Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

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Circulation 2011;123;2892-2896
DOI: 10.1161/CIRCULATIONAHA.110.992362
Circulation is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 0009-7322. Online ISSN: 1524-4539

Hypertension

A Global Perspective

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Case presentation 1: A morbidly obese but nonsmoking and nondiabetic 44-year-old African woman (body mass index, 41 kg/m^2) presents with exertional dyspnea to a primary healthcare clinic in Soweto, adjacent to Johannesburg, South Africa. She seeks medical attention for the first time. Her blood pressure (BP) is 178/115 mm Hg, her total and high-density lipoprotein cholesterol are 2.6 and 0.9 mmol/L (100 and 34 mg/dL), respectively, and her heart rate is 112 bpm. Her initial absolute risk (Framingham algorithm) is calculated at 2% (low) probability of cardiovascular disease (CVD) within 5 years, increasing to 5% (high) when preliminary evidence of left ventricular hypertrophy is subsequently found on 12-lead ECG.

Case presentation 2: A 60-year-old, nondiabetic, Chinese woman (body mass index, 24 kg/m^2) visits a primary healthcare clinic in Beijing, complaining about painful knees. A routine physical examination reveals a BP of 145/90 mm Hg, total and high-density lipoprotein cholesterol of 4.8 and 1.1 mmol/L (185.6 and 42.5 mg/dL), respectively, and heart rate of 72 bpm. Her absolute risk (initially) is calculated as 6% (low) probability of CVD within 5 years. Despite some nonspecific but abnormal ECG findings, she does not qualify as having "ECG evidence of left ventricular hypertrophy," which would increase her absolute risk to 20% (high). However, the woman is questioned more carefully about potential risks, and she admits to smoking 15 cigarettes per day. Her recalculated risk is now 12% (intermediate) and would rise to 16% (high) if, by the age of 65 years, her systolic BP increased to 155/90 mm Hg.

Case presentation 3: A 65-year-old (nonsmoking) white woman (body mass index, 28 kg/m^2) presents to a primary care clinic in Charlotte, NC, and is found to be hypertensive with a BP of 170/110 mm Hg and heart rate of 88 bpm. Her total and high-density lipoprotein cholesterol levels are 6.8 and 0.8 mmol/L (263 and 30.9 mg/dL), respectively. Her initial absolute risk is calculated as 18% (intermediate) probability of CVD within 5 years. Although she is found not to have ECG evidence of left ventricular hypertrophy (which would have increased her risk level to 28%), a glucose tolerance test reveals that she has type 2 diabetes mellitus, confirming her high-risk status.

What Are the Diagnostic Considerations for These Patients, and What Further Investigations Are Indicated?

Much of the global burden of CVD is now borne by low- to middle-income countries. Unfortunately, many of these regions are still grappling with poverty- and infection-related CVD, such as rheumatic heart disease, endomyocardial fibrosis, human immunodeficiency virus infection, tuberculous pericarditis, and Chagas disease. The combination of economic constraints, limited resources, and the overlap of several disease burdens limits the capacity to deal with noncommunicable risk factors and related diseases.

In this Clinician Update, we focus on the diagnostic approach to patients with newly diagnosed hypertension, from different ethnic backgrounds and risk factor profiles, presenting in different regions of the world. Emphasis is placed on diagnosis, overall risk factor profile, lifestyle modification,

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(*Circulation*. 2011;123:2892-2896.)

***Circulation* is available at http://circ.ahajournals.org**

DOI: 10.1161/CIRCULATIONAHA.110.992362

and adherence, taking into account many of the logistic, socioeconomic, cultural, and resource constraints that are widely prevalent in low- to middle-income countries.

Hypertension: A Global Epidemic

There is increasing awareness of a global epidemic of CVD encompassing a range of conditions, from hypertension to acute coronary syndromes, stroke, and chronic heart failure, with potentially devastating consequences for resource-poor countries. Overall, 80% of worldwide cardiovascular-related deaths occur in low- to middle-income countries, and, in comparison with high-income countries, these deaths (and events such as stroke and acute myocardial infarction) occur at a younger age, exerting a profound impact on the family unit and the workforce. It is predicted that noncommunicable forms of CVD will become the leading cause of death and disability, globally, by 2020.[1] Significantly, hypertension as a highly modifiable antecedent for CVD is responsible for more deaths worldwide than any other, including tobacco use, obesity, and lipid disorders.[2] In low- to middle-income countries, the differential pattern in BPs in rural versus urban communities is a key marker of the various stages of epidemiological transition, characterized by dramatic socioeconomic changes and accompanied by parallel changes in the risk status and pattern of illness within affected communities.[3]

The lesson from high-income countries is, of course, that prevention is far more cost-effective than expensive treatments. In low- to middle-income countries, this truism is even more pertinent, particularly when the young age of those affected and the adverse impact on the workforce and family units are considered.[4]

Pattern of Hypertension in Different Regions

Africa is a continent with broad inequities in socioeconomic status, with large-scale migration of populations from rural to urban regions.[5] Overall, there is a lack of effective cardiovascular screening and treatment programs, with suboptimal access to healthcare. Typical of the case study presented above (case presentation 1), recent studies from urban South Africa have shown that the most prevalent cardiovascular risk factors are a combination of obesity and hypertension.[6] Recent data from Soweto suggest that (often undetected) hypertensive heart failure is the most common presentation to the hospital with chronic heart disease. In contrast, cases of coronary artery disease remain scarce.[7]

The pattern of hypertension and its most common complication, stroke (both hemorrhagic and ischemic) in Asia is complex, given the broad diversity of the region experiencing various stages of epidemiological transition. In 2000, it was noted that in India, China, Philippines, Thailand, Sri Lanka, Iran, Pakistan, and Nepal, there had been a rapid increase in both the prevalence of hypertension and the rate of stroke fatalities. The reported prevalence of hypertension in urban-dwelling adults varied widely from 15% to 35%.[8] As in sub-Saharan Africa,[5] the prevalence of hypertension is 2 to 3 times lower in rural- versus urban-dwelling adults.[8] Moreover, the risk of hypertension increases at lower levels of body mass index compared with other ethnic groups (case presentation 2), with CVD events (including stroke) occurring at relatively younger ages. A longitudinal, population cohort study in Chengdu, China, typically documented not only a higher prevalence of hypertension in initially 35- to 64-year-old men (from 13.2% to 51.2%) and women (14.0% to 45.1%) during 1992–2007 but age-matched increases over this period.[9]

In the United States, hypertension is more prevalent and less well treated in individuals who are disadvantaged from a socioeconomic perspective, and among blacks.[10] The diet is typically high in salt, with the majority coming from processed food. Despite recommended daily intake of <5.8 g of salt per day, with a lower target of 3.7 g of salt for those aged >40 years, blacks, and those with hypertension, the average man and woman are estimated to consume 10.4 and 7.3 g of salt per day, respectively.[10] Metabolic disease due to concurrently high levels of sedentary behaviors and poor dietary patterns overall is also common.

Optimizing Blood Pressue Levels: From the Individual to the Population Approach

The Figure shows the often parallel approaches to optimizing BP levels from the individual to the population perspective. At the individual level, hypertension is typically diagnosed and treated with the use of simple cutoff points in BP level (eg, a BP of 140/90 mm Hg). The American Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure recommends BP level–based guidelines that are primarily focused on single cutoff point BP levels.[11] Initiation of pharmacological treatment does not take into account any additional information such as age, ethnicity, lipid levels, smoking status, or the number of risk factors (except diabetes mellitus and chronic renal disease). Consequently, this method does not allow for precise assessment of a patient's true cardiovascular risk.

As demonstrated in the 3 case studies, however, it is important to consider individual circumstances when the combined impact of risk factors on absolute risk is considered. The World Health Organization Choosing Interventions That Are Cost-Effective Program showed that treating those with high absolute risk in various regions of the world was cheaper and saved more lives than one based on target levels of individual risk factors.[12] Although risk calculators can be found readily on the Internet, the use of a chart based on absolute risk calculations was popular and, when used, resulted in better BP control compared with usual care in the primary care setting.[13] However, the pre-

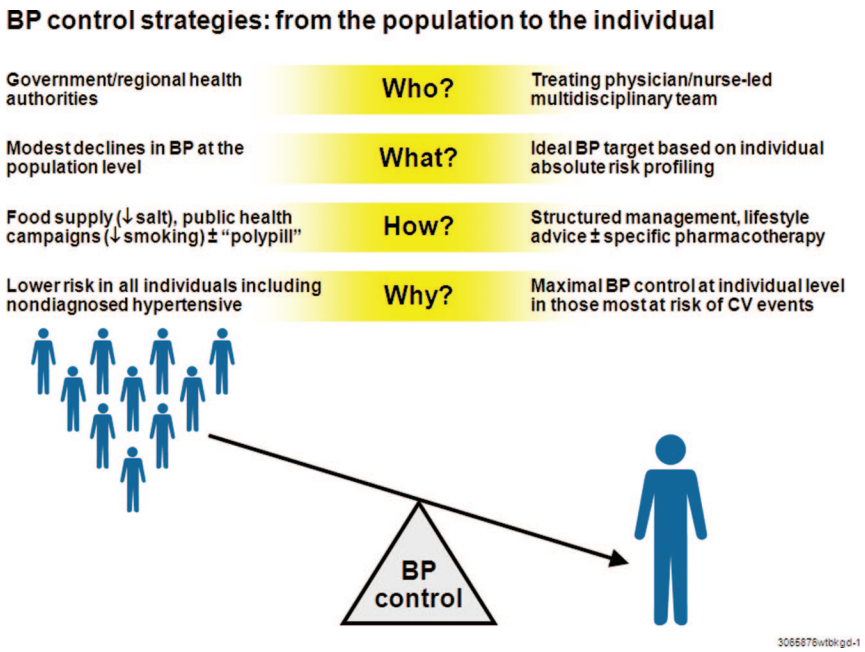

Figure. Optimizing blood pressure (BP) at the individual and population levels. CV indicates cardiovascular.

sented case studies readily demonstrate the limitations when one calculates risk and determines treatment thresholds with reliance on data derived from white cohorts. This observation applies to both the Framingham risk score[14] and its European equivalent.[15] However, the use of quantitative risk-based guidelines for treatment of hypertension could free up major resources, including prevention programs, especially in low- to middle-income countries.[4] Developing accurate ethnic- and region-specific risk tools is clearly a priority in this setting.

A wider approach to BP control is the implementation of population-based policies and strategies to reduce access to tobacco and foods rich in salt and/or saturated fats. A recent study[10] suggests that even modest reductions in dietary salt could substantially reduce cardiovascular events and medical costs and should be a public health priority in low- to middle-income countries.

Diagnostic and Therapeutic Options to Control Blood Pressue on a Global Basis

The 3 case studies presented in this article highlight the many multifaceted challenges in optimizing BP across the globe (Table). In case presentation 1, a 12-lead ECG identified potential left ventricular hypertrophy, and further investigation with a chest x-ray and echocardiography (if available) would therefore be a priority. Brain natriuretic assays are not readily available in Africa (even in tertiary centers). Africans often present with more pronounced end-organ damage, in particular hypertensive heart failure.[7] Importantly, being overweight is culturally acceptable, and even perceived as desirable, and therefore advice and education regarding the importance of weight reduction coupled with a low-salt diet would be highly important. In case presentation 2, the patient is clearly at risk of a premature stroke event; her smoking habit and the need to lose weight are high priorities, with careful consideration of the need to start lipid-lowering therapy. Similarly, in case presentation 3, further investigation typically reveals the presence of type 2 diabetes mellitus. Aggressive treatment to achieve a BP of <130/90 mm Hg is clearly indicated, as is further investigation of subclinical CVD (including renal impairment).

A multidrug regimen to address the most common risk factors has been proposed to be cost-effective and to reduce the occurrence of CVD by half in high-risk individuals. This polypill approach comprises a statin, aspirin, a β-blocker, an angiotensin-converting enzyme inhibitor, a thiazide, and folic acid.[16] Unfortunately, although this would undoubtedly improve adherence

Table. Factors Contributing to Low Hypertension Control Rates

Health System Factor	Patient Factor	Physician Factor	Treatment Factor
Limited access to regular primary care and medication	Lack of health insurance	Lack of knowledge of guidelines (eg, BP thresholds, use in monotherapy, in patients with difficult-to-control BP)	Resistant hypertension (eg, in clinical trials, BP is uncontrolled in approximately one third of patients)
Lack of country- or region-specific guidelines and dissemination	Increased susceptibility to hypertension (eg, obesity, advanced age)	Concern about medication side effects	Side effects
Lack of incentive of hypertension incentives and controls	Noncompliance with therapy (eg, knowledge, deficits, complicated regimens, side effects) Preventative services not sought or received Limited transportation and child care	Failure to titrate medicine when BP is not controlled Lack of time at office visits	

BP indicates blood pressure.

rates, the most effective and affordable constituents of the polypill among different ethnic groups remain open to debate. Moreover, the cost dynamics of applying the polypill (and the support structure to apply and monitor its effects) undoubtedly differ from region to region.[17]

Structured Management

Regardless of the setting, a recent Cochrane review of randomized trials undertaken in primary care concluded that "antihypertensive drug therapy should be implemented by means of a vigorous stepped care approach when patients do not reach target BP levels."[18] From the perspective of resource-poor healthcare systems, a parallel review of nurse-led interventions applying the same stepped care approach provides a potentially cost-effective strategy to manage patients with hypertension.[19] This approach outlines a clear plan for regular BP monitoring and precise algorithms for escalating treatment. However, the importance of lifestyle management cannot be ignored. In all case studies, assessment of anthropometric profile, dietary intake (particularly saturated fats and excess salt intake), exercise levels, exposure to direct and passive tobacco smoke, and the individual's psychosocial status from a culturally sensitive and holistic perspective is vital. Subsequent advice and coaching for agreed-on targets around the key drivers of increased risk factors (ie, smoking, sedentary behavior, and poor diet habits) need to be embedded in any structured program of care. Raising the awareness of CVD, its antecedents, and the importance of adhering to prescribed treatment (and lifestyle changes) represents an important framework to such management.

Achieving Blood Pressure Control in 3 Diverse Settings

In Soweto, South Africa, after more definitive investigation (described above), the 44-year-old African woman (case presentation 1) was diagnosed with moderate left ventricular hypertrophy (left ventricular mass index, 111 g/m^2), but without concurrent evidence of systolic (left ventricular ejection fraction, 58%) or diastolic dysfunction. She was subsequently managed by a cardiologist, dietician, and nurse at the hypertensive clinic at the local tertiary hospital. In addition to specific dietary and lifestyle education (including reducing salt intake and weight loss), she is prescribed an angiotensin-converting enzyme inhibitor in combination with a low-dose diuretic to enhance the effectiveness of the angiotensin-converting enzyme inhibitor, as suggested in particular for black Africans. After a series of visits to the hypertension clinic over 3 months to reinforce key health messages and titrate pharmacotherapy, the patient has lost 10 kg, her BP is 135/90 mm Hg, and her heart rate is 85 bpm. A new program of cross-referral ensures that the patient's management plan and long-term surveillance are now implemented by the primary clinic.

In Beijing, China, the 60-year-old woman (case presentation 2) was informed of the risks posed by her hypertension, metabolic profile, and smoking. Because she was reluctant to immediately quit smoking, and there are few programs to support her in this endeavor, it was agreed (with her healthcare team) that a combination of dietary modification, an exercise program, acupuncture, and traditional herbal medicines will be initially trialed to normalize her BP and address her other risk factors. A review in 6 weeks time revealed that she has lost 3 kg, her resting BP is now 138/85 mm Hg, and her total and high-density lipoprotein cholesterol levels are 4.3 and 1.2 mmol/L (166 and 46 mg/dL), respectively. She was subsequently encouraged to maintain her current therapeutic regimen, aim to steadily reduce her smoking habit, and return for reassessment in 6 months time.

In Charlotte, NC, the 65-year-old woman (case presentation 3) attended a case conference with her primary care physician, primary care nurse, and a diabetic educator. Key therapeutic targets were summarized, including losing 15 to 20 kg, lowering her BP to $<$130/80 mm Hg, lowering her total cholesterol to $<$5.0 mmol/L, and raising her high-density lipoprotein cholesterol to $>$1.0 mmol/L (200 and 40 mg/dL, respectively). To achieve this, a multidisciplinary program of follow-up coordinated by a case manager was implemented, and she was prescribed a long-acting, controlled-release calcium channel blocker and a low-dose diuretic. Over the next 6 months, she managed only modest weight loss of 1.5 kg. However, her diet-controlled glycosylated hemoglobin was 6.5%, she achieved her target lipid profile, and her resting BP has declined to 142/90 mm Hg, with a heart rate of 80 bpm. Case conference review, while noting the positive improvements, identified the need for further weight loss and the addition of third-line antihypertensive therapy; she was subsequently prescribed a β-blocker.

Summary

In summary, there is ample evidence to suggest that the burden of hypertension is already having a profound effect on the health of populations in low- to middle-income countries.[12] The phenomenon of epidemiological transition has certainly contributed to the rise of CVD and will, no doubt, cause a sustained epidemic of noncommunicable forms of CVD for the foreseeable future. Unfortunately, in resource-poor countries, there is often limited scope to respond to this growing problem. It is encouraging to see that the World Health Organization has developed an action plan that advocates key strategies for limiting the impact on noncommunicable diseases.[2]

Disclosures

None.

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