Heart Rate and Subsequent Blood Pressure in Young Adults
The CARDIA Study

Jang-Rak Kim, Catarina I. Kiefe, Kiang Liu, O. Dale Williams, David R. Jacobs, Jr, Albert Oberman

Abstract—The objective of the present study was to examine the hypothesis that baseline heart rate (HR) predicts subsequent blood pressure (BP) independently of baseline BP. In the multicenter longitudinal Coronary Artery Risk Development in Young Adults study of black and white men and women initially aged 18 to 30 years, we studied 4762 participants who were not current users of antihypertensive drugs and had no history of heart problems at the baseline examination (1985–1986). In each race-sex subgroup, we estimated the effect of baseline HR on BP 2, 5, 7, and 10 years later by use of repeated measures regression analysis, adjusting for baseline BP, age, education, body fatness, physical fitness, fasting insulin, parental hypertension, cigarette smoking, alcohol consumption, oral contraceptive use, and change of body mass index from baseline. The association between baseline HR and subsequent systolic BP (SBP) was explained by multivariable adjustment. However, HR was an independent predictor of subsequent diastolic BP (DBP) regardless of initial BP and other confounders in white men, white women, and black men (0.7 mm Hg increase per 10 bpm). We incorporated the part of the association that was already present at baseline by not adjusting for baseline DBP: the mean increase in subsequent DBP was 1.3 mm Hg per 10 bpm in white men, white women, and black men. A high HR may be considered a risk factor for subsequent high DBP in young persons. (Hypertension. 1999;33:640-646.)

Key Words: heart rate ■ blood pressure ■ hypertension ■ regression analysis ■ race

Though evidence has been accumulating that heart rate (HR) is a correlate of blood pressure (BP), HR has not been the central focus of epidemiological investigations of BP.1 Yet numerous cross-sectional or case-control studies2–28 show an independent relationship between HR and hypertension14,17–19 or with both systolic BP (SBP) and diastolic BP (DBP).9,13,16,22,23 Prospective studies2–7,10–15,20,21,24,28 on the association between HR and subsequent BP are inconsistent. Many, but not all, lose statistical significance after adjustment for baseline BP, the most potent predictor of subsequent BP. Important confounders such as physical activity or fitness are not considered in these studies. Thus, whether HR affects BP level remains uncertain. Also, cross-sectional HR-BP associations have been found to be different in blacks compared with whites.7,11,27

We tested the following hypotheses in young black and white participants in the Coronary Artery Risk Development In young Adults (CARDIA) study:
1. Baseline HR is an independent predictor of subsequent BP after adjustment for baseline BP and other confounders.
2. Race-sex is an effect modifier for the association between HR and subsequent BP.

Methods

CARDIA is a multicenter longitudinal epidemiological study of the determinants of cardiovascular risk factors during young adulthood. Methods are described in detail elsewhere.29,30 Briefly, 5115 black and white women and men aged 18 to 30 years at baseline were selected and stratified by race to represent the populations of Birmingham, Ala, Chicago, Ill, Minneapolis, Minn, and Oakland, Calif. Participants were examined at baseline (year 0) in 1985–1986 and were reexamined every 2 to 3 years with follow-up rates of 90.4% at year 2, 85.7% at year 5, 80.6% at year 7, and 78.5% at year 10.

Participants were asked to present fasting in the morning and to refrain from smoking and heavy physical activity. BPs were measured 3 times in the right arm, with participants seated, at 1-minute intervals after 5 minutes of rest. We recorded the first-phase (systolic) and fifth-phase (diastolic) Korotkoff sounds using a random zero sphygmomanometer and appropriately sized cuff. A 30-second HR was recorded at the radial artery by palpation before the first BP measurement.

Body weight with light clothing was measured to the nearest 0.2 lb and body height without shoes was measured to the nearest 0.5 cm. Body mass index (BMI) was computed as weight in kilograms divided by height squared (m²). Physical fitness was assessed by duration of treadmill exercise testing and by an interviewer-administered physical activity history questionnaire that was designed for CARDIA.30,31

Sex, race, years of education, date of birth, history of heart problems, current medications, weekly alcohol consumption,28 parental history of high BP, and cigarette smoking status were determined by structured interview or by self-administered question-
Table 1. Number of Participants and Baseline Characteristics of Continuous SD and Categorical Variables at Baseline Examination by Sex and Race, CARDIA Study, 1985–1986

<table>
<thead>
<tr>
<th>Variable</th>
<th>Black (n=1098)</th>
<th>White (n=1094)</th>
<th>Black (n=1360)</th>
<th>White (n=1210)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, bpm</td>
<td>64.6±9.7</td>
<td>67.2±10.4</td>
<td>71.8±10.6</td>
<td>72.4±11.0</td>
</tr>
<tr>
<td>Age, y</td>
<td>24.2±3.8</td>
<td>25.4±3.4</td>
<td>24.3±3.9</td>
<td>25.4±3.4</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>115.6±10.6</td>
<td>114.2±10.3</td>
<td>108.1±9.8</td>
<td>104.7±9.2</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>70.5±10.3</td>
<td>70.6±9.3</td>
<td>67.4±9.3</td>
<td>66.1±8.5</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>24.5±4.3</td>
<td>24.3±3.6</td>
<td>25.9±6.6</td>
<td>23.1±4.4</td>
</tr>
<tr>
<td>Waist/hip ratio (&gt;100)</td>
<td>81.8±4.7</td>
<td>83.8±4.7</td>
<td>74.1±5.9</td>
<td>72.6±4.9</td>
</tr>
<tr>
<td>Treadmill duration, minutes</td>
<td>11.1±2.4</td>
<td>12.2±2.4</td>
<td>7.2±2.0</td>
<td>9.2±2.2</td>
</tr>
<tr>
<td>Fasting insulin, µU/mL</td>
<td>10.6±8.1</td>
<td>9.2±5.7</td>
<td>13.4±9.3</td>
<td>9.3±6.9</td>
</tr>
<tr>
<td>Education, (&gt;12 years) %</td>
<td>43.1</td>
<td>72.8</td>
<td>52.4</td>
<td>73.1</td>
</tr>
<tr>
<td>Parental history of hypertension, %</td>
<td>53.6</td>
<td>43.5</td>
<td>57.4</td>
<td>44.6</td>
</tr>
<tr>
<td>Cigarette smoker, %</td>
<td>37.3</td>
<td>26.0</td>
<td>31.1</td>
<td>27.1</td>
</tr>
<tr>
<td>Heavy drinker (30+ mL/da), %</td>
<td>17.2</td>
<td>20.4</td>
<td>2.8</td>
<td>6.3</td>
</tr>
<tr>
<td>Oral contraceptive use, %</td>
<td>...</td>
<td>...</td>
<td>34.6</td>
<td>29.0</td>
</tr>
</tbody>
</table>

Continuous variables are mean±SD; categorical, %. SBP indicates systolic blood pressure; DBP, diastolic blood pressure.

Results

Baseline cohort characteristics are summarized for each race-sex subgroup (Table 1). Baseline HR was highest in white women and lowest in black men (Figure 1), but both SBPs and DBPs at all subsequent examinations were highest in black men and lowest in white women (Figure 2).

Cross-sectional associations between HR and SBP and DBP at each examination were significant in men and white women except for SBP at year 10 in black men. In black women, however, the associations were much weaker (Table 2, top). Prospective associations between baseline HR and subsequent SBP and DBP were all significant in men and white women (Table 2, bottom). They were fairly constant over time. Associations were stronger with DBP than with SBP, but in black women the associations with subsequent SBP were null and those with subsequent DBP were weaker. Subsequent HR was associated with baseline HR for all examinations and across all race-sex groups (Table 2). There were some correlations between change in HR and change in BP, but they were much weaker than those between baseline HR and subsequent BP (data not shown).

The unadjusted associations of baseline HR with subsequent SBP were explained mostly by the confounders including baseline BP, except for black women for whom there was a significant negative association after adjustment (model 4, SBP, Table 3). Baseline HR was a highly significant predictor of subsequent DBP after controlling for all the confounders including baseline DBP in black men, in white men, and in white women. The regression coefficient was positive, small,
and not significant in black women (Table 3, DBP). The interaction term between time (examination year) and baseline HR was not significant in any of the 4 race-sex subgroups (data not shown). We considered that inclusion of baseline BP in the model might result in underestimation of the total association between baseline HR and BP because of overadjustment of effects accumulated before baseline. Indeed, in model 5 of Table 3 (DBP), the increase in DBP (mm Hg per bpm) almost doubled. In assessing goodness-of-fit for the models, we noted that the HR-BP association was somewhat stronger at the lowest HRs and weaker at the highest HRs. The coefficient for interaction between baseline HR and baseline BMI was small and not statistically significant (data not shown).

Discussion

In the present study, we found that HR had univariate cross-sectional and prospective associations with BP and that HR was an independent predictor of subsequent DBP regardless of initial BP and other confounders, except for black women. Although the magnitude of the association was modest, it doubled when the results were not adjusted for baseline DBP, thereby incorporating that part of the association that had accumulated before and including baseline. The association between HR and subsequent DBP, however, was largely explained by the baseline characteristics of the cohort, particularly baseline SBP.

Other cross-sectional or case-control studies have also shown significant cross-sectional correlations between HR and BP or hypertension. All the prospective studies reviewed showed significant associations between baseline HR and subsequent BP or hypertension. But only 3 prospective studies specifically investigated BP level, and two showed that the associations of baseline HR with subsequent DBP were independent of initial BP. However, these studies did not consider important confounders such as physical
fitness, and they used different statistical methods than CARDIA.

In CARDIA, baseline resting (supine) HR also was calculated from 12-lead ECG before performing graded exercise treadmill test. The correlations between HR by palpation and that by ECG were not high, and were least in black women: 0.54 for black men, 0.50 for white men, 0.45 for black women, and 0.56 for white women. This may be because of differences in measurement method, time, position of the body, or alarm reaction caused by the expectation of having BP measured. However, in a study that compared the 2 measurements (auscultation for 1 minute versus ECG taken soon after the auscultation), there was a good correlation. The cross-sectional and prospective associations between baseline HR and BP were minimal or absent in black women, which suggests a race-sex effect modifier that has also been suggested in other studies. The correlations between baseline HR and subsequent HR at years 2, 5, 7, and 10 were also not very high and were lowest in black women (Table 3). The relatively high variability of HR in black women may in

**TABLE 2.** Number of Participants and Pearson Correlation Coefficients Between Heart Rate and Blood Pressure Measured at the Same Examination by Year, Sex and Race, CARDIA Study, 1985–1996

<table>
<thead>
<tr>
<th></th>
<th>Men Black</th>
<th>Men White</th>
<th>Women Black</th>
<th>Women White</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline HR correlated with BP at same examination</td>
<td>1098 1094</td>
<td>1360 1210</td>
<td>934 1028</td>
<td>1192 1144</td>
</tr>
<tr>
<td>SBP</td>
<td>0.14†</td>
<td>0.12†</td>
<td>0.06*</td>
<td>0.21†</td>
</tr>
<tr>
<td>DBP</td>
<td>0.14†</td>
<td>0.13†</td>
<td>0.08†</td>
<td>0.17†</td>
</tr>
<tr>
<td>Year 2</td>
<td>855 990</td>
<td>1122 1092</td>
<td>785 945</td>
<td>1050 1026</td>
</tr>
<tr>
<td>SBP</td>
<td>0.16†</td>
<td>0.16†</td>
<td>0.05</td>
<td>0.22†</td>
</tr>
<tr>
<td>DBP</td>
<td>0.14†</td>
<td>0.22†</td>
<td>0.00</td>
<td>0.21†</td>
</tr>
<tr>
<td>Year 5</td>
<td>785 945</td>
<td>1050 1026</td>
<td>761 889</td>
<td>1026 990</td>
</tr>
<tr>
<td>SBP</td>
<td>0.15†</td>
<td>0.17†</td>
<td>0.05</td>
<td>0.13†</td>
</tr>
<tr>
<td>DBP</td>
<td>0.16†</td>
<td>0.25†</td>
<td>0.09†</td>
<td>0.19†</td>
</tr>
<tr>
<td>Year 7</td>
<td>784 945</td>
<td>1050 1026</td>
<td>761 889</td>
<td>1026 990</td>
</tr>
<tr>
<td>SBP</td>
<td>0.15†</td>
<td>0.17†</td>
<td>0.08†</td>
<td>0.22†</td>
</tr>
<tr>
<td>DBP</td>
<td>0.17†</td>
<td>0.31†</td>
<td>0.19†</td>
<td>0.47†</td>
</tr>
<tr>
<td>Year 10</td>
<td>761 889</td>
<td>1026 990</td>
<td>761 889</td>
<td>1026 990</td>
</tr>
<tr>
<td>SBP</td>
<td>0.12†</td>
<td>0.16†</td>
<td>0.03</td>
<td>0.18†</td>
</tr>
<tr>
<td>DBP</td>
<td>0.19†</td>
<td>0.35†</td>
<td>0.12†</td>
<td>0.42†</td>
</tr>
</tbody>
</table>

HR indicates heart rate; BP, blood pressure.

**TABLE 3.** Number of Participants and Population Regression Coefficients of Subsequent SBP and DBP Pooled From Year 2 to Year 10 on Baseline Heart Rate, CARDIA Study, 1985–1996

<table>
<thead>
<tr>
<th></th>
<th>Men Black</th>
<th>Men White</th>
<th>Women Black</th>
<th>Women White</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1, unadjusted</td>
<td>1.13 (0.03)‡</td>
<td>1.12 (0.03)‡</td>
<td>0.01 (0.03)</td>
<td>1.14 (0.02)‡</td>
</tr>
<tr>
<td>No.</td>
<td>1023 1066 1280 1184</td>
<td>1023 1066 1280 1184</td>
<td>922 1012 1163 1116</td>
<td>920 1011 1160 1113</td>
</tr>
<tr>
<td>Model 2, adjusted for only baseline SBP or DBP</td>
<td>0.10 (0.02)†</td>
<td>0.09 (0.02)‡</td>
<td>0.03 (0.02)</td>
<td>0.08 (0.01)†</td>
</tr>
<tr>
<td>No.</td>
<td>1023 1066 1280 1184</td>
<td>1023 1066 1280 1184</td>
<td>922 1012 1163 1116</td>
<td>920 1011 1160 1113</td>
</tr>
<tr>
<td>Model 3, adjusted for baseline SBP or DBP and other baseline confounders (age, body mass index, waist/hip ratio, treadmill duration, fasting insulin, education, parental history of hypertension, cigarette smoking, alcohol amount, oral contraceptive use in women; Model 4, adjusted for baseline SBP or DBP, other baseline confounders, and BMI change; Model 5, adjusted for baseline confounders (except baseline SBP or DBP) and BMI change.</td>
<td>0.13 (0.03)‡</td>
<td>0.13 (0.02)‡</td>
<td>0.02 (0.01)</td>
<td>0.13 (0.02)‡</td>
</tr>
<tr>
<td>No.</td>
<td>920 1011 1160 1113</td>
<td>920 1011 1160 1113</td>
<td>920 1011 1160 1113</td>
<td>920 1011 1160 1113</td>
</tr>
</tbody>
</table>

Number of participants varies because of missing values in the independent variables. Values are mean (SE) measured in mm Hg/bpm unless otherwise indicated.

HR indicates heart rate; BP, blood pressure.

*p<0.05; †p<0.01; ‡p<0.001.
part explain the weaker association between HR and BP. The association with subsequent SBP adjusted for all confounders was even negative for black women. Another 23-year follow-up study of young blacks (mostly men) also showed a negative but nonsignificant association. In another CARDIA analysis, Dyer et al.28 studied elevated BP as a dichotomous variable and found baseline HR to be an independent predictor of 10-year incidence of elevated BP except for black women.

The magnitude of the relationship between baseline HR and subsequent DBP in black and white men and white women did not vary in any systematic way during the 10-year time period. The absence of the expected decrease in effect size over time was perplexing. Perhaps epidemiological data were not sufficiently precise to detect a slowly changing relationship, particularly given the relatively poor repeatability of both HR and BP. In addition, the relatively poor repeatability of HR may have contributed to the small magnitude of the association of resting HR with subsequent DBP.

We studied whether various factors confounded the HR and BP association and found only low levels of confounding (Table 3). A higher HR may indicate merely a low level of physical fitness.2 But our multivariate results indicate that the association between HR and BP is only minimally confounded by level of physical fitness. Others20,39,40 postulate that high insulin in resistant states causes higher HR or sympathetic overactivity and later hypertension. Although acute elevations in plasma insulin levels cause sympathetic activation that could elevate BP, plasma insulin also causes vasodilation.20,39,41 In some epidemiological studies, high baseline fasting insulin concentrations increased the incidence of hypertension in women42 and particularly in lean subjects.43 Stern et al.40 postulated that tachycardia may represent an early stage of insulin resistance syndrome and that higher BP may be a later feature, but this was not supported by their data.

Because our results showed that higher HR preceded higher BP, we wanted to assess whether the former was involved in the process of higher BP development by insulin resistance. If insulin resistance leads to subsequent higher BP and this process is mediated by higher HR, removing baseline fasting insulin level from the regression model should considerably increase the contribution of baseline HR on the subsequent BP. We compared the regression coefficients of subsequent BP on baseline HR in the regression model before and after removing baseline fasting insulin levels. Little changed in the regression coefficients (data not shown), indicating that the relation between baseline HR and subsequent BP was not dependent on baseline fasting insulin level. Further, since there was little difference between adjusted and unadjusted analyses, overadjustment is unlikely to explain our results.

Some studies have shown both greater cross-sectional44 and prospective21 associations between HR and BP in lean persons, although these studies did not adjust for baseline BP. However, we saw no differential between baseline HR and subsequent BP according to BMI. A correlation between HR and BP at any one examination could be explained by a transient increase in sympathetic nervous system activity in some participants.1,21,25,26 Pavlov showed that sympathetic nervous system reactions were weakened by repeated exposure to stimulus, which may explain why there is a gradual fall of BP and HR in a patient who attends an outpatient clinic frequently.25,45 This adaptation effect is consistent with our finding of minimum mean SBP at year 5 and minimum mean DBP at year 2 despite increasing age. Although BP and HR reactions in clinic had many features in common, the correlation between their peak changes was not high (r = 0.37).25 In the present study, the pattern of HR change was different from that of BP change. Nonetheless, the cross-sectional associations between HR and BP at each of the 5 examinations in the present study remained fairly constant through a 10-year time period, which may mean that the adaptation effect did not weaken these associations.

Without confounding as an explanation of the HR-BP association, it may be that increasing BP is causally related to the level of resting HR. Some investigators46,47 suggest that sympathetic overactivity early in life, a potent marker of which is tachycardia, causes later hypertension and insulin resistance, which may explain our findings. But only a small proportion of hypertensive patients have this neurogenic form of hypertension,46 perhaps contributing to the small observed effect sizes. Whether such persons inherit a tendency toward a stable sympathetic overactivity or a susceptibility to greater reactions to environmental stimuli (such as the clinic visit) remains disputed.1,48 However, Julius49 suggested that an association between baseline HR and BP may mean that the presence of chronic, stable sympathetic overactivity precedes the development of hypertension. In addition to its modulation by the autonomic nervous system, HR also is under the direct influence of primary genetic factors according to a recent animal study.50 CARDIA data suggest that in some patients who later develop hypertension, signs of enhanced sympathetic drive exhibited by higher HRs are present before the BP elevation. Diastolic pressure relates most closely to vascular resistance and is less affected by cardiac function.51 The HR elevation reflects an increased sympathetic tone leading to smooth muscle cell proliferation, resulting over the long-term in reduced compliance of the peripheral vasculature and, consequently, elevated DBP.

High sympathetic activity is present especially in young subjects with hypertension and in those with borderline hypertension49,52–54 and decreases with age.52 The participants in our study were young (18 to 30 years old at baseline). This may explain partly why CARDIA showed significant prospective associations between baseline HR and subsequent DBP, independent of initial BP and other confounders in contradistinction to other studies.4,5,11,12,15,20,21,24 More importantly, CARDIA was able to control for very potent confounders, sex and race, that may have masked the effect of baseline HR on the subsequent BP with analyses stratified by 4 race-sex subgroups.

We excluded from the analyses participants who were current users of antihypertensive medications and who reported history of heart problems at the baseline examination,
because their BP and/or HR could be distorted.55 More than half of heart problems were histories of heart murmur, and including both of these groups in the analyses made little change. Excluding measurements when the participant was taking antihypertensive medications during follow-up examinations also had little effect on the analyses. Measures for primary prevention of atherosclerosis may affect HR inconsistently. For example, antihypertensive medications may either decrease (beta blockers) or increase (vasodilators) HR. Other than the lowering effect of physical fitness on HR, little is known about this, so we cannot comment on the potential effect of preventive measures on our results. Though the CARDIA cohort appears quite representative of the population for which it was selected, small differences between participants and nonparticipants56 may be a limitation in the present study.

In conclusion, HR is an independent predictor of DBP over the next 10 years in white men and women and black men regardless of initial BP and other potential confounders. Higher HRs may be considered a risk factor of subsequent high DBP in young persons, except for black women, rather than just a reflection of a temporary state of anxiety. If further research supports this finding, persistently elevated resting HR may be a signal for more aggressive treatment of high normal BP.

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References


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