Original Article

Impact of Changes in Obesity Parameters on Glucose Metabolism and Insulin Resistance Over a One-Year Period

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***Aim*: Changes in indexes of obesity, such as waist circumference (WC) and body mass index (BMI), may influence some glucose metabolism-related parameters in both obese and non-obese subjects. We have investigated the impact of changes in WC and in BMI on data related to glucose metabolism over a one-year period.**
***Methods*: Data from 3213 individuals (2014 men, 1199 women) who underwent a general health screening two years running and were not taking antidiabetic medication were analyzed.**
***Results*: In men, percent changes in WC (%dWC) and BMI (%dBMI) were both significantly correlated with percent changes in fasting glucose (%dFG), in hemoglobin A_{1c} (%dHbA_{1c}), and in HOMA-IR (%dHOMA-IR). In women, these relationships were not significant except for the relationship between %dBMI and %dHOMA-IR. In a multivariate linear regression analysis using age, %dBMI, and %dWC as independent variables, %dBMI, but not %dWC, was found to be an independent predictor of %dHOMA-IR in both genders. Furthermore, in men, %dBMI was also an independent factor predicting %dFG and %dHbA_{1c}.**
***Conclusion*: During the one-year period, a reduction in BMI, and thus weight loss, was found to be associated with the improvement of insulin sensitivity, especially in men. A reduction in WC was also associated with an improvement in insulin sensitivity in men; however, this relationship did not remain significant after controlling for changes in BMI.**

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Key words; Waist circumference, Body mass index, Glucose metabolism, Insulin resistance, Health screening

Introduction

Elevated fasting glucose (FG) and hemoglobin A_{1c} (HbA_{1c}) concentarions, and enhanced insulin resistance are associated with an increased incidence of cardiovascular diseases[1)]. Obesity, which may be reflected as an increase in waist circumference (WC) and in body mass index (BMI), is known to be associated with these glucose metabolism-related parameters[2-6)]. In addition, the relative risk of developing type 2 diabetes increases with a gain in weight and BMI[7)]. The relationship observed between insulin resistance and obesity may be explained by a disproportionate accumulation of visceral fat, leading to a change in levels of adipocytokines, which may underlie various metabolic disorders[8-10)]. On the other hand, it has not been fully established whether changes in BMI or those in WC have the greater impact on glucose metabolism-related data. To this end, here we have analyzed the relationship between changes in obesity parameters and changes in diabetic parameters over a one-year period in Japanese individuals.

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Table 1a. Baseline Characteristics at the First Visit According to %dWC

variables	%dWC-Q1 (range: −21.3–−3.4)	%dWC-Q2 (range: −3.4–−0.1)	%dWC-Q3 (range: 0.0–3.3)	%dWC-Q4 (range: 3.3–33.4)	*p* value
Women					
n	348	202	223	426	
Age, years	53 (52–54)	53 (51–54)	51 (50–53)	51 (50–52)	0.066
Height, cm	156 (156–157)	157 (156–158)	157 (156–158)	157 (157–158)	0.037
Weight, kg	50 (51–52)	52 (52–54)	52 (52–55)	51 (51–53)	0.009
WC, cm	79 (78–80)	77 (77–80)	76 (76–78)	72 (73–74)	<0.001
BMI, kg/m^2	20.7 (20.7–21.3)	21.1 (21.2–22.2)	21.1 (21.2–22.1)	20.8 (20.8–21.3)	0.028
Systolic blood pressure, mmHg	115 (116–119)	118 (118–123)	114 (115–120)	113 (115–118)	0.129
Diastolic blood pressure, mmHg	72 (72–75)	73 (73–76)	72 (72–75)	71 (71–74)	0.198
Pulse rate, bpm	63 (63–64)	63 (62–65)	63 (63–65)	63 (63–64)	0.937
LDL-cholesterol, mg/dL	131 (127–134)	130 (125–134)	127 (124–133)	122 (121–127)	0.021
HDL-cholesterol, mg/dL	68 (68–71)	66 (66–70)	68 (67–70)	68 (68–70)	0.329
Trigryceride, mg/dL	77 (81–91)	77 (84–99)	77 (79–93)	69 (76–83)	0.026
Uric acid, mg/dL	4.5 (4.5–4.7)	4.5 (4.4–4.7)	4.6 (4.5–4.7)	4.4 (4.4–4.5)	0.076
Fasting glucose, mg/dL	87 (87–90)	89 (89–93)	88 (88–91)	88 (88–91)	0.149
Hemoglobin A$_{1C}$, %	5.1 (5.1–5.2)	5.2 (5.1–5.2)	5.1 (5.1–5.2)	5.1 (5.1–5.2)	0.284
Blood urea nitrogen, mg/dL	13.0 (13.0–13.8)	13.0 (13.2–14.2)	13.0 (12.9–13.7)	13.0 (13.2–13.8)	0.705
Serum creatinine, mg/dL	0.60 (0.61–0.70)	0.60 (0.62–0.65)	0.60 (0.61–0.63)	0.60 (0.62–0.64)	0.408
Anti-dyslipidemic medication, *n* (%)	13 (3.7)	11 (5.4)	6 (2.7)	16 (3.8)	0.526
Anti-hypertensive medication, *n* (%)	27 (7.8)	18 (8.9)	9 (4.0)	17 (4.0)	0.022
Current smoker, *n* (%)	36 (10.3)	15 (7.4)	12 (5.4)	44 (10.3)	0.117
Men					
n	462	589	600	363	
Age, years	54 (53–55)	54 (53–54)	54 (53–54)	53 (51–53)	0.040
Height, cm	169 (169–170)	170 (169–170)	169 (169–170)	169 (169–170)	0.975
Weight, kg	68 (68–70)	68 (68–69)	67 (68–69)	67 (67–68)	0.328
WC, cm	88 (87–89)	87 (86–87)	85 (85–86)	82 (82–84)	<0.001
BMI, kg/m^2	23.8 (23.6–24.2)	23.7 (23.6–24.0)	23.6 (23.6–24.0)	23.3 (23.2–23.8)	0.150
Systolic blood pressure, mmHg	128 (127–131)	125 (127–130)	124 (125–127)	121 (121–124)	<0.001
Diastolic blood pressure, mmHg	81 (81–83)	80 (80–82)	79 (79–81)	77 (77–79)	<0.001
Pulse rate, bpm	62 (62–64)	62 (62–64)	62 (62–64)	61 (61–63)	0.347
LDL-cholesterol, mg/dL	132 (129–134)	130 (128–133)	129 (127–132)	125 (124–131)	0.225
HDL-cholesterol, mg/dL	54 (55–58)	54 (54–57)	53 (54–56)	55 (55–58)	0.328
Trigryceride, mg/dL	111 (122–136)	111 (123–134)	111 (126–140)	100 (115–133)	0.037
Uric acid, mg/dL	6.1 (6.0–6.2)	6.1 (6.1–6.3)	6.0 (6.0–6.2)	6.2 (6.0–6.2)	0.290
Fasting glucose, mg/dL	95 (97–100)	95 (97–99)	94 (95–97)	93 (94–97)	0.008
Hemoglobin A$_{1C}$, %	5.3 (5.3–5.4)	5.3 (5.3–5.4)	5.2 (5.2–5.3)	5.2 (5.2–5.3)	0.005
Blood urea nitrogen, mg/dL	14.0 (14.3–15.0)	14.0 (14.4–14.9)	14.0 (14.0–14.6)	14.0 (14.1–14.7)	0.405
Serum creatinine, mg/dL	0.80 (0.83–0.92)	0.80 (0.85–0.87)	0.85 (0.85–0.87)	0.80 (0.84–0.86)	0.647
Anti-dyslipidemic medication, *n* (%)	18 (3.9)	25 (4.2)	28 (4.7)	16 (4.4)	0.942
Anti-hypertensive medication, *n* (%)	58 (12.6)	77 (13.1)	84 (14.0)	42 (11.6)	0.736
Current smoker, *n* (%)	137 (29.7)	194 (32.9)	175 (29.2)	121 (33.3)	0.352

Methods

Study Population

The study was approved by The Ethics Committee of Mitsui Memorial Hospital. Between October 2005 and October 2006, 11558 individuals underwent a general health screening at our institute. Of these, 3325 (2113 men, 1212 women) individuals

Table 1b. Baseline Characteristics at the First Visit According to %dBMI

variables	%dBMI-Q1 (range: −21.8–−1.9)	%dBMI-Q2 (range: −1.9–−0.2)	%dBMI-Q3 (range: −0.2–1.4)	%dBMI-Q4 (range: 1.4–15.7)	*p* value
Women					
n	284	268	305	342	
Age, years	53 (52–54)	54 (52–54)	52 (51–53)	49 (49–51)	0.002
Height, cm	156 (156–157)	157 (156–157)	158 (157–158)	157 (157–158)	0.005
Weight, kg	52 (52–54)	51 (52–53)	51 (51–53)	51 (51–53)	0.325
WC, cm	77 (76–78)	76 (76–78)	75 (75–77)	75 (75–77)	0.115
BMI, kg/m^2	21.3 (21.3–22.0)	20.9 (21.1–21.8)	20.5 (20.6–21.2)	20.7 (20.7–21.3)	0.002
Systolic blood pressure, mmHg	117 (118–123)	115 (115–119)	114 (115–119)	113 (115–118)	0.060
Diastolic blood pressure, mmHg	74 (73–76)	73 (72–75)	71 (72–74)	71 (71–74)	0.057
Pulse rate, bpm	63 (63–65)	64 (63–65)	61 (62–64)	63 (63–65)	0.106
LDL-cholesterol, mg/dL	133 (127–135)	132 (129–136)	125 (123–129)	117 (119–125)	<0.001
HDL-cholesterol, mg/dL	67 (66–70)	68 (67–71)	69 (68–71)	67 (67–70)	0.647
Trigryceride, mg/dL	79 (87–102)	76 (80–89)	74 (79–89)	68 (73–81)	0.002
Uric acid, mg/dL	4.5 (4.4–4.7)	4.4 (4.4–4.6)	4.6 (4.5–4.7)	4.4 (4.4–4.6)	0.408
Fasting glucose, mg/dL	88 (88–91)	88 (88–93)	88 (88–91)	88 (88–90)	0.933
Hemoglobin A$_{1C}$, %	5.1 (5.1–5.2)	5.2 (5.1–5.3)	5.1 (5.1–5.2)	5.1 (5.0–5.1)	0.028
Blood urea nitrogen, mg/dL	13.0 (13.2–14.0)	13.0 (13.1–13.9)	13.0 (13.3–14.2)	13.0 (12.8–13.4)	0.174
Serum creatinine, mg/dL	0.60 (0.61–0.63)	0.60 (0.61–0.63)	0.60 (0.62–0.73)	0.60 (0.61–0.63)	0.002
Anti-dyslipidemic medication, *n* (%)	12 (4.2)	10 (3.7)	12 (3.9)	12 (3.5)	0.972
Anti-hypertensive medication, *n* (%)	23 (8.1)	15 (5.6)	16 (5.2)	17 (5.0)	0.352
Current smoker, *n* (%)	21 (7.4)	22 (8.2)	23 (7.5)	41 (12.0)	0.130
Men					
n	504	531	495	484	
Age, years	54 (53–55)	55 (54–55)	54 (53–54)	51 (51–52)	<0.001
Height, cm	169 (169–170)	169 (168–169)	170 (169–170)	170 (169–171)	0.012
Weight, kg	69 (68–70)	67 (67–68)	68 (68–69)	68 (67–69)	0.097
WC, cm	87 (86–87)	85 (85–86)	86 (85–87)	85 (85–86)	0.011
BMI, kg/m^2	24.0 (23.8–24.3)	23.4 (23.4–23.9)	23.7 (23.6–24.1)	23.5 (23.3–23.8)	0.012
Systolic blood pressure, mmHg	126 (127–130)	124 (125–128)	126 (125–129)	123 (123–126)	0.011
Diastolic blood pressure, mmHg	81 (81–83)	79 (79–81)	80 (80–82)	78 (78–80)	0.019
Pulse rate, bpm	62 (62–64)	62 (62–63)	62 (63–64)	62 (61–63)	0.106
LDL-cholesterol, mg/dL	133 (130–135)	129 (128–133)	130 (126–132)	125 (125–130)	0.014
HDL-cholesterol, mg/dL	54 (54–56)	54 (55–57)	54 (55–58)	54 (54–57)	0.437
Trigryceride, mg/dL	111 (126–141)	108 (123–136)	111 (120–135)	107 (118–132)	0.285
Uric acid, mg/dL	6.1 (6.1–6.3)	6.1 (6.0–6.2)	6.0 (6.0–6.2)	6.1 (6.0–6.3)	0.344
Fasting glucose, mg/dL	95 (97–100)	95 (97–100)	95 (95–97)	93 (94–96)	0.002
Hemoglobin A$_{1C}$, %	5.3 (5.3–5.5)	5.3 (5.3–5.4)	5.2 (5.2–5.3)	5.2 (5.2–5.3)	<0.001
Blood urea nitrogen, mg/dL	14.0 (14.3–15.0)	14.0 (14.3–14.8)	14.0 (13.9–14.4)	14.0 (14.3–15.0)	0.130
Serum creatinine, mg/dL	0.80 (0.84–0.92)	0.80 (0.85–0.87)	0.80 (0.83–0.86)	0.90 (0.85–0.87)	0.303
Anti-dyslipidemic medication, *n* (%)	20 (4.0)	18 (3.4)	28 (5.7)	21 (4.3)	0.334
Anti-hypertensive medication, *n* (%)	72 (14.3)	81 (15.3)	47 (9.5)	61 (12.6)	0.035
Current smoker, *n* (%)	155 (30.8)	167 (31.5)	148 (29.9)	157 (32.4)	0.851

underwent a general health screening during this period (first visit) and again the following year (second visit). Among these 3325 individuals, 3213 (2014 men, 1199 women) who reported not taking antidiabetic drugs at either visit were enrolled in the current study. The mean ± standard deviation (SD) of the interval between the two visits of the individuals enrolled was 356 ± 51 days. The percent difference in

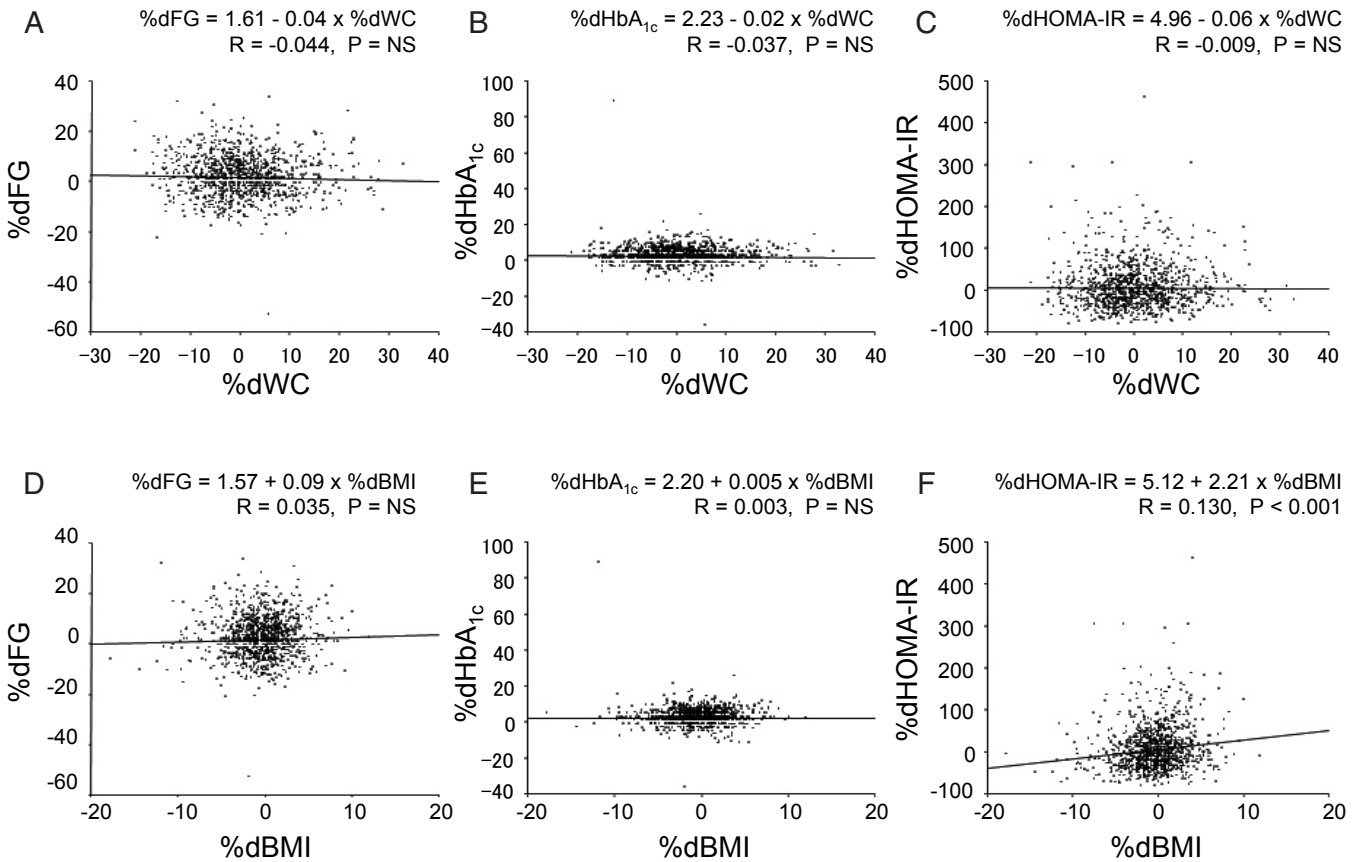

Fig. 1. Scatter plot and linear regression between %dWC and %dFG (A), %dHbA1c (B), and %dHOMA-IR (C) and between %dBMI and %dFG (D), %dHbA1c (E), and %dHOMA-IR (F) in women.

the value of WC, BMI, serum levels of fasting glucose (FG), HbA1c, and HOMA-IR between the first and second visits was designated %dWC, %dBMI, %dFG, %dHbA1c, and %dHOMA-IR, respectively. Blood samples were taken from all subjects after an overnight fast. BMI was expressed as weight (in kilograms) divided by the square of height (in meters). WC was measured at the umbilical level to the nearest 1 cm by trained physicians and technicians[11].

Laboratory Analysis

Serum levels of TC, HDL-C, and TG were determined enzymatically. Serum uric acid was measured by the uricase-peroxidase method; hemoglobin A1C was determined by a latex agglutination immunoassay. Creatinine was measured by TBA-200FR (Toshiba Medical Systems, Tochigi, Japan) using a commercial kit. The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated by the equation: HOMA-IR = (immunoreactive insulin (IRI)) × FBS/405. Blood pressure was measured after about 10 min of rest by an automated sphygmomanometer.

Statistical Analysis

Data are expressed as the median (95% confidence interval (95%CI)) unless stated otherwise. The Kruskal-Wallis test, χ^2 test, logistic regression analysis, and multivariate linear regression analysis were applied as appropriate to assess the statistical significance of differences between groups using computer software, Dr. SPSS II (SPSS Inc., Chicago, IL). A value of $p < 0.05$ was taken to be statistically significant.

Results

Baseline Characteristics

We enrolled 1199 women and 2014 men in this study. The mean age of the individuals enrolled was 51.9 years in women and 53.4 years in men at the first visit. The sex-nonspecific range of the first to fourth %dWC quartiles was −21.3/−3.4, −3.4/−0.1, 0.0/3.3, and 3.3/33.4, respectively, and that of the first to fourth %dBMI quartiles was −21.8/−1.9, −1.9/−0.2, −0.2/1.4, and 1.4/15.7, respectively. Subject characteristics at the first visit are shown according to the

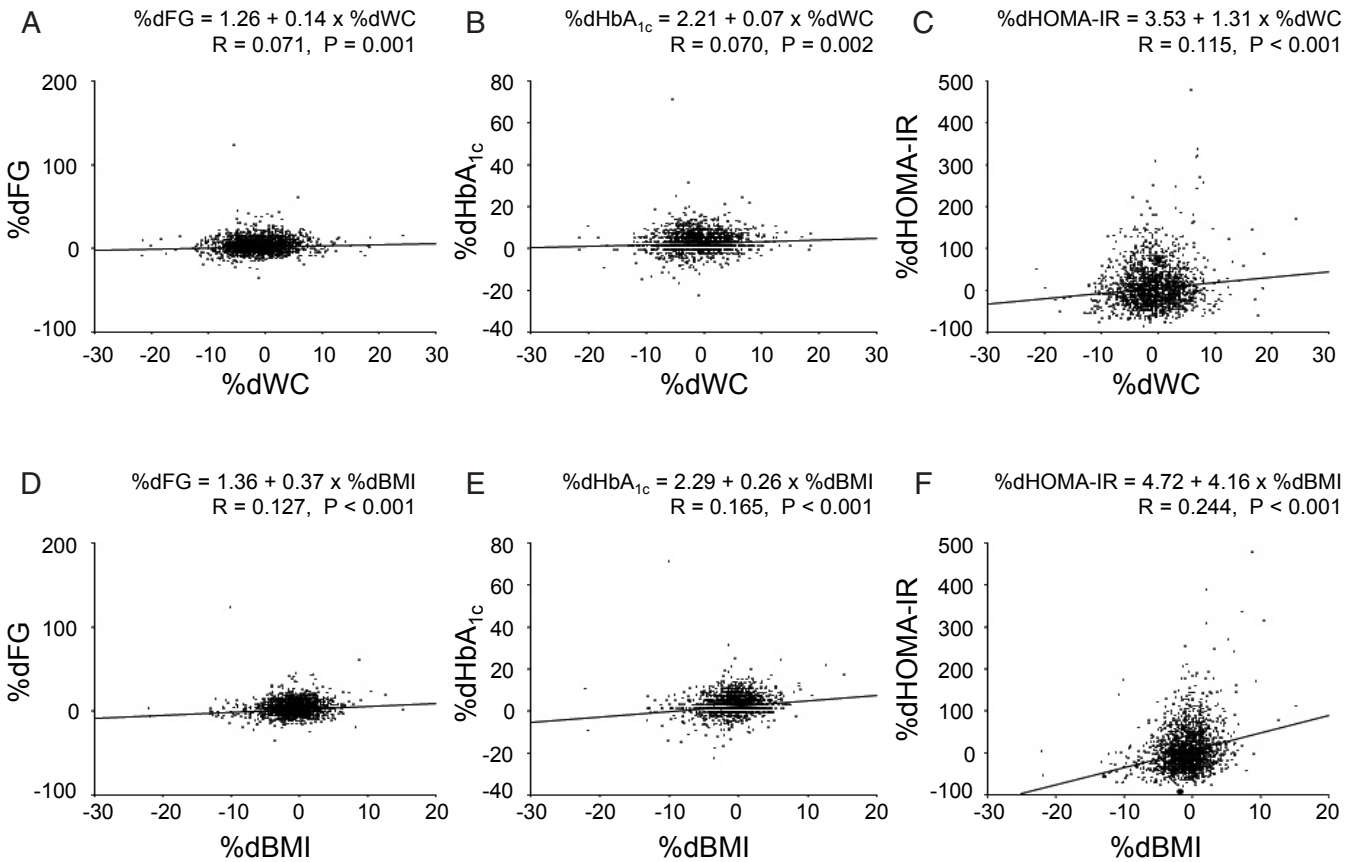

Fig. 2. Scatter plot and linear regression between %dWC and %dFG (A), %dHbA1c (B), and %dHOMA-IR (C) and between %dBMI and %dFG (D), %dHbA1c (E), and %dHOMA-IR (F) in men.

%dWC and %dBMI quartiles in **Table 1**. No statistically significant trends in the rate of anti-dyslipidemic medication or of current smoking were found across the four %dWC or %dBMI quartiles in either gender. The correlation coefficient between %dWC and %dBMI was 0.24 in women and 0.46 in men.

Association between Percent Changes in Obesity Parameters and Percent Changes in Diabetic Parameters

Scatter plots of %dWC and %dBMI versus %dFG, %dHbA1c and %dHOMA-IR, coupled with results of linear regression analyses, are shown in **Fig. 1** and **2**. In women, only the relationship between %dBMI and %dHOMA-IR was significant. In men, by contrast, the relationship was significant between both %dWC and %dBMI and the percent change in each of the diabetic parameters.

Fig. 3 and **4** show the percent changes in diabetic parameters according to the %dWC and %dBMI quartiles. In women, %dHOMA-IR increased with increasing %dBMI. In men, not only %dHOMA-IR but also %dFG and %dHbA1c increased with increasing %dWC and %dBMI.

Logistic Regression Analysis

A multivariate logistic regression analysis, adjusted for age at the first visit, of the second, third, and fourth %dBMI quartiles, showed that the first, second, third, and fourth %dBMI quartiles in men were associated with the highest %dHOMA-IR quartile (%dHOMA-IR >24.3%) with an odds ratio of 1.00 (reference), 1.47 (95%CI 1.08-2.01), 1.51 (95%CI 1.11-2.07), and 2.87 (95%CI 2.13-3.87), respectively. In women, on the other hand, the first, second, third, and fourth %dBMI quartiles were not significantly related to the highest %dHOMA-IR quartile (%dHOMA-IR >24.3%) with an odds ratio of 1.00 (reference), 1.23 (95%CI 0.82-1.85), 1.45 (95%CI 0.98-2.14), and 1.89 (95%CI 1.30-2.74), respectively.

Multivariate Linear Regression Analysis

In a multivariate linear regression analysis with age at the first visit and %dWC as independent vari-

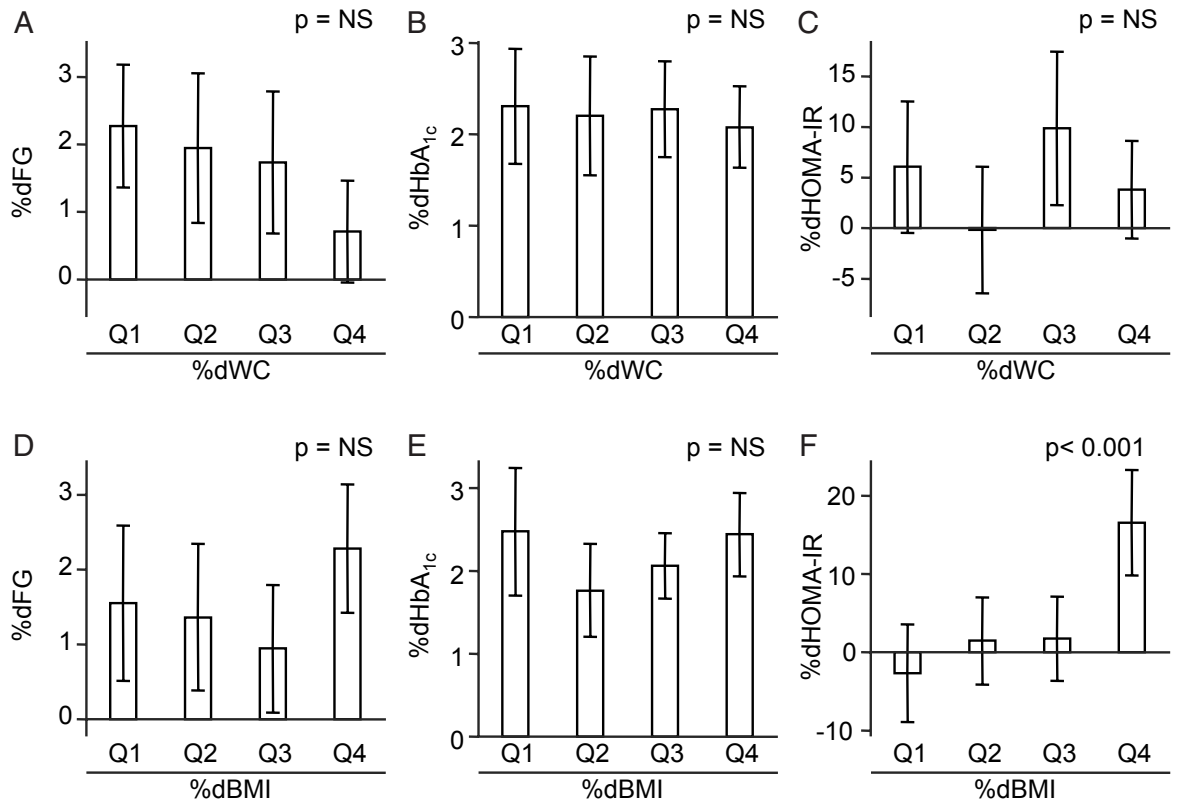

Fig. 3. %dFG (A), %dHbA1c (B), and %dHOMA-IR (C) according to %dWC quartiles, and %dFG (D), %dHbA1c (E), and %dHOMA-IR (F) according to %dBMI quartiles in women. The mean ± 95% confidence interval is shown in each group.

ables (**Table 2**, model 1), %dWC was an independent predictor for %dHOMA-IR in men, but not in women. However, when %dBMI was used as an additional covariate in the statistical model, %dWC did not remain significant (**Table 2**, model 2). In model 2, %dBMI was found to be an independent predictor for %dHOMA-IR, %dFG and %dHbA1c in men, but for only %dHOMA-IR in women.

Discussion

In the current study, we demonstrated that percent changes in obesity parameters (%dWC, %dBMI) were positively correlated with percent changes in glucose metabolism-related parameters (%dFG, %dHbA1c, %dHOMA-IR) in men. In women, by contrast, there was no significant relationship between %dWC and percent changes in diabetic parameters, and %dBMI was not significantly associated with %dFG or %dHbA1c. In the multivariate linear regression analysis, %dWC was a predictor for %dHOMA-IR in men, although it did not remain significant when %dBMI was used as an additional covariate in the statistical model, suggesting that changes in WC are not a predictor for changes in glucose-metabolism-related parameters independent of changes in BMI.

Obesity is associated with a cluster of specific metabolic abnormalities that may be related to cardiovascular risk factors[8, 12]. Wahrenberg *et al*. have reported that WC, which was found to be the strongest regressor among WC, BMI, log-plasma triglycerides, systolic blood pressure, and high-density lipoprotein cholesterol, is a risk factor for insulin resistance[13]. On the other hand, Onat *et al*. prospectively analyzed 1638 men and found that the age-adjusted waist-to-hip ratio (WHR) was significant in predicting diabetes mellitus[14]. Furthermore, Colditz *et al*. analyzed data from 114281 women who did not have diagnosis of diabetes mellitus, coronary heart disease, stroke, or cancer, and showed that BMI was the dominant predictor of risk for diabetes mellitus, although weight gain was also a risk factor for diabetes[15]. It has been shown that even small gains in weight during adulthood lead to a significantly increased risk of many chronic diseases[16]. Several studies showed that weight loss reduced regional depots of adipose tissue and

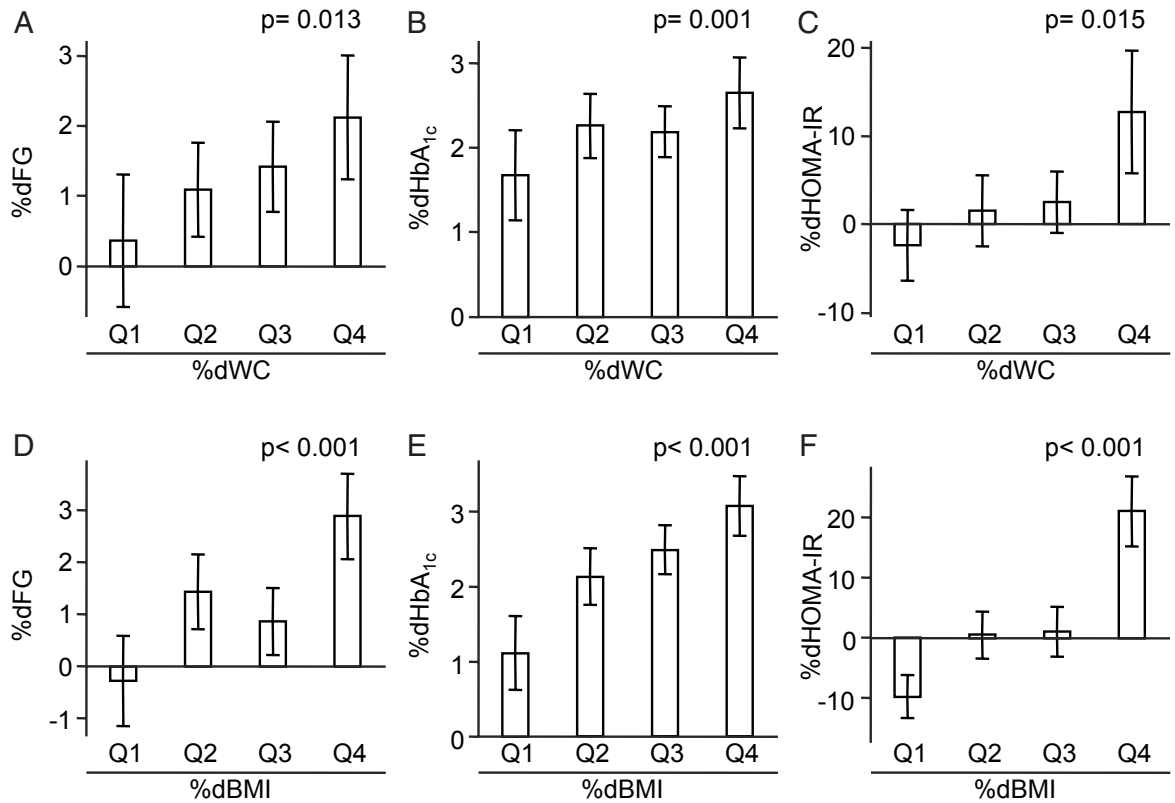

Fig. 4. %dFG (A), %dHbA1c (B), and %dHOMA-IR (C) according to %dWC quartiles, and %dFG (D), %dHbA1c (E), and %dHOMA-IR (F) according to %dBMI quartiles in men. The mean ± 95% confidence interval is shown in each group.

improved insulin sensitivity and cardiovascular risk factors[17, 18]. Pascale *et al.* analyzed 60 women and 33 men participating in a year-long weight loss program and concluded that improvements in FG, fasting insulin, and HbA1c were significantly related to weight loss[19].

Besides body weight, visceral fat has also been reported to be associated with β-cell function in individuals with impaired fasting glycemia and impaired glucose tolerance[9]. In general, BMI is strongly associated with subcutaneous fat area. As parameters of obesity, BMI and WC may have different meanings but similar associations. BMI may have a weaker association with visceral fat; by contrast, WC has a stronger correlation with visceral fat area in both genders[10]. It has been suggested that WC better reflects the accumulation of visceral fat than WHR[20, 21]. Therefore, it is possible that changes in WC have a stronger impact on changes in glucose metabolism as compared with changes in BMI.

In the current study, however, %dBMI was an independent factor predicting %dFG, %dHbA1c, and %dHOMA-IR in men, and %dHOMA-IR in women. %dWC was an independent factor predicting %dHOMA-IR in men, only without adjustment for %dBMI. Why %dBMI had a stronger association with %dFG, %dHbA1c and %dHOMA-IR is not clear.

Because Asian women are relatively lean, subcutaneous fat may have a relatively greater influence on WC[22]. For example, Sakurai *et al.* analyzed 2935 men and 1622 women between 35 and 59 years of age: in a multiple logistic regression analysis, WC was associated with FG in both genders. However, the risk ratio of having two or more metabolic disorders was higher for BMI than for WC in women, suggesting WC to be a relatively poor discriminator of visceral fat, and BMI to be a more appropriate index of total and abdominal fat, especially in women[22, 23].

It has recently been demonstrated that the association between WC and cardiovascular risk markers, such as insulin resistance, weakens with age[24]. Janssen *et al.* reported that, although individuals with a moderate and high WC were likely to have elevated cardiometabolic risk markers irrespective of age, there seemed to be a significant correlation between age and WC, indicating that the relation between WC and insulin

Table 2. Multivariate linear regression analysis between percent changes in diabetic parameters and age, %dWC, and %dBMI

		β	95% CI		Standardized β	p value
Women	Model 1					
	Dependent variable, %dFG					
	age	−0.02	−0.06	0.03	−0.02	0.494
	%dWC	−0.05	−0.10	0.01	−0.05	0.118
	Dependent variable, %dHbA$_{1c}$					
	age	−0.01	−0.04	0.01	−0.03	0.353
	%dWC	−0.02	−0.06	0.01	−0.04	0.181
	Dependent variable, %dHOMA-IR					
	age	0.00	−0.30	0.31	0.00	0.993
	%dWC	−0.06	−0.44	0.32	−0.01	0.753
	Model 2					
	Dependent variable, %dFG					
	age	−0.01	−0.06	0.03	−0.02	0.605
	%dWC	−0.06	−0.12	0.00	−0.06	0.059
	%dBMI	0.12	−0.03	0.27	0.05	0.119
	Dependent variable, %dHbA$_{1c}$					
	age	−0.01	−0.04	0.02	−0.03	0.374
	%dWC	−0.03	−0.06	0.01	−0.04	0.168
	%dBMI	0.02	−0.08	0.11	0.01	0.741
	Dependent variable, %dHOMA-IR					
	age	0.08	−0.22	0.38	0.01	0.610
	%dWC	−0.28	−0.67	0.10	−0.04	0.152
	%dBMI	2.41	1.42	3.40	0.14	<0.001
Men	Model 1					
	Dependent variable, %dFG					
	age	−0.02	−0.06	0.01	−0.03	0.223
	%dWC	0.14	0.05	0.22	0.07	0.002
	Dependent variable, %dHbA$_{1c}$					
	age	−0.01	−0.03	0.01	−0.03	0.250
	%dWC	0.07	0.03	0.12	0.07	0.002
	Dependent variable, %dHOMA-IR					
	age	−0.08	−0.29	0.14	−0.02	0.479
	%dWC	1.30	0.80	1.80	0.11	<0.001
	Model 2					
	Dependent variable, %dFG					
	age	−0.01	−0.05	0.02	−0.02	0.434
	%dWC	0.03	−0.07	0.13	0.02	0.544
	%dBMI	0.35	0.20	0.49	0.12	<0.001
	Dependent variable, %dHbA$_{1c}$					
	age	−0.01	−0.03	0.01	−0.01	0.592
	%dWC	−0.01	−0.06	0.04	−0.01	0.740
	%dBMI	0.26	0.18	0.34	0.17	<0.001
	Dependent variable, %dHOMA-IR					
	age	0.02	−0.19	0.23	0.00	0.840
	%dWC	0.02	−0.52	0.57	0.00	0.932
	%dBMI	4.15	3.33	4.97	0.24	<0.001

For model 1, independent variables include age at the first visit and %dWC. For model 2, independent variables include age at the first visit, %dWC, and %dBMI.

resistance was attenuated in the elderly[24]. With regard to our study, the mean age of the individuals enrolled was 51.9 years in women and 53.4 years in men at the first visit. We may have to analyze the relationship between %dWC or %dBMI and changes in glucose metabolism in a younger population in future studies. In addition, WC measurements may be less reliable or reproducible than weight and height measurements, which might relate to the finding that although %dWC is a predictor for the change in diabetic parameters, the correlation between %dWC and %dBMI was weaker in women, the latter of which is a predictor for the changes in diabetic parameters also in women.

In the current study, interestingly, there was a gender difference in the relationship between %dWC and changes in diabetic parameters. Wing *et al*. reported that the relationship between changes in WHR and changes in lipid parameters differed between women and men: they showed that changes in WHR were associated with changes in total cholesterol and triglycerides levels in men, but not in women[18].

Although we did not look into the mechanisms that may explain the differences in the association of changes in obesity indexes and those in glucose metabolism-related markers between men and women, several explanations may exist. Adipose tissue has been recognized as a significant endocrine organ that releases biologically important cytokines, such as adiponectin, leptin, and vaspin[25, 26]. In several clinical studies, certain gender differences have existed in the serum levels of such adipokines (adiponectin[27, 28], leptin[29], and vaspin[30]), which may account, in part, for the difference in the association between changes in obesity indexes and those in glucose metabolism-related parameters in the current study. Such sexual dimorphism in adipocytokines may be related to the difference in the levels of sex hormones, such as dehydro-epiandrosterone-sulphate (DHEAS), oestradiol, and testosterone[27, 31, 32].

We previously analyzed the relationship between percent changes in obesity parameters and percent changes in serum lipid parameters, uric acid, and systolic blood pressure[33-35]. We found that, as in the current study, the impact of %dBMI was greater than that of %dWC from the viewpoint of changes in serum uric acid and blood pressure.

Our study has several potential limitations. First, we enrolled only individuals who underwent a general health screening at our institute for 2 consecutive years. Second, we analyzed data from participants without considering alcohol consumption or the number of cigarettes smoked. Third, we excluded individuals who were taking antidiabetic drugs at either visit. It has been suggested that these individuals are generally more motivated to improve their own health than those who are not taking such drugs. In addition, a longer follow-up would be required to draw more convincing conclusions in future studies.

In summary, over a one-year period, %dBMI was found to be an independent predictor for %dHOMA-IR in both genders and for %dFG and %dHbA_{1c} only in men. Although %dWC was also associated with percent changes in these diabetic parameters, this relationship did not remain significant after controlling for %dBMI. Conversely, the relationship between %dBMI and percent changes in glucose-related metabolism parameters, especially in men, was independent of %dWC. These findings collectively suggest that controlling body weight, rather than WC, may be the primary target for improving glucose metabolism at least over a one-year period.

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