Regional Body Composition Changes Exhibit Opposing Effects on Coronary Heart Disease Risk Factors

Tomohiro Okura, Yoshio Nakata, Keisuke Yamabuki, Kiyoji Tanaka

Objective—We investigated how regional body composition measured by dual-energy X-ray absorptiometry (DXA) is associated with risk factors for coronary heart disease (CHD) during weight reduction in obese women.

Methods and Results—Data were gathered from 128 overweight and obese women, aged 34 to 66 years, during a 14-week intervention study with diet and exercise. Regional (arms, legs, and trunk) fat tissue (FT) and lean soft tissue (LST) were measured by DXA. The FT change in legs correlated negatively with changes in diastolic blood pressure, low-density lipoprotein cholesterol (LDL-C), fasting plasma glucose (FPG), and the number of CHD risk factors per subject ($r = -0.17$, $P < 0.05$ to $-0.26$, $P < 0.01$) in response to weight reduction, whereas truncal FT change had positive correlations with changes in triglycerides, LDL-C, FPG, and the number of CHD risk factors per subject ($r = 0.17$, $P < 0.05$ to 0.25, $P < 0.01$). LST change in legs correlated negatively with changes in systolic blood pressure, FPG, and the number of risk factors ($r = -0.20$ to $-0.21$, $P < 0.05$).

Conclusions—Regional body composition information is important for evaluating improvement of CHD risk factors during weight-reduction treatment for obesity; differential FTs had opposing effects on CHD risk factors during weight reduction in obese women. (Arterioscler Thromb Vasc Biol. 2004;24:1-8.)

Key Words: obesity ▪ risk factors ▪ exercise ▪ diet

According to several epidemiological studies, obesity is closely associated with some major health risk factors, and the prevalence of obesity continues to increase in developed countries. It is well known that individuals with android-type obesity are at greater risk for coronary heart disease (CHD) and several metabolic disorders. Waist circumference and waist-to-hip ratio (WHR) are widely used anthropometric indices for determining central fat obesity. Intra-abdominal fat measured by computerized tomography (CT) is also an index for evaluating abdominal adiposity and is strongly associated with metabolic disorders independent of whole-body adiposity, including high blood pressure and triglycerides as well as increased incidence of diabetes mellitus. There are also several cross-sectional studies showing an association between regional body composition, especially truncal adiposity measured by dual-energy X-ray absorptiometry (DXA), and several CHD risk factors. Interestingly, some investigators have reported that peripheral fat may confer a negative association against metabolic dysfunction in postmenopausal and elderly women. However, very little information is available on the relationship between changes in regional body composition and CHD risk factors in response to weight reduction.

Based on these studies, we hypothesized that changes in regional body composition during weight reduction would affect or improve CHD risk factors. In this study, we investigate how changes in anthropometric and CT variables and regional body composition measured by DXA are associated with improvement in CHD risk factors in overweight and obese women in response to weight reduction through diet and exercise. We focused on which body region as measured by DXA is most strongly related to the improvement in CHD risk factors.

Methods

One hundred sixty-three sedentary women were recruited through advertisements in local newspapers. Of them, 154 sedentary women (exercise-induced energy expenditure <60 minutes/week) were aged 34 to 66 years, were chosen as subjects after they met the following criteria for high-risk obesity phenotype: (1) BMI ≥25 kg/m² with CHD risk factors that require weight reduction for their improvement or (2) high-risk obesity as specified by an excess of intra-abdominal fat, in which intra-abdominal fat area of 100 cm² was used as a cut-point for high-risk obesity by using a CT scan. We excluded 15 subjects who smoked, had concomitant renal, hepatic, or cardiac disease or diabetes (defined as a 2-hour postload glycemia ≥200 mg/dL), or were being treated with hormone replacement or drugs, which could affect the variables of the study. Eleven subjects were unable to complete the study successfully for personal reasons. Consequently, 128 subjects, consisting of 36 postmenopausal and 92 premenopausal women, completed the study requirements. Menopause was defined as the absence of menses for...
at least 12 months by a questionnaire. Assays and measurements were performed before and after the 14-week intervention period. This study conformed to the principles outlined in the Helsinki Declaration and was approved by the Higashi Toride Hospital Review Board. The aim and design of the study were explained to each subject before they gave their written informed consent.

**Anthropometric Variables**

Body mass was measured to the nearest 0.1 kg using a digital scale, height was measured to the nearest 0.1 cm using a wall-mounted stadiometer, and body mass index (BMI) was calculated as mass (kg) divided by height squared (m²). The WHR was calculated as a ratio of waist circumference measured at the level of the umbilicus to hip circumference.

**Regional Body Composition by DXA**

A DXA machine (DPX-L; Lunar, Madison, Wis) was used to evaluate segmental body composition (arms, trunk, legs, and whole body), which consists of fat tissue (FT) and lean soft tissue (LST). Transverse scans were used to measure FT and LST, and pixels of soft tissue were used to calculate the R value (the ratio of beam attenuation at the lower energy relative to that at the higher energy) of mass attenuation coefficients at 40 to 50 keV (low energy) and 80 to 100 keV (high energy) using software version 1.3Z.

The reproducibility of segmental body composition measurements was evaluated in 34 subjects. Two DXA procedures were performed on the same day, separated by an interval of a few minutes. The average coefficients of variation were 6.0%, 3.1%, and 3.7% for the FT of arms, legs, and trunk, and they were 1.6%, 1.0%, and 1.1% for the LST of arms, legs, and trunk, respectively.

**Abdominal Adipose Tissue Area by CT**

Intra-abdominal fat area (IFA) (cm^2) and subcutaneous fat area (SFA) (cm^2) were measured at the level of the umbilicus (L4-L5) using CT scans (SCCT-6800TX; Shimadzu, Tokyo, Japan) performed on subjects in the supine position. The IFA and SFA were calculated using software version 1.3Z.

The results of abdominal fat area were correlated with the results of IFA and SFA determined according to the Friedewald formula. The number of CHD risk factors per subject had decreased 52% (2.1 ± 1.5 → 1.0 ± 1.1) by the end of the weight-reduction treatment.

**Energy Cost of Physical Activity as Exercise**

The energy cost of physical activity was defined as the sum total of energy expenditures by the bench-stepping exercise and walking. The energy costs of the bench stepping exercise were measured 3 times (once each month) during the study using a metabolic measurement system with the breath-by-breath method (Oxycon alpha System; Mijnhardt, Breda, Netherlands). Portable heart rate monitors monitored subjects’ heart rates during their walking sessions. According to subjects’ diaries (body weight, heart rate, and walking time), energy expenditure while walking was calculated every day by the subjects using the following equation: Energy expenditure (kcal) = 5.04 × VO2 × heart rate × duration (min)/1000 mL.

**Statistical Analysis**

Values are expressed as mean ± SD. Student paired t tests were performed to test the significance of changes in variables measured before and after the intervention program. Qualitative data were analyzed by a χ² test. Relationships between 2 measurement variables were assessed using partial Pearson product moment correlation. Spearman rank-order correlation was used to determine the bivariate associations between number of CHD risk factors and measurement variables. Correlation coefficients were compared using a test based on z-transformed correlation coefficients. In each statistical analysis, P < 0.05 was regarded as significant. The data were analyzed with the Statistical Analysis System (SAS), version 8.2.

**Results**

**Physical Activity as Exercise and Dietary Intake**

Attendance at the bench-stepping exercise (40 sessions) averaged 92% (range 83% to 100%). The frequency of walking was 3.6 ± 1.4 days/wk. Walking duration averaged 187 ± 130 minutes/wk. The mean energy expenditures during the walking and the bench-stepping exercise were calculated as 849 ± 354 kcal/wk and 1166 ± 130 kcal/wk, respectively. The mean dietary intakes per day during intervention period (n = 90) were calculated as 64 ± 12 grams (258 ± 49 kcal) for proteins, 29 ± 8 grams (260 ± 76 kcal) for fat, 134 ± 34 grams (537 ± 135 kcal) for carbohydrates, and 1054 ± 199 kcal for total energy intake.

**Comparison of Measurements Before and After Treatment**

Table 1 shows that significant changes were observed in all variables (anthropometric, DXA, CT variables, and CHD risk factors) as determined by Student paired t tests. Frequency of all CHD risk factors decreased significantly with the exception of HDL-C. The number of CHD risk factors per subject had decreased 52% (2.1 ± 1.5 → 1.0 ± 1.1) by the end of the weight-reduction treatment.
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<th>TABLE 1. Descriptive Characteristics of Subjects at Baseline and After Treatment</th>
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<td><strong>Number of CHD risk factors (%)</strong></td>
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Values are presented as mean ± SD.

ISR indicates intra-abdominal fat area to subcutaneous fat area ratio; CHD, coronary heart disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.
Relationships Between Measurements at Baseline

We investigated how the number of CHD risk factors relates to anthropometric, CT, or DXA measurements. Waist circumference, WHR, IFA, and ISR correlated positively with the number of CHD risk factors ($r = 0.18$, $P < 0.05$ to $r = 0.50$, $P < 0.001$). As Figure 1 shows, truncal FT correlated positively with the number of CHD risk factors ($r = 0.22$, $P < 0.05$), whereas FT in legs and LST in the legs and trunk had significant negative correlations ($r = -0.27$, $P < 0.01$ to $r = -0.33$, $P < 0.001$). The correlation coefficient between IFA and the number of CHD risk factors ($r = 0.50$, $P < 0.001$) was significantly larger than correlation coefficients between the number of CHD risk factors and waist circumference ($r = 0.28$, $P < 0.01$) and WHR ($r = 0.18$, $P < 0.05$).

Relationships Between Measurements in Response to Weight Reduction

Figure 2 and Figure 3 illustrate how change in the number of CHD risk factors relates to changes in anthropometric, CT, or DXA measurements. Spearman rank-order correlation coefficients show that change in the number of CHD risk factors per subject correlated positively with changes in CT measurements ($r = 0.23$, $P < 0.01$ for IFA and $r = 0.22$, $P < 0.05$ for ISR) and truncal FT by DXA ($r = 0.25$, $P < 0.05$). In contrast, change in the number of CHD risk factors per subject had negative significant correlations with changes in FT and LST in legs ($r = -0.26$, $P < 0.01$ and $r = -0.21$, $P < 0.05$, respectively).

Figure 4 shows that change in DBP correlated significantly with change in FT in legs ($r = -0.33$, $P < 0.001$). This suggests that an increase in DBP was associated with a decrease in FT in legs. We also calculated partial Pearson correlation coefficients between changes in CHD risk factors and DXA measurements during the treatment period (Table 2). The FT in legs correlated negatively with DBP, LDL-C, FPG, and the number of CHD risk factors ($r = -0.17$, $P < 0.05$ to $r = -0.25$, $P < 0.01$). In contrast, truncal FT had significant positive correlations with TG, LDL-C, and FPG ($r = 0.17$ to $0.20$, $P < 0.05$). In addition, LST in legs and SBP, FPG, and the number of the risk factors ($r = -0.20$ to $-0.21$, $P < 0.05$). Any difference between correlation coefficients was not statistically significant.

Discussion

To our knowledge, the present study is the first to determine how changes in segmental DXA measurements (FT and LST) may be related to changes in CHD risk factors after weight reduction in a relatively large sample size of obese women. Our main observation is that FT in legs had a negative association against some CHD risk factors. In addition, the positive associations we observed between some CHD risk

Figure 1. Spearman rank-order correlation coefficients between number of CHD risk factors and DXA measurements at baseline. DXA measurements adjusted for age, BMI, menstrual status, whole-body fat tissue, and total lean soft tissue. CHD indicates coronary heart disease; DXA, dual-energy X-ray absorptiometry; BMI, body mass index. *$P<0.05$, §$P<0.01$, †$P<0.001$. 

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factors and anthropometric or CT measurements support findings from previous studies.\textsuperscript{5–7} We confirmed that FT in legs had a protective effect against the metabolic disorders we looked at, similar to recent reports using DXA measurements.\textsuperscript{12,13,18}

We excluded subjects who smoked or were being treated with hormone replacement. It is important to control for these factors when evaluating the effects of regional body composition on CHD risk factors in obese women because estrogens and smoking may independently influence CHD risk factors.\textsuperscript{24,25} In partial correlation analysis of the relationships between changes that occur in response to weight reduction, we used physical activity as a covariate. Because lipid and glucose consumption secondary to physical activity may independently influence CHD risk factors, it is also necessary to adjust for this factor when determining the effects of regional body composition on CHD risk factors during the weight-reduction period.

Regional Fat Tissue and CHD Risk Factors
Truncal and central fat deposition, especially intra-abdominal FT, clearly correlated with hypertension and the glucose and lipid metabolic abnormalities.\textsuperscript{5–10} Excess intra-abdominal FT means there will be increased lipolytic activity of this tissue, resulting in excess release of free fatty acids into the portal circulation.\textsuperscript{26} Subsequently, increased portal free fatty acids may contribute to dyslipidemia, hyperinsulinemia, and other metabolic abnormalities.\textsuperscript{27} In this study, anthropometric measurements and IFA had a positive association with some CHD risk factors at baseline and in response to weight reduction, which is consistent with the previously mentioned studies. It should be noted that truncal FT includes abdominal and gluteal fat tissue. Some studies reported that these 2 fat regions might induce opposing effects on CHD risk factors.\textsuperscript{12,13} Contrary to our expectation, truncal FT correlated positively with some CHD risk factors at baseline and in response to weight reduction when adjusted for the selected variables. Our subjects had a higher WHR (baseline 1.02±0.07) compared with women from western countries (WHR: 0.82 to 0.95),\textsuperscript{11,28} which indicates abdominal fat tissue may contribute to the CHD risk factor profile more than gluteal fat tissue in our subjects.

Peripheral FT has been reported to have a negative association with metabolic dysfunction\textsuperscript{13,17} and atherogenic tendencies.\textsuperscript{12,14} Our results also indicate that FT in legs has a significant negative correlation with CHD risk factors at baseline and in response to weight reduction. Our results and those of previous studies suggest that FT in legs may release...
certain factors constituting protection against atherosclerosis or other CHD risk factors. Berg et al found that peripheral fat tissue may secrete the hormone adiponectin, which correlates negatively to insulin resistance and has putative anti-atherogenic properties that help prevent the formation of atherosclerotic plaques, although no direct evidence is available to confirm this.

**Regional Lean Soft Tissue and CHD Risk Factors**

As we have indicated, little information is available concerning the relationship between regional LST and CHD risk factors during weight reduction. However, because LST is the strongest determinant of resting metabolic rates, which is closely associated with lipid and glucose metabolism, it can be hypothesized that an increase in LST may improve some CHD-related metabolic variables. Resistance training has the potential to increase LST, which results in normalized blood pressure in those with high normal values, and improved glucose tolerance and insulin sensitivity. Abe et al examined the relationship between serum lipid and mid-thigh muscle thickness measured by ultrasound in a cross-sectional study and found that the mid-thigh muscle thickness correlated significantly with HDL-C/TC in both sexes. Our results also indicate that LST in the legs and trunk had significant negative correlations with some CHD risk factors at baseline, and that LST in legs had significant negative correlations with SBP, FPG, and the number of CHD risk factors during weight reduction. These observations suggest that increasing LST, especially in the legs, may help normalize blood pressure and glucose metabolism. However, it is difficult to increase LST during weight-reduction treatment. Exercise intensity is known to influence motor unit activation: only slow-twitch fibers (type I) were activated when exercise was performed at <40% of VO2max, but at >80% of

**Figure 3.** Spearman rank-order correlation coefficients between changes in number of CHD risk factors and DXA measurements in response to weight reduction. DXA measurements adjusted for age, menstrual status, changes in whole-body fat tissue and total lean soft tissue, and physical activity during treatment. CHD indicates coronary heart disease; DXA, dual-energy X-ray absorptiometry.

*P<0.05, §P<0.01.
VO_{2\text{max}}, fast-twitch fatigable fibers (type II B) were also mobilized.\textsuperscript{36} Type II B fibers selectively and predominantly had hypertrophy compared with type I fibers.\textsuperscript{37} Prescribed exercises (walking and bench-stepping exercise) in the present study may be of insufficient intensity to activate the motor units of the type II B fibers. Because resistance training was not performed in the present study, LST in the arms, legs, and trunk decreased $-0.3\, \text{kg}, -0.3\, \text{kg},$ and $-0.9\, \text{kg},$ respectively. Hence, our findings should be interpreted to mean slowing the LST lost during weight reduction could favorably affect CHD risk factors.

There are some limitations of this study. The study design has no randomization and includes selection and information biases. Subject age range was wide (34 to 66 years), and premenopausal and postmenopausal women were included in the study. Because estrogens may independently influence CHD risk factors.\textsuperscript{30} These factors might partly preclude our definitive conclusions. It is well known that menopause is associated with a body fat redistribution toward an increase in visceral adipose tissue, resulting in increase in risks for CHD. However, it was unclear whether menopause would affect our findings. Further studies on effects of menopause on the relationships between changes in regional body composition and CHD risk factors with weight loss are needed.

In conclusion, our study demonstrated that the amount of FT in the legs and trunk had opposing effects on CHD risk factors in response to weight reduction in obese women. In addition, LST in legs has a negative association against CHD risk factors. Regional body composition information is, therefore, important for evaluating the improvement of CHD risk factors during weight-reduction treatment for obesity.

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