 with ROSC.

4P for adults. Good quality, but not directly related to evidence evaluation question. This study supports the use of ETCO2 to document improvement in cardiac output during CPR, but they do not employ a gold standard measurement to assure that the increase in ETCO2 is due to an actual increase in cardiac output with ACD-CPR. Invasive femoral artery pressure was measured in less than a third of patients, but did show a significant increase in the systolic pressure with ACD-CPR. The mixed venous blood gas changes provided further indirect evidence for improved cardiac output.


P5, animal study that shows a good correlation between effective pulmonary blood flow and ETCO2. Therefore, provides support for using ETCO2 to monitor the effectiveness of interventions during CPR to improve cardiac output. They also document the expected effects of changing minute ventilation, but note that the effects of mechanical ventilation on cardiac output are eliminated by use of a mechanical ventricular assist device. Thus, use of ETCO2 for prognosis and to monitor effect of intervention during CPR is best done when minute ventilation is constant.

See similar study reported by this group the same year.


P5, often quoted well done study clearly showing a tight relationship between PETCO2 and cardiac index. In this animal study, minute ventilation was kept constant and cardiac output adjusted using mechanical ventricular assist devices. This study supports using ETCO2 to monitor changes in CO during CPR.

See very similar paper where they adjusted the minute ventilation at low flow.


5P, animal model, good quality

Study supports the relationship between ETCO2 and cardiac output in a model of hypovolemic and cardiogenic circulatory shock.


5P, fair quality for study question. The study supports a relationship between improving cardiac output through BLS and higher ETCO2, but cannot verify that the intervention increased cardiac output. This is similar to Berg's study showing value of audio directed CPR. Also shows that 120/min compression rate appears to produce better CO as measured by end-tidal CO2 (ETCO2).

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This 5P good quality study (3 P for adults) is the largest trial evaluating the association between ETCO2 and outcome in cardiac arrest. This study combines the data from a number of previous trials reported from this group. It is entirely out-of-hospital arrest with a two-tiered system having an emergency medicine physician at the arrest scene. Thus, the results from this trial may not be transferable to other EMS response systems. This study provides good support for the prognostic utility of ETCO2 monitoring to predict outcome during CPR.

The trial documented that initial ETCO2 is different in patients with shockable arrest rhythms versus those without shockable rhythms, suggesting that this difference is because there is more retention of CO2 in the lungs with an asphyxial arrest than seen in the patient with an acute arrhythmia-mediated arrest. In this large retrospective analysis of prospectively collected data during OOH arrest they noted the following key points:

- An ETCO2 of 1.9 kPa (14.3 mmHg) or less measured at 20 mins after the initiation of ALS for cardiac arrest accurately predicts death in patients with a nonshockable rhythm. For ROSC (Table 3), the sensitivity, specificity, PPV and NPV were all 100% using this threshold. The 20 min ETCO2 threshold of 1.9 kPa discriminated between the 402 patients with ROSC and 335 without ROSC.

- A 15 minute ETCO2 of more than 1.8 kPa (13.5 mmHg) has a sensitivity and NPV of 100% for ROSC (Table 3) with specificity and PPV of 98% (328 patients ≤ 1.8 kPa (13.6) versus 409 patients >18 kPa (13.6 mmHg).

- A 20 min ETCO2 value greater than 1.5 kPa (11.3 mmHg) predicted death in patients with a shockable cause of cardiac arrest; the sensitivity, specificity, PPV and NPV were all 100% for this outcome (based on 304 patients, 93 of whom had ROSC. This same threshold had a sensitivity of 100% and NPV of 100% for survival to discharge, but only a specificity of 44% and PPV of 45% for survival. See Table 9. There were 211 patients with ETCO2 >1.5 kPa at 20 mins; 95 survived and 116 died. All 93 patients with ETCO2 < 1.5 kPa died.

- ETCO2 >2.1 kPa (15.8 mmHg) at 20 min in patients with nonshockable rhythm had sensitivity and NPV of 100% in predicting survival to hospital discharge.

- ETCO2 less than 1.5 kPa (11.3 mmHg) after 20 mins of CPR (or <1.8 kPa (<13.5 mmHg) after 15 mins of CPR) are incompatible with ROSC

- No patient with initial, average and maximum ETCO2 was <10 mmHg (1.33 kPa) had ROSC (not sure of number of patient fitting this criteria; likely it was less than 97 out of 737 patients).

- Initial ETCO2 was significantly higher in patients with non-shockable vs. shockable rhythm (3.4± 2.4 vs 2.2±1.2), but by 1 min, ETCO2 was lower in the nonshock vs.
shockable group (2.8±1.5 vs 3.3±1.4). This is consistent with higher likelihood of asphyxial arrest in nonshock group.

- They conclude that ETCO2 should be monitored during CPR since it has prognostic value and can help in the decision-making for termination of resuscitation.


4P adults, 5P children; good quality. Looking at the utility of ETCO2 to predict outcome was not the main point of this study, but ETCO2 concentration did correlate with outcome. No threshold value identified and relatively small study.

It took a fairly long time to attach the device and get it working. The microprocessor is programmed to compress 25% of the AP diameter in adults.


3P for adults, good quality, but study has limited applicability since only looked at 20 min outcome and limited analysis to just those patients with PEA. Prospective observational study, Bellingham, WA. No industry support. They excluded patients with asystole, VF or VT—had to have electrical activity (ie, PEA). Study from 1991 to 1995 in relatively small county (160,000).

They did include patients with post-defibrillation PEA. Excluded CA from hypothermia, trauma, hypovolemia, tamponade, tension pneumothorax, and poisoning. Report no difference in survival based on initial ETCO2 using mainstream monitor. They noted that others have used ETCO2 as predictor of survival, but their purpose was to determine its utility as a predictor of death. 35/150 survived to hospital admission. Initial etco2 was 12.3±6.9 (2-50) in NS vs 12.2±4.6 in S (5-22). Note that upper limit (99%) of survival with Etco2 <10 is 3.9%. 19/35 survivors to admission died in the hospital. Initial and final etco2 did not discriminate between hospital survival groups.

See editorial by Gomersall and the authors' response. The patients with ROSC achieved this outcome prior to 20 mins, so this magnified the difference in ETCO2 levels. They also note that patients with ROSC had initial/early ETCO2 >10 whereas the nonsurvivors did not.


This is very similar to the 2007 paper by Ristagno that showed that effective chest compression was important to ROSC after VF arrest. This is a small study which used temporary LAD occlusion to induce 5 minutes of VF arrest. They used a 15:2 compression:ventilation ratio during CPR. No vasoactive drugs were used during CPR.

Data, as seen in Figure 5, suggests that the threshold ETCO2 for successful resuscitation may be higher than 15 torr in this model. A CPP of 15 torr was clearly critical to achieve ROSC. They used fairly large tidal volumes (15 mL/kg) during CPR. Like other studies from this group, they found that ETCO2 started to fall after about 2 mins of CPR suggesting that
attempts at defibrillation may be best after 2 mins rather than the 3 mins used in this study.
Overall, supports the relationship between ETCO2 and prediction of outcome. Small trial, fair quality for the study question. Animal trial (5P)


This is a nice pig study (5P) documenting the adverse effect of epinephrine and norepinephrine on cardiac output, as seen by a rapid, but transient fall in ETCO2.
Good study design. This study used a short duration of cardiac arrest, which likely resulted in a greater effect from the epinephrine and norepinephrine than observed in other studies with long arrest duration. It seems likely that the effect of vasopressors on PetCO2 depends on the duration of cardiac arrest. This study also shows that vasopressors improve coronary perfusion pressure but reduce global cardiac output (ie, effective pulmonary blood flow). It is also possible that the failure of the PetCO2 to fall after a vasopressor represents a poor prognosis (ie, lack of effect from the vasopressor).
There are good figures in this study that nicely illustrate the changes in ETCO2, CPP and pulmonary blood flow. Pulmonary and carotid blood flow was measured by ultrasonic flow probes.
Study documents need to cautiously interpret ETCO2 for outcome prediction and monitoring the effectiveness of CPR--does not directly contribute to data on those outcomes, except showing that that ETCO2 reflects changes in CO.


4P, good study quality. From prehospital unit in Maribor Slovenia with 2-tiered system; second tier had physicians. Observational prospective study. Collected OOH CA data from Jan 2000 to April 2006, so there is an overlap with this group's previous study. Vasopressin was used routinely for VF arrests requiring medications since 11/03 and in asystole as first drug since 1/06. Initial MAP was the first measured MAP after ROSC (by Lifepack 12). All etco2 by mainstream monitor; recorded initial than q minute until arrival at hospital or discontinuation of CPR efforts. Note that the average etco2 was above the threshold of 1.33 kPa (10 mmHg) in vasopressin group. They note that ALL patients with ROSC had an initial etco2 over 1.33 kPa. There were 452 patients in the epi group and 146 patients in the vasopressin/epi group. They do not state how many of these patients received only vasopressin.

Table: comparison of ETCO2 between CA patients who received epinephrine only or vasopressin±epinephrine
(see worksheet)
In the following table note the odds ratio for the initial etco2 associated with ROSC & hospital admission. For every 10 mmHg increase in initial MAP there is a 1.4 times greater likelihood of hospital survival, suggesting this reflects better cerebral perfusion. It is interesting that the initial end-tidal CO2 was not different between the epinephrine and vasopressin groups, but the average and final end-tidal CO2 was significantly higher in the vasopressin group as was the occurrence of any ROSC (58% vs. 67%; p=0.04) and ROSC and admission to the hospital (46% vs 62%; p=0.01)

Study shows the beneficial effect of combined epi and vasopressin reflected by higher MAP and ETCO2. This was specifically seen in the asystole population. MAP was measured after ED admission. Thus, this study supports utility of ETCO2 to predict outcome and as a monitor of improved quality of CPR (in this case from vasopressin) resulting in higher rate of ROSC and survival to hospital admission.


This observational (5P) study is not directly related to the evidence evaluation worksheet, but is relevant since it illustrates the physiologic principle of correlating effective pulmonary blood flow to ETCO2. In addition, it points out the potential limitation of using ETCO2 monitoring during CPR in infants with univentricular physiology and shunt dependent pulmonary blood flow. It also suggests that monitoring changes in ETCO2 at a constant minute ventilation, as may occur postoperatively, can be useful to detect a fall in effective pulmonary blood flow as may occur with an increase in PVR or with shunt obstruction. Good quality for what the study was designed to measure.


5P for pediatrics, good quality but cannot calculate sensitivity, specificity, PPV and NPV from data reported. No research support. Two tiered EMS system with physicians in second tier. Mainz Germany. Unlike most other trials, they report the end-tidal CO2 every 2 mins up to 10 mins. It is important to note, however, that this prospective trial excluded traumatic and non-cardiac codes, so it is less applicable to pediatrics since asphyxial arrest is not included. VF was initial rhythm in 45%. They used a side stream capnometer and at the time of this study a 5:1 compression:ventilation ratio was used, so hard to compare to current protocols. Indeed, this ratio would result in frequent interruptions in compressions and likely limits the ability to detect a difference between ACD-CPR and standard CPR. Their data clearly supports failure to achieve an end-tidal CO2 >15 torr by 10 min of CPR with non-survival (median of 7.2 min from call to even beginning CPR with only 8.3% having bystander CPR despite almost 70% being witnessed). They also suggest that continuous monitoring of end-tidal CO2 could potentially replace the need to stop CPR and assess for a pulse.

5P, fair quality. This study did not find that there was a relationship between ETCO2 and outcome. ETCO2 was 24±11.1 in non-survivors and 29±13.0 mmHg.


4P for adults, fair quality. No industry support. Study conducted in Japanese prehospital setting. The purpose of this prospective, multicenter study was to evaluate a colorimetric end-tidal CO2 (ETCO2) detector (EASY CAP) as a monitor during prehospital non-traumatic cardiopulmonary resuscitation (CPR) without tracheal intubation. This detector was used for 121 patients during CPR with a laryngeal mask airway (58%), esophageal gastric tube airway (2%) or face mask (40%) by authorized emergency lifesaving technicians. No meds are given in the field. At 7 to 15 minutes after the initiation of CPR, ETCO2 was 2.0% in 45 cases (group C). The rate of return of spontaneous circulation was 17% in group A, 24% in group B, and 48% in group C (groups A v C, P .01). There was a significant difference in the rate of hospital admission between groups A and C. The ETCO2 value may be useful for monitoring during prehospital CPR with a laryngeal mask airway or face mask.

Most patients were in asystole (94/121); only 10 had VF and 17 had PEA. They did not find that having an ETCO2 <4 mmHg (0.5%) predicted outcome, but this may have been effected by not having a secure airway with leak during face mask ventilation or ineffective ventilation.

Overall, this study supports a difference in outcome associated with ETCO2, but prediction was not strong. A major limitation of this study is that the airway was not secured with an endotracheal tube, so the presence of airway leak may affect the ETCO2 reading.


5P, fair quality relatively small study with only the maximal measurement of ETCO2 reported, which precludes using this paper to guide resuscitation. Relatively young patient population. This is not a prognostic trial, but suggests a correlation between ACD-CPR and better blood flow as reflected by the significantly higher peak ETCO2 during the 3 minutes of ACD-CPR compared with 3 mins of standard CPR. Thus, it supports use of ETCO2 to monitor the effectiveness of CPR.

LOE 5P-animal data. Good methodologic quality. Hemorrhagic shock model, not cardiac arrest. Study follows up on observations made by same group in small human observational study (1989). Study supports observations subsequently made by Idris et al in 1994. Prospective, controlled animal study with 14 sheep weighing 23 to 47 kg. They performed 172 simultaneous measurement of thermodilution cardiac output and ETCO2 during controlled arterial hemorrhage. A plot of CO vs. ETCO2 suggested that the relationship was logarithmic, r=.91 (ETCO2 vs log[CO]). They conclude that decreased presentation of CO2 to the lungs is the major, rate-limiting determinant of the ETCO2 during low flow. As CO increases, respiration becomes the rate-limiting factor. Often quoted animal study documenting relationship between hemorrhage and fall in ETCO2. Thus, this study supports use of ETCO2 monitoring as indicator of changes in cardiac output during CPR.


4P for adults, fair quality, small descriptive study
This study was done in very late CPR state when the patient was not likely to have much vascular tone and little cardiac output achieved, so not very helpful. This likely explains why there was no change in PetCO2 with changes in compression rate. Overall, would rate this as neutral for utility of ETCO2 monitoring to identify changes in cardiac output. See follow up study published in 1989 that documents that changing compression force improved ETCO2.


LOE D5, good study that provides animal data supporting the relationship between pETCO2 and cardiac output. Supports earlier work by Weil et al. CCM 1985; 13:907-13. Their estimates of stroke volume, however, are based on TEE, which is not clearly reliable when the SV is being produced by chest compression rather than cardiac contraction. Used a side-stream IR monitor. They used two independent observers to estimate SV. During VF arrest with compressions, the CI by thermodilution decreased from 127±23 to 36±10 ml/min/kg (28±8% of baseline). SVI decreased from 1.22±0.23 to 0.45±0.13 ml/kg/beat (37±11% of baseline). PetCO2 decreased from 37.8±1.6 to 15.5±4.5 mmHg, a decrease to 38±10% of the baseline value. At low CI, there was a linear relationship between SV and PetCO2. In summary, this study supports monitoring of ETCO2 to assess quality of CPR in terms of improvement in cardiac output.

5P, fair methodology for this evidence evaluation since the basis for patient selection and inclusion does not reflect the range of all cardiac arrests. The use of continuous mainstream monitoring with 1 second sampling and use of constant minute ventilation during CPR are strengths of their study. A weakness of the study is the mixed population without clearly distinguishing between asphyxial versus primary cardiac arrests.

Retrospective “case control” study of OOH arrests with ALS in Prague, Czech Republic (~1.5 million) using 2-tiered EMS system with 12 anesthesia or ED physicians in second tier. ALS patients intubated and mechanically ventilated with 7-10 mL/kg, FiO2 = 1.0 at rate of 8-12/min. Used Zoll M monitor with mainstream ETCO2 (noted that some contamination of detector with blood may affect CO2 reading since IR absorption by hgb (430 nm) is close to CO2 (426 nm). Study done from 2004-6 so substantial delay in publication. Part of a larger study funded by Ministry of Education, Youth and Sports of Czech Republic.

Analyzed 140 patients (70 transferred to hospital and 70 who died at scene), 32 excluded such as failure to maintain stable ROSC or if NaHCO3 given. Also, did not include patients who responded to defibrillation rapidly without need for ET intubation. Overall, there were 59 cases with ROSC and 49 without ROSC ranging in age from 0.5 to 90 or 92 years respectively. No data on how many were <19 years. Mean duration of monitoring was 18 min before ROSC and 33 min after ROSC.

There was a very wide range of initial and average ETCO2 during resuscitation; they did not correlate the ETCO2 to the type of arrest. Average (during chest compression) ETCO2 before ROSC was 26.65 mmHg (3.55±1.6 kPa) [note higher than Slovenia data] and 36.6±12.4 (4.8±1.66 kPa) after ROSC. Mean difference before versus after ROSC was 9.95 mmHg (1.32 kPa; 95% CI for difference was 6.5 - 13.5 mmHg) - see figure for changes with ROSC. This is consistent with other reports. In the 49 patients without ROSC, mean ETCO2 was 16.7±9.1 mmHg (2.24±1.2 kPa).

6/59 with ROSC had initial ETCO2 <9.4 mmHg (1.25 kPa); 4/49 without ROSC had initial ETCO2 >41.25 mmHg (>5.5 kPa). All 49 non-ROSC patients had little change in waveform during CPR.

Overall, this study supports monitoring ETCO2, which was associated with ROSC, but no obvious threshold highly predictive of outcome; instead, the higher the ETCO2 the better the outcome. They also demonstrate the rapid rise in ETCO2 with ROSC.


5P, good methodology

Evaluated importance of depth of compression versus timing of defibrillation in a pig VF model. Used a 15:2 compression:ventilation ratio during CPR. VF arrest was 5 min; induced by LAD occlusion, but the coronary balloon was deflated permitting complete restoration of blood flow, so may not be a good AMI model. For the purpose of this study, they convincingly showed that 25% compression of A-P diameter was clearly superior to compressing 70% of that distance (17.5% of AP diameter). There was a clear difference between the ETCO2 in the group receiving more effective chest compressions. Thus, this study provides good support for monitoring ETCO2 as an indicator of the effectiveness of BLS interventions.
They used a fairly large tidal volume for their rescue breaths (15 mL/kg) in these 40 kg pigs. No epinephrine or other vasoactive drug was used during CPR. This study clearly shows that effective chest compression is more important than immediate defibrillation in a model of 5 mins of arrest prior to the availability of an AED.

They used TEE to monitor ventricular function after ROSC--showed a transient decline in cardiac contractility that recovered.

It is interesting that the ETCO2 started to fall after 2 mins of CPR, suggesting that the timing of defibrillation attempt may be after 2 mins rather than the 3 mins used in this trial.


5P, good quality
Used OPS imaging to monitor changes in cerebral cortical blood flow during VF arrest and CPR. Showed a correlation between cortical blood flow and ETCO2 during CPR. It is interesting that cortical blood flow persisted for 3 mins of no cardiac pumping function and thus presumably blood flow; this observation presumably reflects an ongoing pressure gradient between the arterial and venous circuits. They also monitored brain tissue pCO2 and found that the tissue concentration continued to rise even during CPR suggesting there was ongoing ischemia. Tissue pCO2 only came down after ROSC, but took about 7 minutes to return to baseline. This was a relatively short arrest period (3 min) followed by 4 min of CPR before shocking.

Animals received CPR using a 15:2 compression:ventilation ratio.
Study supports monitoring ETCO2 as an indicator of the effectiveness of CPR.


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5P, good methodology.
Study was not designed to assess value of continuous monitoring of ETCO2; instead they used this methodology as a method of monitoring cardiac output and correlated this with directly measured cortical cerebral blood flow.
Study supports monitoring the ETCO2 during CPR as a monitor of cardiac output.

4P, fair quality because of limitations in data collection as noted and inability to calculate predictive values of ETCO2. Prospective clinical observation of nonconsecutive cases conducted in 2 community hospital EDs (St. Lukes Hospital-Bethlehem, PA and Christiana Care, Dover, DE). Mainstream capnography was only available at Christiana. They obtained capnography on arrival if intubated, or after intubation, BUT recorded values during ultrasound and REPORTED only peak value. Capnography data was only available for about half the patients. Survival was admission to hospital. 102 subjects, 53 had capnography with 6 survivors. All survivors had etco2 >10, but there was some overlap with non-survivors, so this threshold ETCO2 is a sensitive indicator of survival to hospital admission, but not a specific discriminator of survival; and this threshold ETCO2 was a specific, but not sensitive indicator of death. No patient with ETCO2 <16 torr survived (0/29), but there were only 6 survivors. 24 subjects had etco2>16 and 6 survived (25%).
No industry support.
Overall, this study supports the predictive ability of ETCO2 for survival and hospital admission.


Case series, good quality, 5P. This is one of the few studies that addresses the initial question regarding the ability of ETCO2 to detect cardiac arrest. Conducted in controlled cath lab setting and showed rapid fall in ETCO2 with induction of VF.


5P, good quality with constant minute ventilation, but this study is not related to cardiac arrest; study shows a correlation between cardiac output and PetCO2 in adults undergoing abdominal aortic aneurism repair with hemorrhage and low cardiac output. This study supports the relationship between changes in cardiac output and PetCO2 when ventilation is held constant, indicating the value of this methodology in patients with critical illness as another method to non-invasively follow the patient's cardiac output. Used a mainstream CO2 detector. Although the CI fell to as low as 1.1 L/min/M2 no patient had an ETCO2 <20 mmHg. It is important to note that the mean decrease in CI was 34% and the decrease in ETCO2 was 11.1%, so numerically the changes were not that large (e.g., from 27 to 24 mmHg). Animal studies show that the CI – ETCO2 relationship is asymptotic with the relationship becoming linear only at very low CI, indicating the creation of a significant increase in dead space ventilation (ie, areas of very high V/Q ratios). Ornato study suggested a logarithmic relationship between CO and ETCO2.


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5P, descriptive study, fair quality and tangentially related to evidence question. This observational study supports the association between ETCO2 and improved effective pulmonary blood flow in association with insertion of a central shunt in children with cyanotic heart disease. This study also supports the value of monitoring ETCO2 in children with shunt dependent pulmonary blood flow.


5P adult non-arrest study. Fair methodology. This study provides indirect evidence regarding the correlation of low output states with changes in ETCO2. Specifically, the ETCO2 correlates most poorly with PaCO2 in those patients with multiple trauma, higher ISS and greater lactate and metabolic acidosis whereas it correlates better in patients with isolated head trauma. This study provides weak support for monitoring ETCO2 during CPR.


P5, good study in minipigs, which are approximately the size of infants so should be applicable to pediatrics. This is one of the first studies showing that end-tidal CO2 during CPR closely correlates with cardiac output. Studied 19 minipigs with pentobarbital anesthesia and cardiac output measured by continuous thermodilution. Induced VF and measured change in ETCO2. Also documented the occurrence of mixed venous hypercapnia and reduced arterial CO2. During CPR, ETCO2 and CO decreased to a mean of 21% and 33% of their baseline values, respectively. With ROSC ETCO2 usually overshot transiently to 140% of prearrest values. The found a good correlation between ETCO2 and CO (when low). They report that ETCO2 correlates linearly with changes in cardiac output during low-flow states, particularly if ventilation is kept constant.


Animal trial (LOE 5) that showed greater cardiac output with the Lifesick. This study is relevant to the worksheet since it showed a good correlation between end-tidal CO2 and cardiac output, cerebral and coronary perfusion pressure and cerebral and coronary blood flows.
decompression on haemodynamics, end-tidal CO2, and ventilation during

P5, good quality animal study. This study was designed to compare ACD-CPR to standard CPR.
They directly measured blood flow and perfusion pressure during different compression
methods in a VF arrest model. The study clearly supports the observation that PetCO2
reflects improved blood flow during CPR.

comparison of 15:2 and 30:2 compression-to-ventilation ratios for cardiopulmonary

5P; Good quality study. Supported by AHA and research gift from the Dwight Opperman
Foundation. This study was focused on evaluating the difference in cardiac output with
30:2 vs. 15:2 compression:ventilation, but also showed that adding ITD even after 6 mins
of VF arrest and 6 mins of standard CPR resulted in further augmentation of cardiac
output, carotid artery flow and coronary perfusion pressure. The mixed venous oxygen
saturation improved and the ETCO2 increased with the 30:2 vs. 15:2 ratio and with the
addition of the ITD device. Thus, the study documents that changes in ETCO2 track
changes in effective pulmonary blood flow. The latter is further supported by a fall in the
PaCO2 - ETCO2 gradient consistent with a fall in physiologic dead space.
It is noteworthy that the 30:2 ratio produced better hemodynamics in this model including mixed
venous oxygen saturation. The ETCO2 was also much higher with the addition of the
ITD. This study has significant clinical implications and supports a correlation between
ETCO2 and cardiac output.