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Babies and Children at Last: Pediatric Cardiac Output Monitoring in the 21st Century

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In this issue of *Anesthesiology*, Sigurdsson et al. report on a new cardiac output monitoring system based on extracorporeal arteriovenous ultrasound measurement in small children[1]. While the technology they are describing is invasive, it is one of the first technologies to be so meticulously tested in this important patient population. Specifically, the authors used the aortic flow probe - the physiological gold standard for cardiac output monitoring - as a reference and they included children presenting with various congenital heart diseases. Rarely have clinical hemodynamic monitoring studies achieved such a level of scientific rigor not only in the pediatric setting, but also in the adult setting.

Dr. Alfred Blalock, one of the great pioneers of pediatric congenital cardiac surgery, made a critical observation on the relationship between cardiac output and blood pressure during his shock experiments in the 1920s. He found that "*the repeated removal of blood is usually associated with a decline in the cardiac output from 30 to 50 per cent below the normal level* ***before*** *a marked diminution in the mean blood pressure occurs*[2]." By Ohm's law, blood pressure is related to cardiac output and systemic vascular resistance. Hence, blood pressure can remain relatively stable despite a significant change in cardiac output due to compensatory changes in systemic vascular resistances. Although blood pressure is imperative for perfusion pressure, cardiac output is essential for oxygen delivery and cardiac output measurement is a vital part of hemodynamic monitoring and management of all critically ill patients including pediatric patients of all ages and sizes[3]. Although almost a century has passed since Dr. Blalock illustrated the critical role of cardiac output in global cardiovascular circulation, despite its shortcomings, blood pressure still remains the

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mainstay for hemodynamic monitoring of cardiovascular function in critically ill pediatric patients. Cardiac output is only rarely measured in this pediatric population, and the methods available for cardiac output monitoring in this population remain either poor surrogate, not validated or inaccurate.

Today, the most common perioperative pediatric cardiac output monitoring only uses surrogates such as mixed venous oxygen saturation, lactate levels, regional venous oxygen saturation, toe-core temperature difference and serial echocardiographic exams[4]. Invasive monitoring based on information from arterial and central venous pressures such as pulse contour analysis methods have been tested in pediatric patients. However, no study to date has ever tested tehse systems against a reference method such as the aortic flow probe and many of the devices that are commonly used in adult patients are not yet FDA approved for children (vascular compliance evaluation used to calculate cardiac output with these systems has not been designed for children)[5]. For these reasons, cardiac output monitoring use in pediatric clinical practice is more the exception than the rule. On the other side of the spectrum, newer non-invasive hemodynamic monitoring modalities such as electrical cardiometry, impedance cardiography, and bioreactance have been described and tested in pediatric populations but again, their real life implementation has been scarce at best[6–9]. Overall, very few commercially available cardiac output monitoring devices are applicable in pediatric patients and most of them present with incomplete validations and/or poor precision and accuracy[9]. So why has this important topic not made it to “prime-time” in the pediatric anesthesia community?

There are a number of challenges to implementing translatable research regarding pediatric cardiac output monitoring. First from a clinical perspective, a subset of pediatric patients for whom hemodynamic monitoring would be beneficial often have shunts and/or complex cardiac anatomy hampering accurate cardiac output measurement. Secondly, pediatric patients represent size limitations when developing either non-invasive or invasive cardiac output monitoring devices – the range of sizes and body habitus varies significantly from patient to patient and the relatively low cardiac output values in children significantly impacts accuracy of the measurements. Heightened regulations around clinical experimentation within non-adult populations coupled with perceived small market size further deters active industry involvement in development of novel cardiac output monitoring technologies. Furthermore, the accuracy and clinical utility of many of these cardiac output monitoring devices though substantiated within adult population have not born out in pediatric population. The majority of these technologies are derivatives from innovations and studies in adult population[9]. In a recently published meta-analysis, our group actually found 20 studies testing cardiac output monitoring systems in children9. In this study, the main finding was that these studies presented with a very high inter-study heterogeneity and a lack of standardization in the way they were conducted regarding stratification by age, device, reference method, settings, invasiveness, and intra-cardiac shunt. Thus, further research is needed to validate the applicability of the adult algorithms and technologies to pediatric population. To this effort Sigurdsson et al. conducted a “state of the art” validation of a relatively new technology (extracorporeal arteriovenous ultrasound) in a very challenging patient population[1]: small children undergoing corrective cardiac surgery. This study is remarkable for many reasons. The methodology follows all of the main criteria for methods comparison studies as emphasized by *Riou et al.* in an Editorial published in *Anesthesiology* in 2013[10]: A clear quantified hypothesis is tested (null hypothesis is that the methods are equivalent in precision and there is no bias in the cardiac output measurements); there is a unique primary endpoint (cardiac output absolute value); the type of the study is indicated (method comparison study); an a priori calculation of the number of patients needed is presented based on previous experiences; and the statistical plan was decided a priori. More impressive is the fact that the authors chose an almost indisputable but highly invasive reference method for cardiac output measurements: The periaortic flow probe, which remains the gold standard for cardiac output monitoring in the clinical setting.

Despite the encouraging results from this study, there are still many challenges in developing the ideal cardiac output monitor for pediatric patients. The perfect pediatric cardiac output monitor would have to be size unlimited, accurate, reproducible, continuous, have a rapid response time, non-invasive, user friendly, operator independent, cost effective, and have the ability to factor in simple and complex intra- and extra-cardiac shunts. No such device is in existence for either adult or pediatric patients yet. However, if we can overcome the other major factors, such as an unfavorable industrial interest and strict research constraints to conduct clinical validation, then innovation will surely drive the invention of such device in the future. Another equally important question that needs to be answered is whether the addition of cardiac output monitoring guided hemodynamic management would affect clinical outcomes the way it has potential to affect outcome in adult major surgery patients[11]. However without reliable, practical and widely adopted device this debate is only academic. This is the reason why we welcome and applaud the study by Sigurdson et al. that offers possibility of a simple and reliable method that uses arterial line and central line to measure cardiac output in children of all sizes.

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