



## Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

Journal Home Page: <https://www.atlantis-press.com/journals/artres>

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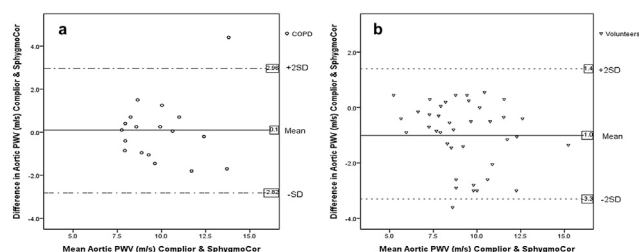
### **P2.27: A ROBUST METHOD FOR AUTOMATIC MEASUREMENTS OF DIAMETER, DISTENSION AND IMT IN HUMANS AND SMALL ANIMALS**

S. Segstedt, T. Nilsson, Å.R. Ahlgren, D. Ley, M. Cinthio

**To cite this article:** S. Segstedt, T. Nilsson, Å.R. Ahlgren, D. Ley, M. Cinthio (2013) P2.27: A ROBUST METHOD FOR AUTOMATIC MEASUREMENTS OF DIAMETER, DISTENSION AND IMT IN HUMANS AND SMALL ANIMALS, Artery Research 7:3\_4, 126–127, DOI: <https://doi.org/10.1016/j.artres.2013.10.088>

**To link to this article:** <https://doi.org/10.1016/j.artres.2013.10.088>

Published online: 14 December 2019



**Figure 1** Bland-Altman plot comparing PWV by Complior and SphygmoCor in a) Patients with COPD b) Volunteers.

### P2.25

#### ECHOCARDIOGRAPHIC VALIDATION OF A NOVEL METHOD FOR NONINVASIVE ESTIMATION OF CARDIAC OUTPUT BASED ON PULSE CONTOUR ANALYSIS

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Surgical or critically ill patients often require continuous assessment of cardiac output (CO) for diagnostic purposes or guiding therapeutic interventions. A new method of non-invasive estimation of CO, based on pressure wave analysis, has been recently developed, but its validity has been examined only *in silico*. Aim of this study was to evaluate the reproducibility, precision and accuracy of the "Systolic Volume Balance" method (SVB).

**Methods:** Twelve subjects underwent 2-D transthoracic echocardiography (Doppler) for CO measurement which was used as reference value. The application of SVB method required aortic pressure wave analysis and estimation of total arterial compliance ( $C_t$ ). Aortic pulses were derived by mathematical transformation of radial pressure waves recorded by applanation tonometry (SphygmoCor).  $C_t$  was estimated by the "pulse pressure" method. The agreement, association, variability, bias and precision between the reference (Doppler) and estimated (SVB) values of CO were evaluated by Spearman correlation coefficient, intraclass correlation coefficient (ICC), coefficient of variation (CV), root mean square error (RPSE), mean difference, SD of differences (SDD), percentage error (PR) and Bland-Altman analysis.

**Results:** Both SVB and Doppler provided highly reproducible measures of CO when two repeated measurements were performed (ICC>0.9, SD of difference <0.4 L/min, CV<5%, PR<17%). CO estimation by the SVB method was comparable with the respective measure by Doppler indicating a good agreement and accuracy (Table).

**Table.** Accuracy and precision of CO estimation by the SVB method compared to the reference method (Doppler).

Parameter	Value
Mean difference (L/min)	0.780
Standard deviation of difference (L/min)	0.323
Limits of agreement (L/min)	0.15–1.41
Coefficient of variation (%)	13.0
Root mean squared error (L/min)	0.678
Spearman correlation coefficient	0.939
Intraclass correlation coefficient	0.797
Percentage error (%)	20

**Conclusion:** CO estimation by the SVB method is highly reproducible and accurate in comparison with the CO measurement by Doppler. Future studies, though, are required to assess the clinical utility of this method.

### P2.26

#### ASSESSING CHARACTERISTICS OF THE CARDIO-ANKLE VASCULAR INDEX (CAVI) AND ITS PWV FOR ARTERIAL FUNCTION – ARM-LEG DIFFERENCES AND REPEATABILITY

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**Background:** Vasera is a machine developed to evaluate arterial stiffness by measuring pulse wave velocity (PWV) and cardio-ankle vascular index (CAVI), apparently independent of blood pressure (BP). The 4-cuff device measures right (R) and left (L) brachial and ankle BP, deriving the CAVI value and cardio-ankle (ca)PWV. We assessed the operating characteristics of this novel technique in clinical practice.

**Method:** A total of 108 patients, (13 healthy controls, 76 hypertensive, 19 with type 2 diabetes) aged 18-80 years, were measured with the Vasera 1500 (Fukuda-Denshi, Tokyo, Japan) after 10 minutes rest in a temperature controlled room. Patients with known vessel disease were excluded. Repeat visits were made after about 2 weeks.

**Results:** Mean±SD BMI and age were 29.6±6.1kg/m<sup>2</sup> and 50.8±16.1y respectively. Within-visit R and L CAVI were 7.8±1.5, and 7.8±1.7 units, and R and L PWV 8.1±1.5 and 8.1±1.6 m/sec. The difference between brachial systolic R and L BP, 2.5±7mmHg, correlated with both R-PWV and L-PWV (r=0.29 for both, p=0.009). No significant correlation was seen between brachial or ankle R and L systolic and diastolic BP differences and R/L-CAVI, nor was there significant correlation between ankle R/ L systolic and diastolic BP difference and R-PWV or L-PWV. In 24 patients, between-visit differences in CAVI (R) were 0.14 (95%CI -0.4 to 0.6, not significant, NS) and in caPWV 0.5 (-0.3 to 1) m/sec – NS.

**Conclusion:** Between-visit repeatability for both CAVI & caPWV was good. The correlation between difference in arm BP and caPWV suggests possible subclinical subclavian or aortic stiffness /disease.

### P2.27

#### A ROBUST METHOD FOR AUTOMATIC MEASUREMENTS OF DIAMETER, DISTENSION AND IMT IN HUMANS AND SMALL ANIMALS

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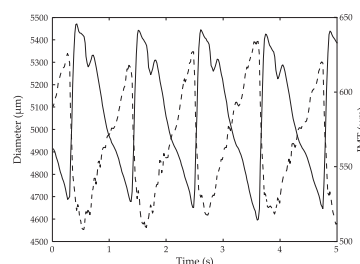
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ARTIC is a new segmentation-based tracking algorithm used to automatically measure diameter, distension and intima media thickness (IMT) in arteries using B-mode ultrasound. ARTIC is initiated with a mark in the center of lumen and can then perform automatic measurements in about 1000 frames/second. To show the robustness and versatility of ARTIC evaluations were made with four different ultrasound scanners, Philips HDI5000, Philips iU22, VisualSonics Vevo 2100 and ULA-OP (Florence University) with different file-formats, including DICOM. The repeatability of automatic measurements of diameter, distension and IMT was evaluated in a) the carotid artery in humans of various age and health and b) the aorta in premature rabbit-pups having a diameter of less than 1 mm. Further the measurements of ARTIC were compared to those of a previously phantom validated method. Finally, differences in measured diameter, distension and IMT when using different scanners were evaluated. The mean diameter of the measurement ranged from 5771-6604 μm (humans) and 768 μm (rabbit pups), the mean distension

Type of evaluation		CV(%)
IJ22 Carotid artery	Diam.	0.7
20 subjects Age 21-62	Dist.	4.1
Healthy Normotensive	IMT	2.3
ARTIC vs Validated method	Diam.	0.4
20 subjects Age 25-57 years	Dist.	2.4
Healthy Normotensive	IMT	1.9
HDI5000 Carotid artery	Diam.	1.8
10 subjects Age 23-39 years	Dist.	4.2
Healthy Normotensive	IMT	4.2
ULA-OP Carotid artery	Diam.	1.4
10 subjects Age 23-39 years	Dist.	6.4
Healthy Normotensive	IMT	5.8
HDI5000 Carotid artery	Diam.	1.4
12 subjects Age 60-76 years	Dist.	8.8
Healthy Normotensive	IMT	6.6
ULA-OP Carotid artery	Diam.	2.0
10 subjects Age 65-86 years	Dist.	8.7
Various Health	IMT	3.6
HDI5000 vs ULA-OP	Diam.	1.8
10 subjects Age 23-39 years	Dist.	8.5
Healthy Normotensive	IMT	9.1
Vevo 2100 Aorta	Diam.	13.0
10 premature rabbit pups	Dist.	19.0
	IMT	6.1



ranged from 501-861  $\mu\text{m}$  (humans) and 40  $\mu\text{m}$  (rabbit pups) and the mean IMT ranged 543-1011  $\mu\text{m}$  (humans) and 88  $\mu\text{m}$  (rabbit pups). The table shows a summary of the obtained coefficients of variation. The figure shows the diameter and IMT during four cardiac cycles measured with ARTIC. In conclusion ARTIC can be a useful tool to automatically characterize the arterial wall in both humans and small animals.

### P3 Population Science

#### P3.01

##### EFFECT OF BODY SIDE ON ATHEROSCLEROTIC PLAQUE DISTRIBUTION IN THE CAROTID AND FEMORAL ARTERIES

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**Objective:** Atherosclerotic disease is caused by a combination of systemic, and local factors. The influence of local geometry (affecting local flow conditions) is often neglected. In contrast to the carotid artery, at the iliac-femoral artery region, a large degree of bilateral asymmetry exists. Therefore, our aim was to determine the influence of body side on the prevalence of atherosclerosis (i.e. plaque and intima-media thickening; IMT) at the carotid and femoral arteries.

**Methods:** Data were used from the ASKLEPIOS study, including 2524 apparently healthy subjects with a mean age of 46 year (range 35-55). Echographic images were obtained bilaterally at the common carotid and common femoral arteries. A single observer approach was used for the acquisition and quantification of plaques and IMT.

**Results:** The carotid artery displays almost no left-right difference in IMT values nor plaques. In contrast, the femoral artery displays substantially more atherosclerosis on the right side. Specifically, the IMT distribution at the right common femoral artery is more skewed (Percentile 90 right: 1.11 mm, left 1.01 mm;  $p < 0.001$ ), which is mirrored by a significantly higher plaque prevalence (right 21.9 vs left 15.7 %;  $p < 0.001$ ).

**Conclusions:** Atherosclerotic lesions are more prevalent at the right than at the left femoral artery. This finding highlights the role of local arterial geometry on the development of atherosclerosis, and underscores the importance of the choice of body side when assessing vascular health.

#### P3.02

##### MORNING BLOOD PRESSURE SURGE, BLOOD PRESSURE VARIABILITY AND AORTIC STIFFNESS IN ESSENTIAL HYPERTENSION

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Morning blood pressure surge is associated with increased cardiovascular risk, possibly due to its ability to reflect short-term BP variability and/or its link with arterial stiffness. The link between morning BP surge and vascular stiffness is not defined.

689 untreated hypertensives ( $48 \pm 10$  years, BP  $149/92 \pm 17/10$  mmHg) underwent c-f PWV and 24-h ambulatory BP measurement. Morning surge was calculated as: sleep-rough surge (STS, 2-hour average SBP after wake-up minus average of 3 SBP centered on the lowest nighttime reading), pre-awakening surge (PAS, 2-hour average SBP after wake-up minus 2-hour average SBP before wake-up), and rising BP surge (RBS, SBP on rising minus the lowest SBP in the 30' before). Average real variability (ARV, 24h average of the absolute differences between consecutive SBP), was considered a measure of short-term SBP variability.

STS and RBS were directly correlated to c-fPWV ( $r = 0.17$  and  $r = 0.12$ ,  $p < 0.01$ ) and ARV ( $r = 0.28$  and  $r = 0.23$ ,  $p < 0.001$ ), while PAS had no such relationships. Patients in the top quartile of STS ( $> 39$  mmHg) had higher age- and 24-h mean BP-adjusted c-fPWV ( $9.73 \pm 2$  vs  $9.29 \pm 2$  m/s,  $p = 0.004$ ), while no difference was found for the top quartile of PAS or RBS. In a multivariate regression, high STS values predicted a high c-fPWV ( $\beta = 0.08$ ,  $p = 0.038$ ), independently of age, sex, 24-h mean BP and nocturnal BP reduction. After adding ARV ( $\beta = 0.17$ ,  $p < 0.001$ ) to the model, the relationship between STS and c-fPWV was no longer significant ( $\beta = 0.05$ ,  $p = 0.17$ ).

Morning SBP surge, calculated as STS, has a positive relation with aortic stiffness in hypertension, which is no longer significant after adjusting for 24-h short-term BP variability.

#### P3.03

##### INTERNATIONAL COMPARISON OF ESTIMATED AORTIC PULSE WAVE VELOCITY (APWV) IN 3 SETTINGS OF AFRICAN- AND EUROPEAN- ORIGIN PATIENTS AND CONTROLS – GHANA, BRITAIN AND BARBADOS

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**Objectives:** In resource-poor settings, aPWV's prognostic power, independent of blood pressure (BP), has potential as an intervention target against 'hypertension' and diabetes (T2DM). We compared simple determinants of aPWV in 3 African-origin settings and British Europeans.

**Methods:** Using methods standardised across 3 hospital sites in Ghana, Britain and Barbados, aPWV was estimated over 8 cardiac cycles up to 3 times by the single cuff-based Arteriograph, whose prognostic impact was recently reported. Sub-samples had repeatability measured separately. With basic anthropometry, data were analysed by regression (MRA), adjusting for temperature (co-linear with site).

**Results:** 527 people, (Ghana 296; UK 128 (35% African-origin); Barbados 103) 54% women, had satisfactory measurements, in 125 hypertensives without T2DM, 248 T2DMs and 154 apparently healthy controls, mean $\pm$ SD age  $50 \pm 15$ , range 20-87y, BMI  $28.1 \pm 6$  kg/m<sup>2</sup>. Cross-site age-/sex / adjusted mean (SD) aPWV were  $8.8 \pm 1.6$ ,  $9.3 \pm 2.3$  and  $8 \pm 1.8$  m/sec for Ghana, UK & Barbados respectively, with sys/diasBP  $147 \pm 23 / 85 \pm 13$ ,  $136 \pm 17 / 82 \pm 13$  and  $126 \pm 26 / 72 \pm 15$  mmHg. Forced into the MRA model, patient group, BMI and temperature did not contribute while systolic BP (standardized Beta (=B) 0.28), age (0.26) site (0.22) or ethnicity as West African, African-Caribbean  $>$  European (0.3), heart rate (0.21) and gender (0.17), were all related to aPWV,  $p < 0.002$ . Pulse, rather than systolic, pressure did not contribute, but central sysBP did (0.3,  $p < 0.0001$ ).

**Conclusions:** These data suggest that aPWV is not only a robust prognostic indicator but a potential treatment target, across the range of BP less affected by anthropometry and these 'disease' states. Are ethnic effects confounded by BP?

#### P3.04

##### GENETIC AND ENVIRONMENTAL CONTRIBUTIONS TO ARTERIAL STIFFENING, ATHEROSCLEROTIC PLAQUE AND CALCIFICATION

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**Introduction:** The prognostic importance of aortic calcification is often attributed to its close association with atherosclerotic plaque but it may relate to its effects on aortic stiffness and be driven by processes distinct from those of atherosclerosis. The aim of the present study was to determine the individual heritability of atherosclerosis plaque, calcification and aortic stiffness.

**Methods:** For heritability we examined 900 female twins from the Twins UK cohort aged 21-81 years and measured pulse wave velocity (PWV) and calcified and non-calcified plaque by carotid ultrasound. Total aortic plaque burden and calcium score were measured in a sub-sample of 100 women who underwent computed tomography (CT) and magnetic resonance imaging (MRI). Heritability and effect of environmental factors were estimated using structural equation modelling

**Results:** In the total cohort, adjusted heritability estimates of PWV and calcified plaque were 38% (confidence interval (CI): 19-59%) and 0.61 (CI: 4-83%), respectively. In contrast heritability of non-calcified plaque was only 5% (CI: 0-61%). Shared genetic factors accounted for 92% of the correlation between PWV and calcified plaque. In a sub-sample of twins with CT/MRI imaging an additive genetic component accounted for 77% (CI: 32%-89%) of variation in total aortic calcification. Shared genetic factors accounted for  $> 99\%$  of the correlation between PWV and calcification.

**Conclusion:** Our findings suggest calcification is driven by processes that are, at least in part, distinct from atherosclerosis. The association between aortic stiffening and calcification can be accounted for by common genetic factors, which contribute little to atherosclerosis.