Pre-hypertension: Concepts and management

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Abstract

Subjects with ‘pre-hypertension’—adults with blood pressure ranging from 120/80 mmHg to 129/89 mmHg—display a higher risk of future hypertension and cardiovascular disease (CVD) including myocardial infarction, stroke, heart failure, and cardiovascular death. Adoption of healthier lifestyles in individuals with BP in this range might lower their BP, delay or prevent hypertension, and reduce the risk of CVD. On the other hand, it might increase public anxiety and lead to unnecessary physician visits. Pre-hypertension should be differentiated from labile (or borderline) hypertension, a term used for subjects who are demonstrated to have paroxysmal hypertension. While majority of subjects found to have pre-hypertension will eventually develop hypertension by the age of 60, about one fifth continue to stay pre-hypertensive or exhibit a fall in BP in optimal range. There is no simple way to predict which pre-hypertensive subjects will develop sustained hypertension though lower body mass index (BMI) and higher physical activity may be associated with a lower risk. Coronary calcium may be a key predictor of future cardiovascular events in patients with pre-hypertension, particularly women. Though no large randomized studies have shown that lifestyle changes will reduce the risk of hypertension, it is well known that lifestyle modifications have a beneficial effect on blood pressure and cardiovascular risk factors. The term “pre-hypertension” was re-introduced in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7, 2003) for adults with blood pressure (BP) ranging from 120–139 mmHg systolic and/or 80–89 mmHg diastolic, dropping the normal and high-normal BP categories of JNC 6 (1998). In children and adolescents, pre-hypertension was defined as systolic and/or diastolic BP above the 90th percentile but less than the 95th percentile for age, gender, and height according to normative tables published in the Working Group report.

Key Words

- Pre-hypertension
- Hypertension
- Cardiovascular disease
- Labile hypertension
- Coronary calcium
- Therapeutic lifestyle changes
- Angiotensin receptor blocker (ARB)
- Angiotensin-converting enzyme inhibitor (ACE-I)
- ACE-I
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Introduction

The concept of pre-hypertension is not new. It was introduced way back in 1939 when a study found that systolic blood pressure (SBP) in the range of 120–140 mmHg, particularly in the young, was associated with progression to hypertension and cardiovascular (CV) events in future. The term “pre-hypertension” was re-introduced in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7, 2003) for adults with blood pressure (BP) ranging from 120–139 mmHg systolic and/or 80–89 mmHg diastolic, dropping the normal and high-normal BP categories of JNC 6 (1998). In children and adolescents, pre-hypertension was defined as systolic and/or diastolic BP above the 90th percentile but less than the 95th percentile for age, gender, and height according to normative tables published in the Working Group report.

The main stimulus for introducing pre-hypertension as a category of BP was Prospective Studies Collaboration (2002), a meta-analysis of 31 prospective epidemiological studies incorporating >1 million subjects which found that in the middle aged and the elderly, each increment of 20 mmHg in SBP or 10 mmHg in diastolic BP (DBP) doubles the risk of coronary artery disease and stroke mortality, starting at 115/75 mmHg. This was consistent with Framingham Heart Study in which subjects with BP in pre-hypertensive range were at increased risk of hypertension during 4 years follow-up, particularly in the elderly (Table 1). In the same study, pre-hypertension was associated with an increase in the risk of cardiovascular disease including myocardial infarction (MI), but not stroke. In Women Health Initiative (WHI), pre-hypertension was associated with MI (hazard ratio, HR 1.76, 95% CI 1.40–2.22) as well as stroke (HR 1.93, 95% CI 1.49–2.50), heart failure (HR 1.36, 95% CI 1.05–1.77), and CV death (HR 1.58, 95% CI 1.12–2.21).

The purpose of introducing pre-hypertension as a category was to increase awareness amongst public and health professionals who adoption of healthier lifestyles in individuals with BP in this range might lower their BP, delay or prevent hypertension, and reduce the risk of CVD. Criticism was soon raised against this term as it might increase public anxiety and lead to unnecessary physician visits for millions. Yet, it was recognized that BP in this range did increase the risk of progression to hypertension and future CVD, particularly when the baseline BP was higher (Table 1). In the same study, pre-hypertension was associated with MI, heart failure, stroke, and CV death (HR 1.58, 95% CI 1.12–2.21).

While majority of subjects found to have pre-hypertension will eventually develop hypertension by the age of 60, about one fifth continue to stay pre-hypertensive or exhibit a fall in BP in optimal range. There is no simple way to predict which pre-hypertensive subjects will develop sustained hypertension though lower body mass index (BMI) and higher physical activity may be associated with a lower risk. Coronary calcium may be a key predictor of future cardiovascular events in patients with pre-hypertension, particularly women. Though no large randomized studies have shown that lifestyle changes will reduce the risk of hypertension, it is well known that lifestyle modifications have a beneficial effect on blood pressure and cardiovascular risk factors. The term “pre-hypertension” was re-introduced in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7, 2003) for adults with blood pressure (BP) ranging from 120–139 mmHg systolic and/or 80–89 mmHg diastolic, dropping the normal and high-normal BP categories of JNC 6 (1998). In children and adolescents, pre-hypertension was defined as systolic and/or diastolic BP above the 90th percentile but less than the 95th percentile for age, gender, and height according to normative tables published in the Working Group report.

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There is no simple way to predict which pre-hypertensive subjects will develop sustained hypertension. Hypertension and Ambulatory Recording Venetia Study (HARVEST) from Italy, presented at the 2013 International Conference on Pre-hypertension and Cardio-metabolic Syndrome has somewhat clarified this issue. In this study, 198 adults with stage 1 hypertension, who became normotensive during long term follow-up had a slightly lower body mass index (BMI) at baseline and less marked increases in BMI over 15 years follow-up, lower triglycerides, higher physical-activity, and lower incidence of pre-diabetes when compared to the those with sustained hypertension.

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Abstract

Subjects with ‘pre-hypertension’—adults with blood pressure (BP) ranging from 120–129 mmHg systolic and/or 80–89 mmHg diastolic—are at increased risk of future hypertension and cardiovascular disease (CVD) including myocardial infarction, stroke, heart failure, and cardiovascular death. Adoption of healthier lifestyles in individuals with BP in this range might lower their BP, delay or prevent hypertension, and reduce the risk of CVD. On the other hand, it might increase public anxiety and lead to unnecessary physician visits. Pre-hypertension should be differentiated from labile (or borderline) hypertension, a term used for subjects who are demonstrated to have paroxysmal hypertension. While majority of subjects found to have pre-hypertension will eventually develop hypertension by the age of 60, about one fifth continues to stay pre-hypertensive or exhibit a fall in BP in optimal range. There is no simple way to predict which pre-hypertensive subjects will develop sustained hypertension through lower body mass index (BMI) and higher physical activity may be associated with a lower risk.

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Pre-hypertension should be differentiated from the so-called labile (or borderline) hypertension, a term often used for subjects who are demonstrated to have paroxysmal hypertension. Unlike pre-hypertension, where BP is consistently below hypertensive range, BP in labile hypertension is intermittently >140 mmHg systolic and/or >90 mmHg diastolic. A common cause of labile hypertension is panic disorder. At other times, it is a precursor of more sustained hypertension when it may be accompanied by a hyper-adrenergic state manifesting as anxiety, sweating, palpitations, sinus tachycardia, and elevation of systolic BP. Rarely, labile hypertension due to phaeochromocytoma though hypertension in this condition is very often sustained. Patients with labile hypertension may benefit from pharmacological intervention, particularly when markers of early target organ damage, such as left ventricular (LV) hypertrophy, increase in LV end diastolic diameter or LV mass index, carotid intimal medial thickness or microalbuminuria are present.**

Predicting sustained hypertension in pre-hypertension

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Table 1: Four year incidence of progression to hypertension²

<table>
<thead>
<tr>
<th>Optimal BP (120 and 80 mmHg)</th>
<th>Normal BP (120-129 and 80-84 mmHg)</th>
<th>High-normal BP (130-139 and 85-89 mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65 Years 5.3% (95% CI 4.6-6.3)</td>
<td>17.6% (95% CI 15.2-20.3%)</td>
<td>37.3% (95% CI 33.3-41.5%)</td>
</tr>
<tr>
<td>&gt;65 Years 10.6% (95% CI 12.0-20.9)</td>
<td>25.5% (95% CI 20.4-31.4)</td>
<td>49.5% (95% CI 42.6-56.4)</td>
</tr>
</tbody>
</table>

n = 4200 men, 5645 women, mean age 52 years

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Prevention of hypertension in patients with pre-hypertension (PREVER-PREVENTion)

The other randomized, double-blind, placebo-controlled trial of drug treatment in pre-hypertension is Prevention of Hypertension in Patients with Pre-hypertension (PREVER-PREVENTion) in which pre-hypertensive subjects whose BP after 3 months of recommended lifestyle changes continues to be in the range of 120-130/80-89 mmHg are being randomized to a combination of low-dose chlorthalidone plus amlopidine or to placebo for 18 months to investigate whether pharmacological treatment of pre-hypertension prevents or delays hypertension and target organ damage manifested by microalbuminuria and electrocardiographic left ventricular hypertrophy. Final results from the trial once again are still several years away.

Conclusion

The concept of pre-hypertension is attractive, but current methods do not allow reliable prediction of future hypertension or cardiovascular events in individual pre-hypertensive subjects. The benefits of drug treatment in pre-hypertension have not been convincingly demonstrated. Even if drug treatment is effective in reducing the burden of hypertension and its complications, cost-effectiveness is an important issue. Lack of demonstrated benefit of pharmacological treatment in reducing blood pressure below the level of 140/90 mmHg in uncomplicated hypertension and <130/80 mmHg in high risk subsets also argue against drug treatment in pre-hypertension. Therefore, at present, lifestyle modification alone is recommended for the majority of pre-hypertensive patients.

References


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Nixe dent study from Germany, presented at the 2013 International Conference on Prehypertension and Cardiometabolic Syndrome recruited 4181 patients without history of coronary artery disease or stroke, all of whom had coronary artery calcium (CAC) at baseline. Over 7 years, the adjusted risk of primary (fatal and nonfatal) cardiovascular events (stroke and coronary revascularizations) across all blood-pressure categories increased significantly with higher levels of CAC, including prehypertensive and normotensive patients even if CAC conventionally was not considered to be high.

### Management of prehypertension

Though no large randomized studies have shown that therapeutic lifestyle changes will reduce the risk of incident hypertension or avert stroke in patients with prehypertension, there seems no controversy about the desirability of healthy lifestyles in prehypertension. These approaches do lower blood pressure modestly, are safe, and likely to reduce global cardiovascular risk. What is not known is whether drug treatment is warranted in this range of BP and the ongoing trials will attempt to answer this question. But even if these trials are able to demonstrate that anti-hypertensive drug therapy in prehypertension will reduce progression to hypertension and its complications, the question of cost-effectiveness will remain unanswered. Cost-effectiveness of drug treatment may be greater in older patients or those with more pronounced CV risk factors, but this also needs to be documented in prehypertensive population. Tilt then drug treatment of prehypertension cannot be adopted as a public health policy.

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### Ongoing drug trials for prehypertension

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