Visceral Fat Is a Major Contributor for Multiple Risk Factor Clustering in Japanese Men With Impaired Glucose Tolerance

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OBJECTIVE — The significance of abdominal visceral fat accumulation was evaluated in Japanese men with impaired glucose tolerance (IGT).

RESEARCH DESIGN AND METHODS — The IGT subjects (n = 123) were aged 55 ± 9 years with a BMI of 24 ± 3 kg/m^2. The 148 control subjects with normal glucose tolerance (NGT) were matched for age and BMI. IGT and NGT were classified according to the 1985 World Health Organization criteria. Abdominal fat distribution was analyzed by computed tomography at umbilical level. Plasma lipid, glucose, and insulin concentrations and blood pressure (BP) were measured.

RESULTS — In subjects with IGT, the average visceral fat area (VFA) was significantly greater than in subjects with NGT. Fasting insulin, the sum of insulin concentrations during an oral glucose tolerance test, insulin resistance according to a homeostasis model assessment for insulin resistance (HOMA-IR), systolic BP, and serum triglyceride were significantly higher, whereas the $\Delta I_{30-0}/\Delta G_{30-0}$ was significantly lower, in subjects with IGT. Subjects with IGT and NGT were then divided into three subgroups according to the number of risk factors they possessed (dyslipidemia, hypertension, neither, or both). In both IGT and NGT subjects, BMI, VFA, subcutaneous fat area, fasting insulin, HOMA-IR, and insulin secretion of the homeostasis model assessment were significantly higher in the double–risk factor subgroup than in the no–risk factor subgroup, and VFA was a potent and independent variable in association with the presence of a double risk factor.

CONCLUSIONS — Visceral fat accumulation is a major contributor for multiple risk factor clustering in Japanese men with IGT and NGT.

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In recent years, the frequency of type 2 diabetes and impaired glucose tolerance (IGT) has been increasing in Japan, reflecting changes in lifestyle and diet. Atherosclerotic vascular disease is well known to be among the most important prognostic factors in patients with type 2 diabetes or IGT (1,2). The frequency of microangiopathy is closely related to severity of glucose intolerance, whereas the prevalence of macroangiopathy, such as coronary artery disease in IGT, is nearly equal to that in type 2 diabetes (3,4). However, because IGT is defined only according to the oral glucose tolerance test (OGTT), various clinical states are included within this large, heterogeneous group. Consequently, identification of patients at particular risk for atherosclerosis among individuals with IGT is highly important. Recently, multiple risk factor–clustering syndromes, such as "syndrome X" and "the deadly quartet," which include glucose intolerance among the major factors, have received wide attention (5,6). Several studies have linked disproportionate accumulation of adipose tissue in the abdominal region, which is easily estimated by anthropometric measurements (such as waist circumference and waist-to-hip ratio), to these syndromes (7–11). We have demonstrated that in particular, intra-abdominal visceral fat accumulation, as detected by computed tomography (CT), is closely related to a clustering of many risk factors (12,13). Several studies, including our own, have demonstrated that visceral fat accumulation is one of the most important factors in the development of diabetes and coronary artery disease (14–16).

In the current investigation, we examined abdominal fat distribution using CT as well as clinical and metabolic characteristics in male subjects with IGT in order to determine whether visceral fat accumulation is a major contributor in the clustering of multiple factors for high atherogenic risk in IGT.

RESEARCH DESIGN AND METHODS

— The 271 subjects (123 case subjects and 148 control subjects) in this study were selected from 471 Japanese men who visited our affiliated hospitals and clinics from January 1999 to April

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Abbreviations: BP, blood pressure; CT, computed tomography; HOMA-IR, homeostasis model assessment for insulin resistance; HOMA-IS, homeostasis model assessment for insulin secretion; IGT, impaired glucose tolerance; NGT, normal glucose tolerance; OGTT, oral glucose tolerance test; SFA, subcutaneous fat area; VFA, visceral fat area; WHO, World Health Organization.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

2000 for medical consultation or a health examination, which included a physical checkup, routine collection of biochemical data, a 75-g OGTT, and a CT evaluation of body-fat distribution. The remaining 200 subjects were excluded from the study. Considering the influence of drugs on the related variables, some patients were excluded because they were taking medication for hypertension (41 subjects) or hyperlipidemia (17 subjects). After the exclusion of these subjects, we performed the subjects' selection for estimating the relation between IGT and normal glucose tolerance (NGT) subjects, who were strictly matched for age and BMI. The protocol for this research was reviewed and approved by the Research Group for Prevention and Epidemiology of Diabetes Mellitus in the Ministry of Health and Welfare. All subjects gave written informed consent before the study. Initially, subjects were classified as having NGT, IGT, or type 2 diabetes based on the results of a 75-g OGTT using World Health Organization (WHO) diagnostic criteria (17). NGT was defined as a fasting plasma glucose value <7.8 mmol/l and a 2-h plasma glucose value <7.8 mmol/l; IGT was defined as a fasting plasma glucose value <7.8 mmol/l and a 2-h plasma glucose value of 7.8–11.1 mmol/l; and diabetes was defined as a fasting plasma glucose value ≤7.8 mmol/l or a 2-h plasma glucose value ≤11.1 mmol/l. A total of 123 IGT subjects, aged 55 ± 9 years with BMI of 24 ± 3 kg/m^2, were selected along with 148 control subjects with NGT, who matched the IGT subjects for age and BMI.

Anthropometric measurements (height-,weight, and waist circumference) were made in a standing position after subjects removed their clothes, shoes, and socks. Waist circumference was measured at the level of the umbilicus during expiration. Blood pressure (BP) was measured in the right arm using a mercury manometer after subjects had briefly rested in a sitting position.

Abdominal fat distribution was determined with subjects in the supine position using CT according to our previously described procedure (18). Ordinary CT parameters were used, specifically 120 kV and 200 mA as well as a slice thickness of 5 mm, a scanning time of 2 s, and a field of view of 400 mm. The subcutaneous fat area (SFA) and intra-abdominal visceral fat area (VFA) were measured at the level of the umbilicus and determined by a standardized method with CT numbers. Briefly, a region of interest of the subcutaneous fat layer was defined by tracing its contour on each scan, and the attenuation range of CT numbers (in Hounsfield units) for fat tissue was calculated. A histogram for fat tissue was computed on the basis of mean attenuation ± 2 SD. Total and intraperitoneal tissue with attenuation within the mean ± 2 SD were considered to be the total fat area and VFA, and the SFA was defined by subtracting the VFA from the total fat area.

Laboratory methods

Blood was drawn after an overnight fast. A 75-g OGTT was performed, including blood sample collection at 0, 30, and 120 min for the determination of glucose and insulin concentrations. Plasma glucose was assayed by the glucose oxidase method, and serum insulin was assayed by double-antibody radioimmunoassay. The sums of the glucose and insulin concentrations during the OGTT were calculated as Σ glucose and Σ insulin. Serum total cholesterol and triglyceride concentrations were determined by enzymatic methods. HDL cholesterol was also measured by an enzymatic method after heparin and calcium precipitation. We used a homeostasis model assessment for insulin resistance (HOMA-IR) or a homeostasis model assessment for insulin secretion (HOMA-IS) and $\Delta I_{30-0}/\Delta G_{30-0}$ as a measure of early secretory response of insulin to an oral glucose load (19,20). The formulas used to calculate the HOMA-IR, HOMA-IS, and $\Delta I_{30-0}/\Delta G_{30-0}$ were as follows: HOMA-IR: [fasting insulin (pmol/l) × fasting glucose (mmol/l)]/135; HOMA-IS: [20 × (fasting insulin/7.175)/(fasting glucose − 3.5)]; $\Delta I_{30-0}/\Delta G_{30-0}$: [Δ insulin (30 min − 0 min)]/[Δ glucose (30 min − 0 min)].

A questionnaire concerning present status of receiving treatment for hypertension or dyslipidemia and past or current smoking habits, as well as a family history concerning diabetes, hypertension, and vascular disease (e.g., ischemic heart disease or cerebral infarction) among first- and second-degree relatives, were completed by each subject.

Risk factors were defined as dyslipidemia (a total cholesterol concentration >5.69 mmol/l, a triglyceride concentration >1.69 mmol/l, and/or an HDL cholesterol concentration <1.03 mmol/l) as well as hypertension (systolic BP >140 mmHg and/or diastolic BP >90 mmHg). The subjects were divided into three groups according to the number of risk factors they possessed. A subject with no risk factors was classified accordingly. A subject with one of the two risk factors was placed in the single–risk factor group, whereas a subject with both risk factors was placed in the double–risk factor group.

Data analysis

Results were expressed as the means ± SD. The significance of differences between average values of variables for IGT and NGT was determined by an unpaired Student's *t* test. Comparisons of several values (serum triglyceride, plasma insulin, Σ insulin during OGTT, HOMA-IR, HOMA-IS, and $\Delta I_{30-0}/\Delta G_{30-0}$) that were not normally distributed were performed using the Mann-Whitney *U* test. The difference in the fraction of subjects with risk factors was compared between IGT and NGT subjects using the χ^2 test. Differences between mean values of each variable between the no–risk factor, single–risk factor, and double–risk factor groups were assessed by Student's *t* tests. The frequency of a history of smoking or a family history of relevant diseases was compared between these three subgroups by a χ^2 test using a 2 × 3 contingency table. Linear regression analysis was used to study the relation between VFA and variables in the IGT and NGT groups, respectively. The influence of significant variables, including BMI, VFA, SFA, HOMA-IR, and HOMA-IS was determined by an unpaired Student's *t* test or the Mann-Whitney *U* test. Double–risk factor occurrence was tested by multinomial logistic regression analysis between the IGT and NGT subjects with no risk factors and double risk factors. $P < 0.05$ was considered to indicate statistical significance.

RESULTS — Table 1 presents the means ± SD for clinical, anthropometric, and metabolic variables in the subjects with IGT and the control subjects with NGT, who were matched with IGT subjects for age and BMI. Mean values for waist circumference and VFA were significantly higher in the IGT group. Although the mean value for SFA tended to be higher in IGT group, the difference was not statistically significant ($P = 0.065$). Fasting glucose, fasting insulin, and Σ

Table 1—*Clinical and anthropometric characteristics and metabolic profiles of male subjects with IGT compared with subjects with NGT, who were matched for age and BMI*

	NGT	IGT
n	148	123
age (years)	55 ± 9	55 ± 9
BMI (kg/m^2)	24 ± 3	24 ± 3
Waist circumference (cm)	85 ± 8	87 ± 7
VFA (cm^2)	105 ± 53	123 ± 55†
SFA (cm^2)	110 ± 46	121 ± 46
Fasting glucose (mmol/l)	5.29 ± 0.40	5.72 ± 0.51‡
Fasting Insulin (pmol/l)	39 ± 24	46 ± 26*
Σ Glucose during OGTT (mmol/l)	19.8 ± 2.1	24.2 ± 2.2‡
Σ Insulin during OGTT (pmol/l)	557 ± 316	643 ± 383*
$\Delta I_{30-0}/\Delta G_{30-0}$(pmol/mmol)	103 ± 11	54 ± 45‡
HOMA-IR	1.29 ± 0.83	1.63 ± 0.97‡
HOMA-IS	63 ± 39	59 ± 32
Total cholesterol (mmol/l)	5.11 ± 0.85	5.22 ± 0.96
Triglyceride (mmol/l)	1.51 ± 1.10	1.78 ± 1.27†
HDL-cholesterol (mmol/l)	1.27 ± 0.38	1.24 ± 0.41
Systolic BP (mmHg)	125 ± 20	131 ± 23*
Diastolic BP (mmHg)	76 ± 14	78 ± 16

Data are means ± SD. *$P < 0.05$, †$P < 0.01$, and ‡$P < 0.001$ versus NGT group by unpaired Student's *t* test or Mann-Whitney *U* test (fasting insulin, Σ insulin during OGTT, $\Delta I_{30-0}/\Delta G_{30-0}$, HOMA-IR, and HOMA-IS). Σ glucose during OGTT, sum of glucose levels (0, 30, and 120 min) during 75-g OGTT; Σ insulin during OGTT, sum of insulin levels (0, 30, and 120 min) during 75-g OGTT. $\Delta I_{30-0}/\Delta G_{30-0}$, HOMA-IR, and HOMA-IS were calculated by fomulas in RESEARCH DESIGN AND METHODS.

glucose and Σ insulin during the OGTT were significantly higher in the IGT group. The mean value of the $\Delta I_{30-0}/\Delta G_{30-0}$ was significantly lower and the mean value of HOMA-IR was significantly higher in the IGT group. Although the mean values of the systolic BP and serum triglycerides were significantly higher in the IGT group, total cholesterol, HDL cholesterol, and diastolic BP were not significantly different between the two groups.

Table 2 shows the means ± SD for the anthropometric and metabolic parameters as well as the frequency of subjects with a smoking history and a pertinent family history in the three subgroups of IGT subjects, defined by the number of risk factors (presence or absence of dyslipidemia and hypertension), as compared with those of the control subjects with NGT. The frequency of the subjects with the cluster of risk factors was significantly higher in the IGT group than in the NGT group ($P < 0.05$). In NGT and IGT subjects, mean values for BMI, waist circumference, VFA, and SFA were significantly higher in the double–risk factor group than in the no–risk factor group. The mean fasting glucose concentration was significantly higher in the single–risk factor group than in the no–risk factor group but did not differ between the double–risk factor group and the no–risk factor group in IGT subjects. In NGT and IGT subjects, fasting insulin concentration was significantly increased in the double–risk factor group, and Σ insulin during OGTT was significantly increased in the double–risk factor group in NGT

Table 2—*Clinical and metabolic characteristics in male NGT and IGT subjects with or without risk factors*

	NGT subjects (*n* = 148)			IGT subjects (*n* = 123)		
	No risk factor	Single risk factor	Double risk factor	No risk factor	Single risk factor	Double risk factor
n	54 (36)	78 (53)	16 (11)	28 (23)	72 (58)	23 (19)*
age (years)	55 ± 7	53 ± 10	57 ± 6	57 ± 9	54 ± 8	56 ± 10
BMI	22.7 ± 2.4	23.9 ± 2.5	25.5 ± 2.1†	23.7 ± 2.8	23.7 ± 2.5	25.5 ± 2.3‡
Waist circumference (cm)	83 ± 7	86 ± 8†	90 ± 6	85 ± 7	87 ± 7	90 ± 9§
VFA (cm^2)	83 ± 51	113 ± 48†	140 ± 56†	108 ± 51	117 ± 51‡	159 ± 59‡
SFA (cm^2)	99 ± 49	114 ± 43‡	130 ± 34‡	109 ± 43	119 ± 44	141 ± 52§
Smoking history	31 (57)	56 (72)	12 (75)	20 (71)	43 (60)	14 (61)
Family history						
Diabetes	6 (11)	13 (17)	4 (25)	3 (11)	16 (22)	9 (39)
Hypertension	9 (17)	25 (32)	9 (56)‖	8 (29)	21 (29)	10 (43)
Vascular disease	5 (9)	18 (23)	4 (25)	7 (25)	15 (21)	6 (26)
Fasting glucose (mmol/l)	5.32 ± 0.38	5.25 ± 0.37	5.31 ± 0.55	5.48 ± 0.41	5.85 ± 0.47†	5.63 ± 0.64
Fasting insulin (pmol/l)	33 ± 15	39.0 ± 25	61 ± 27†	36.7 ± 19.6	47.3 ± 28.6	51.1 ± 19.8§
Σ Glucose during OGTT (mmol/l)	19.8 ± 2.2	19.7 ± 2.1	19.9 ± 2.1	23.6 ± 2.0	24.5 ± 2.3	24.0 ± 2.1
Σ Insulin during OGTT (pmol/l)	472 ± 208	594 ± 372	685 ± 260‡	628 ± 420	631 ± 371	698 ± 388
$\Delta I_{30-0}/\Delta G_{30-0}$	88 ± 72	117 ± 134	85 ± 43	57 ± 41	50 ± 48	64 ± 40
HOMA-IR	1.08 ± 0.53	1.28 ± 0.90	2.02 ± 0.93†	1.25 ± 0.69	1.73 ± 1.1§	1.80 ± 0.74‡
HOMA-IS	51 ± 29	64 ± 39§	97 ± 54†	48 ± 23	56 ± 32	79 ± 34†

Data are *n* (%) or means ± SD. Risk factors: dyslipidemia and hypertension, which are defined in RESEARCH DESIGN AND METHODS. *$P < 0.05$ versus subjects with NGT by χ^2 test; †$P < 0.001$, ‡$P < 0.01$, and §$P < 0.05$ versus each no–risk factor group by unpaired Student's *t* test or Mann-Whitney *U* test (fasting insulin, Σ insulin during OGTT, $\Delta I_{30-0}/\Delta G_{30-0}$, HOMA-IR, and HOMA-IS); ‖$P < 0.01$ among three groups in NGT subjects by χ^2 test.

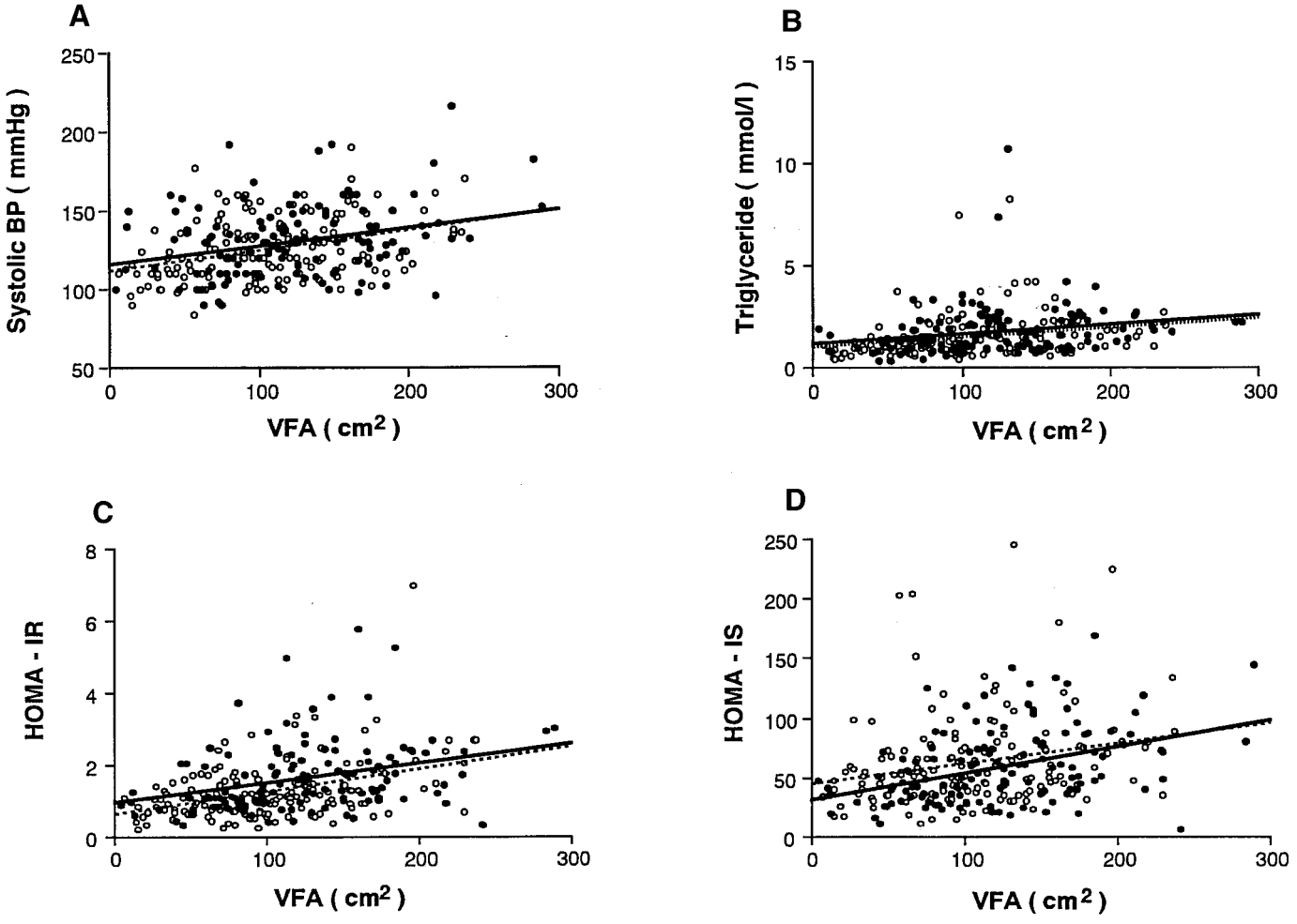

Figure 1—*Correlation between visceral fat area and systolic BP* (A) *(IGT:* r = *0.28,* P < *0.01; NGT:* r = *0.36,* P < *0.0001), serum triglyceride* (B) *(IGT:* r = *0.28,* P < *0.05; NGT:* r = *0.24,* P < *0.01), HOMA-IR* (C) *(IGT:* r = *0.32,* P < *0.001; NGT:* r = *0.40,* P < *0.0001), and HOMA-IS* (D) *(IGT:* r = *0.38,* P < *0.0001; NGT:* r = *0.23,* P < *0.01) in subjects with IGT* (●, n = *123) and NGT* (○, n = *148). The regression lines show a solid line as IGT and a broken line as NGT in each figure.*

subjects. HOMA-IR was significantly increased in both the single– and double–risk factor groups compared with the no–risk factor group, and HOMA-IS was significantly higher in the double–risk factor group compared with the no–risk factor group in IGT. In NGT subjects, HOMA-IR was significantly higher in the double–risk factor group, and HOMA-IS was significantly increased in both the single– and double–risk factor groups compared with the no–risk factor group. Although only the frequency of subjects with a history of hypertension was significantly higher in the double–risk factor group in NGT subjects, other differences in the frequency of smoking history or family history of hypertension or vascular disease were noted among the subgroups. However, the prevalence of subjects with a family history of diabetes had a tendency to be higher in the double–risk factor group ($P = 0.054$) than in the no–risk factor group in IGT subjects. Although there were no statistically significant parameters among the double–risk factor subgroups in IGT and NGT, HOMA-IS and $\Delta I_{30-0}/\Delta G_{30-0}$ tended to be lower in the double–risk factor subgroup in IGT ($P = 0.081$ for both).

Figure 1 shows the relation between VFA and systolic BP, serum triglycerides, HOMA-IR, and HOMA-IS in subjects with IGT and NGT. Significant and similar positive correlations between VFA and these variables were noted in both groups.

Multinominal logistic regression analysis between the no–risk factor group and the double–risk factor group in IGT or NGT subjects was performed to ascertain the influence of parameters, including BMI, VFA, SFA, HOMA-IR, and HOMA-IS on the presence of double risk factors, including hypertension and dyslipidemia. Only VFA was a significant independent predictor when interactions between parameters were considered in both groups ($P = 0.0015$ in IGT and $P = 0.045$ in NGT).

CONCLUSIONS—The current study clarified that VFA and waist circumference were significantly greater in subjects with IGT than in age- and BMI-matched subjects with NGT. Several previous studies, including our own, have demonstrated that there is a close relation between visceral fat accumulation and glucose intolerance (12,14,15). We confirmed this relation in subjects with mild

glucose intolerance. Furthermore, our subjects with IGT had both a significantly greater waist circumference and greater VFA, which correlates with the findings of Pouliot et al. (21), indicating a close relation between waist circumference and VFA. Accordingly, waist circumference might be used to predict VFA in subjects with IGT.

In the present study, various clinical and metabolic parameters were also compared between IGT and NGT. IGT was characterized by a higher fasting glucose level, a higher glucose response to an OGTT, hyperinsulinemia, increasing insulin resistance, and impairment of early-phase insulin response to a glucose load. Several previous studies in Western countries demonstrated that IGT is not only associated with an impairment of early-phase insulin secretion but also with hyperinsulinemia resulting from insulin resistance, which is in agreement with our study (22–24). On the other hand, Matsumoto et al. (25) reported that impairment of early-phase insulin secretion may be an important factor in the development of IGT, but total insulin secretion and insulin resistance are not associated with early progression of glucose intolerance in obese and nonobese Japanese subjects. Their subjects were not matched for age, and NGT subjects were significantly younger than IGT subjects. Furthermore, they did not evaluate the subjects' fat distribution. We had previously reported that aging is one of the most important factors for visceral fat accumulation (26) and showed, in the current study, a positive correlation between visceral fat accumulation and the parameter of insulin resistance or insulin secretion; therefore, these differences may cause this distinction. However, both studies are cross-sectional, and further prospective studies in Japanese subjects will be needed. Although mean systolic BP and serum triglyceride were significantly higher in IGT subjects, mean values of other parameters, including diastolic BP, serum total cholesterol, and HDL cholesterol were not statistically different between groups. However, when we examined these variables according to number of associated risk factors, specifically dyslipidemia and hypertension, the double–risk factor frequency was significantly higher in IGT than in NGT subjects. One reason for the similarity of mean values could be because IGT and NGT subjects were strictly matched for BMI. Other possibilities are that the abnormality of each parameter may be mild in the IGT subjects investigated and that IGT itself is a heterogeneous category.

We also investigated the characteristics of the IGT and NGT subjects who simultaneously possessed dyslipidemia and hypertension, i.e., multiple risk factor–clustering syndrome. Although both subgroups with double risk factors had a high BMI, a large waist circumference, and large subcutaneous and visceral fat volumes, the most remarkable finding among them was a marked accumulation of intra-abdominal visceral fat. Glycemic control was not evidently worse in these subgroups, but insulin resistance was exacerbated. Many studies have compared clinical features between IGT and type 2 diabetes or NGT, but the present study is one of only a few to consider subgroups of IGT and NGT. We determined that VFA was the most powerful factor for identifying members of IGT and NGT subgroups with the cluster of risk factors. We previously demonstrated that a close correlation exists between visceral fat accumulation and hyperlipidemia or hypertension in obesity and also that insulin resistance is more severe in visceral fat obesity than in subcutaneous fat obesity (12,13, 27). In the current study, we also established that in male Japanese subjects with IGT, increased visceral fat is related to an increase in BP and serum triglyceride as well as a worsening of insulin resistance but not to impairment of insulin secretion. Furthermore, it was a remarkable finding that NGT subjects with double risk factors had almost the same characteristics as IGT subjects with double risk factors, suggesting that visceral fat accumulation rather than the deterioration of glucose metabolism may be important for risk factor clustering. It is also of interest to observe whether this NGT subgroup develops IGT or diabetes in the near future. Recently, Pascot et al. (24) demonstrated in a similar study that visceral fat accumulation is an important factor in the deterioration of the lipid profile in Canadian men with IGT. In that study, the IGT subjects were mainly obese and were compared with NGT subjects who were not matched for BMI. The prevalence of obesity, defined by the WHO as BMI $\geq$30 kg/m^2, is no more than 2–3% of the Japanese population, whereas it is 10–20% in Europe and the U.S. (28,29). Thus, the striking feature of obesity in Japan is that the degree of obesity is mild. Moreover, the Japanese are more sensitive to glucose loading than Caucasians when exposed to overnutrition and are thus liable to develop glucose intolerance, even with a mild excess of adiposity (30,31). Consequently, we needed to evaluate the differences between IGT and NGT subjects who were strictly matched for BMI. Although the mean BMI of the subjects was normal by the WHO criteria, lower cutoffs for obesity should be used in Japanese populations. Recently, Fujimoto et al. (32) also prospectively demonstrated that in Japanese-American individuals, the prevalence of coronary artery disease was ~30% during a 10-year interval, whereas plasma glucose and BP were potent independent risk factors along with visceral fat accumulation. This suggests that our IGT subjects with multiple risk factors, predicted by VFA, may have a high atherogenic risk because they have a similar genetic background. However, further prospective studies will be necessary to clarify whether atherosclerotic disease actually occurs more often in subjects with apparent high risk.

Identifying which subgroup of IGT subjects is likely to develop overt diabetes is another interesting problem. Whether metabolic characteristics such as increased insulin resistance or decreased insulin secretion indicate likelihood of overt diabetes is controversial. A recent prospective study (33), in which Mexican-Americans were followed-up for 7 years, demonstrated that converters from the prediabetic state to type 2 diabetes showed greater insulin resistance and atherogenic risk at baseline than nonconverters. On the other hand, previous studies in Japan (25,34) have suggested that decreased insulin secretion rather than increased insulin resistance may be chiefly responsible for deterioration to IGT and type 2 diabetes. One explanation for this difference may be differing genetic predisposition. The insulin-secreting capacity of pancreatic β-cells in Japanese individuals may be smaller than in Caucasians. Chen et al. (35) demonstrated that earlier impairment of insulin secretion and subsequent increases in visceral fat contributed to the development of diabetes in initially nondiabetic Japanese-American men. In the present study, we found that the prevalence of the subjects with a family history of diabetes tended to

be relatively high in the double-risk group, which was associated with increased insulin resistance and insulin secretion; however, no differences in the degree of decrease in early response of insulin secretion to oral glucose load were observed among these subgroups. We suspect that in further follow-up of the IGT subjects, the subjects in the double–risk factor group may develop overt diabetes more often than subjects in the no–risk factor group. Further prospective studies will be needed to draw a firm conclusion.

In conclusion, we demonstrated that visceral fat accumulation is a major contributor for the clustering of multiple risk factors in Japanese men with IGT and NGT.

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