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EDITORIAL

Special Issue: Current evidence and perspectives for hypertension management in Asia

Real-world evidence of the association between blood pressure elevation and coronary artery disease and stroke in Japan

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The brain and heart are major target organs for hypertension, along with the kidneys. A large-scale meta-analysis of 61 prospective observational studies on blood pressure (BP) and mortality that included 958,074 adults with no previous cardiovascular disease demonstrated that the mortality rates for coronary artery disease (CAD) and stroke increase exponentially with elevated systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels, without any evidence of a threshold down to at least 115/75 mmHg [1]. Moreover, similar associations were shown for populations in the age range of 50 to 89 years, regardless of sex. EPOCH-JAPAN, a meta-analysis of 10 cohort studies that included approximately 70,000 individuals in Japan, showed that the association between SBP/DBP level and cardiovascular disease mortality was almost logarithmically linear and that the risk was lowest among individuals with BP levels <120/80 mmHg in both middle-aged (40–64 years) and elderly (65–74 years) age groups [2].

Recently, Yamada et al. investigated the associations between BP and the incidence of CAD or stroke according to glucose status by analyzing data from a nationwide claims-based database that included information on 805,992 adults with no prior cardiovascular disease enrolled with a health insurance provider for company employees and their dependents in Japan [3]. They found a linear relationship between SBP and DBP and CAD or stroke morbidity regardless of the presence or severity of abnormal glucose levels. Compared with the lowest quintile of SBP ≤ 119 mmHg, hazard ratios (HRs) for CAD in the higher SBP quintiles 2–5 (120–129, 130–139, 140–149, and 150≤ mmHg, respectively) progressively increased from 2.10 (95% confidence interval, 1.73–2.56) in quintile 2 to 3.21 (2.37–4.34) in quintile 5 among normoglycemic subjects. The HR for stroke increased from 1.46 (1.27–1.68) in quintile 2 to 4.76 (3.94–5.75) in quintile 5 among normoglycemic subjects. Similarly, the HRs for CAD and stroke progressively increased from 1.39 (1.14–1.69) and 1.70 (1.44–2.01) in quintile 2 to 2.52 (1.95–3.26) and 4.12 (3.38–5.02) in quintile 5, respectively, among borderline hyperglycemic subjects and from 1.50 (1.19–1.90) and 1.72 (1.31–2.26) in quintile 2 to 2.52 (1.95–3.26) and 3.54 (2.66–4.70) in quintile 5, respectively, among those with diabetes. A similar trend was observed for DBP across the highest quintiles 2–5 (75–79, 80–84, 85–89, and 90≤ mmHg, respectively) compared with the lowest quintile of DBP ≤ 74 mmHg. These observations are novel since they show that a linear relationship between SBP/DBP and cardiovascular risks is present not only in the general population but also in populations with normoglycemia and borderline glycemia. Notably, BP elevation and worsening glucose status have an additive effect on CAD morbidity. Compared to individuals with normal glucose levels and an SBP < 120 mmHg, the HR for CAD increased 8.4-fold among those with diabetes and an SBP ≥ 150 mmHg. In contrast, the HRs for stroke remained similar at approximately 5.0, 4.4, and 5.6 for individuals with an SBP ≥ 150 mmHg who had normoglycemia, borderline hyperglycemia, and diabetes, respectively, suggesting that there is no additive effect of hypertension or glycemic status for stroke. The strengths of this study were not only its large sample size but also the accurate definitions of CAD and stroke events that were based on detailed data regarding medications and procedures (i.e., catheter intervention, bypass surgery, thrombolytic therapy, and endovascular thrombectomy) and not solely derived from ICD codes or insurance disease names. Thus, this study allowed the precise identification of almost all patients with incident CAD and CVD during the follow-up period.

This large-scale real-world study in Japan serves as confirmatory evidence that irrespective of glucose status, the risks

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of CAD and stroke begin to increase progressively with SBP/DBP levels that are much lower than the recommended diagnostic threshold for hypertension in current guidelines (i.e., 140/90 mmHg in JSH 2019 and 2018 ESC/ESH [4, 5] and 130/80 mmHg in 2017 ACC/AHA [6]). This finding supports the JSH 2019 recommendation that early initiation of lifestyle modifications, especially salt reduction, is important for the prevention of cardiovascular diseases among all subjects with a BP of 120/80 mmHg or higher [4]. Stroke, especially cerebral hemorrhage, has thus far been the most common sequela of hypertension in Japan and East Asia, although there is an upward trend toward a greater incidence of myocardial infarction in Japan, especially in urban areas, probably due to the westernization of the lifestyle [7–9]. Therefore, strict control of BP and blood glucose through early intervention is necessary for Japanese and Asian populations to prevent and reduce cardiovascular diseases, including CAD and stroke.

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Compliance with ethical standards

Conflict of interest The author declares no competing interests.

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