



## The monthly ESH guide through publications

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### Increased risk of progression to sustained hypertension in patients with white coat and masked hypertension

White-coat and masked hypertension are two not clearly defined entities with respect to their clinical impact. A study by Sivén SS et al. investigated the risk of progression to sustained hypertension among a total of 944 patients of the Finn-Home study with either normotension (n=528) or white-coat HT (n=142) or masked HT(n=63) that were followed for 11 years. Rate of progression to sustained HT increased from 18% in normotension to 52% in white-coat HT to 73% in masked HT. These rates increased progressively with increasing home and office BP. After adjusting for other cardiovascular risk factors (sex, age, smoking, BMI, diabetes and hypercholesterolemia) the relative risk among patients with white-coat HT was 2.8 (95% CI 2.2-3.6) and those with masked HT was 3.8 (95% CI 2.9-5.0). The authors conclude that white-coat and masked HT are not benign phenomena and such patients require close follow-up and lifestyle evaluation.

*Sivén SS, Niiranen TJ, Kantola IM, Jula AM. White-coat and masked hypertension as risk factors for progression to sustained hypertension: the Finn-Home study. J Hypertens. 2016;34(1):54-60.*

### Greater cardiovascular protection of more compared to less intensive BP lowering

The results of the recent independent SPRINT trial have caused a stir among experts with respect to the optimal BP target. In a large meta-analysis of 19 trials published between 1950 and 2015, on a total of 44989 patients, Xie X et al. investigated the effect on cardiovascular risk of more intensive vs less intensive BP

lowering treatment. Mean BP was 133/76mmHg in the more intensive BP lowering group compared to 140/81mmHg in the less intensive BP lowering group. There was a significant relative risk reduction in patients that underwent intensive BP-lowering for major cardiovascular events, myocardial infarction and stroke but not for heart failure, end-stage renal disease and cardiovascular and total mortality. Additional BP lowering had a clear benefit even in patients with systolic BP lower than 140mmHg, while the absolute benefit was greater in trials of patients with vascular or renal disease or diabetes. Severe hypotension was more frequent but overall rare in the more intensive BP lowering approach. It is concluded that intensive BP lowering offers greater protection for cardiovascular events, while there are additional benefits in high-risk patients.

*Xie X, Atkins E, Lv J, Bennett A, Neal B, Ninomiya T, Woodward M, MacMahon S, Turnbull F, Hillis GS, Chalmers J, Mant J, Salam A, Rahimi K, Perkovic V, Rodgers A. Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis. Lancet. 2016 Jan;387(10017):435-43.*

### **Adverse effect of extreme air pollution on blood pressure and insulin resistance**

Increasing data are providing evidence of an adverse impact of air pollution on cardiovascular parameters. In the Air Pollution and Cardiometabolic Disease Study, 65 nonsmoking adults with metabolic syndrome living in Beijing underwent a series of visits across 4 seasons. The high fine particulate matter and personal black carbon levels ranged significantly during follow-up and their cumulative exposure in the previous days to the visits were associated with systolic and diastolic BP elevations respectively. Both black carbon and fine particulate matter were significantly associated with worsening insulin resistance. The study highlights the increased cardiometabolic risk of air pollution that may affect populations living in areas with extremely high concentrations of fine particulate matter such as megacities in Asia.

*Brook RD, Sun Z, Brook JR, Zhao X, Ruan Y, Yan J, Mukherjee B, Rao X, Duan F, Sun L, Liang R, Lian H, Zhang S, Fang Q, Gu D, Sun Q, Fan Z, Rajagopalan S. Extreme Air Pollution Conditions*

*Adversely Affect Blood Pressure and Insulin Resistance: The Air Pollution and Cardiometabolic Disease Study. Hypertension. 2016;67(1):77-85.*

### **Central compared to brachial blood pressure is a better associate to target organ damage**

Central BP has been proposed as a closer correlate of target organ damage compared to brachial BP. In a meta-analysis of cross-sectional data, Kollias A et al. documented a closer association of central compared to brachial BP with left ventricular mass index (n=6431, r=0.30 vs 0.26, p<0.01 for difference), carotid intima-media thickness (n=6136, r=0.27 vs 0.23, p<0.01 for difference) and pulse wave velocity (n=3699, r=0.42 vs 0.39, p<0.01 for difference). Similar correlations of central and brachial BP were reported with urinary albumin excretion. Age did not have a significant effect as shown in meta-regression analysis. It is concluded that central compared to brachial BP is overall more strongly associated with preclinical organ damage.

*Kollias A, Lagou S, Zeniodi ME, Boubouchairopoulou N, Stergiou GS. Association of Central Versus Brachial Blood Pressure With Target-Organ Damage: Systematic Review and Meta-Analysis. Hypertension. 2016;67(1):183-90.*

### **Relative potency, dose equivalence and effects of dose doubling among different categories of potassium sparing diuretics**

Clinical trial data on potassium-sparing diuretics with respect to their effects on BP are overall limited compared to the more widely used thiazides. Roush GC et al. performed a meta-analysis of trials that randomized hypertensive patients using a parallel or cross-over design with a placebo group. The amiloride dose levels of 2.5, 5, 10, 20 and 40mg were considered analogous to eplerenone and spironolactone dose levels of 25, 50, 100, 200 and 400mg. Placebo-adjusted changes in office SBP were -1.9 for triamterene (low dose), -9.9 for amiloride, -13.2 for spironolactone and -9.2 for eplerenone. Doubling amiloride, eplerenone, and spironolactone doses reduced SBP similarly and on average by -2.3 (-3.1, -1.5). Spironolactone was the most potent antihypertensive followed by amiloride and eplerenone. Dose equivalencies were eplerenone to spironolactone 4.5-to-1, amiloride to

spironolactone 3.3-to-1, and eplerenone to amiloride 1.4-to-1. Increases in serum potassium from amiloride and spironolactone at commonly used doses averaged 0.14–0.29 mEq/l. As data on direct comparisons between potassium sparing diuretics are lacking, insights from a systematic review help guide the use of such agents.

*Roush GC, Ernst ME, Kostis JB, Yeasmin S, Sica DA. Dose doubling, relative potency, and dose equivalence of potassium-sparing diuretics affecting blood pressure and serum potassium: systematic review and meta-analyses. J Hypertens. 2016;34(1):11-9.*

### **Risk of incident hypertension associated with parathyroid hormone**

Data are accumulating regarding the vascular effects of parathyroid hormone (PTH) including endothelial dysfunction and renin-angiotensin system activation. The association of PTH with the development of HT was examined among 7504 participants of the Atherosclerosis Risk in Community Study free of cardiovascular disease or HT. Incident HT was defined as BP  $\geq$ 140/90mmHg or reported antihypertensive treatment. During a 6 year follow-up, PTH was not associated with incident HT after adjusting for multiple demographics and behavioural risk factors. No significant interaction between PTH and age, sex, obesity status, or eGFR was detected. However, there was an independent positive association of PHT with incident HT in black patients even after adjustments. Unlike whites, when PTH was defined according to the clinical cut-point ( $\geq$ 65 vs  $<$ 65pg/ml), blacks in the clinically high PTH group were at a significant greater risk for HT. It is concluded that in the study cohort there was no independent association of PHT with incident HT but there may be such an association in blacks.

*Yao L, Folsom AR, Pankow JS, Selvin E, Michos ED, Alonso A, Tang W, Lutsey PL. Parathyroid hormone and the risk of incident hypertension: the Atherosclerosis Risk in Communities study. J Hypertens. 2016; 34(2):196-203.*

### **Cardiovascular effects of unilateral nephrectomy in living kidney donors**

Even though there is a clear association of chronic kidney disease and cardiovascular events, it is still unclear whether this relationship is causative. The

Chronic Renal Impairment in Birmingham (CRIB)-Donor study is a prospective, longitudinal, parallel group study comparing living kidney donors with similar healthy controls (n=124); it was designed to study the association of the reduction in renal function with adverse cardiovascular effects. At 12 months, there was a  $30\pm 12\text{ml/min/1.73m}^2$  decrease in GFR among donors. In donors compared with controls, there were significant increases in left ventricular mass ( $+7\pm 10$  versus  $-3\pm 8$  g;  $P<0.001$ ), while aortic distensibility ( $-0.29\pm 1.38$  versus  $+0.28\pm 0.79\times 10^{-3}$  mm Hg $^{-1}$ ;  $P=0.03$ ) and global circumferential strain decreased ( $-1.1\pm 3.8$  versus  $+0.4\pm 2.4\%$ ;  $P=0.04$ ). Donors had a higher risk of developing detectable highly sensitive troponin T (OR 16.2, CI 95% 2.6–100.1,  $P<0.01$ ) and microalbuminuria (OR 3.8, CI 95% 1.1–12.8,  $P=0.04$ ). No changes in ambulatory BP were documented. Change in GFR was independently associated with change in left ventricular mass ( $R^2=0.28$ ;  $P=0.01$ ). It is concluded that reduced renal function should be regarded as an independent causative cardiovascular risk factor.

*Moody WE, Ferro CJ, Edwards NC, Chue CD, Lin EL, Taylor RJ, Cockwell P, Steeds RP, Townend JN; CRIB-Donor Study Investigators. Cardiovascular Effects of Unilateral Nephrectomy in Living Kidney Donors. Hypertension. 2016; 67(2):368-77.*

### **Isometric exercise for blood pressure management**

Dynamic aerobic endurance is the preferred exercise option for BP management. Isometric activity has previously been associated with exaggerated BP response but there is data that isometric resistance training may lower BP. In a meta-analysis of 11 randomized and crossover trials (n=302) the effects of isometric exercise on BP were examined. Six studies used handgrip and five studies used leg exercise, while study duration ranged from 4 to 10 weeks. After isometric exercise there was a decrease in systolic BP by  $-5.2$  mmHg (95% CI:  $-6.08$  to  $-4.33$ ), in diastolic BP by  $-3.91$  mmHg ( $-5.68$  to  $-2.14$ ) and in mean BP by  $-3.33$  mmHg (95% CI  $-4.01$  to  $-2.66$ ). Males tended to reduce mean BP more than females and subjects aged more than 45 years demonstrated greater reductions in mean BP. Hypertensive patients showed a larger reduction in mean BP compared to normotensives. This form of training may produce significant and clinically meaningful BP reductions

*Inder JD, Carlson DJ, Dieberg G, McFarlane JR, Hess NC, Smart NA. Isometric exercise training for blood pressure management: a systematic review and meta-analysis to optimize benefit. Hypertens Res. 2016;39(2):88-94.*

### **Improving adherence with mobile phone text messages**

Adherence to treatment is a major issue to optimize management of HT. The SMS-Text Adherence Support (StAR) trial is a single-blind, 3-arm randomized trial that assessed the effect of automated adherence support via mobile text messages on BP. A total of 1372 patients were randomized to receive information-only text messages, interactive text messages or usual care. At 12 months, the mean adjusted change in systolic BP compared with usual care was -2.2mmHg (95% CI, -4.4 to -0.04) with information only SMS and -1.6mmHg (95% CI, -3.7 to 0.6) with interactive SMS. There was a 42% greater chance for HT control with information-only messaging and 41% greater chance with interactive messaging compared to usual care. It was concluded that there is a small reduction in systolic BP with mobile phone text messages after 12 months, while an interactive intervention did not provide any additional benefit.

*Bobrow K, Farmer AJ, Springer D, Shanyinde M, Yu LM, Brennan T, Rayner B, Namane M, Steyn K, Tarassenko L, Levitt N. Mobile Phone Text Messages to Support Treatment Adherence in Adults With High Blood Pressure (SMS-Text Adherence Support [StAR]): A Single-Blind, Randomized Trial. Circulation. 2016; 133(6):592-600.*