Developments in Estimating Visceral Fat Area from Medical Examination Data

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Aim: The aim of this study is to develop a simple method for estimating visceral fat area (VFA) using medical examination data.

Methods: The study subjects were 100 males who had undergone medical examinations and computed tomography (CT) at the umbilicus level. Multiple regression analysis was conducted to estimate VFA. The Bland & Altman Method was used to examine the tendency for mean difference between VFA observed by CT and VFA estimated by medical examination data. We calculated cross-validation and sensitivity and specificity at VFA ≥ 100 cm².

Results: As a result of multiple regression analysis, the waist-height ratio (WHtR) and triglyceride (TG) were taken as independent variables (r = 0.910). The Bland & Altman Method showed 0.00 ± 63.88 cm². The cross-validation regression equation was r = 0.889. Sensitivity was 0.833 and specificity was 0.900.

Conclusion: WHtR is a simple index used to diagnose the accumulation of VFA. It has been reported that TG, which increases with accumulating VFA, is a factor in hyperlipidemia; therefore, we consider the obtained independent variables to be appropriate. In addition, the regression equation showed high correlation and good results by cross-validation, the Bland & Altman Method, sensitivity, and specificity. We assert that VFA can be estimated using this method.


Key words: Computed tomography, Metabolic syndrome, Lifestyle-related disease, Waist circumference

Introduction

In Japan, obesity is defined as having a body mass index (BMI) of over 25 kg/m²1). According to Yoshiike et al.2, approximately 25% of males between 35 and 64 years old are obese, with a BMI ≥ 25 kg/m², and this percentage is increasing every year. Obesity has been categorized into two types: visceral fat syndrome and subcutaneous fat syndrome. The categorization depends on differences in fat distribution. The Japan Society for the Study of Obesity has defined a BMI ≥ 25 kg/m² and a visceral fat area (VFA) ≥ 100 cm² as visceral fat syndrome. A diagnostic image using computed tomography (CT) images at the umbilicus level is recommended as a diagnostic method3); however, we were unable to gain unlimited access to CT, due to problems such as radiation exposure. Instead of using CT, the waist circumference (W) at the umbilicus level, men ≥ 85 cm and women ≥ 90 cm, was used to screen for visceral fat syndrome1). It is difficult to perform a quantitative assessment on the degree of accumulated VFA because of the indirect index; however, it has become obvious that visceral fat syndrome promotes not only the incidence of lifestyle-related diseases, but also the risk of coronary artery disease4-10). The expression of angiotensinogen, and the inappropriate secretion of various adipocytokines such as TNA-α and PAI-1 in abdominal accumulated adipose
Anthropometric indeces, area of abdominal tissue, and blood biochemical analysis (mean ± S.D.)

<table>
<thead>
<tr>
<th>Anthropometric indeces</th>
<th>Area of abdominal tissue and blood biochemical analysis</th>
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<tbody>
<tr>
<td>Age (years) [19-80]</td>
<td>44.4 ± 18.4</td>
</tr>
<tr>
<td>Height (cm) [147.0-181.0]</td>
<td>167.4 ± 7.2</td>
</tr>
<tr>
<td>Weight (kg) [39.0-113.0]</td>
<td>66.1 ± 12.6</td>
</tr>
<tr>
<td>W (cm) [62.3-119.5]</td>
<td>83.6 ± 11.4 (Over 85 cm^2: 40%)*</td>
</tr>
<tr>
<td>HIP (cm) [74.0-122.0]</td>
<td>92.4 ± 7.4</td>
</tr>
<tr>
<td>BMI (kg/m^2) [15.4-43.4]</td>
<td>23.6 ± 4.2 (Over 25 kg/m^2: 25%)*</td>
</tr>
<tr>
<td>WHtR [0.34-0.81]</td>
<td>0.50 ± 0.07</td>
</tr>
<tr>
<td>WHR [0.70-1.16]</td>
<td>0.90 ± 0.08</td>
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<tr>
<td>SFA (cm^2) [6.4-320.1]</td>
<td>105.7 ± 67.9</td>
</tr>
<tr>
<td>VFA (cm^2) [3.1-476.3]</td>
<td>76.8 ± 78.5 (Over 100 cm^2: 30%)*</td>
</tr>
<tr>
<td>BPmax (mmHg) [90-170]</td>
<td>125.9 ± 16.4 (Over 130 mmHg: 44%)*</td>
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<tr>
<td>BPmin (mmHg) [50-97]</td>
<td>73.4 ± 10.1 (Over 85 mmHg: 17%)*</td>
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<tr>
<td>TC (mg/dL) [117-310]</td>
<td>191.4 ± 37.1</td>
</tr>
<tr>
<td>HDL-C (mg/dL) [21-130]</td>
<td>52.4 ± 17.4 (Under 40 mg/dL: 23%)*</td>
</tr>
<tr>
<td>TG (mg/dL) [24-399]</td>
<td>120.9 ± 63.9 (Over 150 mg/dL: 26%)*</td>
</tr>
<tr>
<td>GL (mg/dL) [59-348]</td>
<td>151.7 ± 71.2 (Over 110 mg/dL: 59%)*</td>
</tr>
</tbody>
</table>

n = 100
W, waist circumference; HIP, hip circumference; BMI, body mass index; WHtR, waist-height ratio; WHR, waist-hip ratio; SFA, subcutaneous fat area; VFA, visceral fat area; BPmax, systolic blood pressure; BPmin, diastolic blood pressure; TC, total cholesterol; HDL-C, HDL-cholesterol; TG, triglyceride; GL, glucose
[ ] shows range of each value, *Criteria of metabolic syndrome in Japan, †Criteria of obesity in Japan

W, hip circumference, have testified to this cause^{11-14}; therefore, the prevention of excess accumulation of VFA is important to prevent lifestyle-related diseases such as coronary artery disease. For prevention, it is important to know how much VFA has accumulated. Moreover, the development of simple and precise measurement methods is desired to promote primary prophylaxis.

Finally, we considered developing a simple method of estimating VFA using medical examination data, because blood biochemistry analyses increase or decrease depending on the accumulation of adipose tissue.

Subjects

The study subjects were 100 males (mean age ± S.D.: 44.4 ± 18.4 years, range: 19-80 years) who had undergone medical examinations at several hospitals. The study protocol was approved by the Bioethics Committee of Utsunomiya University.

Methods

A CT image at the umbilicus level was taken using the method developed by Tokunaga et al.\(^3\). The CT image was used to analyze the VFA and subcutaneous fat area (SFA) using Fat Scan Version 3.0 (N2 System Corporation, Hyogo, Japan). Height, weight, W, and hip circumference (HIP) were calculated. Blood biochemistry analyses conducted in fasting subjects early in the morning were: systolic blood pressure (BPmax); diastolic blood pressure (BPmin); total cholesterol (TC); HDL-cholesterol (HDL-C); triglyceride (TG); and glucose (GL). Body mass index (BMI) was calculated as weight divided by the square of the height.

Waist-hip ratio (WHR) and waist-height ratio (WHtR) were calculated as W divided by HIP and by height, respectively. Each measurement value was obtained by medical examination.

An individual correlation coefficient was used to determine the correlation between VFA and each measurement value. Stepwise selection of multiple regression analysis was conducted to estimate VFA. Independent variables were age, anthropometry parameters, which admitted the highest correlation with VFA, and individual blood biochemistry analyses. This analysis was applied to all subjects. Cross-validation using 20 other males was employed to evaluate the precision of the multiple regression equations. We used the Bland & Altman Method\(^5\) to examine the tenability of mean difference between VFA observed by CT and VFA estimated by the medical examination data. The upper and lower limits of agreement, defining the range within which 95% of differences between methods are expected to lie, were calculated as a mean difference of ± 1.96 standard deviation (S.D.). The mean difference and the upper and lower limits of agreement are reported as a 95% confidence interval. A p value less than 0.05 was regarded as significant. We calculated the sensitivity, specificity, false positive, and false negative at VFA ≥ 100 cm^2.

Results

The mean of each item and its S.D. are shown in Table 1. A total of 30 males (30%) showed VFA ≥ 100 cm^2: 40 males (40%) showed W ≥ 85 cm; 25 males (25%) showed BMI ≥ 24 kg/m^2.

Strong correlation coefficients between VFA and
Anthropometric indices were WHtR ($r = 0.897$), W ($r = 0.868$), BMI ($r = 0.834$), and WHR ($r = 0.760$). WHtR showed the highest correlation in the anthropometric indices. Thereafter, we used this as an independent variable to perform multiple regression analysis. Correlation coefficients between VFA and blood biochemistry analyses were: BPmax ($r = 0.133$); BPmin ($r = 0.057$); GL ($r = 0.094$); TG ($r = 0.582$); TC ($r = 0.103$); and HDL-C ($r = -0.425$). TG and HDL-C were only observed as significant at a 1% level.

As a result of multiple regression analysis, WHtR and TG were taken as independent variables. The regression was $\text{VFA} = 857.66 \times \text{WHtR} + 0.22 \times \text{TG} - 378.31$ ($r = 0.910$, $p < 0.01$, Fig. 1). This estimation value had a stronger correlation than the estimation value using only WHtR, the regression of which was $\text{VFA} = 951.5 \times \text{WHtR} - 399.1$ ($r = 0.897$, $p < 0.01$). The result of the cross-validation regression equation, obtained using medical examination data, was $r = 0.889$ ($p < 0.01$), a strong correlation (Fig. 2). The Bland & Altman Method of comparison between VFA observed by CT and VFA estimated by medical examination data showed a mean difference and 1.96 S.D. of 0.00 ± 63.88 cm² (Fig. 3). There was no difference between the mean VFA observed by CT and the mean VFA estimated by medical examination data. The result of this method using regression only by WHtR was 0.00 ± 68.05 cm². Moreover, sensitivity and specificity were high (0.833 and 0.900, respectively) when discriminate $\text{VFA} \geq 100$ cm² or $< 100$ cm² was used for this regression equation. However, seven false positives and five false negatives were observed and these were distributed between VFA=70 cm² and 120 cm², centered on VFA=100 cm² (Fig. 4).

**Discussion**

Recently, a diagnostic image using CT at the umbilicus level has been the most precise and objective method of measuring VFA; however, it is not an appropriate screening of visceral fat syndrome for a group, due to problems such as the cost and radiation exposure. Therefore, W, WHtR, BMI, and WHR are recommended as indirect indices for simple screening, which have strong correlations with VFA $^{1,4,16-20}$. However, it has been reported that an accumulation of VFA induces lifestyle-related disease and coronary artery disease, because blood biochemistry analyses increase or decrease along with VFA $^{5-9,21-23}$. Therefore, we conducted multiple regression analysis using medical examination data. We also considered developing a simple estimation method of VFA using anthropometric indices and blood biochemistry analyses for screening at medical examinations.

The obtained independent variables by multiple regression analysis were WHtR ($p < 0.01$) and TG ($p < 0.01$). WHtR is a simple index, used to diagnose the accumulation of VFA. It is also effective in screening for coronary artery disease, which is induced by an excess accumulation of VFA $^{24}$. It has been reported that TG, which increases with accumulating VFA, is a factor in hyperlipidemia $^{25}$. The increase in TG induces flowing free fatty acid into the liver with the excess accumulation of VFA $^{10}$. Firstly, we consider that there
is a close relation between excess accumulation of VFA and increased TG. Secondly, TG exhibited the highest correlation and a significant positive correlation was only observed between blood biochemical analyses and VFA; therefore, we consider the obtained independent variables to be appropriate, because WHtR and TG increased together with the accumulation of VFA and these independent variables showed a significant correlation with VFA in this study.

The Bland & Altman Method was used to examine the tendency for mean difference between VFA observed by CT and VFA estimated by medical examination data. Many high VFA subjects who were over 150 cm² by (VFA observed by CT + VFA estimated by medical examination data)/2, were positive with (VFA observed by CT − VFA estimated by medical examination data). This shows the difference between observed and estimated values. The zero line on the vertical axis represents the mean difference between VFA observed by CT and VFA estimated by medical examination data. An error was admitted ± 63.88 cm² between the values.

**Fig. 3.** Bland & Altman plot for comparison between VFA observed by CT and VFA estimated by medical examination data.

The tendency for mean difference between VFA observed by CT, and VFA estimated by medical examination data was calculated by the Bland & Altman method. Transverse axis is (VFA observed by CT + VFA estimated by medical examination data)/2. Vertical axis is (VFA observed by CT − VFA estimated by medical examination data). This shows the difference between observed and estimated values. The zero line on the vertical axis represents the mean difference between mean VFA observed by CT and mean VFA estimated by medical examination data. There is no difference between the values. Lines between ± 40 and ± 80 on the vertical axis represent the limits of agreement (mean difference ± 1.96 S.D.). An error was admitted ± 63.88 cm² between the values.
tion data). Their feature was high WHtR (mean: 0.65, range: 0.55-0.81), showing a tendency to underestimate subjects who have a high WHtR according to the estimation equation; however, this is not a serious problem because subjects are classified precisely at VFA ≥100 cm²; which is a very high VFA although it is underestimated. This specific tendency was not found under 150 cm² because of the evenly distributed positive and negative with (VFA observed by CT – VFA estimated by medical examination data). In addition, the same tendencies were observed using regression for WHtR alone. The regression obtained using medical examination data is smaller error regression using only WHtR (medical examination data: 63.88 cm², only WHtR: 68.05 cm²); therefore, using medical examination data is more precise than using only anthropometric indices.

We examined the validity of the regression equation for screening. Six were false positives and six were false negatives, even though sensitivity and specificity were high. In particular, 12 of 27 study subjects who had a VFA between 70 cm² and 120 cm² (44.4%), centered on VFA = 100 cm², were misclassified as false positives or false negative. The mean VFA observed by CT was high, 81.8 cm² for seven males classified as false positive. It is detrimental for health to exceed VFA ≥100 cm²; however, it is known that VFA accumulates with age. This could indicate that they will exceed VFA ≥100 cm² in the future, even though they are healthy and do not exceed VFA ≥100 cm² now; therefore, subjects need to amend their lifestyles to keep their VFA < 100 cm² from the perspective of primary prevention, because they have accumulated high VFA, although they were misclassified as VFA ≥100 cm². While the mean VFA observed by CT was 108.1 cm²; five males were classified as false negatives. These subjects were slightly over VFA ≥100 cm²; therefore, it was suggested that the estimated equation possible misclassifies the target value of VFA, which is around 100 cm². Moreover, one subject showed large errors between the VFA observed by CT and the VFA estimated by medical examination data in a misclassification as false positive and false negative. His VFA observed by CT was 117.1 cm² and VFA estimated by medical examination data was 39.8 cm². His feature was a lower WHtR (0.45) independent value than its mean value (0.50); therefore, it is suggested that the value of VFA estimated by the regression equation depends mainly on WHtR. In addition, TG increases not only due to VFA but also alcohol, overeating, and a constitutional abnormality. Considering these points, the value of VFA estimated by the regression equation should be used when we classify VFA ≥100 cm² or <100 cm² during medical examinations.

In conclusion, this study explored the possibility that the estimated value depends on WHtR. This study also pointed out the possibility that subjects with an observed VFA value of around 100 cm² were misclassified using a regression equation to estimate VFA; however, WHtR and TG reflect the accumulation of VFA. We obtained a high correlation, r = 0.910, between VFA observed by CT and VFA estimated by medical examination data. We also obtained a high correlation, r = 0.889, by cross-validation. There was no difference between the mean VFA observed by CT and medical examination data, even though the upper and lower limits of agreement were ± 63.88 cm² according to the Bland-Altman method. The sensitivity and specificity of classifying VFA ≥100 cm² were high in the estimation equation (0.833 and 0.900, respectively). We consider that we can estimate VFA simply and quantitatively with a regression equation using anthropometric indices and blood biochemical analyses. In addition, we can estimate VFA easily by conducting a medical examination because the indices used in this study are measured during medical examinations. We believe that this method is useful for screening VFA ≥100 cm², although we had only 100 study subjects and it appears that a few showed a large error between VFA observed by CT, and VFA estimated from medical examination data. In future studies, we will attempt to increase the number of study subjects, including females, and to develop a more precise estimation equation.

References

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