Impact of Waist Circumference on the Relationship Between Blood Pressure and Insulin

The Quebec Health Survey

Paul Poirier, Isabelle Lemieux, Pascale Mauriègue, Eric Dewailly, Carole Blanchet, Jean Bergeron, Jean-Pierre Després

Abstract—Hyperinsulinemia has been suggested to be involved in the etiology of obesity-associated hypertension. The objective of the present study was to quantify, in a population-based study, the respective contributions of excess adiposity (body mass index [BMI]), waist circumference (WC), fasting insulin levels, and insulin sensitivity to the variation of resting blood pressure. The Quebec Health Survey was used to obtain fasting plasma insulin and glucose levels and resting blood pressure as well as anthropometric measurements in a representative sample of 907 men and 937 women. When the sample was divided into tertiles of BMI and further stratified on the basis of the 50th percentile of WC (88 cm in men), nonobese men in the first BMI tertile (<23.2 kg/m²) but with abdominal obesity were characterized by an increased systolic blood pressure (SBP) compared with nonobese men with low WC (130±18 versus 120±11 mm Hg; mean±SD; P=0.075). The SBP was comparable to SBP values measured among men in the top BMI tertile (129±14 mm Hg for BMI ≥26.6 kg/m²). When subjects were classified into tertiles of fasting insulin and WC, no association between insulin levels and blood pressure was noted, once the variation in WC was considered. Insulin sensitivity (estimated with homeostasis model assessment [HOMA]) did not explain variation in blood pressure in men, whereas the contribution of HOMA in women was of marginal clinical significance (R² of <1.3%; P<0.0001). These results suggest that the documented association between obesity, fasting insulin, insulin sensitivity, and blood pressure is largely explained by concomitant variation in WC. (Hypertension. 2005;45:363-367.)

Key Words: insulin ■ blood pressure ■ obesity

It is well known that there is a greater prevalence of hypertension in obese patients than among normal-weight subjects. However, not every obese patient is hypertensive, another indication that obesity is a heterogeneous condition. Although excess fatness may contribute to hypertension in some obese patients, the mechanisms responsible for the weight-related increase in blood pressure are still unclear. One possible link between weight gain and hypertension is the insulin-resistant and compensatory hyperinsulinemic state frequently observed in obese individuals. Insulin resistance, hyperinsulinemia, and blood pressure have been correlated not only in obese but also in lean hypertensive patients. However, the association between fasting plasma insulin and hypertension has been inconsistent among studies. Nevertheless, insulin has been shown in multiple studies to have acute actions on the sympathetic nervous system, renal function, and the cardiovascular system that could lead to hypertension if these effects are sustained. Despite the fact that abdominal obesity is often accompanied by features of the metabolic syndrome, including (but not always) hypertension, the respective contributions of abdominal obesity versus hyperinsulinemia to high blood pressure are poorly defined. Recently, Hayashi et al reported that visceral obesity was associated with an increased odds of hypertension in Japanese Americans independently of fasting plasma insulin. Of note, ∼40% of the cohort was diagnosed with hypertension. Thus, the aim of the present study was to quantify, in a population-based sample (the Quebec Health Survey), the respective contributions of excess adiposity (as crudely estimated by the body mass index [BMI]), abdominal fat accumulation (estimated by waist circumference [WC]), fasting insulin levels, and insulin sensitivity (assessed with the homeostasis model assessment [HOMA]) to the variation of resting blood pressure.

Methods

As part of the federal–provincial Canadian Heart Health Initiative, Santé Québec (an organization of the Quebec Statistics Institute) conducted the Heart Health and Nutrition Survey among Quebecers. The primary objective of the survey was to determine the prevalence of cardiovascular risk factors and participants’ knowledge and...
awareness of the causes and the consequences of these factors. Individuals excluding the aboriginal populations represented the sample of the Quebec Health Survey. The global sample included 5,000,371 individuals taken from 6,700,000 citizens of the Quebec province, which covered most of the entire adult population. The study population consists of 1944 noninstitutionalized subjects (907 men and 937 women; aged 18 to 74 years). Participants constituted a stratified probability sample of the population and were selected according to a statistical sampling design. The sampling design, developed by the Quebec Bureau of Statistics, has been described previously. In brief, the territory was divided in primary units of sampling (PUS; n = 95); each unit counted 40 participants from a target sample of 3800 individuals. Thereafter, the PUS were stratified and subjects were divided into 6 groups according to age and sex (18 to 34, 35 to 64, and 65 to 74 years of age for men and women). Individuals were selected from health insurance files, and 2056 subjects completed the evaluation, which consisted of interviews, validated questionnaires for medical history, physical examination, and blood sampling. Complete data sets were available from 1944 patients. Participants were asked to fast overnight before giving blood samples. Lipid profile and plasma insulin levels were analyzed as described previously. Insulin sensitivity was estimated from the HOMA (fasting insulin \times fasting glucose/22.5). Written informed consent was obtained from all subjects.

Height was measured in standing position, with shoulders and buttocks against the wall, the subject looking straight ahead, with joined feet, and arms hanging on both sides. Body weight was measured with a calibrated beam scale. WC was obtained using a graduated tape when subjects were in standing position. WC was measured as the narrowest circumference of the trunk. However, when the position of the narrowest circumference could not be identified, the measurement was taken at the level of the last rib. BMI was calculated as weight/height (kg/m²). Resting blood pressure was taken in a sitting position after a 5-minute rest using a mercury sphygmomanometer according to standard procedures. Subjects were asked to refrain from eating or smoking for 30 minutes before the procedure. Per protocol design, trained nurses visited participants at their homes. Also, participants came to the clinic after an overnight fast and met a physician who performed a medical history and physical examination. Blood pressure values are means of 4 views, validated questionnaires for medical history, physical examination, and blood sampling. Complete data sets were available from 1944 patients. Participants were asked to fast overnight before giving blood samples. Lipid profile and plasma insulin levels were analyzed as described previously. Insulin sensitivity was estimated from the HOMA (fasting insulin \times fasting glucose/22.5). Written informed consent was obtained from all subjects.

**Statistical Analysis**

Results presented in this article were derived from weighed data, to re-establish the equiprobability of an individual being selected from the sample and to take into account nonresponse by age, sex, and geographic stratum. To achieve this objective, each respondent was given a value (weight) corresponding to the number of persons he or she represented in the Quebec population. Thus, all the data used in the present analyses were weighed and are representative of the entire Quebec adult population. Pearson correlation coefficients were calculated to quantify the univariate associations among variables. Comparisons among subgroups were performed by an ANOVA with the General Linear Model, and the Duncan post hoc test was used when a significant group effect was observed. Covariance analysis was also conducted to adjust variables for age-related differences among subgroups. Furthermore, multiple regression analyses were performed to quantify the independent contribution of BMI, WC, fasting insulin levels, and insulin sensitivity (HOMA) to the variance of systolic blood pressure (SBP) or diastolic blood pressure. Subjects on hypertensive medications were included. All analyses were performed with the SAS statistical package (SAS Institute).

**Table 1. Characteristics of Men and Women of the Quebec Health Survey**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Men (n=907)</th>
<th>Women (n=937)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>41±15</td>
<td>42±15</td>
<td>0.5738</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>76.2±12.6</td>
<td>62.2±12.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.4±3.9</td>
<td>24.4±4.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>WC, cm</td>
<td>89.7±11.1</td>
<td>77.3±12.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Metabolic profile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholesterol, mmol/L</td>
<td>5.28±1.07</td>
<td>5.21±1.05</td>
<td>0.4863</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
<td>3.28±0.93</td>
<td>3.17±0.92</td>
<td>0.0400</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.19±0.30</td>
<td>1.41±0.34</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.85±1.51</td>
<td>1.39±0.78</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cholesterol/HDL, cholesterol</td>
<td>4.70±1.58</td>
<td>3.90±1.25</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fasting insulin, pmol/L</td>
<td>68±49</td>
<td>64±36</td>
<td>0.4398</td>
</tr>
<tr>
<td>HOMA</td>
<td>17.3±17.8</td>
<td>15.0±11.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fasting glucose, mmol/L</td>
<td>5.5±1.7</td>
<td>5.1±1.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>125±14</td>
<td>119±17</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>78±9</td>
<td>74±9</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values are means±SD.

**Results**

The characteristics of the 907 men and 937 women included in this study are shown in Table 1. The average BMI was 25 kg/m² in both genders, whereas average WC values corresponded to 89.7±11.1 cm in men and 77.3±12.1 cm in women. The range of BMI was 16.7 to 46.9 kg/m² in men and 15.0 to 48.5 kg/m² in women. There were 44 men (4.8%) and 75 women (8%) with hypertension (>140/90 mm Hg) or taking antihypertensive medications. Correlations between BMI, WC, and fasting insulin levels and either resting diastolic blood pressure or SBP were presented in Table 2. There were significant associations between BMI, WC, and fasting insulin concentrations and diastolic blood pressure or SBP in women, whereas no association was found between fasting insulin levels and diastolic blood pressure in men. Therefore, although most correlations were statistically significant, the highest correlations with either SBP or diastolic blood pressure were obtained in both genders with WC. Multivariate analyses revealed that WC was the best variable, explaining a significant proportion of variance of either diastolic blood pressure or SBP (Table 3). Insulin sensitivity estimated from the HOMA did not add statistically significant information in men, whereas the information provided with HOMA in women may be considered clinically nonsignificant.

**Table 2. Correlations Between BMI, WC, and Fasting Insulin Levels and Either Diastolic Blood Pressure (DBP) or SBP**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DBP (mm Hg)</th>
<th>SBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI, kg/m²</td>
<td>r=0.31*</td>
<td>r=0.29*</td>
</tr>
<tr>
<td>WC, cm</td>
<td>r=0.35*</td>
<td>r=0.38*</td>
</tr>
<tr>
<td>Fasting insulin, pmol/L</td>
<td>r=0.05</td>
<td>r=0.09*</td>
</tr>
<tr>
<td>HOMA</td>
<td>r=0.06</td>
<td>r=0.11†</td>
</tr>
</tbody>
</table>

*P<0.0001; †P<0.05.
Nonobese men with abdominal obesity (≥88 cm) were characterized by an elevation in SBP, which was comparable to SBP values measured among men in the top BMI tertile (≥26.6 kg/m²). Regarding diastolic blood pressure, WC seemed to have a greater influence than BMI in the determination of elevated diastolic blood pressure (Figure 1A).

Among women, the highest SBP was observed for subjects who were in the upper tertile of BMI (≥24.8 kg/m²) and characterized by an elevated WC (≥74 cm). Finally, the highest diastolic blood pressure was observed among women in the upper tertile of BMI and with an elevated WC (Figure 1B).

When men (Figure 2A) and women (Figure 2B) were classified on the basis of tertiles of fasting insulin (≥49.6, 49.6 to 66.5, and ≥66.5 pmol/L in men and ≥48.3, 48.3 to 64.9, and ≥64.9 pmol/L in women) and WC (≥84, 84 to 93, and ≥93 cm in men and ≥69, 69 to 79, and ≥79 cm in women), no association was found between variation in insulin and blood pressure once the variation in WC was taken into account. Data were adjusted for age. For instance, diastolic blood pressure and SBP values were elevated in the upper tertiles of WC, irrespective of the presence/absence of hyperinsulinemia (Figure 2A and 2B).

### Discussion

Results of the present study suggest that the well-documented association between obesity, fasting insulin, insulin sensitivity, and blood pressure may largely, if not entirely, be explained by phenomena related to the concomitant variation in the amount of abdominal fat, as estimated by a simple clinical parameter: WC.

In whites, there have been many reports supporting an association between obesity, fasting insulin, insulin sensitivity, and blood pressure may largely, if not entirely, be explained by phenomena related to the concomitant variation in the amount of abdominal fat, as estimated by a simple clinical parameter: WC.

On the other hand, in some studies, >50% of hypertensive subjects were above their recommended weight. Concordance rates of 15% for dizygotic and 31% for monozygotic twins have been reported in those with obesity and hypertension. Obesity and insulin resistance are closely interrelated with “at-risk” obesity (ie, the metabolic syndrome), suggesting also a common underlying pathogenesis for obesity and hypertension. Indeed, it has been reported that WC was the strongest independent predictor (age, gender, BMI, and insulin resistance included) of SBP and diastolic blood pressure in 413 normoglycemic Chinese that included 56% individuals with hypertension. In this previous study, WC was found to be the major determinant of blood pressure, accounting for >20% of its variance. A similar association has been reported recently between the prevalence of hypertension and intra-abdominal fat accumulation but not with WC in a cohort.

### Table 3. Multivariate Regression Analyses Showing the Independent Contribution of WC to the Variance of Diastolic Blood Pressure (DBP) or SBP

<table>
<thead>
<tr>
<th>Dependent Variables</th>
<th>Independent Variables</th>
<th>Partial (R^2\times 100)</th>
<th>Total (R^2\times 100)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men DBP</td>
<td>WC</td>
<td>12.4%</td>
<td>12.4%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Fasting insulin</td>
<td>0.37%</td>
<td>12.8%</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>BMI</td>
<td>0.21%</td>
<td>13.0%</td>
<td>0.1464</td>
</tr>
<tr>
<td>Men SBP</td>
<td>WC</td>
<td>14.4%</td>
<td>14.4%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>BMI</td>
<td>0.24%</td>
<td>14.6%</td>
<td>0.1170</td>
</tr>
<tr>
<td>Women DBP</td>
<td>WC</td>
<td>18.8%</td>
<td>18.8%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>BMI</td>
<td>0.23%</td>
<td>19.0%</td>
<td>0.1047</td>
</tr>
<tr>
<td>Women SBP</td>
<td>WC</td>
<td>22.1%</td>
<td>22.1%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Fasting insulin</td>
<td>0.94%</td>
<td>23.1%</td>
<td>0.0008</td>
</tr>
<tr>
<td></td>
<td>HOMA</td>
<td>0.36%</td>
<td>23.4%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Variables included in the model were BMI, WC, fasting insulin concentrations, and HOMA (fasting insulin×fasting glucose/22.5).
of 563 Japanese Americans. However, this cohort included nearly 40% of individuals with hypertension. On the other hand, the Baltimore Longitudinal Study of Aging reported, in a white population of 649 patients, that the simple correlation between fasting insulin and blood pressure was secondary to the confounding effects of age and obesity. Again, a significant number of patients had hypertension (25%) in that study. Nevertheless, the correlations of blood pressure measurements were considerably stronger in both sexes with BMI, percent body fat, and waist-to-hip ratio than with insulin levels. In contrast to these 3 studies, our cohort only included 6.5% of subjects with hypertension because it was a population-based study. This is important because it is well known that some antihypertensive medications may negatively or positively influence insulin sensitivity and the metabolic risk profile over time. Therefore, our sample had the advantage of being representative of the whole population of adult Quebecers aged 18 to 74 years.

Several mechanisms may contribute to the increase in blood pressure resulting from increasing levels of abdominal adiposity in a manner independent of insulin resistance. Sympathetic activation associated with obesity and molecules released by hypertrophied fat cells are 2 factors that may promote the formation of angiotensin II (Ang II) and aldosterone, which have direct vasopressor and antinatriuretic effects. A local renin-angiotensinogen system (RAS) has been found to be present in human adipose tissue and may act as a distinct system from the plasma RAS. Indeed, all components of the RAS system (angiotensinogen [AGT], Ang II type 1 [AT₁] receptor, and angiotensin-converting enzyme but not renin and AT₂ receptor) are found in adipose tissue.

Fasting insulin may be related to hypertension by being a crude marker of the metabolic abnormalities associated with insulin resistance. However, results of the present study suggest WC may be a better marker of a cluster of blood pressure–raising abnormalities than fasting insulin. Mechanistic studies will be required to validate the above possibilities for a direct role of the expanded abdominal adipose tissue mass on blood pressure modulation.

Limitations
The population of people studied was young, with a lower average BMI and WC than in the US population. The prevalence of the metabolic alterations and the hypertriglyceridemic waist in that cohort has been the subject of previous reports. However, because there is a well-defined linear relationship between blood pressure and mortality from ischemic heart disease such that a lower blood pressure confers lower risk of mortality, our findings may be of clinical importance because even a relatively small rise in blood pressure has been known to increase the risk of cardiovascular death. Our population was predominantly white, with a relatively low prevalence of hypertension. This may limit the generalizability of our findings to other populations such as blacks, Hispanics, etc.

Perspectives
Our results may reconcile some apparently inconsistent results linking insulin resistance with hypertension. Although there is a high correlation between indices of obesity and indexes of insulin sensitivity, the multivariate statistical analysis determined that the documented association between obesity, fasting insulin, insulin sensitivity, and blood pressure was largely explained by variation in WC. Therefore, central obesity assessed by WC may appear to have a predominant role compared with insulin levels in explaining individual differences in blood pressure, at least in a white population. It is plausible that cross-talks exist between visceral adipose tissue, Ang II, and insulin in the overweight/obesity state in human, and this process may contribute to conditions such as development of cardiovascular and dysmetabolic complications. Further studies are needed to document such an association in different ethnic groups.
Acknowledgments
Some of the investigators were supported by a grant from the Canadian Institute of Health Research. P.P. and J.B. are clinical research scholars from the Fonds de la Recherche en Santé du Québec (FRSQ). J.-P.D. is chair professor of human nutrition, lipidology, and prevention of cardiovascular diseases, which is supported in part by Pfizer, Provigo, and by the Foundation of Corporation of the Quebec Heart Institute.

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*Hypertension*. 2005;45:363-367; originally published online January 24, 2005;
doi: 10.1161/01.HYP.0000155463.90018.dc

*Hypertension* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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