Developing Techniques: The Future of Monitoring

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Abstract

The fundamental goal of critical care medicine is to optimize cardiac output to maintain adequate organ perfusion and meet the body's metabolic demands. Historically, monitoring cardiac output was limited to indirect measures of the physical exam and biochemistry. The pulmonary artery catheter was the first widely adapted instrument to quantify cardiac output at the bedside, but its use has been curtailed, especially in pediatrics, due to its invasiveness and associated complications. Newer cardiac output monitoring technologies have recently emerged and are being slowly integrated into routine clinical practice.

Cardiac output devices have evolved to become less invasive in hopes of minimizing side-effect profiles. In general, these devices fall into three broad categories: intermittent measurements based on transpulmonary dilution, continuous monitoring based on analysis and integration of the invasive arterial waveform, and continuous measurements based on changes to electrical impulses across the thoracic cavity. Lastly, commercial devices that determine the adequacy of distal perfusion through tissue-based assessment have also been recently introduced. Volume assessment of physiologic compartments (e.g., intravascular, intrapulmonary) is also possible by several companies. Adult data showing acceptable accuracy and precision exists for many of the newer devices, but validation in pediatric patients, particularly infants and neonates, is scant.

This chapter will provide readers a detailed review of the underlying physiology for the emerging cardiac output devices and present their validation studies in the field of pediatrics. It will also provide a framework for assessing their utility in a pediatric intensive care unit.

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Introduction

Hemodynamic surveillance forms the hallmark of critical care patient monitoring. Historically, adequacy of cardiac output has relied on assessment of clinical indices including patient vital signs, capillary refill, peripheral body temperature, urine output, and biochemistry. However, with increasing evidence of poor physical exam reliability, direct measurement of absolute cardiac output has been sought to direct patient care [1, 2]. Pulmonary artery catheterization with measurement of cardiac output by thermodilution has been used extensively in various adult settings [3]. Unfortunately, due to a significant complication burden and limited utility for children with congenital heart disease who often have residual intracardiac shunts, the use of this technique has always been limited in pediatrics and, over the past decade, has declined even further. Measurement of cardiac output has instead focused on development of newer methods that might offer both accuracy and minimal invasiveness and with the capability of repeated or continuous measurements for pediatric patient monitoring. Furthermore, newer technology has also attempted to address the ability of determining the adequacy of the cardiac output in meeting the hemodynamic and perfusion demands of the body.

This chapter will review emerging technologies for monitoring cardiac output and tissue perfusion that are now slowly transitioning from research tools into clinical applications for monitoring postoperative cardiac patients in the critical care unit. For a summary of the principles, advantages, and disadvantages of the different systems discussed in this chapter, please see Table 50.1.

Transpulmonary Dilution Techniques

Clinically accurate and reliable measurement of cardiac output was first introduced in adults over 40 years ago using the pulmonary artery catheter, which became the clinical standard [3]. However, lack of demonstrable clinical benefit in several studies have led to questions about its utility in goal-directed patient care, particularly in light of the incidence of complications including hemorrhage, thrombosis, infection, and vessel injury. Comparable studies in pediatrics have not been undertaken; however, the side-effect profile has propelled the study of less invasive technologies [4]. These newer techniques largely employ the concept of transpulmonary dilution of an indicator as the core method by which cardiac output is calculated.

Most cardiac output monitoring devices incorporate an indicator dilution method of measurement [5]. Similar to pulmonary artery catheters, cardiac output is based on an indirect Fick calculation using the integral change of the indicator concentration over time. Following injection of an indicator, it is diluted by the blood flow, and the indicator will both appear at the downstream sensor sooner and be cleared faster with a higher cardiac output. The monitoring device generates a curve of the indicator concentration over time (Fig. 50.1); a lower area under the indicator time curve signals a shorter circulation time and thus a higher cardiac output. Test injections are usually conducted in triplicate, with the average forming the final reported cardiac output value. Unlike the traditional pulmonary artery catheter, these devices examine transpulmonary dilution, during which the tracer is injected in a large systemic vein and the downstream measurement occurs in a systemic artery. One important effect of this approach is that the dilution time is

Table 50.1 Summary of cardiac output monitoring devices

Name	Physiologic principles	Age group	Advantages	Disadvantages
PiCCO	TPTD + Arterial pressure-based CCO	Well validated in children	Multiple hemodynamic parameters	Requires central arterial catheter
		CCO less well validated in children	Continuous	
COstatus (Transonic, NY, USA) – transpulmonary	Transpulmonary ultrasound dilution	Validated in animal studies and adults	Standard AC and CVC	Intermittent measurement
		Only one study validation in children	Nontoxic indicator	Circuit needs replacement 24–36 h
			Minimal blood loss	Potential for fluid overload
			Can measure other volume status parameters	
LiDCO (LiDCO Systems, London, UK)	Transpulmonary lithium dilution + arterial pressure-based CCO	One validation in children	Continuous	Potential significant blood loss
		Not approved for use <40 kg		
Dye densitogram analyzer (Nihon Kohden, Tokyo, Japan)	Pulsed dye densitometry	No validation studies in pediatrics	Noninvasive	Appropriate signal detection mandatory
			Use of peripheral venous catheter	
FloTrac/Vigileo system (Edwards Lifesciences, CA, USA)	Arterial pulse contour analysis	Not validated in pediatrics	Continuous	Arterial wave artifacts, irregular pulse influence measurements
			No calibration	
MostCare (PRAM) (Vytech, Padova, Italy)	Arterial pulse contour analysis	One validation study in children	Continuous	Calibration not possible
Nexfin (BMEYE, Amsterdam, The Netherlands)	Arterial pulse contour analysis (finger cuff)	Adults only	Noninvasive	Not feasible for small children
			Continuous	
USCOM (Uscom, Sydney, Australia)	Transcutaneous Doppler	Adults	Noninvasive	Intermittent
		More validation in pediatrics needed		Operator and flow dependent
				Nomogram based estimates
Bioimpedance	Electrical impedance (surface electrodes)	Adults/pediatrics	Noninvasive	Inaccurate in intensive care settings
			Continuous	Not well validated in pediatrics
NICOM (Cheetah Medical, Tel Aviv, Israel)	Bioreactance (surface electrodes)	Validated in adults	Noninvasive	–
		No validation studies in pediatrics	Continuous	
OPS and SDF	Direct, bedside in vivo observation of the microcirculation	Observation studies in pediatric sepsis	Provide assessment of adequacy of oxygen delivery	–
		Adults		

AC arterial catheter, *CCO* continuous cardiac output, *CVC* central venous catheter, *TPTD* transpulmonary thermodilution

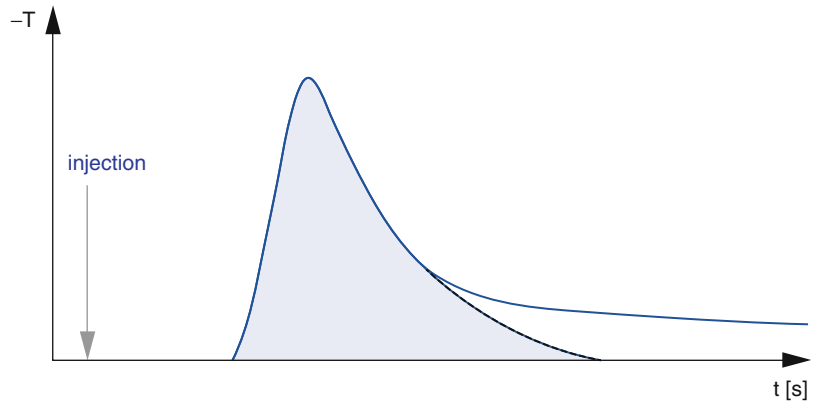

Fig. 50.1 A thermodilution curve from a transpulmonary cardiac output monitoring device: the period from indicator injection to measurement of curve represents the transit time. The dilution curve indicates the measured change in temperature over time (an equivalent curve would be formed using other indicator techniques). Cardiac output is calculated by a modification of the Stewart-Hamilton equation and is inversely related to the area subtended by the dilution curve

lengthened over a period of several cardiac cycles, decreasing the impact of beat-to-beat and respiratory variability on the final value [6].

The accuracy of the transpulmonary dilution method is based on several technical and physiological assumptions that must be met in order for this technique to be accurate. These include adequate mixing of blood and indicator, minimization of indicator loss, and need for constant blood flow through the circulation. Abnormal circulation resulting from valvular regurgitation, intracardiac shunts, or extremely impaired cardiac output result in erroneous results [7]. These devices are therefore limited to children with biventricular anatomy and physiology and thus cannot be used in a large number of children with congenital heart disease.

Nevertheless, when used appropriately, these devices can provide information that may be useful for patient evaluation and management.

Transpulmonary Thermodilution

The Transpulmonary thermodilution (TPTD) technique uses thermal energy as an indicator. Ice-cold saline is injected in a central venous catheter, and a thermistor-tipped catheter positioned in a large systemic artery, usually femoral or axillary, measures downstream temperature. The volume of injectate is weight based and ranges between 2 and 20 mL [8]. In contrast to the traditional pulmonary artery catheter, this method is considered less invasive as both venous and arterial catheters are usually used as part of standard care; thus, placement of additional catheters is not required.

The commercially available PiCCO system (Pulsion®, Munich, Germany) has been widely used in adult and pediatric ICU settings (Fig. 50.2). Thermistor-tipped arterial catheters ranging in size from 3F to 5F are available, allowing for measurement in any patient above 3.5 kg. It has been validated in several juvenile animal and pediatric human studies against perivascular flow probes, pulmonary artery catheters, and direct cardiac output calculation by Fick method [9–11].

With the data acquired by transpulmonary thermodilution, volume for several physiologic compartments can be calculated. The total volume of distribution is determined based on mathematical and experimental models where an indicator is injected into several mixing chambers arranged in series. Specifically, the Stewart-Hamilton principle, in which cardiac output is measured from the total indicator used and the integral of indicator concentration over time, is used to describe the relationship where

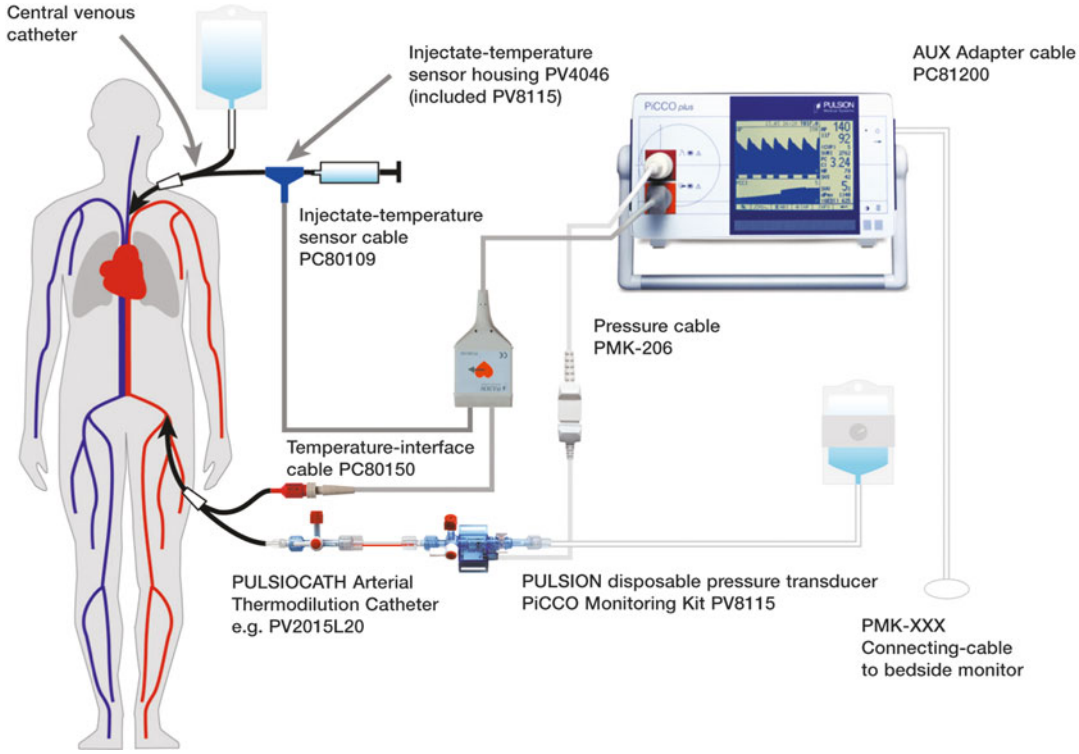

Fig. 50.2 A schematic representation of the PiCCO system by Pulsion®: ice-cold saline is injected into a central venous catheter. A thermistor-tipped arterial catheter measures the change in temperature in a central artery, usually the femoral or axillary. All data are presented in real time on the display screen. Both access catheters can also participate in ongoing hemodynamic monitoring. The arterial pressure curve is also used for continuous cardiac output monitoring by pulse contour analysis

volume equals the product of flow and mean transit time. This calculated volume of distribution is called the intrathoracic thermal volume (ITTV) and is the product of cardiac output and mean transit time (time at which 50 % of indicator detected); ITTV represents the total blood volume in the cardiopulmonary circulation at end of diastole. The total amount of volume in the pulmonary space (pulmonary thermal volume) can also be calculated from the thermodilution curve; when subtracted from the ITTV, the global end-diastolic volume (GEDV) is determined, representing the total volume of blood in all cardiac chambers at the end of diastole. In experimental animal models and neonatal observational trials, GEDV outperformed clinical markers of preload in correlating with stroke volume and cardiac output. Finally, degree of pulmonary edema measured as extravascular lung volume can also be calculated from the above data set. Pediatric studies, compared to adults, are sparse and additional validation is required. The above static volume indices have the potential to form an integral component in a patient's clinical assessment and a valuable tool in guiding therapeutic interventions [12].

Ultrasound Dilution

The COstatus device (Transonic Systems Inc., Ithaca, NY, USA) is based on the changes to ultrasound velocity of circulating blood following dilution by a saline injection. Ultrasound velocity is dependent on protein and ion concentrations and generally measures between 1,560 and 1,585 m/s. Saline dilution decreases the ultrasound velocity, which can be measured over time

and converted to a measure of blood concentration, which is then used to calculate cardiac output [13]. The saline dilution is accomplished via an extracorporeal arterial–venous connection, which is established between a central venous catheter and a central or peripheral arterial line. These connections are primed with approximately 5 mL of heparinized saline, and a roller pump maintains constant blood flow through the circuit at a rate of 8–12 mL/min. Normal isotonic saline, heated to body temperature (37 °C), is injected at a volume of 0.5 mL/kg (maximum 30 mL) into the venous limb of the circuit, and ultrasound velocity of circulating blood is then continuously monitored at the arterial limb. Cardiac output is calculated as the product of the volume of isotonic saline injection and decrease in ultrasound velocity over the integral of ultrasound velocity over time. Consistent with other dilution devices, the injections occur in triplicate with a final mean value ultimately reported.

Ultrasound dilution has been validated in numerous animal and adult models [13–16]. In the only published pediatric series, ultrasound dilution correlated well with cardiac output measured by pulmonary artery catheterization in children undergoing cardiac catheterization following cardiac transplants. This study was limited to children above 1 year of age and 10 kg and showed means bias of 4.1 mL/min with a precision of 0.8 L/min [17].

The major advantage of the COstatus technique is its ability to use peripheral arterial catheters that are part of routine postoperative care of children. Other benefits include the use of nontoxic indicator and minimization of blood loss. Nevertheless, COstatus affords only intermittent measurement of cardiac output using a circuit that must be replaced every 24–36 h. A potential for fluid overload exists with repeated saline injections for each measurement. Ultrasound dilution technology also allows for assessment of total end-diastolic volume (TEDV), central blood volume (CBV), and active circulating volume (ACV). ACVI is defined as the volume of blood in which the indicator mixes in 1 min from the time of injection and represents the total amount of blood in the circulatory system, actively participating in cardiac output. The ACV may have clinical value in assessing a patient's volume status [18]. CBV is the product of cardiac output and the mean indicator transit time from the injection site (central vein) to the recording site (peripheral artery) and represents the volume of blood in the heart, lungs, and great vessels [19]. Finally, TEDV is analogous to the GEDV as determined by the PiCCO system and is considered to be equivalent to the preload volume of the heart. This is based on the underlying assumption that the majority of time of the arterial curve versus the venous curve is due to indicator traversing the heart chambers; TEDV is then calculated using the width of the arterial and venous curves at one-half the maximum height [20]. Although several small adult cohort data show a correlation between TEDV and CBV and cardiac preload, no pediatric studies are currently available.

Lithium Dilution

Transpulmonary lithium dilution uses an isotonic solution of lithium chloride as the indicator and requires standard venous and arterial catheters and a lithium sensor [21]. The commercially available device is marketed under the name LiDCO (LiDCO Systems, London, UK). Similar to COstatus, LiDCO makes use of usual arterial access such as the radial artery. Following injection of lithium chloride (0.002–0.004 mmol/L) into a standard central venous or peripheral venous catheter, the resulting arterial lithium concentration-time curve is recorded by a lithium sensor attached to the patient's existing arterial line and is interpreted by the LiDCO device. A constant flow of 3–4 mL/min is established by a roller pump directing arterial blood through a three-way connector to pass by the lithium sensor that detects the voltage across a lithium selectively permeable membrane. The voltage is related to the concentration of lithium (corrected for sodium). Each measurement requires approximately 3 ml of blood. Cardiac output is the product of the injected lithium dose, the area subtended by the lithium dilution curve and

1 − packed cell volume. The packed cell volume is calculated by dividing hemoglobin concentration (g/dl) by 34, the correction factor accounting for the distribution of lithium in the plasma. Cardiac output measurements are an average of 2–3 injections.

LiDCO has been validated in pediatric patients using transpulmonary thermodilution as the reference technique. Seventeen patients in a pediatric intensive care unit were studied and the results demonstrated safety, feasibility, and reasonable correlation with transpulmonary thermodilution measurements [22].

With three injections required for every cardiac output measurement, and 3–4 mL blood loss per reading, recurrent measurements can lead to significant blood loss for small infants. Furthermore, the maximum recommended total cumulative dose of lithium chloride is 3 mmol, corresponding to approximately 20 individual injections of 0.15 mmol for adults. The dose used in children for a single CO measurement is 0.002–0.009 mmol/kg, which has no known pharmacological effect [23]; however, repeat cardiac output measurements should be limited to avoid overaccumulation of lithium. The LiDCO device has not received FDA approval for children weighing less than 40 kg.

Pulsed Dye Densitometry

With pulsed dye densitometry, intermittent cardiac output measurements can be obtained at the bedside using a finger or nose clip device and a dye densitogram analyzer based on the same principles that are applied to pulse oximetry [24]. However, for substances in the blood other than hemoglobin, the alteration due to arterial pulsation is used to estimate its concentration in the blood. In this dye dilution technique, indocyanine green, a nontoxic substance, is employed as the indicator. Indocyanine green is cleared exclusively by the liver, with a half-life of approximately 4 min, and it takes >20 min to be metabolized completely in the blood. It is injected into a central vein with a measured arterial concentration change based on transcutaneous signal detection adapted from pulse oximetry. In contrast to the conventional dye dilution method, this technique does not require blood sampling. Cardiac output and circulating blood volume can be calculated by analyzing the pulsatile change in dye concentration in the arterial blood. Appropriate signal detection is mandatory and high heart rate, poor peripheral circulation, interstitial edema, and movement artifacts negatively influence this.

Studies in adults are limited and this technique has not been validated in pediatrics, but an animal study comparing it with ultrasound flow probe showed good correlation [25]. Its applicability in clinical practice is unknown.

Arterial Waveform Analysis

Continuous analysis of pulse contour allows for beat-to-beat assessment of cardiac output, in contrast to the repeated intermittent measures inherent in transpulmonary dilution techniques. Pulse contour analysis is a based on the principle that the area subtended by the arterial pulse wave reflects stroke volume and arterial compliance. Proprietary computer algorithms analyze the arterial pressure waveform and calculate cardiac output as the product of the determined stroke volume and the instantaneous heart rate [26]. Some devices providing pulse contour analysis require calibration against an indicator dilution technique, whereas others do not. Those that require calibration have generally been incorporated into devices that already use transpulmonary dilution techniques.

Pulse contour cardiac output algorithms have been designed for the adult population and have not been extensively studied in pediatrics. Several patient characteristics in children may affect the reliability of these monitors. Firstly, the developing vascular system is structurally and functionally different in children than adults. Since vascular capacitance plays an integral role in pulse contour analysis, such changes may make measurement in children less accurate. Secondly, an optimal pressure transducing system requires low compliance tubing and careful calibration. Dampened waveforms,

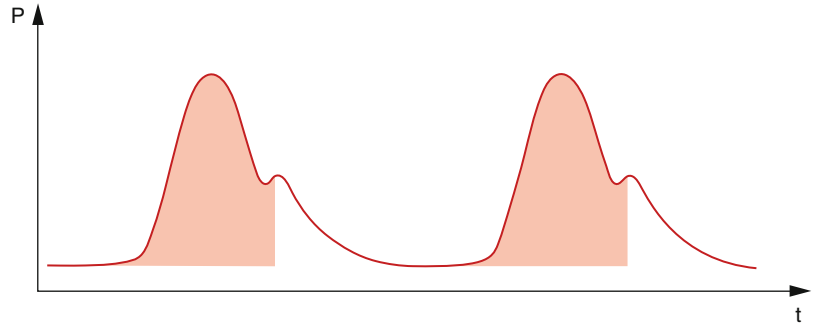

Fig. 50.3 Pulse contour analysis: cardiac output is continuously calculated by an algorithm that incorporates the area subtended by systolic portion of the arterial waveform (*shaded area* flanked by the systolic upstroke until the dicrotic notch), aortic compliance, and a patient-specific factor derived from calibration with thermodilution. Repeat calibration with thermodilution is required every 8 h and when significant hemodynamic shifts occur

movement artifacts, and catheter kinking are common in infants and small children and may adversely affect the derived cardiac output from the arterial waveform.

Pulse Contour Analysis

The PiCCO2 system (Pulsion®, Munich, Germany) integrates pulse contour analysis to the PiCCO system described above. To determine continuous pulse contour cardiac output, an algorithm incorporating the area under the systolic portion of the arterial waveform, aortic compliance, and a patient-specific calibration factor determined by the bolus thermodilution measurement of cardiac output is used (Fig. 50.3). It requires an initial calibration using transpulmonary thermodilution, with regular recalibration at a maximum interval of 8 h necessary to ensure measurement accuracy. More frequent calibration is required when patient-related factors, such as profound alterations in hemodynamic status, change [27].

To date, the use of the PiCCO2 pulse contour system in pediatric patients has not been adequately validated. A comparative cardiac output study in children prior to and following cardiac surgery showed poor agreement (percentage error $\pm$ 52 %) between pulse contour analysis measurements and TPTD [28]. The weak agreement persisted despite surgical correction of all intracardiac shunts. Smaller patient size, lower absolute cardiac output values, higher heart rates, and greater aortic compliance compared with adults may affect or limit the accuracy and precision of PiCCO2 analysis in children necessitating its cautious use. Its clinical strength and utility may be in its ability to detect changes in the hemodynamic profile. The absolute cardiac output may be considered a rough estimate, but changes in measured cardiac output could alert the clinician, which would make it a useful tool.

Another potential physiologic parameter evaluated by the PiCCO2 system is fluid responsiveness. Variations in the pulse pressure analysis are detected across the respiratory cycle and calculated as the difference of max stroke volume and mean stroke volume divided by the mean stroke volume [29]. Since pulse pressure reflects stroke volume, variations to measured pulse pressure through the respiratory cycle are thought to correspond to the effects of positive pressure ventilation on stroke volume in intubated children. Several adult studies have shown that elevation to stroke volume variation was associated with an increased fluid responsiveness. Although data in adults is sparse, there is an absence of pediatric data.

LiDCO/PulseCo

The PulseCo method (LiDCO Systems, London, UK), incorporated in the LiDCO device, converts

the arterial waveform to a nominal stroke volume using a pressure–volume transformation [23]. Unlike the PiCCO2 algorithm that uses only the systolic portion of the pulse pressure wave, the entire arterial pressure curve is incorporated into the PulseCo Pulse Power Analysis. In doing so, this device theoretically incorporates the influence of peripheral resistance. The proprietary algorithm used by PulseCo analyzes the pressure waveform against a table derived from the curvilinear relationship of pressure and volume which seems to be similar in different subjects. In this way, a standardized volume waveform is constructed from the original arterial pressure input, which reflects the power generated by each heart beat and becomes the source of cardiac output assessment. The area subtended by standardized volume waveform when calibrated against transpulmonary lithium dilution is used as the basis for calculating stroke volume and, therefore, cardiac output. Periodic calibration against the transpulmonary dilution technique is required to maintain accuracy. Theoretically, this analysis is less vulnerable to inaccuracy due to damping of pulse pressure waveform and can be used in any artery.

This measurement technique has been validated in a pediatric study against pulmonary artery thermodilution. Twenty children with structurally normal hearts undergoing routine catheterization hemodynamic assessment for transplantation surveillance or investigation of primary pulmonary hypertension were studied. Patients with known intracardiac or extracardiac shunting were excluded [30]. PulseCo was determined to be very precise and accurate, with a percentage error of 8.8 % and relative bias of 6 % between measurements.

The method seems promising, but further studies are warranted and the use of lithium should be considered, although the integration of continuous CO analysis from arterial pulse pressure by the LiDCO device may limit the frequency of lithium use. As with PiCCO2, the accuracy and precision are dependent on the frequency of recalibration, which place limitations to its long-term use. Unfortunately, for those caring for large numbers of patients with residual shunts, the need to validate the measurement against a transpulmonary dilution technique may also be problematic.

FloTrac/Vigileo

The FloTrac/Vigileo system (Edwards Lifesciences, Irvine, CA) is another cardiac output monitoring system based on analysis of the systemic arterial pressure wave. An important distinction for this device is that it does not require calibration. The stroke volume is derived by a proprietary algorithm, using the patient's vascular resistance and arterial compliance based on sex, height, weight and age, and the pulse pressure waveform characteristics [31].

The FloTrac algorithm does not calculate the area under the pressure waveform. Instead, stroke volume is calculated by waveform analysis. Together with patient demographic information, the waveform is analyzed to calculate the standard deviation of the arterial pressure, which is proportional to pulse pressure. The standard deviation of the arterial pressure is multiplied by a conversion factor, which incorporates the effects of resistance and compliance and also converts the standard deviation of the arterial pressure into ml/beat. This relationship can vary widely between patients and also in a single individual as hemodynamics change. Its calibration constant is recalculated every 60 s.

There is a growing body of adult-based evidence characterizing its utility in critical illness for which it is FDA approved [32, 33]. Only one validation study has been done in the pediatric population. Teng et al. compared this device with pulmonary artery catheter derived intermittent cardiac output measurements in pediatric patients with cardiomyopathy, pulmonary hypertension, or post-cardiac transplant who presented for heart catheterization [34]. An unacceptably high percentage error (80 %) was found between the two methods. Since the algorithm used by the device is based on the vascular properties of elderly patients, it should be used cautiously in other populations with different vascular compliance, which most certainly includes children.

PRAM

The Pressure Recording Analytical Method (PRAM) (Vytech, Padova, Italy) also analyzes the systemic arterial pressure waveform morphology to calculate cardiac output [35]. The results of this beat-to-beat analysis allow for determination of the stroke volume, which is then used to calculate cardiac output multiplying stroke volume by heart rate. This method, studied in children by Calamandrei et al. [36], has been compared with transthoracic Doppler echocardiographic measurements. The study showed that the mean difference between the two methods was 0.12 ± 0.27 L·min^{-1} (95 % CI -0.54 to 0.77 L·min^{-1}) with a percent error of 21 %. The major problem with this comparison is that echocardiographic determination of cardiac output in children is a poor gold standard and has shown to be generally unreliable due to high interoperator variability in being a reliably precise measure of cardiac output [37]. Nevertheless, PRAM might still be useful in pediatric patients, but clearly, additional clinical validation studies are warranted.

Noninvasive Continuous Finger Arterial Pressure and Cardiac Output Monitoring

Blood pressure and cardiac output can be obtained using a continuous, noninvasive, finger arterial pressure measurement technique. This method requires an inflatable finger cuff that incorporates a photoplethysmographic sensor, a rapid-reacting pneumatic servo system and a device that can interpret the signal. The plethysmographic signal drives the servo system in such a way that the finger arterial wall is constantly kept unloaded. The cuff pressure then is a reflection of the finger arterial pressure. After application of a software algorithm, a brachial pressure curve is generated [38]. The Nexfin HD device (BMEYE, Amsterdam, the Netherlands) incorporates an arterial pressure-based pulse contour continuous cardiac output monitoring method that can be applied to the arterial waveform from the finger artery.

Thus far, it has been limited to adult studies, which have shown acceptable results in healthy volunteers. However, acceptable reliability reflected by a relative error of 29 % was found in a single study comparing Nexfin with pulmonary artery catheter data in ICU patients [39]. Due to physical characteristics of infants and small children, it is unlikely that this device would ever have clinical relevance in this population. Further validation studies are needed.

Other Methods

Continuous Wave Doppler Ultrasound

The Ultrasonic Cardiac Output Monitor (USCOM) (Uscom, Sydney, Australia) is a portable apparatus for measuring cardiac output through transcutaneous analysis of aortic or pulmonary artery flow using continuous wave Doppler ultrasound. The Doppler flow is measured using a handheld probe positioned on the thorax. The subject's height and a nomogram incorporated into the software estimates the valve cross-sectional area so that cardiac output can be calculated from the measured flow across the aortic or pulmonary valve [40, 41]. In one animal study, USCOM compared favorably with data obtained from an ultrasound flow probe around the ascending aorta [42]. Nevertheless, a validation study in children comparing USCOM with pulmonary artery thermodilution found measurements unreliable in representing the absolute cardiac output in children undergoing cardiac catheterization [40].

The USCOM technology has inherent weaknesses that may lead to poor reliability. First, cardiac output measurements are operator and flow signal dependent. Second, its usage of nomogram based estimates of the cross-sectional area of the aorta and pulmonary valves could introduce error into the results. The validity of this technique requires further studies.

Thoracic Bioreactance/Impedance

Thoracic bioreactance is a noninvasive method that analyzes intrabeat variations of transthoracic voltage in response to an injected high-frequency current [43]. Bioreactance uses a high-frequency sine wave generator and four dual electrodes. The variation in the frequency spectra of a delivered oscillating current that occurs when the current traverses the thoracic cavity is analyzed. The signal-to-noise ratio in bioreactance is approximately 100-fold greater than in traditional bioimpedance, which reduces the amount of error due to artifact. Thoracic bioimpedance provides continuous hemodynamic data [44]. In this system, a high-frequency electrical current of known amplitude and frequency is applied at source electrodes, and the change in voltage across the thorax is measured at the receiving electrodes. A ratio is obtained between the voltage and current amplitudes corresponding to a measure of transthoracic current resistance (impedance). Cardiac output is determined by converting variations to impedance to the proportion of fluid in the thorax. The amount of intrathoracic fluid is, in turn, related to blood flow in the aorta, which is systemic cardiac output.

Studies determining accuracy of cardiac output measured by bioimpedance in adults have shown discrepant results. Although, there is adequate correlation with pulmonary artery catheter thermodilution in some clinical settings [45], cardiac output determined by bioimpedance has been shown to be inaccurate in intensive care units and other settings where significant signal noise exists [46]. In one pediatric study comparing bioimpedance with the direct Fick method in children with repaired and palliated congenital heart disease, only 55 % of measurements were within 30 % of each other, making it an unreliable tool in this population [47].

With regard to bioreactance instead of bioimpedance, studies in adults have validated the basic principles of this technique and have found a good correlation and concordance between bioreactance and other methods for the measurement of cardiac output [48, 49]. Only one study has attempted to use this technique to measure cardiac output in children, and no validation studies have been done [50].

Microcirculatory Changes

Utility of cardiac output guided therapy has been questioned in large adult trials that demonstrated no benefit in pulmonary artery catheter use in several disease states. One potential explanation is that this device measures absolute cardiac output and not effective cardiac output and adequacy of distal organ perfusion. Efforts to better quantify perfusion to the microcirculation have been undertaken to provide bedside assessment of the adequacy of tissue oxygen delivery, which in many ways is the Holy Grail of intensive care therapy. Research has demonstrated that in various disease states, including cardiogenic or hemorrhagic shock, discernable changes occur in the microcirculation that could serve as an indicator of tissue hypoperfusion and could be of prognostic value [51, 52].

Several modalities have been designed to quantify these microcirculatory changes but have been generally confined to the laboratory setting. Nevertheless, selective devices including Orthogonal Polarization Spectroscopy (OPS) and Sidestream DarkField imaging (SDF) have been translated to bedside tests. These technologies are video-based devices that have recently been implemented in handheld form.

OPS and SDF are based on properties of light rays passing through tissue. As a light source is applied against tissue, light rays are reflected by the deeper tissue layers providing transillumination of the superficial tissue [53]. These techniques employ different light sources; however, both the wavelengths selected emit light rays that are absorbed by the hemoglobin contained in the red blood cells. As such, blood vessels are seen as black or gray bodies, making the microvascular vessels clearly visible and easily analyzed [54, 55]. Different variables including vascular density and heterogeneity of perfusion can then be measured; with the estimate of capillary density and

assessment of the proportion vessels perfused being the most relevant for tissue perfusion [56].

Adult studies have shown that patients admitted to the ICU for severe heart failure or cardiogenic shock had microvascular circulatory alterations, consisting of a decrease in vessel density and in the proportion of perfused capillaries [57]. Most of the literature, including studies of pediatric populations, has looked at the microcirculatory changes that occur secondary to sepsis and modeled with endotoxin. In pediatric patients with septic shock, Top et al. used OPS to examine the microcirculatory changes that occurred in the buccal mucosa and found that compared with non-survivors, survivors had an increase in the density of the functional capillaries [58].

While most of the adult literature has focused on the microcirculatory changes that occur in sepsis, it is rational to think that these devices could also play a role in assessing the microcirculation of other low flow states. This may form the foundation of future investigation.

Conclusion

Improving cardiac output monitoring in the pediatric cardiac intensive care unit forms the foundation of numerous new technologies that are being introduced to bedside care. Each technology strives to improve accuracy, precision, and versatility, allowing reliable measurements across several disease states and cardiac physiologies while minimizing their invasiveness. Bedside tests are now available to analyze cardiac output intermittently or on a continuous basis. Furthermore, additional physiologic data may be available depending on the manufacturer.

At this time, the majority of validation studies have been completed in adult settings. Although the results may be extrapolated to the pediatric patients, differences in size, vascular compliance, and other tissue characteristics mandate that pediatric specific studies be completed. Additionally, the challenges posed by the unusual physiologic situations frequently encountered in pediatric cardiac patients such as residual shunts, valvular dysfunction, and non-pulsatile pulmonary circulations may limit applicability of some of these techniques and require careful study. Nevertheless, there is optimism that new methods of hemodynamic surveillance will be available at a reduced side-effect burden.

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