Dr. BobbieJean Sweitzer: Hello. I’m BobbieJean Sweitzer, Professor of Anesthesiology at Northwestern University and an Associate Editor for Anesthesiology and you are listening to an Anesthesiology podcast designed for physicians and scientists interested in the research that appears in our journal.

Today we are speaking with two authors of publications that appear in the May 2019 issue of the journal. With us is Dr. Jin-Tae Kim. Dr. Kim is the lead author of an article titled “Respiratory Variation of Internal Carotid Artery Blood Flow Peak Velocity Measured by Transfontanelle Ultrasound to Predict Fluid Responsiveness in Infants: A Prospective Observation Study.”

Dr. Kim is a Professor in the Department of Anesthesiology and Pain Medicine, Seoul National University Hospital, Seoul National University College of Medicine in Seoul, Republic of Korea. Welcome, Dr. Kim.

Dr. Jin-Tae Kim: Hello, Dr. Sweitzer.

Dr. BobbieJean Sweitzer: It’s good to have you again. I know we had you interviewed a few months ago, so it’s nice to have you join us again.

Joining Dr. Kim is Dr. Elliot Long who wrote an accompanying editorial, “Can the Brain Predict Fluid Responsiveness?” Thank you, Dr. Long, for having that be a much shorter title than Dr. Kim’s.

Dr. Long is from the Department of Emergency Medicine, the Royal Children’s Hospital, Victoria, Children’s Research Institute, Parkville, the Department of Pediatrics, Faculty of Medicine, Dentistry and Health Science, the University of Melbourne, Victoria, all in Australia. Welcome, Dr. Long.

Dr. Elliot Long: Thanks very much, Dr. Sweitzer and hello, Dr. Kim, as well.

Dr. BobbieJean Sweitzer: So, let’s start with you, Dr. Kim. Can you just give us an overview of what you set out to do with this study?

Dr. Jin-Tae Kim: Sure. Prediction of fluid responsiveness in pediatric patients has been a many researched topic of my research team. Several ultrasound parameters for assessing fluid responsiveness have been described. Previous studies have identified a relationship between fluid responsiveness and respiratory variation in the arterial blood flow peak velocity in the ascending aorta or the proximal branch of the aorta.

On the other hand, we apply transfontanelle ultrasonography to assess cerebral blood flow when cerebral oxygen saturation value decreased during congenital cardiac surgery. When we measured cerebral blood flow velocity using transfontanelle ultrasonography, we observed respiratory variation in internal carotid artery blood flow peak velocity like stroke volume variation.

So, we designed this study to evaluate the potential role of point-of-care transfontanelle ultrasonography by determining whether the respiratory variation of internal carotid artery blood flow peak velocity of fluid responsiveness measured by transfontanelle Doppler ultrasound can predict fluid responsiveness in pediatric cardiac patients.

Dr. BobbieJean Sweitzer: So, what method did you use to determine if the patients were fluid responsive or what were you comparing (sounds like: nexus) carotid artery measurements to?

Dr. Jin-Tae Kim: We used the respiratory variation of the aortic blood flow peak velocity to determine fluid responsiveness. The respiratory variation of the aortic blood flow peak velocity is known to be an accurate predictor of fluid responsiveness in pediatric patients.

The respiratory variation of the aortic blood flow peak velocity was measured using transesophageal echocardiography. We also compared pulse pressure variation as intravenous pressure with the respiratory variation of the internal carotid artery below the flow of peak velocity that the pulse pressure variation and central venous pressure had no ability to predict fluid responsiveness in pediatric patients.

Dr. BobbieJean Sweitzer: So, Dr. Long, how is fluid responsiveness defined?

Dr. Elliot Long: Fluid responsiveness is defined as an increase in cardiac output after the administration of a fluid challenge. The precise definition from a research standpoint is slightly variable, meaning that in some cases the volume of fluid that’s administered as a fluid challenge is different ranging from 500 ml to a liter of fluid in adults and 10 ml/kg to 20 ml/kg in children as well as a maneuver called the passive leg raise maneuver.

In addition, the change in cardiac output that’s used to define fluid responsiveness is slightly variable, ranging from 10% to 15%.

Dr. BobbieJean Sweitzer: So, Dr. Kim, what fluid did you use, how much was administered and over what time period?

Dr. Jin-Tae Kim: We administered 10 ml/kg crystalloid over 10 minutes at the completion of surgery and closure of the sternum.

Dr. BobbieJean Sweitzer: Did you only study patients who were likely to be dehydrated or hypotensive or were you trying to find those who were more likely to need fluids to begin with?

Dr. Jin-Tae Kim: Yes. We included the patients suspicious of volume depletion or patients with hypotension. The inclusion criteria were as follows: central venous pressure less than 7 mmHg, systolic blood pressure less than 85% of baseline value measured after anesthetic induction and before incision, decreased end-diastolic volume compared with a baseline value or presence of other clinical signs of dehydration, such as decreased urine output less than 0.5 ml/kg/hr.

Dr. BobbieJean Sweitzer: Dr. Long, what percentage of patients—either pediatric or adults—with acute circulatory failure are likely to be fluid responsive?

Dr. Elliot Long: Yes, I think this is where the story starts to get really interesting because in the majority of studies that have looked at the frequency of fluid responsiveness in critically unwell adults and children, that percentage sits at roughly 50%.

So, only half of the patients that we think have acute circulatory failure that we are thinking of administering fluid to are likely to be fluid responsive and most of those studies have been performed in the intensive care unit setting or the anesthetic setting and those patients aren’t always fluid naïve.

And in fluid naïve patients, that percentage may be slightly higher, but it’s still a surprisingly small number of patients that we think of administering fluid to that are likely to respond in terms of a change in cardiac output.

Dr. BobbieJean Sweitzer: So, in other words, without a good measurement or some objective evaluation, we have about a 50/50 chance of giving people fluids who don’t need fluids.

Dr. Elliot Long: Yes, that’s correct. So, in patients that we think are circulatory compromised, we have about a 50/50 chance of administering fluid to the correct patient without measuring some marker of fluid responsiveness or actually measuring the change in cardiac output when fluid’s administered.

Dr. BobbieJean Sweitzer: That puts Dr. Kim’s study in a very interesting perspective here because if this technique does prove to be very useful, it sounds like there’s a real need for those kinds of objective measurements.

Dr. Kim, can you tell us a bit about the population you studied, the type or types of surgeries these patients were having, the ages of the patients?

Dr. Jin-Tae Kim: Sure. The study population was infants undergoing cardiac surgery due to atrial or ventricular septal defect. The patient had no pulmonary hypertension, aortic arch abnormalities, severe cardiac dysfunction and lung disease. Age of patient was about 5 months.

Dr. BobbieJean Sweitzer: Dr. Long, what other ultrasound parameters for assessing fluid responsiveness have been described or are currently in use today and how do they compare to each other?

Dr. Elliot Long: So, there are a few different methods that have used ultrasound to predict fluid responsiveness. So, if we move from the venous to the arterial side, both respiratory variation and inferior vena cava size or diameter with respiration, both in spontaneously and mechanically ventilated
patients, has been evaluated as has respiratory variation in superior vena cava
diameter. And both of those tests tend to have fairly poor predictive ability
for fluid responsiveness.

And then moving to the arterial side, the respiratory variation in aortic
blood flow peak velocity, as Dr. Kim alluded to, has been evaluated in a
number of pediatric studies and found to be a good predictor of fluid
responsiveness.

And then arterial vessels distal to the proximal aorta have also been
evaluated including the internal carotid artery and the brachial artery. And
I think it’s fair to say the farther away from the aorta the measurements are
taken, the less predictive of fluid responsiveness that vessel tends to be.

Dr. BobbieJean Sweitzer: Dr. Kim, how easy or difficult is it to learn this
ultrasound technique to evaluate the respiratory variation of the carotid
artery?

Dr. Jin-Tae Kim: I think this technique may be difficult to learn if a
physician is not familiar with echocardiography; however, I believe the
physician able to perform echocardiography can learn this technique easily
through some practice.

But, in fact, we need to define characteristics of transfontanelle ultrasono-
graphy such as the learning curve and intra- and interoperative variability.

Dr. BobbieJean Sweitzer: Can these ultrasound techniques be used in
spontaneously breathing patients as Dr. Long described the IVC evaluation
or are there specific ventilation requirements?

Dr. Jin-Tae Kim: I think transfontanelle ultrasonography can be used
even in spontaneously breathing patients if this technique is used to assess
brain perfusion; however, for the determination of fluid responsiveness, we
can apply this technique only in mechanically ventilated patients and tidal
volume should be at least 8 to 10 ml/kg.

Changes in tidal volume is associated with changes in intrathoracic pres-
ture. The change of intrathoracic pressure alters the ability to predict fluid
responsiveness and its cutoff value.

Dr. BobbieJean Sweitzer: Does the presence of lung disease interfere
with this technique?

Dr. Jin-Tae Kim: Definitely. The pulmonary disease can change the lung
compliance. The change of lung compliance can alter intrathoracic pressure
in patients receiving volume-controlled ventilation.

The change of intrathoracic pressure affects the respiratory variation of
an aortic or internal carotid artery blood flow peak velocity. Accordingly,
the lung disease can change the cutoff value for the determination of fluid
responsiveness.

In this study, the cutoff value of the respiratory variation of an aortic blood
flow peak velocity was 13% and that of internal carotid artery was 7.8%. If
the lung compliance has changed, these values will be also changed.

Dr. BobbieJean Sweitzer: So, Dr. Long, in your editorial you talk about
static hemodynamic variables and dynamic hemodynamic variables to pre-
dict fluid responsiveness. Can you define these for us and tell us more about
how they compare and which are more useful than others?

Dr. Elliot Long: So, the static variables are referred to single measurements
in time and they tend to be less predictive of fluid responsiveness or not
predictive of fluid responsiveness and those methods include central venous
pressure and the left ventricular pulmonary occlusion blood pressure or left
atrial pressure.

Dynamic variables refer to changes in certain parameters over time and they
tend to be more predictive of fluid responsiveness. Most of these rely
on cardiopulmonary interactions to give small fluid shift changes or changes
in preload during the cardiac cycle. And the only problem with dynamic
variables is most of them have only been tested under kind of pure research
conditions or ideal study conditions.

That means that the patient is being mechanically ventilated, the patient
is muscle relaxed, not spontaneously triggering the ventilator. As Dr. Kim
alluded to, the tidal volumes need to be large, greater than 8 ml/kg, and the
patient needs to be in sinus rhythm.

So, under research conditions, those dynamic variables have been found
to be quite predictive of fluid responsiveness, but there is some question
about the generalizability of those parameters in real patient conditions or
in unwell patients.

Dr. BobbieJean Sweitzer: So, Dr. Kim, what did you conclude after
completing this study?

Dr. Jin-Tae Kim: We concluded the respiratory variation of the internal
carotid artery blood flow peak velocity as measured using transfontanelle
ultrasound predicts an increase in stroke volume in response to an intrave-
nous fluid administration in infants having cardiac surgery.

Additionally, point-of-care transfontanelle ultrasound can be a good
modality to evaluate a brain perfusion in pediatric patients intraoperatively.

Dr. BobbieJean Sweitzer: Did you find any significant differences in
patient characteristics between those who were fluid responders and those
who were not?

Dr. Jin-Tae Kim: Actually, we found no significant difference in patient
characteristics and intraoperative variables between responders and nonre-
sponders; however, the respiratory variation of the internal carotid artery
and the aortic blood flow peak velocity before fluid administration were
significantly higher in the responders than in the nonresponders.

Dr. BobbieJean Sweitzer: So, Dr. Long, I recall in Dr. Kim’s study that
the responders actually had a slightly higher CVP, I think the average was
8 +/- 2 compared to the nonresponders who had a CVP of 6 +/- 3 before
fluid administration.

So, kind of circling back to our conversation around being correct 50%
of the time or wrong 50% of the time in predicting ahead of time who was
going to respond to fluids, I know in the old days we would predominantly
use CVP as the measure of fluid status, but we would have been misled, it
seems like even more so than even the 50/50 chance.

Is this another nail in the coffin for CVP monitoring, especially to be used
for fluid responsiveness at least?

Dr. Elliot Long: Yes. I guess it really gets down to the question of why the
central venous pressure is being monitored in the first place. Certainly its
use as a predictor of fluid responsiveness has largely been debunked, I think.

My coauthor in the editorial, Dr. Paul Merrick, has written a systematic
review looking at central venous pressure as—and change in central venous
pressure with fluid administration as predictors of volume status and fluid
responsiveness.

And, as you correctly pointed out, it’s very poorly predictive or not pre-
dictive at all of fluid responsiveness.

So, I think this is more evidence—and particularly evidence in a pediatric
population—that central venous pressure is a poor marker of volume status
or fluid responsiveness.

Dr. BobbieJean Sweitzer: So, Dr. Kim, does the technique that you
describe in this paper have advantages over just simply using transesoph-
ageal echocardiography to assess stroke volume in fluid responsiveness or
ultrasound to measure aortic parameters to predict fluid responsiveness as
you used as the gold standard in this study?

Dr. Jin-Tae Kim: Regarding the stroke volume measurement, transesoph-
ageal echocardiography is better than transfontanelle ultrasonography with
no doubt. However, transfontanelle ultrasonography has several advantages
over transesophageal echocardiography to assess fluid responsiveness.

For obtaining the respiratory variation of the aortic blood flow peak
velocity, transesophageal echocardiography or transesophageal echocardio-
gerphy is needed. If the surgical field is close to the chest, the transesophageal
ehocardiography cannot be applied.

Transesophageal echocardiography also has some problems associated with
its probe, especially in infants. Insertion of the TEE probe is relatively inva-
sive; it can compress the left main bronchus and cause respiratory problems
in small infants. Sometimes the TEE probe is not available.

On the other hand, the respiratory variation of internal carotid artery
blood flow peak velocity can be applied without these limitations if the
fontanelle remains open.

Furthermore, the respiratory variation of internal carotid artery blood flow
peak velocity as measured using transfontanelle ultrasound has less potential
bias associated with the Doppler beam angle adjustment than the respiratory
important to assess for fluid responsiveness because of this observation that show that excessive fluid administration and a positive net fluid—cumulative leading to excess mortality. And multiple studies in adult and children that the FEAST study that fluid bolus administration may be harmful in terms of certain patient groups—particularly in patients with sepsis—that fluid bolus administration may be harmful.

Dr. Elliot Long: Yes. It’s interesting that we, as clinicians, often use fluid bolus administration to improve blood pressure. But there is certainly good randomized evidence in children through the Sub-Sahara in Africa that’s conducted a follow-on study to try and address some of the mechanistic questions about why fluid bolus administration may be harmful.

And in their animal model of sepsis they found that sepsis that were administered a fluid bolus had a higher requirement for vasoactive support to maintain an equivalent blood pressure to sepsis that had not been administered a fluid bolus.

So, it seems that there’s some direct effect either on the vascular endothelium or a neurohormonal effect that fluid boluses have that may result in a decrease in systemic vascular resistance and a higher inotrope requirement in certain patients.

So, this is a “watch this space” kind of area, but an active area of research interest.

Dr. Elliot Long: It’s always fascinating how little we know, actually, about what we do. Dr. Kim, currently, do you think the ultrasound technique that you described in your paper of using the measurement of the carotid artery via fontanelle is the best-to-preferred method to use when faced with a decision to administer fluid or not, at least in an infant population having cardiac surgery such as you studied?

Dr. Jin-Tae Kim: Although I believe point-of-care transfontanelle ultrasonography is very useful for assessing brain perfusion and determining fluid responsiveness in pediatric patients, transfontanelle ultrasonography is not best but preferred method depending on situation. Currently, only the respiratory variation of aortic blood flow peak velocity has been recognized to be predictive in pediatric patients according to previous systematic analysis.

However, it has limited utility in some clinical situations. So, we need more study to find the perfect method to determine fluid responsiveness in pediatric patients.

Dr. BobbieJean Sweitzer: Sounds like it’s just another good tool to have. So, I hope today’s discussion will interest many of our listeners and lead you to read this important article and editorial to learn more. Thank you, Drs. Kim and Long, for discussing your work with us today. I wish you well.