



## Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

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

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### 8. USEFULNESS OF BRACHIAL-ANKLE AND CAROTID-FEMORAL PULSE WAVE VELOCITY AS PREDICTIVE VALUES OF CARDIOVASCULAR EVENTS

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**To cite this article:** Takashi Takagi, Mitsuru Ohishi, Miyuki Onishi, Yuji Tatara, Hiromi Rakugi (2009) 8. USEFULNESS OF BRACHIAL-ANKLE AND CAROTID-FEMORAL PULSE WAVE VELOCITY AS PREDICTIVE VALUES OF CARDIOVASCULAR EVENTS, Artery Research 3:3, 96–96, DOI: <https://doi.org/10.1016/j.artres.2009.06.020>

**To link to this article:** <https://doi.org/10.1016/j.artres.2009.06.020>

Published online: 14 December 2019

(hcPWV), heart-femoral PWV (hfPWV), femoral-ankle PWV (faPWV) using carotid and femoral sensor of form PWV/ABI. Therefore we examined prognostic impact of each regional PWV on stroke and cardiovascular disease (CVD) compared with baPWV in the cohort study of hypertensive patients.

**Methods:** This study included 387 patients with essential hypertension (male/female = 218/169, mean age  $61.1 \pm 11.8$ , mean follow period 43 months) whose ba- and regional PWV could be measured from October, 2000 to December, 2004. We set up stroke ( $n = 20$ ) and CVD ( $n = 21$ ) as a primary end point by the questionnaire. We classified the participants by the highest quartile of each PWV; high baPWV group, high hcPWV, high hfPWV and high faPWV; by the lowest quartile of ABI as low ABI group.

**Results:** There was a significant correlation between baPWV and regional PWV; faPWV ( $r = 0.560$ ), hcPWV ( $r = 0.253$ ) and hfPWV ( $r = 0.506$ ). By Kaplan-Meier analysis, only high baPWV group showed the prognostic impact of stroke and CVD ( $p = 0.0099$ ) but not high faPWV ( $p = 0.6982$ ), high hcPWV ( $p = 0.5740$ ), high hfPWV ( $p = 0.0773$ ) and low ABI group ( $p = 0.8008$ ). Only low ABI group showed the prognostic impact on mortality ( $p = 0.0223$ ), high baPWV on stroke ( $p = 0.0155$ ) and high hcPWV on CVD ( $p = 0.0382$ ).

**Conclusion:** As a further, larger, multicenter cohort study is needed, our study indicated that higher level of baPWV might be a risk factor of stroke and CVD, but prognostic impact of regional PWV is not still unclear in hypertension.

## 6.

### BRACHIAL-ANKLE PULSE WAVE VELOCITY AND CHRONIC KIDNEY DISEASE AS A PROGNOSTIC IMPACT IN HYPERTENSION

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**Background:** Many reports have shown that brachial-ankle pulse wave velocity (baPWV) has an effect on evaluation of atherosclerotic change and would be one of the prognostic factors for hypertension (HT). It has been reported that chronic kidney disease (CKD) would influence the prognosis of HT or diabetes mellitus. Therefore we examined how baPWV and CKD effects the incidence of cardiovascular disease (CVD) by the cohort study in hypertensive patients using the AT-form which we can measure PWV easily.

**Methods:** This study included 380 patients with essential HT (male/female 206/174, mean age  $60.9 \pm 12.1$ , mean follow period 41 months) whose baPWV could be measured from October, 2000 to December, 2004. We set up stroke ( $n = 19$ ) and CVD ( $n = 18$ ) as a primary end point by the questionnaire. We estimated CKD as lower glomerular filtration rate (GFR) with MDRD formula and proteinuria. We produced quartile groups according to the baseline measurements of baPWV or the presence of CKD and assessed the prognostic impact on stroke and CVD.

**Results:** There was a significant negative correlation between baPWV and GFR ( $P < 0.0001$ ,  $r = 0.256$ ). The baPWV with CKD ( $n = 287$ ;  $1654 \pm 331$  cm/sec) was significantly higher than that without CKD ( $n = 93$ ;  $1771 \pm 333$  cm/sec). By Kaplan-Meier analysis, highest quartile of baPWV was the prognostic impact of stroke ( $p = 0.0062$ ) but not CKD ( $p = 0.3947$ ). The incidence of stroke and CVD did not correlated with baPWV ( $p = 0.0912$ ) or CKD ( $p = 0.1381$ ). When we classified into 4 groups; high PWV + CKD, high PWV + non CKD, low PWV + CKD and low PWV + non CKD, high PWV + CKD showed significantly higher prognostic impact of stroke and CVD.

**Conclusion:** Our study indicated that higher level of baPWV and the existence of CKD might be a risk factor of stroke and CVD in hypertension.

## 7.

### THE VALUE OF PULSE WAVE VELOCITY AS AN INDEX FOR THE PREDICTION OF CORONARY ATHEROSCLEROSIS

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**Background:** Arterial stiffness has been known as an independent contributory factor for coronary artery disease (CAD). Pulse wave velocity (PWV) is widely accepted as a simple non-invasive measure of arterial stiffness. The aim of our study was to test whether abnormal PWV could identify patients with significant CAD

**Methods:** We enrolled 174 consecutive patients who were referred for evaluation of suspected CAD and underwent PWV measurement and cardiac CT for calcium scoring. Age-matched normative data was used to define

subgroups with normal or abnormal PWV. The severity of CAD was categorized based on the coronary artery calcium score (CACS) and the number of obstructive CAD was also defined in patients who underwent subsequent invasive coronary angiogram.

**Results:** Brachial-ankle PWV (baPWV) was correlated with  $\ln(\text{CACS} + 1)$  and the number of obstructive CAD ( $p < 0.05$ ). However, after adjustment for age, baPWV did no longer correlate with them. Furthermore, abnormal baPWV were neither sensitive nor specific index for detection of moderate to severe coronary calcification (CACS  $\geq 700$ , or  $\geq 75$ th percentile), and the presence of obstructive CAD (sensitivity: 0.61, 0.62 and 0.55; specificity: 0.56, 0.63 and 0.70, respectively).

**Conclusion:** Our findings suggest that PWV was associated with the severity of CAD, however, which may primarily attributed to common risk factors such as age. Furthermore, abnormal PWV failed to predict significant CAD. Therefore, PWV may be of limited value in identifying patients at increased risk of cardiovascular events.

## 8.

### USEFULNESS OF BRACHIAL-ANKLE AND CAROTID-FEMORAL PULSE WAVE VELOCITY AS PREDICTIVE VALUES OF CARDIOVASCULAR EVENTS

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**Background:** The measurement of carotid-femoral pulse wave velocity (cfPWV) is useful to predict stroke and cardiovascular events in hypertensive patients as our previous cohort study Non-invasive Atherosclerotic evaluation in Hypertension (NOAH) study. As the cfPWV is useful, but not easy to measure, it couldn't be suitable for a practical use. Therefore we evaluated the usefulness of brachial-ankle PWV (baPWV) as a predicting factor of cardiovascular events, which was measured by widely-used equipment formPWV/ABI (Colin Co. Ltd.), compared with cfPWV.

**Methods:** We designed this study as a part of NOAH study. We selected 414 outpatients (male/female = 242/172, mean age =  $61.2 \pm 12.0$  y.o.) from participants of NOAH study ( $n = 813$  with essential hypertension), who were simultaneously undergone baPWV and cfPWV measured by AT-form, and their prognoses were followed by questionnaire or medical records. Mean follow-up period was  $43.0 \pm 17.2$  months. We set stroke and/or cardiovascular disease (CVD) as primary endpoint, and stroke, CVD, coronary artery disease (CAD) and mortality as secondary endpoint. During this follow-up period, 36 primary endpoints, 18 brain attacks, 19 heart diseases, 15 CADs and 10 deaths were recorded.

**Results:** The baPWV were strongly correlated with cfPWV (regression analysis;  $r = 0.580$ ). Patients were equally divided into 4 groups by either baPWV or cfPWV and evaluated the prognostic impact by Kaplan-Meier analysis (Log-rank test). For primary endpoint, baPWV and cfPWV showed significant distributions ( $p = 0.0268$  and  $0.0002$ , respectively). The baPWV did not show significant distribution for CVD, CAD, and mortality, but only for stroke ( $p = 0.0015$ ). On the other hand, cfPWV showed significant distribution for CVD, stroke ( $p = 0.0094$  and  $0.0338$ , respectively), but neither for CAD nor mortality. By Cox proportional hazard model adjusted with confounders; age, sex, blood pressure, serum creatinine, diabetes and dyslipidemia, only cfPWV was adopted as predictive factor, but not baPWV.

**Conclusion:** Although a further large scale multicenter trial is necessary, measurement of cfPWV may be better to predict cardiovascular event, but baPWV also can be a useful screening marker and predictor of future cardiovascular event.

## 9.

### HMG-COA REDUCTASE INHIBITOR IMPROVES ENDOTHELIAL DYSFUNCTION IN SPONTANEOUS HYPERTENSIVE RATS VIA DOWN-REGULATION OF CAVEOLIN-1 AND ACTIVATION OF ENOS

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Hypertension is associated with endothelial dysfunction and increased cardiovascular risk. Caveolin-1 regulates nitric oxide (NO) signaling by modulating endothelial nitric oxide synthase (eNOS). The purpose of this study was to examine whether HMG-CoA reductase inhibitor improves impaired endothelial function of the aorta in spontaneous hypertensive rat (SHR) and to determine the underlying mechanisms involved.

Eight-week-old male SHR were assigned to either a control group (CON,  $n = 11$ ) or a rosuvastatin group (ROS,  $n = 12$ ), rosuvastatin (10 mg/kg/day) administered for eight weeks. Abdominal aortic rings were prepared and responses to acetylcholine ( $10^{-9}$ – $10^{-4}$  M) were determined in vitro. To evaluate