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Original Article

# Comparison of the SphygmoCor XCEL device with applanation tonometry for pulse wave velocity and central blood pressure assessment in youth

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**Background:** Vascular phenotype by assessing carotid–femoral pulse wave velocity (cf-PWV) and central SBP (cSP) in the young could be used as an intermediate cardiovascular outcome measure. Tonometry is considered the gold-standard technique, but its use is challenging in clinical practice, especially when used in children. The purpose of this study was to validate cf-PWV and cSP assessment with novel oscillometric device (SphygmoCor XCEL) in children and adolescents.

**Methods:** cf-PWV and cSP were measured in 72 children and adolescents aged 6–20 years. Measurements were performed by applanation tonometry and by the SphygmoCor XCEL device at the same visit under standardized conditions. Regression analysis and Bland–Altman plots were used for comparison of the tonometer-based with oscillometric-based method.

**Results:** Mean cf-PWV measured by applanation tonometry was $4.85 \pm 0.81$ m/s and measured by SpygmoCor XCEL was $4.75 \pm 0.81$ m/s. The mean difference between the two devices was $0.09 \pm 0.47$ m/s ($P$ = NS). cSP measured by SpygmoCor XCEL was strongly correlated with cSP measured by applanation tonometry ($R^2 = 0.87$, $P < 0.001$). Mean cSP measured by applanation tonometry was $103.23 \pm 9.43$ mmHg and measured by SpygmoCor XCEL was $103.54 \pm 8.87$ mmHg. The mean cSP difference between the two devices was $-0.30 \pm 3.34$ mmHg ($P$ = NS), and fulfilled the AAMI criterion 1. The estimated intersubject variability was 2.17 mmHg.

**Conclusion:** The new oscillometric SphygmoCor XCEL device provides equivalent results for cf-PWV and cSP values to those obtained by tonometry in children and adolescents. Thus, the SphygmoCor XCEL device could be appropriate for assessing cf-PWV and cSP in the pediatric population.

**Keywords:** arterial stiffness, central blood pressure, children and adolescents, device validation, pulse wave velocity

**Abbreviations:** cf-PWV, carotid–femoral pulse wave velocity; cSP, central aortic SBP; $cSP_{osc}$, central SBP measured by SpygmoCor XCEL; $cSP_{ton}$, central SBP measured by applanation tonometry; $PWV_{osc}$, carotid–femoral pulse wave velocity measured by SpygmoCor XCEL; $PWV_{ton}$, carotid–femoral pulse wave velocity measured by applanation tonometry

## INTRODUCTION

Carotid–femoral pulse wave velocity (cf-PWV) is a well established marker of arterial stiffness [1,2]. Routine use of cf-PWV is recommended in adults for the assessment of total cardiovascular risk [3], whereas in the pediatric population, there is increasing evidence supporting the role of cf-PWV as a reliable marker of early vascular aging in children with high cardiovascular risk [4–6]. Central aortic SBP (cSP) seems promising in prediction of cardiovascular events in adults beyond peripheral blood pressure (BP) [3,7]. Evidence on clinical significance of cSP in children and adolescents is limited, but it has been suggested that it may provide additional data on vascular phenotype in the young with isolated systolic hypertension [4,8].

During the last years, the publication of reference values for both cf-PWV and cSP in the pediatric age range has enable their widespread use [9,10]. Numerous devices for the assessment of cf-PWV and cSP using a variety of noninvasive techniques are available [11,12]. Applanation tonometry has been regarded as the gold standard of measurement. Cuff-based devices requiring less operator skills, and being less intrusive, facilitating young individuals' cooperation are more attractive for use in pediatric patients [13]. However, significant concerns are often highlighted in the literature regarding the validation of these devices in the pediatric population. A few devices have been compared for their validity on cf-PWV

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assessment against applanation tonometry, whereas no devices have been validated against invasive measurements in the young. The aim of the current study was to compare a cuff-based device (SphygmoCor XCEL; AtCor Medical, Sydney, New South Wales, Australia) with applanation tonometry for the assessment of cf-PWV and cSP in children and adolescents.

# METHODS

## Participants

Seventy-two children and adolescents, aged 6–20 years, were recruited subsequently and were distributed in two age groups (preadolescent children, and adolescents), each including a minimum of 40% male. The institutional ethics committee approved the study protocol and informed consent was obtained from the participants' parents and from both the parents and the participants in case of age older than 12 years.

Participants were instructed to refrain from meal, caffeine or smoking for 3 h prior to test. Before measurement ,all participants were allowed to rest for 15 min in a quiet room with stable temperature.

## Carotid–femoral pulse wave velocity measurement

cf-PWV was measured with the CvMS Sphygmocor device (software version 9, AtCor Medical), which was used as the reference for comparison, and with the SphygmoCor XCEL device (software version 1.2). cf-PWV was measured with the CvMS Sphygmocor system by applanation tonometry ($PWV_{ton}$) sequentially at the carotid and femoral artery gated by a simultaneously recorded ECG signal [14]. cf-PWV was measured with the SphygmoCor XCEL device ($PWV_{osc}$) from carotid and femoral arterial pulses assessed noninvasively and simultaneously [14]. The carotid pulse was measured using tonometer, whereas the femoral pulse was measured using volumetric displacement within a cuff placed around the thigh.

Transit time ($t$) was measured as the time between diastolic feet of the carotid and femoral pulse for both devices [15]. Distance ($d$) for the CvMS device was measured as the linear distance from the suprasternal notch to the femoral pulse palpation site minus the linear distance from the carotid pulse palpation site to the suprasternal notch. Distance ($d$) for the XCEL device was measured as the linear distance from the suprasternal notch to the top of the thigh cuff at centerline of the location of femoral artery minus the linear distance from the carotid pulse palpation site to the suprasternal notch. An algorithm, built into the SphygmoCor XCEL device, reduces the distance by an operator-measured distance from the site wherein the femoral pulse can be palpated to the top of the cuff.

Brachial cuff BP and heart rate (HR) were recorded before and after cf-PWV assessments to check for hemodynamic stability. Measurements were performed in supine position at the right carotid and femoral arteries. Speaking and sleeping were avoided during measurements. Six sequential recordings were obtained, three with each device, alternating devices between recordings in randomized order by two investigators (S.S. and C.Z.). The ARTERY Society guidelines criteria were used to assess the performance of the SphygmoCor EXCEL device [16].

## Central blood pressure measurement

cSP was measured by the CvMS Sphygmocor device using radial applanation tonometry ($cSP_{ton}$) and by the SphygmoCor XCEL device ($cSP_{osc}$). Radial tonometry waveforms were calibrated using brachial cuff SBP and DBP immediately before tonometry assessment. The SphygmoCor XCEL system derives the central aortic pressure waveform from cuff pulsations recorded at the brachial artery [14]. A general transfer function, built in the manufacturer's software, is applied to the noninvasively acquired peripheral signal to calculate the aortic waveform. The brachial cuff is initially inflated to measure patient's brachial SBP and DBP. Five seconds later, the cuff reinflates to a subdiastolic level of pressure to acquire a volumetric displacement signal and automatically capture the pulse wave analysis waveform for 5 s. Appropriate cuff size according to participant's arm circumference was selected among three different cuff sizes available by the manufacturer (small adult 17–25 cm, adult 23–33 cm, large adult 31–40 cm). Measurements were obtained with the participants in seated position and their back and arm supported during the measurement. Calibration for the radial tonometry and the XCEL device was performed with the same SBP and DBP obtained by the brachial cuff. For each individual, three recordings with each device, alternating devices between recordings by two investigators (S.S. and C.Z.), were performed. The ANSI/AAMI/ISO 2013 criteria were used to assess the accuracy of agreement between devices [12,17].

## Statistical analysis

Sample size calculation was based on the available literature that the SD of the difference between two devices should be less than 0.8 m/s. For a mean difference less than 0.5 m/s, which is the criterion of excellent accuracy by the ARTERY Society guidelines for validation of noninvasive hemodynamic measurement devices, we calculated that a sample size of 55 individuals would be necessary to have a 0.90 power and a two-sided alpha = 0.05. For each participant, the average of three measurements for cf-PWV and cSP was calculated. The mean difference and SD of the difference between devices were calculated. Regression analysis and Bland–Altman plots were used for the comparison of the two devices [18]. The slope and $R$ coefficient of the relation between the two devices were calculated. Finally, analysis of covariance (ANCOVA) was used to test possible interactions between method of measurement and age, sex and brachial BP. Statistical analysis was performed with the IBM SPSS statistics version 24 (IBM Corp., Armonk, New York, USA). Statistical significance was defined at the two-tailed $P$ less than 0.05 levels.

# RESULTS

## Carotid–femoral pulse wave velocity

Four individuals were excluded from the analysis because of failure to obtain high-quality recordings with applanation tonometry, two at the carotid site, and two at the femoral site. The characteristics of the remaining 68 children and adolescents are shown in Table 1. Mean pulse

**TABLE 1. Participants' characteristics**

| Parameter | PWV $n = 68$ | cSP $n = 67$ |
|---|---|---|
| Age (years) | 11.54 ± 3.67 | 11.5 ± 3.7 |
| Sex (male) | 32 (47.1%) | 31 (46.3%) |
| Height (cm) | 145.78 ± 17.56 | 145.54 ± 17.59 |
| BMI (kg/m$^2$) | 19.15 ± 3.67 | 19.14 ± 3.62 |
| Brachial SBP (mmHg) | 116.74 ± 10.36 | 121.42 ± 12.64 |
| Brachial DBP (mmHg) | 71.59 ± 10.39 | 72.69 ± 10.38 |

cSP, central aortic SBP; PWV, pulse wave velocity.

transit time was 81.48 ± 12.55 ms with the CvMS device, and 82.25 ± 11.87 ms with the XCEL device ($P$ = NS) (Supplementary Fig. 1, http://links.lww.com/HJH/A958). Mean $PWV_{ton}$ (4.85 ± 0.81 m/s) and mean $PWV_{osc}$ (4.75 ± 0.81 m/s) were significantly correlated ($R = 0.82$, $P < 0.001$) (Fig. 1a). The mean difference between the two devices was 0.09 ± 0.47 m/s ($P$ = NS) (Fig. 1b). Therefore, the accuracy of the XCEL device was rated 'excellent' according to the ARTERY Society guidelines (mean difference less than 0.5 m/s, SD of difference less than 0.8 m/s). Bland–Altman analysis showed good agreement with limits of agreement (LoA) ranging from −0.83 to 1.01. No proportional bias was detected by linear regression analysis with dependent variable the mean difference between devices and independent variable mean PWV of the two devices ($B = 0.005$, $P$ = NS). Bland–Altman plots showed similar performance in the preadolescent and adolescent age groups (Supplementary Fig. 2a, http://links.lww.com/HJH/A958). In ANCOVA analysis, age and sex had no statistically significant effect on the mean difference between devices. However, SBP was found to have a significant effect on the method of cf-PWV measurement ($B = 0.018$, $P = 0.002$). XCEL device presented lower values than CvMS device for SBP levels below 120 mmHg ($P < 0.05$) (Fig. 2).

## Central blood pressure

Five participants were excluded from the analysis due to low quality of recordings, four with tonometric technique and one with both devices. The remaining 67 participants had mean peripheral SBP and DBP 121.42 ± 12.64 and 72.69 ± 10.38 mmHg, respectively. $cSP_{osc}$ was strongly

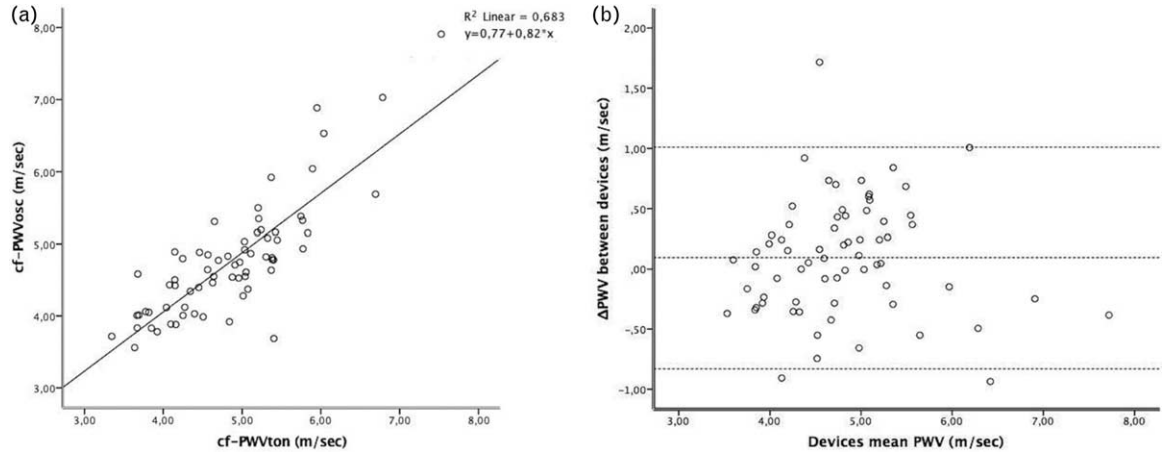


**FIGURE 1** Comparison of carotid–femoral pulse wave velocity measured by SpygmoCor XCEL with applanation tonometry: (a) Scatter plot with regression line and (b) Bland–Altman plot of the difference between carotid–femoral pulse wave velocity measured by SpygmoCor XCEL with applanation tonometry.

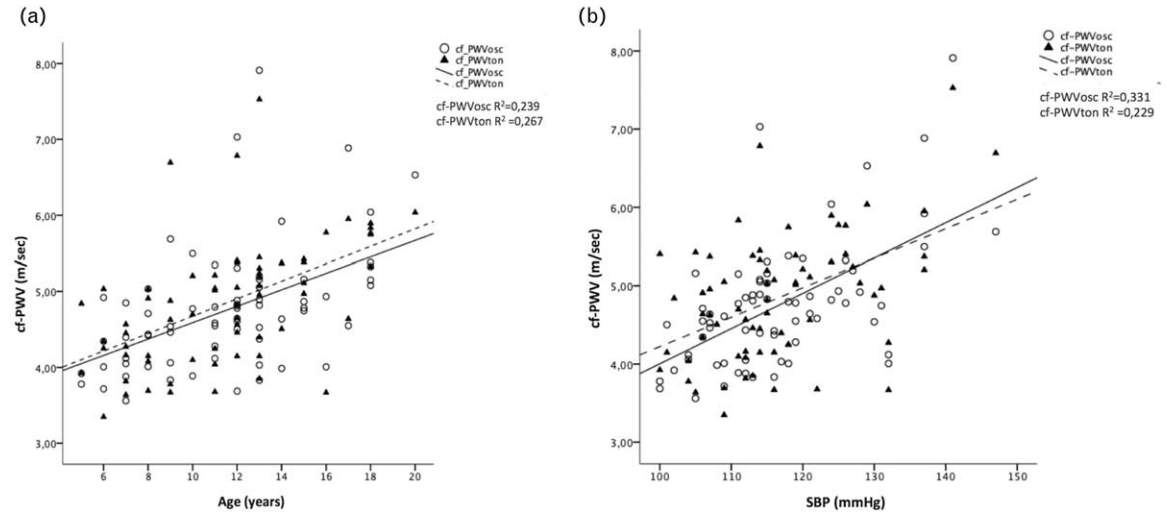


**FIGURE 2** Interaction between (a) age and method of carotid-femoral pulse wave velocity and (b) SBP and method of carotid–femoral pulse wave velocity assessment.

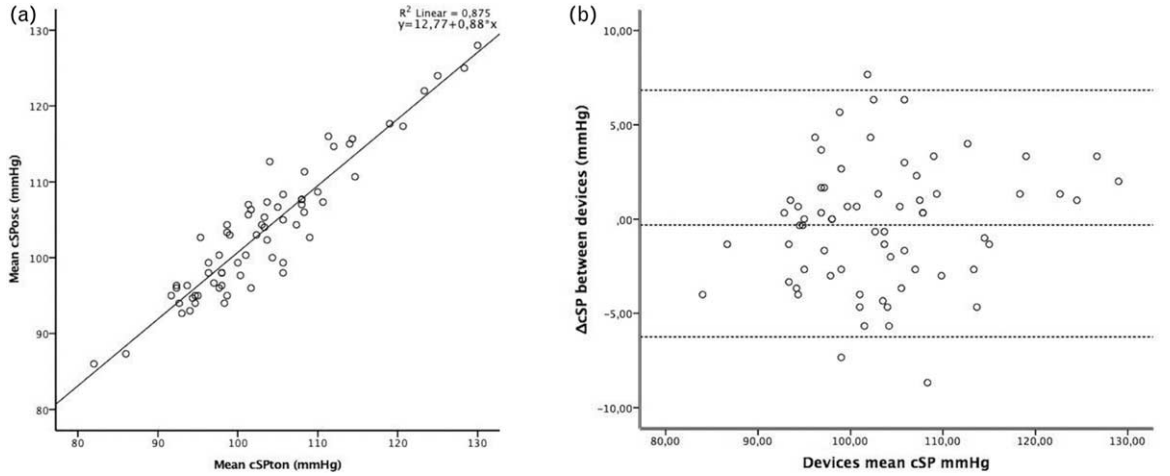


**FIGURE 3** Comparison of central SBP measured by SpygmoCor XCEL with applanation tonometry: (a) Scatter plot with regression line (b) Bland–Altman plot of the difference between central SBP measured by SpygmoCor XCEL with central SBP measured by applanation tonometry.

correlated with $cSP_{ton}$ ($R = 0.93$, $P < 0.001$) (Fig. 3a). Mean $cSP_{ton}$ was $103.23 \pm 9.43$ mmHg and mean $cSP_{osc}$ was $103.54 \pm 8.87$ mmHg. The mean cSP difference between the two devices was $-0.30 \pm 3.34$ mmHg ($P$ = NS), and fulfilled the AAMI criterion 1 (difference $\leq 5.0 \pm 8.0$ mmHg). The estimated SD (intersubject variability) was 2.17 mmHg, and fulfilled AAMI criterion 2 (SD $\leq 8$ mmHg). Bland–Altman analysis showed good agreement with LoA −6.24 to 6.84 (Fig. 3b). No proportional bias was detected by linear regression analysis with dependent variable the mean differences between devices and independent variable mean cSP of the two devices ($B = 0.06$, $P$ = NS). Bland–Altman plots showed similar performance in the preadolescent and adolescent age groups (Supplementary Fig. 2b, http://links.lww.com/HJH/A958). In ANCOVA analysis, age and sex had no significant effect on the method of cSP measurement, but there was a significant SBP effect ($B = 0.124$, $P < 0.05$) (Fig. 4).

## DISCUSSION

The current study showed that the cuff-based SphygmoCor XCEL device provides similar cf-PWV and cSP values with applanation tonometry in children and adolescents. The results are in line with those of previous studies validating the SphygmoCor XCEL device against conventional SphygmoCor device in adults [19–21].

The lack of hard end points in childhood has emerged the need of intermediate outcome measures. Assessing noninvasively the vascular phenotype in young individuals may provide evidence for the effect of known cardiovascular risk factors on early aging process and cardiovascular outcomes [5,22,23]. Available knowledge about cf-PWV and cSP is rather scarce in this age group and further insights are necessary to establish recommendations for routine clinical practice [4]. In line with 2013 European Society of Hypertension and European Society of Cardiology guidelines for the management of hypertension recommendations,

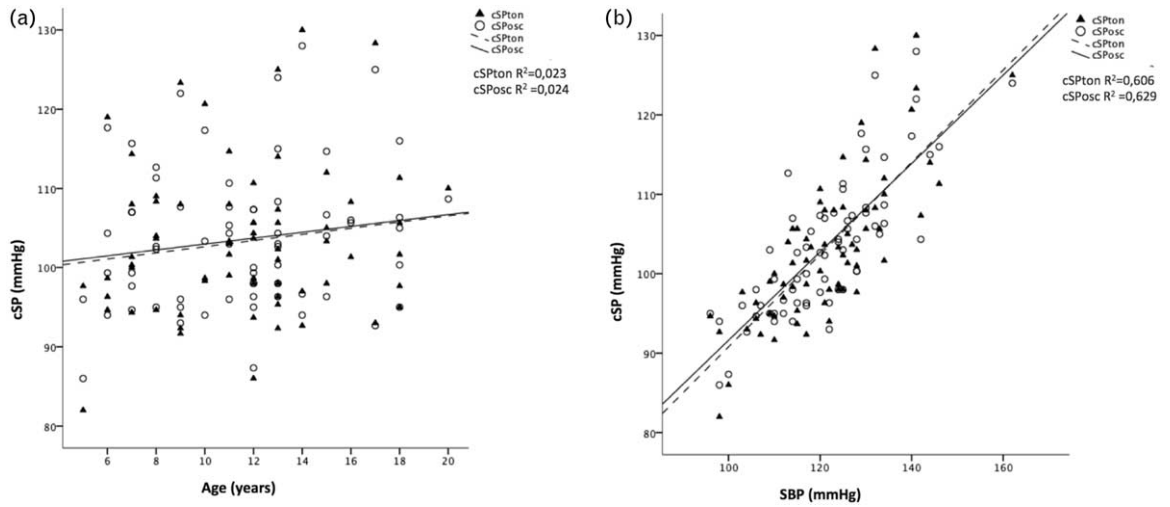


**FIGURE 4** Interaction between (a) age and method of central aortic SBP assessment and (b) SBP and method of central aortic SBP assessment.

numerous devices for noninvasive assessment of vascular phenotype have been validated in the adult population with those based on pressor sensors, either using mechanotranducers or high fidelity applanation tonometers to be considered the gold standard [11].

Applanation tonometry is feasible and reproducible in children and adolescents [24]. However, significant challenges including operator training and expertise may compromise the quality and reliability of measurements. Lowenthal *et al.* [24] performed cf-PWV measurements in children and adolescents by applanation tonometry on 2 consecutive days and found a better quality of acquired cf-PWV measurements the 2nd day of assessment for the same operator. Moreover, measuring cf-PWV at two different sites (carotid and femoral) critically depends on patients' cooperation, as he/she should remain still and irresponsive to environmental stimuli throughout the study period to ensure similar HRs during measurements at both sites [13]. Keehn *et al.* [25] compared applanation tonometry with cuff-based measurements by Vicorder device (Skidmore Medical Ltd, Bristol, UK) and reported nonsuccessful assessment of cf-PWV in the 22% of their study population by applanation tonometry caused by failure of cooperation or pulse palpation. In young children, obtaining high-quality radial or femoral pulse signal may be difficult, resulting in longer assessment times challenging the cooperation of the child [13,14]. Cuff-based devices may encounter with the above challenges facilitating the assessment of cf-PWV and cSP in children and adolescents, as they require less time for the assessment, are more convenient for the patient, are simpler to use and operator independent.

Kis *et al.* [26] compared a cuff-based device with two devices using applanation tonometry for cf-PWV assessment in children showing good accordance among devices. Similarly, we found excellent accordance between the two devices suggesting that Sphygmocor XCEL provides interchangeable results with applanation tonometry for cf-PWV assessment in the pediatric population. Moreover, the LoA for cf-PWV obtained with Sphygmocor XCEL are much narrower than those reported in pediatric studies comparing other cuff-based devices with applanation tonometry [25–27]. Therefore, it may be used in clinical studies allowing extrapolation of data and comparison with published reference data for cf-PWV [9].

The ideal assessment of arterial distances has not been thoroughly examined in children. In adults, it is currently recommended to use the 0.8× direct distance (carotid pulse palpation site to the femoral pulse palpation), as it has been shown to more accurately reflect the real traveled aortic path [15,28]. The subtraction method (suprasternal notch to the femoral pulse palpation site minus the linear distance from the carotid pulse palpation site to the suprasternal notch) has been used in the current study to be in line with previous studies on cf-PWV in children, and taking into account that published cf-PWV reference values in the pediatric age range are based on the subtracted travel distance [9]. This distance assessment has been shown to be clinically equivalent to invasive measurements in adults and is acceptable by the European Society of Hypertension Expert Consensus on measurement of arterial stiffness [15,29]. Importantly distances for both devices were measured by the same manner.

Cuff-based devices have been reported to underestimate cf-PWV compared with measurements obtained with tonometer [18,26]. However, this underestimation was nonsignificant in the current study, possibly because both devices used the same algorithm to detect foot waveform. On the other hand, there was a significant effect of SBP on cf-PWV measured by the two devices, resulting in underestimation of cf-PWV levels with the cuff-based device at lower DBPs, possibly associated with low oscillation at femoral site with lower SBP level in children. A previous study also showed that the only parameter reported to interfere with tonometric cf-PWV measurements reproducibility was high SBP [24]. The implications of this finding need to be further investigated upon its implications to individual measurements and cardiovascular risk assessment.

In the current study, we also found an excellent performance of SphygmoCor XCEL device for the assessment of cSP compared with applanation tonometry. Two previous validation studies for SphygmoCor XCEL device in adults showed equivalent values of cSP with applanation tonometry by SphygmoCor 'conventional' device performing calibration with brachial SBP and DBP measured by XCEL device [20,21]. A recent study validating SphygmoCor XCEL device against invasive cSP measurement in 36 patients undergoing coronary angiography, reported strong correlation, but underestimation of cSP by the SphygmoCor XCEL device compared with invasive measurement [30], which has also been shown for cSP values obtained by the 'conventional' SphygmoCor device [31]. This underestimation was mainly attributed to calibration issues due to differences between invasive and noninvasive brachial SBP and DBP measurements [12,30]. Of note, data were based on elderly patients with coronary disease being under vasoactive medications and cannot be safely extrapolated in the young. In the current study, including children and adolescents the SphygmoCor XCEL device was compared against applanation tonometry and fulfilled pass criteria by ANSI/AAMI/ISO 2013, validating its clinical use for cSP in this age group [12]. The underestimation of cSP derived from peripheral pressure waveforms by generalized transfer function built in SphygmoCor devices has been also reported in children and adolescents, and development of age-specific generalized transfer functions may further improve accuracy in the future [32].

Children and adolescents present different growth stages and puberty may add further to differences among age groups. Significant considerations have been expressed with regard to interpretation of data in the young age [33]. In the absence of validated devices in the young, investigators have used devices developed for adults [34]. Differences in body size, vascular tree morphology, HR and mean BP are some of the arguments that challenge the reliability of the devices for assessment of cSP. In the current study, we found similar performance of the XCEL device for cSP in the preadolescent and adolescent group.

In conclusion, cuff-based devices are particularly appealing for vascular phenotype assessment in the young

population. The new cuff-based SphygmoCor XCEL device provides equivalent results for cf-PWV and cSP values to those obtained by applanation tonometry in children and adolescents. Thus, the SphygmoCor XCEL device could be appropriate for assessing cf-PWV and cSP in the young and may be used in clinical studies in the pediatric population. Further studies are needed to evaluate the use of noninvasive assessment of cSP in the pediatric population.

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### Conflicts of interest

There are no conflicts of interest.

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## Reviewer's Summary Evaluation

### Referee 1

This study appears to be the first to validate the novel cuff-oscillometric ShygmoCor XCEL against conventional tonometric SphygmoCor devices in the pediatric population. The findings of equivalent values for carotid-femoral pulse wave velocity and central aortic blood pressure provide a practical rationale for using the XCEL device among children and adolescents. This study clearly shows that further research is needed in the young population to validate the noninvasive estimates by comparing invasive measures, standardize the methodology for path length measurements, establish the normative reference values, and investigate the clinical rationale for cardiovascular risk assessment.