Cardiovascular risks of hypertension

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INTRODUCTION

Hypertension is quantitatively the most important modifiable risk factor for premature cardiovascular disease [1]; it is more common than cigarette smoking, dyslipidemia, and diabetes, which are the other major risk factors (table 1). Hypertension accounts for an estimated 54 percent of all strokes and 47 percent of all ischemic heart disease events globally [2]. (See "Overview of established risk factors for cardiovascular disease".)

The impact of hypertension on the risk for cardiovascular disorders and the impact of cardiovascular risk on therapeutic decisions in the treatment of hypertension are discussed in this topic. The effects of different antihypertensive drugs and of different blood pressure goals on cardiovascular outcomes are presented elsewhere:

- (See "Choice of drug therapy in primary (essential) hypertension".)
- (See "Goal blood pressure in adults with hypertension".)

IMPACT OF HYPERTENSION ON CARDIOVASCULAR DISEASE

Hypertension increases the risk for a variety of cardiovascular diseases [3-5], including stroke, coronary artery disease, heart failure, atrial fibrillation [6], and peripheral vascular disease.

The risk for both coronary disease and stroke increases progressively with incremental increases in blood pressure above 115/75 mmHg, as shown in numerous epidemiologic studies (figure 1A-B) [7-12]. For each 20/10 mmHg increase in systolic/diastolic blood pressure, there

is a doubling of coronary heart- and stroke-related mortality. However, these observations do not prove a causal relationship, since increasing blood pressure could be a marker for other risk factors such as increasing body weight, which is associated with dyslipidemia, glucose intolerance, and the metabolic syndrome. The best evidence for a causal role of increasing blood pressure in cardiovascular complications is an improvement in outcome as blood pressure is reduced with antihypertensive therapy [13]. (See "Goal blood pressure in adults with hypertension".)

The increase in cardiovascular risk has primarily been described in terms of elevated systolic pressure in older adults [14] and elevation in both systolic and diastolic pressure in younger individuals. Pulse pressure, which is the difference between the systolic and diastolic blood pressures and is determined primarily by large artery stiffness, is also a strong predictor of risk [14]. Conversely, isolated diastolic hypertension, in which the diastolic pressure is elevated but the systolic pressure is normal, is uncommon and not associated with a higher cardiovascular risk [15]. (See "Increased pulse pressure".)

Out-of-office blood pressure measurements may predict cardiovascular risk better than routine clinic measurements, a fact that has led to increased reliance upon home and ambulatory blood pressure monitoring (ABPM) to make the diagnosis of hypertension [5,16]. These issues are presented elsewhere:

- (See "Overview of hypertension in adults", section on 'Making the diagnosis of hypertension'.)
- (See "Blood pressure measurement in the diagnosis and management of hypertension in adults".)
- (See "Out-of-office blood pressure measurement: Ambulatory and self-measured blood pressure monitoring".)

Impact of hypertension on specific cardiovascular disorders — The magnitude of the association between hypertension and cardiovascular disease varies according to the specific cardiovascular outcome. In one large cohort study, for example, hypertension (which was defined as a blood pressure ≥140/90 mmHg) increased the relative risk of stroke (by 3.8 and 2.6 in men and women, respectively). In addition, heart failure was increased (by 4.0 and 3.0 in men and women, respectively) and to a greater degree than the relative risk of coronary heart disease (by 2.0 and 2.2, respectively) [17].

Projections have been made for the expected decrease in morbidity and mortality resulting from a 10 to 12 mmHg reduction in systolic pressure and a 5 to 6 mmHg reduction in diastolic

pressure using data from multiple clinical trials performed over the past 30 years. Although not proving cause-and-effect, the estimated benefit from this degree of blood pressure lowering is a 38 percent reduction in risk of stroke and a 16 percent reduction in risk of coronary disease [18]. As noted above, the best evidence for a causal role of increasing blood pressure in cardiovascular complications is an improvement in outcome as blood pressure is reduced with antihypertensive therapy [13]. (See "Goal blood pressure in adults with hypertension".)

Additive effects of hypertension and other risk factors — The different cardiovascular risk factors have an additive effect on the likelihood of developing coronary heart disease and other cardiovascular outcomes [19,20]. In addition to hypertension, the major risk factors are older age, elevated plasma and low-density lipoprotein (LDL) cholesterol, a low high-density lipoprotein (HDL) cholesterol, diabetes mellitus, and cigarette smoking. Thus, individual patients who have significant hypertension but none or few of the other risk factors are at relatively lower overall risk than patients with less hypertension but more of the other risk factors (figure 2) [19,21]. (See "Overview of established risk factors for cardiovascular disease".)

Multiple risk prediction models using these and other risk factors have been developed, most notably the Framingham risk score [19,20]. The ability of the Framingham risk criteria to predict cardiovascular disease has been widely reproduced [22-24], but the degree of cardiovascular risk related to the Framingham risk criteria may not apply to all patient populations [25-27]. Other risk factors have been proposed to improve upon the Framingham risk assessment, including C-reactive protein, brain natriuretic peptide, echocardiography, and other studies for detecting subclinical vascular disease [28-30]. However, none have been proven to add significantly to the Framingham scoring, and they are probably not cost effective.

Other risk prediction models exist, including one developed by the American Heart Association (AHA) and the American College of Cardiology (ACC) that incorporated data from multiple patient cohorts and includes risk of all cardiovascular events, including stroke, rather than coronary heart disease alone (calculator 1) [31].

A detailed discussion on estimation of cardiovascular risk in an individual without known disease is presented elsewhere. (See "Cardiovascular disease risk assessment for primary prevention in adults: Our approach".)

APPLICATION OF RISK ASSESSMENT TO THERAPEUTIC DECISIONS

Use of baseline cardiovascular risk to guide treatment decisions — A central question in the care of hypertensive patients is whether or not treatment decisions (eg, use of antihypertensive medications, goal blood pressure) should be applied uniformly to the entire hypertensive

population or, instead, tailored according to a patient's risk for future cardiovascular events. The benefit a patient receives from blood pressure lowering depends upon the balance between the **absolute** (rather than relative) reduction in risk for adverse outcomes and the potential harms and burdens of antihypertensive therapy. (See "Cardiovascular disease risk assessment for primary prevention in adults: Our approach" and "Cardiovascular disease risk assessment for primary prevention: Risk calculators".)

Although the relative cardiovascular risk reduction appears to be the same regardless of the baseline cardiovascular risk, the absolute number of cardiovascular events prevented by therapy is significantly greater in the population with higher baseline cardiovascular risk. This concept is presented in detail elsewhere. (See "Goal blood pressure in adults with hypertension".)

A group from New Zealand, for example, took various cardiovascular risk factors into account in determining the overall risk status of individual patients, including their level of blood pressure, age, gender, and other factors (figure 2) [21]. They then examined the evidence of benefits of antihypertensive therapy from the clinical trials and considered the costs of such therapy. They concluded that antihypertensive therapy could be justified only if the risk for a major cardiovascular event over the next five years was 10 percent or greater or if the level of blood pressure was so high as to mandate therapy regardless of overall risk status (≥170/100 mmHg).

Several professional organizations have recommended that markers of overall cardiovascular risk be incorporated in treatment decisions [32-34]. As an example, guidelines from the American College of Cardiology/American Heart Association (ACC/AHA) suggest initiating hypertensive medications in higher-risk individuals at lower blood pressures than those with lower overall cardiovascular risk [5]. Details of our approach are presented elsewhere. (See "Goal blood pressure in adults with hypertension".)

Current risk versus prior risk — In addition to the specific patient population [25], another problem with the use of such data is that the risk status that is currently assessed may not reflect what was previously present. This is an important issue because it is the **prior** risk status that is more likely to be responsible for the current health of the individual.

As an example, although blood pressure at the time of risk assessment (current blood pressure) is typically used in most prediction algorithms, this does not accurately reflect an individual's past blood pressure experience; the use of long-term, average blood pressure is more accurate. This is supported by the following observations:

- In a study of 3560 individuals, the presence of elevated blood pressure before age 35 years was associated with coronary calcification (which is a strong predictor of future coronary

heart disease) later in life. This association was observed after adjusting for blood pressure and other coronary risk factors that were present after age 35 years [35].

- A report from the Framingham Heart Study found that recent and remote antecedent blood pressure (systolic, diastolic, and pulse pressure) predicted cardiovascular risk incrementally over current blood pressure [36]. This effect was seen in men and women, younger and older subjects, and lower and higher blood pressure groups.

- In another study, 1604 men whose risk status was first assessed when they were aged 45 to 64 years and free of clinically obvious cardiovascular disease were then reassessed 25 years later when they were aged 70 to 90 years [37]. Most patients changed their risk status over this time period, moving forward or backward. When the current risk status of the 342 subjects who developed cardiovascular disease (myocardial infarction, angina, coronary bypass surgery, angioplasty, or stroke) during the follow-up period was compared with that of the 279 who remained healthy, there were few differences. However, the results were different when the original risk status was used. Those patients who remained healthy had significantly lower blood pressure (121/79 versus 134/83 mmHg) and plasma cholesterol levels (211 versus 226 mg/dL [5.45 versus 5.84 mmol/L]) 25 years before.

Based upon these data, clinicians need to be cautious about only using current cardiovascular risk estimates to predict subsequent events [37].

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Beyond the Basics topics (see "Patient education: High blood pressure in adults (Beyond the Basics)" and "Patient education: High blood pressure treatment in adults (Beyond the

Basics)")

SUMMARY AND RECOMMENDATIONS

- Hypertension is quantitatively the most important risk factor for premature cardiovascular disease; it is more common than cigarette smoking, dyslipidemia, and diabetes, which are the other major risk factors (table 1). (See 'Introduction' above.)

- Hypertension increases the risk for a variety of cardiovascular diseases, including stroke, coronary artery disease, heart failure, atrial fibrillation, and peripheral vascular disease. The risk for both coronary disease and stroke increases progressively with incremental increases in blood pressure above 115/75 mmHg, as shown in numerous epidemiologic studies (figure 1A-B). However, the best evidence for a causal role of increasing blood pressure in cardiovascular complications is an improvement in outcome with antihypertensive therapy. (See 'Impact of hypertension on cardiovascular disease' above.)

- The magnitude of the association between hypertension and cardiovascular disease varies according to the specific cardiovascular outcome. Using data from multiple studies, a 10 to 12 mmHg reduction in systolic pressure and a 5 to 6 mmHg reduction in diastolic pressure are projected to produce a 38 percent reduction in risk of stroke and a 16 percent reduction in risk of coronary disease. (See 'Impact of hypertension on specific cardiovascular disorders' above.)

- The different cardiovascular risk factors have an additive effect on the likelihood of developing coronary heart disease and other cardiovascular outcomes. Multiple risk prediction models using these and other risk factors have been developed, including one developed by the American Heart Association (AHA) and the American College of Cardiology (ACC) that incorporated data from multiple patient cohorts and includes risk of all cardiovascular events, including stroke, rather than coronary heart disease alone (calculator 1). (See 'Additive effects of hypertension and other risk factors' above.)

- The benefit a patient receives from blood pressure lowering depends upon the balance between the **absolute** (rather than relative) reduction in risk for adverse outcomes and the potential harms and burdens of antihypertensive therapy. We, and several professional organizations, recommend that markers of overall cardiovascular risk be incorporated in treatment decisions. (See 'Application of risk assessment to therapeutic decisions' above.)

Topic 3850 Version 22.0

GRAPHICS

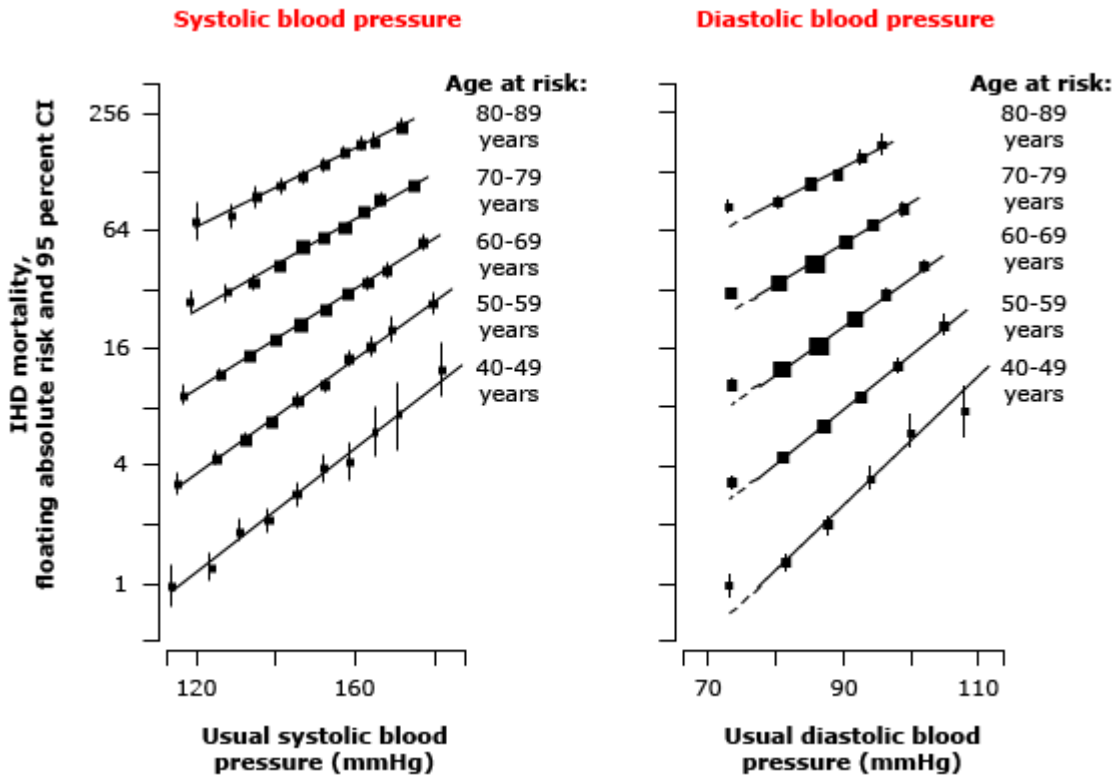
Components of cardiovascular risk factors in patients with hypertension

Major risk factors	Target organ damage
Hypertension	Heart disease
Cigarette smoking	Left ventricular hypertrophy
Obesity (BMI ≥30 kg/m2)	Angina or prior myocardial infarction
Physical inactivity	Prior coronary revascularization
Dyslipidemia	Heart failure
Diabetes mellitus	Stroke or transient ischemic attack
Microalbuminuria or estimated GFR <60 mL/min	Chronic kidney disease
Age >55 years for men, >65 years in women	Peripheral arterial disease
Family history of premature coronary disease	Retinopathy
Men - <55 years	
Women - <65 years	

Data from The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood pressure. The JNC 7 report. JAMA 2003; 289:2560.

Graphic 81993 Version 1.0

Coronary heart disease mortality related to blood pressure and age

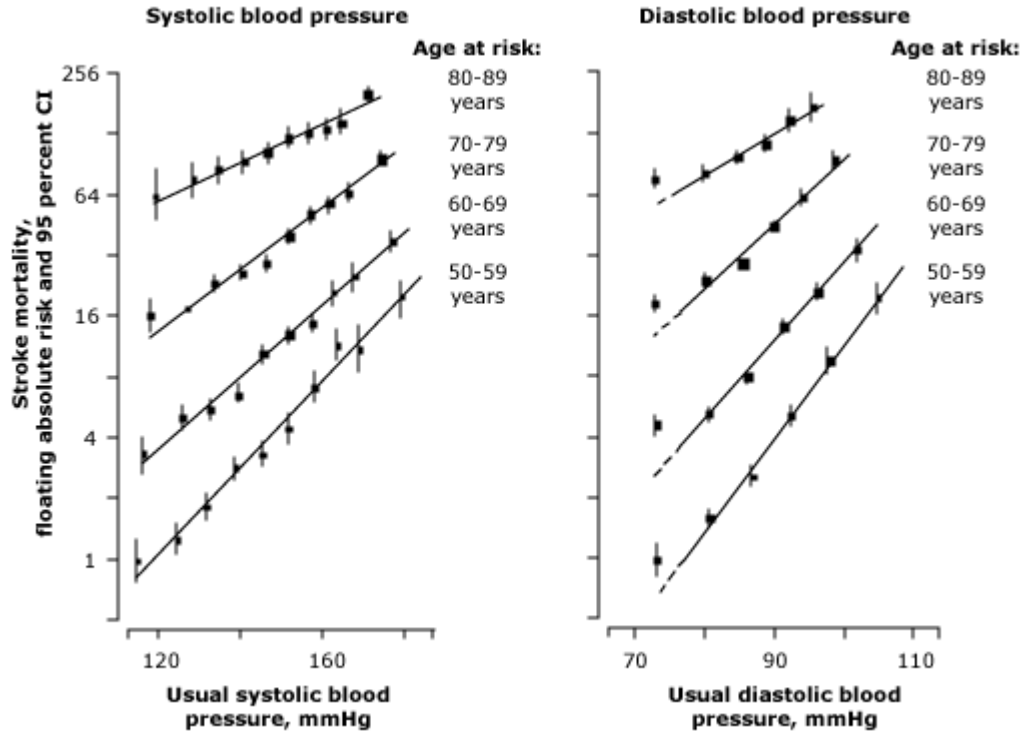


Coronary heart disease (CHD) mortality rate, pictured on a log scale with 95% confidence intervals (CI), in each decade of age in relation to the estimated usual systolic and diastolic blood pressure at the start of that decade. CHD mortality increases with both higher pressures and older ages. For diastolic pressure, each age-specific regression line ignores the left-hand point (ie, at slightly less than 75 mmHg) for which the risk lies significantly above the fitted regression line (as indicated by the broken line below 75 mmHg).

IHD: ischemic heart disease.

Graphic 75106 Version 9.0

Stroke mortality related to blood pressure and age



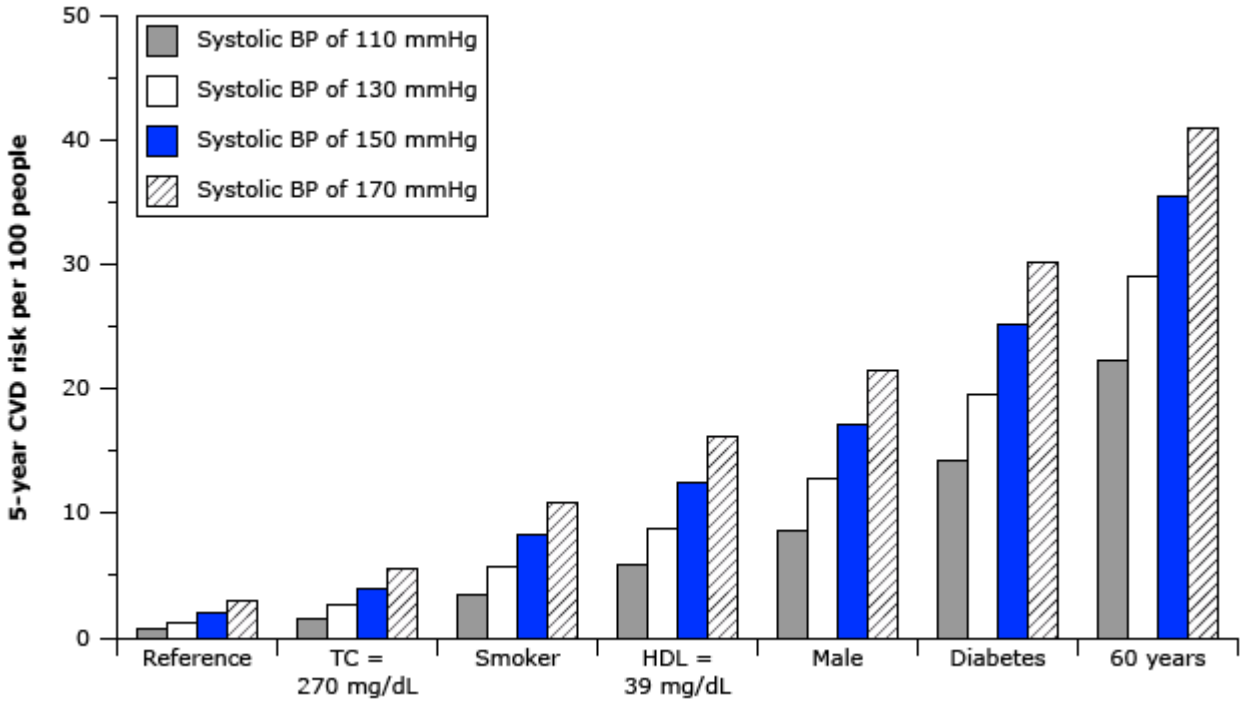
Stroke mortality rate, pictured on a log scale with 95% CI, in each decade of age in relation to the estimated usual systolic and diastolic blood pressure at the start of that decade. Stroke mortality increases with both higher pressures and older ages. For diastolic pressure, each age-specific regression line ignores the left-hand point (ie, at slightly less than 75 mmHg) for which the risk lies significantly above the fitted regression line (as indicated by the broken line below 75 mmHg).

CI: confidence interval.

Data from Prospective Studies Collaboration, Lancet 2002; 360:1903.

Graphic 66793 Version 5.0

Additive effects of risk factors on cardiovascular disease at 5 years



Cumulative absolute risk of CVD at 5 years according to systolic blood pressure and specified levels of other risk factors. The reference category is a non-diabetic, non-smoking 50-year-old woman with a serum TC of 154 mg/dL (4.0 mmol/L) and HDL cholesterol of 62 mg/dL (1.6 mmol/L). The CVD risks are given for systolic blood pressure levels of 110, 130, 150, and 170 mmHg. In the other categories, the additional risk factors are added consecutively. As an example, the diabetes category is a 50-year-old diabetic man who is a smoker and has a TC of 270 mg/dL (7 mmol/L) and HDL cholesterol of 39 mg/dL (1 mmol/L).

BP: blood pressure; CVD: cardiovascular disease; HDL: high-density lipoprotein; TC: total cholesterol.

Adapted from: Jackson R, Lawes CM, Bennett DA, et al. Lancet 2005; 365:434.

Graphic 55353 Version 12.0