

VIEWPOINT

Treatment of Hypertension

Addressing a Global Health Problem

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Hypertension is the most common preventable cause of cardiovascular disease (CVD) worldwide. It is commonly referred to as a "silent killer" because it gradually damages the heart, blood vessels, and other organs without any apparent symptoms. Elevated blood pressure (BP) is a major risk factor for myocardial infarction, heart failure (HF), stroke, chronic kidney disease, peripheral artery disease, and atrial fibrillation. Although hypertension can be readily diagnosed, and in most instances successfully treated with improvements in lifestyle and with well-tolerated inexpensive medications, hypertension continues to be a major cause of global morbidity and mortality.

Historical Perspective

The consequences of hypertension have been known for many decades. In 1930, Weiss¹ commented that: "Persistently elevated arterial pressure...is probably responsible, directly or indirectly, for more disability and death than any other single pathological condition, including cancer and tuberculosis. Persistent hypertension combined with vascular pathology is the etiological factor in

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the bulk of instances of cerebral accident, myocardial failure and chronic insufficiency of the kidneys." In the late 1930s, President Roosevelt was diagnosed as having hypertension, which over a short span of time was complicated by HF, renal failure, and stroke, the latter resulting in his untimely death at the age of 63 years in 1945. At that time, treatment of hypertension was limited to a low-salt diet, bed rest, and sedatives; antihypertensive therapy included drugs such as veratrum alkaloids, ganglion-blocking agents, and thiocyanates, which had serious adverse effects and marginal BP lowering. "Skillful neglect" and reassurance were considered acceptable management approaches.

Since then, medicine has witnessed a remarkable evolution in the understanding of the pathophysiology and treatment of hypertension. In the 1950s and 1960s, several effective and well-tolerated antihypertensive agents became available, including thiazides and β -blockers. However, their role in reducing morbidity and mortality from hypertension was unclear and many physicians were reluctant to use these drugs. Significant progress was made in resolving this uncertainty by

2 seminal Veterans Administration randomized clinical trials that demonstrated treatment of hypertension significantly reduced cardiovascular events, including mortality. These findings, reported in *JAMA* in 1967 and 1970,^{2,3} established the scientific basis for prevention of clinical complications of hypertension with antihypertensive drugs. Since then, the effectiveness of multiple other medications have been evaluated in many well-designed and adequately powered clinical trials that have consistently shown substantial reduction in cardiovascular events with lowering of BP. In a meta-analysis of 123 BP-lowering trials comprising 613 815 patients, every 10-mm Hg reduction in systolic BP was associated with a reduction in the risk of HF by 28%, stroke by 27%, coronary heart disease by 17%, and all-cause mortality by 13%.⁴

Burden of Hypertension

Despite continuing advances in the development of effective and generally well-tolerated pharmacological treatments of hypertension and the markedly reduced costs as these drugs have become generic, hypertension continues to be a leading cause of mortality and morbidity in the United States and worldwide. According to the National Health and Nutrition Examination Survey data from 2011 to 2014, in the United States, an estimated 85.7 million adults (one-third of the adult population and two-thirds of persons aged ≥ 60 years) have hypertension, defined as BP greater than or equal to 140/90 mm Hg. Among adults with hypertension in the United States, 84% were aware that they had hypertension, three-fourths were treated, and only one-half had their BP optimally controlled. As a result, high BP remains a major contributor to deaths and health care costs in the United States.

While the high frequency of hypertension and its relatively poor control in the United States are concerning, the global trends are even more concerning, particularly those in low- and middle-income countries. Based on data from 844 studies in 154 countries, including nearly 9 million participants, from 1990 to 2015, the rate of systolic BP of 140 mm or higher increased from 17 307 to 20 526 per 100 000, the estimated annual death rate associated with this BP level increased from 97.9 to 106.3 per 100 000, and the loss of disability-adjusted life-years increased from 95.9 million to 143.0 million.⁵

Hypertension and CVD

Hypertension predates the diagnosis of HF in more than three-fourths of patients; it enhances the risk of HF by

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accelerating the progression of coronary artery disease and, especially in elderly individuals, it is also frequently associated with other risk factors for HF such as diabetes, renal impairment, and obesity. In many patients with longstanding poorly controlled hypertension, concentric left ventricular hypertrophy and resultant diastolic ventricular dysfunction are the initial manifestations of hypertensive heart disease, often progressing to HF with preserved ejection fraction. Myocardial infarction may cause dilated cardiomyopathy and HF with reduced ejection fraction.

Treatment of Hypertension

The definition of hypertension and the optimal BP goal of antihypertensive therapy have evolved as a consequence of epidemiologic studies and clinical trials. Until recently, treatment of hypertension to a BP goal less than 140/90 mm Hg was considered adequate. However, in 2015, the Systolic Blood Pressure Intervention Trial (SPRINT) demonstrated that among individuals without diabetes at high cardiovascular risk, targeting systolic BP to less than 120 mm Hg, compared with less than 140 mm Hg, significantly reduced cardiovascular events, including HF and all-cause mortality, in the overall study population⁶ and among those older than age 75 years.⁷ Subsequently, the 2017 American College of Cardiology/American Heart Association guidelines for the management of high BP now define normal BP as less than 120/80 mm Hg, elevated BP as 120-129/<80 mm Hg, and hypertension as BP greater than or equal to 130/80 mm Hg and recommend targeting BP to less than 130/80 mm Hg in all patients.⁸ This lower threshold for hypertension identifies approximately 18 million more US adults at an elevated risk of CVD than those recognized by previous higher BP cutoffs. Two studies in this issue of *JAMA* report a higher risk of cardiovascular

events among young adults with BP of 120-129/<80 mm Hg or 130-139/80-89 mm Hg compared with those with BP less than 120/80 mm Hg.^{9,10} These findings emphasize the importance of early recognition and initiation of lifestyle modification and antihypertensive therapy in those with BP of 120-139/80-89 mm Hg.

Future Directions

Controlling hypertension should be a key component of the global mission to reduce the incidence of CVD, the most common cause of death. As the burden of hypertension remains high despite the availability of effective, affordable antihypertensive therapy, innovative strategies to attack this problem need to be developed. First, as nonadherence to medications is a major cause of uncontrolled hypertension, approaches such as intensive patient education, self-measured BP monitoring, and the use of mobile health technology should be used. Second, strategies involving diagnosis and management of hypertension in nontraditional settings, such as pharmacies, barbershops, hair salons, and grocery stores, should be undertaken.

Clinicians have known for almost a century that hypertension is a major cause of multiple diseases and deaths. The current persistence of this silent killer should not be tolerated, and a worldwide "call to action" is now indicated. Collaborative efforts of physicians, other health professionals, and governmental and nongovernmental agencies are required to control this pandemic. In addition, because patients with elevated BP (120-139/>80 mm Hg) have a greater risk of CVD than those with normal BP, lifestyle modifications and management of concomitant cardiovascular risk factors, such as hypercholesterolemia, diabetes, obesity, and cigarette smoking, must also be strongly encouraged to lower the risk for the development of CVD.

ARTICLE INFORMATION

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