Measurement of pulse wave velocity in children: comparison of volumetric and tonometric sensors, brachial-femoral and carotid-femoral pathways

Louise Keehn^a, Laura Milne^a, Karen McNeill^a, Phil Chowienczyk^a, and Manish D. Sinha^{a,b}

Background: Pulse wave velocity (PWV), a measure of arterial stiffness strongly predictive of cardiovascular risk in adults, is usually measured by sequential ECG-referenced carotid and femoral tonometry. A simplified technique, more suitable for use in children, employs simultaneous volumetric recording from a sensor applied over the carotid artery and a cuff applied over the femoral artery or arm and thigh pressure cuffs applied over the brachial and femoral arteries. The purpose of this study was to compare PWV computed over the carotid-femoral path (PWVcf) with that over the brachial-femoral path (PWVbf) using a volumetric system (Vicorder) and to compare values of PWVcf obtained by the volumetric and a tonometric method (SphygmoCor) in children.

Method: Vicorder PWVcf and PWVbf were compared in 156 children (3–18 years, 110 with chronic kidney disease), and PWVcf by Vicorder was compared to PWVcf by SphygmoCor in a subset of 122 patients.

Results: PWVcf by Vicorder was moderately correlated with PWVcf by SphygmoCor ($R = 0.50$, $P < 0.000$). PWVbf and PWVcf by Vicorder were more closely correlated ($R = 0.75$, $P < 0.0001$), but with a significant systematic difference. Applying a correction factor to PWVbf measurements gave results similar to those obtained over the carotid-femoral path. Within-patient coefficients of variation for repeated measures were 5.9, 7.8, and 8.5% for PWVbf (Vicorder), PWVcf (Vicorder) and PWVcf (SphygmoCor), respectively. All PWV values showed a similar relation to age.

Conclusion: Volumetric methods appear reproducible and are easy to use in children, but values obtained by Vicorder and SphygmoCor are not interchangeable even when measured over the same pathway.

Keywords: arterial stiffness, children, pulse wave velocity, SphygmoCor, Vicorder

Abbreviations: CKD, chronic kidney disease; ERF, established renal failure; LoA, limits of agreement; PWVcf, pulse wave velocity, measured over the carotid-femoral path; PWVbf, pulse wave velocity, measured over the brachial-femoral path

INTRODUCTION

Pulse wave velocity (PWV) is a measure of arterial stiffness which when measured along large elastic arteries such as the aorta is highly predictive of cardiovascular risk in adults [1], particularly in patients with chronic kidney disease (CKD) [2]. Children with CKD, including those with established renal failure (ERF) requiring renal replacement therapy, have an increased risk of mortality secondary to cardiovascular disease, both during childhood and as young adults [3–5]. These young adults with ‘childhood-onset’ ERF exhibit mortality rates about 30-fold higher than age-matched peers with no renal disease [4,5]. It is now widely accepted that the risk factors for these adverse cardiovascular events develop during childhood and that they are likely to evolve with progressive renal dysfunction [6].

In these children with moderate to severe CKD, arterial stiffness may contribute to cardiovascular morbidity or mortality, either through remodelling of the left ventricle predisposing to sudden cardiac death [7] or through other mechanisms. Therefore, measurement of arterial stiffness in children with CKD may be particularly important. Reference values for PWV in children have recently been published [8], which may aid evaluation of PWV in paediatric clinical studies.

Pulse wave velocity is usually measured between the carotid artery and the femoral artery by sequential ECG-referenced arterial applanation tonometry (using a pressure sensitive transducer to lightly compress the artery) or other arterial pressure or flow velocity sensors. The SphygmoCor system (AtCor Medical, Australia) uses ECG-referenced applanation tonometry and is one of the

Journal of Hypertension 2014, 32:1464–1469

^aKings College London, British Heart Foundation Centre and ^bDepartment of Paediatric Nephrology, Evelina Children’s Hospital, Guys & St Thomas NHS Foundation Trust, London, UK

Correspondence to Louise Keehn, Clinical Pharmacology, 4th Floor, North Wing, St Thomas Hospital, Westminster Bridge Road, London SE1 7EH, UK. Tel: +44 20 7188 4770; fax: +44 20 7118 5116; e-mail: louise.keehn@kcl.ac.uk

Received 2 August 2013 Revised 11 March 2014 Accepted 11 March 2014

J Hypertens 32:1464–1469 © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 3.0 License, where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially.

DOI: 10.1097/HJH.0000000000000203

most widely used systems in adults for measurement of carotid-femoral PWV (PWVcf). There are some limitations of this system for use in children: tonometry requires a trained operator and access to the femoral artery in the inguinal area may be distressing particularly in adolescents.

The Vicorder PWV system (Skidmore Medical, UK) uses simultaneous volumetric pressure recordings from a sensor placed over the carotid artery and a thigh cuff placed over the femoral artery (which can be placed over light clothing) is less operator-dependent than a tonometric system and does not require the patient to undress. The Vicorder system can also be used to measure brachial-femoral PWV (PWVbf), whereby the proximal sensor is a cuff placed over the brachial artery. This may be more acceptable to young children than the neck cuff.

The relation of Vicorder brachial-femoral measurements to carotid-femoral measurements is unknown. Nor is it clear whether there is a close correlation between carotid-femoral measurements obtained by Vicorder and SphygmoCor systems. Good agreement between the devices has been reported in children and young adults [9,10], in older adults [11] and in pregnant women [12]. However, others have questioned the suitability of the Vicorder device as an alternative to more established methods [13].

The purpose of this study was to compare PWVcf and PWVbf obtained using the Vicorder system and to compare values of PWVcf obtained by the Vicorder and SphygmoCor in children with and without CKD.

METHODS

One hundred and fifty-six patients were recruited from paediatric renal and hypertension outpatient clinics at the Evelina Children's Hospital, London, UK. The local research ethics committee approved the study, and written consent was obtained from all parents or guardians. In older children, written assent was also obtained. Seated blood pressure was measured in triplicate using a calibrated aneroid measurement by a single trained observer.

All 156 patients had measurements of both PWVcf and PWVbf by Vicorder. Measurements were performed supine using appropriately-sized cuffs as recommended by the manufacturer. Path lengths were determined using a measuring tape. The path length for PWVcf was taken as the distance from the suprasternal notch to the top of the thigh cuff, and that for PWVbf as the distance from the top of the arm cuff to the top of the thigh cuff. Three measurements were performed in each mode if the patient remained comfortable. Data were considered acceptable

when there were at least five sequential good-quality waveforms obtained from each cuff.

Those patients who were able to tolerate the measurement also had measurements of PWVcf by SphygmoCor. SphygmoCor PWVcf path length was measured from the suprasternal notch to the femoral pulse at the point of applanation. Measurements were rejected if the SD of the mean transit time exceeded 6% (automatically flagged by SphygmoCor). As with Vicorder, measurements were done in triplicate whenever possible. All measurements were made by two experienced trained observers (L.K. and L.M.).

Data analysis was performed using SPSS 19.0 (SPSS, Chicago, Illinois, USA). Pearson's correlation was used to assess the correlation between measures obtained by the different methods. Mean and SD of differences between methods were calculated and presented as Bland-Altman plots. Within-patient SD and coefficients of variation (SD as percentage of mean) were used to assess the repeatability of successive measures. Linear regression analysis was used to test the association of PWV with age and blood pressure. The regression equation between PWVcf and PWVbf Vicorder was used to adjust PWVbf (Vicorder) to obtain the best estimate of PWVcf (Vicorder), by multiplying PWVbf by 0.67, the reciprocal of the slope of the regression of PWVbf vs. PWVcf and adjusting for the small average difference, 0.5 m/s, between the two measures.

RESULTS

One hundred and fifty-six children (42% female), aged 3–18 years, were recruited. Of these, 110 (71%) had CKD, 27 (17%) had hypertension and 19 (12%) were normal healthy individuals. There were no significant differences in clinical characteristics between the entire cohort and the subset able to tolerate carotid and femoral tonometry (Table 1).

Comparison of pulse wave velocity by Vicorder over carotid-femoral and brachial-femoral paths

The mean difference between Vicorder PWVcf and PWVbf was 1.81 ± 1.21 m/s. Vicorder PWVbf measurements were significantly higher than Vicorder PWVcf measurements ($P < 0.001$), but were closely correlated ($R = 0.75$, $P < 0.001$; Fig. 1a). Limits of agreement (LOA, = mean difference $\pm$ 2SD) between Vicorder PWVcf and PWVbf were 0.62 to -4.25 m/s (Fig. 1b), with a significant systematic difference between the two measurements. When corrected by linear regression to obtain the best prediction

TABLE 1. Patient demographic data

Parameter	All patients (n = 156)		SphygmoCor cohort (n = 122)		P
	Range	Mean $\pm$ SD	Range	Mean $\pm$ SD	
Age (years)	3.2–17.9	11.7 $\pm$ 3.6	4.3–17.9	12.2 $\pm$ 3.3	0.21
Height (cm)	89.5–189.2	146.9 $\pm$ 22.4	102.8–189.2	150.5 $\pm$ 19.8	0.16
Weight (kg)	12.8–116.1	48.0 $\pm$ 22.9	16.6–111.8	50.3 $\pm$ 22.0	0.41
BMI	13.1–41.7	20.9 $\pm$ 5.6	13.6–41.7	21.1 $\pm$ 5.4	0.78
SBP (mmHg)	71–147	107 $\pm$ 16	71–147	108 $\pm$ 17	0.64
DBP (mmHg)	22–97	57 $\pm$ 12	22–97	57 $\pm$ 12	0.78

FIGURE 1 (a) Correlation between Vicorder PWVcf and PWVbf, (b) Bland-Altman plot of agreement between Vicorder PWVcf and Vicorder PWVbf, (c) Bland-Altman plot of agreement between Vicorder PWVcf and corrected PWVbf. PWVbf, brachial-femoral pulse wave velocity; PWVcf, carotid-femoral pulse wave velocity.

of PWVbf, the mean difference between PWVcf (Vicorder) and PWVbf (Vicorder) was 0.00 ± 0.77 m/s, with LoA -1.54 to 1.54 m/s (Fig. 1c).

Comparison of pulse wave velocity by Vicorder and SphygmoCor

Of the 156 patients, 122 (78.2%) were able to tolerate carotid and femoral tonometry, with at least one valid result acquired. In comparison to the overall cohort, those with failed tonometry were significantly younger (9.84 ± 4.2 vs. 11.7 ± 3.6 years; $P = 0.008$), but with no difference between groups for BMI ($P = 0.53$) and sex ($P = 0.66$). Declining

FIGURE 2 (a) Correlation between SphygmoCor PWVcf and Vicorder PWVcf, (b) Bland-Altman plot of agreement between SphygmoCor PWVcf and Vicorder PWVcf. PWVbf, brachial-femoral pulse wave velocity; PWVcf, carotid-femoral pulse wave velocity.

tonometry ($n = 6$), failure to stay still ($n = 6$), and failure to palpate one or more pulse and/or poor-quality trace ($n = 5$ each) were the commonest causes of failed tonometry. PWVcf by Vicorder was significantly lower than that measured by SphygmoCor ($P < 0.001$) and only moderately correlated with SphygmoCor PWVcf ($R = 0.50$, $P < 0.001$; Fig. 2a). The mean difference between Vicorder PWVcf and SphygmoCor PWVcf was 0.31 ± 0.88 m/s. The LoA between Vicorder PWVcf and SphygmoCor PWVcf were -1.46 to 2.07 m/s (Fig. 2b). The path lengths used for the two instruments were highly correlated ($R = 0.84$, $P < 0.0001$) and the correlation between Vicorder transit time and SphygmoCor transit time was similar to that between corresponding values of PWV ($R = 0.52$ and $R = 0.50$ for correlations between transit times and PWV, respectively; both $P < 0.001$). Vicorder PWVbf was marginally less well correlated with SphygmoCor PWVcf ($R = 0.451$, $P < 0.001$), with a mean difference of 1.48 ± 4.54 m/s. Using corrected values of PWVbf against SphygmoCor PWVcf, the mean difference was -0.34 ± 1.11 m/s (Fig. 3a and b), with LoA -2.56 to 1.88 m/s.

We observed no significant difference between boys and girls for the difference between corrected PWVbf (Vicorder) and SphygmoCor PWVcf (-0.43 vs. -0.22 m/s; $P = 0.49$). Similarly, there was no significant difference by age subgroups (<10 , $10-15$, >15 years) for the difference between corrected PWVbf (Vicorder) and SphygmoCor PWVcf (Table 2).

FIGURE 3 (a) Correlation between SphygmoCor PWVcf and corrected Vicorder PWVbf, (b) Bland-Altman plot of agreement between SphygmoCor PWVcf and corrected Vicorder PWVbf. PWVbf, brachial-femoral pulse wave velocity; PWVcf, carotid-femoral pulse wave velocity.

Repeatability of Vicorder and SphygmoCor measurements

Within-patient coefficients of variation were calculated for those with at least two measurements for each device. Duplicate or triplicate PWVbf measurements were obtained for all patients. Six patients only had one PWVcf (Vicorder) recorded, as some measurements were discarded due to poor-quality traces or intolerance of the neck cuff. Of the 122 patients included in the SphygmoCor subset, 101 had duplicate or triplicate measurements of acceptable quality. The time taken to perform three consecutive measurements was approximately 5 and 10 min for Vicorder and SphygmoCor, respectively. Within-patient variations for repeated measures were 5.9, 7.8, and 8.5% for PWVbf (Vicorder), PWVcf (Vicorder) and PWVcf (SphygmoCor), respectively.

Correlation of Vicorder and SphygmoCor measurements with age

Linear regression was used to determine the correlation between PWV and age for each device. Pearson's correlation coefficients were 0.50, 0.53 and 0.401 (each $P < 0.001$) for SphygmoCor, Vicorder PWVcf and Vicorder PWVbf (Fig. 4). There was no significant difference in these correlation coefficients ($P = 0.36$).

Discrimination of blood pressure with Vicorder and SphygmoCor

Two groups of children ($n = 20$) at the extremes of the blood pressure distribution (and thus assumed to have stiff and compliant arteries for the high and low blood pressures, respectively), but matched for age, were used to test the discriminatory ability of the PWV measurements to detect stiff and compliant aortae. Receiver-operating characteristic curves show the sensitivity and specificity of the devices (Fig. 5). The area under the curves was 0.913 [95% confidence interval (CI) 0.82–1.00] for PWVcf (SphygmoCor), 0.863 (95% CI 0.73–1.00) for PWVcf (Vicorder) and 0.900 (95% CI 0.78–1.00) for PWVbf (Vicorder). Therefore, there was no significant difference in the discriminatory ability of each method.

DISCUSSION

Carotid-femoral measurements have until recently been used to estimate large-artery PWV, but such an approach can be difficult to use, especially in children. In the present study, carotid-femoral tonometry data could not be acquired in 22% of our children (34 out of 156). Usually, this was due to practical problems in the younger children such as the need to sit still, difficulty in palpating pulses or obtaining traces of adequate quality. In a few patients with arrhythmias, such as benign sinus tachycardia of childhood, the SphygmoCor was unable to compute the PWV accurately. Although we do not have any formal data regarding tolerance and comfort of patients for either system, the Vicorder volumetric recording system was used successfully (for both carotid-femoral and brachial-femoral measurements) in all children, and measurements showed similar or better repeatability than those obtained using the SphygmoCor system. When comparing the repeatability and tolerability of Vicorder and SphygmoCor, it is important to note that our results could have been influenced by the order in which the instruments were used.

When comparing the agreement between Vicorder PWVcf and SphygmoCor PWVcf, there was only moderate correlation and LoA were relatively broad. LoA for

TABLE 2. Comparison of the differences between corrected PWVbf (Vicorder) and PWVcf (SphygmoCor) according to sex and age

Subset	n	Mean	SD	P
Female	53	−0.22	1.05	0.49
Male	69	−0.43	1.15	
Aged <10 years	34	−0.16	0.99	0.34
Aged 10–15 years	59	−0.49	1.15	
Aged >15 years	29	−0.26	1.11	

PWVbf, brachial-femoral pulse wave velocity; PWVcf, carotid-femoral pulse wave velocity.

FIGURE 4 Variation of mean PWV according to age, as calculated by each device. PWV, pulse wave velocity.

carotid-femoral measurements for the two devices were -1.46 to 2.07 m/s, slightly greater than the LoA of -1.0 to 1.7 m/s obtained by Kracht *et al.* [9] in a study on children and adolescents, the mean age (11.1 years) of which was similar to the children in our study (11.7 years). Our LoA were also slightly greater than those reported by Kis *et al.* [10] (-0.91 to 2.1 , using the manufacturer's recommended calculation of path length) in a slightly older group (mean age 16.7 years). Our LoA were, however, better than those reported by van Leeuwen Segarceanu *et al.* [13], and thus sit within the range reported to date. Although the agreement between PWV obtained by the Vicorder and SphygmoCor methods has been described as 'excellent', it is worth noting that since the mean PWV with SphygmoCor was 5.62 m/s, a LOA value of 2 m/s represents an error of 36%. Thus, values of PWV obtained by the two methods can hardly be regarded as interchangeable. Differences between methods could arise as a result of inaccuracies in estimating the true path lengths, differences in the true path lengths, the point of pulse recording for the Vicorder system being distal to that for the SphygmoCor, and differences in estimation of the timing of the arterial pulse waveforms at the two sites. The close correlation between the estimates of path length used for the two systems and the fact that the correlation between transit times was similar to that between values of PWV suggest that differences arise in large part through differences in timing algorithms. It is also noteworthy that in

other studies which have used a variety of correction factors to adjust for inaccuracies in estimation of length, the impact on the SD of the mean difference is negligible, which would again point to a difference in timing algorithm as the main source of variation between the methods. The SphygmoCor system (as in this study) is usually used with a well established intersecting tangent algorithm to identify the foot of the arterial pulse, whereas the Vicorder uses a cross-correlation algorithm which may be influenced by differences in waveform morphology between the carotid and femoral sites [14].

To our knowledge, this is the first study to evaluate the measurement of brachial-femoral PWV. This is an even simpler technique requiring very little user training, which is well tolerated by children. Good-quality waveforms can be acquired from most brachial arteries, with no venous artefacts, as are often seen with a neck cuff. The brachial-femoral measurement measures the difference between pulse transit from the aorta to brachial artery and aorta to femoral rather than that between the aorta to carotid and aorta to femoral. The two measurements might, therefore, be expected to differ because of the longer and more muscular route from the aorta to the brachial artery compared to that to the carotid: the right innominate being common to both routes but the former incorporating the subclavian and brachial arteries rather than just the common carotid. However, provided there is a close correlation between PWV in the carotid and subclavian/brachial arteries, PWV obtained over the two pathways might be expected to correlate well. This was indeed the case with a high correlation of R (0.75) between PWVbf and PWVcf. When adjusted for differences in estimation of path length, PWVbf by Vicorder agreed almost as well with SphygmoCor PWVcf as did PWVcf by Vicorder.

In conclusion, the Vicorder technique is easy to use, is well tolerated by children and gives excellent repeatability. Values obtained over the brachial-femoral path are closely correlated with those from the carotid-femoral path. However, Vicorder carotid-femoral values are only moderately correlated with those obtained from the SphygmoCor system, with the difference likely to be due to differences in the timing algorithms used in the two systems. Although measurements are not interchangeable, PWVbf appears as reproducible and as likely to discriminate between

FIGURE 5 ROC curve showing area under the curve for each method of PWV measurement. PWV, pulse wave velocity; ROC, receiver-operating characteristic curve.

groups with differing arterial stiffness as other measures. Since it is the simplest measure to use, we would recommend this is applied more widely in children and our findings tested in larger cohorts to ascertain its clinical utility.

ACKNOWLEDGEMENTS

We thank Paula Sofocleous for her help in recruiting patients from the Evelina Children's Hospital into our study.

This research was supported by Guy's & St Thomas's Charity, the British Heart Foundation and by the National Institute for Health Research (NIHR) award to the Biomedical Research Centre and Clinical Research Facility at Guys & St Thomas NHS Foundation Trust and King's College London.

Conflicts of interest

P.C. and King's College London have an interest in Centron Diagnostics, a company that produces instruments for the measurement of blood pressure (not used in this study).

REFERENCES

1. Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness. *J Am Coll Cardiol* 2010; 55:1318–1327.
2. Blacher J, Guerin AP, Pannier B, Marchais SJ, Safar ME, London GM. Impact of aortic stiffness on survival in end-stage renal disease. *Circulation* 1999; 99:2434–2439.
3. Parekh RS, Carrol CE, Wolfe RA, Port FK. Cardiovascular mortality in children and young adults with end-stage kidney disease. *J Pediatr* 2002; 141:191–197.
4. Groothoff JW, Gruppen MP, Offringa M, Hutten J, Lilien MR, Van De Kar NJ, *et al.* Mortality and cause of death of end-stage renal disease in children: a Dutch cohort study. *Kidney Int* 2002; 61:621–629.
5. McDonald SP, Craig JC. Long-term survival of children with end-stage renal disease. *N Engl J Med* 2004; 350:2654–2662.
6. Schaefer F. Cardiac disease in children with mild-to-moderate chronic kidney disease. *Curr Opin Nephrol Hypertens* 2008; 17:292–297.
7. Mitsnefes MM. Cardiovascular complications of pediatric chronic kidney disease. *Pediatr Nephrol* 2008; 23:27–39.
8. Reusz GS, Cseprekál O, Temmar M, Kis É, Cherif AB, Thaleb A, *et al.* Reference values of pulse wave velocity in healthy children and teenagers. *Hypertension* 2010; 56:217–224.
9. Kracht D, Shroff R, Baig S, Doyon A, Jacobi C, Zeller R, *et al.* Validating a new oscillometric device for aortic pulse wave velocity in children and adolescents. *Am J Hypertension* 2011; 24:1294–1299.
10. Kis E, Cseprekál O, Kerti A, Salvi P, Benetos A, Tisler A, *et al.* Measurement of pulse wave velocity in children and young adults: a comparative study using three different devices. *Hypertension Res* 2011; 34:1197–1202.
11. Hickson SS, Butlin M, Broad J, Avolio AP, Wilkinson IB, McEniery CM. Validity and repeatability of the Vicorder apparatus: a comparison with the SphygmoCor device. *Hypertension Res* 2009; 32:1079–1085.
12. Everett TR, Mahendru A, McEniery CM, Lees CC, Wilkinson IB. A comparison of SphygmoCor and Vicorder devices for measuring aortic pulse wave velocity in pregnancy. *Artery Res* 2012; 6:92–96.
13. Van Leeuwen Segarceanu E, Tromp WF, Bos WJB, Vogels OJM, Groothoff JW, van der Lee J. Comparison of two instruments measuring carotid-femoral pulse wave velocity: Vicorder versus SphygmoCor. *J Hypertens* 2010; 28:1687–1691.
14. Gaddum NR, Alastruey J, Beerbaum P, Chowienzyk P, Schaeffer T. A technical assessment of pulse wave velocity algorithms applied to noninvasive arterial waveforms. *Ann Biomed Eng* 2013; 41:2617–2629.

Reviewers' Summary Evaluations

Reviewer 1

This study examines the measurement of carotid-femoral (aortic) and brachial-femoral pulse wave velocity in children, comparing volumetric cuff-based techniques with tonometric techniques. The finding is that although both techniques show general agreement, values are not readily interchangeable due to a significant systematic difference which increases with the magnitude of pulse wave velocity. In addition, a corrected volumetric brachial-femoral measurement is shown to provide a measure of aortic pulse wave velocity. This is of potential interest as a more convenient measurement of pulse wave velocity for screening procedures in children.

Reviewer 2

Keehn *et al.* present an interesting study on the evaluation of the pulse wave velocity in children with two noninvasive methods: the volumetric and a tonometric method and evaluate the measurement of the brachial-femoral vs. carotid-femoral pulse wave velocity. They used two different available systems (SphygmoCor and Vicorder) in a sequential manner in children. According to these results, both methods are not comparable with significant differences in measurement. The study raises the problem of this evaluation in children and emphasizes the need for population-based studies to help clinicians using these automated systems on a routine basis.