Host: Welcome to the Anesthesiology journal podcast, an audio interview of study authors and editorialists.

Dr. James P. Rathmell: Hello. I’m Jim Rathmell, Professor of Anesthesia at Harvard Medical School and Chair of the Department of Anesthesiology, Perioperative and Pain Medicine at Brigham and Women’s Hospital in Boston. I’m one of the Executive Editors for Anesthesiology and you’re listening to an Anesthesiology podcast that we’ve designed for physicians and scientists interested in the research that appears in the journal.

Today we’re going to talk with the lead author of an original research article that appears in the May 2019 issue and the author of an editorial view designed to explain more about that original research article.

With us today is Dr. Theodor Sigurdsson. Dr. Sigurdsson is a doctoral student in the Department of Pediatric Anesthesiology and Intensive Care Medicine at the Children’s Hospital of the University Hospital of Lund in Lund, Sweden. He’s also a Consultant, Anesthesiology in Reykjavik, Iceland and it’s snowing today in Iceland.

Dr. Sigurdsson is the lead author of an article that appears in the May 2019 issue of the journal titled “Extracorporeal Arteriovenous Ultrasound Measurement of Cardiac Output in Small Children.” Dr. Sigurdsson, thank you for joining us today.

Dr. Theodor S. Sigurdsson: Thank you, Dr. Rathmell. Pleased to be here.

Dr. James P. Rathmell: Also with us is Dr. Maxime Cannesson. Dr. Cannesson is Professor of Anesthesiology and Vice Chair for Perioperative Medicine at UCLA Medical Center in Los Angeles, California. Dr. Cannesson wrote an editorial view that accompanies this research article and it also appears in the May 2019 issue of the journal. It’s titled, “babies and children at last: Pediatric Cardiac Output Monitoring in the 21st Century.” Dr. Cannesson, thank you for joining us.

Dr. Maxime Cannesson: Thank you, Dr. Rathmell, for having me.

Dr. James P. Rathmell: Dr. Sigurdsson, congratulations on the publication of your work. I want to start by giving listeners a bit of context about your research. The technology that most of us are familiar with for measuring cardiac output is by thermodilution of a small bolus of saline injected into the central circulation.

In this new research article, you use a technology for cardiac output and blood volume measurements that’s based on blood dilution with a small bolus of physiologic body-temperature saline which after transcardiopulmonary mixing is detected with ultrasound sensors that are attached to an extracorporeal arteriovenous loop and that extracorporeal loop uses an existing central venous and peripheral arterial catheters.

Now, that’s a pretty confusing description. Can you walk us through how this technology works?

Dr. Theodor S. Sigurdsson: Absolutely. This new technology is based on the Stewart-Hamilton Indicator Dilution principle similar to the thermal dilution that has been considered that standard reference method regarding cardiac output estimations. The theory behind the technology is the physiologic principle that the ultrasound velocity of blood is not the same as the ultrasound velocity for isotonic saline. The baseline ultrasound velocity is the function of the total blood protein concentration; some of proteins in the plasma are (sounds like: dried) cells.

The injection of the body-temperature isotonic saline as an indicator caused a reduction in the blood ultrasound velocity that is then detected at the transpulmonary passage. This change in ultrasound velocity can then be used to estimate the cardiac output.

Measurements are performed using a single-use extracorporeal arteriovenous loop primed with heparin saline, as you said before, connected between an internal radial arterial catheter (sounds like: at the site of) of (inaudible) central venous catheters.

The two multi-use ultrasound (sounds like: cloth) dilution sensors are placed on the arteriovenous sensor at the AV loop. The AV central clamped on the venous (sounds like: limp) of the loop calculates the exact amount, (sounds like: absent) of injection indicators and the quality of injection. A peristatic pump is then used to prevent stasis of blood and to provide the stable blood flow through the AV loop from the artery to the vein at this slow rate for the duration of the measurements.

Body-temperature isotonic saline is injected into the venous (sounds like: site of the) AV loop. The arterial stents are clamped on, the arterial (sounds like: limp) of the loop detects the change in ultrasound velocity. This change is then transformed into a dilution curve (sounds like: that’s placed) on the specific monitor estimating cardiac output from the area onto the curve as well as a number of other hemodynamic parameters.

At the end of the measurement cycle, the AV loop is flushed and the blood from the extracorporeal system is returned into the patient’s circulation.

Dr. James P. Rathmell: Well, that’s pretty interesting. So, it’s a loop between an existing arterial line and an existing central venous catheter that uses a pump outside and the saline’s injected outside and extrapolates the cardiac output from there. So, not too hard to understand how the setup is; but the actual derivation is pretty sophisticated. So, you use this new technology in this study. What did you set out to learn in this study that you’ve conducted and what was your hypothesis as you started?

Dr. Theodor S. Sigurdsson: Well, I’ve always been fascinated about the human hemodynamics and the question what makes us tick and how. (Sounds like: I was handed) the dynamic data and as I read in young children, I welcomed this opportunity to learn more about this specific group of patients.

Our hypothesis was that this new technology would have a good agreement with a well-established reference method and a comparable precision and estimation of cardiac output in young children.

Dr. James P. Rathmell: So, you set out to compare the precision in agreement of this technology to measure cardiac output with a reference method and that reference method was a perivascular flow probe placed around the aorta in young children.

The null hypothesis was that the methods are equivalent in precision and there’s no bias in the cardiac output measurements, meaning that there was no systematic higher or lower measurement with one device or another.

Why type of patients did you enroll and how did you carry out the study?

Dr. Theodor S. Sigurdsson: Well, my coauthor and mentor, Dr. Lindberg, had conducted a small pilot study that showed that this new technology had a very promising agreement; however, we felt that the jury was still out regarding the precision. We, therefore, not only needed the higher number of patients to confirm earlier results, but also a repeated measurement for each patient to be able to estimate the precision.

As our focus was on the youngest age group, we only enrolled patients with parental consent on the 15 kg that were to undergo correction of arterial or venricular septal defects.

We conducted the study and our lower measurements while maintaining anesthesia and stable conditions of the surgical correction. With the aorta exposed, the surgeon fitted the flow probe around the ascending aorta while we preferred and confirmed that all signals and devices were up and running.

All measurements were done simultaneously and consecutively with both methods five times; each measurement took about 45 seconds and each measurement session took about five to eight minutes.

Dr. James P. Rathmell: So, you ended up with 215 cardiac output measurements in 43 children who had elective cardiac surgery. What did you learn about the new technology and its reliability as a means for measuring cardiac output in children?

Dr. Theodor S. Sigurdsson: We learned that the technology was very reliable, easy to apply and safe in young children. The major advantages included the use of existing arterial and venous catheters, nontoxic indicators, absence of blood loss and a very good agreement on precision.

Dr. James P. Rathmell: So, it’s precise. What do you conclude? How can you explain the differences between the measurements provided by the new method and the reference standard of the periaortic flow probe?

Dr. Theodor S. Sigurdsson: Well, the position was excellent. 3.6% compared to the (sounds like: reference) method of 5%. It is important to remember that the cardiac output is not the stationary value which can fluctuate due to physiological factors like respiration.
The periaortic flow probes’ measurements are probably more prone to be influenced by these fluctuations as well as there are some technical issues regarding the selection of the right (inaudible) size, probe size and obtaining a satisfactory alignment with the vessel in question.

The difference in agreement, 0.08 liters per minute, can be simply explained by the missing coronary flow that is usually around 6% to 8% of the total cardiac output. We had seen earlier that the placement of the flow probe around the pulmonary trunk could sometimes cause the mechanical compression of the coronaries, thus influencing the cardiac output.

As our main focus in this study was to estimate the precision, we not only chose to place the flow probe around the ascending aorta, thus missing that part of the cardiac output (inaudible) with the coronaries, but without disturbing the cardiac output.

These issues tend to be less of a problem in the experimental trappings where the surgeon has much more freedom to test the margins, but not in clinical studies. Overall, we had a percentage error of 26.6% which was within the allowed 30% limit. Both methods were, therefore, considered comparable.

Dr. James P. Rathmell: Dr. Cannesson, I want to turn to your editorial view. The title is “Babies and Children at Last: Pediatric Cardiac Output Monitoring in the 21st Century.” The title hints at how you feel about this new technology and you start out by telling us that this an unusual study because the new method was meticulously tested against a gold standard method. Can you elaborate on why such validation studies are uncommon and how this study stands apart?

Dr. Maxime Cannesson: Of course. First I’d like to really congratulate Dr. Sigurdsson and colleagues for this work because, as you just mentioned, Dr. Rathmell, the studies in terms of the methodology that he chose is extremely remarkable.

The reason why I find it very strong is that they clearly used the gold standard for measuring cardiac output which is the aortic flow probe. And when you look at what kind of studies are published in this field and have been published in this field over the past 15 or 20 years, what everybody knows, that the aortic flow probe is the gold standard.

Obviously this technology is very rarely used as a reference in clinical studies. It’s probably that because that takes a lot of work, it requires a strong collaboration between the anesthesiologist and surgeon because this can only be done in cardiac surgery and you need to really work very closely with your cardiac surgery teams to be able to develop this kind of data.

But still, it remains the gold standard. So, any kind of technology in the past should have been tested at some point either in animals or in some specific setting with this kind of— with the aortic flow probe.

The bottom line is that most of the time when cardiac output monitoring studies are performed they use other reference methods; they use mostly the Swan-Ganz catheter, so the classic thermodilution or the noninvasive cardiac output monitoring methods or even sometimes they use ultrasound.

And that creates a little bit of an issue because these systems are not gold standard for measuring cardiac output and it always raises the question to know whether the inaccuracy that you could observe in a new technique is related to the lack of accuracy of the gold standard or lack of accuracy of the new method.

And in the study by Dr. Sigurdsson, I really believe that the reasons we get are extremely valid and accurate because they clearly use what’s the best method for measuring cardiac output physiologically and also clinically.

Dr. James P. Rathmell: So, a rare study that actually uses a real gold standard. That’s terrific. Can you describe as you did in your editorial Dr. Alfred Blalock and the observations that he made about the relationship between cardiac output and blood pressure? And tell us why cardiac output is still seldom measured in pediatric patients.

Dr. Maxime Cannesson: So, I would expand and say that actually cardiac output is seldom measured in any kind of patients undergoing surgery. Maybe in adult cardiac surgery cardiac output is measured more frequently, but outside of it it’s pretty rare still.

So, Dr. Alfred Blalock was a pediatric surgeon and one of the pioneers of pediatric cardiac surgeries, obviously the inventor of the Blalock-Taussig shunt, and in the 1920’s he conducted some of the landmark studies on the cardiovascular physiology.

And what he would do in these studies is that he would induce hemorrhagic shocks in animal models and he demonstrated something that’s been demonstrated again and again—and which is probably one of the strongest evidence in cardiovascular physiology—is that you can decrease the blood volume of a living organism, a mammal, an animal or even a human being, you decrease the blood volume down to 30% of their baseline without seeing any change in the arterial pressure.

Why? Because when the venous return decreases because of the hemorrhage and the cardiac output decreases, there is a compensatory mechanism that’s going to maintain the arterial pressure and this mechanism is the increase in the systemic vascular resistances.

And what you demonstrated back in the days about a century ago is that if you just look at the blood pressure, you’re going to miss hemorrhagic patients. If you want to detect hemorrhage very early, you have to measure cardiac output because that’s what decreases first in the setting of hemorrhage.

And this is something we’ve known for more than a century that something that’s been demonstrated again and again and again, but still when it comes to clinical practice we very rarely measure cardiac output.

Dr. James P. Rathmell: Well, can you tell us a little bit more about the problems or the limitations with measuring cardiac output in small children? And describe the data that existed before this new study.

Dr. Maxime Cannesson: So, one of the main limitations in the pediatric setting is that there is a lack, actually, of a gold standard that’s easily accessible to measure cardiac output in the clinical setting, something that you can use as a reference. And that’s why, again, the study by Dr. Sigurdsson is so important because they used this aortic flow probe.

So, because these kind of studies are very difficult it’s obviously very difficult to validate new devices and new technologies. However, the technologies available for pediatric patients are basically the same as the technologies that exist for adult patients, but they are facing a bit more challenges when it comes to their clinical application.

First, the size, obviously, of pediatric patients is completely different from what you observe in adult patients and the size varies from one patient to the other in the pediatric setting. It’s different to measure cardiac output in an infant versus measuring cardiac output in a patient that’s ten years old.

The size is important because the cardiac output in this setting is going to be very different. The cardiac output in an infant could be down to 700 cc per minute, so any change in the accuracy of the cardiac output measuring device is going to induce a big mean percent error. The smaller the value you’re trying to measure, the more likely you are to make a mistake in your measurement.

Another limitation of cardiac output monitoring in children also comes from the regulatory approval. We don’t have much of these technologies being approved in children. For example, technologies like the arterial pressure, cardiac output monitoring system are only validated for adults.

And what we explain in the editorial is maybe one of the problems with that is that the market of pediatric anesthesia is pretty small compared to the other markets; and, unfortunately, it may be that some companies are not willing to go through the FEDA regulatory process for such a small market.

But even if the market is small, these patients are extremely important and I believe that it will be extremely important to have these devices in this setting.

Dr. James P. Rathmell: So, is this new device the answer to making routine cardiac output measurements in children or are there still some challenges that need to be overcome?

Dr. Maxime Cannesson: Personally, I’ve never used this device in my clinical setting, but what I can foresee as one of the main limitations is that it’s still pretty invasive to measure cardiac output. Even though it’s been extremely well-validated in this study, I would say that the field of potential application for this technology in the clinical practice remains probably as of today the critical care setting and the cardiac surgery setting.

You want systems that are less invasive so that you can use them in more patients: you don’t have the barrier of placing a very invasive device to measure cardiac output. However, I do believe that this step toward the cardiac output monitoring in small children, this study is probably the first step toward this goal.

Dr. James P. Rathmell: Well, it’s probably not made for the general pediatrician’s office. Dr. Sigurdsson, where do you see this new technology fitting into clinical practice?
Dr. Theodor S. Sigurdsson: Well, I must agree with everything that’s been said; this is an extremely important group of patients that are really sensitive to all fluctuation and circulation in hemodynamics.

With regard to the cardio output estimations, we finally have a safe and reliable bedside technology that we can easily apply in the pediatric ICU settings.

A patho-clinical estimation of the critically ill patients or children on cardiac output response to different treatment is now possible. However, this technology does not provide us with the continuous cardiac output measurements and, in that respect, I really see that this new technology could act as a bridge between two worlds: from the invasive to the noninvasive.

There are many exciting continuous noninvasive cardiac output monitors emerging and I think this new technology could certainly help in the future for the patients.

Dr. James P. Rathmell: So, what comes next for you and your research group?

Dr. Theodor S. Sigurdsson: Well, we are currently working on data from earlier, current and ongoing studies in pediatric patients using this technology as well as looking into other aspects of pediatric hemodynamics. Just now we are mostly focusing on shunt detection and estimation of volume status in pediatric patients.

Dr. James P. Rathmell: Well, terrific. I hope today’s discussion will lead many of you listening to read this new article and the editorial view that appear in the May 2019 issue of Anesthesiology. You can learn more about measurement of cardiac output in small children using this new technology. Dr. Jonathon Wænderer from Vanderbilt and I also created an infographic that appears in the same issue and better explains the new technology and how it compares with other methods for measuring cardiac output.

Drs. Sigurdsson and Cannesson, thank you for joining me today and for the terrific explanations.

Dr. Theodor S. Sigurdsson: Thank you.

Dr. Maxime Cannesson: Thank you very much.