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Le malattie dell'anziano
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L'IPERTENSIONE: QUANDO E COME TRATTARE
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Riferimenti bibliografici

- (1) **Alderman MH, Cohen HW, Sealey JE, Laragh JH. Plasma renin activity levels in hypertensive persons: their wide range and lack of suppression in diabetic and in most elderly patients.** *Am J Hypertens* 2004; 17(1):1-7.
Ref ID: 225
Keywords: Age Factors/Angiotensin II/blood/Creatinine/Diabetes Mellitus/epidemiology/Ethnic Groups/Female/Humans/Hypertension/Logistic Models/Male/methods/Middle Aged/Morbidity/mortality/physiology/physiopathology/Potassium/Prognosis/Renin/Renin-Angiotensin System/Risk Factors/Sex Factors/therapy/urine
Abstract: **BACKGROUND:** The renin-angiotensin system (RAS) maintains hemodynamic integrity by modulating both volume and vasoconstriction through a cybernetic feedback control mechanism. In addition, angiotensin II, the active component of the RAS, can be vasculotoxic and, in hypertensive individuals, is associated with increased cardiovascular morbidity and mortality. The objective of this study was to determine the distribution and determinants of plasma renin activity (PRA) in a representative sample of hypertensive persons. **METHODS:** We systematically measured PRA in 4170 untreated participants in a systematic work site-based, hypertension treatment program. **RESULTS:** In this multiethnic employed population, patients were classified as follows: low renin, <0.65 ng/mL/h (30% of the sample); medium renin, 0.66 to 4.5 mg/mL/h (60%); or high renin, >4.5 ng/mL/h (10%). Low renin patients were more likely to be African American, female, and slightly older. However, the majority of women and African American individuals were not low renin. The 469 diabetic subjects distributed across renin categories, as did the group as a whole. **CONCLUSIONS:** This systematic study of PRA in a large community sample of hypertensive patients reveals a wide distribution of activity level, with identifiable differences according to ethnicity, age, and sex but not diabetic status. However, these demographic differences were more quantitative than qualitative and do not provide a useful basis for estimation of the activity of the RAS. Instead, in hypertensive subjects, direct measurement of PRA is necessary, both for prognosis and for guiding hypertensive therapy
- (2) **Andersen UO, Jensen G. Decreasing population blood pressure: 15 years of follow-up in the Copenhagen City Heart Study (CCHS).** *Blood Press* 2004; 13(3):176-182.
Ref ID: 253
Keywords: Adult/Aged/Aged,80 and over/Antihypertensive Agents/blood/Blood

Pressure/Body Mass Index/Cardiovascular Diseases/Cholesterol/Cross-Sectional Studies/Denmark/drug therapy/epidemiology/etiology/Female/Follow-Up Studies/Heart/Humans/Hypertension/Longitudinal Studies/Male/methods/Middle Aged/physiopathology/Research Support,Non-U.S.Gov't/Risk/Risk Factors/Smoking/therapeutic use/therapy

Abstract: OBJECTIVE: Population blood pressure (BP) levels from a longitudinal study were analysed for trends during a period of 15 years. Trends from unadjusted data are reported as well as trends adjusted for major cardiovascular (CV) risk factors and use of antihypertensive therapy, thus allowing assessment of independent BP trends. DESIGN: The Copenhagen City Heart Study is a longitudinal epidemiological study of CV risk in a random population sample of both genders aged 20 and above. Three cross-sectional population surveys were performed: 1976-78 (n=14000), 1981-83 (n=12675) and 1991-94 (n=9661). METHODS: BP was measured by a London School of Hygiene Sphygmomanometer. Weight and height were measured and body mass index (BMI) calculated. Non-fasting plasma cholesterol was determined. A questionnaire concerning smoking status and diabetes was completed. Measurement methods were strictly standardized and unchanged in the three cross-sectional surveys. RESULTS: Unadjusted systolic BP (SBP) levels decreased during 15 years of follow-up, and unadjusted diastolic BP (DBP) levels increased. An investigation of the effect of major CV risk factors, both singly and jointly on BP levels, revealed a pattern of correlations contributing to BP variability. Adjustments for BMI, cholesterol, diabetes, use of antihypertensive therapy and smoking status were made in the final analyses of BP trend. The adjusted trend model demonstrated that SBP levels remained lower than SBP levels in the first survey. DBP levels increased slightly. CONCLUSIONS: The results demonstrate a decrease in population SBP. The decrease is independent of major CV risk factors. Possible contributing factors are discussed

- (3) **Bakris GL, Fonseca V, Katholi RE, McGill JB, Messerli FH, Phillips RA et al. Metabolic effects of carvedilol vs metoprolol in patients with type 2 diabetes mellitus and hypertension: a randomized controlled trial.** JAMA 2004; 292(18):2227-2236.

Ref ID: 15

Keywords: Adrenergic beta-Antagonists/Adult/Aged/Aged,80 and over/analysis/Angiotensin-Converting Enzyme Inhibitors/Antihypertensive Agents/blood/Blood Glucose/Blood Pressure/Carbazoles/Comparative Study/complications/Diabetes Mellitus/Diabetes Mellitus, Type 2/Double-Blind Method/drug therapy/Hemoglobin

A,Glycosylated/Humans/Hydrochlorothiazide/Hypertension/metabolism/Metoprolol/Middle Aged/Propranolamines/Renin-Angiotensin System/Research Support,Non-U.S.Gov't/Research Support,U.S.Gov't,P.H.S./Risk/Risk Factors/therapeutic use

Abstract: CONTEXT: Beta-blockers have been shown to decrease cardiovascular risk in patients with hypertension and type 2 diabetes mellitus (DM); however, some components of the metabolic syndrome are worsened by some beta-blockers. OBJECTIVE: To compare the effects of beta-blockers with different pharmacological profiles on glycemic and metabolic control in participants with DM and hypertension receiving renin-angiotensin system (RAS) blockade, in the context of cardiovascular risk factors. DESIGN, SETTING, AND PARTICIPANTS: A randomized, double-blind, parallel-group trial (The Glycemic Effects in Diabetes Mellitus: Carvedilol-Metoprolol Comparison in Hypertensives [GEMINI]) conducted between June 1, 2001, and April 6, 2004, at 205 US sites that compared the effects of carvedilol and metoprolol tartrate on glycemic control. The 1235 participants were aged 36 to 85 years with hypertension (>130/80 mm Hg) and type 2 DM (glycosylated hemoglobin [HbA1c], 6.5%-8.5%) and were receiving RAS blockers. Participants were

followed up for 35 weeks. INTERVENTIONS: Participants were randomized to receive a 6.25- to 25-mg dose of carvedilol (n = 498) or 50- to 200-mg dose of metoprolol tartrate (n = 737), each twice daily. Open-label hydrochlorothiazide and a dihydropyridine calcium antagonist were added, if needed, to achieve blood pressure target. MAIN OUTCOME MEASURES: Difference between groups in mean change from baseline HbA1c following 5 months of maintenance therapy. Additional prespecified comparisons included change from baseline HbA1c in individual treatment groups, treatment effect on insulin sensitivity, and microalbuminuria. RESULTS: The 2 groups differed in mean change in HbA1c from baseline (0.13%; 95% confidence interval [CI], -0.22% to -0.04%; P = .004; modified intention-to-treat analysis). The mean (SD) HbA1c increased with metoprolol (0.15% [0.04%]; P < .001) but not carvedilol (0.02% [0.04%]; P = .65). Insulin sensitivity improved with carvedilol (-9.1%; P = .004) but not metoprolol (-2.0%; P = .48); the between-group difference was -7.2% (95% CI, -13.8% to -0.2%; P = .004). Blood pressure was similar between groups. Progression to microalbuminuria was less frequent with carvedilol than with metoprolol (6.4% vs 10.3%; odds ratio, 0.60; 95% CI, 0.36-0.97; P = .04). CONCLUSIONS: Both beta-blockers were well tolerated; use of carvedilol in the presence of RAS blockade did not affect glycemic control and improved some components of the metabolic syndrome relative to metoprolol in participants with DM and hypertension. The effects of the 2 beta-blockers on clinical outcomes need to be compared in long-term clinical trials

- (4) **Baruch L. Hypertension and the elderly: more than just blood pressure control.** J Clin Hypertens (Greenwich) 2004; 6(5):249-255.

Ref ID: 204

Keywords: Aged/Aging/Angiotensin-Converting Enzyme Inhibitors/Antihypertensive Agents/blood/Blood Pressure/Cardiovascular Diseases/Clinical

Trials/Compliance/complications/drug therapy/Elasticity/etiology/Europe/Humans/Hypertension/physiopathology/Practice Guidelines/prevention & control/Renin/Risk/Risk Assessment/therapeutic use

Abstract: Hypertension is a major risk factor for cardiovascular disease in both young and elderly persons; therefore, good blood pressure control is at the center of improved cardiovascular health. The recently issued seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure and the European Society of Hypertension/European Society of Cardiology 2003 guidelines for hypertension management emphasize the importance of treatment efficacy rather than age in treating elderly persons with hypertension. Most hypertension clinical trials have been carried out with younger hypertensives, but this is changing with trials such as the Systolic Hypertension in the Elderly Program, the first Swedish Trial of Old Patients With Hypertension, and the Systolic Hypertension in Europe trial. These trials have clearly demonstrated the benefits of good blood pressure control in reducing the risk of stroke in elderly persons. With many safe and effective antihypertensive drugs on the market, the question becomes how elderly persons should be treated. Elderly patients often have isolated systolic hypertension, which is related to loss of arterial elasticity or compliance with aging and is more recalcitrant to treatment than essential hypertension. In addition, with advancing age there is the likelihood that other disease states are present in addition to hypertension. The newer antihypertensive drugs that interfere with the renin angiotensin system, such as angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers, have the potential of improving cardiovascular outcomes in elderly persons in addition to offering effective blood pressure reduction. Their use should be considered within a comprehensive risk assessment that includes individualized risk-benefit considerations

- (5) **Bellelli G, Frisoni GB, Lucchi E, Guerini F, Geroldi C, Magnifico F et al. Blunted reduction in night-time blood pressure is associated with cognitive deterioration in subjects with long-standing hypertension.** Blood Press Monit 2004; 9(2):71-76.
Ref ID: 63
Keywords: Aged/Aged,80 and over/blood/Blood Pressure/Blood Pressure Monitoring,Ambulatory/Cerebrovascular Disorders/Circadian Rhythm/Cognition Disorders/complications/Confidence Intervals/etiology/Female/Humans/Hypertension/Italy/Male/methods/Multivariate Analysis/physiology
Abstract: OBJECTIVE: Data about the relationship of blunted reduction of night-time blood pressure (BP) with cognitive deterioration (CD) are conflicting. This study aims to explore this possible association in elderly people with long-standing hypertension. METHODS: Twenty-six hypertensive subjects consecutively admitted to a rehabilitation unit over a six-month period were recruited. Exclusion criteria concerned all clinical conditions potentially related to BP variability or leading to CD. All patients underwent a clinic and 24-h BP non-invasive monitoring assessment of BP, as well as a cognitive assessment with the Mini Mental State Examination (MMSE). The presence of cerebrovascular disease (CVD) was assessed on CT films, with a standardized visual rating scale. RESULTS: Blunted reduction of both systolic and diastolic night-time BP were significantly associated with poorer cognitive performances ($r=0.61$, $p=0.001$ for systolic; and $r=0.57$, $p=0.002$ for diastolic, respectively). In a multiple regression model, blunted reduction of night-time BP ($B=0.17$, [95% confidence intervals: 1.1-1.3], $p=0.008$ for systolic; and $B=0.15$, [95% confidence intervals: 1.0-1.3], $p=0.02$ for diastolic) independently predicted poorer cognitive performances. CONCLUSIONS: In subjects with long-standing hypertension the blunted reduction of night-time BP is independently associated with lower cognitive performances
- (6) **Berry KL, Cameron JD, Dart AM, Dewar EM, Gatzka CD, Jennings GL et al. Large-artery stiffness contributes to the greater prevalence of systolic hypertension in elderly women.** J Am Geriatr Soc 2004; 52(3):368-373.
Ref ID: 222
Keywords: Aged/analysis/Aorta,Thoracic/Arteries/blood/Blood Pressure/Brachial Artery/Carotid Arteries/Comparative Study/Compliance/complications/Elasticity/epidemiology/etiology/Female/Humans/Hypertension/Male/Multivariate Analysis/physiology/Prevalence/Pulse/Sex Characteristics/ultrasonography
Abstract: OBJECTIVES: To determine whether sex differences in large-artery stiffness contribute to the greater prevalence of systolic hypertension in elderly women than in elderly men. DESIGN: During a single visit arterial stiffness was assessed in the unmedicated state using four parameters. PARTICIPANTS: Three hundred seventy-four women with a mean age \pm standard deviation of 72 \pm 5 and 296 men aged 71 \pm 5 participated. SETTING: Hypertensive patients were recruited from general practice as part of the second Australian National Blood Pressure Study in Melbourne, Australia. MEASUREMENTS: Large-artery stiffness was assessed using multiple methodologies, including aortic arch stiffness (beta-index) using M-mode ultrasound and arterial compliance and augmentation index using noninvasive carotid pressure and aortic flow measurements. RESULTS: Women had greater carotid and brachial pulse pressure (PP) than men ($P<.001$), despite higher mean arterial pressure in men. Mean arterial compliance was lower in women (0.20 \pm 0.12 vs 0.28 \pm 0.16 mL/mmHg, $P<.001$) even after correction for aortic area, and aortic arch stiffness was higher (30 \pm 36 vs 23 \pm 22; $P<.01$). Consistent with both a stiffer proximal circulation and a shorter distance to reflection sites, women had higher augmentation index (38 \pm 11% vs 29 \pm 12%, $P<.001$). In multivariate analysis, sex

was an independent determinant of all arterial stiffness indices. **CONCLUSION:** Independently of known confounders, elderly hypertensive women have stiffer large arteries, greater central wave reflection, and higher PP than elderly men. Stiffer large arteries likely contribute to the greater prevalence of systolic hypertension in elderly women and may partly explain the acceleration in postmenopausal cerebrovascular and cardiac complications

- (7) **Bjorklund K, Lind L, Zethelius B, Berglund L, Lithell H. Prognostic significance of 24-h ambulatory blood pressure characteristics for cardiovascular morbidity in a population of elderly men.** *J Hypertens* 2004; 22(9):1691-1697.

Ref ID: 111

Keywords: analysis/blood/Blood Pressure/Geriatrics/methods/Morbidity/Pulse/Risk/Risk Assessment/Risk Factors/Sweden

Abstract: **OBJECTIVE:** This study aimed to investigate the prognostic significance of 24-h ambulatory systolic (SBP), diastolic (DBP) and pulse pressure (PP), and blood pressure (BP) variability for cardiovascular morbidity in elderly men. **DESIGN AND METHODS:** Twenty-four hour ABP monitoring was performed in 70-year-old men (n = 872) participating in a longitudinal population-based study. The population was followed for up to 9.5 years, and the relationship between different blood pressure components and cardiovascular (CV) morbidity was assessed by Cox proportional hazard analysis. **RESULTS:** During follow-up, 172 CV events occurred (2.97 per 100 person-years). SBP and PP, both office and ambulatory, were significant predictors of CV morbidity. Twenty-four hour ambulatory PP [hazard ratio (HR) for 1 SD increase in BP 1.32, 95% confidence interval (CI) 1.15-1.52] and daytime ambulatory PP (HR 1.29, 95% CI 1.13-1.48) predicted CV morbidity independently of office PP and other established CV risk factors. Addition of night-time PP to a regression model with daytime PP and covariates did not increase the predictive value. However, the variability of daytime SBP (adjusted HR 1.24, 95% CI 1.07-1.42) provided additional prognostic power, independently of the 24-h SBP level. **CONCLUSIONS:** Ambulatory PP was a powerful predictor of CV morbidity in elderly men, independently of office PP and other established cardiovascular risk factors. Moreover, variability of daytime SBP added important prognostic information, suggesting that 24-h ambulatory BP monitoring may contribute to an improved risk assessment in elderly subjects

- (8) **Bo S, Ciccone G, Grassi G, Gancia R, Rosato R, Merletti F et al. Isolated systolic hypertension in a cohort of type 2 diabetic patients.** *Nutr Metab Cardiovasc Dis* 2004; 14(3):157-161.

Ref ID: 246

Keywords: adverse effects/Age Distribution/Aged/Blood Pressure Determination/Cohort Studies/Comorbidity/Comparative Study/Confidence Intervals/Diabetes Mellitus, Type 2/diagnosis/epidemiology/Female/Humans/Hypertension/Italy/Male/methods/Middle Aged/Prevalence/Probability/Prognosis/Proportional Hazards Models/Risk/Risk Assessment/Severity of Illness Index/Sex Distribution/Systole

Abstract: **BACKGROUND AND AIMS:** Previous studies of the adverse effects of isolated and borderline isolated systolic hypertension excluded or under-represented type 2 diabetic patients. The aim of this study was to evaluate the prevalence and role of isolated and borderline isolated systolic hypertension in a cohort of 3892 type 2 diabetic patients. **METHODS AND RESULTS:** The hypertensive patients were classified as treated (n= 1806; 46.4%), untreated diastolic hypertension (n=407; 10.4%), untreated isolated systolic hypertension (n=166; 4.3%) and untreated borderline isolated systolic hypertension (n=625; 16%). A Cox proportional hazard model including several confounders showed that the patients with untreated isolated systolic hypertension were at significantly higher risk of

hospital admissions due to cerebrovascular diseases than the normotensive and untreated diastolic hypertensive patients (HR=2.05; 95% CI: 1.2-3.4 and HR=1.97; 95%CI: 1.1-3.5, respectively). In the same model, borderline isolated systolic hypertension significantly correlated with admissions for cerebrovascular diseases in comparison with normotensive patients (HR=1.73; 95% CI: 1.2-2.6). CONCLUSIONS: This is the first report concerning the prevalence of isolated and borderline isolated systolic hypertension in a large cohort of type 2 diabetic patients. The results are in line with population-based estimates. Our data show that isolated systolic hypertension is an independent predictor of hospital admissions due to cerebrovascular diseases

- (9) **Bobrie G, Chatellier G, Genes N, Clerson P, Vaur L, Vaisse B et al. Cardiovascular prognosis of "masked hypertension" detected by blood pressure self-measurement in elderly treated hypertensive patients.** JAMA 2004; 291(11):1342-1349.

Ref ID: 75

Keywords: Aged/Aged,80 and over/Arteries/blood/Blood Pressure/Blood Pressure Determination/Cardiovascular Diseases/Cohort Studies/Comparative Study/Coronary Artery Bypass/diagnosis/epidemiology/Family Practice/Female/Heart/Hospitalization/Humans/Hypertension/Incidence/Male/methods/Middle Aged/mortality/Myocardial Infarction/Office Visits/Prognosis/Research Support,Non-U.S.Gov't/Risk/Risk Factors/Self Care/Sphygmomanometers/surgery

Abstract: CONTEXT: Blood pressure (BP) measurement in clinicians' offices with a mercury sphygmomanometer has numerous drawbacks. In contrast, the use of home BP measurement improves measurement precision and reproducibility. However, data about its prognostic value are lacking. OBJECTIVE: To assess the prognostic value of home vs office BP measurement by general practitioners in a European population of elderly patients being treated for hypertension. DESIGN, SETTING, AND PARTICIPANTS: Office and home BP and cardiac risk factors were measured at baseline in a cohort of 4939 treated hypertensive patients (mean age, 70 [SD, 6.5] years; 48.9% men) who were recruited and followed up by their usual general practitioners without specific recommendations about their management. The cohort was then followed up for a mean of 3.2 (SD, 0.5) years. The thresholds defining uncontrolled hypertension were at least 140/90 mm Hg for office BP and 135/85 mm Hg for home BP. MAIN OUTCOME MEASURES: The primary end point was cardiovascular mortality. Secondary end points were total mortality and the combination of cardiovascular mortality, nonfatal myocardial infarction, nonfatal stroke, transient ischemic attack, hospitalization for angina or heart failure, percutaneous transluminal coronary angioplasty, or coronary artery bypass graft surgery. RESULTS: At the end of follow-up, clinical status was known for 99.9% of patients. At least 1 cardiovascular event had occurred in 324 (incidence, 22.2/1000 patient-years). For BP self-measurement at home, each 10-mm Hg increase in systolic BP increased the risk of a cardiovascular event by 17.2% (95% confidence interval [CI], 11.0%-23.8%) and each 5-mm Hg increase in diastolic BP increased that risk by 11.7% (95% CI, 5.7%-18.1%). Conversely, for the same increase in BP observed using office measurement, there was no significant increase in the risk of a cardiovascular event. In a multivariable model with patients having controlled hypertension (normal home and office BP) as the referent, the hazard ratio of cardiovascular events was 1.96 (95% CI, 1.27-3.02) in patients with uncontrolled hypertension (high BP with both measurement methods), 2.06 (95% CI, 1.22-3.47) in patients with normal office BP and elevated home BP, and 1.18 (95% CI, 0.67-2.10) in patients with elevated office BP and normal home BP. CONCLUSIONS: Our findings suggest that home BP measurement has a better prognostic accuracy than office BP measurement. Blood pressure should systematically be measured at home in patients receiving treatment for hypertension

- (10) **Bryson CL, Smith NL, Kuller LH, Chaves PH, Manolio TA, Lewis W et al. Risk of congestive heart failure in an elderly population treated with peripheral alpha-1 antagonists.** J Am Geriatr Soc 2004; 52(10):1648-1654.
Ref ID: 31
Keywords: Adrenergic alpha-Antagonists/adverse effects/Aged/Antihypertensive Agents/blood/Blood Pressure/chemically induced/Cohort Studies/Diuretics/Diuretics,Thiazide/drug effects/drug therapy/epidemiology/Female/Health Services/Heart/Heart Failure,Congestive/Humans/Hypertension/Male/Research Support,U.S.Gov't,P.H.S./Risk/Risk Factors/United States
Abstract: OBJECTIVES: To compare the risk of congestive heart failure (CHF) in elderly individuals treated with any peripheral alpha-1 antagonist for hypertension with any thiazide, test whether the risk persists in subjects without cardiovascular disease (CVD) at baseline, and examine CHF risk in normotensive men with prostatism treated with alpha antagonists. DESIGN: Prospective cohort study. SETTING: Four U.S. sites: Washington County, Maryland; Allegheny County, Pennsylvania; Sacramento County, California; and Forsyth County, North Carolina. PARTICIPANTS: A total of 5,888 community-dwelling subjects aged 65 and older. MEASUREMENTS: Adjudicated incident CHF. RESULTS: The 3,105 participants with treated hypertension were at risk for CHF; 22% of men and 8% of women took alpha antagonists during follow-up. The age-adjusted risk of CHF in those receiving monotherapy treated with alpha antagonists was 1.90 (95% confidence interval=1.03-3.50) compared with thiazides. In subjects without CVD at baseline receiving monotherapy, women taking an alpha antagonist had a 3.6 times greater age-adjusted risk of CHF, whereas men had no difference in risk. Adjustment for systolic blood pressure attenuated statistical differences in risk. There were 930 men without hypertension at risk for CHF; 5% used alpha antagonists during follow-up, with no observed increase in CHF risk. CONCLUSION: Subjects receiving alpha antagonist monotherapy for hypertension had a two to three times greater risk of incident CHF, also seen in lower-risk subjects, but differences in blood pressure control partly explained this
- (11) **Chaudhry SI, Krumholz HM, Foody JM. Systolic hypertension in older persons.** JAMA 2004; 292(9):1074-1080.
Ref ID: 50
Keywords: Aged/Aged,80 and over/Antihypertensive Agents/blood/Blood Pressure/Calcium Channel Blockers/Clinical Trials/diagnosis/Diuretics/Humans/Hypertension/Research Support,Non-U.S.Gov't/Research Support,U.S.Gov't,P.H.S./Risk/Systole/therapeutic use/therapy/Veterans
Abstract: CONTEXT: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure emphasizes the importance of systolic hypertension (SH), defined as systolic blood pressure (SBP) of at least 140 mm Hg and diastolic blood pressure of less than 90 mm Hg, in older persons (> or =60 years). OBJECTIVE: To systematically review the literature on clinical management of SH in older persons. DATA SOURCES: We performed a MEDLINE search of English-language literature from 1966-2004 to identify reports about SH in older persons, with particular emphasis on data from randomized clinical trials. STUDY SELECTION AND DATA EXTRACTION: We selected 1064 studies by using the search terms hypertension combined with the terms systole (or systolic) and aged. DATA SYNTHESIS: There is strong evidence from clinical trials to support the treatment of SH in older persons with SBP of at least 160 mm Hg. Large-scale trials to assess the value of antihypertensive therapy for older patients with SBP of 140 to 159 mm Hg have not been performed, and recommendations to treat these patients are based on observational studies that show a graded relationship of cardiovascular risk with increasing SBP. The studies most strongly

support the use of thiazide diuretics and long-acting calcium channel blockers as first-line therapy to treat SH. CONCLUSIONS: Treatment of SH in older patients with SBP of at least 160 mm Hg is supported by strong evidence. The evidence available to support treatment of patients to the level of 140 mm Hg or those with baseline SBP of 140 to 159 mm Hg is less strong; thus, these treatment decisions should be more sensitive to patient preferences and tolerance of therapy

- (12) **Dart AM, Gatzka CD, Cameron JD, Kingwell BA, Liang YL, Berry KL et al. Large artery stiffness is not related to plasma cholesterol in older subjects with hypertension.**

Arterioscler Thromb Vasc Biol 2004; 24(5):962-968.

Ref ID: 74

Keywords: Age Factors/Aged,Aged,80 and

over/analysis/Aorta,Thoracic/Arteries/Biomechanics/blood/Blood Pressure/Body Height/Cholesterol/Cohort Studies/Comparative Study/Elasticity/Female/Heart/Heart Rate/Humans/Hypertension/Lipoproteins,HDL/Lipoproteins,HDL

Cholesterol/Male/methods/pathology/Prospective Studies/Research Support,Non-U.S.Gov't/Risk/Risk Assessment/Sex Factors/Single-Blind Method/ultrasonography

Abstract: OBJECTIVE: Previous studies have demonstrated a prognostic role of large artery stiffness in hypertensive subjects and increased stiffness in subjects with coronary artery disease. Although plasma cholesterol is an established risk factor for cardiovascular disease, its relationship with large artery properties in a hypertensive population is unclear. METHODS AND RESULTS: Plasma cholesterol and large artery properties were measured at baseline in a subset of participants of a randomized controlled trial (ANBP2) evaluating hypertension treatment in older (65 to 84 years) subjects. Noninvasive measures of large artery behavior were central augmentation index (AI), systemic arterial compliance (SAC), and transverse expansion of the aortic arch (aortic distensibility). Arterial waveforms acceptable for analysis were obtained in approximately 80% of cases yielding valid measurements of AI in 868, SAC in 846, and aortic distensibility in 680 subjects. Mean total and high-density lipoprotein (HDL) concentrations were 5.5+/-1.0 and 1.4+/-0.5 mmol L(-1). Total and HDL cholesterol and AI were greater in females than males, whereas SAC and aortic distensibility were greater in males. In multiple regression analyses there were no significant associations between stiffness parameters and total or HDL cholesterol. Significant independent associations in such analyses were found for mean arterial blood pressure, gender, age, height, and heart rate, in keeping with previous findings. CONCLUSIONS: In the largest cohort of elderly hypertensive subjects studied to date, plasma cholesterol per se was not associated with large artery stiffness. Such independence from cholesterol increases the potential for artery stiffness measurements to additionally contribute to cardiovascular risk assessment in this population

- (13) **de Leeuw FE, Richard F, de Groot JC, van Duijn CM, Hofman A, Van Gijn J et al. Interaction between hypertension, apoE, and cerebral white matter lesions.** Stroke

2004; 35(5):1057-1060.

Ref ID: 213

Keywords: Aged/Aged,80 and over/Apolipoproteins E/blood/Blood Pressure/Brain/Brain Diseases/Cerebrovascular Disorders/Comorbidity/Comparative

Study/Dementia/diagnosis/epidemiology/etiology/Female/Follow-Up

Studies/genetics/Genotype/Heterozygote/Humans/Hypertension/Magnetic Resonance Imaging/Male/methods/Middle

Aged/Netherlands/pathology/Polymorphism,Genetic/Research Support,Non-

U.S.Gov't/Risk/Risk Factors

Abstract: BACKGROUND AND PURPOSE: Cerebral white matter lesions (WMLs) are

frequently found on magnetic resonance imaging scans in both cognitively intact and demented elderly persons. Vascular risk factors, especially hypertension, are related to their presence. However, not every person with vascular risk factors has WMLs, which suggests interaction with other determinants, eg, genetic factors. The epsilon4 allele of the apolipoprotein E gene (apoE) may be a candidate because this allele is associated with both the vascular risk factors and the consequences (cognitive impairment, dementia) of WMLs. METHODS: We investigated apoE genotype, blood pressure levels, and their interaction in relation to subcortical and periventricular WMLs in 971 participants in the Rotterdam Scan Study. RESULTS: ApoE epsilon4 carriers had a significantly higher subcortical WML volume than did apoE epsilon3epsilon3 carriers (adjusted mean difference, 0.5; 95% confidence interval, 0.2 to 0.8), irrespective of hypertension. This was not found for periventricular WMLs. Participants with both hypertension and at least 1 apoE epsilon4 allele had the highest degree of both types of WML; the interaction was statistically significant for subcortical WMLs (P=0.016). CONCLUSIONS: apoE epsilon4 carriers are at increased risk for WMLs if they suffer from hypertension as well. This may reflect a diminished capacity for neuronal repair in apoE epsilon4 carriers

- (14) **de Leeuw FE, Barkhof F, Scheltens P. Alzheimer's disease--one clinical syndrome, two radiological expressions: a study on blood pressure.** J Neurol Neurosurg Psychiatry 2004; 75(9):1270-1274.
 Ref ID: 258
 Keywords: Age Factors/Aged/Alzheimer Disease/analysis/Arteriosclerosis/Atrophy/blood/Blood Pressure/Brain/complications/epidemiology/Female/Humans/Hypertension/Magnetic Resonance Imaging/Male/methods/Middle Aged/Netherlands/pathology/physiopathology/Prevalence/Pulse/Regression Analysis/Research Support, Non-U.S. Gov't/Risk/Risk Factors/Syndrome
 Abstract: BACKGROUND: Vascular risk factors could play a role in the aetiology of Alzheimer's disease, but this has not been investigated in relation to neuroimaging findings OBJECTIVE: To evaluate the distribution of blood pressure and an indicator of atherosclerosis (pulse pressure) in patients with Alzheimer's disease with and without small vessel disease. METHODS: 152 Alzheimer patients underwent 1.0T MRI scanning. Blood pressure was measured with a sphygmomanometer. Small vessel disease was assessed by the presence of lacunar infarcts and white matter lesions. The distribution of blood pressure and pulse pressure, with or without small vessel disease, was assessed by linear regression analysis. RESULTS: Patients with small vessel disease had a higher blood pressure, a wider pulse pressure, and an increased prevalence of hypertension. These findings were strongly age dependent: for patients under 65, mean systolic blood pressure was higher in the subpopulation with small vessel disease than in those without (mean (SD): 149.9 (19.3) v 135.7 (20.5) mm Hg; p = 0.02). Hypertension was more common in patients with white matter lesions than in those without (75.6% v 45.1%; p = 0.03) and the pulse pressure was higher (61.9 (14.4) v 51.7 (11.5) mm Hg; p = 0.01). There was no relation between blood pressure and the degree of (sub)cortical and hippocampal atrophy in patients without small vessel disease. CONCLUSIONS: There was heterogeneity in Alzheimer's disease patients with respect to blood pressure and pulse pressure. Alzheimer's disease encompasses a heterogeneous group of disorders which share a common cognitive profile but with distinct radiological features with respect to white matter lesions

- (15) **de Leeuw PW, Ruijter LM, Palmer CR, Brown MJ, Castaigne A, Mancina G et al. Clinical significance of renal function in hypertensive patients at high risk: results**

from the INSIGHT trial. Arch Intern Med 2004; 164(22):2459-2464.

Ref ID: 5

Keywords: Aged/Amiloride/blood/Cardiovascular Diseases/Comparative Study/complications/Creatinine/Diuretics/Double-Blind Method/drug therapy/etiology/Female/Heart/Humans/Hydrochlorothiazide/Hypertension/Kidney/Kidney Failure/Male/Middle Aged/Nifedipine/physiopathology/prevention & control/Research Support,Non-U.S.Gov't/Risk/Risk Factors/therapeutic use/Vasodilator Agents

Abstract: BACKGROUND: Increasing evidence suggests renal involvement in hypertension-related cardiovascular and cerebrovascular complications. To assess this role of renal function in more detail, we studied the evolution of renal function and the relationship of renal function with mortality and morbidity in the Intervention as a Goal in Hypertension Treatment (INSIGHT) study. METHODS: The INSIGHT study was a double-blind, randomized, multicenter trial in patients with hypertension and at least 1 additional cardiovascular risk factor. Treatment consisted of nifedipine gastrointestinal therapeutic system, 30 mg/d, or hydrochlorothiazide-amiloride (25 mg/d of hydrochlorothiazide and 2.5 mg/d of amiloride hydrochloride). Primary outcome was a composite of cardiovascular death, myocardial infarction, heart failure, and stroke. Renal function was assessed by measuring creatinine clearance, serum creatinine level, and serum uric acid level and by the presence of proteinuria. RESULTS: Creatinine clearance fell more in nifedipine recipients than in hydrochlorothiazide-amiloride recipients. Renal insufficiency developed in 2% of nifedipine recipients and 5% of hydrochlorothiazide-amiloride recipients. Primary outcomes occurred in 15% of patients with increased serum creatinine levels and 6% of patients with normal levels (odds ratio [OR] 2.89; 95% confidence interval [CI], 1.92-4.36; $P < .001$). Primary outcomes were more likely in patients with low creatinine clearance (< 60 mL/min) than in those with higher clearances (9% vs 5%, respectively [OR, 1.51, 95%CI, 1.22-1.88; $P < .001$]). CONCLUSIONS: Renal function is an important predictor of risk in hypertensive patients at high risk. Antihypertensive treatment with a long-acting dihydropyridine calcium channel blocker may better preserve renal function than would treatment with diuretics

- (16) **DegliInnocenti A, Elmfeldt D, Hofman A, Lithell H, Olofsson B, Skoog I et al. Health-related quality of life during treatment of elderly patients with hypertension: results from the Study on COgnition and Prognosis in the Elderly (SCOPE).** J Hum Hypertens 2004; 18(4):239-245.

Ref ID: 73

Keywords: Aged/Aged,80 and over/analysis/Antihypertensive Agents/Benzimidazoles/blood/Blood Pressure/Cognition/Comparative Study/diagnosis/Diuretics/Double-Blind Method/drug effects/drug therapy/epidemiology/Europe/Female/Follow-Up Studies/Health Status Indicators/Humans/Hydrochlorothiazide/Hypertension/Male/physiopathology/Prognosis/psychology/Quality of Life/Research Support,Non-U.S.Gov't/Tetrazoles/therapeutic use/therapy/Treatment Outcome/United States

Abstract: The Study on COgnition and Prognosis in the Elderly (SCOPE) was a multinational, randomised, double-blind study to assess the effects of candesartan 8-16 mg daily on cardiovascular events and cognitive function in elderly patients (aged 70-89 years) with mild to moderate hypertension. A total of 4937 patients were randomised to candesartan or placebo with other antihypertensive drugs (mostly diuretics, beta-blockers, and calcium antagonists) added as needed to control blood pressure. Only 16% of the patients in the control group received placebo alone. The mean follow-up was 3.7 years. The aim of this health-related quality of life (HRQL) substudy analysis was to investigate changes in HRQL during antihypertensive treatment, and possible differences in patients

receiving candesartan-based or other antihypertensive treatment. Three validated HRQL instruments were used: the Psychological General Well-being (PGWB) Index, the Subjective Symptoms Assessment Profile (SSA-P), and the EuroQoL Health Utility Index (EuroQoL). The HRQL was generally good at baseline and well preserved during follow-up in the presence of substantial blood pressure reductions in both treatment groups. Several of the observed changes in score from baseline to last visit favoured candesartan-based compared to control treatment, particularly the changes in PGWB Anxiety (-0.5 vs -1.0, $P=0.01$), PGWB Positive well-being (-0.8 vs -1.1, $P=0.04$), SSA-P Cardiac symptoms (0.03 vs 0.10, $P=0.03$), and EuroQoL Current health (-3.1 vs -5.3, $P=0.008$). This favourable result may be related to the somewhat lower blood pressure associated with candesartan-based treatment. In conclusion, there should be no reason to withhold modern antihypertensive therapy in elderly patients due to concerns for a negative effect on HRQL

- (17) **Erkinjuntti T, Roman G, Gauthier S, Feldman H, Rockwood K. Emerging therapies for vascular dementia and vascular cognitive impairment.** *Stroke* 2004; 35(4):1010-1017. Ref ID: 81

Keywords: Activities of Daily Living/Alzheimer Disease/Brain/Carbamates/Cardiovascular Diseases/Cerebrovascular Accident/Cerebrovascular Disorders/Cholinesterase Inhibitors/Clinical Trials/Cognition/Cognition Disorders/complications/Controlled Clinical Trials/Dementia/Dementia,Vascular/diagnosis/etiology/Finland/Galantamine/Humans/Hyperlipidemia/Hypertension/Incidence/Indans/Phenylcarbamates/Piperidines/prevention & control/Risk Factors/Terminology/therapeutic use/therapy
 Abstract: BACKGROUND: Cerebrovascular disease (CVD) and ischemic brain injury secondary to cardiovascular disease are common causes of dementia and cognitive decline in the elderly. CVD also contributes to cognitive loss in Alzheimer disease (AD). SUMMARY: Progress in understanding vascular cognitive impairment (VCI) and vascular dementia (VaD) has resulted in promising symptomatic and preventive treatments. Cholinergic deficits in VaD due to ischemia of basal forebrain nuclei and cholinergic pathways can be treated with cholinesterase inhibitors used in AD. Controlled clinical trials with donepezil and galantamine in patients with VaD, as well as in patients with AD plus CVD, have demonstrated improvement in cognition, behavior, and activities of daily living. The N-methyl-D-aspartate receptor antagonist memantine stabilized progression of VaD compared with placebo. Primary and secondary stroke prevention, in particular with control of hypertension and hyperlipidemia, can decrease VaD incidence. CONCLUSIONS: From a public health viewpoint, recognition of VCI before the development of dementia and correction of vascular burden on the brain may lead to a global decrease of incident dementia

- (18) **Kahonen-Vare M, Brunni-Hakala S, Lindroos M, Pitkala K, Strandberg T, Tilvis R. Left ventricular hypertrophy and blood pressure as predictors of cognitive decline in old age.** *Aging Clin Exp Res* 2004; 16(2):147-152. Ref ID: 129

Keywords: Aged/Aged,80 and over/Aging/anatomy & histology/blood/Blood Pressure/Cognition/Cognition Disorders/complications/Data Interpretation,Statistical/Dementia/diagnosis/Echocardiography/Echocardiography,Doppler, Color/Electrocardiography/etiology/Female/Finland/Follow-Up Studies/Geriatrics/Heart/Heart Ventricles/Humans/Hypertension/Hypertrophy,Left Ventricular/Male/Mental Status Schedule/methods/Organ Size/pathology/physiology/physiopathology/Prognosis/Prospective Studies/psychology/Risk
 Abstract: BACKGROUND AND AIMS: The relationships between blood pressure (BP) and cognition are complex and are still partly unclear. The impact of history of hypertension,

present BP levels, and left ventricular hypertrophy (LVH) on cognition was investigated in a 10-year follow-up study of an aged population. **METHODS:** The population-based sample consisted of 75-, 80- and 85-year-old individuals at baseline (N=650). Their history of hypertension was investigated, and present BP values were recorded several times. Echocardiographic examinations were performed twice at 3-year intervals, and electrocardiography (ECG) at entry. Cognitive function was assessed by the Mini-Mental State Examination (MMSE) at baseline and at 10 years, and by the Clinical Dementia Rating (CDR) at baseline, at 1, 5 and 10 years. **RESULTS:** At baseline, elderly individuals with impaired cognition or dementia had lower BP, but thicker left ventricle posterior wall (LVPW), greater cardiac mass, and more often signs of LVH in ECG than those without cognitive deficits. Echocardiographic LVH, but not BP, predicted cognitive decline in a 5-year follow-up. Patients who died demented within 5 years were characterized by low BP and thin LVPW. Baseline BP and echocardiographic variables were not significantly different between those who had and had not cognitive decline at 10 years, but declining BP tended to precede cognitive deficits. **CONCLUSIONS:** Results indicate that, the closer cognitive decline, the lower the BP, and suggest that, although LVH is a risk factor of cognitive decline, it loses its predictive value in old age

- (19) **Kannel WB, Wilson PW, Nam BH, D'Agostino RB, Li J. A likely explanation for the J-curve of blood pressure cardiovascular risk.** Am J Cardiol 2004; 94(3):380-384.

Ref ID: 112

Keywords: Adult/Age Distribution/Aged/blood/Blood Pressure/Blood Pressure Determination/Cardiovascular Diseases/Cohort Studies/Comorbidity/Comparative Study/Confidence Intervals/diagnosis/Diastole/epidemiology/Female/Heart/Heart Rate/Humans/Hypertension/Incidence/Male/Middle Aged/physiology/Probability/Prognosis/Proportional Hazards Models/Prospective Studies/Pulse/Research Support,Non-U.S.Gov't/Research Support,U.S.Gov't,P.H.S./Risk/Risk Assessment/Risk Factors/Sex Distribution/Survival Analysis/Systole

Abstract: We prospectively tested in the combined original and offspring Framingham cohorts the hypothesis that the increase in cardiovascular disease (CVD) incidence at low diastolic blood pressure (BP) is largely confined to subjects with increased systolic BP and hence an increased pulse pressure. The 10-year risk of 951 nonfatal CVD events and 204 CVD deaths was estimated at diastolic pressures of <80, 80 to 90, and > or =90 mm Hg, according to concomitant systolic BP. An increasing tendency for a J-curve relation of CVD incidence to diastolic BP was observed with successive increments in accompanying systolic BP. In both genders, a statistically significant excess of CVD events was observed at a diastolic BP of <80 mm Hg only when accompanied by a systolic BP of >140 mm Hg that persisted after adjustment for age and associated CVD risk factors. Patients with this condition of isolated systolic hypertension have been shown to benefit from antihypertensive treatment

- (20) **Kazmierki R, Watala C, Podsiadly E, Dorszewska J, Adamczewska-Goncerzewicz Z, Tylewska-Wierzbanowska S et al. Carotid intima-media thickness better differentiates between groups of stroke patients and persons without cerebrovascular disease than other conventional and novel risk factors.** Folia Morphol (Warsz) 2004; 63(3):253-260.

Ref ID: 25

Keywords: Aged/anatomy & histology/Carotid Arteries/Case-Control Studies/Cerebrovascular Accident/Cerebrovascular Disorders/Cross-Sectional Studies/Heart/Humans/Hypertension/Male/Middle Aged/pathology/Risk/Risk

Factors/Smoking/Tunica Intima/Tunica Media/ultrasonography

Abstract: When measured by ultrasound, the morphological markers of carotid atherosclerosis such as intima-media thickness (IMT) and cross-sectional plaque area have been associated with the risk of ischaemic stroke. We set out to determine whether the morphological parameters of the carotid arteries made it possible to better differentiate between groups of older atherothrombotic stroke patients and persons without cerebrovascular disease than conventional and novel risk factors of stroke. Of the total number of 623 persons examined, 54 stroke patients (mean age 63.3 years) and 74 controls without cerebrovascular disease (mean age 66.3 years) fulfilled the inclusion criteria for this investigation and were enrolled in the case-control study. After adjustment for age, gender and education level, the strongest associations were found between stroke and carotid IMT [odds ratio (OR) = 10.6; 95% confidence interval (CI): 4.3-26.9] and plaque area (OR = 5.4; 95%CI: 2.3-13.1). Other risk factors showed weaker associations with stroke occurrence. Of the clinical risk factors, a significant association was found between stroke and coronary heart disease (OR = 3.5; 95%CI: 1.2-10.2), hypertension (OR = 3.2; 95%CI: 1.5-7.2) and smoking (OR = 2.7; 95%CI: 1.1-6.4). From the laboratory-derived risk factors a significant association was found between stroke and triglyceride levels (OR = 4.4; 95%CI: 1.9-10.0), and an inverse correlation was observed between stroke occurrence and HDL-cholesterol level (OR = 0.4; 95%CI: 0.2-0.8). The carotid IMT and plaque area, measured with the use of ultrasonography, showed a better correlation with stroke occurrence than currently recognised clinical and biochemical risk factors. The intima-media thickness and plaque area of the carotid arteries could be useful parameters in the development of strategies to identify patients at high risk of atherothrombotic ischaemic stroke

- (21) **Kono I, Mori S, Nakajima K, Nakagawa M, Watanabe Y, Kizu O et al. Do white matter changes have clinical significance in Alzheimer's disease?** *Gerontology* 2004; 50(4):242-246.

Ref ID: 124

Keywords: Aged/Aged,80 and over/Alzheimer Disease/Brain/Case-Control Studies/Dementia/Diabetes Mellitus/Heart/Humans/Hypertension/Japan/Magnetic Resonance Imaging/methods/pathology/Statistics,Nonparametric

Abstract: BACKGROUND: Although white matter changes visible with MRI are generally considered to result from ischemia, it has become clear that these changes also appear in patients with Alzheimer's disease (AD). However, their significance in AD is unknown. OBJECTIVE: We evaluated the clinical significance of white matter changes in AD. METHODS: Ninety-six AD patients (79.4 +/- 5.92 years old) and 48 age-matched control subjects (80.0 +/- 7.03 years old) participated in the study. Three neuroradiologists assessed the degree of periventricular hyperintensities (PVH) and deep white matter hyperintensities (DWMH) using a modified Fazekas' rating scale. We examined whether there was a difference in the severity and the histogram pattern of the white matter changes, or in vascular factors (hypertension, diabetes mellitus, and ischemic heart disease) between the two groups. We also analyzed the association between the severity of the white matter changes and the degree of dementia (MMSE score and disease duration). RESULTS: There were no differences in the vascular factors between AD and control subjects. The degree of PVH in AD was severe compared with that in the control subjects. In histograms of the number of subjects with each degree of PVH severity, the distribution of AD patients had peaks at both the low and intermediate degrees of PVH, while most of the controls had a low degree of PVH. There was no difference in the degree or the histogram pattern of DWMH between the two groups. The severity of white matter changes was not associated with severity of dementia in AD. CONCLUSIONS: Although

PVH might have several causative factors, and may have some clinical significance, the change itself does not contribute to the progression of AD

- (22) **Lapu-Bula R, Ofili E. Diastolic heart failure: the forgotten manifestation of hypertensive heart disease.** *Curr Hypertens Rep* 2004; 6(3):164-170.

Ref ID: 55

Keywords: Aged/Aging/Clinical Trials/Coronary Arteriosclerosis/diagnosis/Diastole/etiology/Heart/Heart Failure, Congestive/Hospitalization/Humans/Hypertension/Hypertrophy, Left Ventricular/mortality/physiology/physiopathology/Research Support, U.S. Gov't, Non-P.H.S./Research Support, U.S. Gov't, P.H.S./Risk/Risk Factors/therapy/Ventricular Dysfunction, Left

Abstract: Heart failure (HF) is a progressively debilitating disorder characterized by frequent hospital admissions and high annual mortality rates. Coronary artery disease (CAD), hypertension, and aging are major risk factors for the development/progression of HF. For years, most of the attention has been focused on HF caused by reduced left ventricular (LV) systolic function, largely attributable to CAD. It is now generally accepted that nearly 50% of elderly patients with HF might have normal or preserved LV systolic function. This condition is commonly referred to as a distinct type of HF caused by LV diastolic dysfunction, and it often accompanies hypertensive heart disease. Isolated diastolic HF is increasingly recognized as the dominant cause of symptoms and hospitalizations from HF in a large proportion of individuals aged 65 and older. However, the clinicians caring for patients with diastolic HF do not fully understand its cause, how it progresses, or how it could be appropriately diagnosed and treated. Because varying degrees of systolic and diastolic dysfunction might coexist in any individual patient, and given the limitation of current diagnostic tools, the overall impact of isolated diastolic HF continues to evolve. Ongoing clinical trials are testing new strategies for treatment of diastolic HF

- (23) **London GM, Asmar RG, O'Rourke MF, Safar ME. Mechanism(s) of selective systolic blood pressure reduction after a low-dose combination of perindopril/indapamide in hypertensive subjects: comparison with atenolol.** *J Am Coll Cardiol* 2004; 43(1):92-99.

Ref ID: 116

Keywords: administration & dosage/adverse effects/Antihypertensive Agents/Aorta/Arteries/Atenolol/blood/Blood Pressure/Carotid Arteries/Comparative Study/drug effects/drug therapy/Drug Therapy, Combination/Female/Follow-Up Studies/France/Humans/Hypertension/Indapamide/Male/methods/Middle Aged/Perindopril/Pulse/Research Support, Non-U.S. Gov't/Risk/therapeutic use

Abstract: OBJECTIVES: The goal of this study was to determine if a low-dose combination of the angiotensin-converting enzyme inhibitor perindopril (Per) and the diuretic indapamide (Ind) reduces central (thoracic aorta, carotid artery) as well as brachial systolic blood pressure (SBP) more than the beta-blocker atenolol and to determine the hemodynamic factors influencing independently brachial and central SBP: pulse wave velocity (PWV) and pattern of wave reflections. BACKGROUND: In high cardiovascular risk populations, angiotensin blockade improves survival without affecting brachial SBP and diastolic blood pressure (DBP). Whether central SBP, which is physiologically lower than brachial SBP, is significantly reduced has never been investigated. METHODS: This study was a double-blind randomized trial for one year in patients with essential hypertension. RESULTS: For a similar DBP reduction, Per/Ind decreased SBP significantly more than atenolol, with a more pronounced reduction for central than for brachial SBP. After one year, the difference between brachial and central SBP was maintained by Per/Ind (8.28 +/- 1.53 mm Hg) and

significantly attenuated by atenolol (0.29 +/- 1.61 mm Hg). Under atenolol, the principal factor modulating SBP reduction was mean blood pressure. Under Per/Ind, this parameter played a minor role, and the central SBP reduction implied a major role for disturbed PWV and wave reflections. CONCLUSIONS: Under Per/Ind, but not atenolol, normalization of brachial SBP is achieved with a significantly greater reduction of central SBP. This hemodynamic profile reflects changes of wave reflections issued from distal arterial and arteriolar territory, where Per/Ind, but not atenolol, is known to improve vessel wall structure

- (24) **Mattace-Raso FU, van der Cammen TJ, van Popele NM, van der Kuip DA, Schalekamp MA, Hofman A et al. Blood pressure components and cardiovascular events in older adults: the Rotterdam study.** J Am Geriatr Soc 2004; 52(9):1538-1542. Ref ID: 49
Keywords: Adult/Age Distribution/Age Factors/Aged/Aged,80 and over/blood/Blood Pressure/Blood Pressure Determination/Cause of Death/Cerebrovascular Accident/Cohort Studies/Comparative Study/complications/Confidence Intervals/diagnosis/epidemiology/etiology/Female/Humans/Hypertension/Incidence/Male/methods/mortality/Myocardial Infarction/Netherlands/Predictive Value of Tests/Proportional Hazards Models/Prospective Studies/Pulse/Risk/Risk Factors/Sex Distribution/standards/statistics & numerical data/Suburban Health
Abstract: OBJECTIVES: To compare the strength of the relative risks of systolic (SBP) diastolic blood pressure (DBP) and pulse pressure (PP) as predictors of myocardial infarction and stroke in older adults. DESIGN: Prospective cohort study. SETTING: The Rotterdam Study, a Dutch population-based study. PARTICIPANTS: A total of 4,234 subjects aged 55 and older with no previous myocardial infarction (MI) or stroke at baseline. MEASUREMENTS: Blood pressure levels at baseline, first MI and stroke, all-cause mortality during follow-up. RESULTS: During follow-up, 205 subjects had an MI (average follow-up period 7 years), 137 subjects had a stroke (average follow-up period 6.1 years), and 748 subjects died. A 1-standard deviation difference in SBP, DBP, and PP was associated with relative risks of MI of 1.24 (95% confidence interval (CI)=1.06-1.46), 1.07 (0.92-1.25), and 1.25 (1.07-1.48), respectively. Corresponding relative risks for stroke were 1.59 (1.37-1.86), 1.27 (1.10-1.48), and 1.48 (1.27-1.72). For all-cause mortality the corresponding relative risks and 95% CI were 1.21 (1.11-1.31), 1.06 (0.99-1.14), and 1.20 (1.10-1.31). CONCLUSION: The results of this study suggest that, in a population of apparently healthy older adults, PP is not a better predictor of cardiovascular events and all-cause mortality than SBP
- (25) **McEniery CM, Wallace S, Dakham Z, Pusalkar P, Ashby MJ, Cockcroft JR et al. Matrix Metalloproteinase-9 (MMP-9), MMP-2, and Serum Elastase Activity Are Associated With Systolic Hypertension and Arterial Stiffness.** Arterioscler Thromb Vasc Biol 2004. Ref ID: 245
Keywords: blood/Blood Pressure/C-Reactive Protein/Hypertension/methods/pharmacology/Pulse/Risk
Abstract: Background--Arterial stiffness is an independent determinant of cardiovascular risk, and arterial stiffening is the predominant abnormality in systolic hypertension. Elastin is the main elastic component of the arterial wall and can be degraded by a number of enzymes, including matrix metalloproteinase-9 (MMP-9) and MMP-2. We hypothesized that elastase activity would be related to arterial stiffness and tested this using isolated systolic hypertension (ISH) as a model of stiffening and separately in a large cohort of healthy individuals. METHODS AND RESULTS: A total of 116 subjects with ISH and 114 matched controls, as well as 447 individuals free from cardiovascular disease were studied. Aortic

and brachial pulse wave velocity (PWV) and augmentation index were determined. Blood pressure, lipids, C-reactive protein, MMP-9, MMP-2, serum elastase activity (SEA), and tissue-specific inhibitor 2 of metalloproteinases were measured. Aortic and brachial PWV, MMP-9, MMP-2, and SEA levels were increased in ISH subjects compared with controls ($P=0.001$). MMP-9 levels correlated linearly and significantly with aortic ($r=0.45$; $P=0.001$) and brachial PWV ($r=0.22$; $P=0.002$), even after adjustments for confounding variables. In the younger, healthy subjects, MMP-9 and SEA were also independently associated with aortic PWV. CONCLUSIONS: Aortic stiffness is related to MMP-9 levels and SEA, not only in ISH, but also in apparently younger, healthy individuals. This suggests that elastases including MMP-9 may be involved in the process of arterial stiffening and development of ISH

- (26) **McGreevy C, Mulrooney J, O'Keefe ST, Mulkerrin EC. Do older people tolerate ambulatory blood pressure monitoring?** J Am Geriatr Soc 2004; 52(10):1780-1781.
Ref ID: 30
Keywords: Adult/adverse effects/Age Distribution/Aged/blood/Blood Pressure/Blood Pressure Monitoring,Ambulatory/Comparative
Study/diagnosis/Female/Humans/Hypertension/Male/psychology/Questionnaires/Reproducibility of Results
- (27) **Mogi N, Umegaki H, Hattori A, Maeda N, Miura H, Kuzuya M et al. Cognitive function in Japanese elderly with type 2 diabetes mellitus.** J Diabetes Complications 2004; 18(1):42-46.
Ref ID: 77
Keywords: Adult/Aged/analysis/Analysis of Variance/Cognition/Diabetes Mellitus/Diabetes Mellitus,Type 2/Educational Status/epidemiology/Female/Hemoglobin A,Glycosylated/Humans/Hyperlipidemia/Hypertension/Insulin/Japan/Male/psychology/Questionnaires/Reference Values
Abstract: The current study was conducted to investigate the cognitive function in Japanese elderly with type 2 diabetes mellitus (DM). Participants included 69 diabetic and 27 nondiabetic subjects (60 to 85 years old). The cognitive functional tests conducted were the Mini-Mental State Examination (MMSE), Word Lists Recall (immediate, delayed), Digit Symbol Test (Wechsler Adult Intelligence Scale-Revised [WAIS-R]), and the Stroop Color Word Test. Hemoglobin A1c (HbA1c) was measured as the index of glycemic control, and information about recent hypoglycemic episodes was gathered by using questionnaires. Student's t test showed that DM subjects had significantly lower scores in the MMSE ($P<.01$) and Digit Symbol Test ($P<.05$) than non-DM subjects. The scores of the Digit Symbol Test in diabetes subjects had a significant negative relationship with HbA1c ($r=-.433$; $P<.001$), and insulin-use had a significant relationship with the scores of the MMSE and Digit Symbol Test. Subjects in the DM group were further divided by insulin use. Comparison of insulin-treated DM subjects, non-insulin-treated DM subjects, and nondiabetic subjects by analysis of variance followed by Bonferroni's post hoc test showed that insulin-treated DM subjects had significantly lower scores in the MMSE and Digit Symbol Tests than both non-insulin-treated DM subjects ($P<.05$) and nondiabetic subjects ($P<.01$). Our study suggests that Japanese elderly DM subjects, especially those with insulin treatment, have poor cognitive function
- (28) **Muller M, van den Beld AW, Bots ML, Grobbee DE, Lamberts SW, van der Schouw YT. Endogenous sex hormones and progression of carotid atherosclerosis in elderly men.** Circulation 2004; 109(17):2074-2079.
Ref ID: 64

Keywords: Aged/Aged,80 and over/Aging/blood/Body Mass Index/Carotid Arteries/Carotid Artery Diseases/Carotid Artery,Common/Cholesterol/Disease Progression/epidemiology/Estradiol/Humans/Hypertension/Male/methods/Netherlands/Prospective Studies/Risk/Risk Factors/Smoking/Testosterone/Tunica Intima/Tunica Media/ultrasonography

Abstract: **BACKGROUND:** The burden of atherosclerosis especially afflicts the increasing older segment of the population. Recent evidence has emphasized a protective role of endogenous sex hormones in the development of atherosclerosis in aging men.

METHODS AND RESULTS: We studied the association between endogenous sex hormones and progression of atherosclerosis in 195 independently living elderly men. Participants underwent measurements of carotid intima-media thickness (IMT) at baseline in 1996 and again in 2000. At baseline, serum concentrations of testosterone (total and free) and estradiol (total and free E2) were measured. Serum free testosterone concentrations were inversely related to the mean progression of IMT of the common carotid artery after adjustment for age (beta=-3.57; 95% CI, -6.34 to -0.80). Higher serum total and free E2 levels were related to progression of IMT of the common carotid artery after adjustment for age (beta=0.38; 95% CI, -0.11 to 0.86; and beta=0.018; 95% CI, -0.002 to 0.038, respectively). These associations were independent of body mass index, waist-to-hip ratio, presence of hypertension and diabetes, smoking, and serum cholesterol levels
CONCLUSIONS: Low free testosterone levels were related to IMT of the common carotid artery in elderly men independently of cardiovascular risk factors

- (29) **Papademetriou V, Farsang C, Elmfeldt D, Hofman A, Lithell H, Olofsson B et al. Stroke prevention with the angiotensin II type 1-receptor blocker candesartan in elderly patients with isolated systolic hypertension: the Study on Cognition and Prognosis in the Elderly (SCOPE).** J Am Coll Cardiol 2004; 44(6):1175-1180.

Ref ID: 41

Keywords: administration & dosage/Aged/Aged,80 and over/analysis/Angiotensin II Type 1 Receptor Blockers/Antihypertensive Agents/Benzimidazoles/blood/Blood Pressure/Cerebrovascular Accident/Comparative Study/Diuretics/Double-Blind Method/drug effects/drug therapy/epidemiology/Europe/Female/Follow-Up Studies/Humans/Hydrochlorothiazide/Hypertension/Male/methods/mortality/physiopathology/prevention & control/Prognosis/Receptor,Angiotensin,Type 1/Research Support,Non-U.S.Gov't/Risk/Risk Factors/Systole/Tetrazoles/therapeutic use/therapy/Time Factors/Treatment Outcome/Veterans

Abstract: **OBJECTIVES:** The aim of this study was to test the hypothesis that the angiotensin II type 1 receptor blocker (ARB) candesartan can reduce the risk of stroke in elderly patients with isolated systolic hypertension (ISH). **BACKGROUND:** Isolated systolic hypertension is the predominant form of hypertension in the elderly, and stroke is the most common cardiovascular (CV) complication. **METHODS:** In the Study on Cognition and Prognosis in the Elderly (SCOPE), 4,964 patients age 70 to 89 years were randomly assigned to double-blind candesartan or placebo with open-label antihypertensive therapy (mostly thiazide diuretics) added as needed to control blood pressure. Of the 4,964 patients, 1,518 had ISH (systolic blood pressure >160 mm Hg and diastolic blood pressure <90 mm Hg). The present study is a predefined subgroup analysis of outcome results in the ISH patients. **RESULTS:** Of the ISH patients, 754 were randomized to the candesartan group and 764 to the control group. Over the study period, blood pressure was reduced by 22/6 mm Hg in the candesartan group and by 20/5 mm Hg in the control group (difference between treatments 2/1 mm Hg; p = 0.101 and 0.064). A total of 20 fatal/non-fatal strokes occurred in the candesartan group (7.2/1,000 patient-years) and 35 in the control group (12.5/1,000 patient-years); relative risk (RR) was 0.58 (95% confidence interval 0.33 to

1.00), that is, a RR reduction of 42% ($p = 0.050$ unadjusted, $p = 0.049$ adjusted for baseline risk). There were no marked or statistically significant differences between the treatment groups in other CV end points or all-cause mortality. **CONCLUSIONS:** In elderly patients with ISH, antihypertensive treatment based on the ARB candesartan resulted in a significant 42% RR reduction in stroke in comparison with other antihypertensive treatment, despite little difference in blood pressure reduction

- (30) **Pasqualini R, Foroni M, Salvioli G, Mussi C. The "nondipper" elderly: a clinical entity or a bias?** *J Am Geriatr Soc* 2004; 52(6):967-971.

Ref ID: 257

Keywords: Aged/Aged,80 and over/analysis/Artifacts/blood/Blood Pressure/Blood Pressure Monitoring,Ambulatory/Circadian

Rhythm/Comorbidity/complications/diagnosis/Female/Geriatrics/Humans/Hypertension/Italy /Male/Middle Aged/Monitoring,Ambulatory/Movement/Multivariate

Analysis/physiology/physiopathology/Polypharmacy/Prevalence/Pulse/Sleep/Sleep Disorders

Abstract: **OBJECTIVES:** To determine the prevalence of nondipper (ND) blood pressure profile in the elderly and to ascertain whether the ND pattern of ambulatory blood pressure in the elderly is an artifact or represents a specific clinical entity. **DESIGN:** Cross-sectional, observational study. **SETTING:** Cardiovascular diagnostic center, division of geriatrics, secondary care, institutional practice. **PARTICIPANTS:** Sixty-five consecutive community-dwelling elderly hypertensive patients referred to the cardiovascular center. **MEASUREMENTS:** The patients underwent actigraphy and ambulatory blood pressure monitoring and completed a sleep assessment questionnaire. Patients were divided based on the night-time decrease in blood pressure ($>10\%$: "dippers" ($n=19$); $<10\%$: "NDs" ($n=46$)). **RESULTS:** Nondippers displayed poorer quality of sleep, as demonstrated objectively by actigraphic data; they obtained a higher mean score \pm standard deviation on the sleep questionnaire (4.6 ± 2.9 vs 3.0 ± 1.1 , $P=.030$) and were taking more benzodiazepines (33.1% vs 10.7% , $P=.035$), indicating that their usual sleep quality was worse than that of dippers. Multivariate analysis showed a strong correlation between nondipper profile and quality of sleep and also with comorbidity, total number of drugs being taken, and pulse pressure. **CONCLUSION:** Actigraphy demonstrates impaired sleep in the nondipper elderly. Nevertheless, the nondipping pattern seems independent of the discomfort of cuff-inflation during the night and occurs in association with higher comorbidity and polypharmacy; therefore, it cannot be considered a "bias," but is related to detrimental clinical conditions that should be studied in depth

- (31) **Psaltopoulou T, Naska A, Orfanos P, Trichopoulos D, Mountokalakis T, Trichopoulou A. Olive oil, the Mediterranean diet, and arterial blood pressure: the Greek European Prospective Investigation into Cancer and Nutrition (EPIC) study.** *Am J Clin Nutr* 2004; 80(4):1012-1018.

Ref ID: 33

Keywords: administration & dosage/Adult/Aged/Aged,80 and over/Alcohol Drinking/analysis/blood/Blood Pressure/Cereals/Cohort

Studies/diagnosis/Diet,Mediterranean/drug effects/epidemiology/etiology/Female/Food Habits/Fruit/Greece/Humans/Hypertension/Male/Meat/Middle Aged/mortality/Plant

Oils/Prospective Studies/Questionnaires/Research Support,Non-U.S.Gov't/Vegetables

Abstract: **BACKGROUND:** Diet has been reported to influence arterial blood pressure, and evidence indicates that the Mediterranean diet reduces cardiovascular mortality.

OBJECTIVE: The objective was to examine whether the Mediterranean diet, as an entity, and olive oil, in particular, reduce arterial blood pressure. **DESIGN:** Arterial blood pressure

and several sociodemographic, anthropometric, dietary, physical activity, and clinical variables were recorded at enrollment among participants in the Greek arm of the European Prospective Investigation into Cancer and Nutrition (EPIC) study. Of these participants, 20 343 had never received a diagnosis of hypertension and were included in an analysis in which systolic and diastolic blood pressure were regressed on the indicated possible predictors, including a 10-point score that reflects adherence to the Mediterranean diet and, alternatively, the score's individual components and olive oil. RESULTS: The Mediterranean diet score was significantly inversely associated with both systolic and diastolic blood pressure. Intakes of olive oil, vegetables, and fruit were significantly inversely associated with both systolic and diastolic blood pressure, whereas cereals, meat and meat products, and ethanol intake were positively associated with arterial blood pressure. Mutual adjustment between olive oil and vegetables, which are frequently consumed together, indicated that olive oil has the dominant beneficial effect on arterial blood pressure in this population. CONCLUSIONS: Adherence to the Mediterranean diet is inversely associated with arterial blood pressure, even though a beneficial component of the Mediterranean diet score-cereal intake-is positively associated with arterial blood pressure. Olive oil intake, per se, is inversely associated with both systolic and diastolic blood pressure

- (32) **Schlienger RG, Kraenzlin ME, Jick SS, Meier CR. Use of beta-blockers and risk of fractures.** JAMA 2004; 292(11):1326-1332.

Ref ID: 38

Keywords: Adrenergic beta-Antagonists/Adult/Aged/analysis/Angiotensin-Converting Enzyme Inhibitors/Antihypertensive Agents/Body Mass Index/Calcium Channel Blockers/Case-Control Studies/diagnosis/Diuretics/Diuretics,Thiazide/drug therapy/Drug Therapy,Combination/epidemiology/Female/Fractures/Humans/Hypertension/Male/Middle Aged/Osteoporosis/pharmacology/Research Support,Non-U.S.Gov't/Risk/Smoking/therapeutic use/therapy

Abstract: CONTEXT: Animal studies suggest that the beta-blocker propranolol increases bone formation, but data on whether use of beta-blockers (with or without concomitant use of thiazide diuretics) is associated with reduced fracture risk in humans are limited.

OBJECTIVE: To determine whether use of beta-blockers alone or in combination with thiazides is associated with a decreased risk of fracture in adults. DESIGN, SETTING, AND PARTICIPANTS: Case-control analysis using the UK General Practice Research Database (GPRD). The study included 30,601 case patients aged 30 to 79 years with an incident fracture diagnosis between 1993 and 1999 and 120,819 controls, matched to cases on age, sex, calendar time, and general practice attended. MAIN OUTCOME MEASURES: Odds ratios (ORs) of having a fracture in association with use of beta-blockers or a combination of beta-blockers with thiazides. RESULTS: The most frequent fractures were of the hand/lower arm (n = 12,837 [42.0%]) and of the foot (n = 4627 [15.1%]). Compared with patients who did not use either beta-blockers or thiazide diuretics, the OR for current use of beta-blockers only (> or =3 prescriptions) was 0.77 (95% confidence interval [CI], 0.72-0.83); for current use of thiazides only (> or =3 prescriptions), 0.80 (95% CI, 0.74-0.86); and for combined current use of beta-blockers and thiazides, 0.71 (95% CI, 0.64-0.79). Data were adjusted for smoking; body mass index; number of practice visits; and use of calcium channel blockers, angiotensin-converting enzyme inhibitors, antipsychotics, antidepressants, statins, antiepileptics, benzodiazepines, corticosteroids, and estrogens. CONCLUSIONS: Our data suggest that current use of beta-blockers is associated with a reduced risk of fractures, taken alone as well as in combination with thiazide diuretics. Many elderly patients with hypertension who are at risk of developing osteoporosis may potentially benefit from combined therapy with beta-blockers and thiazides

- (33) **Sierra C, De La SA, Salamero M, Sobrino J, Gomez-Angelats E, Coca A. Silent cerebral white matter lesions and cognitive function in middle-aged essential hypertensive patients.** Am J Hypertens 2004; 17(6):529-534.
Ref ID: 108
Keywords: Aged/blood/Blood Pressure/Brain/Brain Diseases/Cerebral Ventricles/Cognition/Comparative Study/Depression/Diastole/Female/Humans/Hypertension/Magnetic Resonance Imaging/Male/Memory/methods/Middle Aged/pathology/physiology/physiopathology/radiography/Research Support, Non-U.S.Gov't/Severity of Illness Index/Spain/Statistics/Systole
Abstract: BACKGROUND: An association between midlife blood pressure levels and late-life cognitive impairment has been reported. Hypertension is one of the most important factors related to the presence of cerebral white matter lesions, which is a prognostic factor for the development of cognitive impairment. Studies have shown a relationship between white matter lesions and cognitive decline in elderly hypertensive patients. The aim of the present study was to evaluate cognitive function in asymptomatic middle-aged hypertensive patients according to the presence or absence of white matter lesions. METHODS: Sixty never-treated essential hypertensive patients (38 men, 22 women), aged 50 to 60 years (mean age, 54.4 +/- 3.8 years), without clinical evidence of target organ damage, were studied. All patients underwent brain magnetic resonance imaging to establish the presence or absence of white matter lesions, using the Rotterdam criteria. Cognitive function was evaluated by a neuropsychologic test battery measuring attention, memory, intelligence, anxiety, and depression. RESULTS: Twenty-three hypertensive patients (38%) were found to have white matter lesions on brain resonance. These patients exhibited a significantly worse performance on digit span forward, a standardized measure of attention than hypertensives without white matter lesions (4.86 +/- 1.14 v 5.51 +/- 0.97; P = .027). Hypertensive patients with white matter lesions showed no differences on both visual and logical memory tests when compared with patients without lesions. CONCLUSIONS: We conclude that the presence of silent cerebral white matter lesions in middle-aged hypertensive patients is associated with a mild decline in basic attention
- (34) **Staessen JA, Thijs L, Fagard R, Celis H, Birkenhager WH, Bulpitt CJ et al. Effects of immediate versus delayed antihypertensive therapy on outcome in the Systolic Hypertension in Europe Trial.** J Hypertens 2004; 22(4):847-857.
Ref ID: 135
Keywords: administration & dosage/Aged/Antihypertensive Agents/blood/Blood Pressure/Calcium Channel Blockers/Cerebrovascular Accident/Comparative Study/complications/Diabetes Mellitus/Dihydropyridines/Double-Blind Method/Drug Administration Schedule/drug effects/drug therapy/Drug Therapy, Combination/Enalapril/epidemiology/Europe/Female/Follow-Up Studies/Heart Failure, Congestive/Humans/Hydrochlorothiazide/Hypertension/Incidence/Linear Models/Male/methods/mortality/Myocardial Infarction/Nitrendipine/Research Support, Non-U.S.Gov't/Survival Rate/therapeutic use/therapy/Time Factors/Treatment Outcome
Abstract: BACKGROUND: To assess the impact of immediate versus delayed antihypertensive treatment on the outcome of older patients with isolated systolic hypertension, we extended the double-blind placebo-controlled Systolic Hypertension in Europe (Syst-Eur) trial by an open-label follow-up study lasting 4 years. METHODS: The Syst-Eur trial included 4695 randomized patients with minimum age of 60 years and an untreated blood pressure of 160-219 mmHg systolic and below 95 mmHg diastolic. The double-blind trial ended after a median follow-up of 2.0 years (range 1-97 months). Of 4409 patients still alive, 3517 received open-label treatment consisting of nitrendipine (10-40 mg

daily) with the possible addition of enalapril (5-20 mg daily), hydrochlorothiazide (12.5-25 mg daily), or both add-on drugs. Non-participants (n = 892) were also followed up. RESULTS: Median follow-up increased to 6.1 years. Systolic pressure decreased to below 150 mmHg (target level) in 2628 participants (75.0%). During the 4-year open-label follow-up, stroke and cardiovascular complications occurred at similar frequencies in patients formerly randomized to placebo and those continuing active treatment. These rates were similar to those previously observed in the active-treatment group during the double-blind trial. Considering the total follow-up of 4695 randomized patients, immediate compared with delayed antihypertensive treatment reduced the occurrence of stroke and cardiovascular complications by 28% (P = 0.01) and 15% (P = 0.03), respectively, with a similar tendency for total mortality (13%, P = 0.09). In 492 diabetic patients, the corresponding estimates of long-term benefit (P < 0.02) were 60, 51 and 38%, respectively. CONCLUSIONS: Antihypertensive treatment can achieve blood pressure control in most older patients with isolated systolic hypertension. Immediate compared with delayed treatment prevented 17 strokes or 25 major cardiovascular events per 1000 patients followed up for 6 years. These findings underscore the necessity of early treatment of isolated systolic hypertension

- (35) **Steckelings UM, Stoppelhaar M, Sharma AM, Wittchen HU, Krause P, Kupper B et al. HYDRA: possible determinants of unsatisfactory hypertension control in German primary care patients.** Blood Press 2004; 13(2):80-88.

Ref ID: 256

Keywords: administration & dosage/Adolescent/Adult/Aged/analysis/Antihypertensive Agents/blood/Blood Pressure/Cross-Sectional Studies/diagnosis/drug effects/drug therapy/Drug

Therapy,Combination/epidemiology/Female/Germany/Humans/Hypertension/Male/Middle Aged/Patient Education/pharmacology/physiopathology/Primary Health Care/Research Support,Non-U.S.Gov't/therapeutic use

Abstract: The Hypertension and Diabetes Screening and Awareness (HYDRA) study is a cross-sectional point-prevalence study performed in September 2001; 45,125 primary care attendees were recruited from a representative nationwide sample of 1912 primary care practices in Germany. Around 42% of all patients presenting in these practices had hypertension (WHO definition). In approximately 70% of these patients, hypertension was diagnosed by doctors and 84% of diagnosed patients were on antihypertensive medication, but in less than 30% of treated patients was blood pressure controlled (< 140/90 mmHg). The control rate in all patients presenting with hypertension (including those patients unrecognized) was as low as 19%. The present analysis aimed to find explanations for this unsatisfactory outcome of hypertension control. The main finding was that the rate of diagnosis of hypertension is alarmingly low in young people, probably due to insufficient blood pressure screenings. The data further indicated that doctors still set their target of treatment according to outdated guidelines and that doctors still orientate their treatment primarily with regard to the diastolic pressure. These insights into the causes of unsatisfactory hypertension control may help to direct future educational programmes designed to improve hypertension management specifically to these deficits and thereby to improve control rates

- (36) **Steffen HM. Use of calcium channel antagonists for the treatment of hypertension in the elderly.** Drugs Aging 2004; 21(9):565-581.

Ref ID: 123

Keywords: Adult/Aged/Amlodipine/Antihypertensive Agents/blood/Blood Pressure/Calcium Channel Blockers/Cardiovascular Diseases/Comparative

Study/complications/Dementia/Diabetes Complications/Diabetes Mellitus/Diuretics/drug therapy/Drug Therapy,Combination/epidemiology/etiology/Heart/Humans/Hypertension/mortality/Prevalence/prevention & control/Pulse/Randomized Controlled Trials/Research Support,Non-U.S.Gov't/Risk/therapeutic use

Abstract: Systolic blood pressure and pulse pressure increase continuously throughout adult life and the prevalence of arterial hypertension rises accordingly, reaching 53-78% among those aged 65-74 years. Estimates of the prevalence of isolated systolic hypertension in the elderly range from 34-65%, with more women than men affected. It has been shown that within all age groups a difference in usual systolic blood pressure of 20 mm Hg or a difference in usual diastolic blood pressure of 10 mm Hg is associated with an approximately 2-fold difference in the risk of dying from stroke or ischaemic heart disease. Intervention trials using predominantly diuretics and/or beta-adrenoceptor antagonists have proven the efficacy and tolerability of antihypertensive treatment in elderly patients. For many years there have been ongoing discussions about the safety of calcium channel antagonists, especially in patients with diabetes mellitus. However, according to a recently published large prospective, randomised, double-blind, controlled clinical trial with more than 33,000 patients enrolled, no indications for increased total mortality, cancer rate or gastrointestinal bleeding for participants on amlodipine, a long-acting dihydropyridine calcium channel antagonist, were found. With calcium channel antagonists, protective effects against cardiovascular disease have been proven in large trials with elderly patients, particularly against stroke. There is good evidence to suggest that calcium channel antagonists may be superior to other antihypertensive agents in diabetic patients with isolated systolic hypertension. These agents are well tolerated and probably delay the progression of dementia. The lack of adverse metabolic effects that, in the case of a diuretic-based regimen, may have important long-term implications concerning cardiovascular risk, make calcium channel antagonists an attractive choice when antihypertensive treatment decisions need to be made in a predominantly overweight or obese elderly population

- (37) **van Dijk EJ, Prins ND, Vermeer SE, Hofman A, van Duijn CM, Koudstaal PJ et al. Plasma amyloid beta, apolipoprotein E, lacunar infarcts, and white matter lesions.**

Ann Neurol 2004; 55(4):570-575.

Ref ID: 70

Keywords: Aged/Aged,80 and over/Amyloid beta-Protein/Apolipoproteins E/blood/Brain/Brain Infarction/Comparative Study/Confidence Intervals/Creatinine/Cross-Sectional

Studies/Dementia/epidemiology/Female/genetics/Genotype/Humans/Hypertension/Linear Models/Magnetic Resonance Imaging/Male/metabolism/Middle Aged/Nerve Fibers,Myelinated/Netherlands/Odds Ratio/pathology/Research Support,Non-U.S.Gov't

Abstract: Lacunar brain infarcts and cerebral white matter lesions are frequently observed on magnetic resonance imaging scans in elderly subjects. These lesions are also frequent in patient with cerebral amyloid angiopathy. We examined whether plasma amyloid beta peptide (Abeta) levels are associated with lacunar infarcts and white matter lesions in the general population, and whether the apolipoprotein E (APOE) genotype modifies these associations. We studied 1,077 participants within the population-based Rotterdam Scan Study, who were 60 to 90 years of age and free of dementia. Cross-sectional associations were analyzed by regression models with adjustments for age, sex, creatinine levels, and hypertension. In APOE epsilon4 carriers, plasma Abeta levels were positively associated with lacunar infarcts and white matter lesions, whereas in noncarriers no associations were observed. Per standard deviation increase in Abeta(1-40) and Abeta(1-42) levels the odds

ratios for lacunar infarcts were 1.72 (95% confidence interval [CI] = 1.22-2.43) and 1.93 (95% CI = 1.31-2.85), the periventricular white matter lesion grade increased by 0.32 (95% CI = 0.08-0.57) and 0.29 (95% CI = 0.00-0.57), and the subcortical white matter lesion volume increased by 0.48 ml (95% CI = 0.04-0.91) and 0.24 ml (95% CI = -0.27-0.75). Higher Aβ levels are associated with more lacunar infarcts and white matter lesions in elderly subjects who carry an APOE ε4 allele

- (38) **Wang Y, Wang QJ. The prevalence of prehypertension and hypertension among US adults according to the new joint national committee guidelines: new challenges of the old problem.** Arch Intern Med 2004; 164(19):2126-2134.

Ref ID: 255

Keywords: Adult/African Americans/analysis/blood/Blood Pressure/Body Weight/classification/Hypertension/methods/Prevalence/United States

Abstract: **BACKGROUND:** The recently released Seventh Report of the Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure provides a new classification of blood pressure levels. Little is known about the current situation of elevated blood pressure in the United States, according to the new guidelines. **METHODS:** Cross-sectional analysis of national representative data collected from 4805 adults 18 years and older surveyed in the 1999-2000 National Health and Nutrition Examination Survey. We examined the prevalence of prehypertension and hypertension according to the new JNC guidelines, people's awareness and management of hypertension, and the differences across sociodemographic and body weight groups. **RESULTS:** Elevated blood pressure is a serious problem in the United States. Approximately 60% of American adults have prehypertension or hypertension, and some population groups, such as African Americans, older people, low-socioeconomic-status groups, and overweight groups, are disproportionately affected. The prevalence of hypertension has increased by approximately 10 percentage points during the past decade. The awareness and appropriate management of hypertension among hypertensive patients remain low: 31% were not aware of their disease, only two thirds (66%) were told by health professionals to adopt lifestyle modifications or take drugs to control hypertension, and only 31% controlled their hypertension. **CONCLUSIONS:** With 60% of the population affected, the United States is facing a serious challenge in the prevention and management of prehypertension and hypertension. People's awareness and control of hypertension remain poor. This study highlights the seriousness of the problem and the importance of promoting lifestyle modifications

- (39) **Wassertheil-Smoller S, Psaty B, Greenland P, Oberman A, Kotchen T, Mouton C et al. Association between cardiovascular outcomes and antihypertensive drug treatment in older women.** JAMA 2004; 292(23):2849-2859.

Ref ID: 3

Keywords: Adrenergic beta-Antagonists/Aged/Angiotensin-Converting Enzyme Inhibitors/Antihypertensive Agents/blood/Blood Pressure/Calcium Channel Blockers/Cardiovascular Diseases/complications/Diuretics/drug therapy/Drug Therapy,Combination/epidemiology/Female/Follow-Up Studies/Heart/Humans/Hypertension/Middle Aged/Postmenopause/prevention & control/Proportional Hazards Models/Prospective Studies/Research Support,U.S.Gov't,P.H.S./Risk/therapeutic use/Treatment Outcome

Abstract: **CONTEXT:** Diuretic-based therapy is at least as effective as newer classes of agents for hypertension. However, many patients with hypertension require treatment with more than 1 drug class to achieve blood pressure control. The relative benefits or risks of 2-drug-class combinations are not well known. **OBJECTIVE:** To prospectively evaluate if

there are differences in cardiovascular mortality among postmenopausal women with hypertension but no history of cardiovascular disease (CVD) treated with different classes of antihypertensive agents, singly or in combination. DESIGN, SETTING, AND PARTICIPANTS: Women with hypertension enrolled in the Women's Health Initiative Observational Study, a longitudinal multicenter cohort study of 93 676 women aged 50 to 79 years at baseline (1994-1998), assessed for a mean of 5.9 years. MAIN OUTCOME MEASURES: Relationship between baseline use of ACE inhibitors, beta-blockers, calcium channel blockers, or diuretics, or a combination of these, and incidence of coronary heart disease, stroke, and CVD mortality. RESULTS: Among 30,219 women with hypertension but no history of CVD, 11 294 (57%) were receiving monotherapy with an ACE inhibitor, beta-blocker, calcium channel blocker, or diuretic, and 4493 (23%) were treated at baseline with a combination of diuretic plus either ACE inhibitor, beta-blocker, or calcium channel blocker or ACE inhibitor plus calcium channel blocker. Monotherapy with calcium channel blockers vs diuretics was associated with greater risk of CVD death (hazard ratio, 1.55; 95% confidence interval, 1.02-2.35), controlling for multiple covariates. Women treated with a diuretic plus a calcium channel blocker had an 85% greater risk of CVD death vs those treated with a diuretic plus a beta-blocker, after adjustment for age, race, smoking, high cholesterol levels requiring medication, body mass index, physical activity, use of hormone therapy, and diabetes. After exclusion of women with diabetes the hazard ratio was 2.16 (95% confidence interval, 1.16-4.03). Analyses adjusting for propensity to be receiving a particular treatment did not change the results. For morbid events of coronary heart disease or stroke, diuretics plus ACE inhibitors or calcium channel blockers did not differ from diuretics plus beta-blockers. CONCLUSIONS: Among women with hypertension but no history of CVD, a 2-drug-class regimen of calcium channel blockers plus diuretics was associated with a higher risk of CVD mortality vs beta-blockers plus diuretics. Risks were similar for ACE inhibitors plus diuretics and beta-blockers plus diuretics. Monotherapy with diuretics was equal or superior to other monotherapy in preventing CVD complications of high blood pressure

- (40) **Wolf-Maier K, Cooper RS, Kramer H, Banegas JR, Giampaoli S, Joffres MR et al. Hypertension treatment and control in five European countries, Canada, and the United States.** Hypertension 2004; 43(1):10-17.

Ref ID: 117

Keywords: Adolescent/Adult/Aged/blood/Blood Pressure/Canada/Cardiovascular Diseases/Comparative Study/complications/Cross-Sectional Studies/drug therapy/epidemiology/etiology/Europe/Female/Humans/Hypertension/Italy/Male/methods/Middle Aged/Prevalence/Research Support,Non-U.S.Gov't/Research Support,U.S.Gov't,P.H.S./Risk/Risk Factors/Spain/Sweden/United States

Abstract: Levels of hypertension treatment and control have been noted to vary between Europe and North America, although direct comparisons with similar methods have not been undertaken. In this study, we sought to estimate the relative impact of hypertension treatment strategies in Germany, Sweden, England, Spain, Italy, Canada, and the United States by using sample surveys conducted in the 1990s. Hypertension was defined as a blood pressure of 160/95 mm Hg or 140/90 mm Hg, plus persons taking antihypertensive medication. "Controlled hypertension" was defined as a blood pressure less than threshold among persons taking antihypertensive medications. Among persons 35 to 64 years, 66% of hypertensives in the United States had their blood pressure controlled at 160/95 mm Hg, compared with 49% in Canada and 23% to 38% in Europe. Similar discrepancies were apparent at the 140/90 mm Hg threshold, at which 29% of hypertensives in the United States, 17% in Canada, and $\leq 10\%$ in European countries had their blood pressure controlled. At the 140/90 mm Hg cutpoint, two thirds to three quarters of the hypertensives

in Canada and Europe were untreated compared with slightly less than half in the United States. Although guidelines vary among countries, resulting in different case definitions, this does not account entirely for the varying success of different national control efforts. Low treatment and control rates in Europe, combined with a higher prevalence of hypertension, could contribute to a higher burden of cardiovascular disease risk attributable to elevated blood pressure compared with that in North America