Should the Treatment of Hypertension be based on Blood Pressure Level Only or on Total Cardiovascular Risk?

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Abstract

The treatment of hypertension is a mainstay of cardiovascular medicine. This was not always the case but was established only 60 years ago with the publication of the Framingham study in 1961. Despite the compelling findings of this landmark study which established the link to coronary heart disease, the medical community was slow to take up blood pressure control to strict targets. The philosophy of care has evolved in the ensuing years, and there is now universal support for this approach. However, an understanding of the goals and targets of hypertensive therapy as related to an individual patient’s overall cardiovascular risk is somewhat less clear. This paper provides a review of relevant literature with regard to the question of whether total cardiovascular risk should be taken into consideration when treating the hypertensive patient.

Key words: Blood pressure targets, end-organ damage, cardiovascular risk

Background

Hypertension is an important determinant in the spectrum of cardiovascular disease (CVD), and treating hypertension is a central tenet of modern cardiac care. However, the decision of whether to initiate therapy based on cardiovascular risk factors or absolute blood pressure (BP) measurements is less defined. The Framingham study began the cardiology community’s focus on epidemiological risk in the pursuit of the etiology of cardiac disease.[¹] Historically, antihypertensive therapy was determined by signs of the development of overt end-organ damage in patients but became modified with accumulation of epidemiological data. Hypertension was established as a causal risk factor, with a significant reduction in BP being correlated with a reduction in hypertensive heart failure in those with CVD.

The Framingham study established cardiovascular prospective population epidemiological research and preventative cardiology. The “risk factor” concept evolved, indicating that multiple interrelated factors promote increased risk of the development of coronary heart disease (CHD).[²] To date, no single essential factor has been identified. Epidemiologists began to conceptualize vascular disease as an outcome of multiple forces, and hypertension is primed among these. This research determined the influence of hypertension on the full clinical spectrum of CVD including sudden death, silent and overt myocardial infarction, heart failure, and clinical and silent strokes.

The study determined population CVD incidence attributable to hypertension at a time when only mortality statistics was available, and most recently, the lifetime risk of developing it and its vascular consequences. The study also provided some valuable insights into mechanisms of hypertension-induced CVD. In the past, initiation of antihypertensive treatment was often delayed until there was evidence of target organ involvement. Framingham study data indicated that this practice was imprudent as 40–50% of hypertensive persons developed overt cardiovascular events before evidence of target organ damage such as proteinuria, cardiomegaly, or electrocardiogram abnormalities. However, patients with CVD appear to also benefit, with reductions in hypertensive heart failure. Within the original Framingham study subgroup of patients who have...
hypertension, there was benefit from significant BP reduction and evidence of end-organ damage seems to be an increased risk for cardiovascular complication.

There appears to be a group of patients with accelerated disease that seems to benefit from aggressive antihypertensive treatment. Patients who have had significant cardiovascular risk in the past particularly benefit from intervention for their hypertension. The link between hypertension and coronary artery disease is long established but the link between cerebrovascular disease and hypertension appears more compelling. Several studies such as ALLHAT have shown that significant reduction in BP directly correlates with reduction in cerebrovascular disease end points.\(^1\)

**Risk Stratification**

Risk stratifying patients according to the hypertensive risk appear to benefit in the management of patients with CVD. Elevated BP is a causal risk factor for CVD. Epidemiological analyses have established the graded and continuous association between higher BP and CVD. In a population-based study of older adults, although all measures of BP were strongly and directly related to the risk of coronary and cerebrovascular events, SBP was the best single predictor of cardiovascular events.\(^3\) Moreover, randomized clinical trials among individuals with hypertension have demonstrated, in aggregate, a reduction in CVD events by 20%, CHD by 17%, stroke by 27%, and heart failure by 28% for every 10 mmHg systolic BP (SBP) lowering with medical therapy.\(^4\) This approximately correlates with a doubling in cerebrovascular and cardiovascular events for every 20 mmHg rise in SBP over 120 mmHg. Therefore, prevention, detection, treatment, and control of elevated BP are an important public health priority and a primary target for CVD prevention. This suggests that stratifying patients according to BP may be beneficial in targeting the treatment of hypertension in patients who should be aggressively managed.

**Concerns and Special Populations**

There are concerns about the potential harm from aggressive BP management at lower BP.\(^5\) The common adverse effects of antihypertensive therapy can be grouped two ways:

- Effects of the particular drug chosen (e.g., cough associated with ACE inhibitors)
- Effects of BP lowering (often hypotension and syncope).\(^6\)

For example, there are risks in overzealous treatment in hypertensive patients, particularly in the elderly and those with isolated systolic hypertension. These patients often have quite low diastolic BP and with aggressive reduction in mean arterial pressure often lead to an increased risk of falls. Diastolic hypertension is often present in pediatric and obstetric patients although systolic hypertension also is of significance.

Concerns have also been raised about renal safety due to the statistically significant difference in participants without chronic kidney disease experiencing at least 30% reduction in estimated glomerular filtration rate (eGFR) in SPRINT.\(^7\) This measure is not a clinically meaningful outcome in those with eGFR above 60 mL/min/1.73 m\(^2\). For those with chronic kidney disease, there was no significant difference in the composite renal outcomes, but there was insufficient power to determine if there was any effect on long-term dialysis.

Alternatively, a systematic review by Xie et al. revealed no significant differences in severe adverse events associated with BP lowering, dizziness, or adverse events leading to discontinuation of more intensive BP lowering therapy. However, there was a small difference in severe hypotension.\(^8\)

**Conclusion**

There appears to be significant benefit in BP reduction over and above end-organ damage, particularly in patients with cardiovascular risk. The treatment of absolute BP measurements rather than cardiovascular risk alone seems to be of value, particularly given the insidious onset of end-organ damage in many patients, and the lack of symptoms of CVD until significant macro- and microvascular damage has occurred. Patients with cardiovascular risk may warrant BP treatment to more aggressive BP targets. However, there are also limitations to aggressive BP reduction, particularly in certain populations such as the elderly. In view of this, the authors recommend that ongoing vigilance in primary care and physician settings to tight BP control will be associated with better outcomes, although certain populations may require more pragmatic approach. Most patients will require vigilance and careful cardiac risk management including BP monitoring to ensure the avoidance of the long-term sequelae of CVD.

**References**

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