Influence of Carboxyhemoglobin, Gamma-Glutamyl-Transferase, Body Weight, and Heart Rate on Blood Pressure in Middle-Aged Men

NELS CHRISTIAN HENNINGSEN, M.D., LARS JANZON, M.D., AND ERIK TRELL, M.D.

SUMMARY Carboxyhemoglobin (COHb%) and gamma-glutamyl-transferase (GGT) are indicators of tobacco and alcohol consumption; similarly, body weight broadly reflects dietary habits. Relationships between COHb%, GGT, relative body weight, heart rate and blood pressure were studied in 242 48-year-old men attending a general health screening program in Malmö, Sweden. All were without treatment for high blood pressure. Positive correlations were found between blood pressure and body weight, GGT, and pulse, and a reciprocal correlation between blood pressure and COHb%. Use of objective markers for known or suspected risk factors, such as alcohol consumption, smoking, or overweight, were studied to elucidate their usefulness for further prospective studies.

(Hypertension 5: 560-563, 1983)

KEY WORDS • hypertension • multi-variate analysis • risk factors

ARTERIAL hypertension constitutes one of the most important risk factors for cardiovascular morbidity and mortality.1,2 One of the major aims in several population screening trials has therefore been measurement of blood pressure (BP), with subsequent treatment of individuals with consistently elevated levels.3,4 Several factors have been shown to covary with BP, namely, heredity,5 body weight,6,7 salt intake,8 age,5,8 and alcohol consumption.7,9-11 However, smoking and potassium intake seem to be inversely related to BP.9,14,15 Thus, many exogenous factors may be of pathogenetic and pathophysiologic, as well as methodological, importance to the BP levels recorded, reproducibility, predictive value, clinical interpretation, and resulting treatment.

Although body weight at least partly reflects dietary habits in the population, it is usually more difficult to get a reliable history of alcohol consumption, at least in individuals with high consumption levels.16 Recent studies tend to indicate a linear relationship between BP and alcohol consumption7,9-13 and BP and gamma-glutamyl-transferase (GGT),14-21 although a flattened relationship has been suggested11 after a consumption level of 180 g/week.

In a recent statistical evaluation of the relationship between alcohol intake and BP,12 it was suggested that the individual’s “immediate” (24-hour) intake was better correlated to the BP. However, others have found good correlation between BP level and amount of alcohol consumed over several weeks and up to 3 months.11,13 In our ongoing preventive study22 of men with persistent hypertension, we found that the higher the GGT level the higher the incidence of moderate-to-severe hypertension; this could also indicate a longer acting effect of high alcohol consumption. Carboxyhemoglobin (COHb%) is today frequently used for the short-term and objective assessment of tobacco consumption.23

The aim of the present study was to evaluate univariate and multivariate correlations between BP, COHb%, relative bodyweight, GGT, and heart rate in a random subsample of untreated healthy middle-aged (48-year-old) men, and to assess how much of the variability in the blood pressure measurements could be accounted for by these other factors.

Methods

Selection of Subjects

In November 1974, consecutive middle-aged birth-year cohorts in Malmö, Sweden (230,000 inhabitants)
were invited to a health screening and intervention program at the Department of Preventive Medicine, Malmö General Hospital. The details of the program have been given elsewhere. About 75% of these cohorts agreed to participate. From a consecutive total random sample of 1028 untreated men born in 1930–1931 and investigated in 1978–1979, 242 were selected at random to the analysis. All these individuals were investigated according to the previously described screening routines. All were asked not to smoke in the morning prior to the investigation and during the study.

Protocol
Analysis of GGT was done according to the recommendations of the Scandinavian Enzyme Committee, and of COHb% according to the method of Collison et al. Actual/ideal (A/I) weight was calculated as the quotient of actual (measured) weight over the ideal weight for sex, age, and height according to the nomograms worked out by Lindberg et al. The BP and HR were measured by nurses specially trained in screening for this investigation. In all subjects, BP was obtained in the morning (8 to 9 a.m.) by a mercury manometer with the appropriate cuff size after the subjects had rested supine for 10 minutes and then after standing for 2 minutes. Diastolic blood pressure was defined as the appearance of the fifth Korotkoff sound and expressed in millimeters of mercury (mm Hg).

Statistical Analysis
COHb%, GGT, A/I weight, and HR were related to diastolic blood pressure (DBP) and systolic blood pressure (SBP). Partial correlation coefficients were used to express the association between BP and COHb%, GGT, A/I weight, and HR. In this analysis the influence of each factor was assessed after adjustment for differences in the other. The multiple linear regression equation was calculated for DBP = C + x1 COHb% + x2 GGT + x3 A/I weight + x4 HR. The multiple R2 was used to assess how much of the variability of BP could be attributed to COHb%, A/I weight, GGT, and HR together.

Table 3 represents the matrix for the multiple linear correlations between COHb%, GGT, A/I weight, HR, and the supine DBP. The GGT, A/I-weight, and HR had a significant positive correlation to DBP, but COHb% was negatively related to DBP.

Table 1. Mean Values (± sd) and Range of All BP Values (Supine and Erect), Heart Rate, COHb%, GGT, and A/I Weight (n = 242)

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>sd</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine (10 min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>87</td>
<td>10</td>
<td>60-140</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>129</td>
<td>16</td>
<td>100-200</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>68</td>
<td>11</td>
<td>36-108</td>
</tr>
<tr>
<td>Standing (2 min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>89</td>
<td>11</td>
<td>50-140</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>127</td>
<td>16</td>
<td>90-190</td>
</tr>
<tr>
<td>COHb%</td>
<td>1.3</td>
<td>1.0</td>
<td>0.0-5.8</td>
</tr>
<tr>
<td>GGT (μkat/liter)</td>
<td>0.68</td>
<td>0.62</td>
<td>0.12-2.79</td>
</tr>
<tr>
<td>(IE)</td>
<td>(40)</td>
<td>(37)</td>
<td>(7-167)</td>
</tr>
<tr>
<td>A/I weight</td>
<td>1.09</td>
<td>0.14</td>
<td>0.63-1.63</td>
</tr>
</tbody>
</table>

DBP = diastolic blood pressure; SBP = systolic blood pressure; COHb% = carboxyhemoglobin; GGT = gamma-glutamyl-transferase; 1.00 μkat = 10E; normal value = < 1.00 μkat/l.

Table 2. Univariate Correlation Coefficients between COHb%, GGT, A/I Weight and Heart Rate (10 min Supine) and All BPs Measured (DBP, SBP Supine 10 min) + DBP, SBP (Standing 2 min)

<table>
<thead>
<tr>
<th></th>
<th>Supine 10 min</th>
<th>Standing 2 min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DBP</td>
<td>SBP</td>
</tr>
<tr>
<td></td>
<td>DBP</td>
<td>SBP</td>
</tr>
<tr>
<td>COHb%</td>
<td>-0.16*</td>
<td>-0.12*</td>
</tr>
<tr>
<td>GGT (μkat/liter)</td>
<td>0.22*</td>
<td>0.19†</td>
</tr>
<tr>
<td>A/I weight</td>
<td>0.26*</td>
<td>0.24†</td>
</tr>
<tr>
<td>Heart rate (supine)</td>
<td>0.30†</td>
<td>0.32‡</td>
</tr>
</tbody>
</table>

*p < 0.05.
†p < 0.01.
‡p < 0.001.
§Not significant.

Table 3. Partial Correlation Coefficients between COHb% (1), GGT (2), A/I Weight (3), Heart Rate (4), and DBP 10 Supine (10 min) with Diastolic BP Supine

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. COHb%</td>
<td>r = -0.16*</td>
</tr>
<tr>
<td>2. GGT</td>
<td>r = 0.19†</td>
</tr>
<tr>
<td>3. A/I weight</td>
<td>r = 0.42†</td>
</tr>
<tr>
<td>4. Heart rate</td>
<td>r = 0.24†</td>
</tr>
<tr>
<td>5. COHG% + GGT + A/I weight + HR</td>
<td>R = 0.28*</td>
</tr>
</tbody>
</table>

*p < 0.05; + p < 0.01. R = multiple correlation coefficient; R2 = 0.08. DBP supine (10 min) = 39.8 - 2.0 (COHb%) + 5.5 (GGT) + 28.5 (A/I weight) + 0.23 (heart rate).
Discussion

It is well known that BP varies in the same individual from one time to another. Several studies in the past have established different factors that correlate with BP, i.e., body weight or body weight change, salt intake, alcohol consumption, and, especially in the industrialized countries, age. Other studies have shown a negative correlation between BP and smoking and potassium intake. All the above studies looked at populations with a wide age span except for the Gothenburg study, which examined men born in 1913, and ours.

The evaluation of alcohol consumption and smoking has usually been accomplished by questionnaires, which could underestimate the true role of alcohol. By using actual values of GGT and COHb%, which seem to have a relatively good correlation to the long-term effects of alcohol consumption and the amount of tobacco smoke inhaled and absorbed by the body during the preceding 24 hours, it may be possible to better understand the complex interrelationships between these factors and their contribution to recorded BP levels as well as their reproducibility and clinical interpretation.

The negative correlation between COHb% and BP found in this study is in accordance with earlier reports. The reason for this reciprocal association is not clear. Except for the vasodilating effect of nicotine, no biochemical or physiological explanation has been established. A negative correlation between smoking and body weight has also been shown, but this correlation was not statistically significant in our study. A positive correlation between smoking and alcohol consumption has previously been found, and can be traced also in the interrelations of COHb% and GGT in our multiple linear regression analysis. However, co-variation of amount of tobacco and alcohol consumption, as expressed in their linear correlation, seems to be less pronounced than the coexistence of the habits per se.

The positive correlation between A/I weight and BP in this normal, untreated population of 48-year old men is similar to other results; it is also well known that in established hypertensives overweight is common. Although weight loss may be useful in the treatment program for essential hypertension, the results are difficult to maintain over longer periods of time (i.e., more than 2 years) and are not directly related to the BP decrease as seen in the placebo-treated group of about 1500 mildly hypertensive patients in the Australian trial. In the study made by Reisin et al., the obese patients were told to eat more vegetables. Although potassium intake seems to have a beneficial effect on BP, urinary excretions were not reported, nor were changes in alcohol consumption, which may explain some of the BP reduction.

Severe overweight, as such, may partly be the phenotype of a genetic disorder characterized as increased intracellular sodium induced by abnormally low activity (or amount) of the cellular membrane-bound sodium-pump (Na\textsuperscript{+}, K\textsuperscript{+}-ATPase). Increased intracellular sodium content and decreased activity of the Na\textsuperscript{+}, K\textsuperscript{+}-ATPase enzyme have been proposed as explanations for essential hypertension and have also been found in the offspring of such patients.

The positive correlation between GGT and BP is in accordance with other surveys of alcohol consumption and BP. Such a relationship is particularly evident in established hypertensive patients, but in the present analysis, which was mainly confined to the normal BP range, GGT accounted for only 4% of the BP variation. This may also indicate that alcohol is one of the main causative factors in the establishment of definite hypertension in predisposed individuals. Such predisposition could be the increased intracellular sodium content, which is found especially in male offspring of established hypertensive patients, in whom significant correlations between GGT and BP were also found.

The results of our present analysis indicate that COHb%, GGT, A/I weight, and HR, independent of each other and in combination, are factors that affect BP. These factors should be kept in mind when interpreting BP measurements and considering further investigation and intervention.

The question as to whether GGT and COHb% are better indicators than self-reported consumptions of alcohol and tobacco has not been solved. However, other reports have shown a significant relationship between these markers and self-reports. Furthermore, GGT and COHb% may be strong indicators of the biological effects of alcohol consumption and smoking, as shown by the relationship between COHb% and cardiovascular symptoms (angina pectoris, dyspnea) in smoking patients. The number of premature deaths in screened men with elevated GGT levels and high alcohol consumption is at least three to six times higher than in men without these features. In New Zealand, a positive correlation has been documented between alcohol consumption and mortality in cardiac deaths (myocardial infarction, sudden death). Although utilization of an elevated GGT level seems to be effective in the control of heavy drinking in middle-aged men, the usefulness of GGT as an objective risk marker has to be evaluated further in prospective studies.

References

27. Management Committee of the Australian Therapeutic Trial in Mild Hypertension: Untreated mild hypertension. Lancet 1: 185, 1982
Influence of carboxyhemoglobin, gamma-glutamyl-transferase, body weight, and heart rate on blood pressure in middle-aged men.
N C Henningsen, L Janzon and E Trell

Hypertension. 1983;5:560-563
doi: 10.1161/01.HYP.5.4.560

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1983 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/5/4/560

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/