Effect of Longitudinal Changes in Visceral Fat Area and Other Anthropometric Indices to the Changes in Metabolic Risk Factors in Japanese Men

The Hitachi Health Study

OBJECTIVE—The effects of longitudinal changes in the visceral fat area (VFA), and other anthropometric indices, on the risk factors of metabolic syndrome were not studied. We calculated the changes in metabolic risk factors in relation to changes in certain anthropometric indices in a large-scale study of Japanese men.

RESEARCH DESIGN AND METHODS—The subjects were 1,106 men participating in the Hitachi Health Study who received a computed tomography examination in both 2004 and 2007. VFA, subcutaneous fat area (SFA), and waist circumference were measured using the computed tomography. We examined how longitudinal changes in each anthropometric index over a 3-year period influenced the value of each metabolic risk factor.

RESULTS—Changes (Δ) over a 3-year period in body weight, SFA, and waist circumference strongly correlated, while the changes in body weight and VFA were weakly correlated. Changes in the VFA were associated with changes in metabolic risk factors, especially changes in triglyceride and HDL; we found these changes to be independent of the Δbody weight and Δwaist circumference.

CONCLUSIONS—Change in body weight is not a precise surrogate marker of ΔVFA, and repeated VFA measurements over time are useful. Adopting a lifestyle that does not increase the VFA is important in preventing metabolic syndrome.
Changes in VFA and incidence of CVD risk

At the time of both surveys. Body height and weight were measured using an automated scale (BF-220; Tanita), and the BMI was defined as the weight in kilograms divided by the square of the height in meters. VFA, SFA, and waist circumference were measured using a computed tomography scanner and protocols previously described (20). In brief, single-slice imaging was performed at the umbilical level in a spine position using a Redix turbo CT machine (Hitachi Medico). The imaging conditions were 120 kV, 50 mA, and a slice thickness of 5 mm. VFA, SFA, and waist circumference were calculated using fatPointer software (Hitachi Medico). Triglyceride and HDL cholesterol levels were measured using the enzymatic method with a Hitachi 7600 device (Sekisu Medical). Blood glucose levels were measured using the glucose electrode technique with an ADAMS glucose GA-1170 device (Arkrey). Blood pressure was measured using an oscillometric method with a Kentaro ADVANCE BP-203RV III A/B device (Colin) while the patient was in a sitting position and after the patient had rested for 3 min. Informed consent was obtained from each examinee regarding the use of his or her data for research purposes. The current study was approved by the ethics review committee of the National Center for Global Health and Medicine.

Definition of the state of risk factor clustering

Subjects with two or more of the following four factors, defined by the National Cholesterol Education Program’s Adult Treatment Panel III guidelines (21), with the exception of waist circumference, were defined to have clustering of metabolic risk factors: 1) triglyceride $\geq 150$ mg/dL (1.69 mmol/L), 2) HDL cholesterol $< 40$ mg/dL (1.03 mmol/L), 3) systolic blood pressure (SBP) $\geq 130$ mmHg or diastolic blood pressure (DBP) $\geq 85$ mmHg, or 4) fasting plasma glucose $\geq 110$ mg/dL (6.11 mmol/L). Subjects currently receiving treatment for hyperlipidemia, hypertension, or diabetes were deemed as having the respective risk factor, regardless of the biochemical value.

Statistical analyses

The baseline data and the 3-year changes in CVD risk-related variables (i.e., BMI, VFA, SFA, VFA/SFA, waist circumference, SBP, DBP, triglyceride, HDL cholesterol, and glucose) were calculated for subjects who had not received a medical treatment in both surveys. The P value between baseline and the 3-year follow-up period was calculated using a paired t test. Pearson correlation coefficients for the changes in the anthropometric and CVD risk variables were calculated. To establish the independent contribution of each anthropometric variable, multiple linear regression analyses were used to obtain the standardized partial regression coefficients, where the change in the CVD risk variable was the dependent variable and the changes in the anthropometric indices were the independent variables; a stepwise procedure was used to select significant variables. All analyses were performed using SPSS (version 15.0; SPSS, Chicago, IL).

RESULTS—The anthropometric and CVD risk variables at the baseline survey and changes during the 3-year follow-up period are shown in Table 1. The mean (SD) age of the subjects was 52.7 (8.4)

### Table 1—Anthropometric and CVD risk variables at baseline and changes during the 3-year follow-up period (n = 1,106)

|               | Baseline Mean | SD | Changes in 3-year period Mean | SD | P* |
|---------------|---------------|----|-------------------------------|----|----|
| Height (cm)   | 169.0         | 6.1| 0.3                          | 0.5| <0.001|
| Weight (kg)   | 67.6          | 9.4| 0.0                          | 3.1| 0.61 |
| BMI (kg/m²)   | 23.6          | 2.7| 0.1                          | 1.1| 0.018|
| VFA (cm²)     | 120.0         | 52.2| 0.0                         | 32.5| 0.99 |
| SFA (cm²)     | 122.6         | 52.2| 4.2                         | 24.7| <0.001|
| VFA/SFA       | 1.03          | 0.54| -0.03                       | 0.48| 0.055|
| WC (cm)       | 85.6          | 8.1| -0.2                        | 4.6| 0.088|
| SBP (mmHg)    | 121.5         | 11.7| -1.1                        | 10.8| 0.001|
| DBP (mmHg)    | 76.9          | 8.2| -0.1                        | 7.1| 0.62 |
| TG (mg/dL)    | 137.6         | 92.6| -9.0                        | 80.0| <0.001|
| HDL cholesterol (mg/dL) | 56.4  | 14.2  | -1.8                     | 7.9  | <0.001|
| Fasting glucose (mg/dL) | 105.2 | 13.0  | 1.5                       | 8.7  | <0.001|

TG, triglyceride; WC, waist circumference. *Paired t test between values at baseline and at the 3-year follow-up.

### Table 2—Pearson correlation coefficients among changes in anthropometric and CVD risk variables (n = 1,106)

| Change variable | ΔVFA | ΔSFA | ΔBody weight | ΔWaist circumference | ΔBMI | ΔSBP | ΔDBP | ΔFasting glucose | ΔLog triglycerides | ΔHDL |
|-----------------|------|------|--------------|----------------------|------|------|------|-----------------|-------------------|------|
| ΔVFA            | 1    | 0.632| 0.672        | 0.756                | 0.671| 0.138| 0.162| 0.188           | 0.197             | -0.234|
| ΔSFA            | 0.632| 1    | 0.738        | 0.765                | 0.738| 0.174| 0.177| 0.187           | 0.171             | -0.238|
| ΔBody weight    | 0.672| 0.738| 1            | 0.722                | 0.989| 0.155| 0.210| 0.203           | 0.222             | -0.252|
| ΔWaist circumference | 0.756 | 0.765 | 0.722 | 1 | 0.718 | 0.140 | 0.156 | 0.168 | 0.196 | -0.233 |
| ΔBMI            | 0.671| 0.738| 0.989        | 0.718                | 1    | 0.150| 0.203| 0.204           | 0.225             | -0.253|
| ΔSBP            | 0.138| 0.174| 0.155        | 0.140                | 0.150| 1    | 0.627| 0.055           | 0.096             | -0.003|
| ΔDBP            | 0.162| 0.177| 0.210        | 0.156                | 0.203| 0.627| 1    | 0.093           | 0.097             | -0.004|
| ΔFasting glucose | 0.188| 0.187| 0.203        | 0.168                | 0.204| 0.055| 0.093| 1              | 0.039             | 0.041|
| ΔLog triglycerides | 0.288| 0.280| 0.350        | 0.295                | 0.353| 0.109| 0.117| 0.079           | 1                | -0.288|
| ΔHDL cholesterol | -0.234| -0.238| -0.252       | -0.233               | -0.253| -0.003| -0.004| 0.041           | -0.250            | 1 |

The absolute value of a correlation coefficient $>0.06$ was statistically significant at $P<0.05$. The correlation coefficients were essentially unchanged after adjustments for age (data not shown).
years at baseline. The mean BMI was 23.6 (2.7) kg/m², the mean VFA was 120.0 (52.2) cm², and the mean waist circumference was 85.6 (8.1) cm at baseline. The 3-year changes in each of these parameters were relatively small.

Pearson correlation coefficients for the changes in the anthropometric measurements and CVD risk variables are shown in Table 2. Strong correlations among the changes in the four adiposity indices were observed, with a colinearity observed among the indices. Correlations among the Δbody weight, ΔSFA, and Δwaist circumference were also strong, but the correlation between the Δbody weight and ΔVFA was weak. These findings suggested that the Δbody weight was not an exact surrogate marker of ΔVFA. We also analyzed correlations among the changes in anthropometric measurements and CVD risk variables. Significant correlations between the Δlog triglyceride and ΔVFA, the Δlog triglyceride and Δbody weight, the ΔSBP and ΔSFA, the ΔSBP and Δbody weight, and the Δglucose and Δbody weight were observed. The correlation coefficients were essentially unchanged after adjustments for age (data not shown).

Multiple linear regression analyses showed that the changes in VFA, SFA, body weight, and waist circumference were independently associated with the changes in CVD risk factors during the 3-year follow-up period (Table 3). The ΔDBP, Δglucose, Δlog triglyceride, and ΔHDL cholesterol were significantly affected by both the ΔVFA and ΔSFA. In contrast, the ΔSBP was only significantly affected by the ΔSFA. The Δlog triglyceride and ΔHDL cholesterol values were more strongly affected by the ΔVFA than by the ΔSFA. These results suggest that the ΔVFA and ΔSFA contribute differently to the ΔCVD risk variables. A multiple regression analysis showed that the ΔVFA were significantly related to the Δlog triglyceride and ΔHDL cholesterol and were independent of the Δbody weight and Δwaist circumference.

**CONCLUSIONS**—This study investigated the change in metabolic risk factors between a baseline examination and a 3-year follow-up examination, measured using computed tomography. The changes in body weight, SFA, and waist circumference strongly correlated. The changes in body weight and VFA showed weak correlation, suggesting that changes in body weight are not an exact surrogate marker of changes in VFA. A multiple regression analysis showed that the ΔVFA was significantly related to Δtriglyceride and ΔHDL cholesterol independently of Δbody weight and Δwaist circumference, suggesting the importance of monitoring VFA over time.

In previous cross-sectional studies, positive correlations between VFA and SBP and between VFA and serum triglyceride were reported to be significant when VFA was measured by computed tomography (14). In previous longitudinal studies, the effects of changes in BMI (22), weight (23), and waist circumference (24, 25) on metabolic risk factors were examined. One such report showed a strong linear trend between increasing BMI and a worsening of various variables of metabolic risk factors, including blood pressure and lipid

| Table 3—Independent associations of changes in VFA, SFA, body weight, and waist circumference with changes in the CVD risk factors during the 3-year follow-up period according to multiple linear regression analyses |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| Dependent variable | Independent variables | Model 1 | Model 2 |
|---------------------|---------------------|--------|--------|
| ΔSBP | ΔVFA | 0.056 | 0.115 | --- | --- |
| ΔSFA | 0.161 | <0.001 | 0.194 | <0.001 | --- | --- |
| Age | 0.034 | 0.216 | --- | --- |
| ΔDBP | ΔVFA | 0.093 | 0.008 | 0.093 | 0.008 | --- | --- |
| ΔSFA | 0.135 | <0.001 | 0.135 | <0.001 | --- | --- |
| Age | −0.105 | <0.001 | −0.105 | <0.001 | --- | --- |
| ΔFasting glucose | ΔVFA | 0.100 | 0.002 | 0.100 | 0.002 | --- | --- |
| ΔSFA | 0.127 | <0.001 | 0.127 | <0.001 | --- | --- |
| Age | −0.071 | 0.005 | −0.071 | 0.005 | --- | --- |
| ΔLog triglycerides | ΔVFA | 0.207 | <0.001 | 0.206 | <0.001 | --- | --- |
| ΔSFA | 0.141 | <0.001 | 0.143 | <0.001 | --- | --- |
| Age | −0.026 | 0.295 | --- | --- |
| ΔHDL cholesterol | ΔVFA | −0.154 | <0.001 | −0.154 | <0.001 | --- | --- |
| ΔSFA | −0.134 | <0.001 | −0.134 | <0.001 | --- | --- |
| Age | −0.082 | 0.001 | 0.082 | 0.001 | --- | --- |
| ΔSBP | ΔVFA | 0.031 | 0.480 | --- | --- |
| ΔSFA | 0.121 | 0.011 | 0.128 | 0.002 | --- | --- |
| ΔBody weight | 0.084 | 0.067 | 0.089 | 0.031 | --- | --- |
| ΔWaist | −0.009 | 0.866 | --- | --- |
| Age | 0.041 | 0.142 | --- | --- |
| ΔDBP | ΔVFA | 0.055 | 0.203 | --- | --- |
| ΔSFA | 0.070 | 0.139 | --- | --- |
| ΔBody weight | 0.157 | 0.001 | 0.220 | <0.001 | --- | --- |
| ΔWaist | −0.035 | 0.507 | --- | --- |
| Age | −0.092 | 0.001 | −0.088 | 0.001 | --- | --- |
| ΔFasting glucose | ΔVFA | 0.080 | 0.040 | --- | --- |
| ΔSFA | 0.085 | 0.045 | --- | --- |
| ΔBody weight | 0.158 | <0.001 | 0.223 | <0.001 | --- | --- |
| ΔWaist | −0.082 | 0.070 | --- | --- |
| Age | −0.053 | 0.037 | --- | --- |
| ΔLog triglycerides | ΔVFA | 0.112 | 0.003 | 0.127 | <0.001 | --- | --- |
| ΔSFA | 0.008 | 0.846 | --- | --- |
| ΔBody weight | 0.229 | 0.000 | 0.248 | <0.001 | --- | --- |
| ΔWaist | 0.031 | 0.483 | --- | --- |
| Age | −0.006 | 0.813 | --- | --- |
| ΔHDL cholesterol | ΔVFA | −0.105 | 0.04 | −0.112 | 0.001 | --- | --- |
| ΔSFA | −0.065 | 0.106 | −0.073 | 0.043 | --- | --- |
| ΔBody weight | −0.116 | 0.003 | --- | --- |
| ΔWaist | −0.017 | 0.684 | −0.119 | 0.002 | --- | --- |
| Age | −0.092 | <0.001 | −0.093 | <0.001 | --- | --- |

Model 1: All independent variables were entered into the model. Model 2: Significant variables were selected using the stepwise method. β, regression coefficient.
profiles (24). Likewise, another report showed that weight changes were linearly related to all measurements of each component of the metabolic risk factors (23). Other studies have shown that a reduction in the waist circumference and the VFA achieved through lifestyle modifications is closely linked to an improvement in metabolic risk factors (19,23). These studies suggest that the changes in BMI, weight, waist circumference, and VFA are related to risk factors for CVD. However, the impact of the change in the VFA (measured twice in the same person), which is regarded as the strongest indicator of CVD risk among the anthropometric variables, has remained uncertain. To our knowledge, this is the first study to analyze the relationships between changes in VFA and changes in metabolic risk factors, compared with other anthropometric variables, in a large population. Our findings clearly showed that the ΔVFA were significantly related to the Δlog triglyceride and ΔHDL cholesterol and were independent of Δbody weight and Δwaist circumference. In previous studies (22), the mean value of each component of metabolic risk factors or the prevalence of metabolic risk factors and its components were compared according to changes in BMI, body weight, and waist circumference. This is the first study that compared the strength of the association of metabolic risk factors with the change in VFA in a large population.

The current study has the following strengths: the study had a longitudinal design and examined the relationships between metabolic risk factors and the change in VFA using computed tomography scans performed twice on the same subject. The number of subjects was relatively large, with >1,000 subjects being followed over a 3-year period. Our study is thought to have a small measurement bias because VFA and SFA were measured using the same computed tomography machine, in the same region, and at the same state of expiration during both the baseline examination and the 3-year follow-up examination. A random measurement error could have diluted the relationship between ΔVFA and the metabolic risk factors. Thus, the real relationship may be stronger than the observed one. Nevertheless, the current study also has a limitation. The study subjects were limited to men, and further studies in women are needed.

In conclusion, the current study of Japanese men showed that changes in the VFA were associated with changes in metabolic risk factors. The ΔVFA was significantly related to Δlog triglyceride and ΔHDL cholesterol and was independent of Δbody weight and Δwaist circumference, suggesting the importance of measuring the VFA repeatedly over time. The adoption of a lifestyle that does not result in an increase in VFA is important in preventing metabolic syndrome.

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