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Accuracy and repeatability of pediatric cardiac output measurement using Doppler: 20-year review of the literature

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Abstract *Objective:* Review of the accuracy and repeatability of Doppler cardiac output (CO) measurements in children. *Design:* Publications in the scientific literature retrieved using a computerized Medline search from 1982–2002 and a manual review of article bibliographies. Studies comparing Doppler flow measurements with thermodilution, Fick, or dye dilution methods in the pediatric critical care setting were identified to assess the bias, precision, and intra- and interobserver repeatability of Doppler CO measurement. Where results were not suitable for comparison and the original measurements available, data were re-analyzed using appropriate statistical methods and presented in

comparative tables. *Results:* The precision of pediatric Doppler CO measurements compared to thermodilution, dye dilution, or Fick methods is around 30% and repeatability varies from less than 1% to 22%. Bias is generally less than 10% but varies considerably. *Conclusions:* The bias, precision, and repeatability from study to study indicate that Doppler CO measurements are acceptably reproducible in children, with best results when used to track changes rather than absolute values, and using the transesophageal approach.

Keywords Pediatric · Doppler · Cardiac output · Accuracy · Reproducibility

Introduction

Cardiac output (CO) measurements are not frequently used in children. There may be several reasons for this, including technical and size constraints, perceived lack of usefulness and questionable reliability of the various techniques for measurement, and not least a limited but significant risk of complications. In addition, industrial interest is generally directed towards adult critical care medicine. Several methods for CO measurement in children have been described, including clinical estimation, thermodilution, Fick, and dye indicator techniques, bioimpedance, and Doppler echocardiography. Of these clinical judgement is the most frequently used method despite the fact that it is poorly correlated with objective measurements [1].

The rationale for measuring CO is not entirely clear. Traditional indices such as blood pressure and pulse rate

may not immediately reflect mild to moderate blood loss [2], and it seems intuitively correct to optimize CO and hence tissue oxygen delivery in critically ill patients. Even in adults whether CO measurement has a beneficial effect on clinical outcome is unknown [3, 4, 5, 6, 7]. In children a review by Thompson [8] suggested that substantial value may be obtained from the information made available by the use of the pulmonary artery catheter in selected patients. It would seem reasonable to conclude that CO measurement is clinically useful, provided that it is not taken as the sole determinant of tissue oxygen delivery. Therefore studies addressing the potential benefits of hemodynamic measurement in the pediatric population deserve attention.

An essential but often unmentioned premise of clinical outcome studies is that an accurate and reproducible measuring tool is available to draw adequate conclu-

sions from the data. Secondly, it must not cause further morbidity/mortality. In this regard minimally invasive techniques have a priority, particularly in children. Doppler ultrasonography is capable of measuring blood flow non- or semi-invasively, and advances in probe and data-processing technology have made it possible to utilize Doppler measurements even in small infants. The use of Doppler for flow measurements, however, remains an enigma for most clinicians. This is probably due to a perceived lack of usefulness, cost, inadequate education, and/or the fact that many children in cardiac intensive care do not have normal biventricular physiology. Nevertheless, a growing population of intensivists acknowledge the importance of the knowledge of Doppler echocardiography. This contribution provides a 20-year literature review for Doppler CO measurement in children, focusing on its repeatability, bias, and precision in comparison to current clinically accepted methods such as thermodilution, dye dilution, and Fick techniques.

Materials and methods

A computerized Medline search was conducted with a limit of 20 years (1982–2002). This limit corresponded to the time of publication of the first clinical measurements of pediatric CO using Doppler methods. Articles were retrieved, and a manual review of bibliographies was also conducted in which the authors identified publications missed by the Medline search. Studies comparing Doppler CO to dye dilution, Fick, and thermodilution techniques in the pediatric setting were included.

Table 1 Accuracy of traditional Doppler CO measurements compared to reference technique in children given as mean difference ± 2 standard deviations of differences unless otherwise stated. All measurements were made using the suprasternal approach unless otherwise indicated. (TED transesophageal Doppler, DBD dual-

The Bland-Altman [9] method was used to compare data from two measurement techniques, where the bias (mean difference) between the two techniques was taken to indicate accuracy and the limits of agreement (± 2 SD of differences) were taken to indicate precision. The coefficient of variation (CV) was used as an indicator of repeatability, defined as the standard deviation of repeated measurements divided by their mean, expressed as a percentage. We extracted results from articles reporting their findings using these methods. In studies where statistical analyses were conducted using other methods we extracted actual data given in tables or in graphs, and reanalyzed them using the Bland-Altman method and calculated CVs.

Results

Bias and precision of Doppler flow measurements

Eleven articles describing Doppler CO measurements in 285 children were retrieved. The precision of Doppler flow measurements compared to Fick, thermodilution, or dye dilution methods are summarized in Table 1. The precision of Doppler cardiac output measurements compared to the other techniques is in the order of 30%. The bias of measurements was generally less than 10%, but was more than 15% in 4 of the 11 papers.

Repeatability

Twelve articles in which 344 children were studied were retrieved. The inter- and intraobserver repeatabilities of Doppler cardiac output measurements are shown in Ta-

beam Doppler, CWD continuous-wave Doppler, TEE transesophageal Doppler, PWD pulsed-wave Doppler, AA ascending aorta, DA descending aorta, AN aortic annulus, leaflet aortic maximal leaflet separation, TD thermodilution, dye dye dilution, NA not available)

Study	<i>n</i>	Method	Site	Reference	CO range	<i>R</i>	Difference
Alverson et al. [32]	33	PWD	AA	Fick	0.4–5.54 l/min	0.98	5 \pm 27%
Mellander et al. [15]	10	PWD	AA	TD	1–4.5 l/min	0.97	–18.3 to 75.5% range of mean difference
Morrow et al. [18]	12	CWD	AN	TD	1–6 l/min	0.94	–37 \pm 43%
Notterman et al. [17]	17	PWD	AN	TD	1.02–6.26 l/min	0.84	12.7% (0.41–102.5%) mean difference (range)
Rein et al. [21]	25	CWD	AN	TD	1.9–5.6 l/min	0.86	1.2 \pm 30.3%
Sholler et al. [16]	21	PWD	AA leaflet	Dye	0.5–5.5 l/min	0.930.99	16.3 \pm 30.7%–8.1 \pm 19.5%
Tibballs et al. [19]	18	PWD	AA	Dye	0.23–5.76 l/min	0.97	7.1 \pm 19.6%
Wipperman et al. [20]	18	PWD DBD	AA	TD	0.4–2.2 l/min	NA	1.9 \pm 22.4%
Wodey et al. [10]	20	PWD	DA	CWD	2–6 l/min	NA	–0.02 \pm 36%
Murdoch et al. [12]	11	CWD (TED) minute distance	DA	TD	2.91–5.02 l min ^{–1} m ^{–2}	–	–0.5 \pm 10% ^a
Tibby et al. [11]	100	CWD (TED) minute distance	DA	TD	1.44–8.97 l min ^{–1} m ^{–2}	NA	0.87 \pm 16.8% ^a

^a refers to 2 SDD of the relative change in minute distance or CO

Table 2 Repeatability of traditional Doppler CO measurements in children defined as the coefficient of variation (CV), unless otherwise stated. All measurements were made at the aorta using the

suprasternal approach unless otherwise indicated (*PWD* pulsed-wave Doppler, *CWD* continuous-wave Doppler, *CO* cardiac output, *VTI* velocity time integral *TED* transesophageal Doppler)

Study	n	Variable	Reproducibility of measurement V (%)	
			Intraobserver	Interobserver
Childs et al. [26]	72	VTI	0.3–0.8	8
Claflin et al. [24]	10	CO	7.0–12.1	3.1
		VTI	6.6–11.7	2.5
Hanseus et al. [25]	10	VTI	3.5	5.8
		Minute distance	7.5	6.5
Hirsimaki et al. [27]	37	Mean velocity	6.77 (SEM)	–
		Max velocity	5.65 (SEM)	–
Hudson et al. [23]	12	CO PWD	7.9–16.1	14.8
		CO CWD	7.1–18.4	12.6
Mellander et al. [15]	10	Mean velocity	6.4	–
		Max. velocity	4.5	–
Mohan et al. [13]	20	Minute distance	16.0	–
Notterman et al. [17]	17	CO	Median 2.5, range 0.34–10.6	–
Rein et al. [21]	25	CO	–	21.7
Wodey et al. [10]	20	Mean velocity	5.0–20.1 (mean difference)	–
		CO	7.0–22.0 (mean difference)	–
Murdoch et al. [12]	11	MD (TED)	2.8–3	–
Mohan et al. [13]	20	MD (TED)	2.1	–
Tibby et al. [11]	100	Minute distance (TED)	Median 3.3, interquartile range 2.1–4.7	–

ble 2. The range of intraobserver and interobserver repeatabilities for CO were 2.5–22.0% and 3.1–21.7%, respectively.

Discussion

The precision of Doppler cardiac output measurements compared to thermodilution, dye dilution, or Fick techniques is in the order of 30%, with a bias of less than 10% in the majority of studies. The available literature mostly describes measurements using the suprasternal approach although transesophageal Doppler has also been recently reported [10, 11, 12, 13]. Regarding transesophageal measurements it is important here to clearly differentiate between transesophageal echocardiography with Doppler flow measurements and the esophageal Doppler technique. With the former a two-dimensional image is obtained, and the Doppler sampling site is placed, guided by the two-dimensional image. With the latter the Doppler sample is placed in the direction of flow in a blind fashion and adjusted to obtain the best signal. The studies referred to here concern the esophageal Doppler technique only; there were no data available on cardiac output measurements using transesophageal Doppler echocardiography, which is in contrast to adults.

As is the case for adults, a common limitation for Doppler validation studies is the lack of a true gold standard and the various types of statistical analyses used. In general, the method described by Bland and Altman

seems to be most appropriate when comparing Doppler flow measurements against another method whose accuracy is questionable [9]. This method uses the mean of the two methods as the yardstick, and reports accuracy in terms of the mean difference (bias) between the two methods ± 2 standard deviations, the latter also termed the limits of agreement, an indicator of precision.

Critchley et al. [14] further expanded on Bland and Altman's method by quantifying the acceptable limits of agreement, given a known error in the reference method. The basis of this approach was that when two methods are compared, the limits of agreement intuitively are larger than the precision of the reference method alone. Thus using the precision of the reference method as a criterion for acceptance or rejection of the test method would be flawed, since the limits of agreement would invariably be larger due to the error component of the reference method alone. By using a Pythagorean approach where the variances of both reference and test methods are added to give a combined "expected" variance the expected limits of agreement between the two methods can be calculated. Critchley's method adjusts for errors in the reference method itself, and the criteria for acceptance of the test method may thus be more appropriate.

Most studies report a bias of less than 10%, with a range from –37% to 16%. In 4 of the 11 studies a bias of greater than 15% and of up to 102% was noted [15, 16, 17, 18]. There were large variations in the precision of Doppler CO measurements. At best a precision of 19% was calculated for measurements using pulsed-wave Doppler at the ascending aorta, compared to the dye di-

lution method [16, 19]. When relative change instead of absolute CO value is used for statistical analyses, the accuracy of Doppler CO measurements compared to thermodilution improves [11, 12]. Murdoch et al. [12] followed children (16–169 months) after cardiac surgery and found that Doppler is able to measure *changes* in CO with limits of agreement within 10% of the change in thermodilution measurements. Other studies suggest considerably larger errors. Mellander et al. [15] obtained best results using a combination of Doppler mean velocity and area measurements at the aortic root (mean difference 1.5% compared to thermodilution), but noted considerably larger mean differences (–18.3% to 75.5%) using other combinations. Similarly, Notterman et al. [17] detected a mean difference of 12.7% between suprasternal pulsed wave Doppler CO measurements of the ascending aorta compared with thermodilution, with a range of 0.41–102.5%. The authors noted also that the difference between thermodilution and Doppler CO was greater than 15% in 45% of measurements, and greater than 25% in 25% of measurements.

The causes of the sometimes large variations in CO data between the reference method and Doppler echocardiography are well known. They include optimal measurements of the area under the Doppler flow velocity signal, the angle of insonation, and the correct measurement of the cross-sectional area. An adequate Doppler signal can be often produced with Doppler echocardiography. The angle of insonation must be below 20°, otherwise incurring unacceptably large errors due to its cosine relationship with flow.

Cross-sectional area measurements have been identified as the major source of error of Doppler flow measurements. Wipperman's group [20] used a dual-beam Doppler technique, described as “angle and diameter independent” with a mean difference ± 2 SD of $1.9 \pm 23\%$ compared to thermodilution. However, this was an isolated finding using the dual beam technique, and we found no other pediatric study using this approach. From the data of Sholler et al. [16] we calculated the agreement between pulsed-wave Doppler and Fick CO to be $-8.1 \pm 19.5\%$ when cross-sectional measurements were taken at the level of maximal aortic leaflet separation, and $16.3 \pm 30.7\%$ at the level of the ascending aorta. In Rein et al. [21] Doppler and thermodilution CO differed by $1.2 \pm 30.3\%$ when the data were reanalyzed. The authors noted the importance of the site of aortic cross-sectional area measurements, with the most consistent results at the annulus. Reasoning that cross-sectional area was a major contributor of error in Doppler CO measurements, Tibby and coworkers [11] used minute distance (=time velocity integral multiplied by heart rate) measured using transesophageal continuous-wave Doppler at the descending aorta as a surrogate for cardiac output. The *change* in minute distance after hemodynamic manipulation agreed well with the *change* in femoral ther-

modilution CO with bias ± 2 SD of $0.87 \pm 16.82\%$. This is also supported by the study by Murdoch et al. [12], which showed, that minute distance was able to track changes in cardiac output with good accuracy and precision.

The large errors in pediatric CO measurement are in contrast to what is found in the extensive literature of adult clinical research. Although various techniques, major vessels, and cardiac structures have been assessed, the estimation of cross-sectional area seems to be particularly important. The technique of mean aortic valve area as closest estimation of output area [22] seems to provide good results in adults and similar meticulous evaluation of the mean effective aortic valve area in children may improve the accuracy and precision of measurements. In addition, transesophageal echocardiography with Doppler flow measurements, in which a two-dimensional image is used to guide placement of the Doppler sample volume has not been reported and may be worth investigating in children.

The repeatability of Doppler CO measurements relates to both intra- and inter-observer repeatabilities. Further, there is a distinction between the repeatability of the entire measurement procedure and the repeatability of data analyses. In our review of the literature it was often difficult to distinguish between these two types of repeatabilities. Different measures are often quoted, including the CV, mean percentage difference, and ± 2 SD difference between repeated measurements. For ease of comparison we recalculated repeatability as the CV.

The intraobserver repeatability for CO measurements ranges from 2.1% to 22% [10, 17, 23, 24]. Removing area calculations and focusing on minute distance, the velocity time integral, or mean or maximum velocity did not seem to improve the repeatability of the measurements (range 0.3–20.1%) [10, 11, 12, 13, 15, 24, 25, 26, 27]. Interobserver repeatability was of the same order as the intraobserver case, with a range from 3.1 to 21.7% for CO [21, 23, 24]. For the velocity-time integral alone the interobserver repeatability was better, 2.5–8% [24, 25, 26]. Although there are few data, transesophageal Doppler measurements seem to be more repeatable than suprasternal Doppler measurements [11, 12, 13], with intraobserver repeatability in the order of 3%. Supporting this, Mohan et al. [13] demonstrated the superiority of transesophageal over suprasternal Doppler for minute distance measurements in terms of intraobserver repeatability. This may relate to the angle of insonation of the ultrasound beam, which appears easier to maneuver using transesophageal Doppler, so that the beam lies more parallel to the direction of blood flow.

Doppler CO seems to be most useful when used to track changes in CO rather than achieving absolute values [11, 12]. Since only two articles were retrieved regarding this issue, additional research is desirable. Changes in velocity indices rather than flow may be a

more accurate hemodynamic monitor and needs further evaluation.

The findings here suggest that Doppler CO measurements in children are reasonably precise. Using the criteria described by Critchley et al. [14], most studies had limits of agreement within the calculated “expected” range. There were a few exceptions, however, and we also note that there seems to be a discrepancy between suprasternal and transesophageal measurements, with the latter being more reproducible. The findings here are encouraging, since pediatric cardiac output measurements are inherently more difficult than in adults. For example, one may expect poorer spatial resolution relative to the size of the aorta, increased aortic compliance, inadequate temporal resolution due to faster heart rates, and complex velocity profiles due to reduced filling times. The studies reported here included a wide range of pathologies and ages ranging from 0.7 months to 18 years. The heterogeneity of these data may have contributed to the range of errors; however it was not possible to conduct subset analyses from the information given. We note that even in controlled, laboratory conditions, Doppler CO measurements have a precision of 20% at best, although the intra- and interobserver repeatabilities seem to be better [28, 29].

Although transesophageal Doppler measurements are available in the pediatric setting, we found only three studies describing minute distance measurements. Furthermore, none of the studies utilized Doppler measurements guided by two-dimensional echocardiography images. This may reflect the cost of ultrasound scanners and pediatric transesophageal probes as well as technical limitations. Complications during transesophageal echocardiography using a conventional probe, although minimal, should not be denied. A recent study in 1650 children found airway obstruction in 1%, inadvertent extubation (0.5%), vascular compression (0.6%), and advancement of the endotracheal tube in 0.2%, apparently representing the most important problems [30]. The smaller and more pliable transesophageal Doppler probe used for flow measurements would presumably be associated with less adverse effects; however, the complication rate is unknown. Nevertheless, this does not detract from issues such as patient tolerability, the need for fixation, difficulty in probe fixation, and the ability to ensure a

good and constant signal. More studies are required to assess the utility, accuracy, and reproducibility of transesophageal CO measurements in children. Transtracheal Doppler flow measurements have also been described but have not gained wide acceptance, possibly due to its invasiveness and lack of accuracy [31].

Traditional Doppler flow measurements are limited by the fact that they only provide one- or two-dimensional measurements of flow, which is a three-dimensional entity. Velocity is measured along the direction of the beam emitted by the ultrasound transducer, and hence a cosine correction is needed to obtain the mean velocity, especially when the intercept angle is above 20°. Difficulty arises when the angle of insonation becomes large, due not only to the large cosine correction required but also to failing signal quality. Furthermore, to make the correction the direction of flow is assumed to be parallel to the vessel, which may not be the case in complex structures such as the cardiac valves. Three-dimensional flow measurements are becoming available and may be a way of providing more accurate and reproducible CO measurements; however, these techniques are not yet available for clinical use.

Conclusions

Pediatric Doppler CO measurements are less well investigated than adults. The error of such measurements compared to thermodilution, dye dilution, or Fick method is around 30%, and repeatability varies widely from less than 1% to 20% for both intra- and interobserver cases. Taken together, the accuracy, precision, and repeatability in this study indicate that pediatric Doppler CO measurements are acceptably reproducible. Doppler is most useful when used to track changes, particularly when cross-sectional measurements are not made, and when using transesophageal rather than suprasternal probes. There are few reports of transesophageal approaches and no reports of measurements at sites other than the aorta. Other approaches such as those using velocity indices, the “effective aortic valve area” and three-dimensional methods may improve the quality of CO measurements. These issues deserve further investigation.

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