Relationship of serum leptin to total and truncal body fat

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1. In this study we investigated the relationship between serum leptin levels and body fat distribution in a random sample of women of widely ranging age and body mass index. Anthropometry and dual energy X-ray absorptiometry were used to measure body fat and its distribution.

2. Leptin levels (log transformed) were not significantly correlated with age, but were significantly positively correlated (P < 0.001) with most anthropometric measures except waist-to-hip circumference ratio. The strongest correlations were with total grams of body fat and percentage body fat (r = 0.68 and 0.76 respectively, P < 0.001). When corrected for percentage body fat the partial correlation coefficients for all other measures became non-significant. The correlation with truncal body fat fell significantly from 0.66 to −0.05 after correction, but the partial correlation with total body fat remained significant (P < 0.005) when grams of truncal fat were controlled for (r = 0.21).

3. These results indicate that the relationship of serum leptin to percentage body fat is the strongest, and that truncal body fat, although the most metabolically active, does not appear to have an independent association with serum leptin.

INTRODUCTION

Leptin, the soluble 16 kDa protein product of the adipose specific obese (ob) gene, is considered to be an important regulator of food intake and energy expenditure [1]. In the ob/ob mouse, mutations in the ob gene resulting in leptin deficiency are the cause of obesity [2]. However, studies in humans have found that peripheral blood leptin concentration is higher in obese than lean individuals and that women have higher levels than men [3–5]. Weight loss has been reported to reduce serum leptin levels [6].

A strong correlation between serum leptin and body mass index (BMI) has been found in several studies but the absolute level for a given body weight has been noted to be quite variable [3, 5–7]. A possible explanation for this could be a different relationship between leptin and body fat in different sites; either because of different rates of production or differences in metabolism related to size of the body compartment. The levels of a 4.5 kb mRNA product of the ob gene, found in abundance in human adipose tissue in subcutaneous, omental, peri-lymphatic, and other sites, varied from region to region even in the same individual [7].

Body fat content in people with a high BMI varies considerably, as lean body tissue, water and fat all contribute to BMI. The distribution of body fat is also variable, being strongly dependent on gender and age. In premenopausal women adipose tissue is most often distributed on the hips and thighs and is known as ‘gynoid’ fat distribution [8]. In postmenopausal women, adipose tissue deposition shifts from the lower body to the trunk (abdominal) region of the body. This is referred to as truncal obesity and is associated with a higher incidence of diabetes, hyperlipidaemia, hypertension and coronary heart disease [8–10].

Indirect measures of obesity, such as waist-to-hip circumference ratio (WHR) and BMI, are commonly used to assess fat distribution. An increase in BMI is usually associated with an increase in the WHR, and in women BMI is an independent risk factor for cardiovascular disease. However, an elevated WHR is a stronger predictor for cardiovascular disease than BMI [10]. BMI measures are a crude index of obesity and do not distinguish between fat and fat-free mass [11]. WHR is an acceptable index of intra-abdominal fat but does not quantify the regional fat or measure fat and fat-free mass.

DEXA is a relatively safe, convenient, accurate and precise method of analysing total body fat and the distribution pattern. DEXA can be used to
measure specific sites, such as trunk or legs, and to determine the percentage of fat and fat-free mass. This direct method of analysis is more reliable than using anthropometry to calculate the percentage of body fat [8, 12]. In this study we have investigated the relationship between serum leptin levels and body fat distribution in a random sample of women with a wide range of age and BMI.

SUBJECTS AND METHODS

We studied 183 women, between 20 and 80 years of age, predominantly Caucasian, with a BMI between 17 and 42 kg/m², who were drawn from a random population-based study of bone density in the Barwon Statistical Division, Victoria, Australia, known as the Geelong Osteoporosis Study. The study was conducted in accordance with the Declaration of Helsinki (1989), with approval of the Ethics Committee of Geelong Hospital and written consent from participants. Weight and height measures were obtained and BMI (weight/height²) calculated. Waist and hip circumference measurements were taken using a non-extensive flexible tape at the minimum circumference of the abdomen and the maximum extension of the buttocks, respectively, and the WHR calculated.

Body fat content and fat-free mass were determined from a total body scan using DEXA (DPX; Lunar Radiation Corp., Madison, WI, U.S.A.) and truncal fat was estimated using the method of Ley et al. [8]. From the total body scans measures of lean tissue and fat tissue were generated by the default measures of the software. Sections of the body were isolated with oblique lines through the hip joints, through the shoulder joints, and under the chin. This produced distinct regions of lower body (area below the hip joint), upper body or trunk (area above the hip joint, but not including arms or head), the arms, and the head region. Subjects were not included in the study if total body scans were not complete, as was the case in a number of obese subjects who were larger than the scanning bed could accommodate.

Venous blood specimens were collected after an overnight fast and separated by centrifugation. Serum leptin concentrations were measured by radioimmunoassay (Linco Research, MO, U.S.A.). The limit of sensitivity for the leptin radioimmunoassay is 0.5 ng/ml. The inter-assay coefficient of variation ranged from 4.1 to 8.2% and the intra-assay coefficient of variation is 5%.

Statistical analysis was performed using SPSS 6.1. Non-normally distributed parameters, including leptin concentrations, were log₁₀ transformed before analysis. A Pearson–product moment correlation matrix was established. Partial correlation was used to assess the relationship between serum leptin concentrations (log) and individual anthropometric and DEXA measurements, controlling for the contribution of other measured variables.

RESULTS

The DEXA scans of 183 women were analysed for total body fat and truncal body fat. The ranges were 6–55 kg and 2–33 kg, respectively. Median (range) serum leptin was 20.3 (1.8–73.0) ng/ml. Leptin levels (log transformed) were not significantly correlated with age, but were significantly positively correlated (P < 0.001) with most anthropometric measures except WHR (Table 1). However, when corrected for the influence of total grams of fat from DEXA analysis the partial correlation coefficients became non-significant and, generally, slightly negative for most parameters. Correlation of serum leptin was strongest with percentage body fat (r = 0.76), and remained strong (r = 0.46) even when corrected for total grams of fat. After correction for the percentage body fat there were no statistically significant partial correlations of anthropometric or body composition measures. The correlation with truncal body fat fell significantly from 0.66 after correction for grams of total fat or percentage body fat,

<table>
<thead>
<tr>
<th>Table 1. Correlation coefficients for the association of age, anthropometric and DEXA measures with serum leptin (log).</th>
<th>Bivariate correlation</th>
<th>Partial correlation corrected for total grams of fat</th>
<th>Partial correlation corrected for % body fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.11</td>
<td>0.17</td>
<td>0.02</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>0.59**</td>
<td>-0.32**</td>
<td>-0.06</td>
</tr>
<tr>
<td>BMI</td>
<td>0.62**</td>
<td>-0.002</td>
<td>-0.08</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>0.55**</td>
<td>-0.02</td>
<td>-0.05</td>
</tr>
<tr>
<td>WHR</td>
<td>0.22</td>
<td>-0.03</td>
<td>-0.07</td>
</tr>
<tr>
<td>Total fat (g)</td>
<td>0.68**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trunk fat (g)</td>
<td>0.66**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Truncal/total fat</td>
<td>0.28**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral fat (g)</td>
<td>0.63**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat-free mass (g)</td>
<td>0.29**</td>
<td>-0.29**</td>
<td>0.46**</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>0.76**</td>
<td></td>
<td></td>
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</tbody>
</table>
whereas the partial correlation of leptin with total body fat remained significant \( r = 0.21, P < 0.005 \) when the grams of truncal fat were controlled for.

Figure 1 shows the relationship between leptin and total body fat \( (r^2 = 0.56) \), with the best fit regression being a quadratic equation. Figure 2 shows the relationship between plasma leptin and percentage body fat, unadjusted and adjusted for age, BMI, total body fat and truncal body fat. In Fig. 2 it can be seen that adjustment for these factors made little difference to the values. The confidence interval was greatest at the highest range, but the number of measures was also smallest \((n = 22)\) in this group.

**DISCUSSION**

In this study we have described a significant relationship between serum leptin levels and most anthropometric and DEXA measures in a large group of women across a wide range of age, BMI and percentage body fat. The most significant correlation was seen between serum leptin (log transformed) and total grams of body fat and percentage body fat. The results indicate that percentage body fat, irrespective of site, is the most important correlate.

Recently Dua et al. \[13\] conducted a similar investigation of the correlation between plasma leptin levels with total body and visceral fat in a small group of healthy premenopausal African-American women aged 20–45 years. They also found that leptin levels strongly correlated \( (r = 0.797, P < 0.001) \) with total body fat mass as measured by DEXA, but not with visceral fat measured by computerized axial tomography when total body fat was accounted for.

Haffner et al. \[14\] examined the relationship of serum leptin levels to body fat distribution in 147 Mexican Americans from the San Antonio Heart Study. They concluded that leptin concentrations are highly correlated with total adipose tissue deposits, as determined by BMI or sum of skinfolds, in both men and women, but not with regional distribution of fat. After adjusting for adiposity, the gender difference in leptin levels was reduced but leptin continued to be significantly higher in women \[14\]. In contrast, Considine et al. \[15\] found no differences in leptin levels between men and women when compared for equivalent percentages of body fat.

Our results support the theory that serum leptin concentrations reflect the total amount of adipose tissue in the body, rather than just truncal or visceral fat, despite the fact that the latter is generally considered to be the most metabolically active component. This may partly explain why women, who tend to have a greater percentage body fat for a given BMI, have higher leptin levels compared with men \[3\].

The relationship between total body fat and leptin levels appears weakest at extreme values of body fat content, particularly at the higher levels with body fat of over 35 kg, which may be consistent with a different relationship in the morbidly obese, but the scatter of points at the extremes make the relationship difficult to delineate clearly. At the other
extreme, during prolonged undernutrition leading to a reduction in body mass, leptin concentrations fall and may contribute to neuroendocrine abnormalities, such as reduced fertility [16,17].

In summary, in predominantly Caucasian women with a wide range of body fat distribution serum leptin concentrations appear to reflect the total amount of adipose tissue in the body with the strongest relationship being to the percentage body fat. Truncal obesity does not appear to independently affect serum leptin levels.

REFERENCES