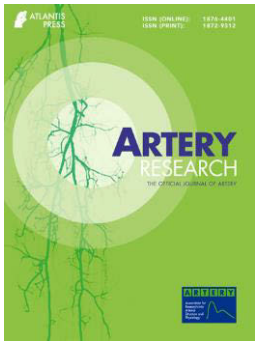

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14. USING CENTRAL BLOOD PRESSURE TO GUIDE THERAPY IN HYPERTENSION: BP GUIDE STUDY DESIGN AND INITIAL FINDINGS

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the potential role of NO and caveolin-1, we examined the plasma activity of NOx, eNOS, phosphorylated-eNOS and expression of caveolin-1. The relaxation in response to acetylcholine was significantly enhanced in ROS compared to CON. Expression of eNOS RNA was unchanged, whereas NOx level and phosphorylated-eNOS at serine-1177 was increased accompanied with depressed level of caveolin-1 in ROS.
We conclude that HMG-CoA reductase inhibitor can improve impaired endothelial dysfunction in SHR, and its underlying mechanisms are associated with increased NO production. Furthermore, HMG-CoA reductase inhibitor can activate the eNOS by phosphorylation related to decreased caveolin-1 abundance. These results imply the therapeutic strategies for the high blood pressure-associated endothelial dysfunction through modifying caveolin status.

10.
THE USEFULNESS OF ESTIMATED CAROTID SYSTOLIC BLOOD PRESSURE USING FORM PWV/ABI IN BLOOD PRESSURE LOWERING THERAPY

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Background: Central systolic blood pressure (central-SBP) can be estimated noninvasively and antihypertensive drugs may exert different effects on central-SBP. We investigated the usefulness of carotid systolic blood pressure (carotid-SBP) estimated by form PWV/ABI in blood pressure lowering therapy.
Methods: We evaluated pulse wave velocity, carotid augmentation index (AI), carotid-SBP in 329 patients (301 hypertensives, 172 men, 65 ± 12 yeasrs old) using form PWV/ABI. Antihypertensive drugs were evaluated in those patients.
Results: Mean brachial blood pressure (b-SBP) was 136 ± 21 mmHg and carotid-SBP was 147 ± 25 mmHg. We determined delta-SBP as carotid-SBP - b-SBP, and we divided the subjects into group A (delta-SBP $<$ 0mmHg) and group B (delta-SBP $>$ 0mmHg). The number of group A was 22 patients and that of group B was 307 patients. There were no differences of mean age between these two groups. Although b-SBP of group A (137 ± 21 mmHg) was similar to that of group B (136 ± 21 mmHg), b-diastolic BP of group A (83 ± 12mmHg) was different from that of group B (77 ± 13 mmHg, $p = 0.0456$). Carotid AI of group A ($13 \pm 14\%$) is lower than that of group B ($23 \pm 18\%$, $p = 0.0160$). The evaluation of the effect of antihypertensive agents showed that Ca antagonists, angiotensin receptor blockers, angiotensin converting enzyme inhibitors and diuretics did not affect delta-SBP significantly. However, those who had β blockers or blockers showed higher delta-SBP compared to those who without these drugs.
Conclusion: Estimation of carotid-SBP using form PWV/ABI is useful for the evaluation of the effects of antihypertensive drugs on brachial and central BPs.

11.
THE EFFECT OF LONG-TERM ADMINISTRATION OF HYDROCHLOROTHIAZIDE ON CENTRAL BLOOD PRESSURE

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Background: It's unknown wheather there is much benefit on central aortic pressure than brachial pressure while long-term administration of hydrochlorothiazide in patients with essential hypertension.
Methods: The retrograde analysis was conducted at three of the participating centers in the Felodipine Event Reduction (FEVER) study. 76 of 129 patients in placebo group, who kept hydrochlorothiazide monotherapy over 36 months period, and took pulse wave recording at randomization, 12 month, 24 month and 36 month, were included into the final analysis. Radial artery pressure waveforms were measured with applanation tonometry, and convolved into the ascending aortic pressure waveforms, using the FDA-approved SphygmoCor system. The analysed parameters in aortic pressure waveform included first peak pressure, secondary peak pressure, diastolic pressure, pulse pressure, augmentation and augmentation index.
Results: In comparison with baseline, there were substantial falls ($P < 0.001$) in brachial SP/DP and in central aortic SP/DP with no difference, slight falls ($P < 0.05$) in aortic augmentation, and no significant falls ($P > 0.05$) in augmentation index and heart rate.
Conclusion: Long-term administration of hydrochlorothiazide resulted in the similar reduction of both brachial pressure and central aortic pressure without the change of augmentation index, which could exclude definite benefit on central aortic pressure than brachial pressure.

12.
THE EFFECT OF ORALLY SINGLE DOSE OF SLOW-RELEASE ISOSORBIDE-5-MONONITRATE ON CENTRAL BLOOD PRESSURE IN HEALTHY VOLUNTEERS

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Background: The cuff sphygmomanometer failed to show consistent alteration in brachial blood pressure with slow-release isosorbide-5-mononitrate(IS-5-MN), even though the drug proved very effective in relieving angina pectoris.Sofar, the effect of orally single dose of slow-release isosorbide-5-mononitrate on central blood pressure is not known.
Methods: Using self-control study before and after treatment in a total of 22 healthy volunteers, the effects of slow-release IS-5-MN 60 mg in single dose form were assessed over a tweenty four hour period through analysis of the radial pulse waveform, calibrated against conventional cuff sphygmomanometry. Ascending aortic pressure waveforms were generated from the radial waves, using a validated generalised transfer function. The concentration of 5-ISMN were measured by HPLC-MS.
Results: After taken the drug, the concentration of 5-ISMN was rapidly increased to peak at 4 h, then linearly decreased to 187.6 ng/ml at 24 h. There was no consistent change in heart rate or brachial pressures except for a decrease in systolic pressures and a increase in heart rate ($p < 0.01$) at 2-6 hour. In contrast, there were substantial and significant decreases in aortic systolic pressures, augmented pressures, augmentation index and ejection duration ($p < 0.001$) at 0.5 h-16 h.
Conclusion: Pulse waveform analysis exposes concentration dependent effects of 5-ISMN on the aortic waveform, suggesting muscular conduit arterial dilatation with reduced wave reflection and venous dilatation with reduced ejection duration at the low and intermediate concentration, arteriolar dilatation and decreased peripheral resistance at the high concentration.

13.
THE LONG-TERM EFFECT BETWEEN CO-ADMINISTRATION OF SIMVASTATIN AND EZETIMIBE AND ATORVASTATIN ON CENTRAL PULSE WAVE VELOCITY IN ADULTS WITH HYPERCHOLESTEROLEMIA

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Daegu Catholic University Medical Center

Background: The various statin might contribute to a change in arterial stiffness independent of the cholesterol-lowering effects of statin therapy. The aim of this study was to compare the short-term effect between co-administration of simvastatin and ezetimibe (vytorin) and atorvastatin (lipitor) on pulse wave velocity (PWV).
Methods: We enrolled 27 patients with hypercholesterolemia (Total cholesterol $>$ 200 mg/dL). The patients were randomly divided into two groups according to statin (vytorin: 13 patients, lipitor : 14 patients). They were treated vytorin 10/20 mg and Lipitor 20 mg for 1 month, then vytorin 10/10 mg and Lipitor 10 mg for 5 months. We measured the carotid-femoral PWV (cfPWV), and lipid profile at baseline, 1 month, and 6 months after treatment with the statin.
Results: The total cholesterol and LDL levels in both groups were significantly decreased 1 month later, and they were slightly increased 6 months later. In addition, the change of total cholesterol was not different in both groups. The central PWV(cfPWV) in lipitor group was significantly decreased compared with those in vytorin group after 6 months (-0.61 ± 1.23, 0.24 ± 1.24 m/sec, respectively).
Conclusion: Although co-administration of simvastatin and ezetimibe for 6 months might show similar lipid lowering effect compared with atorvastatin, only atorvastatin might show pleiotrophic effect for long-term treatment in hypercholesterolemia.

14.
USING CENTRAL BLOOD PRESSURE TO GUIDE THERAPY IN HYPERTENSION: BP GUIDE STUDY DESIGN AND INITIAL FINDINGS

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Background: Estimated central blood pressure (BP) predicts cardiovascular mortality independent of brachial BP, but whether central BP may be useful in

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 randomised 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)

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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 (AIx). 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 AIx 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 different between two drugs in aspect of PWV and AIx. 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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The Catholic University of Korea

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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The Catholic University of Korea

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, Myeng Chan Cho, Byung Hee Oh, Nam Sik Chung., on behalf of Korean Vascular Research Working Group
Cheil General Hospital, Kwandong University College of Medicine

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,