

#### **NEWSLETTER**

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## The monthly ESH guide through publications

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#### Effects of hypertension treatment on heart failure: insights from a metaanalysis

A recent meta-analysis of a total of 35 BP-lowering randomized controlled trials investigated the contribution of antihypertensive treatment and different classes of antihypertensive drugs on new-onset heart failure. Relative risk with BP lowering was 0.63 (CI: 0.52-0.75) for heart failure and 0.58 (CI: 0.49-0.68) for stroke. There was an association of relative risk reduction with systolic and diastolic BP and pulse pressure reduction. Further analysis of head to head comparisons of different antihypertensive drug classes at first showed that calcium antagonists are inferior in preventing new onset heart failure (RR:1.16, CI: 1.01-1.33). However, after limiting the analysis to trials allowing concomitant use of diuretics, b-blockers or RAS blockers, this inferiority disappeared (RR: 0.96, CI:0.81-1.12). It is concluded that BP-lowering treatment effectively prevents new-onset heart failure. After considering trial design, calcium antagonists are as affective as other drugs in preventing heart failure

Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure-lowering treatment. 6. Prevention of heart failure and new-onset heart failure - meta-analyses of randomized trials. J Hypertens. 2016 Mar; 34(3):373-84.

# Protective effect of allopurinol for cardiovascular outcomes in hypertensive adults

Data from the United Kingdom Clinical Research Practice Datalink were used to investigate the hypothesis that allopurinol is associated with improved cardiovascular outcomes among hypertensive adults older than 65 years. A total of 2032 allopurinol-exposed patients and 2032 matched non-exposed patients were studied. Exposure to allopurinol was a time-dependent variable and was defined as any exposure and then as high ( $\geq$ 300 mg daily) or low-dose exposure. Allopurinol use was associated with a significantly lower risk of both stroke (HR: 0.50, 95% CI: 0.32–0.80) and cardiac events (HR: 0.61, 95% CI: 0.43–0.87) compared tononexposed control patients. In exposed patients, high-dose treatment with allopurinol (n=1052) was associated with a significantly lower risk of both stroke (HR: 0.58, 95% CI: 0.36–0.94) and cardiac events (HR: 0.65, 95% CI: 0.46–0.93) than low-dose treatment (n=980). It is concluded that allopurinol use is associated with lower rates of stroke and cardiac events in older adults with hypertension, particularly at higher doses.

MacIsaac RL, Salatzki J, Higgins P, Walters MR, Padmanabhan S, Dominiczak AF, Touyz RM, Dawson J. Allopurinol and Cardiovascular Outcomes in Adults With Hypertension. Hypertension. 2016 Mar; 67(3):535-40.

### Blood pressure lowering for prevention of cardiovascular disease and mortality: a meta-analysis focusing on baseline pressure, comorbidities and drug classes

A systematic review and meta-analysis was performed to clarify the extent to which the benefits of BP lowering for prevention of cardiovascular disease differ by baseline BP, comorbidities and drug classes. A total of 123 randomized controlled trials (613815 participants) were included in the analysis. Every 10 mm Hg reduction in SBP significantly reduced the risk of major cardiovascular disease events (RR: 0.80, 95% CI: 0.77–0.83), coronary heart disease (RR: 0.83, 0.78–0.88), stroke (RR: 0.73, CI: 0.68–0.77), heart failure (RR: 0.72, 0.67–0.78) and all-cause mortality (RR: 0.87, CI: 0.84–0.91). The effect on renal failure was not significant (RR: 0.95, 0.84–1.07). Similar proportional risk reductions (per 10 mm Hg lower systolic blood pressure) were noted in trials with higher and lower mean baseline SBP. Proportional risk reductions in major cardiovascular disease did not differ by baseline disease history, except for diabetes and chronic kidney disease. B-blockers were inferior to other drugs for the prevention of major cardiovascular disease events,

stroke, and renal failure. Calcium channel blockers were superior to other drugs for the prevention of stroke. For the prevention of heart failure, calcium channel blockers were inferior and diuretics were superior to other drug classes. This meta-analysis strongly supports lowering BP to SBP less than 130 mm Hg and providing BP lowering treatment to individuals with a history of cardiovascular disease, coronary heart disease, stroke, diabetes, heart failure, and chronic kidney disease.

Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, Chalmers J, Rodgers A, Rahimi K. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet. 2016 Mar 5; 387(10022):957-67

## Increased prevalence of psychiatric disorders among patients with hypertension

In a study that used administrative healthcare data in Stockholm County 1 (of the total of 2058408 residents), the prevalence of concomitant hypertension and psychiatric disorders in the general population was investigated. Data of certain psychiatric diagnoses including specifically depression, anxiety disorders, bipolar disorder, and schizophrenia were obtained. The age-adjusted ORs for depression in persons with hypertension were 1.293 (95% CI 1.256–1.331,) for men and 1.036 (95% CI 1.013–1.058) for women. The age-adjusted ORs for anxiety in persons with hypertension were 1.279 (95% CI 1.238–1.322) for men and 1.050 (95% CI 1.024–1.076) for women. The OR for bipolar disease were 0.904 (95% CI 0.826–0.990) for men and 0.709 (95% CI 0.656–0.767) for women. For schizophrenia, the ORs were 0.568 (95% CI 0.511–0.632) for men and 0.537 (95% CI 0.478–0.603) for women. The authors conclude that increased awareness of the risk of depression and anxiety among hypertensive patients is needed to combat hypertension and psychiatric diseases in the population. In addition, hypertension is probably underdiagnosed and neglected in individuals with severe psychiatric disorders.

Sandström YK, Ljunggren G, Wändell P, Wahlström L, Carlsson AC. Psychiatric comorbidities in patients with hypertension - a study of registered diagnoses 2009-2013 in the total population in Stockholm County, Sweden. J Hypertens. 2016 Mar; 34(3):414-20.

## Pulse pressure is the strongest predictor of 30-day mortality among different blood pressure indices in patients with STEMI

A retrospective study in 7033 consecutive STEMI patients without cardiogenic shock was performed in order to compare admission SBP, DBP, pulse pressure and mean arterial pressure in predicting 30-day all-cause mortality. Cox proportional hazard analysis was used to calculate HRs with a 10mmHg increment and quartiles of each BP. Of the 4 indexes, only SBP (HR: 0.94 per 10mm Hg, Cl: 0.91-0.98; P = 0.001) and PP (HR: 0.89 per 10 mmHg, 95% Cl 0.85-0.94; P < 0.001) were significantly associated with 30-day all-cause mortality. Compared with SBP, PP was a better predictor for mortality in both men ( $\chi^2 = 5.9$  for per 10mm Hg,  $\chi^2 = 10.8$  for quartiles) or women ( $\chi^2 = 15.1$  for per 10mm Hg,  $\chi^2 = 19.5$  for quartiles), and the relationship remained significant after adjustment of SBP. There was a pattern of declining risk with increasing blood pressures for mortality, and this trend was mainly observed in age groups of more than 70 years. It is concluded that pulse pressure was an independent predictor of mortality in patients with STEMI, and low admission blood pressure should serve as a warning sign.

Ma WF, Liang Y, Zhu J, Yang YM, Tan HQ, Yu LT, Gao X, Feng GX, Li JD. Comparison of 4 Admission Blood Pressure Indexes for Predicting 30-Day Mortality in Patients With ST-Segment Elevation Myocardial Infarction. Am J Hypertens. 2016 Mar;29(3):332-9.

#### Measurement of night-time blood pressure with home blood pressure monitoring as a determinant of target organ damage

The association of night-time BP assessed by home blood pressure (HBP) or ambulatory blood pressure (ABP) monitoring with preclinical target organ damage was investigated in 131 middle-aged untreated hypertensive patients. Measurement of BP was performed with ABP monitoring (24-h) and HBP monitoring during daytime (6 days, duplicate morning and evening measurements) and night-time (automated asleep measurements, three nights, 3-hourly measurements/night). Daytime and night-time HBP were slightly higher than the respective ABP values (mean difference for systolic daytime/night-time 3.5±10.6/2.6±9.8mmHg, P<0.01). Target organ damage was assessed by echocardiographic left ventricular mass index (LVMI), common carotid intima–media thickness (cIMT), urine albumin excretion (UAE), and ankle-brachial index (ABI). Daytime as well as nighttime ABP were strongly correlated with their respective HBP counterparts. Both ABP and HBP night-time measurements were strongly and comparably correlated with all the indices of preclinical target organ damage. It is concluded that in untreated hypertensives, night-time BP assessed by home monitoring appears to be as good as night-time ambulatory monitoring in determining preclinical target organ damage.

Andreadis EA, Agaliotis G, Kollias A, Kolyvas G, Achimastos A, Stergiou GS. Night-time home versus ambulatory blood pressure in determining target organ damage.J Hypertens. 2016 Mar; 34(3):438-44.

## Aortic stiffness is associated with cognitive function and brain aging in young to middle aged adults

The associations of aortic stiffness with cognitive function and brain aging at a young age were examined in the Framingham Heart Study Third Generation cohort (47% men; mean age, 46 years). Participants completed the assessment of aortic stiffness (carotid–femoral pulse wave velocity), a neuropsychological test battery assessing multiple domains of cognitive performance and magnetic resonance imaging to examine subclinical markers of brain injury. In adjusted regression models, higher aortic stiffness was associated with poorer processing speed and executive function (Trail Making B–A;  $\beta$ ±SE,  $-0.08\pm0.03$ ; P<0.01), larger lateral ventricular volumes ( $\beta$ ±SE,  $0.09\pm0.03$ ; P<0.01) and a greater burden of white-matter hyperintensities ( $\beta$ ±SE,  $0.09\pm0.03$ ; P<0.01). In young adults (30–45 years) aortic stiffness was associated with white-matter injury and cognition. It is concluded that aortic stiffness was associated with cognitive function and markers of subclinical brain injury in young to middle-aged adults.

Pase MP, Himali JJ, Mitchell GF, Beiser A, Maillard P, Tsao C, Larson MG, DeCarli C, Vasan RS, Seshadri S. Association of Aortic Stiffness With Cognition and Brain Aging in Young and Middle-Aged Adults: The Framingham Third Generation Cohort Study. Hypertension. 2016 Mar; 67(3):513-9.

#### Lowering blood pressure below 140mmHg compared to 150mmHg may be more protective from stroke in elderly individuals

The effect of less compared to more intensive BP lowering on cardiovascular outcomein patients aged ≥60 years and free of stroke, diabetes mellitus, and chronic kidney disease was investigated in the Northern Manhattan Study. 1750 participants (mean age at baseline 72±8 years) had SBP measured at baseline and were annually followed up for incident stroke. Among all participants, 40% were on antihypertensive medications; 43% had SBP <140 mm Hg, 20% had 140 to 149 mm Hg, and 37% had  $\geq$ 150 mm Hg. Over a median follow-up of 13 years, 182 participants developed stroke. The crude stroke incidence was greater among individuals with SBP≥150 mm Hg (10.8 per 1000 person-years) and SBP 140 to 149 (12.3) than among those with SBP<140 (6.2). After adjusting for demographics, vascular risk factors, diastolic BP, and medication use, participants with SBP 140 to 149 mm Hg had an increased risk of stroke (HR, 1.7; 95% CI, 1.2-2.6) compared with those with SBP <140 mm Hg. The increased stroke risk was most notable among Hispanics and non-Hispanic blacks. It is concluded that raising the SBP target from 140 to 150 mm Hg in older individuals free from diabetes mellitus or chronic kidney disease may be detrimental for stroke risk reduction, especially among minority US populations.

Evidence to Maintain the Systolic Blood Pressure Treatment Threshold at 140 mm Hg for Stroke Prevention: The Northern Manhattan Study.Dong C, Della-Morte D, Rundek T, Wright CB, Elkind MS, Sacco RL.Hypertension. 2016 Mar;67(3):520-6.