

Blood pressure and control of cardiovascular risk

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Abstract: Two key early 20th century notions, the first the primacy of diastolic pressure in determining risk, and the second that hypertension is a discrete disorder, have proved to be incorrect. We now recognize the primacy of systolic pressure as a risk factor for cardiovascular disease and that hypertension is an arbitrary definition. In the early 21st century, we are moving away from a dichotomous approach to risk classification, and away from notions of hypertension and normotension towards an appreciation that blood pressure-related risk is continuous. In parallel, there has been a paradigm shift from a single risk factor approach to comprehensive cardiovascular disease risk prevention. Accordingly, prevention of cardiovascular disease requires a focus on lowering of blood pressure and modification of associated risk factors rather than simply treatment of hypertension. This emphasis is reflected in the World Health Organization (WHO)–International Society of Hypertension (ISH) 2003 statement on management of hypertension.

Keywords: blood pressure, hypertension, cardiovascular risk, treatment

Introduction

The definition of hypertension has long been recognized to be arbitrary and problematic, as reflected by the numerous changes in definition over the years. At about the time of the great “two cultures” debate around the relative values of science and the humanities (Snow 1959), the great divide in hypertension was the debate between the two giants of the field in the mid-twentieth century, Pickering and Platt. The former, whose view ultimately triumphed, held that high blood pressure was simply the upper end of a continuous distribution, whereas Platt regarded hypertension as a discrete disorder (Swales 1985). Perhaps the definition that has best stood the test of time is that hypertension should be defined in terms of blood pressure level above which investigation and treatment do more good than harm (Evans and Rose 1971).

For much of the 20th century, the emphasis in hypertension was on diastolic pressure. It is now recognized that systolic pressure is more important as a marker of risk and that isolated systolic hypertension is itself an important entity (Neaton and Wentworth 1992). At the same time, there has been downward revision of the definition of what constitutes hypertension, eg, from 160/100 to 140/90 mmHg over the last 20 years. Indeed JNC 7 now has a pre-hypertensive category (120/80 to 139/89 mmHg) (JNC 7 2003).

But, more importantly, it is now clear that changes in blood pressure, even over a range, which by any definition would be regarded as normotensive, are associated with changes in cardiovascular risk. MacMahon and colleagues (1990) showed unequivocally that the risk of cardiovascular disease (CVD) was continuously associated with diastolic blood pressure over 70–110 mmHg and that there was no

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threshold for the association. The same is true of systolic pressure (MacMahon et al 1990).

The WHO recognized this reality: “Increasingly, the very terms hypertension, hyperglycemia and hypercholesterolemia will probably disappear, as the focus moves from treating a theoretically decided cut-off point, towards managing continuous distributions of risks that intersect and interact with each other: blood pressure, blood sugar and blood cholesterol should be the focus of control” (WHO 2002a, p 13).

In that World Health Report (WHO 2002b), the association of systolic blood pressure (above a theoretical minimum of 115 mmHg) with CVD risk for stroke, ischemic heart disease, hypertensive disease, and other cardiac disease was continuous; and globally, around 62% of cerebrovascular disease and 49% of ischemic heart disease was attributable to suboptimal blood pressure (systolic blood pressure >115 mmHg). The report pointed out that blood pressure ranks third globally, in terms of risk for burden of disease, behind underweight (number 1) and unsafe sex and in front of tobacco, alcohol, unsafe water, cholesterol, and overweight (number 10). It estimated that hypertension worldwide causes over 7 million premature deaths, 4.5% of the global disease burden, and some 64 million disability adjusted life years lost (WHO 2002a).

The World Health Organization (WHO)–International Society of Hypertension (ISH) statement on management of mild hypertension was published in 2003 (Kaplan et al 2003), shortly after the European (ESH–ESC 2003) and US guidelines, JNC 7 (2003).

The three documents were different in purpose with different target audiences. The WHO–ISH document was a statement for a global audience, which updated the very comprehensive 1999 WHO–ISH guidelines (Chalmers et al 1999) in three key areas:

- ascertainment of overall cardiovascular risk to establish thresholds of, and goals for, treatment;
- treatment strategies;
- cost-effectiveness.

The other two documents were comprehensive guidelines for European and North American audiences, respectively.

This difference in target audience is of substantial practical importance, as the global capacity to access and manage hypertension is very different from that in the developed countries of Europe and the USA. A global capacity assessment of 167 countries by WHO found 61% had no national hypertension guidelines, 45% did not have

Table 1 WHO, US, and European classifications of hypertension (mmHg)

WHO–ISH			
<i>Grade 1</i>	<i>Grade 2</i>	<i>Grade 3</i>	
140–159/ 90–99	160–179/ 100–109	≥ 180 ≥ 110	
JNC 7			
<i>Normal</i>	<i>Pre-HT</i>	<i>Stage 1</i>	<i>Stage 2</i>
< 120	120–139/ < 80	140–159/ 90–99	≥ 160 ≥ 100
ESH–ESC			
<i>Optimal</i>	<i>Normal</i>	<i>High normal</i>	
< 120	120–129/ < 80	130–139/ 85–89	
<i>Grade 1</i>	<i>Grade 2</i>	<i>Grade 3</i>	<i>ISH</i>
140–159/ 90–99	160–179/ 100–109	≥ 180 ≥ 110	≥ 140 < 90

Abbreviations: ESH–ESC, European Society of Hypertension–European Society of Cardiology; HT, hypertension; ISH, International Society of Hypertension; JNC 7, The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; WHO, World Health Organization.

health professionals trained to manage hypertension, antihypertensives were not affordable in 25% of countries, basic drugs for hypertension were not available in 12%, and basic equipment for managing hypertension was not available in 8% (Alwan et al 2001). Low- and middle-income countries have limited capacity to address comprehensive cardiovascular risk, particularly in primary care. Customized risk assessment and management approaches are essential for such low resource settings (WHO 2002a, 2002c).

The classifications of hypertension used in the three documents are summarized in Table 1. The differences reflect arbitrary division of a continuous risk.

Stratification of risk from the WHO–ISH statement and the European guidelines is shown in Table 2. Risk stratification was less prominent in JNC 7. The European guidelines made the important point that risk in this context means “added” risk, ie, low risk means low *added* risk. The differences between the two charts are more apparent than real and reflect the emphasis on simplicity in the WHO–ISH statement, where added risk is low, medium, or high; whereas the European guidelines use low, moderate, high, and very high.

Thresholds for treatment were the same in all three documents, as were targets for blood pressure lowering. Thresholds are 140/90 mmHg for low- and medium-risk subjects, but lower for high-risk patients. Targets are <140 mmHg systolic in low–medium risk and <130/80 mmHg in high-risk patients.

Table 2 Stratification of risk

WHO-ISH					
BP (mmHg)	Grade 1 140–159/ 90–99	Grade 2 160–179/ 100–109	Grade 3 ≥ 180		
Other risks					
Nil	Low	Medium	High		
1–2	Medium	Medium	High		
≥ 3/TOD/ACC	High	High	High		
ESH-ESC					
BP (mmHg)	Normal SBP 120–129 or DBP 80–84	High normal SBP 130–139 or DBP 85–89	Grade 1 SBP 140–159 or DBP 90–99	Grade 2 SBP 160–179 or DBP 100–109	Grade 3 SBP ≥ 180 or DBP ≥ 110
Other risk factors and disease history					
No other risk factors	Average	Average	Low	Moderate	High
1–2 risk factors	Low	Low	Moderate	Moderate	Very high
3 or more or TOD or diabetes	Moderate	High	High	High	Very high
ACC	High	Very high	Very high	Very high	Very high

Abbreviations: ACC, associated clinical conditions; DBP, diastolic blood pressure; SBP, systolic blood pressure; TOD, target organ damage.

All three documents recommend lifestyle measures for prevention and management of hypertension. Recommendations are for weight loss in the overweight, physical activity, moderation of alcohol intake, healthy diet (fruit, vegetables, and low saturated fat), reduction of dietary sodium and increased dietary potassium.

The documents differ in choice of initial therapy. All, however, agree the emphasis on initial therapy is outdated because most patients will not be controlled on monotherapy. The WHO–ISH statement emphasizes that trial data suggest benefits largely derived from blood pressure reduction, while recognizing the strong evidence that specific agents benefit patients with compelling indications. Accordingly, for patients without compelling indications, on the basis of comparative trial data, availability, and cost, it recommends (low dose) diuretic be considered for first-line therapy. JNC 7 makes a similar recommendation for low dose diuretic, and adds that if BP is >20/10 mmHg above target, then starting with 2 drugs should be considered.

The European guidelines take a different position, and recommend any of 5 major classes as initial therapy: diuretics, β -adrenoreceptor blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers.

The three documents give similar compelling indications for specific drugs. The WHO–ISH statement puts more emphasis on feasibility and cost-effectiveness, which are of greater importance globally than in the rich countries of USA and Europe. It points out that cost-effectiveness equals benefits for expenditure, whereas affordability equals

prevalence and total cost of treatment in a specific setting. Thus, where resources are limited, cost-effective treatment may not be affordable. Where resources are limited, priority for drug therapy should be given to those at higher risk. The statement noted that in many (but not all) settings, thiazide diuretics are cheapest and hence most cost-effective, but where there are compelling indications, classes that provide additional benefits, even if more expensive, may be more cost-effective. In patients with low added risk, treatment may not be cost-effective unless drugs are cheap, but in high-risk patients with large benefits from treatment, even expensive drugs may be cost-effective.

JNC 7 suggests use of generic drugs or combination drugs should be considered to reduce prescription costs, whereas the European guidelines state that cost of drugs should not predominate over individual efficacy and tolerability.

The WHO–ISH statement reflects the World Health Report (WHO 2002a) and the WHO–ISH 2000 statement on prevention (Chockalingam et al 2000) in stressing that worldwide population strategies to reduce blood pressure are very cost-effective. The WHO–ISH statement points out that prevention of CVD requires both population-based and high-risk group strategies targeting unhealthy lifestyle: diet, tobacco, inactivity; hypertension, glucose intolerance, hyperlipidemia; and CVD management.

The three documents, written as they are for different audiences, vary in emphasis, but their similarities far outweigh their differences. If we are to prevent and control the current worldwide epidemic of cardiovascular disease,

we need a comprehensive and aggressive approach directed at both populations and high-risk individuals, focussing on global risk-factor reduction.

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