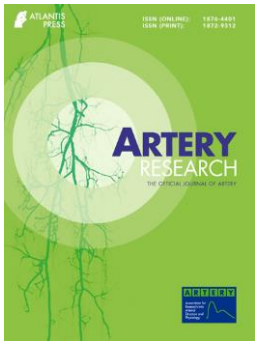

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P3.20: CLINICAL SIGNIFICANCE OF AMBULATORY ARTERIAL STIFFNESS INDEX (AASI) IN YOUNG STAGE 1 HYPERTENSIVE' S

F. Saladini, E. Benetti, C. Fania, L. Mos, P. Ballerini, E. Cozzutti, G. Garavelli, S. Cozzio, E. Casiglia, P. Palatini

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1.269, p=0.038). Male, diabetes, hypertension, low HDL-C and smoking were also significant independent predictors of events.
Conclusion: CAVI is an independent predictor of cardiovascular events in subjects with coronary risks.

P3.17
EFFECT OF HYPERTENSION ON ARTERIAL STIFFNESS IN GHANAIAN SUBJECTS WITH TYPE 2 DIABETES

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Background: Hypertension exacerbates cardiovascular disease in type 2 diabetes (T2DM) but the ACCORD trial suggested limited impact on CVS events by hypertensive treatment. Our hypothesis is that arterial stiffness, measured as aortic pulse wave velocity (PWV) may underlie these events. Few data exist on arterial stiffness in hypertensive diabetes patients in sub-Saharan Africa, where the two conditions are becoming epidemic. We compared indices of arterial stiffness in T2DM subjects with (T2DM+HT), without (T2DM-HT) hypertension and normotensive non-diabetes (NDM).
Methods: Forty eight T2DM+HT, 45 T2DM-HT and 34 NDM volunteers (as screened by OGTT), between the ages of 40-70 years, were randomly recruited. Weight, height and waist circumference (WC) were measured. Indices of arterial stiffness, pulse wave velocity (PWV), aortic systolic blood pressure (aSBP), and aortic augmentation index(aAIx) were measured with Arteriograph (Tensiomed, Hungary) and Cardio-Ankle Vascular Index (CAVI) with Vasera 1500 (Fukuda-Denshi, Tokyo, Japan) in supine subjects after 10 minutes rest in a temperature controlled room.
Results: In a univariate analysis, after adjusting for gender, age in decade, BMI and waist circumference, mean values of CAVI (8.43±1.31 vs. 7.4±1.05 vs. 7.00±0.87; p<0.001), PWV (9.16±1.04 vs. 7.98±1.28 vs. 7.64±1.42; p<0.001), aSBP (153.94±25.62 vs. 115.72±11.11 vs. 117.06±11.11; p<0.001) and aAIx (28.53±12.43 vs. 19.18±11.47 vs. 26.21±14.08; p=0.026) were higher in T2DM+HT than T2DM-HT, which was also higher than NDM. Contrast analysis showed no significant difference between aSBP between T2DM-HT and NDM.
Conclusion: Hypertension increases arterial stiffness in T2DM subjects in Ghana.

P3.18
ENDOTHELIAL FUNCTION BUT NOT IN INTIMA-MEDIA THICKNESS RELATES TO RENIN STATUS IN A MULTI-ETHNIC GROUP OF YOUNG HEALTHY ADULTS

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Subjects of African and African-Caribbean ethnicity have been reported to have lower plasma renin activity (PRA), decreased endothelium-dependent vasomotor function and increased intima-media thickening relative to white European subjects. We explored whether vascular structure and function might be associated with renin status, since both may be influenced by endothelium-derived nitric oxide (NO). Flow mediated dilation (FMD, a measure of endothelium-derived NO) of the brachial artery and common carotid intima-media thickness (CIMT) were measured using high resolution ultrasound in a multi-ethnic group of 143 subjects (mean ± SD 30±10 years) including 84 black subjects of African or African-Caribbean self defined ethnicity; the remainder were of white European ethnicity. Subjects were additionally characterized by anthropometric and biochemical measurements including plasma renin activity (PRA) and underwent ambulatory blood pressure monitoring. PRA was lower (0.6 ± 0.67 vs. 0.9 ± 0.6 ng ml^{-1} hr^{-1}, medians ± IQR, P< 0.092) and IMT greater (0.47± 0.09 vs. 0.43 ± 0.08 mm) in black compared to white subjects. FMD tended to be lower in black compared to white subjects but the difference was not significant. FMD was independently correlated with PRA after adjustment for age, ethnicity, sex and blood pressure (standardized regression coefficient 0.31, P<0.005). However, IMT was not significantly correlated with FMD nor with PRA. These results suggest that availability of endothelium-derived NO is closely associated with PRA but does not explain ethnic differences in CIMT.

P3.19
AORTIC PULSE PRESSURE BETTER PREDICTS INCREASES ARTERIAL STIFFNESS COMPARED TO BRACHIAL AND AMBULATORY MEASUREMENTS

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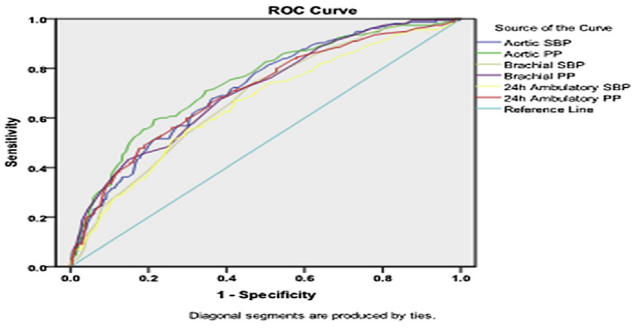
Objectives: Hypertension is associated with increased arterial stiffness, which is an independent predictor of cardiovascular risk. Aortic systolic blood pressure (SBP) and/or pulse pressure (PP) better predicts cardiovascular events than peripheral blood pressure. The present study compared the discriminative ability for increased arterial stiffness of aortic BP with ambulatory peripheral BP, with reference to office brachial SBP or PP in never treated hypertensives.
Methods: We enrolled 619 consecutive essential hypertensives (mean age 52.2±12.0 years, 325 men). Arterial stiffness was determined with carotid-femoral pulse wave velocity (PWV) using the Complior® device. Aortic pressures were measured using the Sphygmocor® device and 24h ambulatory SBP and PP were obtained from 24h ambulatory blood pressure monitoring. We employed dichotomous outcome variable (PWV≥75th percentile [8.55 m/s]). Receiver operating characteristic (ROC) curves were generated to evaluate the ability of the pressures to discriminate subjects with and without significant arterial stiffness (PWV ≥75th percentile [8.55 m/s]).
Results: All different types of blood pressure significantly discriminated subjects with significant arterial stiffness (all p<0.001). Aortic pulse pressure had the highest area under the curve (AUC=0.741) and 24h ambulatory SBP the lowest (AUC=0.655). (Figure, Table).
Conclusions: PP is more valuable than SBP pressure in the prediction of increased arterial stiffness. Moreover, aortic PP may better predict increased arterial stiffness than brachial or ambulatory BP measurements.

Variable	AUC	95% CI
Aortic pulse pressure	0.741*†‡	0.696—0.786
Aortic systolic blood pressure	0.717*†	0.672—0.762
Brachial pulse pressure	0.710*	0.664—0.756
Brachial systolic blood pressure	0.681*¶	0.634—0.727
24h ambulatory pulse pressure	0.705*†	0.657—0.753
24h ambulatory systolic blood pressure	0.655*#¶§	0.605—0.705

* P<0.001 compared to the null hypothesis that the AUC is 0.5 and the examined variables cannot discriminate subjects with low or high pulse wave velocity values.† P<0.05 compared to 24h ambulatory systolic blood pressure# P<0.05 compared to 24h ambulatory pulse pressure.
‡ P<0.05 compared to brachial systolic blood pressure.
¶ P<0.05 compared to aortic pulse pressure.
§ P<0.05 compared to aortic systolic blood pressure.



P3.20
CLINICAL SIGNIFICANCE OF AMBULATORY ARTERIAL STIFFNESS INDEX (AASI) IN YOUNG STAGE 1 HYPERTENSIVE' S

F. Saladini [1], E. Benetti [1], C. Fania [1], L. Mos [2], P. Ballerini [3], E. Cozzutti [3], G. Garavelli [4], S. Cozzio [5], E. Casiglia [1], P. Palatini [1]

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Objective: The aim of the study was to examine the relationship between AASI and age in a cohort of stage I hypertensives < 50 years of age and to investigate its predictive capacity for future established hypertension.
Methods: We studied 1157 subjects from the HARVEST study (mean follow-up 5.9 years). AASI and 24-h pulse pressure (PP) were calculated from 24-h ambulatory recordings. The predictive value of AASI for incident hypertension was evaluated with Cox regression analysis adjusting for age, sex, mean 24-h blood pressure (BP).
Results: Baseline office BP was 145.5±10.4/93.6±5.6 mmHg, 24-h PP was 49.6±11.2 mmHg, AASI was 0.56±0.2. AASI was correlated with 24-h PP ($r=0.41$, $p<0.0001$), and showed a U-shaped correlation with age. In our population age was inversely correlated with 24-h PP ($r=-0.32$, $p<0.0001$). The highest sex-adjusted AASI values were found in the two bottom and the top age deciles (mean±SEM, 0.62±0.02, 0.61±0.02, and 0.60±0.02, respectively). During follow-up 55.7% of the subjects developed established hypertension needing pharmacological treatment. In a multivariate Cox analysis, AASI showed a negative predictive value for the development of future hypertension ($p<0.001$). Participants in the middle AASI tertile (H.R. and 95%CI: 0.81, 0.67-0.97, $p=0.03$) and top tertile (0.71, 0.57-0.87, $p=0.001$) had a lower risk of developing hypertension compared to subjects in the bottom tertile.
Conclusions: AASI shows a U-shaped relationship with age in a population of young-to-middle-age hypertensives and it may be even a predictor of better outcome. So, the clinical significance of AASI in hypertension appears to be heavily dependent on age.

P3.21
CENTRAL HEMODYNAMICS PARAMETERS IN BLACK HYPERTENSIVE PATIENTS BORN AND LIVING IN SUB-SAHARAN AFRICA

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Background: Few studies assessed arterial stiffness in Black hypertensive patients Born and living in sub-Saharan Africa, where cardiovascular disease reaches epidemic proportions.
Methods: The Newer versus Older Antihypertensive Agents in African Hypertensive Patients (NOAAH) trial had recruited native African patients to compare the efficacy of various Antihypertensive drugs given once daily as single-pill combinations. Two centers engaged in Pulse wave analysis and measured carotid femoral pulse wave velocity (PWV). Statistical Methods included single and multiple linear regressions.
Results: Of 172 patients screened, 116 entered the ancillary study on central hemodynamics (51.3% women; mean age 52.7 years; untreated blood pressure 147.6/87.1 mm Hg).the augmentation indexes were higher ($p<0.0001$) in women than men, both peripherally (pAI, 11.1 vs.10.6%) and centrally (cAI, 39.0 vs. 28.0%). PWV (8.91 m/s) and central pulse pressure (cPP, 48.7 mm Hg) were similar ($p>0.844$) in both sexes. pAI and cAI increased with female sex and mean arterial pressure, but decreased with heart rate and body mass index. cPP increased with age and mean arterial pressure. PWV increased with age and mean arterial pressure. Patients with measurements above the age-specific thresholds determined in healthy Black South Africans amounted to 0 for cAI, 1 (1.2%) for cPP, and 11 (18.3%) for PWV.
Conclusion: NOAAH patients have measures of arterial stiffness similar to those of a healthy Black reference population with determinants as reported in the literature. Our observations Highlight the potential for the prevention of irreversible arterial damage by timely treating Sub-Saharan hypertensive patients to target blood pressure levels.

P3.22
CHROMOSOME 9P21 LOCUS AND CORONARY ARTERY DISEASE — COLLABORATIVE META-ANALYSIS ON ANGIOGRAPHIC BURDEN AND MOLECULAR FUNCTION ANALYSIS

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Objective: Chromosome 9p21 variants showed robust association with coronary heart disease in genome-wide association studies, but questions remain on the mechanism. We investigated the relationship of 9p21 locus with (1) angiographic coronary artery disease (CAD) burden and progression to myocardial infarction (MI); and (2) biological function of vascular smooth muscle cell (VSMC).
Methods and results: We established a collaboration of 21 studies (33,673 patients) with information on both CAD and MI status along with 9p21 genotype. We first confirmed an association between 9p21 and CAD using angiographic ally defined cases and controls (pooled odds ratio (OR)=1.31 (95% CI 1.20-1.43) per copy of risk allele). Among subjects with angiographic CAD, random-effects model identified an association with multi-vessel CAD, compared to those with single-vessel disease (OR=1.10 (95% CI 1.04-1.17)). However, there was no significant association between 9p21 and prevalent MI when both cases and controls had underlying CAD (OR=0.99 (95% CI 0.95-1.03)).Immunohistochemical staining of human atherosclerotic plaque showed co-localization of VSMC with the cell-cycle regulator proteins $p16^{INK4a}$, $p14^{ARF}$ and $p15^{INK4b}$, which are encoded by the genes *CDKN2A* and *CDKN2B* genomically located nearby the 9p21 locus. The 9p21 risk genotype confers reduced $p15^{INK4b}$ levels ($p=3.7\times10^{-2}$) and higher VSMC content ($p=5.6\times10^{-4}$) in the plaques. We further examined the influence of 9p21 genotype on primary cultures of VSMC isolated from human umbilical cord. The risk genotype was associated with reduced expression of $p16^{INK4a}$, $p15^{INK4b}$ ($p=1.2\times10^{-5}$, 1.4×10^{-2}), and increased VSMC proliferation ($p=1.6\times10^{-2}$).
Conclusions: The 9p21 locus primarily mediates an atherosclerotic phenotype, by influencing CDKN2A/CDKN2B expression and hence VSMC proliferation.

P3.23
URINARY ALBUMIN EXCRETION FROM SPOT URINE SAMPLES PREDICT ALL-CAUSE AND STROKE MORTALITY IN AFRICANS

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Twenty-four hour urinary albumin excretion reflects general endothelial damage, relates to arterial stiffness, and predicts adverse health outcomes. Albumin determined from easily collected spot urine samples is also predictive. No prognostic evidence for albumin excretion from any means of urine collection exists for Africans. We followed health outcomes in 1061 randomly selected non-diabetic, HIV negative Africans (mean age: 51.5 years; 62.0% women). We determined the baseline urinary albumin-to-creatinine ratio from spot urine samples. Over a median follow-up of 4.52 years, 132 deaths occurred of which 47 were cardiovascular-related. The urinary albumin-to-creatinine ratio averaged 0.68 (5th to 95th percentile interval; 0.13, 4.54 mg/mmol). In multivariable-adjusted analyses, albumin excretion predicted all-cause mortality (hazard ratio, 1.26; 95% confidence interval, 1.07, 1.48; $P=0.006$), and a tendency existed for cardiovascular (1.26; 0.97, 1.63; $P=0.087$) mortality, which seemed driven by stroke (1.72; 1.17, 2.54; $P=0.006$) and not cardiac mortality (0.67; 0.41, 1.07; $P=0.094$). The predictive value remained in 528 hypertensives for both all-cause (1.38; 1.13, 1.69; $P=0.001$) and cardiovascular mortality (1.45; 1.07, 1.96; $P=0.017$), but again driven by stroke. Our findings remained significant after excluding participants with macroalbuminuria and those on anti-hypertensive treatment. In conclusion, in non-diabetic HIV-negative