Blood Pressure Single-Nucleotide Polymorphisms and Coronary Artery Disease (page 995)

Blood pressure (BP) is considered a major cardiovascular risk factor that is influenced by multiple genetic and environmental factors. However, the precise genetic underpinning influencing interindividual BP variation is not well characterized; and it is unclear whether BP-associated genetic variants also predispose to clinically apparent cardiovascular disease. Such an association of BP-related variants with cardiovascular disease would strengthen the concept of BP as a causal risk factor for cardiovascular disease. In this issue of Hypertension, analyses within the Coronary ARtery Disease Genome-Wide Replication And Meta-Analysis consortium indicate that common genetic variants associated with BP in the population, indeed, contribute to the susceptibility for coronary artery disease (CAD). Lieb et al tested 30 single-nucleotide polymorphisms—that based on prior studies were known to affect BP—for their association with CAD. In total, data from 22,233 CAD cases and 64,762 controls were analyzed. The vast majority (88%) of BP-related single-nucleotide polymorphisms were also shown to increase the risk of CAD (as defined by an odds ratio for CAD >1; Figure). On average, each of the multiple BP-raising alleles was associated with a 3% (95% confidence interval, 1.8%–4.3%) risk increase for CAD.

Masked Hypertension in Diabetes Mellitus (page 964)

The first important finding in the IDACO study of masked hypertension (MH) in the population with diabetes mellitus and non–diabetes mellitus was that antihypertensive treatment converted some sustained hypertensives into sustained normotensives; this resulted in an increased cardiovascular disease risk in the treated versus untreated normotensive comparator group (Figure). Not surprisingly, normalization of blood pressure (BP) with treatment did not eliminate the lifetime cardiovascular disease burden associated with prior elevated BP nor did it correct other cardiometabolic risk factors that clustered with the hypertensive state.

The second important IDACO finding was that treatment increased the prevalence of MH by decreasing conventional BP versus daytime ambulatory BP (ABP) by a ratio of ≈3 to 2. The clinical implication of increased prevalence of MH with therapy in the population of both diabetes mellitus and non–diabetes mellitus was that these subjects did not receive sufficient antihypertensive therapy to convert MH into normalized ABP (ie, treated, normalized ABP being the gold standard for minimizing cardiovascular disease risk). Indeed, there is a transformation-continuum from sustained hypertension to MH and finally to sustained normotension with increasing antihypertensive therapy. These IDACO findings strongly suggest that many physicians mistakenly have their primary focus on normalizing in-office rather than out-of-office home BP and/or 24-hour ABP values and this results in an increased prevalence of MH. However, what constitutes optimal normalized ABP will remain empirical until established in randomized controlled trials.

Genetic Risk Score for Blood Pressure (page 987)

Elevated blood pressure (BP) is a strong, independent, and modifiable risk factor for stroke and heart disease. BP is a heritable trait, and genome-wide association studies have identified several genetic loci that are associated with systolic BP, diastolic BP, or both. Although the variants have modest effects on BP, typically 0.5 to 1.0 mm Hg, their presence may act over the entire life course and, therefore, lead to substantial increase in risk of cardiovascular disease (CVD). However, the independent impact of these variants on CVD risk has not been established in a prospective setting. Havulinna et al genotyped 32 common single-nucleotide polymorphisms in several Finnish cohorts, with up to 32,669 individuals after exclusion of prevalent CVD cases. The median follow-up was 9.8 years, during which 2295 incident CVD events occurred. Genetic risk scores were created for systolic BP and diastolic BP by multiplying the risk allele count of each single-nucleotide polymorphism by the effect size estimated in published genome-wide association studies on BP traits. The GRSs were strongly associated with baseline systolic BP, diastolic BP, and hypertension (all P<0.05). Hazard ratios for incident CVD increased roughly linearly by quintile of systolic BP or diastolic BP GRS (Figure). GRSs remained significant predictors of CVD risk after adjustment for traditional risk factors, even including BP and use of antihypertensive medication. These findings are consistent with a lifelong effect of these variants on BP and CVD risk.