Association Between Resting Heart Rate and Hypertension Treatment in a General Population
Jean Ferrière and Jean-Bernard Ruidavets

Epidemiologic studies have reported a relationship between resting heart rate (RHR) and cardiovascular mortality, particularly in hypertensive subjects. In a representative sample (n = 1175) of women and men aged 35 to 64 years, we studied the associations between RHR and hypertension. RHR was associated with sex (P < .001), socioeconomic and marital status (P < .05), physical fitness (P < .001), smoking (P < .05), hypercholesterolemia (P < .01), body mass index (P < .01), blood pressure (P < .01), triglyceride levels (P < .01), glycemia (P < .05), hematocrit (P < .001 in men, not significant in women), and white blood cell count (P < .01). Logistic regression models adjusted for the above variables were developed with RHR coded as a polytomous outcome variable (RHR < 65/min; 65 < RHR < 75/min; 75 < RHR < 85/min; RHR > 85/min). Subjects unaware of their hypertension had significant adjusted odds ratios for high RHR categories [75 < RHR < 85/min: 2.11 (1.37 to 3.23), P < .001; RHR ≥ 85/min: 4.71 (2.06 to 10.78), P < .001]. People treated for hypertension had nonsignificant odds ratios whatever the RHR categories. After adjustment for numerous risk factors, elevated RHR were associated with high blood pressure in unaware hypertensive subjects. The impact of antihypertensive drugs with different RHR lowering effects remains to be studied on a population basis. Am J Hypertens 1999; 12:628–631 © 1999 American Journal of Hypertension, Ltd.

KEY WORDS: Hypertension, heart rate, population.

Previous studies have shown positive associations between resting heart rate (RHR) and both all-cause and cardiovascular mortality. Furthermore, RHR may be an independent risk factor for cardiovascular deaths in hypertensive subjects. Few studies have examined the relationships between RHR and hypertension detection and treatment in a general population. The aim of the present study was to identify the relationships between RHR and hypertension in a representative cross-sectional sample of 1175 women and men.

METHODS

Study Population We selected our study population among the third MONICA (MONItoring of trends and determinants in Cardiovascular disease) survey on cardiovascular risk factors. The MONICA Project was an international 10-year program coordinated by the World Health Organization. Its aim was to monitor deaths attributable to coronary heart disease, myocardial infarction, coronary care, and cardiovascular risk factors. Forty-one collaborating centers from 27 countries were participating in this program. They carried out a registration of acute coronary events. These cen-
Questionnaire and Clinical Parameters Each subject had to complete an informed consent and, with the help of a specially trained medical staff, fill in a questionnaire on medical history, hormonal status, cardiovascular risk factors, drug intake, tobacco and alcohol consumption, nutritional habits, lifestyle, and socioeconomic status. The number of years of education represented the number of years spent at school or in full-time study (from the beginning of the primary school until graduation or left school). The economic status of the subjects was determined according to their yearly income tax (income tax: free, low, medium, and high). Physical activity was evaluated in four different classes by using a standardized questionnaire: none, light (ie, light physical activity almost every week), moderate (ie, intensive physical activity during at least 20 min once or twice a week), and intense (ie, intensive physical activity during at least 20 min three times a week or more). Alcohol consumption was quantified in grams of alcohol per day. The participants were asked about their smoking habits: never smoked, ex-smokers, and current smokers. Height, weight, and blood pressure were measured according to standard protocols. Body mass index (BMI) was calculated as weight divided by height squared (kg/m²). Two blood pressure and RHR (pulse palpation for 60 sec) measurements were made on subjects after at least a 5-min rest. The participants were in a sitting position for the measurements. A standard sphygmomanometer was used. All blood pressure measurements were taken at the nearest 2 mm Hg. The averages of the two blood pressure and RHR measurements were used for the analysis.

Biological Measurements A blood sample of 20 mL was obtained and placed in tubes containing Na₂EDTA after the subjects had fasted for at least 10 h, kept at room temperature, and centrifuged within 4 h. Serum total cholesterol and triglycerides were measured by enzymatic methods (Boehringer, Mannheim, Germany). HDL-cholesterol measurement was done after sodium phosphotungstate–magnesium chloride precipitation of apolipoprotein B-containing lipoproteins (Boehringer). Fasting plasma glucose was measured with a hexokinase-glucose-6-phosphate dehydrogenase method (Boehringer).

Statistical Analysis When the distribution of variables was skewed (triglycerides and glycemia), logarithmically transformed values were used in statistical computations. Qualitative data were analyzed by χ² test. For quantitative data, we used linear regression.

Then we introduced potential confounding factors into multivariate models. For modeling ordinal response data as RHR³ (RHR < 65/min; 65 ≤ RHR < 75/min; 75 ≤ RHR < 85/min; RHR ≥ 85/min), we used the polytomous logistic model. The polytomous logistic model is a straightforward extension of the logistic model for binary responses, to accommodate multinomial responses.

### RESULTS

Women (69.0 ± 8.6 beats/min) had higher (P < .001) RHR than men (65.7 ± 9.1 beats/min) (Table 1). Socioeconomic (P < .05) and marital (P < .05) status (higher RHR in widowed and divorced than in married and single subjects), smoking habits (higher RHR in current smokers than in ex-smokers or nonsmokers, P < .05), physical fitness (higher RHR in current smokers than in ex-smokers or nonsmokers, P < .05), and diastolic blood pressure (DBP) blood pressures (P < .01), triglyceride levels (P < .01), fasting blood glucose (P < .05), hematocrit (P < .001 in men, P = NS in women), and white blood cell count (P < .01) (Table 2). Because there were no major sex differences in the association of RHR with the other variables, the groups were lumped together for subsequent analyses.

Unaware hypertensive subjects (SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg; 69.8 ± 9.8 beats/min, n = 241) had higher RHR (one-way analysis of variance, P <
than normotensive subjects (SBP <140 mm Hg and DBP <90 mm Hg; 66.3 ± 8.6 beats/min, n = 766) or treated (with a drug) and noncontrolled (SBP ≥140 mm Hg or DBP ≥90 mm Hg; 67.9 ± 9.3 beats/min, n = 117) or treated and controlled subjects (SBP <140 mm Hg and DBP <90 mm Hg; 69.3 ± 8.4 beats/min, n = 51). Logistic regression models adjusted for the above variables (clinical and biological variables associated with RHR) were developed with RHR coded as a polytomous outcome variable (RHR < 65/min; 65 ≤ RHR < 75/min; 75 ≤ RHR < 85/min; RHR ≥ 85/min).

Unaware hypertensive subjects had significant adjusted odds ratios (OR) for high RHR categories [75 ≤ RHR < 85/min; OR: 2.11 (1.37 to 3.23), P < .001; RHR ≥ 85/min; OR: 4.71 (2.06 to 10.78), P < .001]. Treated (controlled and not controlled) subjects had nonsignificant adjusted OR whatever the RHR categories (Table 3). Similar results were obtained after eliminating the subjects (n = 75) taking β-blockers or non-dihydropyridine calcium antagonists [75 ≤ RHR < 85/min; OR: 2.12 (1.38 to 3.26), P < .001, in unaware hypertensive subjects and OR: 1.30 (0.64 to 2.65), P = NS, in treated subjects; RHR ≥85/min; OR: 4.45 (1.92 to 10.29), P < .001, in unaware hypertensive subjects and OR: 2.08 (0.54 to 7.96), P = NS, in treated subjects].

**DISCUSSION**

Associations between RHR and blood pressure have been assessed in numerous studies. But only very few reports have studied the relationships between RHR and blood pressure awareness and treatment in a general population. In this work, we show that the detection of hypertension during a systematic examination is associated with elevated RHR and that the use of antihypertensive drugs with or without control of blood pressure values (even after eliminating the subjects taking β-blockers and non-dihydropyridine calcium antagonists) is associated with RHR similar to RHR found in normotensive subjects.

In the present study, elevated RHR was associated with general poor health factors, for instance tobacco

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**TABLE 2. PEARSON CORRELATION COEFFICIENTS OF RESTING HEART RATE WITH OTHER VARIABLES BY SEX**

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>BMI</th>
<th>SBP</th>
<th>DBP</th>
<th>TC</th>
<th>HDL-C</th>
<th>TG</th>
<th>GLU</th>
<th>HT</th>
<th>WBC</th>
<th>ALC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td>0.04</td>
<td>0.11†</td>
<td>0.20‡</td>
<td>0.20‡</td>
<td>0.09</td>
<td>−0.08*</td>
<td>0.20‡</td>
<td>0.09*</td>
<td>0.19†</td>
<td>0.18‡</td>
<td>−0.04</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td>−0.01</td>
<td>0.12†</td>
<td>0.13†</td>
<td>0.12†</td>
<td>0.03</td>
<td>−0.05</td>
<td>0.13†</td>
<td>0.13†</td>
<td>0.01</td>
<td>0.11†</td>
<td>−0.02</td>
</tr>
</tbody>
</table>

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL-C, HDL cholesterol; TG, triglycerides; GLU, fasting glucose; HT, hematocrit; WBC, white blood cell count; ALC, alcohol.

* P < .05; † P < .01; ‡ P < .001.

**TABLE 3. ODDS RATIOS FOR RHR CATEGORIES ACCORDING TO BLOOD PRESSURE STATUS POLYTOPIC LOGISTIC MODEL (n = 1175)**

<table>
<thead>
<tr>
<th>Blood Pressure Thresholds, 140/90 mm Hg</th>
<th>&lt;65/min</th>
<th>≥65/min and &lt;75/min</th>
<th>≥75/min and &lt;85/min</th>
<th>≥85/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated and controlled hypertensive subjects (n = 51)</td>
<td>1</td>
<td>2.44‡</td>
<td>1.27</td>
<td>2.04</td>
</tr>
<tr>
<td>Treated and not controlled hypertensive subjects (n = 117)</td>
<td>1</td>
<td>1.07</td>
<td>0.84</td>
<td>2.72</td>
</tr>
<tr>
<td>Unaware hypertensive subjects (n = 241)</td>
<td>1</td>
<td>(0.66–1.73)</td>
<td>(0.45–1.57)</td>
<td>(0.92–8.06)</td>
</tr>
<tr>
<td>Model 2*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated hypertensive subjects (n = 168)</td>
<td>1</td>
<td>1.37</td>
<td>0.93</td>
<td>2.44</td>
</tr>
<tr>
<td>Unaware hypertensive subjects (n = 241)</td>
<td>1</td>
<td>(0.89–2.08)</td>
<td>(0.54–1.62)</td>
<td>(0.90–6.60)</td>
</tr>
</tbody>
</table>

* reference: normotensive subjects (n = 766).
† 95% confidence interval.
‡ P < .05; § P < .001.
Odds ratios adjusted for sex, socioeconomic and marital status, physical fitness, smoking habits, history of hypercholesterolemia, fasting blood glucose, triglyceride levels, hematocrit, body mass index, and white blood cell count.
consumption, low socioeconomic status, or low physical activity.\textsuperscript{1,7–9} This is why it seems accurate to consider RHR as a prognostic factor for noncardiovascular death.\textsuperscript{1,13} In our study, RHR was also associated with coronary heart disease risk factors; this was the case for blood pressure, glyceria, trigylceride levels, hematocrit, and white blood cell count (Table 2). Other studies have shown these same relationships.\textsuperscript{1,6–9} The role of sympathetic overactivity associated with elevated RHR, considered as a determining factor in the occurrence or the worsening of insulin resistance, dyslipidemia or blood viscosity seems to be clearly demonstrated.\textsuperscript{1}

In our study, an hypertensive subject who was not aware of his or her blood pressure status had a higher probability of elevated RHR (OR = 2.11 for 75 ≤ RHR <85/min, and OR = 4.71 for RHR ≥85/min). Because of the relationship between RHR and the prognosis,\textsuperscript{1–5} unaware hypertensive subjects with high RHR should be treated with drugs acting on the sympathetic nervous system. In a recently published paper, Materson et al\textsuperscript{14,15} have shown that antihypertensive drugs differed in their ability to reduce RHR and to change RHR in groups with high or low rates at baseline. Further studies are needed to compare antihypertensive drugs such as β-blockers, dihydropyridine, and non-dihydropyridine calcium antagonists,\textsuperscript{15} to disentangle the effect of therapy on blood pressure and on RHR.

Conversely, hypertensive subjects aware of their hypertension and treated with a drug, after adjustment for numerous associated factors, had RHR similar to RHR observed in normotensive subjects. These results are quite difficult to explain. It would be very useful to know blood pressure values before and after the beginning of the treatment. A significant decrease of blood pressure might be sufficient to reach a threshold where the relationship between RHR and blood pressure might become less dangerous for the prognosis. We have tried to study the impact of antihypertensive drugs on RHR\textsuperscript{14} according to therapeutic classes (data not shown). Unfortunately, the size of each sample was not sufficient to perform such an analysis. Nevertheless, it would be very valuable to know whether the effectiveness of the treatment on RHR was attributable to its impact on blood pressure values or to the impact on the decrease of the sympathetic tone (such as β-blockers), or both. Further studies are needed.

In conclusion, RHR is associated with many coronary heart disease risk factors. These risk factors are often connected to each other. But after adjustment for all these factors, elevated RHR values are associated with high blood pressure in unaware hypertensive subjects. After adjustment for these same risk factors, the relationship between blood pressure and elevated RHR seems to disappear with an antihypertensive drug. Further studies remain necessary to confirm this relationship and to analyze the different therapeutic classes with different heart rate-lowering effects on a population basis.

REFERENCES