



## The monthly ESH guide through publications

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Before we dive into the recent publications, we would like to invite you to the 26th ESH Annual Meeting that will take place in June 10-13 2016. As always, it will offer a great chance for an update on evolving research and clinical practice in all fields of hypertension through various session designs, as well as the ground for networking and fruitful discussions among scientists and experts interested in cardiovascular protection.

### The antihypertensive effect of spironolactone is positively related to urinary sodium excretion regardless of aldosterone status in patients with resistant hypertension.

Resistant hypertension (RHT) is associated with high dietary sodium and hyperaldosteronism, while mineralocorticoid receptor antagonists are recommended for treatment of RHT. In a retrospective analysis of 79 patients with RHT (baseline SBP  $153.6 \pm 22.3$  mmHg; women 53.2%; African-American 55.8%; obese 76%) the BP response to adding spironolactone 12.5-25mg to existing medications was investigated. A favourable BP response was defined as a reduction in SBP of at least 10 mmHg. Addition of spironolactone resulted in a mean reduction of  $15.5 \pm 20.7$  mmHg. Patients with high urinary sodium excretion ( $\geq 200$  mEq/24h) had a significantly greater BP reduction compared with patients with normal excretion ( $< 200$  mEq/24h) ( $P=0.008$ ). Multivariable analysis identified 24h urinary sodium excretion as a significant predictor of BP response ( $P=0.021$ ) after controlling for potential confounders, including primary aldosteronism. It is concluded that the antihypertensive effect of spironolactone is positively related to urinary sodium excretion regardless of aldosterone status and that mineralocorticoid receptor

antagonists may be of preferential benefit in counteracting the BP effects of high dietary sodium.

*Ghazi L, Dudenbostel T, Lin CP, Oparil S, Calhoun DA. Urinary sodium excretion predicts blood pressure response to spironolactone in patients with resistant hypertension independent of aldosterone status. J Hypertens. 2016 May;34(5):1005-10.*

### **Renal nerve stimulation in accessory renal arteries after sympathetic renal denervation leads to persistent increase in blood pressure.**

The role of accessory renal arteries too small for denervation with respect to BP response to renal denervation is of interest. A study of 21 patients assessed renal nerve stimulation-induced BP increase before and after renal sympathetic denervation in main and accessory renal arteries of anaesthetized patients with drug-resistant hypertension. Nine patients had at least 1 accessory renal artery in which renal denervation was not feasible. Renal nerve stimulation was performed in the main arteries of all patients and in accessory renal arteries of 6 of 9 patients with accessory arteries, both before and after renal sympathetic denervation. Renal nerve stimulation before renal denervation elicited a substantial increase in systolic blood pressure, both in main ( $25.6 \pm 2.9$  mm Hg;  $P < 0.001$ ) and accessory ( $24.3 \pm 7.4$  mm Hg;  $P = 0.047$ ) renal arteries. After renal denervation, renal nerve stimulation-induced systolic blood pressure increase was blunted in the main renal arteries ( $\Delta$  systolic blood pressure,  $8.6 \pm 3.7$  mm Hg;  $P = 0.020$ ), but not in the non denervated renal accessory renal arteries ( $\Delta$  systolic blood pressure,  $27.1 \pm 7.6$  mm Hg;  $P = 0.917$ ). It is concluded that this residual source of renal sympathetic tone may result in persistent hypertension after ablation and partly account for the large response variability.

*de Jong MR, Hoogerwaard AF, Gal P, Adiyaman A, Smit JJ, Delnoy PP, RamdatMisier AR, van Hasselt BA, Heeg JE, le Polain de Waroux JB, Lau EO, Staessen JA, Persu A, Elvan A. Persistent Increase in Blood Pressure After Renal Nerve Stimulation in Accessory Renal Arteries After Sympathetic Renal Denervation. Hypertension. 2016 Jun;67(6):1211-7.*

### **Low adherence to antihypertensives and statin is associated with an increased risk for fatal stroke.**

The risk of fatal stroke associated with nonadherence to statin and/or antihypertensive therapy was assessed in a population-based study using electronic medical and prescription records from Finnish national registers in 1995 to 2007. Of the 58,266 hypercholesterolemia patients age 30+ years without pre-existing stroke or cardiovascular disease, 532 patients died of stroke (cases), and 57,734 remained free of incident stroke (controls) during the mean follow-up of 5.5 years. Year-by-year adherence to statin and antihypertensive therapy in both study groups was captured and the excess risk of stroke death associated with nonadherence was estimated. In all hypercholesterolemia patients, the adjusted odds ratio for stroke death for nonadherent compared with adherent statin users was 1.35 (95% CI 1.04 to 1.74) 4 years before and 2.04 (95% CI: 1.72 to 2.43) at the year of stroke death or the end of the follow-up. In hypercholesterolemia patients with hypertension, relative to those who adhered to statins and antihypertensive therapy, the odds ratio at the year of stroke death was 7.43 (95% CI: 5.22 to 10.59) for those nonadherent both to statin and antihypertensive therapy, 1.82 (95% CI: 1.43 to 2.33) for those non-adherent to statin but adherent to antihypertensive therapy, and 1.30 (95% CI: 0.53 to 3.20) for those adherent to statin, but nonadherent to antihypertensive, therapy. It is concluded that individuals with hypercholesterolemia and hypertension who fail to take their prescribed statin and antihypertensive medication experience a substantially increased risk of fatal stroke. The risk is lower if the patient is adherent to either one of these therapies.

*Herttua K, Martikainen P, Batty GD, Kivimäki M. Poor Adherence to Statin and Antihypertensive Therapies as Risk Factors for Fatal Stroke. J Am CollCardiol. 2016 Apr 5;67(13):1507-15.*

### **Effects of more compared to less intensive blood pressure lowering and different achieved blood pressure levels: data from an updated meta-analysis.**

In an updated meta-analysis, optimal BP targets of antihypertensive treatment were investigated. Among randomized-controlled trials (RCTs) of BP lowering treatment between 1966 and 2015, 16 (52235 patients) compared more vs. less intense treatment, and in 34 (138127 patients) SBP in the active (vs. placebo) or the more (vs. less) intense treatment was below (vs., respectively, above) three predetermined cutoffs. More intense BP lowering significantly reduced risk of stroke

[RR 0.71 (0.60-0.84)], coronary events [0.80 (0.68-0.95)], major cardiovascular events [0.75 (0.68-0.85)] and cardiovascular mortality [0.79 (0.63-0.97)], but not heart failure and all-cause death. When the 16 RCTs were stratified according to cardiovascular death risk, relative risk reduction did not differ between strata, but absolute risk reduction increased with cardiovascular risk, though the residual risk also increased. Stratification of the 34 RCTs according to the three different SBP cutoffs (150, 140 and 130mmHg) showed that a SBP/DBP difference of -10/-5mmHg across each cutoff significantly reduced risk of all outcomes to the same proportion (relative risk reduction), but absolute risk reduction of most outcomes had a significant trend to decrease at lower cutoffs. It is concluded that more versus less intense BP lowering can reduce not only stroke and coronary events, but also cardiovascular mortality. Including data from recent RCTs also shows that all major outcomes can be reduced by lowering SBP a few mmHg below vs. above 130mmHg, but absolute risk reduction becomes smaller, suggesting patients at lower initial SBP were at a lower level of cardiovascular risk.

*Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension: 7. Effects of more vs. less intensive blood pressure lowering and different achieved blood pressure levels - updated overview and meta-analyses of randomized trials. J Hypertens. 2016 Apr;34(4):613-22.*

### **Relationship between outpatient visit frequency and hypertension control: a 9-year occupational cohort study.**

A 9-year cohort study investigated the relationship between the frequency of outpatient visits and hypertension control as determined from health insurance records. 518 participants with hypertension who underwent health checkups in 2004 were included. Participants were aged 35-56 years and none had a history of cardiovascular or cerebrovascular disease. Mean annual outpatient visit days at a hospital/clinic during the 9-year period were classified within four quartiles (Q1, Q2, Q3, Q4). The median (25th-75th percentile) annual outpatient visit days was 9.4 (4.0-15.5). Uncontrolled hypertension was observed in 62.4% of the participants in 2013. The multivariable-adjusted ORs and 95% CIs for uncontrolled hypertension in Q1, Q2 and Q3 vs. Q4 were 4.03 (2.28-7.12), 1.67 (0.99-2.81) and 1.44 (0.86-2.41), respectively. Uncontrolled hypertension increased significantly as the number of

outpatient visits decreased (P for trend <0.001). This tendency was maintained when participants taking antihypertensive agents at baseline were excluded. It is concluded that there is an inverse relationship between outpatient visit frequency and uncontrolled hypertension.

*Shima A, Tatsumi Y, Ishizaki T, Godai K, Kawatsu Y, Okamura T, Nishikawa T, Morimoto A, Morino A, Miyamatsu N. Relationship between outpatient visit frequency and hypertension control: a 9-year occupational cohort study. Hypertens Res. 2016 May;39(5):376-81.*

### **Dynamic penile peak systolic velocity as a predictor of major adverse cardiovascular events in hypertensive patients with erectile dysfunction.**

Reduced dynamic penile peak systolic velocity (D-PSV) correlates with adverse cardiovascular outcomes. In a study on 298 hypertensive men ( $55 \pm 9$  y/o) without known cardiovascular disease or diabetes, the authors investigated whether abnormal penile blood flow predicts major adverse cardiovascular events (MACE). Cavernous vascular disease severity was evaluated by dynamic penile Doppler ultrasound. The whole population was divided into tertiles according to D-PSV reduction (low tertile <25 cm/s; middle tertile 25-35 cm/s; and high tertile >35 cm/s). During a mean follow-up period of 4.9 years, a total of 22 (7%) MACE occurred. D-PSV level was associated with MACE and the differences between the tertiles were significant (Mantel log-rank test: 6.54;  $P < 0.01$ ). A Cox proportional hazard model showed that study participants in the lowest D-PSV tertile had an approximately 3.5-fold higher MACE risk compared with those in the highest D-PSV tertile after adjustment for age, systolic pressure, metabolic parameters, smoking, C-reactive protein, and testosterone levels. When only intermediate-risk patients were evaluated, the risk reclassification beyond traditional risk factors resulted in a clinical net reclassification index of 9.2% that was marginally significant ( $P = 0.07$ ). It is concluded that low-penile blood flow predicts MACE in hypertensive patients free of clinical atherosclerosis. This predictive ability was independent of the severity of hypertension and decreased testosterone levels.

Ioakeimidis N, Vlachopoulos C, Rokkas K, Kratiras Z, Angelis A, Samentzas A, Fassoulakis C, Tousoulis D. Dynamic penile peak systolic velocity predicts major adverse cardiovascular events in hypertensive patients with erectile dysfunction. *J Hypertens*. 2016 May;34(5):860-8.

### **Chlorthalidone/amiloride is more effective compared to losartan in patients with stage I hypertension.**

A randomized, double-blind, controlled trial was performed to compare the blood pressure (BP)-lowering efficacy of a chlorthalidone/amiloride combination pill with losartan during initial management of stage I hypertension. 655 participants with stage I hypertension after 3 months of a lifestyle intervention (aged 30-70 years, BP 140-159 or 90-99 mmHg) were followed for 18 months in 21 Brazilian academic centers. Participants were randomized to 12.5/2.5 mg of chlorthalidone/amiloride (N=333) or 50 mg of losartan (N=322). If BP remained uncontrolled after 3 months, study medication dose was doubled, and if uncontrolled after 6 months, amlodipine (5 and 10 mg) and propranolol (40 and 80 mg twice daily) were added as open-label drugs in a progressive fashion. The difference in SBP during 18 months of follow-up was 2.3 (95% confidence interval: 1.2 to 3.3) mmHg favoring chlorthalidone/amiloride. Compared with those randomized to diuretic, more participants allocated to losartan had their initial dose doubled and more of them used add-on antihypertensive medication. The authors conclude that treatment with a combination of chlorthalidone and amiloride compared with losartan yielded a greater reduction in BP.

Fuchs FD, Scala LC, Vilela-Martin JF, de Mello RB, Mosele F, Whelton PK, Poli-de-Figueiredo CE, de Alencastro PR, E Silva RP, Gus M, Bortolotto LA, Schlatter R, Cesarino EJ, Castro I, Neto JA, Chaves H, Steffens AA, Alves JG, Brandão AA, de Sousa MR, Jardim PC, Moreira LB, Franco RS, Gomes MM, Neto AA, Fuchs FC, Filho DC, Nóbrega AC, Nobre F, Berwanger O, Fuchs SC. Effectiveness of chlorthalidone/amiloride versus losartan in patients with stage I hypertension: results from the PREVER-treatment randomized trial. *J Hypertens*. 2016 Apr;34(4):798-806.

### **Cumulative hypoxemia during sleep predicts vascular endothelial dysfunction in patients with sleep-disordered breathing.**

A study was performed to clarify what SDB-related parameters most predict endothelial dysfunction. In 50 outpatients suspected of SDB polysomnography (PSG) was conducted and flow-mediated vasodilation response (%FMD) was measured. Evaluated indices included: apnea-hypopnea index (AHI), 3% oxygen desaturation index (3%ODI), averaged arterial oxygen saturation (averaged SpO<sub>2</sub>), lowest arterial oxygen saturation (lowest SpO<sub>2</sub>), ratio of arterial oxygen saturation <90% (<SpO<sub>2</sub> 90%), and averaged time desaturation summation index (TDS: [100%-averaged SpO<sub>2</sub>] × total sleep time). Significant differences were observed only in the TDS between the first and third ( $P = 0.03$ ) and between the first and fourth ( $P = 0.04$ ) quartile groups, stratified by %FMD. The %FMD showed a significant relationship with TDS ( $\beta = -0.47$ ,  $P = 0.001$ ), even after adjusting for confounding factors ( $\beta = -0.33$ ,  $P = 0.02$ ). In contrast, AHI, 3%ODI, averaged SpO<sub>2</sub>, lowest SpO<sub>2</sub>, and <SpO<sub>2</sub> 90% showed no significant relationships. The authors conclude that this study shows the validity of TDS in predicting endothelial damage in patients with SDB. Cumulative hypoxemia, rather than the frequency of hypoxemic events presented as AHI, may be a greater contributing factor in causing endothelial dysfunction.

Sawatari H, Chishaki A, Nishizaka M, Tokunou T, Adachi S, Yoshimura C, Ohkusa T, Ando S. Cumulative Hypoxemia During Sleep Predicts Vascular Endothelial Dysfunction in Patients With Sleep-Disordered Breathing. *Am J Hypertens*. 2016 Apr;29(4):458-63

### **Effects of antihypertensive agents on central systolic blood pressure and augmentation index: insights from a meta-analysis.**

A meta-analysis assessing the impact of antihypertensives on central systolic blood pressure (cSBP) and augmentation index (AI) was performed. Fifty-two and 58 studies incorporating 4,381 and 3,716 unique subjects were included for cSBP and AI analysis, respectively. Overall, antihypertensives reduced pSBP more than cSBP (WMD 2.52mm Hg, 95% CI 1.35 to 3.69;  $I^2(2) = 21.9\%$ ).  $\beta$ -Blockers (BBs) posed a significantly greater reduction in pSBP as compared to cSBP (WMD 5.19mm Hg, 95% CI 3.21 to 7.18).  $\alpha$ -Blockers, angiotensin converting enzyme inhibitors, angiotensin II receptor blockers, calcium channel blockers, diuretics, renin-angiotensin aldosterone system inhibitors and nicorandil reduced cSBP and pSBP in



a similar manner. The overall reduction in AI from baseline was 3.09% (95% CI 2.28 to 3.90;  $I^2(2) = 84.5\%$ ). A significant reduction in AI was seen with angiotensin converting enzyme inhibitors, angiotensin II receptor blockers, calcium channel blockers, and diuretics but not with BBs. It is concluded that BBs are not as beneficial as the other antihypertensives in reducing cSBP and AI.

*McGaughey TJ, Fletcher EA, Shah SA. Impact of Antihypertensive Agents on Central Systolic Blood Pressure and Augmentation Index: A Meta-Analysis. Am J Hypertens. 2016 Apr;29(4):448-57.*

### **Home blood pressure strongly predicts coronary artery disease.**

Data from the HONEST (Home blood pressure measurement with Olmesartan Naive patients to Establish Standard Target blood pressure) study were used to investigate the relationship between morning HBP and incidence of stroke and CAD events. In 21,591 treated hypertensive patients (mean age 64.9 years; mean follow-up 2.02 years), 127 stroke events (2.92 per 1,000 patient-years), and 121 CAD events (2.78 per 1,000 patient-years) occurred. The incidence of stroke events was significantly higher in patients with morning home systolic blood pressure (HSBP)  $\geq 145$  mm Hg compared with  $< 125$  mm Hg, and in patients with clinic systolic blood pressure (CSBP)  $\geq 150$  mm Hg compared with  $< 130$  mm Hg. Morning HSBP predicted stroke events similarly to CSBP. Incidence of CAD events was significantly higher in patients with morning HSBP  $\geq 145$  mm Hg compared with  $< 125$  mm Hg and in patients with CSBP  $\geq 160$  mm Hg compared with  $< 130$  mm Hg. The HR for morning HSBP  $\geq 155$  mm Hg was 6.24 (95% CI: 2.82 to 13.84) and for CSBP  $\geq 160$  mm Hg was 3.51 (95% CI: 1.71 to 7.20); therefore, compared with morning HSBP, CSBP may underestimate CAD risk. Goodness-of-fit analysis showed that morning HSBP predicted CAD events more strongly than CSBP. It is concluded that morning HBP is a strong predictor of future CAD and stroke events, and may be superior to clinic BP in this regard. There did not appear to be a J-curve in the relationship between morning HBP and stroke or CAD events.

*Kario K, Saito I, Kushi T, Teramukai S, Tomono Y, Okuda Y, Shimada K. Morning Home Blood Pressure Is a Strong Predictor of Coronary Artery Disease: The HONEST Study. J Am Coll Cardiol. 2016 Apr 5;67(13):1519-27.*



### **Prognostic value of nocturnal blood pressure fall independent of 24-hour systolic blood pressure.**

The Ambulatory Blood Pressure Collaboration in Patients With Hypertension (ABC-H) examined the prognostic importance of the nocturnal systolic blood pressure (SBP) fall, adjusted for average 24-hour SBP levels, in a meta-analysis of 17 312 hypertensives from 3 continents. Risks were computed for the systolic night-to-day ratio and for different dipping patterns (extreme, reduced, and reverse dippers) relative to normal dippers. There were 1769 total CVEs, 916 coronary events, 698 strokes, 450 cardiovascular deaths, and 903 total deaths. After adjustment for 24-hour SBP, the systolic night-to-day ratio predicted all outcomes: from a 1-SD increase, summary HRs were 1.12 to 1.23. Reverse dipping also predicted all end points: HRs were 1.57 to 1.89. Reduced dippers, relative to normal dippers, had a significant 27% higher risk for total CVEs. Risks for extreme dippers were significantly influenced by antihypertensive treatment ( $P<0.001$ ): untreated patients had increased risk of total CVEs (HR, 1.92), whereas treated patients had borderline lower risk (HR, 0.72) than normal dippers. The authors conclude that among hypertensives the nocturnal BP fall provided substantial prognostic information, independent of 24-hour SBP levels.

*Salles GF, Reboldi G, Fagard RH, Cardoso CR, Pierdomenico SD, Verdecchia P, Eguchi K, Kario K, Hoshida S, Polonia J, de la Sierra A, Hermida RC, Dolan E, O'Brien E, Roush GC; ABC-H Investigators. Prognostic Effect of the Nocturnal Blood Pressure Fall in Hypertensive Patients: The Ambulatory Blood Pressure Collaboration in Patients With Hypertension (ABC-H) Meta-Analysis. Hypertension. 2016 Apr;67(4):693-700.*

### **Effects of baroreflex activation therapy on ambulatory blood pressure in patients with resistant hypertension.**

There is no information on the effect of the currently used, unilateral Baroreflex activation therapy (BAT) neo device on ambulatory BP measurements (ABPM). In the present study, patients treated with the BAT neo device for uncontrolled resistant hypertension were prospectively included. ABPM was

performed before BAT implantation and 6 months after initiation of BAT. A total of 51 patients were included into this study, 7 dropped out from analysis because of missing or insufficient follow-up. After 6 months, 24-hour ambulatory systolic (from  $148\pm 17$  mm Hg to  $140\pm 23$  mm Hg,  $P<0.01$ ), diastolic (from  $82\pm 13$  mm Hg to  $77\pm 15$  mm Hg,  $P<0.01$ ), day- and night-time systolic and diastolic BP (all  $P\leq 0.01$ ) significantly decreased while the number of prescribed antihypertensive classes could be reduced from  $6.5\pm 1.5$  to  $6.0\pm 1.8$  ( $P=0.03$ ). BAT was equally effective in reducing ambulatory BP in all subgroups of patients. It is concluded that BAT might be considered as a new therapeutic option to reduce cardiovascular risk in patients with resistant hypertension.

*Wallbach M, Lehnig LY, Schroer C, Lüders S, Böhning E, Müller GA, Wachter R, Koziol MJ. Effects of Baroreflex Activation Therapy on Ambulatory Blood Pressure in Patients With Resistant Hypertension. Hypertension. 2016 Apr;67(4):701-9.*

### **Plasma aldosterone concentration in the adrenal veins shows significant variation and lateralization gradient even in non-PA hypertensive patients.**

In a retrospective study, the results of cosyntropin-stimulated adrenal venous sampling in 40 hypertensive patients who showed positive screening testing but negative results in 2 confirmatory tests/captopril challenge test and saline infusion test were analyzed. Plasma aldosterone concentration, aldosterone/cortisol ratio, its higher/lower ratio (lateralization index) in the adrenal vein with cosyntropin stimulation were measured. Median plasma aldosterone concentration in the adrenal vein was 25 819 pg/mL (range, 5154-69 920) in the higher side and 12 953 (range, 1866-36 190) pg/mL in the lower side ( $P<0.001$ ). There was a significant gradient in aldosterone/cortisol ratio between the higher and the lower sides (27.2 [5.4-66.0] versus 17.3 [4.0-59.0] pg/mL per  $\mu\text{g/dL}$ ;  $P<0.001$ ) with lateralization index ranging from 1.01 to 3.87. The aldosterone lateralization gradient was between 1 to 2 in 32 patients and 2 to 4 in 8 patients. None of the patients showed lateralization index  $\geq 4$ . It is concluded that plasma aldosterone concentration in the adrenal veins shows significant variation and lateralization gradient even in non-PA hypertensive patients; adrenal venous sampling aldosterone lateralization gradients between 2 and 4

should be interpreted with caution in patients with PA because these gradients can be found even in patients with negative confirmatory testing for PA.

*Umakoshi H, Naruse M, Wada N, Ichijo T, Kamemura K, Matsuda Y, Fujii Y, Kai T, Fukuoka T, Sakamoto R, Ogo A, Suzuki T, Nanba K, Tsuiki M; WAVES-J Study Group. Adrenal Venous Sampling in Patients With Positive Screening but Negative Confirmatory Testing for Primary Aldosteronism. Hypertension. 2016 May;67(5):1014-9.*

### **Effect of obstructive sleep apnea in acute coronary syndromes.**

In a prospective longitudinal cohort study of 73 patients admitted on cardiac intensive care unit for ACS, the prevalence of OSA and the prognostic impact of OSA and continuous positive airway pressure (CPAP) therapy were investigated. Cardiorespiratory sleep study and/or polysomnography were performed in all patients. CPAP was recommended if Apnea-Hypopnea Index  $\geq 5$ . The main study outcome was a composite of death for any cause, myocardial infarction, and myocardial revascularization. OSA was diagnosed in 46 patients (63%). Age and cardiovascular risk factors were not significantly different between groups. OSA was classified as mild (m-OSA) in 14 patients (30%) and as moderate-to-severe (s-OSA) in 32 patients (70%). After a median follow-up of 75 months, patients with s-OSA had lower event-free survival rate. After adjustment for gender, patients with s-OSA showed a significantly higher incidence of the composite end point (hazard ratio 3.58, 95% CI 1.09 to 17.73,  $p = 0.035$ ). 19 patients adhered to CPAP (41%), but compliance to CPAP therapy did not reduce the risk of the composite end point (hazard ratio 0.87, 95% CI 0.31 to 2.46,  $p = 0.798$ ). In conclusion, OSA is an under diagnosed disease with high prevalence in patients with ACS.

*Leão S, Conde B, Fontes P, Calvo T, Afonso A, Moreira I. Effect of Obstructive Sleep Apnea in Acute Coronary Syndrome. Am J Cardiol. 2016 Apr 1;117(7):1084-7.*

### **Changes in systolic blood pressure through time and cardiovascular disease**

Data from the Atherosclerosis Risk in Communities (ARIC) cohort were used to examine the contribution of longitudinal patterns of blood pressure change to incidence of heart failure, coronary heart disease, stroke, and cardiovascular disease mortality. Latent class growth models were used to identify patterns of change in

blood pressure across 4 clinical examinations (1987-1998) among 9845 participants (mean age, 53.7 [SD 5.7] years). Patterns of change in systolic blood pressure included slowly and steeply increasing, a decreasing and a sustained elevated blood pressure. Changes in diastolic and mid-blood pressure ( $\frac{1}{2}$  systolic +  $\frac{1}{2}$  diastolic) were less pronounced. The association of blood pressure pattern group membership with incidence of clinical outcomes was examined in follow-up using Poisson regression models adjusted for demographic and metabolic characteristics, and hypertension medication use. A gradient of rates of all events was observed across the identified patterns. Associations were attenuated after adjustment for covariates. It is concluded that cumulative systolic blood pressure load, rather than the temporal pattern of change in systolic blood pressure itself, plays a role in determining the risk of cardiovascular disease, in particular, of heart failure and cardiovascular disease mortality, independent of blood pressure level measured at one point in time.

*Petruski-Ivleva N, Viera AJ, Shimbo D, Muntner P, Avery CL, Schneider AL, Couper D, Kucharska-Newton A. Longitudinal Patterns of Change in Systolic Blood Pressure and Incidence of Cardiovascular Disease: The Atherosclerosis Risk in Communities Study. Hypertension. 2016 Jun;67(6):1150-6.*

### **Renal resistive index is associated with systemic vascular changes in hypertension**

Renal resistance index (RRI) emerges as a good indicator of systemic vascular changes. In the present study, the authors assessed the independent relationships of carotid intima-media thickness (cIMT), aortic pulse wave velocity (aPWV), and peripheral pulse pressure (PP) with RRI in hypertensives with various degrees of renal function. 463 hypertensive patients (30-70 years) with normal renal function (group 0; n = 280) and with chronic kidney disease (groups I-V; n = 183) were enrolled. All subjects underwent ultrasonographic examination of intrarenal and carotid vasculature, as well as a 24-h ambulatory blood pressure monitoring. RRI correlated with cIMT ( $r = 0.460$ ,  $P < 0.001$ ), aPWV ( $r = 0.386$ ,  $P < 0.001$ ), clinic PP ( $r = 0.279$ ,  $P < 0.001$ ), and 24-h PP ( $r = 0.229$ ,  $P < 0.001$ ) in the entire study population. These correlations were similar in subjects with and without renal dysfunction. In the overall study population, the association between RRI, cIMT, and

clinic PP remained statistically significant even after adjustment for various confounding factors, whereas the relationship between RRI and aPWV was lost in multivariate analysis. It is concluded that cIMT and clinic PP rather than directly aPWV are associated with intrarenal hemodynamics; in hypertensives RRI not only detects derangement of intrarenal circulation but may also be considered as a sensor of systemic vascular changes, independently of level of renal function.

*Geraci G, Mulè G, Costanza G, Mogavero M, Geraci C, Cottone S. Relationship Between Carotid Atherosclerosis and Pulse Pressure with Renal Hemodynamics in Hypertensive Patients. Am J Hypertens. 2016 Apr;29(4):519-27.*