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Is Intrathoracic Pressure Regulation at the Threshold of New Resuscitation Science?

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Cardiac arrest remains common in the United States, and nearly 600,000 people suffer sudden cardiac death in Europe and US yearly. Survival, however, has remained low, estimated to be 5–12%.^{1, 2} In part, the poor survival is due to the inefficiency of standard cardiopulmonary resuscitation, resulting in less than 25% of normal blood flow to the brain and heart.³

In an effort to optimize the thoracic pump mechanics and augment forward and vital organ blood flow during resuscitation by harnessing the elastic properties of the chest during decompression, the inspiratory impedance threshold device has been introduced to the world to resuscitation about 20 years ago. The inspiratory impedance threshold device (ITD) is attached to the airway either via a facemask or an endotracheal tube. The ITD impedes air entry into the chest cavity during the decompression phase of CPR, generating more negative intrathoracic pressure than standard CPR. This vacuum has been demonstrated to improve venous return to the heart as well as reduce intracranial pressure.⁴ In a porcine model of cardiac arrest, the use of an ITD led to improved 24-hour survival with improved neurologic outcomes.^{5–7} As a result of favorable hemodynamic, survival, and neurologic outcomes in animal studies, there have been several clinical trials that investigated the ITD in animals and humans.^{8–10} The ITD has been cleared by the FDA as a circulatory enhancer during resuscitation. Most of the animal and clinical studies have shown benefits in different endpoints. The ITD has been shown to improve aortic pressure during CPR¹¹, increase in resuscitation rates in humans and hospital admission rates when it was applied appropriately and during the early phases of cardiac arrest; namely the circulatory phase (4–10 minute of untreated cardiac arrest).¹² In a recent study the ITD demonstrated no benefit compared to a sham valve in 10,000 patients.⁸ While this was the largest clinical trial in CPR to date, it was confounded by the fact that the ITD was placed on average 11–14 minutes after the 911 call, well into the metabolic phase of cardiac arrest where it is very unlikely that any circulation-enhancing device could demonstrate benefits.

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Disclosures/Conflicts:

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The concept of intrathoracic pressure regulation and its efficacy in clinical practice has been shown broadly in 5 clinical studies where active compression decompression CPR has been combined with the ITD. The combination is hemodynamically superior and has resulted in improvement in all the endpoints of resuscitation science. A recent study showed that ACD +ITD (and for the first time for a new CPR method) significantly increased survival to hospital discharge with favorable neurologic outcomes (defined as modified Rankin score <3) by 50% when compared with standard CPR (6% vs 9%, $p=0.019$).⁹ The benefits were maintained up to one year survival which was also improved by 53%.

In this edition of Critical Care Medicine, Xanthos et al. tested the addition of an ITD in a porcine model of asphyxial cardiac arrest.¹³ This is an important study. As the authors correctly point out, it is the first investigation of the use of the ITD in asphyxial cardiac arrest. The study is very innovative since inspiratory impedance during resuscitation of asphyxial cardiac arrest appears to be counterintuitive. The authors provide evidence of improvement in clinically relevant endpoints such as return of spontaneous circulation, 48-hour survival, and neurologic alertness score. In addition to the improved neurologic outcomes, the measurement of early serum NSE and S-100 levels provides additional evidence of decreased neurologic insult during resuscitation. As such their results are intriguing and very supportive of the literature of cardiac etiology cardiac arrest and therefore expand the benefits of the ITD into another etiology.

The potential mechanism of how the ITD may be neuroprotective and improve outcomes compared to standard CPR in this model may be due to direct transfer of intrathoracic pressure into intracranial pressure. A lower intrathoracic pressure therefore is translated into lower diastolic intracranial pressure. The lower ICP combined with the higher aortic pressure leads to more cerebral perfusion and blood flow that could alleviate the injury during the resuscitation even after asphyxia provided that ventilation and oxygenation has been reestablished.

One limitation of the current study by Xanthos et al. is that epinephrine was not used. Epinephrine is routinely used in human resuscitation and enhances successful ROSC¹⁵ but has been shown to reduce neurologically-intact survival in high doses. The beneficial effects of the ITD may be mitigated by the use of vasopressors often required in substrates less healthy than this animal model, however previous animal studies have demonstrated mixed outcomes in this respect. Further translation of this model is limited due to its low prevalence, however adds to the substantial body of animal studies and growing number of clinical trials investigating the use of intrathoracic pressure regulation therapy such as the ITD.

In conclusion, although the results of animal studies must be scrutinized carefully regarding their translation into clinical medicine, the results presented by Xanthos et al. in the journal can be combined with the observations from clinical and animal investigations to date. The data suggest that when an ITD is applied in a timely fashion before the metabolic phase of cardiac arrest, it provides not only favorable hemodynamics during CPR, but also improves ROSC rates and survival with good neurologic outcomes even in an a model of asphyxia.

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