The relationship between visceral adiposity and cognitive performance in older adults

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Abstract

Background: a direct association between visceral adiposity on abdominal computed tomography (CT) and cognitive performance has not been reported.

Objectives: to investigate the associations between total and regional adiposity measured with abdominal CT, and cognitive performance in elderly persons and to explore their modification by age.

Design: cross-sectional study.
Setting: a health promotion centre of a tertiary university hospital.
Subjects: two-hundred and fifty individuals aged 60 years and above who underwent anthropometric measurements, abdominal CT and cognitive testing.

Methods: adiposity measures included body mass index (BMI), waist circumference and visceral and subcutaneous adiposity by abdominal CT. Poor cognitive performance was defined as Mini-Mental State Examination score being at or below 1 SD of age, sex and education-normative values.

Results: in multivariate logistic regression analyses obesity [odds ratio (OR) 2.61, 95% confidence interval (CI) = 1.21–6.01, P = 0.015] and being in the top tertile of the visceral adiposity area (OR: 2.58, 95% CI = 1.001–6.62, P = 0.045) were associated with poor cognitive performance in subjects younger than 70 years, but not in those 70 years and older.

Conclusion: high adiposity, particularly visceral adiposity, was associated with poor cognitive functioning in younger elderly persons.

Keywords: cognition, intra-abdominal fat, body mass index, obesity, visceral, elderly

Introduction

Studies of high body mass index (BMI) as a risk factor for dementia or cognitive decline have shown conflicting results [1–5]. Nevertheless, the studies with statistically significant results had larger sample sizes, longer follow-up periods and younger participants at baseline [3–5]. High BMI in middle age may be associated with a higher risk for dementia [4, 5]. The association between high BMI and dementia risk also decrease in older age [3]. Weight loss seems to occur during the preclinical stage of dementia, and recent follow-up studies have suggested that low BMI could actually be an early sign of dementia [6].

Another commonly used surrogate measure of adiposity is waist circumference that measures the accumulation of adipose tissue in the abdomen. A large waist circumference also predicts obesity-related health risk [7], and some studies have shown that it is a better predictor of adverse cardiovascular outcomes compared with BMI [7, 8]. Central obesity in midlife increases risk of dementia independently of BMI, diabetes and cardiovascular co-morbidities [9]. A small waist circumference may also represent a potentially useful preclinical marker of amnestic mild cognitive impairment (MCI) and Alzheimer's disease (AD) [10].

Abdominal adiposity can be measured directly and separated into visceral and subcutaneous adipose tissue by computed tomography (CT). Visceral adipose tissue is more metabolically active than subcutaneous adipose tissue and is thought to have a stronger influence on adipocytokine production and insulin resistance [11]. However, a recent study has shown that worsening cognitive function was not associated with visceral adipose tissue, but with subcutaneous...
adipose tissue measured with abdominal CT [12]. This study was not able to evaluate the relationship between abdominal adiposity on the CT and cognitive change in persons aged less than 70 years because the study participants were above 70 years of age [12].

We hypothesised that higher adiposity is related to lower cognitive function, that this relation is attenuated by age and that visceral adipose tissue is more strongly associated with lower cognitive function than subcutaneous adipose tissue. To test these hypotheses, we examined the cross-sectional associations between BMI, waist circumference, visceral and subcutaneous adipose tissue areas measured with abdominal CT scans and cognitive performance in older adults and explored their modification by age.

Methods

Subjects

Subjects were those who participated in a health screening programme at the health promotion centre of the Seoul National University Hospital Healthcare System Gangnam Center from October 2004 to February 2009, were at least 60 years old, underwent abdominal CT scans for a screening of the digestive system and were administered the Korean Version of the Mini-Mental State Examination for Dementia (MMSE-KC) [13]. Subjects with a history of cerebrovascular accidents, major depressive disorders or psychoses were excluded.

Cognitive performance

In this study, poor cognitive performance was defined as the MMSE-KC total score being at or below 1 standard deviation (SD) of the age, sex and education-normative values of the Korean population [13].

Anthropometric measurements of adiposity

Subjects’ weight and height were measured while they were wearing light clothing. BMI was calculated as weight (kg) divided by the square of height (m^2). Obesity was defined as BMI ≥25 kg/m^2 according to the modified WHO criteria from the Asia-Pacific guidelines [14]. The measurements of waist circumference were made at the WHO recommended site, which is the midpoint between the lower border of the rib cage and iliac crest [15].

Confounding risk factors

All subjects underwent physical examinations by trained personnel who used a written systematic protocol with standardised instruments. After a rest of at least 10 min, blood pressure was measured on the right upper arm with an automated sphygmomanometer. The levels of fasting glucose, total cholesterol, triglyceride and high-density lipoprotein cholesterol (HDL-C) were measured using 12-h fasting blood samples. Structured questionnaires were administered to collect information on the confounding variables related to cognitive impairment including current smoking (smoked regularly during the previous 12 months) and current drinking (≥140 g/week or ≥20 g/day).

Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or use of antihypertensive medication based on the WHO guidelines for the management of hypertension [16]. Diabetes was defined based on current treatment with insulin or oral hypoglycaemic medication or 8-h fasting plasma glucose ≥126 mg/dl as recommended by the American Diabetes Association [17].

Measurement of abdominal adipose tissue areas by computed tomography scan

The technique used for the adipose tissue area measurements in CT cross-sectional images has been previously reported [18] and has negligible inter-observer variation [19].

The study protocol was reviewed and approved by the institutional review board in Seoul National University Hospital.

Statistical analysis

The continuous variables measured in this study were expressed as means and their SDs. Continuous variables were analysed with Student’s t-test, and the categorical variables were analysed with the Chi-square test or Fisher’s exact test between group comparisons. Logistic regression analysis was used to assess the influence of explanatory variables on cognitive performance. Using a dichotomous approach, the reference group comprised the subjects with the MMSE-KC score above 1 SD of the age, sex and education-normative values of the Korean population.

Given the lack of data regarding normative values for the healthy abdominal adipose tissue area and any gender differences in the abdominal fat composition, the visceral and subcutaneous adipose tissue areas on the CT were categorised into sex-specific tertiles within subjects younger than 70 years and those 70 years and older separately. Odds ratios (ORs) were calculated by using the sex-specific lowest tertiles of the visceral and subcutaneous adipose tissue area as the reference groups. We analysed the associations between BMI, waist circumference, abdominal visceral and subcutaneous adipose tissue area, (respectively) and poor cognitive performance with logistic regression models adjusted for age, gender, education level, diabetes (younger group only) and hypertension (younger group only). A two-tailed P-value of <0.05 was considered statistically significant. We analysed with inclusion of ‘interaction term’ to provide a formal test for an interaction of age and anthropometric measures in predicting cognitive performance. All statistical analyses were performed by using the SPSS 12.0 program (SPSS, Inc., Chicago, IL, USA).
Results

We have divided the total population into younger and older age groups using a 70-year-old cut-off point, and anthropometric and adipose tissue characteristics of the subjects are presented in Table 1. Prevalence of diabetes was statistically significantly higher in the older person than in the younger. In addition, the older group had statistically significantly more visceral adipose tissue (VAT) and waist circumference than did the younger group.

Baseline demographic and clinical characteristics of the subjects are classified according to BMI category (<25 versus ≥25 kg/m²) in subjects younger than 70 years and in those 70 years and older (Supplementary data are available in Age and Ageing online, Table S1). Because few subjects (n = 3) had low body weight (BMI <18.5 kg/m²), subjects with very low relative weights were combined with non-obese subjects. Among subjects younger than 70 years, the obese subjects were older, were more likely to be male, have higher prevalence of poor cognitive performance and have higher hypertension prevalence compared with the non-obese subjects. In subjects 70 years and older, the obese subjects had a higher proportion of men and had higher levels of triglyceride and HDL-C compared with the non-obese subjects.

The univariate and multivariate analyses of the risk for poor cognitive performance with variables including BMI, waist circumference and visceral and subcutaneous adipose tissue areas in subjects younger than 70 years are shown in Table 2. In a univariate analysis, high BMI was associated with the risk of poor cognitive performance in the younger group [OR: 2.44, 95% confidence interval (CI) = 1.19–5.01, P = 0.013]. The top tertile of the visceral adipose tissue area (>149.0 cm² in men and >123.7 cm² in women) showed a tendency to be associated with poor cognitive performance compared with the bottom tertile (<110.0 cm² in men and <91.0 cm² in women) (OR: 2.26, 95% CI = 0.93–5.52, P = 0.070). Increasing waist circumference did not show a tendency of increasing risk of poor cognitive performance (OR: 1.13, 95% CI = 0.55–2.35, P = 0.742). Tertiles of the subcutaneous adipose tissue area were not related to poor cognitive performance. Multivariate logistic regression analyses were used to determine the independent relationship between each variable and cognitive performance after controlling for age, sex, education, hypertension and diabetes (Table 2). In the multivariate analysis, high BMI (OR: 2.61, 95% CI = 1.21–5.66, P = 0.015) and the top tertile of the visceral adipose tissue area (OR: 2.58, 95% CI = 1.001–6.62, P = 0.045) were significantly associated with poor cognitive performance.

In subjects 70 years and older, high BMI, waist circumference and visceral and subcutaneous adipose tissue area tertiles were not associated with poor cognitive

Table 1. Clinical characteristics of the study population according to age group

<table>
<thead>
<tr>
<th></th>
<th>Persons &lt;70 years (n = 188)</th>
<th>Persons ≥70 years (n = 62)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (years)</td>
<td>64.2 ± 2.7</td>
<td>73.2 ± 2.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male, %</td>
<td>42.6</td>
<td>56.5</td>
<td>0.077</td>
</tr>
<tr>
<td>Education, years</td>
<td>13.5 ± 3.5</td>
<td>13.7 ± 3.2</td>
<td>0.773</td>
</tr>
<tr>
<td>TAT (cm²)</td>
<td>286.6 ± 83.1</td>
<td>297.8 ± 106.9</td>
<td>0.460</td>
</tr>
<tr>
<td>VAT (cm²)</td>
<td>121.7 ± 46.3</td>
<td>139.8 ± 63.7</td>
<td>0.042</td>
</tr>
<tr>
<td>SAT (cm²)</td>
<td>164.9 ± 61.1</td>
<td>158.0 ± 66.5</td>
<td>0.453</td>
</tr>
<tr>
<td>BMI (cm²)</td>
<td>23.8 ± 2.45</td>
<td>24.10 ± 3.10</td>
<td>0.467</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>87.18 ± 6.75</td>
<td>89.83 ± 9.06</td>
<td>0.037</td>
</tr>
<tr>
<td>Total cholesterol, mg/dl</td>
<td>191.1 ± 35.5</td>
<td>185.2 ± 32.0</td>
<td>0.253</td>
</tr>
<tr>
<td>Triglyceride, mg/dl</td>
<td>108.2 ± 51.6</td>
<td>107.3 ± 51.2</td>
<td>0.911</td>
</tr>
<tr>
<td>HDL-C, mg/dl</td>
<td>54.4 ± 13.9</td>
<td>55.6 ± 13.8</td>
<td>0.566</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>50.5</td>
<td>53.2</td>
<td>0.770</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>11.7</td>
<td>32.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>8.5</td>
<td>6.5</td>
<td>0.789</td>
</tr>
<tr>
<td>Current drinker, %</td>
<td>12.8</td>
<td>9.7</td>
<td>0.654</td>
</tr>
<tr>
<td>Poor cognitive</td>
<td>21.3 (40)</td>
<td>37.1 (23)</td>
<td>0.018</td>
</tr>
<tr>
<td>performance, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than 1 exercise per week</td>
<td>70.7</td>
<td>77.4</td>
<td>0.331</td>
</tr>
</tbody>
</table>

Table 2. Results of univariate and multivariate analyses of body mass index, waist circumference and visceral and subcutaneous adipose tissue areas as predictors of poor cognitive performance in subjects younger than 70 years

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P-value</td>
</tr>
<tr>
<td>Body mass index ≥25 kg/m²</td>
<td>2.44 (1.19–5.01)</td>
<td>0.013</td>
</tr>
<tr>
<td>Waist circumference ≥90.0 cm (M), F ≥80 cm (F)</td>
<td>1.13 (0.55–2.35)</td>
<td>0.742</td>
</tr>
<tr>
<td>Visceral adipose tissue tertile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M&lt;110.0 cm², F&lt;91.0 cm²</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>110.0 cm² ≤ M ≤ 149.0 cm², 91.0 cm² ≤ F ≤ 123.7 cm²</td>
<td>1.50 (0.59–3.82)</td>
<td>0.39</td>
</tr>
<tr>
<td>M&gt;149.0 cm², F&gt;123.7 cm²</td>
<td>2.26 (0.93–5.52)</td>
<td>0.07</td>
</tr>
<tr>
<td>P-value for trend</td>
<td>0.070</td>
<td>0.049</td>
</tr>
<tr>
<td>Subcutaneous adipose tissue tertile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M&lt;109.4 cm², F&lt;171.8 cm²</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>109.4 cm² ≤ M ≤ 131.9 cm², 171.8 cm² ≤ F ≤ 219.2 cm²</td>
<td>1.18 (0.48–2.93)</td>
<td>0.72</td>
</tr>
<tr>
<td>M&gt;131.9 cm², F&gt;219.2 cm²</td>
<td>2.12 (0.88–5.11)</td>
<td>0.096</td>
</tr>
<tr>
<td>P-value for trend</td>
<td>0.090</td>
<td>0.10</td>
</tr>
</tbody>
</table>

M, males; F, females; OR, odds ratio.

*Adjusted for age, sex, education, hypertension, diabetes.
performance in univariate and multivariate analyses controlling for age, sex and education (Table 3).

We found that interactions of age*anthropometric measures were not statistically significant (data were not shown).

Discussion

This study demonstrates that higher BMI and visceral adipose tissue area calculated from cross-sectional abdominal CT images are associated with poor cognitive functioning and that these relations are attenuated by age. The evidence was that compared with no obesity (BMI < 25 kg/m²), obesity (BMI ≥ 25 kg/m²) was associated with poor cognitive performance in subjects younger than 70 years and that the top tertile of the visceral adipose tissue area was also associated with poor cognitive performance compared with the bottom tertile in those younger than 70 years (Table 2). The evidence that these relations may be attenuated by age was that the relations between BMI, visceral adipose tissue area and poor cognitive performance were not significant in those aged 70 years and older (Table 3).

Compared with the subcutaneous adipose tissue, the visceral adipose tissue has been considered as a pathogenic adipose tissue compartment. One of the mechanisms for this is that the sustained exposure of the liver to an increased flux of free fatty acid via the portal circulation from the visceral adipose tissue may be antecedent to the disturbances in glucose and lipid metabolism [20]. The other mechanism is related to the fact that visceral adipose tissue is more metabolically active than subcutaneous adipose tissue and is thought to have a stronger influence on insulin resistance and adipocytokine production such as adiponectin, tumour necrosis factor-α and plasminogen activator inhibitor type I [12]. In contrast, subcutaneous adipose tissue is less strongly associated with cardiovascular disease and may even exert a protective effect [21].

To the best of our knowledge, this is the first report establishing a positive association between the visceral adipose tissue area measured with CT scans and low cognitive functioning.

In this study, obesity was independently associated with poor cognitive performance after controlling for cardiovascular co-morbidities in subjects younger than 70 years. This result is consistent with those of the previous studies [3–5]. Obesity is associated with carotid artery wall thickening [22] and the presence and severity of white matter lesions [23]. Obesity may be also a risk factor for AD [4]. Leptin was found to reduce Aβ secretase activity as well as increase APOE-mediated clearance of Aβ fibrils [24]. In an animal model, the impairment of the leptin receptor function in the hippocampus reduced long-term potentiation and spatial memory [25]. Leptin resistance occurring in obesity may play a role in cognitive impairment [26].

In the present study, the relations between obesity and poor cognitive performance were not significant in subjects 70 years and older, but were significant in those younger than 70 years. This is also consistent with previous reports [3, 5]. Ageing is characterised by lean body mass loss and adipose tissue increase without weight gain, which may not be captured by BMI, and traditional adiposity measures like BMI are less useful in elderly persons [27]. A higher BMI is related to lower dementia risk in the oldest old [6]. It is possible that persons with low BMI lost their weight because of pre-morbid dementia [6, 10]. It is also possible that a low BMI is the consequence of hyperinsulinaemia, which precedes weight loss [28] and is related to higher dementia risk. The present study shows that the relation of visceral adiposity directly measured with CT scans and poor cognitive functioning is also attenuated by age.

In this study, increasing waist circumference showed a tendency of a positive association with poor cognitive performance in a univariate analysis, but this relation was not significant in multivariate analysis. We suggest two possible explanations of why waist circumference was not associated with poor cognitive performance. First, waist circumference is influenced by subcutaneous as well as visceral adipose tissue. Therefore, a direct measurement of visceral adipose tissue with the CT may have been more valid than

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\begin{array}{c|c|c|c|c|c}
\hline
\text{Univariate analysis} & \text{OR (95% CI)} & \text{P-value} & \text{Multivariate analysis} & \text{OR (95% CI)}^a & \text{P-value} \\
\hline
\text{Body mass index} \geq 25 \text{ kg/m}^2 & 1.73 (0.59–5.04) & 0.312 & 1.73 (0.54–5.33) & 0.358 \\
\text{Waist circumference} > 90.0 \text{ cm (M), F >80 cm (F)} & 2.02 (0.62–6.61) & 0.243 & 2.01 (0.54–7.42) & 0.296 \\
\text{Visceral adipose tissue tertile} & & & & & \\
M <118.8 \text{ cm}^2, F <99.5 \text{ cm}^2 & 1.00 & & 1.00 & \\
118.8 \text{ cm}^2 \leq M \leq 169.9 \text{ cm}^2, 99.5 \text{ cm}^2 \leq F \leq 149.7 \text{ cm}^2 & 0.93 (0.26–3.38) & 0.910 & 0.86 (0.23–3.20) & 0.823 \\
M >169.9 \text{ cm}^2, F >149.7 \text{ cm}^2 & 1.39 (0.40–4.92) & 0.607 & 1.35 (0.38–4.79) & 0.646 \\
\text{P-value for trend} & 0.60 & & 0.632 & \\
\text{Subcutaneous adipose tissue tertile} & & & & & \\
M <109.1 \text{ cm}^2, F <161.3 \text{ cm}^2 & 1.00 & & 1.00 & \\
109.1 \text{ cm}^2 \leq M \leq 159.4 \text{ cm}^2, 161.3 \text{ cm}^2 \leq F \leq 219.0 \text{ cm}^2, & 0.60 (0.16–2.21) & 0.442 & 0.59 (0.16–2.20) & 0.430 \\
M >159.4 \text{ cm}^2, F >219.0 \text{ cm}^2 & 1.13 (0.32–3.90) & 0.853 & 1.02 (0.28–3.71) & 0.979 \\
\text{P-value for trend} & 0.84 & & 0.986 & \\
\hline
\end{array}
\]

M, males; F, females; OR, odds.

\(^a\)Adjusted for age, sex, education.
anthropometric measurements like waist circumference. Secondly, waist circumference has been associated with a higher risk of vascular dementia and not AD in a previous study [3]. If we investigate the relation of waist circumference with poor cognitive performance according to the underlying causes of poor cognitive function, different associations may be observed with poor cognitive function according to the underlying causes.

This study had several limitations. This was a cross-sectional analysis; thus, strong causal inferences cannot be made. The cognitive data in this analysis were limited to the data on MMSE-KC, a measure of global cognitive functioning. We did not investigate associations with domain-specific cognitive functioning. We did not determine whether the cognitive impairment that occurred was due to underlying AD or vascular dementia processes. MMSE has limitations for measuring minute cognitive dysfunction due to the problem of sensitivity and specificity. Another limitation of the study could be that we operationally defined subjects below 1 SD of MMSE as the poor cognitive performance group. Despite these limitations, the results of this study suggest a significant association between global cognitive function and visceral fat in asymptomatic healthy subjects. Further investigation according to the diagnostic criteria of MCI or AD is warranted.

In addition, the sample size of the older group was small and might influence the non-significant results of this group. However, the results in the older group were consistent with the results from previous reports [2, 6]. Our findings need to be confirmed by prospective large population study. Finally, VAT is associated with several complications and mortality. Subject whose VAT played adverse effects did not survive or were less likely to be included in the baseline assessment while those assessed were the ones with ‘uncomplicating’ VAT.

In conclusion, our results showed that high adiposity may be associated with poor cognitive functioning, particularly in younger elderly persons and that visceral adipose tissue is more strongly associated with poor cognitive functioning than subcutaneous adipose tissue. However, this association could be confounded by weight loss due to preclinical disease and was attenuated in older age groups. Our findings have important public health implications. The prevention of obesity, particularly central obesity, might be important for the prevention of cognitive decline or dementia.

**Key points**

- Higher BMI is related to lower cognitive function in older people.
- This study showed a direct association between visceral adiposity on abdominal CT and poor cognitive performance in older people.
- The relation between higher total and visceral adiposity and poor cognitive performance is attenuated by age in older people.

**Conflicts of interest**

None declared.

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**Supplementary data**

Supplementary data mentioned in the text is available to subscribers in *Age and Ageing* online.

**References**

Managing patients with COPD exacerbation: does age matter?

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