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Research Article

Antecedent blood pressure as a predictor of cardiovascular disease

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Abstract

Elevated blood pressure (BP) is associated with greater risk of cardiovascular disease (CVD), and evidence suggests that prior BP levels may be at least as important as current BP in prediction models. We analyzed the determinants of CVD risk in Offspring Framingham Heart Study participants (n = 3344). The baseline Cox model included the traditional risk factors and current systolic BP to predict 20-year risk of CVD (643 events). Current systolic BP was significant, and the associated hazard ratio was 1.09 for 10 mm Hg (confidence interval [CI] 95%: 1.04–1.15). A second model used the traditional risk factors plus antecedent BP (hazard ratio [HR] = 1.19; CI 95%: 1.10–1.24). In a third model that included traditional risk factors and both current and antecedent BP, the antecedent BP was significant (HR = 1.18; CI 95%: 1.08–1.23), but the current BP was not statistically significant (HR = 1.01; CI 95%: 0.97–1.09). Antecedent BP showed a significantly stronger effect on risk of CVD than current BP. J Am Soc Hypertens 2015;9(9):690–696.

Keywords: Hypertension; statistics.

Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide and within the United States.[1,2] The American Heart Association reports that approximately 800,000 deaths in the United States are attributable to CVD every year.[3] The CVD burden in the United States exceeds 400 billion dollars in health care and lost productivity.[4] Many of the causes of CVD are controllable through medication or lifestyle change, so improving our knowledge of risk factors over time and how they may affect CVD risk is worthy of investigation.

Prior research has identified many risk factors for CVD, including age, sex, cholesterol, smoking, diabetes, and elevated levels of BP.[5] Most risk estimate models use a patient's current BP and ignore history of BP.[6] Clinical studies have indicated that a patient's BP history may be an important factor.[7–9] Many patients exhibit high BP variability over time,[10,11] and the most recent point estimate may not capture this information. Furthermore, long-term exposure to elevated BP levels may have important effects on CVD risk. Antecedent BP includes some of this information and may have meaningful effects on a patient's CVD risk status.

In this study, we examined the potential effects of incorporating antecedent BP into modern CVD risk prediction models. Previous studies examining antecedent BP as a risk factor[8] have examined an older cohort in the Framingham Original study. Antihypertensive treatment has improved since the data examined in that study, and more detailed cholesterol information is available. Other CVD risk studies examining changes in BP over time only classify individuals by stage of hypertension.[9] Studies that incorporate antecedent pressures report current, recent, and remote measures, without considering trends within an individual.[12] In this study, we considered the improvement in risk prediction from adding additional BP measurements over time. We further considered whether stage of antecedent hypertension was sufficient to improve risk

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prediction or if exact antecedent pressures were necessary. This study motivates further questions regarding how much BP history is relevant to CVD prediction and how best to weigh past measurements.

Methods

Population Sample

The Framingham Heart Study (FHS) is a longitudinal observational study that began in 1948 in Framingham, Massachusetts, and has had long-term funding from the National Heart, Lung, and Blood Institute. The Offspring Cohort began in 1971 with approximately 5000 participants and was used to undertake the data analyses. Examination 1 collected data from 1971–1975, examination 2 from 1979–1983, and examination 3 from 1983–1987. The current project was approved by the Emory Institutional Review Board, and public-use data were accessed through the National Institutes of Health.

Study Inclusion

We included data from Offspring Study participants who attended examination 3 if they met the following criteria: (1) individuals must not have had any cardiovascular event (myocardial infarction, angina pectoris, stroke, intermittent claudication, or cardiac failure) at the time of examination 3 or before that date, (2) participants had a systolic BP measurement from examination 1 and potentially from examination 2, (3) all other CVD predictors were recorded at examination 3, and (4) study subjects must have either a recorded death time or last known time alive. Of 3765 participants who attended examination 3, a total of 3344 met these selection criteria (1604 men and 1740 women). Persons with missing data values were omitted, and no interpolation was performed. There was an 8-year interval between examinations 1 and 2, and 4 years between examinations 2 and 3.

Clinical Measurements

There were 3344 participants who satisfied the selection inclusion criteria. BP was measured at the FHS with the subject sitting for at least five minutes using an appropriate cuff size. The BP measurements for this project were performed using a mercury column sphygmomanometer with quality control evaluations of the staff who made the measurements. BP was measured twice by a clinician for each participant at each examination, and the average of these determinations was used as the BP in the analyses. Antecedent systolic BP was defined as the simple average of the BP measurements at examinations 1 and 2. For the 416 participants missing BP measurements at examination 2, the examination 1 measurement was used as the antecedent. A study subject was considered on treatment for hypertension if the participant either reported currently taking one of a number of drugs designed to lower BP or if the offspring examination records indicated that the person was being treated for hypertension. The specific drugs included at examination 1: diuretics for fluid retention or BP and hypotensive medications; examination 2: propranolol, hypotensive medications, aldomet, spironolactone, and diuretics for hypertension or other; examination 3: calcium channel blockers, beta blockers, peripheral vasodilators, diuretics, potassium-sparing diuretics, reserpine derivatives, methyldopa, clonidine, wytensin, ganglionic blockers, renin angiotensin blockers, and other antihypertensive drugs. Cigarette smoking was assessed by questionnaire based on regular smoking over the past year.

Cholesterol was determined using enzymatic methods, and high-density lipoprotein (HDL) cholesterol was measured after precipitation of plasma with dextran sulfate. Diabetes was considered present if the subject took glucose lowering medication or if fasting glucose was greater than 126 mg/dL.

Follow-Up for CVD Outcomes

Participants were followed until they first experienced a CVD event or until 20 years after the examination 3. We defined a CVD event as death by CVD, myocardial infarction, coronary insufficiency, cerebrovascular disease, intermittent claudication, or congestive heart failure. Cardiovascular events were adjudicated by a panel of three Framingham clinicians using end point criteria that have in place since the start of the study and have been published elsewhere. Participants not experiencing an event were censored at the time of their death or at the time they were last known to be alive.

Statistical Methods

Cox survival models were used to evaluate the strength of various variables in predicting CVD risk. We first created simple age- and sex-adjusted risk models using current systolic BP, antecedent systolic BP, and both BP measures. We next created multivariate Cox models. The conventional model used age, cholesterol, HDL cholesterol, and systolic BP at examination 3 as continuous variables. Sex, smoking, diabetes, and BP treatment were used as categorical variables. The antecedent model included all these variables, except antecedent BP was used in place of systolic BP. Finally, a full model contained all these variables and both BP measurements. We also created models examining history of hypertension (examination 1 or 2 BP measurement $\geq$140 or on BP treatment) as a predictor instead of the exact antecedent BP.

To compare the predictive power of these models and explore if the differences were significant, we used C statistic (concordance) tests,[13] net reclassification (NRI),[14] and integrated discrimination improvement (IDI).[14] The IDI test is a measure of the new models' improvement in