Diabetologia (1994) 37: 757–764

**Diabetologia**


# Are gender differences in cardiovascular disease risk factors explained by the level of visceral adipose tissue?

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**Summary** It has been suggested that the lower prevalence of cardiovascular disease in women before menopause in comparison with men may be explained by differences in body fat distribution, plasma lipoprotein levels and indices of plasma glucose-insulin homeostasis. Thus, gender differences in visceral adipose tissue accumulation measured by computed tomography and metabolic variables were studied in 80 men and 69 pre-menopausal women, aged 23–50 years. Despite the fact that women had higher levels of total body fat ($p < 0.0001$), they displayed lower areas of abdominal visceral adipose tissue ($p < 0.06$) and a lower ratio of abdominal visceral to mid-thigh adipose tissue areas than men ($p < 0.0001$). After adjustment for body fat mass, women generally displayed a more favourable risk profile than men which included higher plasma $HDL_2$-cholesterol and lower plasma insulin, apolipoprotein B and triglyceride levels ($p < 0.01$). Metabolic variables adjusted for body fat mass were then compared between genders after control for differences in abdominal visceral adipose tissue area. After such controls, variables related to plasma glucose-insulin homeostasis were no longer significantly different between men and women. Gender differences for plasma concentrations of triglyceride, apolipoprotein B and the ratio of $HDL_2$-cholesterol/$HDL_3$-cholesterol also disappeared, whereas plasma concentrations of HDL-cholesterol, $HDL_2$-cholesterol as well as the ratio of HDL-cholesterol/total cholesterol remained significantly higher in women than in men ($p < 0.01$). These results suggest that abdominal visceral adipose tissue is an important correlate of gender differences in cardiovascular disease risk. However, additional factors are likely to be involved in gender differences in plasma HDL-cholesterol levels. [Diabetologia (1994) 37: 757–764]

**Key words** Visceral fat, sex dimorphism, lipoprotein, glucose metabolism, computed tomography.

It is well established that the prevalence of cardiovascular disease is greater in men than in women [1, 2]. The reason for this difference among genders is not fully understood. Sex hormones are likely to be involved in the relative protection from cardiovascular disease noted in women before menopause [1]. Accordingly, changes in hormones occurring during menopause are associated with an increased risk of cardiovascular disease and after menopause, the prevalence of cardiovascular disease progressively increases to the levels found in men [3].

The regional distribution of body fat is a distinct characteristic of sexual differentiation. Vague [4] was the first to document that men are more susceptible to upper body fat accumulation whereas women generally have a predominant accumulation of fat in the gluteo-femoral region. Since then, many studies have demonstrated that an excessive accumulation of fat in the abdominal region, which is often observed among obese men, was strongly associated with metabolic alterations such as a disturbed plasma lipoprotein profile [5–7], hyperinsulinaemia, insulin resistance and glucose intolerance [8–10]. In contrast, gluteo-femoral adipose tissue accumulation, which generally charac-

Received: 15 December 1993
and in revised form: 1 March 1994

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*Abbreviations:* Chol, Cholesterol; TG, triglycerides; apo, apolipoprotein; NIDDM, non-insulin-dependent diabetes mellitus.

terizes obese women, does not appear to substantially increase cardiovascular disease risk. It has therefore been suggested that, when similar levels of total body fat are present, obese men are more inclined to develop metabolic alterations potentially leading to NIDDM and cardiovascular disease than obese women [11, 12]. In that regard, it has been proposed that gender differences in body fat distribution could explain most of the differences observed in the prevalence of cardiovascular disease between men and women [13–15]. These studies have not, however, considered visceral fat accumulation as they have rather relied on the waist-to-hip or waist-to-thigh circumference ratios as anthropometric indices of adipose tissue distribution.

To our knowledge, no study has investigated the contribution of gender differences in visceral fat accumulation to the sex dimorphism found in cardiovascular disease risk factors. The first aim of the present study was therefore to verify whether gender differences in cardiovascular disease risk factors would remain significant after adjustment for the level of abdominal visceral adipose tissue measured by computed tomography. Another objective of the study was to compare among genders, the relationships of the level of body fat, as well as visceral fat accumulation with cardiovascular disease risk factors, for variables that include plasma lipoprotein concentrations and indices of plasma glucose-insulin homeostasis. These analyses were performed in order to verify whether similar elevations in body fat mass or in the abdominal visceral fat area would be associated with comparable alterations in cardiovascular disease risk factors in men and in premenopausal women.

## Subjects and methods

*Subjects.* Eighty men, aged 30–42 years, and 69 pre-menopausal women, aged 23–50 years, were recruited from the Québec City area by solicitation through the media. Subjects were free from metabolic diseases that would require treatment (diabetes, hypertension, coronary heart disease). However, 11 men and 13 women were diagnosed as having impaired glucose tolerance according to the classification of the National Diabetes Data Group [16]. All participants were subjected to a medical examination and were also asked to sign an informed consent document. This study was approved by the Medical Ethics Committee of Laval University.

*Body composition and anthropometry.* Body density was measured by the hydrostatic weighing technique [17] and the mean of six measurements was used in the calculation of body density. Pulmonary residual volume was measured before immersion in the hydrostatic tank, using the helium dilution method of Meneely and Kaltreider [18]. Total fat mass was derived from body density using the equation of Siri [19]. Height, body weight and waist and hip circumferences were measured following the procedures recommended by the Airlie Conference [20], and the waist-to-hip ratio was calculated.

*Computed tomography.* Computed tomography was performed on a Siemens Somatom DRH scanner (Erlanger, FRG) using the procedure of Sjöström et al. [21] as previously described [22]. Briefly, subjects were examined in the supine position with both arms stretched above their heads. Computed tomography scans were performed at the abdominal (between L4 and L5 vertebrae) and at the femoral (mid-distance between the knee joint and the iliac crest) levels, using a radiograph of the skeleton as a reference to establish the position of the scan to the nearest millimeter. Total adipose tissue areas were calculated by delineating these surfaces with a graph pen and then computing the adipose tissue surfaces using an attenuation range of −190 to −30 Hounsfield units [21, 23]. The visceral adipose tissue area was measured by drawing a line within the muscle wall surrounding the abdominal cavity.

*Metabolic variables.* A 75-g oral glucose tolerance test was performed in the morning after an overnight fast. Blood samples were collected in EDTA and Trasylol containing tubes (Miles Pharmaceuticals, Rexdale, Ontario, Canada) through a venous catheter from an antecubital vein at −15, 0, 15, 30, 45, 60, 90, 120, 150 and 180 min for the determination of plasma glucose and insulin concentrations. Plasma glucose was measured enzymatically [24], whereas plasma insulin was measured by radioimmunoassay with polyethylene glycol separation [25]. The total glucose and insulin areas under the curve during the oral glucose tolerance test were determined with the trapezoid method. Fasting blood samples were also collected from an antecubital vein into vacutainer tubes containing EDTA for the measurement of plasma lipid and lipoprotein levels. Chol and TG levels were determined in plasma and lipoprotein fractions using an autoanalyser [26] as previously described [27]. Plasma VLDL (density < 1.006 g/ml) were isolated by ultracentrifugation [28], and the HDL fraction was obtained after precipitation of LDL in the infranatant (density > 1.006 g/ml) with heparin and $MnCl_2$ [29]. The chol and TG content of the infranatant fraction was measured before and after the precipitation step. Apo B concentration was measured in plasma by the rocket immunoelectrophoretic method of Laurell [30], as previously described [31]. The lyophilized serum standards for apo measurement were prepared in our laboratory and calibrated with reference standards obtained from the Centers for Disease Control, (Atlanta, Ga., USA). The concentrations of LDL-chol were obtained by difference. The cholesterol content of $HDL_2$-chol and $HDL_3$-chol subfractions prepared by a precipitation method [32] was also determined. For all women, measurements were performed while subjects were in the early follicular phase of their menstrual cycle.

The cumulative coefficients of variation for these various lipid and lipoprotein determinations in our laboratory are 2.1% for high cholesterol value, 2.7% for low cholesterol value, 3.3% for HDL-chol, 3.0% for TG and 3.5% for apo B.

### *Statistical analyses*

The unpaired Student's *t*-test was used to compare mean values among men and women. Pearson correlation coefficients were used to quantify the univariate associations among variables. An analysis of covariance was performed in order to compare male and female samples after removing the effect of a given independent variable (adjusted means). Linear regression analyses were performed, and slopes of regression lines were also compared among genders [33]. All these analyses were performed on the SAS statistical package (SAS institute, Cary, N. C. USA).

**Table 1.** Body fat and adipose tissue distribution variables in women and men of the study

| Variable | Women ($n = 69$) (range) | Men ($n = 80$) (range) |
|---|---|---|
| Age (years) | 35.3 ± 4.8 (22.8–49.5) | 36.2 ± 3.3 (29.6–41.8) |
| Body mass index (kg/m$^2$) | 30.2 ± 7.2 (17.5–46.5) | 27.1 ± 3.7[b] (19.4–33.8) |
| Body fat mass (kg) | 33.2 ± 14.6 (8.0–66.8) | 21.8 ± 7.8[c] (6.4–37.3) |
| Percentage of fat | 40.5 ± 10.0 (15.6–58.3) | 25.9 ± 6.4[c] (9.7–37.4) |
| Waist circumference (cm) | 86.8 ± 15.2 (62.0–121.0) | 95.1 ± 15.2[b] (72.1–121.0) |
| Waist-to-hip ratio | 0.79 ± 0.05 (0.64–0.91) | 0.93 ± 0.06[c] (0.78–1.03) |
| *Computed tomography* | | |
| Abdominal visceral adipose tissue area (cm$^2$) | 104.0 ± 54.6 (23.7–234.0) | 120.0 ± 49.4[a] (28.0–253.0) |
| Abdominal visceral: mid-thigh | 0.25 ± 0.09 (0.08–0.54) | 0.61 ± 0.22[c] (0.23–1.23) |

Results are means ± SD. Gender differences: [a] $p < 0.06$; [b] $p < 0.001$; [c] $p < 0.0001$

**Table 2.** Metabolic variables in the study sample of women and men

| Variable | Women ($n = 69$) | Men ($n = 80$) |
|---|---|---|
| *Lipids* | | |
| Cholesterol (mmol/l) | 5.17 ± 0.98 | 5.00 ± 0.82 |
| Triglycerides (mmol/l)[a] | 1.51 ± 1.19 | 1.59 ± 0.84 |
| *Lipoproteins* | | |
| LDL-chol (mmol/l) | 3.49 ± 0.94 | 3.41 ± 0.76 |
| Apo B (g/l) | 0.92 ± 0.30 | 0.92 ± 0.22 |
| LDL-apo B/LDL-chol (× 100) | 23.04 ± 3.86 | 24.79 ± 3.12[b] |
| HDL-chol (mmol/l) | 1.21 ± 0.27 | 1.02 ± 0.22[c] |
| $HDL_2$-chol (mmol/l) | 0.48 ± 0.16 | 0.36 ± 0.15[c] |
| $HDL_3$-chol (mmol/l) | 0.73 ± 0.13 | 0.66 ± 0.13[b] |
| $HDL_2$-chol: $HDL_3$-chol | 0.65 ± 0.16 | 0.55 ± 0.24[b] |
| HDL-chol: total chol | 0.24 ± 0.08 | 0.21 ± 0.06[b] |
| *Fasting glucose (mmol/l)* | 5.0 ± 0.6 | 5.1 ± 0.5 |
| *Fasting insulin (pmol/l)* | 81 ± 52 | 79 ± 30 |
| *Oral glucose tolerance test* | | |
| Glucose area (mmol·l$^{-1}$·min$^{-1}$) × $10^{-3}$ | 1.18 ± 0.22 | 1.18 ± 0.23 |
| Insulin area (pmol·l$^{-1}$·min$^{-1}$) × $10^{-3}$ | 81.51 ± 48.01 | 73.06 ± 35.26 |
| Insulin area: glucose area | 67.45 ± 34.61 | 60.93 ± 23.86 |

Results are means ± SD. [a] Values were log – 10 transformed. Gender differences: [b] $p < 0.01$; [c] $p < 0.0001$

## Results

Table 1 presents physical characteristics of both samples of 80 men and 69 pre-menopausal women. Women had higher body mass index and body fat mass values than men ($p < 0.0001$). Despite the fact that women were fatter than men, they had lower levels of abdominal visceral adipose tissue (bordeline significance, $p < 0.06$) as well as lower waist-to-hip ratios than men ($p < 0.0001$). In addition, a substantial gender difference was noted for the ratio of abdominal visceral to mid-thigh adipose tissue areas ($p < 0.0001$).

Gender differences for metabolic variables are presented in Table 2. All variables related to the HDL fraction were significantly higher in women than in men ($0.0001 < p < 0.01$). In contrast, the ratio of LDL-apo B/LDL-chol was significantly higher in men than in women ($p < 0.01$). Despite the fact that women were fatter than men, no difference could be found for any indices of plasma glucose-insulin homeostasis.

Because body fat mass is a well-known correlate of the metabolic profile, and also considering the very significant gender difference in the levels of body fat mass, a covariance analysis was performed to adjust metabolic variables for gender differences in the levels

**Table 3.** Comparison of metabolic variables between women and men after adjustment for gender differences in body fat mass

| Variable | Women ($n = 69$) | Men ($n = 80$) |
|---|---|---|
| *Lipids* | | |
| Cholesterol (mmol/l) | 5.04 ± 0.92 | 5.11 ± 0.92 |
| Triglycerides (mmol/l)[a] | 1.35 ± 1.00 | 1.73 ± 1.03[d] |
| *Lipoproteins* | | |
| LDL-chol (mmol/l) | 3.36 ± 0.86 | 3.52 ± 0.86 |
| Apo B (g/l) | 0.87 ± 0.26 | 0.96 ± 0.26[b] |
| LDL-apo B/LDL-chol ( × 100) | 22.85 ± 3.70 | 24.95 ± 3.67[c] |
| HDL-chol (mmol/l) | 1.26 ± 0.24 | 0.97 ± 0.23[d] |
| $HDL_2$-chol (mmol/l) | 0.51 ± 0.15 | 0.33 ± 0.15[d] |
| $HDL_2$-chol: $HDL_3$-chol | 0.68 ± 0.21 | 0.53 ± 0.21[d] |
| HDL-chol: total chol | 0.26 ± 0.07 | 0.19 ± 0.07[d] |
| *Fasting glucose (mmol/l)* | 4.85 ± 0.47 | 5.28 ± 0.46[d] |
| *Fasting insulin (pmol/l)* | 65.86 ± 33.85 | 91.60 ± 33.57[d] |
| *Oral glucose tolerance test* | | |
| Glucose area ($mmol \cdot l^{-1} \cdot min^{-1}) \times 10^{-3}$ | 1131.01 ± 220.17 | 1219.22 ± 218.36[b] |
| Insulin area ($pmol \cdot l^{-1} \cdot min^{-1}) \times 10^{-3}$ | 68.97 ± 36.83 | 83.87 ± 36.53[b] |
| Insulin area: glucose area | 59.70 ± 27.28 | 67.61 ± 27.05 |

Results are means ± SD. [a] Values were log – 10 transformed. Gender differences: [b] $p < 0.05$; [c] $p < 0.01$; [d] $p < 0.001$

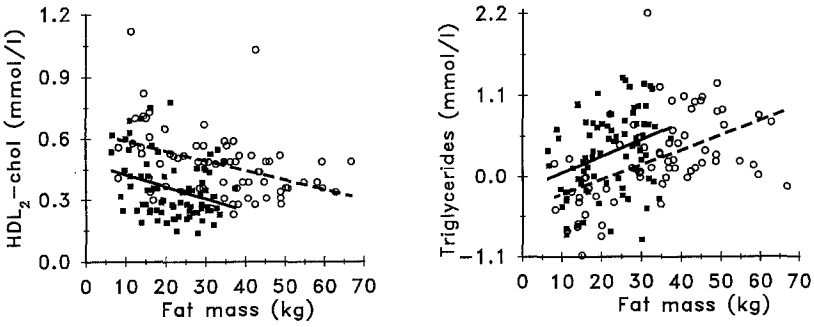
**Table 4.** Comparison of metabolic variables between women and men after adjustment for gender differences in body fat mass and abdominal visceral adipose tissue

| Variable | Women ($n = 69$) | Men ($n = 80$) |
|---|---|---|
| *Lipids* | | |
| Cholesterol (mmol/l) | 5.13 ± 1.06 | 5.03 ± 1.04 |
| Triglycerides (mmol/l)[a] | 1.53 ± 1.17 | 1.57 ± 1.15 |
| *Lipoproteins* | | |
| LDL-chol (mmol/l) | 3.42 ± 1.00 | 3.46 ± 0.97 |
| Apo B (g/l) | 0.91 ± 0.30 | 0.93 ± 0.29 |
| LDL-apo B/LDL-chol ( × 100) | 23.41 ± 4.22 | 24.48 ± 4.11 |
| HDL-chol (mmol/l) | 1.22 ± 0.27 | 1.01 ± 0.26[c] |
| $HDL_2$-chol (mmol/l) | 0.48 ± 0.17 | 0.36 ± 0.17[c] |
| $HDL_2$-chol: $HDL_3$-chol | 0.63 ± 0.24 | 0.57 ± 0.24 |
| HDL-chol: total chol | 0.25 ± 0.08 | 0.20 ± 0.07[b] |
| *Fasting glucose (mmol/l)* | 4.92 ± 0.53 | 5.23 ± 0.52[b] |
| *Fasting insulin (pmol/l)* | 72.91 ± 37.99 | 85.52 ± 37.10 |
| *Oral glucose tolerance test* | | |
| Glucose area ($mmol \cdot l^{-1} \cdot min^{-1}) \times 10^{-3}$ | 1193.86 ± 239.90 | 1165.01 ± 234.24 |
| Insulin area ($pmol \cdot l^{-1} \cdot min^{-1}) \times 10^{-3}$ | 80.95 ± 39.35 | 73.54 ± 38.42 |
| Insulin area: glucose area | 65.91 ± 30.41 | 62.25 ± 29.70 |

Values are mean ± SD. [a] Values were log – 10 transformed. Gender differences: [b] $p < 0.01$; [c] $p < 0.001$

of body fat mass. As shown in Table 3, after adjustment for gender differences in body fat mass, plasma concentrations of TG ($p < 0.001$) and apo B ($p < 0.05$) as well as the ratio of LDL-apo B/LDL-chol ($p < 0.01$) were significantly higher in men than in women. Conversely, plasma concentrations of HDL-chol, $HDL_2$-chol as well as the ratios of $HDL_2$-chol/$HDL_3$-chol and of HDL-chol/total chol ($p < 0.0001$) were all significantly lower in men than in women. No gender differences were seen for plasma concentrations of LDL-chol. Fasting values for plasma glucose and insulin concentrations ($p < 0.0001$) as well as plasma glucose ($p < 0.01$) and insulin ($p < 0.05$) areas following glucose load were significantly higher in men than in women after adjustment for body fat mass.

In order to determine whether gender differences in abdominal visceral adipose tissue areas could account for the sex dimorphism observed in metabolic variables, we performed further covariance analysis. Means of metabolic variables were compared between men and women, after adjustment for both body fat mass and abdominal visceral adipose tissue area (Table 4). Mean plasma concentrations of TG, apo B as well as $HDL_2$-chol/$HDL_3$-chol and LDL-apo B/LDL-chol ratios became identical in men and women with this adjustment. However, women still displayed higher plasma concentrations of HDL-chol ($p < 0.0001$) and



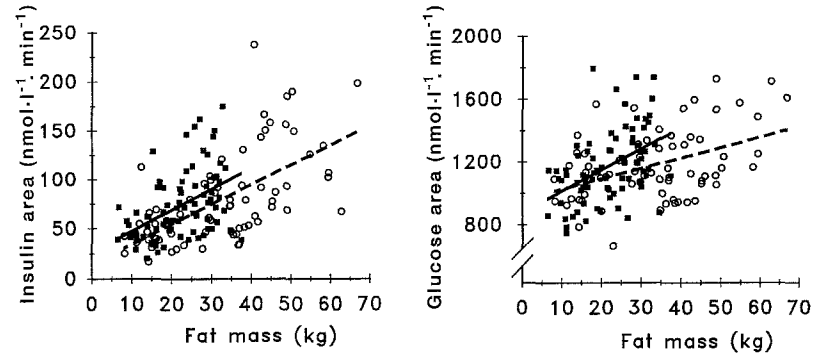
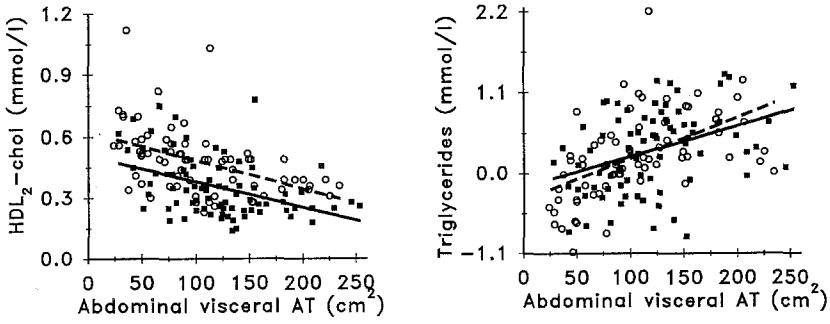




**Fig. 1.** Relationships between body fat mass and plasma $HDL_2$-cholesterol concentration, plasma triglyceride levels, plasma insulin and plasma glucose areas under the curve measured during the oral glucose tolerance test in 69 pre-menopausal women (O---O) and 80 men (■—■). Triglyceride values were log transformed. Correlation coefficients reached $r = -0.42$ and $r = -0.32$ in men and women, respectively for $HDL_2$-cholesterol, $r = 0.51$ (men) and $r = 0.32$ (women) for triglycerides, $r = 0.61$ (men) and $r = 0.47$ (women) for insulin area, $r = 0.43$ (men) and $r = 0.46$ (women) for glucose area. Regression slope for men for the relationship between body fat mass and plasma glucose area was significantly steeper ($\beta = 13.47$) than that of the women ($\beta = 6.64$) ($p < 0.05$)



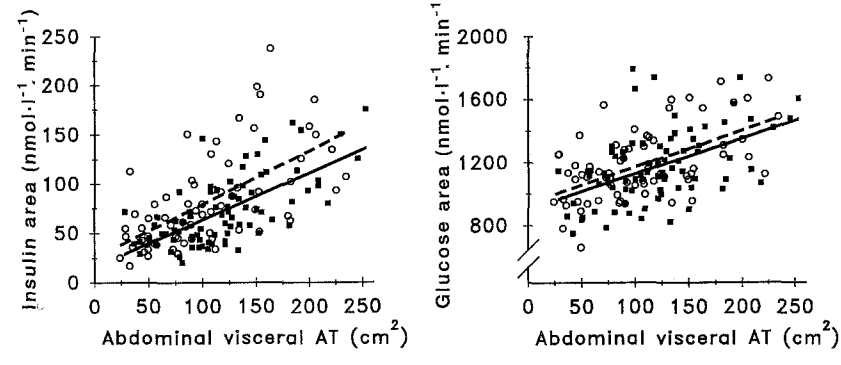




**Fig. 2.** Relationships between the level of abdominal visceral adipose tissue measured by computed tomography and plasma $HDL_2$-cholesterol concentration, plasma triglyceride levels, plasma insulin and plasma glucose areas under the curve measured during the oral glucose tolerance test in samples of 69 pre-menopausal women (O---O) and 80 men (■—■). Triglyceride values were log transformed. Correlation coefficients reached $r = -0.47$ and $r = -0.43$ in men and women respectively for $HDL_2$-cholesterol, $r = 0.53$ (men) and $r = 0.37$ (women) for triglycerides, $r = 0.62$ (men) and $r = 0.67$ (women) for insulin area, $r = 0.56$ (men) and $r = 0.48$ (women) for glucose area. AT, adipose tissue

$HDL_2$-chol ($p < 0.0001$) as well as a higher ratio of HDL-chol/total chol compared to men ($p < 0.01$). In addition, plasma glucose-insulin variables were no longer significantly different between men and women, with the exception of fasting glucose concentration which was still significantly higher in men than in women ($p < 0.01$) after adjustment for both total fat mass and abdominal visceral adipose tissue area.

Finally, we were interested in the potential gender differences in the relationships between body fat mass or abdominal visceral adipose tissue area and selected metabolic variables. Our selection of metabolic variables for these additional analyses was based on the magnitude of their correlations with body fat mass or abdominal visceral adipose tissue area. We also attempted to choose metabolic variables which could

produce relevant information on the risk of cardiovascular disease and NIDDM. No difference in regression slopes was noted when plasma $HDL_2$-chol concentrations, plasma TG concentrations or plasma insulin area following the glucose load were plotted against body fat mass (Fig. 1). However, the regression slope for plasma glucose area was significantly steeper in men than in women ($p < 0.05$).

Figure 2 shows the relationships with abdominal visceral adipose tissue area. No difference in regression slopes was seen for either plasma $HDL_2$-chol concentrations, plasma TG concentrations or plasma insulin area. In contrast to the relationship with body fat mass, the regression slopes for the relationship between plasma glucose area and abdominal visceral adipose tissue area were not different among genders.

## Discussion

Many studies have demonstrated that men and women generally display marked differences in regional fat distribution [4, 34, 35], lipoprotein profile [37] and indices of plasma glucose-insulin homeostasis [12, 38, 39]. Our results agree with these previous reports, as our sample of men had higher levels of abdominal adipose tissue, lower plasma HDL-chol concentrations, higher plasma TG levels, and higher plasma insulin and glucose areas measured during the oral glucose tolerance test in comparison with women, after adjustment for differences in body fat mass.

Body fat mass was the first covariable selected as it was markedly different between men and women. As body fat mass was associated with most of the metabolic variables examined in the present study, adjustment for body fat mass appeared relevant to control for its potential confounding effect. After adjustment for body fat mass, most of the metabolic variables studied remained significantly different among genders. Indeed, men still showed lower HDL-chol values, higher TG, higher ratio of LDL-apo B/LDL-chol as well as higher values of indices of plasma glucose-insulin homeostasis. High TG levels as well as low HDL-chol levels have been identified as significant risk factors for cardiovascular disease in numerous studies [40–43]. Furthermore, our results suggest that for a similar amount of body fat, men had smaller and denser LDL particles than pre-menopausal women (higher ratio of LDL-apo B/LDL-chol) as an elevated LDL-apo B concentration in the presence of "normal" LDL-chol levels suggests the presence of an increased plasma concentration of cholesterol ester-depleted and dense LDL particles [44], which have been found to be associated with increased cardiovascular disease risk [45, 46]. In addition, hyperinsulinaemia has been shown to be associated with an increased cardiovascular disease risk [47–49]. Thus, these results suggest that when men and pre-menopausal women with similar levels of total body fat are compared, women exhibit a more advantageous cardiovascular disease and NIDDM risk profile.

One of the main objectives of the present study was to determine whether gender differences in body fat distribution could account for metabolic differences observed between men and women. Freedman et al. [13] have recently reported that differences in lipid and lipoprotein levels between men and women were reduced to a large extent after adjustment for the waist-to-hip ratio. Larsson and co-workers [14] have also shown that, after controlling for the waist-to-hip ratio, the gender difference in the incidence of coronary heart disease almost disappeared. Since abdominal visceral adipose tissue has been shown to be an important correlate of the metabolic disturbances associated with an altered distribution of body fat [5–10], one of our objectives was to determine whether gender differences in cardiovascular disease risk would be eliminated by controlling for level of abdominal visceral fat assessed by computed tomography after having taken fat mass into account. In the present study, most gender differences in metabolic variables investigated disappeared after adjustment for abdominal visceral fat. Thus, abdominal visceral adipose tissue accumulation appeared to be an important correlate of the sex dimorphism found for cardiovascular disease and NIDDM risk factors. However, adjustment for the amount of total body fat and abdominal visceral adipose tissue area was not sufficient to eliminate the significant gender differences in plasma HDL-chol and $HDL_2$-chol concentrations, the ratio of HDL-chol/total chol as well as for fasting plasma glucose concentration. Thus, for similar amounts of body fat mass and abdominal visceral adipose tissue, women still displayed higher HDL-chol concentrations than men. Sex hormones have been shown to be linked to both visceral adipose tissue accumulation [36] and plasma HDL-chol concentrations [37]. Our results are concordant with these previous observations as men of the present study displayed significantly higher levels of abdominal visceral adipose tissue and lower plasma HDL-chol concentrations than pre-menopausal women. Thus, it is possible that the complex relationships between sex hormones, visceral adipose tissue and plasma HDL-chol are not similar in men vs pre-menopausal women. This could explain, at least partially, why pre-menopausal women display higher HDL-chol levels, even after adjustment for the levels of abdominal visceral adipose tissue. Finally, the results of the present study indicate that a statistical control for visceral fat eliminated most gender differences in the risk profile. It should be kept in mind however that these results cannot be considered as evidence that visceral fat is causally related to metabolic complications.

Another important aspect of the present study was to compare, between men and women, the regression lines of body fat mass as well as abdominal adipose tissue area with selected metabolic variables. No difference in regression slopes was found when $HDL_2$-

chol, TG or plasma insulin area were plotted against body fat mass or abdominal visceral adipose tissue area. However, adjustment for visceral fat was particularly efficient for the glycaemic response to the oral glucose challenge (glucose area). Indeed, when plasma glucose area was plotted against body fat mass, the regression slope for men was significantly steeper than that for women. These results suggest that excess fatness seems to be associated with a greater deterioration of glucose tolerance in men than in women. This sex dimorphism is unlikely to be explained by differences in plasma insulin concentrations during the oral glucose tolerance test as the regression lines between plasma insulin area and body fat mass were similar in both men and women. Our observations suggest that with increased body fat mass, insulin action seems to be more rapidly impaired in men than in women. When the relationship between abdominal visceral adipose tissue area and plasma glucose area was studied, gender differences in regression slopes disappeared i.e. a given abdominal visceral fat deposition was accompanied by a similar glycaemic response in both men and women, irrespective of total fatness. Our results thus suggest that pre-menopausal women must accumulate more body fat mass than men before showing a deterioration in glucose tolerance comparable to men. However, an increasing abdominal visceral adipose tissue mass seems to be associated with similar deterioration in plasma glucose areas in both genders. These results are not surprising since we have previously shown that for a given fat mass value, men have about twice the amount of visceral fat than what can be measured in pre-menopausal women [50]. Thus, our results agree with the notion that increased total adiposity is associated with greater health hazards in men than in pre-menopausal women [11, 12]. However, prospective studies are clearly warranted on this issue.

In summary, our results confirm that there are marked gender differences in the metabolic profile when men and pre-menopausal women of similar body fatness are compared. However, after controlling for both total body fat and abdominal visceral fat, most of the gender differences in the risk profile disappear with the exception of plasma HDL-chol levels which remained significantly lower and fasting plasma glucose concentration which remained significantly higher in men than in women. A given body fat mass was associated with a higher glycaemic response in men than in women. These gender differences were not found when the plasma glucose area was plotted against the abdominal visceral adipose tissue area. Thus, these results suggest that abdominal visceral adipose tissue is an important correlate of the gender differences in risk factors for cardiovascular disease and NIDDM. At this stage, it would be useful to undertake prospective studies to better delineate the relationships between total body fat content and fat topography with the cardiovascular and NIDDM risk factors and to define the nature of the gender differences in these relationships if any.

*Acknowledgements.* The authors would like to express their gratitude to the subjects for their excellent collaboration and to the staff of the Lipid Research Center, the Diabetes Research Unit and the Physical Activity Sciences Laboratory for their contribution to this study. We particularly want to thank Ms. J. Maheux, J. Hovington, M.-F. Verdon, S. Brulotte, M. Marcotte and Mr. H. Bessette and C. Leblanc for their help in the collection and analysis of the data. The dedicated work of Ms. Y. Montreuil, M. Martin and R. Duchesne is also acknowledged. Supported by the Québec Heart and Stroke Foundation, the Canadian Diabetes Association, the Medical Research Council of Canada and by the Fonds de la recherche en santé du Québec. S. Lemieux is a Medical Research Council fellow.

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