Interpreting Blood Pressure in Young Adults*

Michael A. Weber, MD

Epidemiologic studies show a strong relationship between blood pressure (BP) measurements and the incidence of major cardiovascular events (1). The primary basis for the treatment of hypertension has been the belief that reducing BP provides cardiovascular protection. This is supported by evidence from pivotal clinical trials (2–7), conducted mostly in older patients at high cardiovascular risk, because they experience sufficient events to power the analysis of outcomes. An unfortunate consequence is the scarcity of data for younger, less complex patients.

Even so, published guidelines on the management of hypertension have tended to treat all adults (>18 years of age) alike, despite the probability of age-dependent differences in outcomes. But 1 group of U.S. experts recently recommended a higher BP threshold for diagnosis and treatment of hypertension in adults ≥60 years of age than in younger adults (8), and an expert opinion in another guideline recommended treating young adults to a lower BP than recommended for middle-aged and older adults (9).

IMPORTANT NEW OBSERVATIONS IN YOUNG ADULTS

In this issue of the Journal, Yano et al. (10) report a study in which they used the database of the Chicago Heart Association Detection Project in Industry, a 31-year longitudinal observation of cardiovascular outcomes in young to middle-aged adults (11), to establish a relationship between baseline BP and long-term cardiovascular outcomes, specifically cardiovascular death and coronary heart disease (CHD) death, in subgroups of individuals with normal BP and with hypertension.

This work focused on isolated systolic hypertension (ISH), defined as systolic BP ≥140 mm Hg and diastolic BP <90 mm Hg. Using a reference patient group with optimal-normal BP (<130/85 mm Hg), the investigators calculated hazard ratios for major events in patients defined as high-normal (130 to 139/85 to 89 mm Hg), ISH (defined previously), isolated diastolic hypertension (<140/≥90 mm Hg), and systolic diastolic hypertension (≥140/90 mm Hg). In both sexes, the risks for death from cardiovascular disease and CHD in the high-normal and the ISH groups were significantly higher. Men, but not women, with isolated diastolic hypertension also had a greater risk, although relatively few patients had this condition. Patients with combined systolic and diastolic hypertension had the greatest incidence of events.

Whether these elevated BP category definitions provide insights beyond simply establishing higher than normal BP as a cardiovascular risk is uncertain. For instance, systolic and diastolic BPs were both clearly higher in patients with ISH compared with the normal reference group. Furthermore, those with systolic and diastolic hypertension had both higher systolic and diastolic BPs than those with ISH. Thus, it is difficult to ascertain whether diastolic and systolic BPs are independent major determinants of outcomes and whether these various BP categories—on the basis of the traditional 140/90 mm Hg threshold—provide practical assistance.

Still, ISH in younger people has largely been unrecognized, so this report resolves an important uncertainty (10). Consistent with recommendations...
from current clinical hypertension guidelines (8,9,12), elevated systolic or diastolic BP or both should clearly be considered abnormal in young adults and lead to therapy.

CONFUNDING FACTORS

ISH patients had a higher incidence of concomitant risks than control patients, including a higher body mass index, and higher likelihood of being smokers, having abnormal lipid profiles, and having type 2 diabetes (10). However, when these factors were incorporated into models for calculating hazard ratios for major events, the cardiovascular event rate in the ISH group was still significantly higher.

It is not possible to account for every factor that might influence these analyses, and so-called residual confounding (as acknowledged by Yano et al. [10]) can include diet, alcohol intake, and psychological characteristics. Important physiologic mediators also influence hypertension outcomes. The renin-angiotensin system plays an important mechanistic role in raising BP as well as also increasing the risk for cardiovascular outcomes. For instance, in a work-site study of men with hypertension, those with high renin levels had significantly higher myocardial infarction rates (13).

FURTHER CONSIDERATIONS IN THE YOUNG

BP has 2 separate roles in hypertension: 1) as a biomarker of underlying vascular disease; and 2) accelerating the progress of vascular pathology and precipitating clinical events. It is strongly believed that vascular changes start in childhood and that early, effective management may be critical in protecting against later cardiovascular outcomes. Unfortunately, a recent U.S. Preventive Services Task Force evaluation of childhood hypertension concluded that, without direct evidence linking control of childhood hypertension to prevention of events in adults, it is not possible to make recommendations for dealing with BP abnormalities in children (14). This apparently nihilistic opinion was strongly disputed by pediatric hypertension experts (15). Given the financial and logistic barriers to long-term outcomes studies originating in children and adolescents, developing a strategy to provide direction in this area—even if it depends on surrogate endpoints—is critical.

EPIDEMIOLOGY AND CLINICAL TRIAL EVIDENCE

Experts in writing guidelines argue that recommendations for managing hypertension must be driven by clinical trial outcomes that define optimal BP thresholds for diagnosis and treatment. Despite many trials conducted in middle-aged and elderly patients with hypertension, this type of evidence is limited. The 2 trials that prospectively compared outcomes of differing BP treatment targets resulted in only limited data (16,17); thus, most knowledge depends on post-hoc extrapolations from trials designed for other purposes. The Systolic Hypertension in the Elderly Program, a study of ISH (defined as 160/90 mm Hg rather than 140/90 mm Hg) in patients ≥60 years of age, demonstrated a clear benefit of active treatment compared with placebo (2). Although this authoritative trial strongly influenced contemporary guidelines (8,9,12), it was not designed to identify a BP threshold. Post-hoc analyses from several trials have led to the belief that certain levels of BP appear to be associated with reductions in events (2–7,17). Figure 1 depicts BP targets associated with the best protection against major outcomes and suggests that clinical evidence does not fully correspond with epidemiologic data, particularly at the lower end of the BP spectrum. Further prospective trials to guide clinical practice are needed.
A NEED FOR ACTION

A lesson from the study of Yano et al. (10) is that even in a young (mid-30s) cohort, systolic BP and CHD death have a relationship resembling that in the Prospective Studies Collaboration, in which systolic BP increments of 20 mm Hg were associated with an approximate doubling of CHD risk (1). The Collaboration’s million-person database also demonstrated that, independent of BP, increasing age is a powerful determinant of events. It could unwisely be argued that absolute event rates in young people, even when increased by high BP, remain relatively low. In fact, the growing prevalence of hypertension, along with obesity, lipid disorders, and diabetes, in young people has become a major public health issue. Indeed, it is to be hoped that early management of hypertension in young adults might beneficially alter its natural history and reduce the incidence of cardiovascular events in later life.

REFERENCES


KEY WORDS cardiovascular diseases, coronary diseases, hypertension, renin-angiotensin system, risk factors