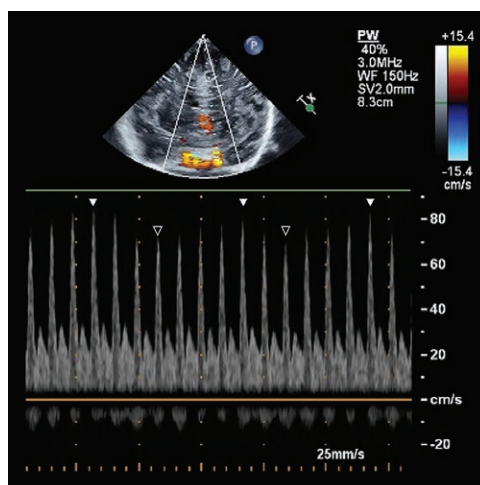# Can the Brain Predict Fluid Responsiveness?

Elliot Long, B.M.B.S., F.R.A.C.P., Paul E. Marik, M.D., F.C.C.P., F.C.C.M.

Resuscitation with IV fluid is a ubiquitous first-line form of acute circulatory support in emergency medicine, critical care, and anesthesiology. In this edition of ANESTHESIOLOGY, Kim *et al.* examine the ability of transcranial ultrasound of the internal carotid artery peak velocity variability to predict fluid responsiveness in mechanically ventilated children after cardiac surgery.[1] In a cohort of 30 postoperative cardiac infants, respiratory variation of the internal carotid artery blood flow peak velocity was measured using transfontanelle ultrasound, before and after the administration of 10 ml/kg saline. Stroke volume index was measured using transesophageal echocardiography to identify fluid responders (greater than 15% increase in stroke volume index). Before fluid loading, respiratory variation of the internal carotid artery velocity was 13 ± 3% in the fluid responders (n = 17) and 8 ± 3% in the nonresponders (n = 13). Transfontanelle respiratory variation in internal carotid artery blood flow peak velocity predicted an increase in stroke volume with an area under the receiver operating characteristics curve of 0.83 (95% CI, 0.65 to 0.94).

"**Transfontanelle measurement of respiratory variation in internal carotid artery blood flow peak velocity is a novel method for predicting fluid responsiveness [in infants].**"

Fluid responsiveness refers to an increase in cardiac output after the rapid administration of a calibrated volume of IV fluid (a fluid bolus). This increase in cardiac output (or stroke volume), expressed as a percentage, provides an estimate of the position of the patient's heart on the Frank–Starling curve. Varying fluid volumes (10 ml/kg or 20 ml/kg in children; 500 ml or 1,000 ml in adults; and passive leg raise), content (crystalloid or colloid), and threshold values for change in cardiac output (10% or 15%) have been used to define fluid responsiveness.

In health, cardiac output increases after the administration of a fluid bolus. For this to occur, both ventricles need to be operating on the ascending portion of the Frank–Starling curve, and fluid bolus administration must increase the stressed venous blood volume, increasing the pressure gradient for venous blood flow to the right atrium.[2] Yet, only 50% of pediatric and adult patients with acute circulatory failure are fluid responsive. The remainder receive none of the benefits of fluid bolus administration and may be harmed through tissue and end-organ edema after fluid redistribution. Fluid bolus administration itself may exacerbate this process through damage to the endothelial glycocalyx and increased venous pressure. Paradoxically, large volume fluid administration may decrease vascular tone and attenuate the cardiovascular compensatory mechanisms of hemodynamically unstable patients. This mechanism has been postulated to explain the increased mortality of patients randomized to the fluid bolus groups in the Fluid Expansion as Supportive Therapy (FEAST) trial.[3] Large volume fluid resuscitation and a positive cumulative net fluid balance have been associated with worsening renal function, acute lung injury, prolonged intensive care unit and hospital length of stay, and mortality, when corrected for disease severity. This holds true for the patient population studied by Kim *et al.*, highlighting the importance of fluid management in influencing patient outcome after cardiac surgery and critical illness.

The ability to predict fluid responsiveness allows fluid bolus administration to be restricted to those likely to benefit, while sparing those who are not fluid responsive from potential harms.

Image: TranscranialUS.

This editorial accompanies the article on p. 719.

Multiple methods for measuring fluid responsiveness have been reported in children.[4] In general, continuous cardiac output monitors are more accurate for detecting trends in cardiac output over time, while intermittent cardiac output monitors are more accurate for measuring absolute values.

Multiple hemodynamic variables have been used to predict fluid responsiveness in children.[5,6] *Static variables*, based on single observations in time, include clinical observations (heart rate and blood pressure), and preload indices (central venous pressure and pulmonary artery occlusion pressure), and have poor test characteristics for predicting fluid responsiveness. *Dynamic variables*, based on the variation in preload induced by mechanical ventilation, by performing the passive leg raise maneuver or by the administration of a fluid challenge, have better test characteristics for predicting fluid responsiveness. Methods for predicting fluid responsiveness based on cardiopulmonary interactions require the patient to be mechanically ventilated with large tidal volumes (greater than 8 ml/kg), not spontaneously triggering the ventilator, and in sinus rhythm. In addition, these methods are influenced by the level of positive end-expiratory pressure, lung and chest wall compliance.

Transfontanelle measurement of respiratory variation in internal carotid artery blood flow peak velocity is a novel method for predicting fluid responsiveness. Similar measurements of the common carotid artery have been validated as predictors of fluid responsiveness in adults, as have changes in carotid artery blood flow induced by passive leg raise and carotid artery flow time. The external validity of the results of the study by Kim *et al.* are supported by the findings of Ibarra-Estrada *et al.*, who reported that the respiratory variation in carotid peak systolic velocity (common carotid) predicted fluid responsiveness in mechanically ventilated adult patients with septic shock, while other commonly used static and dynamic variable were poor predictors of fluid responsiveness.[7]

The generalizability of the study by Kim *et al.* may be limited in part by the study population. In this study, central venous pressure less than 7 mmHg, systolic blood pressure less than 85% of baseline (preoperative) value, decreased end-diastolic ventricular volume compared with preoperative values, and urine output less than $0.5\,ml \cdot kg^{-1} \cdot hr^{-1}$ were used as markers of circulatory failure. Central venous pressure may not reflect volume status or fluid responsiveness. End-diastolic ventricular volume will vary with cardiac contractility and afterload, as well as with preload. Urine output may not reflect renal perfusion, and may not be influenced by fluid bolus administration. In addition, patients with a closed anterior fontanelle, pulmonary hypertension, aortic arch abnormalities, cardiac dysfunction (defined as an ejection fraction less than 40%), and lung disease were excluded from the study and the results may not be generalizable to these children. As previously outlined, the results of this study may not be generalizable to patients receiving low tidal volume ventilation, those spontaneously triggering the ventilator, and those in cardiac rhythms other than sinus.

Not all patients who are fluid responsive "need" a fluid bolus. In patients who are fluid responsive, the decision to administer a fluid bolus should be guided by the presence of signs of hypoperfusion. An assessment of the risks and benefits of fluid bolus over other forms of acute circulatory support should be made before administration. Both the magnitude and duration of effect are important when assessing fluid responsiveness. Studies in critically unwell children and adults that have demonstrated that the duration of effect of fluid bolus therapy on cardiac output in fluid responders lasts less than 1 h.

This important study by Kim *et al.* contributes to our understanding of the physiologic response to fluid bolus administration and the predictors of fluid responsiveness. It provides evidence for a novel method for predicting fluid responsiveness, which, in the right clinical circumstances, gives clinicians another option for hemodynamic monitoring and titrating fluid bolus therapy.

Competing Interests

Dr. Marik is on the advisory board of Baxter Healthcare (USA) and has received an honorarium for presentation at an international scientific meeting. Dr. Long is not supported by and does not maintain any financial interest in any commercial activity that may be associated with the topic of this article.

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ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

Not Just Ethyl Chloride or Somnoform: Anestile, a Refrigerant Anesthetic by Bengué

Vapocoolants or refrigerant topical anesthetics provided surface chilling from the rapid evaporation of a sprayed-on liquid. Such brisk local anesthetics were used for brief surgical procedures (*e.g.*, lancing a boil), for limited dental work, and even for massage therapies. The earliest available and longest used vapocoolant was ethyl chloride, which later was found to be a general anesthetic. The widest used vapocoolant was Somnoform, a mixture of ethyl chloride, methyl chloride, and ethyl bromide. Marketed heavily from 1896 through 1906, Anestile (*bottom*) was a vapocoolant with a 5:1 ratio of ethyl chloride to methyl chloride. For convenience, the manufacturer of Anestile, Bengué, provided a variety of dispensers (an "automatic" one, *top*). That company is better known today under its anglicized label "Bengay" for its arthritis liniments. (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

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