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18. ARTERIAL STIFFNESS IN GERIATRIC MEDICINE

Jeong Bae Park, Kee Sik Kim, Ho Joong Youn, Sang Hong Baek, Kyu Hyung Ryu, Shung Chull Chae, Jang Ho Bae, Jang Ho Bae, Chang Gyu Park, Moo Yong Rhee, Soo Yeun Choi, Dong Ju Choi, Sung Ha Park, Se Joong Rim, Dong Gu Shin, Gae Hoon Kim, Jong Chun Park, Won Ho Kim, Wang Seong Ryu, Kyung Ho Youn, Jin Won Jeong, Young Moo Ro, Young Dae Kim, Dong Soo Kim, Myeng Chan Cho, Byung Hee Oh, Nam Sik Chung

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clinical practice is unknown. This study aimed to test the value of central BP as a management tool for physicians treating patients with essential hypertension.

Methods: Patients with hypertension ($n = 84$; 61 ± 8 years) were randomized to 12 months of treatment decisions guided by usual care (UC, $n = 39$) or, in addition, by central BP (CBP, $n = 45$; based on age and gender-specific normal central systolic BP [SBP] values). Titration recommendations were provided to each patient's general practitioner, as well as the patient themselves. Relevant clinical information (eg left ventricular [LV] mass, blood biochemistry and symptoms) were considered when making titration recommendations in all patients. Central BP was estimated by SphygmoCor 8.0. Primary outcome measures were; 1) change in LV mass 2) use of medication and 3) quality of life. We hypothesized that there will be no significant difference in LV mass between groups (study powered for equivalence). However, it was expected that there will be significantly less use of medication and improved quality of life in the CBP group because more appropriate titration choices will be made to maintain normal central SBP.

Results: Baseline LV mass index (CBP, 27.6 ± 5.7 v UC, 29.7 ± 5.9 g/m^{2.7}), brachial SBP (CBP, 130 ± 14 v UC 130 ± 14 mmHg) and central SBP (CBP, 118 ± 13 v UC 118 ± 15 mmHg) were similar between groups ($P > 0.05$ for all). However, in the CBP group, 33% ($n = 15$) received a recommendation to reduce medication, whilst there were 3% ($n = 1$) in the UC group ($P = 0.001$). Moreover, 8 CBP patients were recommended to cease antihypertensive medication but maintained normal BP, indicating that they may have been incorrectly diagnosed with hypertension and unnecessarily taking medication based on brachial BP assessments.

Conclusion: Therapeutic decisions based on CBP are different from those based on standard BP. Follow up data and final results ($N = 312$) are expected in 2011.

15.

OPEN LABEL, RANDOMIZED, ACTIVE DRUG COMPARATIVE, PARALLEL GROUP, MULTI-CENTER, PHASE IV STUDY TO COMPARE THE EFFECT OF BENIDIPINE AND LOSARTAN ON ARTERIAL STIFFNESS AND CENTRAL BLOOD PRESSURE IN MILD TO MODERATE ESSENTIAL HYPERTENSIVE PATIENTS (BELASCO TRIAL)

Sang-Hyun Ihm, Shung Chull Chae, Do Sun Lim, Kee Sik Kim, Dong Ju Choi, Jong Won Ha, Dong Soo Kim, Kye Hun Kim, Myeong Chan Cho, Hui Kyung Jeon, Sang Hong Baek., The BELASCO trial investigators, Korea

Objectives: The purpose of this study was to compare the effect of benidipine (calcium channel blocker) and losartan (angiotensin receptor blocker) on arterial stiffness and central blood pressure (BP) in mild to moderate essential hypertensives.

Methods and Results: This 24 weeks, multi-center, open label, randomized, active drug comparative, parallel group study was designed as a noninferior study. Eligible patients ($n = 200$) were randomly assigned to receive benidipine ($n = 101$) or losartan ($n = 99$). Radial artery applanation tonometry and pulse wave analysis were used to derive central aortic pressure, pulse wave velocity (PWV) and augmentation index (Alx). No significant differences were found in the mean changes in central BP between 2 groups [-16.66 (systolic BP)/-10.70 (diastolic BP) mmHg in the benidipine group and -18.44/-11.79 mmHg in the losartan group; $P = NS$]. The mean changes in central, brachial and femoral PWV were -0.06, +0.06 and -0.51 m/sec for the benidipine group and -0.02, -0.15 and -0.06 m/s for losartan group (respectively; $P = NS$). No significant differences were found in the mean changes in Alx between two groups [-5.46 in the benidipine group and -4.22 in the losartan group; $P = NS$].

Conclusion: The reduction in central BP after 24 weeks of benidipine was non-inferior to that of losartan in mild to moderate essential hypertensives. There were no significant difference between two drugs in aspect of PWV and Alx. Both drugs had similar central BP lowering effect and affected similarly arterial stiffness.

16.

IS IT POSSIBLE TO PREDICT CORONARY ARTERY STENOSIS BASED ON CAROTID ARTERY INTIMA MEDIA THICKNESS IN DIABETIC PATIENTS

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Background: Noninvasive measurement of carotid artery intima media thickness (IMT) has been widely used as a surrogate marker of coronary atherosclerosis. However, evidence for the clinical implications of increased carotid IMT in diabetic patients is not well established. The aim of this study

was to determine if coronary artery disease (CAD) can be predicted based on carotid IMT, intimal, and medial thickness.

Methods: A total of 569 type 2 diabetic patients (male:female = 311:258, mean age = 63 ± 9 years) who underwent coronary angiography were divided into two groups. Group 1 was composed of patients with no significant CAD ($n = 105$, male% = 37.1%, mean age = 61 ± 10 years) on angiography. Group 2 was composed of patients with significant CAD ($n = 464$, male% = 58.6%, mean age = 64 ± 9 years). Carotid intimal, medial thickness, and IMT were compared between the two groups. Sensitivity and specificity for detecting significant CAD by carotid ultrasound were evaluated.

Results: There were significant differences in the right maximal IMT, mean IMT, and medial thickness for both carotid arteries. However, there were no significant differences in the left maximal IMT and intimal thickness (Table). A right IMT of 1.13 mm and a left IMT of 1.19 mm had 94% sensitivity and 80% specificity for CAD, respectively. A right medial thickness of 0.99 mm and a left medial thickness of 1.03 mm had 100% sensitivity and 86% specificity. **Conclusion:** Carotid medial thickness and IMT were useful as screening methods for detecting significant CAD in patients with diabetes.

17.

CAROTID INTIMA-MEDIA THICKNESS IN A LARGE COHORT STUDY AND REALLY NORMAL SUBJECTS

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Background: Carotid intima-media thickness (IMT) has been widely used as a surrogate of early atherosclerosis. However, the characteristics of patients in cohort-based studies of carotid IMT are very heterogeneous. We evaluated the carotid intima, media, and IMT in really normal (RN) subjects who had no coronary artery disease or other coronary risk factors.

Methods: Among the 3041 patients (male:female = 1819:1222, mean age = 61 ± 11 years) who have undergone carotid ultrasound at our institution since 2003, 124 patients (male:female = 84:40, mean age 54 ± 12 years) who had no coronary artery stenosis confirmed by coronary angiography and no diabetes, hypertension, hypercholesterolemia, or renal dysfunction were enrolled in this study. The carotid intima, media, and IMT were compared between the general population group and the RN subjects.

Results: Right maximal, mean IMT, intimal thickness, and medial thickness were 0.93 ± 0.25 , 0.78 ± 0.16 , 0.24 ± 0.36 , and 0.51 ± 0.15 mm in RN subjects, respectively. The left maximal, mean IMT, intimal thickness, and medial thickness were 0.92 ± 0.33 , 0.79 ± 0.24 , 0.23 ± 0.03 , and 0.55 ± 0.24 mm, respectively. The maximal and mean IMT and medial thickness of both carotid arteries were significantly higher in subjects from the general population.

Conclusion: In a large Korean cohort for carotid IMT, the carotid medial thickness and IMT were significantly related to atherosclerotic risk factors. We must be careful in defining the normal reference values of carotid IMT due to heterogeneous characteristics in the population.

18.

ARTERIAL STIFFNESS IN GERIATRIC MEDICINE

Jeong Bae Park, Kee Sik Kim, Ho Joong Youn, Sang Hong Baek, Kyu Hyung Ryu, Shung Chull Chae, Jang Ho Bae, Jang Ho Bae, Chang Gyu Park, Moo Yong Rhee, Soo Yeun Choi, Dong Ju Choi, Sung Ha Park, Se Joong Rim, Dong Gu Shin, Gae Hoon Kim, Jong Chun Park, Won Ho Kim, Wang Seong Ryu, Kyung Ho Youn, Jin Won Jeong, Young Moo Ro, Young Dae Kim, Dong Soo Kim, Myeong Chan Cho, Byung Hee Oh, Nam Sik Chung., on behalf of Korean Vascular Research Working Group
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Background: Aging exerts a number of deleterious changes in the cardiovascular system, and, in particular, on the large arteries. Previous studies have suggested that augmentation index (Aix) and aortic pulse wave velocity (aPWV) increase linearly with age, yet epidemiological data concerning arterial stiffness suggest that large artery stiffening predominantly occurs later in life. Therefore, the aim of the study was to test the hypothesis; 1) age-related changes in Aix are more prominent in younger individuals, whereas changes in aortic stiffness per se are more marked in older individuals, 2) whether these changes are similar between Caucasians and Koreans.

Methods: 1,188 subjects aged 17 to 87 years (mean age of 45.5 years and female 52%) were included and all were apparently healthy and free of any medication for hypertension, diabetes and dyslipidemia. Aix and aPWV were measured by pp-1000 and Gaon 21 (both Hanbyul Medtech, Korea). **Results:** Women showed significantly higher central Aix (15.4 vs. 22.5 of men, $p < 0.001$) even with lower peripheral pressure ($117/72$ vs. $126/78$ of men,

both $p < 0.001$), but there was no difference in aPWV between sexes. Peripheral and central Alx, and aortic PWV all increased significantly with age; however, the age-related changes in Alx ($r = 0.333$, $p < 0.001$) and aortic PWV ($r = 0.194$, $p < 0.001$) were non-linear, with Alx increasing more in younger individuals, whereas the changes in PWV were more prominent in older individuals, which were similar to the changes in Caucasians (The Anglo-Car-diff Collaborative Trial (ACCT)).

Conclusion: These data suggest that 1) there is sex-difference in Alx according to aging, 2) Alx might be a more sensitive marker of arterial stiffening and risk in younger individuals but aortic PWV is likely to be a better measure in older individuals.

19.

AORTIC DISTENSIBILITY IS MORE CLOSELY ASSOCIATED WITH CAROTID INTIMA MEDIA THICKNESS THAN AORTIC INTIMA-MEDIA THICKNESS IN THE PATIENTS WITH ISCHEMIC STROKE

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Background: The aorta plays a central role for a modulator in whole cardiovascular system by its elasticity. If the elasticity was decreased, aortic distensibility was also decreased and stiffness index was elevated. In this study, we investigated the relationship between aortic distensibility calculated from descending thoracic aorta and intima media thickness (IMT) from aorta and carotid artery which was known as a surrogate maker for atherosclerosis and a predictor of cardiovascular events.

Methods: A total of 500 patients with acute ischemic stroke were enrolled in this study. Most of patients were performed transesophageal echocardiography for detection of embolic sources. We evaluated the association of arterial stiffness index, calculated by distensibility of descending thoracic aorta and systemic blood pressure, and aortic IMT as well as carotid IMT with age, sex, potential vascular risk factors, and cardiac function by echocardiography.

Results: Arterial stiffness index significantly correlated with IMT of descending thoracic aorta and carotid artery ($r = 0.279$, $p = 0.014$, $r = 441$, $p < 0.001$). It also correlated with age ($r = 0.410$, $p = 0.001$) and hypertension history ($r = 0.341$ $p = 0.003$). Arterial stiffness index significantly negative correlation with common carotid artery blood flow peak systolic velocity ($r = 0.248$, $p = 0.010$). A stepwise multivariate regression analysis demonstrate that arterial stiffness index was independently associated with carotid IMT ($\beta = 0.308$, $p = 0.013$), whereas aortic IMT was not an independent predictors of aortic distensibility.

Conclusion: Arterial stiffness index by using distensibility of descending thoracic aorta significantly correlates with other proven surrogate for atherosclerosis such as aortic and carotid IMT. Aortic distensibility is more closely associated with carotid IMT than aortic IMT in the Patients with Ischemic Stroke.

20.

CORRELATION OF AORTIC DISTENSIBILITY WITH CORONARY ATHEROSCLEROSIS IN ANGINA PATIENTS

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Background: Arterial stiffness is associated with an increased risk of cardiovascular disease. However, limited evidence exists on whether arterial stiffening correlates not only with cardiovascular events, but also with subclinical atherosclerotic lesions. This study aimed to provide information on arterial stiffening by the measurements of distensibility at aortic site in angina patients in whom angiographic evaluation allowed quantification of coronary atherosclerosis.

Methods: We studied 137 patients with angina admitted to our hospital for coronary angiography. The measurements of aortic distensibility were carried out in the proximal ascending aorta, 3 cm from the origin of the aorta by a Echocardiography System (Acuson). Patients were classified into three groups according to the angiographic findings: nonsignificant coronary lesions (lumen narrowing $< 50\%$, group A); one (group B); and two or three (group C) coronary vessels.

Results: Age, previous cardiac disease and interventions were progressively greater or more common from group A to C. Other risk factors (serum cholesterol, smoking, history of hypertension) did not differ between the

three groups. Aortic distensibility decreased progressively from group A to C (2.41 ± 1.77 , 1.76 ± 1.33 , 1.62 ± 1.09 cm² dyne⁻¹ 10-6) The decrease in aortic distensibility from group A to group B and C remained significant after adjustment for variables that showed between-group differences such as gender, age, and systolic pressure and showed it to be a specific marker of coronary atherosclerosis.

Conclusion: In patients with angina, aortic distensibility is related to the severity of coronary atherosclerosis. Larger elastic artery (aortic) stiffening can be considered as a marker of the severity of coronary atherosclerosis, providing non-invasive information.

21.

THE ASSOCIATION OF BETWEEN CORONARY SPASM AND B-TYPE NATRIURETIC PEPTIDE AND PULSE WAVE VELOCITY

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Background: Coronary spasm cause transient LV dysfunction and consequently may increase BNP by chance. However, the correlation between coronary spasm and BNP has not been verified. We investigated the association between coronary spasm and BNP and pulse wave velocity (PWV) in patients with preserved LV function.

Methods: A patients with chest pain who have ejection fraction $>50\%$ underwent both diagnostic coronary angiography with acetylcholine provocation and NT-proBNP measurement simultaneously were enrolled for the study. PWV were done in all patients. Significant coronary artery spasm was defined as focal ($>70\%$) or diffuse severe transient luminal narrowing ($>90\%$) with/without chest pain or ST-T change of ECG.

Results: Among total 1,342 patients, 793 patients with heart failure, arrhythmia, CAD or VHD were excluded and 549 patients were enrolled. Thirty five percent (192/549) of enrolled subjects showed positive result at acetylcholine provocation test. Baseline characteristics were well balanced between the spasm group and control group. In the univariate analysis, the BNP levels of spasm group were lower than control group (146 ± 363 pg/mL vs. 197 ± 532 pg/mL, $P = 0.050$). But in the multivariate analysis, there was no significant difference of BNP between two groups. Also there is no difference of PWV value between the groups.

Conclusion: There is no significant relationship between BNP, PWV and vasospastic angina. These finding suggest that vasospastic angina with normal left ventricular systolic function is not associated with BNP or PWV.

22.

BP VARIABILITY AS WELL AS MEAN BP FROM AMBULATORY BLOOD PRESSURE AND HOME BLOOD PRESSURE CORRELATES WELL WITH TARGET ORGAN DAMAGE IN UNTREATED HYPERTENSIVE PATIENTS

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Background: We sought to assess the relation of ambulatory blood pressure (ABP) measurement and home blood pressure (HBP) measurement with target organ damage using BP variability (BPV) as well as mean BP in untreated hypertensive patients.

Methods: Seventy-nine untreated patients with hypertension (men : 52 and female : 27, mean age, 47.5 ± 13.1 years) underwent measurements of ABP, HBP and OBP. The ABP was recorded for 24hrs, HBP was measured for 1week, and OBP was measured at least in two visits. All BP measurements were taken using automatic BP measuring device. The parameters indicating target organ damage were the left-ventricular mass index (LVMI) by transthoracic echocardiography, urinary albumin excretion rate (AER), carotid-femoral pulse-wave velocity (PWV), and carotid intima-media thickness (IMT).

Results: The LVMI was significantly correlated with systolic HBP, systolic/diastolic 24hrs ABP, and systolic ABP variability (ABPV), but was not correlated with OBP. The AER, PWV and IMT were significantly correlated with systolic HBP. In a binary logistic regression analysis, systolic HBP was only predictor of LVMI ($p = 0.003$) and systolic HBP, systolic 24hrs ABP and systolic HBPV were significant predictors of PWV (HBP; $p = 0.001$, ABP; $p = 0.027$, HBPV; $p = 0.036$). Also, systolic HBP was independent predictor of AER and PWV by multiple regression analysis (AER; $p = 0.004$, PWV; $p = 0.009$).

Conclusion: Our data suggest that ABP and HBP measurements are closely related to hypertension-induced target organ damage as assessed by LVMI, AER and PWV. Therefore, ABP and HBP measurements using BP variability as well as mean BP may give additive information for the prediction of cardiovascular target organ damage in hypertension.