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Carotid peak flow velocity variation as a surrogate of aortic peak flow velocity variation in a pediatric population

Federico Cristiani[1*], Juan Pablo Bouchacourt[2], Juan Riva[2] and Pablo Motta[3]

Abstract

Background Carotid peak velocity variation ($\Delta Vpeak_{Car}$) is an alternative to aortic peak velocity variation ($\Delta Vpeak_{Ao}$) and has been used in the pediatric population. Children's physiology and anatomy are heterogeneous throughout their growth. For this reason, the predictive value of ΔVpeakCar as a surrogate of ΔVpeakAo can vary at different ages. We hypothesize that the ability of $\Delta Vpeak_{Car}$ as a surrogate of $\Delta Vpeak_{Ao}$ changes throughout childhood.

Aim Analyze the concordance and the tracking ability of $\Delta Vpeak_{Car}$ and the $\Delta Vpeak_{Ao}$ at different stages of development.

Methods Patients from 0 to 12 years were included. Three groups were defined: under 12 months (G1), between 12 and 60 months (G2), and over 60 months (G3). After anesthesia induction and mechanical ventilation, maximal and minimal aortic and carotid peak flow were measured. $\Delta Vpeak_{Ao}$ and $\Delta Vpeak_{Car}$ were calculated. Pearson test and simple linear regression were performed. Bland-Altman analysis was performed to determine concordance. 4-quadrant analysis was used, followed by polar analysis of the vectors, to complement the concordance analysis and determine the tracking ability of $\Delta Vpeak_{Car}$ to surrogate $\Delta Vpeak_{Ao}$.

Results Sixty-seven patients were enrolled. 22 (32.4%) patients in G1, 21 (31.3%) in G2 and 24 (35.8%) in G3. The determination coefficient (r) between $\Delta Vpeak_{Ao}$ and $\Delta Vpeak_{Car}$ in G1 was 0.44 ($p < 0.001$) with a slope value of 0.61 (SE = 0.11; 95% CI:0.3–0.91). In G2, $r^2 = 0.56$ ($p < 0.001$) with a slope value of 0.59 (SE = 0.14; 95% CI:0.35–0.82); and in G3, $r^2 = 0.85$ ($p < 0.001$) with a slope value of 1.11 (SE = 0.10; 95% CI:0.91–1.31). Bland-Altman analysis showed to G1 a mean bias of -0.37 (LOA − 7.87 to 7.53), to G2 -0.07 (LOA − 7.37 to 7.23) and G3 0.55 (-3.81 to 4.91). Concordance rates were 100% in G3, 95% in G2, and 93% in G1.

Conclusions $\Delta Vpeak_{Car}$ showed good correlation and tracking ability with $\Delta Vpeak_{Ao}$ in schoolchildren. In younger children, it was not reliable enough.

Keywords Paediatric anaesthesia, Doppler ultrasonography, Fluid therapy, Haemodynamic monitoring

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Introduction

Responsiveness to fluid challenges is essential in clinical practice, especially for critically ill and surgical patients. Fluid overload or under-resuscitation may affect outcomes after surgery; hence, identifying patient fluid responsiveness is essential [1, 2]. Many indexes have been used to identify patients who will increase their cardiac output after a fluid challenge [3]. While indexes like pulse and stroke volume variation are good predictors of fluid responsiveness and volume expansion in the adult population, those variables are poor predictors in the pediatric population [4]. There is a lack of supporting evidence about using pressure indexes of heart-lung interaction, like systolic pressure and pulse pressure variation in children. Durant et al. validated aortic peak velocity variation ($\Delta Vpeak_{Ao}$) in the pediatric population and emphasized that respiratory variations in aortic blood flow are reliable indicators of cardiac preload reserve [4]. In a meta-analysis, Desgranges et al. demonstrated that $\Delta Vpeak_{Ao}$ was a good predictor of fluid responsiveness in children under mechanical ventilation [5].

$\Delta Vpeak_{Ao}$ measurement requires transthoracic five chambers apical window of the left ventricular outflow tract. This measurement requires specific training and is not easily reproducible or obtainable. In addition, this window may not be accessible during pediatric surgical procedures.

Peak velocity variation can also be measured in the great vessels distal to the heart. Recently, ultrasound carotid echography with pulse Doppler flow variation has been used to surrogate $\Delta Vpeak_{Ao}$ in adults and children [6, 7]. Carotid peak velocity variation ($\Delta Vpeak_{Car}$) has been proven to be an excellent alternative to $\Delta Vpeak_{Ao}$ and used in the pediatric population. A recently published study by De Souza and co-workers observed that $\Delta Vpeak_{Car}$ could identify fluid responsiveness in 30 critically ill pediatric patients with high sensitivity and specificity [8]. Niyogi and collegues observed concordance with $\Delta Vpeak_{Ao}$ and indicated that $\Delta Vpeak_{Car}$ might be easily measurable and a potential surrogate of $\Delta Vpeak_{Ao}$ in monitoring fluid responsiveness in children. A challenge in this population is that children's physiology and anatomy are heterogeneous throughout their growth. For this reason, the predictive value of $\Delta Vpeak_{Car}$ as a surrogate of $\Delta Vpeak_{Ao}$ can be unreliable at different ages [7]. There is scarce information about the behavior of $\Delta Vpeak_{Car}$ at the different stages of development.

We hypothesize that the ability of $\Delta Vpeak_{Car}$ as a surrogate of $\Delta Vpeak_{Ao}$ is not the same throughout childhood. Therefore, the objective was to analyze the concordance and the tracking ability of $\Delta Vpeak_{Car}$ and the $\Delta Vpeak_{Ao}$ at different stages of childhood.

Patients and methods

This project was presented and approved for implementation by the Pediatric Hospital Center Pereira Rossell Institutional Ethical Committee and registered with the Ministry of Public Health (#8035177). Informed and signed consent was obtained from all the children's parents or responsible guardians. All procedures in this study were performed in accordance with the Declaration of Helsinki. A prospective, observational, and cross-sectional study was conducted from April 2019 to April 2021.

Patients from 0 to 12 years of age scheduled for elective surgery under general anesthesia with mechanical ventilation were included. Three study groups were defined: under 12 months (G1), between 12 and 60 months (G2), and over 60 months (G3). Patients with conditions that may affect the validity of echocardiographic indexes, such as heart disease, irregular rhythm, thoracic surgery, and increased intra-abdominal or intrathoracic pressure, were excluded. Urgent and emergency surgeries and all those procedures where echocardiographic imaging interferes with the surgical field were excluded.

Study protocol

The night before surgery, the anesthesiologist conducted the preoperative visit, explained the anesthetic-surgical procedure, recommended a fasting period according to institutional guidelines, and consented to enter the study.

Before surgery, the following variables were recorded: gender, age in months, weight, height, the surgical procedure, fasting time in hours, preoperative fluid administration, medication, and comorbidities.

During anesthesia induction, children were monitored with electrocardiogram, pulse oximeters, and non-invasive blood pressure. After induction of anesthesia, a peripheral venous line was placed, followed by orotracheal intubation. The maintenance of anesthesia was according to the preference of the attending anesthesiologist. It was ensured that, regardless of the ventilatory mode used, the tidal volume (Vt) was maintained between 6 and 8 ml/Kg, PEEP of 5 cmH_2O, and respiratory rate (RR) consistent with normocapnia. The ratio between heart rate (HR) and RR (HR/RR) was kept at >3.6. Expired Vt, peak inspiratory pressure (PIp), PEEP, and plateau pressure (Pp) were recorded using the anesthesia station. Vt was indexed to the patient's weight, and dynamic compliance was estimated (Vt/[PIp-PEEP]). Fluid therapy during surgery was performed according to Holliday's formula for the patient's weight [9].

Ultrasonographic data acquisition

Data acquisition was made after induction and before surgical incisions during stable hemodynamics. Echocardiographic parameters were measured using a

multi-probe ultrasound system (SonoSite MicroMaxx, USA) with a 1–5 MHz phased array transthoracic echocardiography probe (MicroMaxx P17, SonoSite) and a 5–10 MHz linear probe (MicroMaxx L38e SonoSite).

$\Delta Vpeak_{Ao}$ was measured in apical five-chamber view, keeping the pulse wave Doppler sample volume in the left ventricular outflow tract (LVOT) below the aortic valve. $\Delta Vpeak_{Car}$ was measured with a linear probe, interrogating the common carotid artery longitudinally in the neck, keeping pulsed wave Doppler sample volume centrally in the vessel, and limiting the interrogation angle to a maximum of 60°. Ultrasonographic data acquisition is shown in Fig. 1.

In both echographic sites, maximal and minimal peak velocity flow was measured, and the variability was calculated as

$$\Delta\, velocity = \frac{Maximal\ velocity - Minimal\ velocity}{Mean\ velocity} \times 100$$

All measurements were performed by the same operator, an anesthesiologist experienced in ultrasound. To reduce variability three consecutive measurements were taken and those with a difference of more than 15% between them were discarded. The average of the three measurements was used.

Statistical analysis

Results are expressed as mean ± standard deviation (SD) or median (Q1-Q3) when applicable. The Shapiro-Wilk test was used to confirm the normal distribution of the study variables. The T-tests for independent variables or analysis of variance (ANOVA) with Bonferroni as post hoc were used for means comparison.

A sample size was established of 44 patients to compare $\Delta Vpeak_{Ao}$ and $\Delta Vpeak_{Car}$ means, and 54 patients for means groups comparison. For sample size estimation, a type I error of 0.05, a type II error of 0.9, and an effect

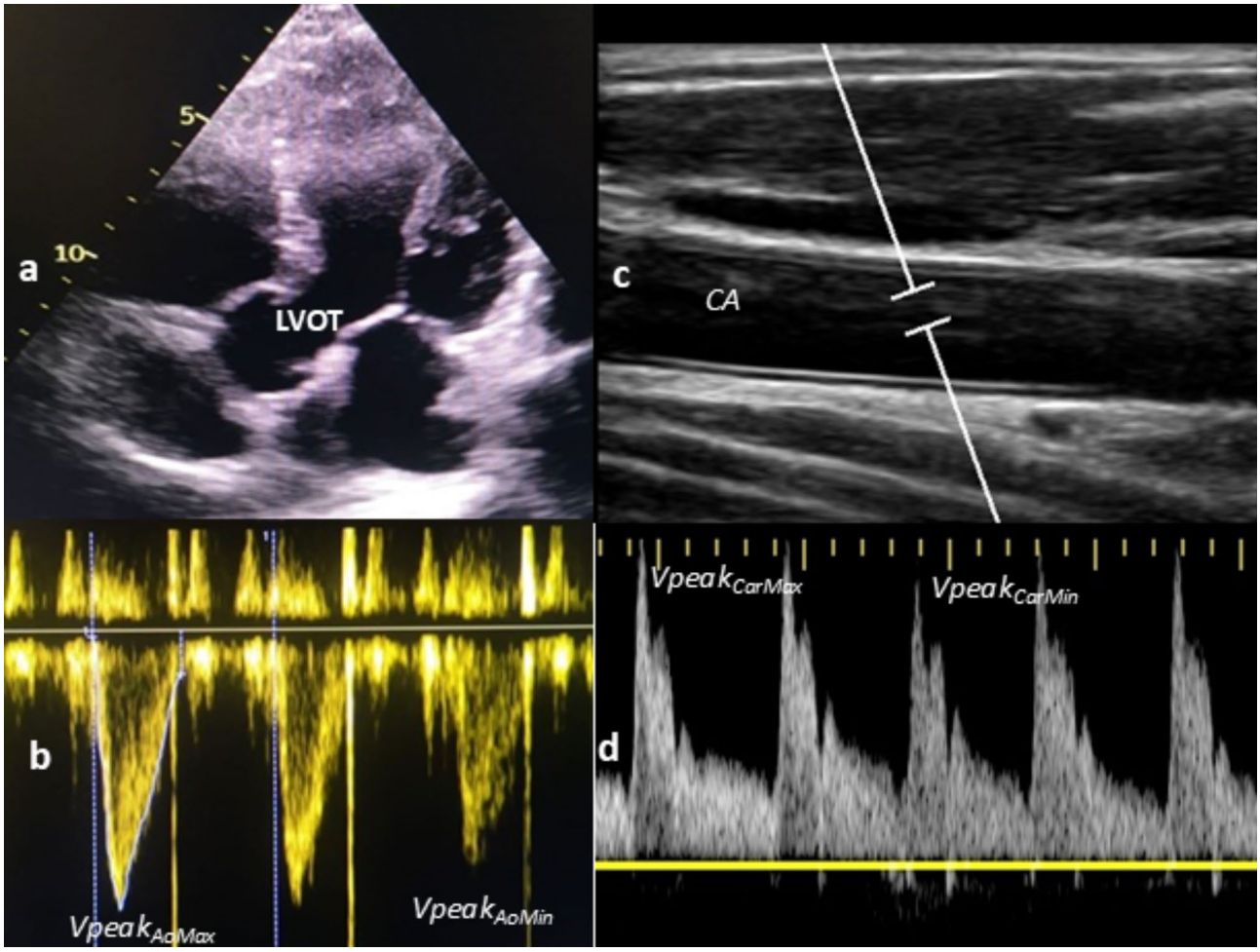

Fig. 1 Ultrasonographic data acquisition. **Figure 1a and b**: $Vpeak_{AoMax}$ and $Vpeak_{AoMin}$ measurement. **c** and **d**: $Vpeak_{CarMax}$ and $Vpeak_{CarMin}$ measurement. LVOT: left ventricular outflow tract, $Vpeak_{AoMax}$: maximal aortic peak velocity, $Vpeak_{AoMin}$: minimal aortic peak velocity, CA: carotid artery, $Vpeak_{CarMax}$: maximal carotid peak velocity, $Vpeak_{CarMin}$: minimal carotid peak velocity

size of 0.5 were considered. In both cases, we consider a power of 90% and a significance level of 5%.

A Pearson test and simple linear regression were performed to determine the correlation and the coefficient of determination between $\Delta Vpeak_{Ao}$ and $\Delta Vpeak_{Car}$.

The Bland-Altman analysis was performed to determine if both variables were interchangeable. The bias (mean difference between two variables), precision (SD of bias), and limits of agreement (LOA) as bias ± 2SD were calculated. The percentage error (PE) was calculated as the ratio of 2SD of the bias to the mean velocities variations and was considered clinically acceptable if it was less than 30%. The usefulness of this analysis is limited, so to complement the concordance analysis and determine the tracking ability of $\Delta Vpeak_{Car}$ to surrogate $\Delta Vpeak_{Ao}$, the 4-quadrant analysis was used, followed by a polar analysis of the vectors. The change or delta values were plotted using a 4-quadrant X-Y Cartesian plot, allowing the direction of change or rate of agreement to be assessed. The concordance rate was defined as the percentage of values included in the upper right and lower left quadrants of the quadrants. Agreement between variables was considered weak when this percentage was less than 90%. An exclusion zone was used to eliminate central data with a significant random error. For numeric data, we used a radial limit of 1.8% (percentage change data of 15%).

The polar analysis allowed a more precise evaluation of the trend and the magnitude of the changes between the study variable ($\Delta Vpeak_{Car}$) and the reference variable ($\Delta Vpeak_{Ao}$). From the center point, changes in the pairs of computed values are represented as vectors with defined angles and magnitude. The mean angular bias (q) and standard deviation represent all angles measured from the polar reference axis (0°). In turn, the radial limits of agreement were estimated as the radial sector containing 95% of the values (1.96 SD). A mean angular value ± 5° and a radial limit of agreement ± 30° were the defined limits for the polar plot analysis [10].

Statistical comparisons between variables were performed using statistics software SPSS 29.0 (SPSS Inc., Chicago, IL). A $p < 0.05$ was considered significant.

Results

Sixty-seven patients were enrolled in the study. Twenty-two were in orthopedic surgery (32.8%), nineteen in general surgery (28.4%), sixteen in urologic surgery (23.9%), and 10 (14.9%) in otorhinolaryngologic surgery.

In the general population, 47 patients (70.1%) were male. The median age was 32 months (12–90 months) with a mean weight of 22.5 ± 19.2 kg. Respiratory variables recorded during the study included Vt = 7.6 ± 0.9 mL/kg, PIp = 15.7 ± 4.1 cmH_2O, PEEP = 5 ± 0.5 cmH_2O, and Cdyn = 11.5 ± 7.4 mL/cmH_2O. At the time of echocardiographic data acquisition, the median fasting duration was 6 h (0–10 h).

Table 1 Demographic and ventilatory variables by subgroup. *N* = 67

	G1 (*n* = 22) < 12	G2 (*n* = 21) 12–60	G3 (*n* = 24) > 60	Sig
Age (months)	8.6 ± 5.7	34.5 ± 15.6[a]	106.3 ± 25.6[a, b]	$p < 0.001$
Weight (Kg)	8.4 ± 3.9	15.7 ± 7.0[a]	41.5 ± 19.9[a, b]	$p < 0.001$
Vt (ml/Kg)	7.7 ± 0.8	7.8 ± 0.8	7.2 ± 1.3	$p = 0.147$
PI_p (cmH_2O)	15.0 ± 2.3	17.1 ± 6.7	15.5 ± 2.6	$p = 0.304$
C_{dyn} (ml/cmH_2O)	6.9 ± 3.1	10.7 ± 4.9	20.4 ± 7.4[a, b]	$p < 0.001$
Fasting (hours)	3.5 ± 4.5	5.9 ± 5.4	7.2 ± 5.2	$p = 0.099$

Vt: volume tidal, PI_p: peak inspiratory pressure. C_{dyn}: dynamic compliance

[a] $p < 0.05$ vs. G1; [b] $p < 0.05$ vs. G2

Table 2 Cardiac and carotid sonographic parameters. *N* = 67

	G1 (*n* = 22)	G2 (*n* = 21)	G3 (*n* = 24)	Sig
$\Delta Vpeak_{Ao}$ (%)	9.1 ± 4.5	8.0 ± 5.6	9.8 ± 7.5	$p = 0.606$
$\Delta Vpeak_{Car}$ (%)	8.7 ± 4.0	8.1 ± 4.3	9.8 ± 9.0	$p = 0.636$
$Vpeak_{Ao}$max (cm/sec)	91.3 ± 23.5	93.4 ± 22.4	84.7 ± 14.0	$p = 0.325$
$Vpeak_{Ao}$min (cm/sec)	83.5 ± 22.1	86.1 ± 20.0	76.6 ± 11.8	$p = 0.201$
$Vpeak_{Car}$max (cm/sec)	127.9 ± 34.4	126.5 ± 44.9	123.9 ± 32.5	$p = 0.933$
$Vpeak_{Car}$min (cm/sec)	117.4 ± 31.8	116.9 ± 42.0	113.3 ± 33.4	$p = 0.913$
D_{LVOT} (mm)	8.6 ± 2.3	13.2 ± 3.4[a]	18.0 ± 3.4[a, b]	$p < 0.001$
D_{Car} (mm)	3.5 ± 0.7	4.5 ± 1.0[a]	5.6 ± 0.8[a, b]	$p < 0.001$
HR (rpm)	121 ± 13	92 ± 17[a]	80 ± 17[a]	$p < 0.001$

$\Delta Vpeak_{Ao}$ & $\Delta Vpeak_{Car}$: aortic and carotid peak velocity variation. $Vpeak_{Ao}$max & $Vpeak_{Car}$max: aortic and carotid maximum peak velocity. $Vpeak_{Ao}$min & $Vpeak_{Car}$min: aortic and carotid minimum peak velocity. D_{LVOT}: left ventricular outflow tract diameter. D_{Car}: carotid diameter

[a] $p < 0.001$ vs. G1; [b] $p < 0.001$ G2

The maximum and minimum mean aortic peak velocities at the LVOT were 89.6 ± 20.3 cm/sec and 81.9 ± 18.5 cm/sec, respectively. Similarly, the maximum and minimum mean common carotid velocities were 126.0 ± 36.8 cm/sec and 115.8 ± 35.3 cm/sec. There was no significant difference observed between $\Delta Vpeak_{Ao}$ and $\Delta Vpeak_{Car}$ across all patients, with values of 9.0 ± 6.0% and 8.9 ± 6.3%, respectively. A strong correlation was found between the two measurements, with a correlation coefficient of 0.84 ($p < 0.05$) and a determination coefficient 0.70 ($p < 0.001$).

Bland-Altman analysis showed a mean bias of 0.29 (LOA −5.9 to 6.48; PE = 72%) with a concordance rate in the quadrant plot of 85%. The vectorial analysis of the tracking ability of $\Delta Vpeak_{Car}$ in the whole population showed an angular bias of 0.7° (95% CI -8.4° to 7.1°) with a radial limit of agreement of 60.4°.

The entire population was divided in three target study groups with 22 (32.4%) patients in G1, 21 (31.3%) in G2 and 24 (35.8%) in G3. Demographic and ventilatory

variables of each group are presented in Table 1 and cardiac and carotid sonographic parameters in Table 2.

The r^2 between $\Delta Vpeak_{Ao}$ and $\Delta Vpeak_{Car}$ in G1 was 0.44 ($p < 0.001$) with a slope value of 0.61 (SE = 0.11; 95% CI:0.3–0.91). In G2, $r^2 = 0.56$ ($p < 0.001$) with a slope value of 0.59 (SE = 0.14; 95% CI:0.35–0.82); and in G3, $r^2 = 0.85$ ($p < 0.001$) with a slope value of 1.11 (SE = 0.10; 95% CI:0.91–1.31). Linear regression fit and correlation coefficient in each study group is presented in Fig. 2.

Bland-Altman analysis showed in G1 a mean bias of 0.37 ± 3.43 (LOA −6.50 to 7.14; PE = 77%), in G2 a mean bias of -0.07 ± 3.65 (LOA −7.37 to 7.23; PE = 90%) and in G3 a mean bias of 0.55 ± 2.18 (LOA −3.81 to 4.90; PE = 49%).

A multidimensional approach of tracking ability of $\Delta Vpeak_{Car}$ as a surrogate $\Delta Vpeak_{Ao}$ is presented in Fig. 3; Table 3. Cartesian analysis of the relationship between $\Delta Vpeak_{Car}$ and $\Delta Vpeak_{Ao}$ differences for each group is shown in the quadrant plot. Concordance rate of 80% in G1, 93% in G2 and 100% in G3. The vectorial analysis showed an increase in the radial limits of agreement with the age increment.

Two groups of patients were identified: those who presented with non-replaced fasting (NR) and those who had intravenous fluid infusion after fasting (R) at the moment of data acquisition. In 28 (42%) patients, the ultrasonographic data acquisition variables were obtained after fluid fasting restitution (R); in 34 (51%) patients, the measurements were performed before that (NR); and in 5 (7%) patients, fasting was not recorded. A significant difference was found in the dynamic ultrasound indexes: $\Delta Vpeak_{Ao}$ (10.6 ± 6.8% vs. 7.4 ± 4.3%) and $\Delta Vpeak_{Car}$ (10.4 ± 7.3% vs. 7.1 ± 4.2%) between NR and R groups, respectively.

Discussion

In this study, we explored the feasibility of $\Delta Vpeak_{Car}$ as a surrogate of $\Delta Vpeak_{Ao}$ in children. When the individual age groups were evaluated, it was found that the ability of $\Delta Vpeak_{Car}$ to serve as a substitute for $\Delta Vpeak_{Ao}$ varied with age. Most importantly, the coefficient of determination, concordance, and ability to follow the changes between the two variables were stronger in children older than 60 months. In contrast, the relationship of $\Delta Vpeak_{Car}$ and the ability to follow the changes of $\Delta Vpeak_{Ao}$ were lower in children younger than 12 months.

$\Delta Vpeak_{Ao}$ has been proposed to be one of the best dynamic index predictors of volume responsiveness in positive-pressure ventilated children [11]. Niyogi et al., when analyzing a similar population, found a correlation coefficient of $r = 0.73$ between $\Delta Vpeak_{Ao}$ and $\Delta Vpeak_{Car}$ [7]. The authors concluded that performing carotid ultrasonography with the recording of $\Delta Vpeak_{Car}$ is a viable technique and more accessible for children in the operating room setting. This index would be a good surrogate for $\Delta Vpeak_{Ao}$ to guide volume resuscitation. However, these authors found wide limits of agreement, which makes clinical decision making difficult if one wants to interchange the variables. These authors do not discriminate the performance of these variables in the different stages of childhood. They only use the Bland-Altman analysis to determine the concordance, unable to decide on the accuracy of one variable to substitute the other.

In our study, when analyzing the coefficient of determination of $\Delta Vpeak_{Car}$, it was found that this value improves as the child grows, being 0.44 at less than 12 months, 0.56 between 12 and 60 months and 0.85 at more than 60 months.

Similar results were observed when considering the tracking ability of $\Delta Vpeak_{Car}$ to replace $\Delta Vpeak_{Ao}$ using cartesian and polar data analysis. Older children present a 4-quadrant plot concordance rate of 100%, with an angular mean of 0.2° and radial limits of 48° in the vectorial polar analysis. The Bland-Altman analysis by subgroups also showed better concordance in this group with a mean of 0.6, with limits of concordance −3.8 to 4.9, with broader limits in younger children. As far as we know, this is the first study that separately analyzes the different age groups. As can be seen, the ability of $\Delta Vpeak_{Car}$ to replace $\Delta Vpeak_{Ao}$ is not uniform at all ages and could lead to incorrect clinical decisions.

It is not established that the cut-off point for $\Delta Vpeak_{Ao}$ identifies the pediatric patient responders with high sensitivity and specificity. The established values vary with the authors and are between 7% and 20%, with different sensitivity and specificity for each [5, 7, 12]. This problem makes it even more challenging to analyze $\Delta Vpeak_{Car}$ and its usefulness when replacing $\Delta Vpeak_{Ao}$ in children.

As mentioned, throughout growth and development, the pediatric patient presents various physiological changes that may affect the correlation between $\Delta Vpeak_{Ao}$ and $\Delta Vpeak_{Car}$. Given that these indexes derive from the heart-lung interaction, children show physiological differences in all their systems compared to adults. The factors explaining this behavior will focus on pleuropulmonary and cardiovascular physiology. When comparing the recording of flow variations at the peripheral level in pediatrics, the ability to replace $\Delta Vpeak_{Ao}$ is better the closer to the thorax. The peak velocity variation recorded at the suprasternal level has better concordance and ability to identify the responders than the $\Delta Vpeak_{Car}$ [7]. Lung and chest wall compliance are higher in the pediatric population, so intrathoracic pressure variations with usual tidal volumes might not determine changes in the circulatory system. These changes are more pronounced in younger children. Children under two years of age are those with the highest compliance both at the

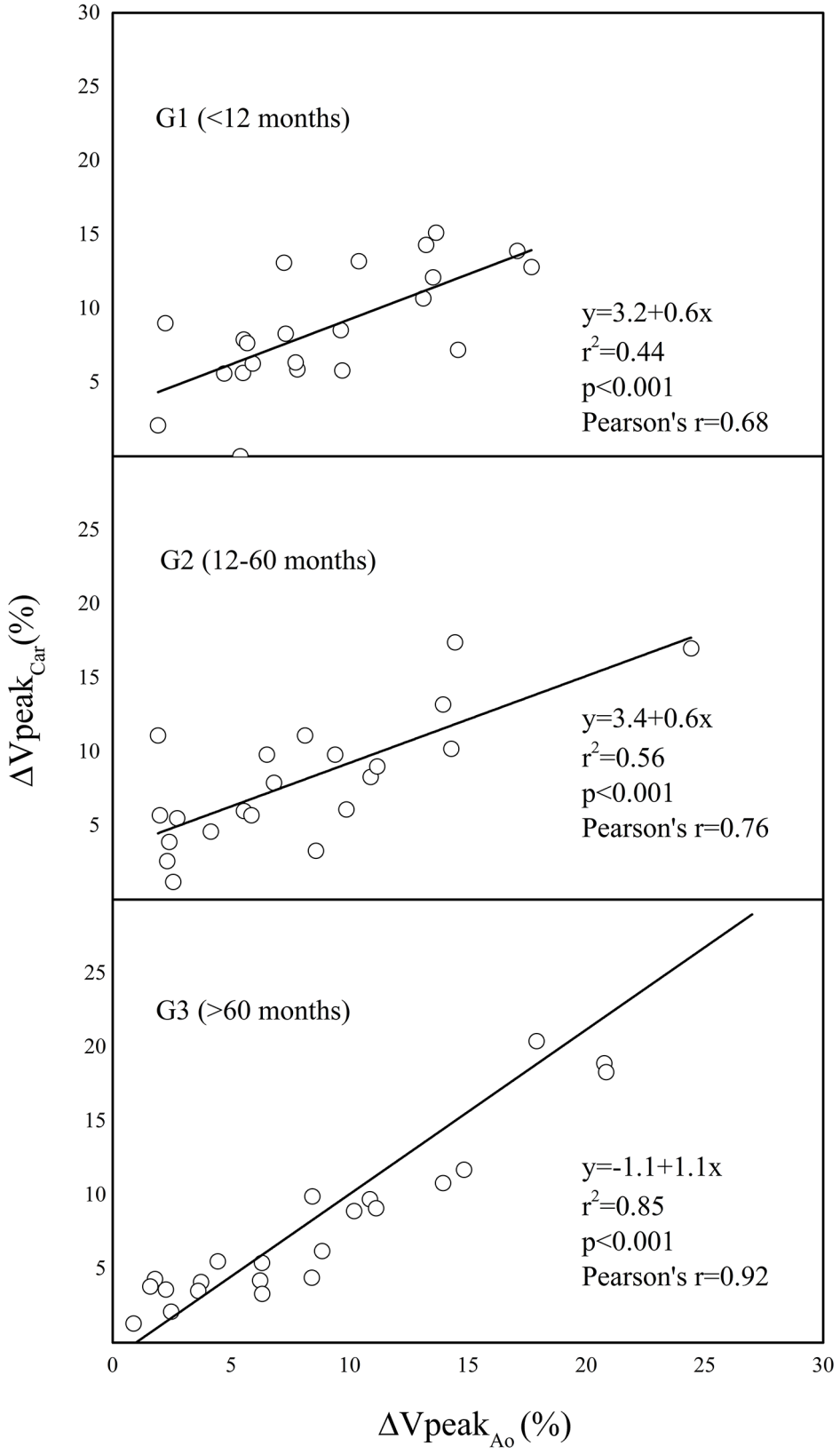

Fig. 2 Linear simple regression fit and correlation between velocity peak variation measured at left ventricular outflow tract ($\Delta Vpeak_{Ao}$) and common carotid ($\Delta Vpeak_{Car}$) level

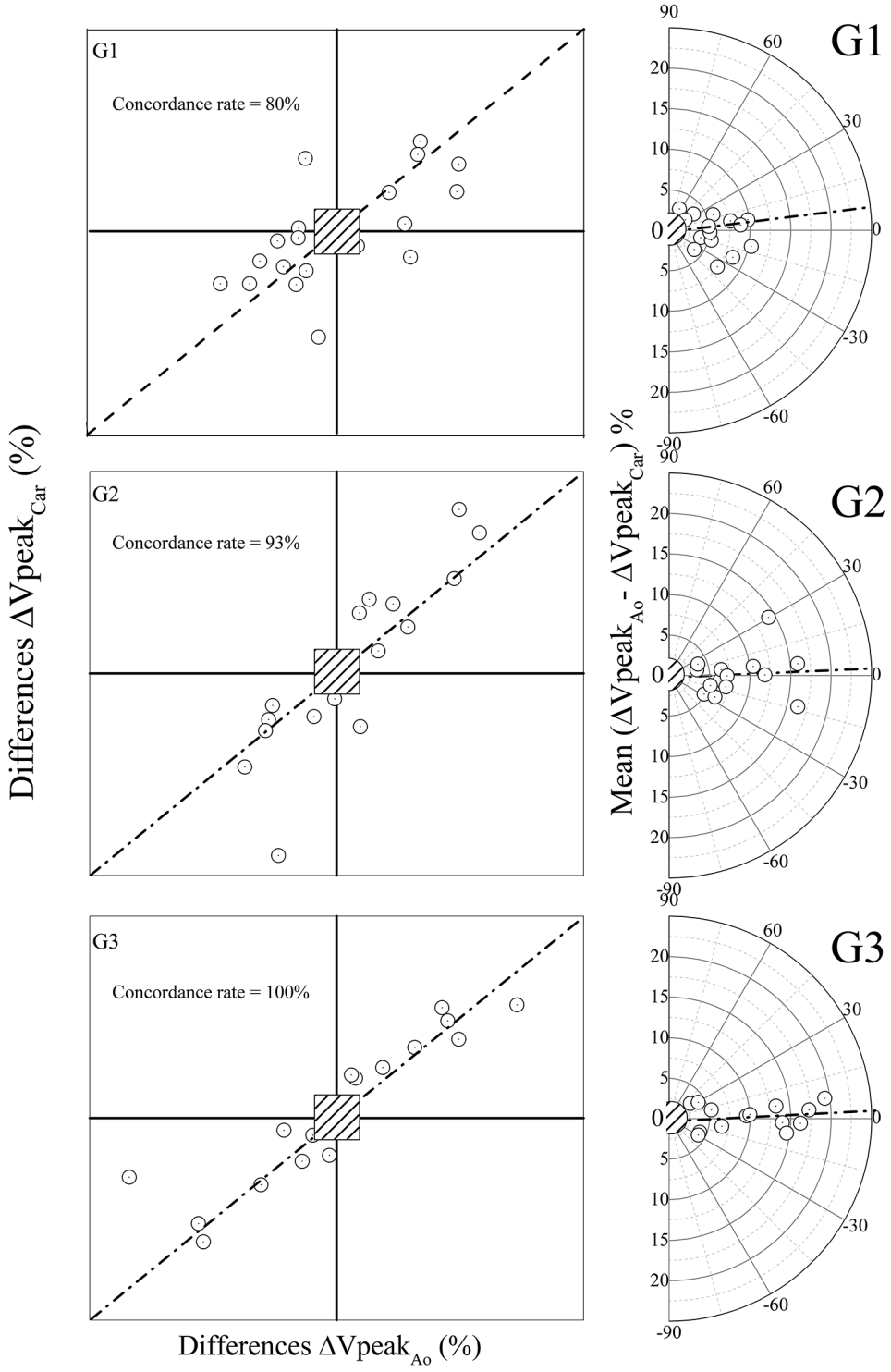

Fig. 3 Multidimensional approach of tracking ability of $\Delta Vpeak_{Car}$ as a surrogate $\Delta Vpeak_{Ao}$. The left side of the figure shows the Cartesian relationship between the differences of variables $\Delta Vpeak_{Ao}$ and $\Delta Vpeak_{Car}$ in each group. The concordance index in respective group is given. On the right side, the agreement of these variables is shown in a polar representation of the relationships between variables $\Delta Vpeak_{Ao}$ and $\Delta Vpeak_{Car}$

level of the rib cage and the lungs. At this age, when the child achieves bipedalism, the thoracic wall ossification stage begins, progressively leading to changes in respiratory dynamics until it becomes like an adult [13]. For this reason, it may be expected that school children have a physiology and behavior of the dynamic indexes more like adults. It is important to note that it is an ongoing process that accompanies growth. It is conceivable that

Table 3 Quadrant and Polar plot analysis data between ΔVpeakCar and ΔVpeakAo of the studied groups

	Concordance rate	Mean Angular Bias	95% CI	Radial limits of agreement
G1 (< 12 months)	80%	2.5º	-19 to 14º	73º
G2 (12–60 months)	93%	0.7º	-13 to 14º	59º
G3 (> 60 months)	100%	0.2º	-12 to 12º	48º

$\Delta Vpeak_{Car}$ will gradually correlate more with $\Delta Vpeak_{Ao}$ with increasing age.

Mechanical ventilation is another factor associated with the low predictability of dynamic indexes in pediatrics. Lower volumes and pressures are recommended, usually using a VT between 6 and 8 ml/kg. Given the high thoracic-pulmonary compliance, these volumes may not cause significant intrathoracic pressure changes capable of affecting the cardiocirculatory system without generating apparent variations in stroke volume [14, 15]. While respiratory compliance increases, the transmission of intrathoracic pressure to venous vessels is less likely to generate stroke volume variation. This factor could affect the interchangeability of these variables and their impact on clinical decision making.

Graham and colleagues, in 2014, compared the pulse pressure variation (PPV) in immature vs. mature animals for different degrees of hypovolemia and observed that immature animals presented lower PPV than mature ones [16]. Infants have reduced ventricular compliance and greater aortic and arterial tree elastance, which would explain why pressure variations can be damped, making it difficult to predict the response to volume. A compliant arterial tree determines that the dynamic indexes derived from flow variations are better predictors than those derived from pressure variations. Changes in arterial size and maturation of wall structure occur during childhood and affect arterial elastic properties. Vascular compliance is determined by vessel size and vessel wall distensibility. Arterial compliance and distensibility could influence the ability of $\Delta Vpeak_{Car}$ to follow changes in $\Delta Vpeak_{Ao}$.

The immature ventricles, being less compliant, tolerate less volume loading, so cardiac output tends to be less preload dependent. They generally work in the flat part of the Frank-Starling curve. It has also been observed that cardiac output is more dependent on the heart rate than the stroke volume in newborns [17]. At the venous level, these physiological characteristics of children determine that venous return is less affected by the changes caused by mechanical ventilation. Byon et al. find that respiratory variation in vena cava diameter is not a good predictor of fluid responsiveness in children since it is affected by the same arterial factors [18].

Carotid pulsed Doppler was used to estimate stroke volume and cardiac index [19]. This study, which included 50 patients between 1 month and 13 years of age, found that carotid Doppler allowed the estimation of cardiac index and stroke volume. Although this work did not evaluate volume responsiveness or differentiate by age group, it does assess the correlation between values measured by echocardiography and pulsed carotid Doppler.

We compared volume-replenished fasting patients ("euvolemic") with non-replenished fasting patients ("hypovolemic"). We found that both $\Delta Vpeak_{Ao}$ and $\Delta Vpeak_{Car}$ followed the usual behavior of the dynamic indexes. This could lead us to think these indexes could predict volume responsiveness using the usually established cut-off points.

Only the tracking ability and concordance of $\Delta Vpeak_{Car}$ were studied, and $\Delta Vpeak_{Ao}$ was used as a reference. We did not use other dynamic indexes, like pressure indexes, and we did not make a fluid challenge to determine the ability to identify responders' patients. More information is required to determine if $\Delta Vpeak_{Car}$ can identify fluid responders independently. For this, a study would have to be designed to evaluate the behavior of $\Delta Vpeak_{Car}$ after a fluid challenge and be able to verify the changes in stroke volume or cardiac outcome after it. However, cardiac outcome measurements are not frequently used in pediatric population in the operating room, especially in infants. Usually, these techniques are invasive and require specific training, so they are relegated to unique situations in children in critical condition.

Although our sample size calculation ensured adequate statistical power, a larger cohort would provide more robust validation of our results. Future studies with larger and more diverse populations are needed to confirm these findings and enhance their clinical applicability. Another limitation of our study is the classification of the population by age to account for anatomical and physiological differences. This approach may introduce bias in the results.

Conclusion

$\Delta Vpeak_{Car}$ showed a good correlation and tracking ability with $\Delta Vpeak_{Ao}$ in schoolchildren. However, in younger children, especially infants, the ability of $\Delta Vpeak_{Car}$ to substitute $\Delta Vpeak_{Ao}$ could lead to errors in clinical decision making. Therefore, absolute values are not substitutable, and caution should be considered in the clinical decision.

Abbreviations

$\Delta Vpeak_{Car}$	Carotid peak velocity variation
$\Delta Vpeak_{Ao}$	Aortic peak velocity variation
Vt	Tidal volume
RR	Respiratory rate

HR	Heart rate
Pip	Peak inspiratory pressure
Pp	Plateau pressure
LVOT	Left ventricular outflow tract
$Vpeak_{AoMax}$	Maximal aortic peak velocity
$Vpeak_{AoMin}$	Minimal aortic peak velocity
CA	Carotid artery
$Vpeak_{CarMax}$	Maximal carotid peak velocity
$Vpeak_{CarMin}$	Minimal carotid peak velocity
SD	Standard deviation
ANOVA	Analysis of variance
LOA	Limits of agreement
C_{dyn}	Dynamic compliance
D_{LVOT}	Left ventricular outflow tract diameter
D_{Car}	Carotid diameter
PPV	Pulse pressure variation

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Author contributions
FC, JPB, JR: study design. JPB: Statistic analysis. FC, JPB, JR, PM: wrote tht main document. All authors reviewed the manuscript.

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Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This project was presented and approved for implementation by the Pediatric Hospital Center Pereira Rossell Institutional Ethical Committee and registered with the Ministry of Public Health (#8035177). Informed and signed consent was obtained from all the children's parents or responsible guardians.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Attestation
All authors approved the final manuscript.

Prior presentation
Interim data from this work were presented at International Anesthesia Society Research (IARS) Meeting 2022. 18th -21th March, 2022. This study was presented and approved for implementation by the Pediatric Hospital Center Pereira Rossell Institutional Ethical Committee and registered with the Ministry of Public Health (clinical trial registration number: 8035177). Informed and signed consent was obtained from all the children's parents or responsible guardians.

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