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EM - COMMENTARY

Not the end of end-tidal CO2

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McGillicuddy et al. [1] should be commended on their attempt to identify a non-invasive method of screening febrile patients for possible sepsis. It is now well accepted that sepsis is a life-threatening disease that needs to be identified as soon as possible; multiple studies have demonstrated that early, aggressive resuscitation leads to better outcomes [2, 3]. If end-tidal capnography (ETCO2) could identify septic patients among the numerous febrile patients seen in the hospital everyday, a significant advance in medicine would be made.

In theory, use of ETCO2 is ideal physiologically and practically. When patients become septic, hypoperfusion at the cellular level leads to a metabolic acidosis that results in a compensatory respiratory alkalosis to maintain homeostasis. ETCO2 should reflect these physiologic changes as it has in identifying hypovolemic shock in trauma patients and respiratory status for procedural sedation. ETCO2 is also non-invasive and simple to use; it can be performed at triage, at the bedside or even en route to the hospital by emergency medicine personnel. In fact, in New York City, ETCO2 will be present on all advanced life support ambulances in 2009. Identification of potential sepsis patients even before hospital arrival would allow maximal time for immediate mobilization of any and all resources necessary for early, goal-directed therapy for sepsis.

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Unfortunately, the evaluation of ETCO2 in predicting elevated SOFA scores and lactic acidosis by McGillicuddy et al. did not yield a strong enough correlation for reliable clinical decision-making. The sensitivity of ETCO2 was 60 and 73% for predicting lactate $\geq$4 and SOFA $\geq$2, respectively. The positive and negative likelihood ratios I calculated (1.04 and 0.94 for lactate; 1.49 and 0.52 for SOFA score) were too low for any true impact.

I would propose that, given the theoretical value of ETCO2 as described above and the less than ideal study design, the results of this study should not halt further research on ETCO2 as a possible non-invasive marker of sepsis.

The first and biggest error in study design was using a surrogate marker (ETCO2) for another surrogate marker (SOFA score or lactate level) of sepsis. Although both SOFA scores and lactate levels are predictive of sepsis, they are not perfect [4, 5]. Among the five patients with an elevated lactate and 34 patients with an elevated SOFA, how many of these patients had sepsis? It is not entirely clear in this study. Testing or correlating ETCO2 with "sepsis" rather than against surrogate markers would be a much more substantial study.

Future studies should also attempt to identify an ideal cutoff or threshold for ETCO2. This study used only ETCO2 less than 35 as abnormal but the sensitivity could be higher with a lower or higher threshold. This has yet to be determined. The study design would be further helped by not only studying the patients with sepsis, but a control group that clearly does not have sepsis if one is to determine what range of the CO2 is going to indicate possible sepsis.

Finally, having a larger cohort of patients with true sepsis would yield more accurate test characteristics (i.e. sensitivity) with tighter confidence intervals for a more accurate assessment of ETCO2 as a marker for sepsis.

The authors acknowledge that their study alone should not be used to make a determination on the utility of ETCO2. More studies need to be done. The value of this study was in the innovative hypothesis and the demonstration that ETCO2 can be easily obtained in febrile patients.

Conflict of interest statement The author declares that he has no conflict of interest related to the publication of this manuscript.

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