

Clinical Usefulness of the Thickness of Preperitoneal and Subcutaneous Fat Layer in the Abdomen Estimated by Ultrasonography for Diagnosing Abdominal Obesity in Each Type of Impaired Glucose Tolerance in Man

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Abstract. For this study we enrolled 1,615 males who were admitted to our hospital for a general health check-up. Plasma glucose (PG) and insulin were measured during 75 g OGTT, and abdominal obesity was assessed by ultrasonography in all subjects. We divided them into several groups: normal glucose tolerance (NGT), high-normal glucose tolerance (h-NGT) who showed >10.0 nmol/l at 1 hr PG among those with NGT, impaired fasting glucose (IFG), impaired glucose tolerance (IGT), IFG + IGT, and DM, according to the results of 75 g OGTT. The aim of the present study was to clarify the clinical characteristics of pre-diabetic disorders relating to metabolic syndrome by comparing various parameters including body mass index (BMI), blood levels of various lipids and abdominal wall fat index (AFI) calculated from the thickness of preperitoneal (Pmax) and subcutaneous (Smin) fat layer in the abdomen estimated by ultrasonography with insulin sensitivity determined by homeostatic model assessment (HOMA-IR) in each type of abnormal glucose regulation as classified by PG changes in 75 g OGTT. We also investigated the relationship between insulin secretion capability and insulin sensitivity to delineate the characteristics of each type of abnormal glucose regulation, and compared the area under the insulin curve (AUCins) and the time axis, and the ability of early insulin secretion by glucose loading (insulinogenic index: I.I.) in each type of abnormal glucose regulation. There was a significant positive correlation between HOMA-IR and Smin or Pmax, suggesting that Smin and Pmax may reflect insulin sensitivity. Abdominal obesity, which was diagnosed from the data of AFI, was present in the h-NGT and IFG + IGT groups, suggesting that those groups belong to the clinical entity of metabolic syndrome. HOMA-IR was higher in IFG than in IGT, although I.I. was reduced and AUCins was increased in IFG as well as in IGT. h-NGT demonstrated a slightly lower I.I. and higher AUCins, compared with IGT. IFG demonstrated much stronger insulin resistance than IGT, although I.I. was reduced and AUCins was increased in IFG and IGT. Thus, it is suggested that insulin sensitivity may partly account for the difference in pathogenesis between IFG and IGT; and that h-NGT, which showed abdominal obesity assessed as AFI by ultrasonography, should be recognized as a disease state of metabolic syndrome with impaired glucose regulation.

Key words: Abdominal wall fat index (AFI), Insulin resistance, Insulin secretion, Impaired glucose regulation
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METABOLIC syndrome is now accepted as an important disorder, inducing cerebro-cardiovascular events

such as cerebral infarction and myocardial infarction [1]. It is widely accepted that insulin resistance is the main pathogenesis of metabolic syndrome, although various abnormalities including abnormal glucose regulation, hypertension, dyslipidemia and abdominal obesity are usually observed in this clinical entity. We have already reported that abdominal wall fat index (AFI) reflects metabolic disorders such as lipid metabolism and glucose metabolism disorders [2]. Thus,

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we attempted to clarify the effect of abdominal obesity examined by the thickness of the preperitoneal and subcutaneous fat layer in the abdomen estimated by ultrasonography (abdominal wall fat index: AFI) instead of waist circumference on insulin sensitivity determined as HOMA-IR in various types of abnormal glucose regulation classified by the PG changes in 75 g OGTT, and also to investigate the relationship between insulin secretion capability and insulin sensitivity to delineate the characteristics of each type of impaired glucose regulation in patients who underwent a general health check-up.

The American Diabetes Association (ADA) [3] and the World Health Organization (WHO) [4] have revised the diagnostic criteria of diabetes and glucose intolerance, so as to include impaired fasting glycemia (IFG), impaired glucose tolerance (IGT), IFG + IGT, and DM. Insulin resistance and impaired secretion occur in the progression toward diabetes and glucose intolerance, but it is unclear which defect arises first [5, 6] and which relates to either IFG or IGT, which reflect different alterations in glucose homeostasis [7]. Although some studies reported that subjects with IFG have hyperinsulinemia and/or worsening of insulin resistance, those with IGT have a defective secretion in response to glucose loading [8–10]. Other studies demonstrate a pronounced defect in early insulin secretion in IFG and marked insulin resistance in IGT [11–13]. Thus, the characteristics of metabolic abnormalities of IFG, compared with IGT, remain to be elucidated.

With the above background, we conducted a study on subjects who had an overnight hospital stay and comprehensive health check between 1991 and 1998. From the time course of 75 g OGTT, the subjects were classified by the WHO and ADA criteria. In addition, we divided the subjects with normal glucose tolerance (NGT) into two groups: high NGT (h-NGT) showing >10.0 mmol/l at 1 hr PG, and NGT demonstrating completely normal PG during 75 g OGTT, according to the criteria of the Japan Diabetes Society (JDS) [14].

The aim of this study was to clarify the clinical characteristics of pre-diabetic disorders relating to metabolic syndrome by comparing various parameters including the body mass index (BMI), blood levels of various lipids and abdominal wall fat index (AFI) with insulin sensitivity determined as HOMA-IR in each type of abnormal glucose regulation as classified by PG changes in 75 g OGTT, and also to investigate the relationship between insulin sensitivity and the insulin secretion

capability to delineate the characteristics of each type of impaired glucose regulation.

Subjects and Methods

The study was performed in the general internal medicine ward with in-patient facilities of Yokohama Rosai Hospital. Those enrolled were subjects admitted for two consecutive days between 1991 and 1998, who underwent a general health check-up to screen for cerebro-cardiovascular disorders, gastrointestinal diseases, and metabolic abnormalities. As a baseline, we measured body composition, and performed blood analysis of the liver and kidney functions in addition to lipid concentrations. We enrolled 1,615 males, with an age distribution (mean \pm SD: 54.7 ± 11.0 years old) ranging from 19 to 89 years old. The distribution of the body mass index (BMI) (mean \pm SD: 23.7 ± 2.8 kg/m²) was as follows; 4 subjects showing <16 of BMI; 20 subjects between 16 and 18 of BMI; 105 subjects between 18 and 20 of BMI; 309 subjects between 20 and 22 of BMI; 472 subjects between 22 and 24 of BMI; 408 subjects between 24 and 26 of BMI; 184 subjects between 26 and 28 of BMI; 81 subjects between 28 and 30 of BMI; 26 subjects between 30 and 32 of BMI; 4 subjects between 32 and 34 of BMI; 2 subjects between 34 and 36 of BMI. None was taking medication affecting glucose or insulin metabolism.

Using ADA and WHO criteria [3, 4] we classified patients into five groups based on glycemic values expressed in mmol/l: 1) NGT with FPG <6.1 and 2-hr PG <7.8 ; 2) IFG (FPG 6.1–6.9 and 2-hr PG <7.8); 3) IGT (FPG <6.1 and 2-hr PG 7.8–11.1); 4) IFG + IGT (FPG 6.1–6.9 and 2-hr PG 7.8–11.1); and 5) DM with FPG >7 and/or 2-hr PG >11.1 . In addition, we divided the subjects with NGT into two groups: h-NGT showing more than 10.0 mmol/l at 1-hr PG with normal PG at 30 min, 90 min and 120 min during 75 g OGTT, and NGT demonstrating completely normal PG in each time during 75 g OGTT.

PG concentrations were determined by the glucose oxidase method, and serum immunoreactive insulin (IRI) concentrations using a radioimmunoassay kit (Eiken Chemical Co., Tokyo). Plasma glycohemoglobin A1c (HbA1c) was determined by high performance liquid chromatography. Serum concentrations of cholesterol and triglycerides were analyzed in a Nippon Denshi autoanalyzer (JCA-RX20, Tokyo, Japan). HDL-

cholesterol was measured by the heparin-manganese method. LDL-cholesterol was calculated using the following formula: LDL-cholesterol = (total cholesterol) – (HDL-cholesterol) – (triglycerides/5).

On the morning of OGTT, we measured BMI (kg/m^2) and the thickness of the preperitoneal and subcutaneous fat layer estimated by abdominal ultrasonography as an index of body fat distribution instead of waist circumference (Fig. 1) [2]. AFI was estimated by calculating the ratio of Pmax to Smin [2]. We calculated insulin resistance from fasting glucose and insulin concentrations using homeostatic model assessment (HOMA-IR) [13]. HOMA-IR is directly related to insulin resistance and is calculated as follows: $\{\text{fasting insulin } (\mu\text{U}/\text{ml}) \times \text{fasting glucose } (\text{mg}/\text{dl})\} / 405$. The area under the glucose curve and the time axis (values before glucose loading, at 30 min, 60 min, 90 min and 120 min) and the area under the insulin curve and the time axis were calculated and designated as the glucose area (AUC_{glucose}) and insulin area (AUC_{ins}), respectively [15]. The insulinogenic index (I.I.) is well known to reflect the function of early insulin secretion induced by glucose from the pancreas, and was calculated using the following formula: the ratio of the net increase of IRI determined from the value of 0 min-IRI subtracted from 30 min-IRI, to the net increase of PG determined from the value of 0 min-PG subtracted from 30 min-PG.

Statistical analyses

Values were expressed as mean \pm SD or SE. Continuous variables were compared by unpaired Student's *t* test. A computer program (SAS) was used in all analyses. Results were considered statistically significant when P values were less than 0.05.

Results

1. Correlation between HOMA-IR and various parameters

Various clinical parameters including age, BMI, blood levels of total cholesterol, triglycerides, HDL-cholesterol, LDL, HbA1c, GOT, GPT, and each parameter of Smin, Pmax and AFI estimated by ultrasonography were compared with HOMA-IR (Table 1A and B). There was a significant positive correlation between HOMA-IR and BMI or blood levels of total cholesterol, triglycerides, HbA1c, GOT and GPT, while there was a significant negative correlation between HOMA-IR and HDL-C level (Table 1A). There was a significant positive correlation between HOMA-IR and Smin or Pmax, although AFI was negatively correlated with HOMA-IR (Table 1B). R value of correlation between HOMA-IR and AFI was very small such as -0.06512 (Table 1B). Those data apparently

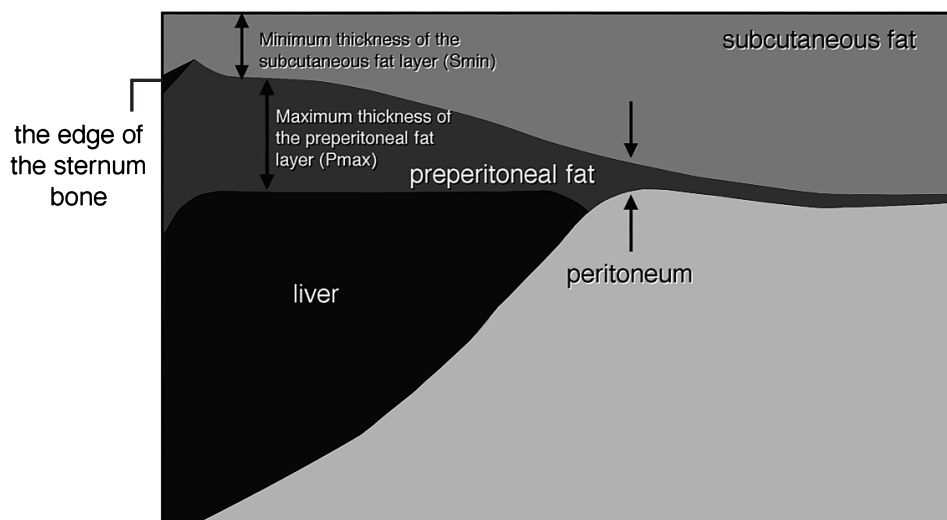


Fig. 1. Measurement of thickness of the preperitoneal and subcutaneous fat layer by abdominal ultrasonography. Abdomen is sagittally scanned from the end of sternum to navel by ultrasonography. Maximum thickness of the preperitoneal fat layer (Pmax) and minimum thickness of the subcutaneous fat layer (Smin) are estimated.

Table 1.**A.** Co-relationship between HOMA-IR and various parameters in 1615 subjects

		Age	BMI	TC	TG	HDL-C	LDL-C	HbA1c	GOT	GPT
HOMA-IR	R=	0.02809	0.28557	0.08756	0.22539	-0.11652	0.00579	0.42861	0.14955	0.26075
	P=	0.2597	<0.0001	0.0004	<0.0001	<0.0001	0.8165	<0.0001	<0.0001	<0.0001

B. Co-relationship between HOMA-IR and the thickness of the maximum preperitoneal (Pmax) and the minimum subcutaneous (Smin) fat layer, or the ratio of Pmax to Smin (AFI) in 1615 subjects

		Smin	Pmax	AFI
HOMA-IR	R=	0.17847	0.11485	-0.06512
	P=	<0.0001	<0.0001	0.0098

Table 2. Regression analysis of each parameter including Smin, Pmax and AFI, affecting on HOMA-IR of which value was log transformed.

Parameter	R-Square
Smin	0.0592
Pmax	0.0235
AFI	0.0114

Statistical analysis was done as described below.

HOMA-IR was log10 transformed to approximately normal distribution.

Correlations between the variables were calculated using Pearson's correlations. Logistic regression analyses were performed to determine which variables were related to the values of HOMA-IR, and R-Square was calculated.

mean that the linearity of co-relationship between HOMA-IR and AFI is almost flat so as to be virtually parallel to X-axis. Thus we further analyzed each value of Smin, Pmax and AFI in order to estimate the most effective factor contributing to HOMA-IR by R-square selection methods (Table 2). The proportions of Smin, Pmax and AFI contributing to the value of HOMA-IR as a determinant factor were 5.92%, 2.35% and 1.14%, respectively. Thus, Smin is the strongest effective factor influencing HOMA-IR, other than Pmax and AFI.

2. Classification of all subjects according to the response of PG to 75 g OGTT

The response of PG and IRI to 75 g OGTT was examined in all subjects, according to the methods described in detail above (Fig. 2). There were 1,615 males, comprising 558 cases (34.6%) of NGT, 273 cases (16.9%) of h-NGT, 448 cases (27.2%) of IGT, 28 cases (1.7%) of IFG + IGT, 19 cases (1.2%) of IFG,

and 289 cases (17.9%) of DM (Table 3).

The comparison of age, BMI, blood pressure (BP), HbA1c, Smin, Pmax, AFI, FPG, IRI, AUC glucose, and serum lipid levels among each type is shown in Table 3. BMI in IGT, IFG + IGT, IFG, and DM was significantly greater than that in NGT. AFI in h-NGT and IFG + IGT was significantly higher than that in NGT. Smin in h-NGT was significantly lower than that in NGT. Triglycerides level in IGT, IFG + IGT, IFG, and DM was significantly higher than that in NGT. Systolic and diastolic BP was significantly higher in IFG + IGT, IFG and DM than in NGT, and diastolic BP was also significantly higher in IGT than in NGT.

3. Comparison of I.I., HOMA-IR and AUCins during 75 g OGTT in various groups

I.I. was significantly lower in DM, IFG, IFG + IGT, IGT and h-NGT, compared with NGT, and the index was in descending order of NGT>IGT>IFG>h-NGT>IFG + IGT>DM. I.I. was also significantly decreased in h-NGT, compared with that in IGT (Table 4).

When comparing the total insulin secretion during OGTT (AUCins), AUCins was significantly increased in IGT and h-NGT, but was significantly decreased in DM, compared with NGT (Table 4).

HOMA-IR, reflecting the state of insulin resistance, was significantly higher in IFG + IGT, IFG and DM than that in NGT (Table 4).

4. Characteristics of h-NGT

We analyzed various parameters including I.I., AUCins, Smin, Pmax, AFI, HbA1C, BMI and HOMA-IR for detecting the strongest determinant ex-

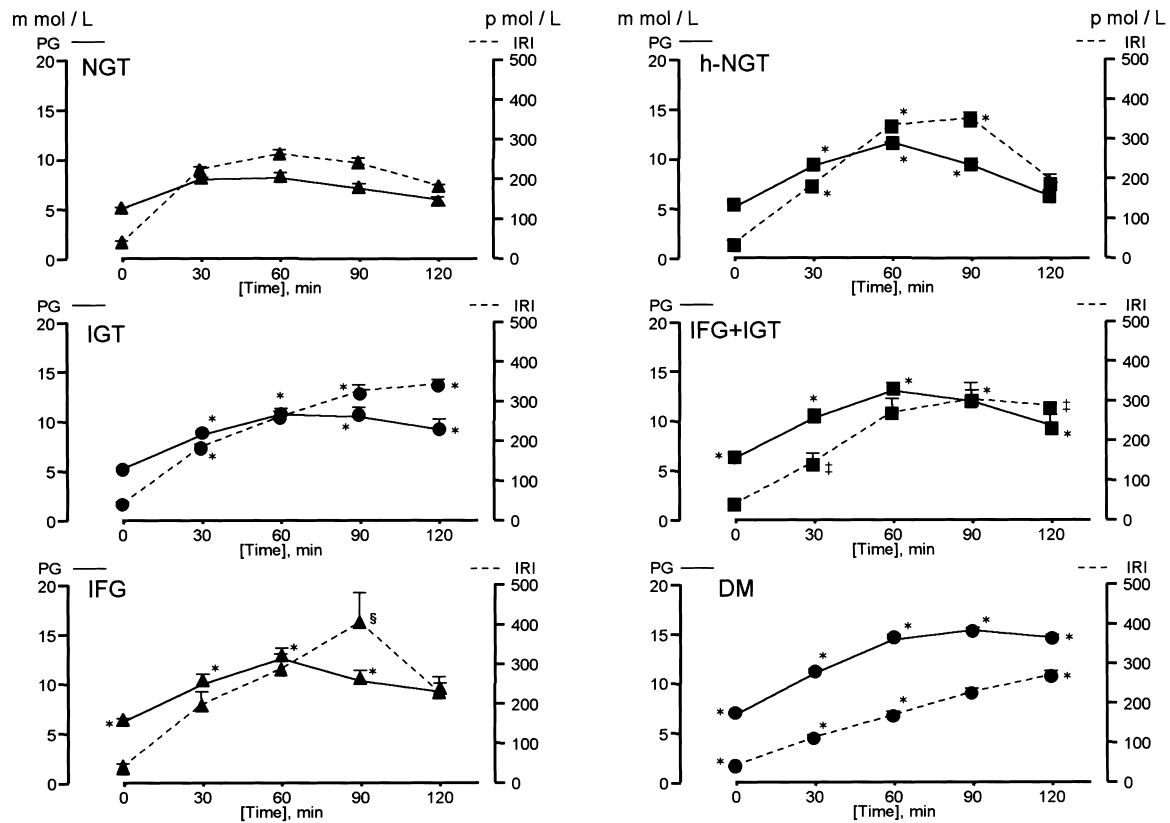


Fig. 2. Time course of plasma glucose (PG) and insulin (IRI) during 75 g OGTT in each type of all subjects. Vertical bars indicate mean \pm SE, and the solid and dotted lines express PG and IRI levels, respectively. * $p < 0.0001$, † $p < 0.01$, § $p < 0.05$, vs NGT

Table 3. Comparison of baseline variables according to each type, classified by 75 g OGTT

Variables	NGT	h-NGT	IGT	IFG + IGT	IFG	DM
Number of cases	558	273	448	28	19	289
Age (years old)	53.2 \pm 11.4	53.2 \pm 10.6	55.2 \pm 10.9 [‡]	56.1 \pm 9.1	53.9 \pm 10.1	57.8 \pm 9.8 [†]
BMI (kg/m ²)	23.1 \pm 2.6	23.5 \pm 2.7	23.8 \pm 2.8 [†]	25.2 \pm 1.4 [†]	25.0 \pm 2.7 [‡]	24.6 \pm 3.0 [†]
BP (mmHg)	124.0 \pm 17.8/ 77.6 \pm 10.4	125.4 \pm 17.3/ 78.6 \pm 10.6	128.3 \pm 17.8/ 80.0 \pm 10.9**	135.1 \pm 21.5 [‡] / 83.6 \pm 10.6 [‡]	132.8 \pm 21.8*/ 82.6 \pm 12.1*	132.2 \pm 19.0 [†] / 81.5 \pm 11.4 [†]
Smin (mm)	7.439 \pm 2.647	6.873 \pm 2.649 [‡]	7.584 \pm 2.567	7.052 \pm 2.767	7.316 \pm 2.595	7.706 \pm 2.707
Pmax (mm)	7.287 \pm 2.701	7.221 \pm 2.729	7.521 \pm 2.731	7.341 \pm 2.265	8.147 \pm 2.750	7.493 \pm 2.717
AFI (ratio)	1.049 \pm 0.408	1.138 \pm 0.485 [‡]	1.048 \pm 0.364	1.224 \pm 0.856*	1.194 \pm 0.437	1.044 \pm 0.423
FPG (mmol/l)	4.98 \pm 0.39	5.11 \pm 0.44 [#]	5.09 \pm 0.44 [#]	6.36 \pm 0.24 [†]	6.33 \pm 0.18 [†]	6.81 \pm 2.06 [†]
IRI (pmol/l)	37.2 \pm 16.8	36.0 \pm 31.8	39.6 \pm 21.0	40.8 \pm 19.2	41.4 \pm 12.0	44.4 \pm 19.8 [†]
HbA1c (%)	5.0 \pm 0.5	5.1 \pm 0.5	5.1 \pm 0.5*	5.3 \pm 0.5*	5.3 \pm 0.6	6.3 \pm 1.6 [†]
AUC glucose (mmol/l·min)	845.25 \pm 97.64	1,055.13 \pm 98.14	1,098.99 \pm 135.28 [†]	1,288/23 \pm 132.11	1,164.88 \pm 166.36 [†]	1,520.09 \pm 348.16 ^{†#}
Total cholesterol (mmol/l)	5.24 \pm 0.92	5.23 \pm 0.99	5.36 \pm 0.89*	5.40 \pm 0.85	5.18 \pm 1.47	5.43 \pm 1.09 [‡]
Triglycerides (mol/l)	1.34 \pm 0.76	1.47 \pm 0.97	1.64 \pm 1.05 [†]	1.86 \pm 1.19*	1.94 \pm 1.40*	2.02 \pm 1.90 [†]
HDL-C (mmol/l)	1.36 \pm 0.37	1.38 \pm 0.41	1.33 \pm 0.37	1.46 \pm 0.53	1.36 \pm 0.49	1.28 \pm 0.36 [‡]
LDL-C (mmol/l)	3.26 \pm 0.86	3.17 \pm 1.00	3.28 \pm 0.83	3.09 \pm 0.81	2.92 \pm 1.39	3.21 \pm 1.00

Results are expressed as Mean \pm SD.

[†] $p < 0.0001$, ** $p < 0.001$, [‡] $p < 0.01$, * $p < 0.05$, vs NGT

[#] $p < 0.0001$, ^{||} $p < 0.05$, vs IFG

Table 4. Comparison of insulinogenic index (I.I.), AUCins, HOMA-IR among all subjects with NGT, h-NGT, IGT, IFG + IGT, IFG and DM

	NGT	h-NGT	IGT	IFG + IGT	IFG	DM
AUCins ($\times 10^3$ pmol/l·min)	25.42 \pm 15.19	29.83 \pm 16.88*	29.09 \pm 17.42*	26.50 \pm 17.04	30.96 \pm 16.62	20.23 \pm 11.02*
I.I. (pmol/l per mmol/l)	74.81 \pm 71.39	37.66 \pm 29.30* [§]	45.63 \pm 41.58*	28.77 \pm 25.20*	41.28 \pm 31.07	18.73 \pm 21.54*
HOMA-IR	1.37 \pm 0.65	1.37 \pm 1.20	1.47 \pm 0.81	1.93 \pm 0.97	1.94 \pm 0.57 [†]	2.29 \pm 1.43*

Results are expressed as Mean \pm SD.

* $p < 0.0001$, $^{\dagger}p < 0.001$, $^{||}p < 0.01$, $^{\ddagger}p < 0.05$, vs NGT

$^{\S}p < 0.05$, vs IGT

Table 5. Multivariate logistic regression analysis of each parameter including I.I., AUCins, Smin, Pmax, AFI, HbA1C, BMI and HOMA-IR, in relation to difference in blood glucose level at 60 min during 75 g OGTT between NGT and h-NGT

Parameter	Odds ratio	(95% CI)	P value
I.I.	0.002	(<0.001 – 0.006)	<0.0001
AUCins	1.001	(1.000 – 1.001)	<0.0001
BMI	1.134	(1.047 – 1.228)	0.0019
HOMA-IR	0.198	(0.071 – 0.554)	0.0020
HbA1c	1.410	(0.965 – 2.060)	0.0755
Smin	0.906	(0.764 – 1.075)	0.2578
AFI	1.207	(0.469 – 3.107)	0.6959
Pmax	1.025	(0.875 – 1.200)	0.7630

Multiple logistic regression analyses were performed to determine which variables were related to difference in blood glucose level at 60 min during 75 g OGTT between NGT and h-NGT. Odds ratios and 95 percent intervals were calculated.

Statistical analysis was done as described below. Differences between the groups were analyzed with ANOVA, and multiple comparisons were unadjusted P-values. Correlations between the variables were calculated using Pearson's correlations. Logistic regression analyses were performed to determine which variables were related to difference in blood glucose level at 60 min during 75 g OGTT between NGT and h-NGT. The results of univariate and multivariate logistic regression analyses were reported as odds ratios with 95 percent confidence intervals. P value less than 0.05 (2-tailed) was considered to indicate significance. All analyses were performed with the use of SAS software (version 8.02, SAS Institute).

plaining the reason why h-NGT shows hyperglycemia at 60 min during 75 g OGTT. As shown in Table 5, I.I. among various variables showed a significant odds ratio, and AUCins, BMI and HOMA-IR also demonstrated a significant odds ratio, while Pmax, Smin, AFI and HbA1C did not show any significant odds ratio. Thus the abnormal regulation of glucose metabolism in h-NGT is mainly explained by I.I., AUCins, BMI and HOMA-IR. It is therefore suggested that the disturbed function of both early insulin secretion and insulin resistance may account for abnormal glucose metabolism

in h-NGT. The present data also suggested that Pmax, Smin and AFI were not directly related to abnormal glucose metabolism in h-NGT of which patients possessed the greatest value of AFI among all of the groups.

Discussion

We have already reported that AFI is useful for assessing the visceral fat volume [2], which is well known to induce insulin resistance. The present data demonstrated that a significant negative co-relationship between AFI and HOMA-IR exists (Table 1), although this negative co-relationship between HOMA-IR and AFI was quite weak so as to be almost a flat line parallel with the X-axis. On the other hand, Smin and Pmax were significantly and positively related to HOMA-IR, suggesting that each parameter such as Smin and Pmax rather than AFI is a good marker reflecting HOMA-IR. It is therefore suggested that AFI does not always account for the state of insulin resistance, which is calculated from fasting glucose and insulin concentrations using homeostatic model assessment (HOMA-IR). The data demonstrated that AFI in h-NGT and IFG + IGT was significantly higher than that in NGT, although there was no significant difference in AFI between NGT and IFG, or IGT or DM. The present studies also showed that Smin in h-NGT was significantly lower than that in NGT, although there was no significant difference in Smin and Pmax between NGT and IGT or IFG + IGT or IFG or DM. It was reported that AFI demonstrated a highly significant correlation with the ratio of visceral fat area to the subcutaneous fat area as determined by CT scan [2]. Thus it is suggested that abdominal obesity, which can be easily evaluated by AFI, may be present in the patients with h-NGT and IFG + IGT. It is possible to differentiate h-NGT from IFG + IGT by determining fasting glucose level. We must carefully follow up pa-

tients with h-NGT because they always show normal levels of fasting glucose with high values of AFI reflecting abdominal obesity. Moreover, HOMA-IR was significantly higher in IFG + IGT, IFG and DM than NGT. Thus, it is suggested that AFI may be a good predictor for assessing the pre-stage of insulin resistance in such cases of h-NGT, or that HOMA-IR is not always in parallel with the value of AFI. AFI may be useful to assess the distribution of visceral fat in order to diagnose metabolic syndrome in patients with h-NGT and IFG + IGT, although further experiments are needed to clarify the cut-off value of AFI.

As mentioned above, the point to be noted in this study is the subdivision of the normal type according to JDS into two subtypes: completely normal type (NGT) and h-NGT. Insulin sensitivity determined by HOMA-IR was similar in NGT and h-NGT, which showed a slightly lower early insulin secretion (I.I.) and higher total insulin secretion (AUCins) compared with IGT. Moreover, I.I. among various variables showed a significant odds ratio (Table 5), and AUCins, BMI and HOMA-IR also demonstrated a significant odds ratio, while Pmax, Smin, AFI and HbA1C did not show any significant odds ratio. Thus the abnormal regulation of glucose metabolism in h-NGT is mainly explained by I.I., AUCins, BMI and HOMA-IR. It is therefore suggested that the disturbed function of both early insulin secretion and insulin resistance may account for abnormal glucose metabolism in h-NGT. Abdominal obesity, which shows high AFI values as assessed by ultrasonography, was also observed in h-NGT. As a result, h-NGT, which is thought to belong to the clinical entity of metabolic syndrome, is presumed to represent the activation state of the compensatory mechanism to maintain the blood glucose at a normal level by promoting total insulin secretion (AUCins). It is of interest to determine whether abdominal obesity or impaired early insulin secretion is the first trigger inducing the abnormal glucose metabolism in h-NGT. Rather than regarding h-NGT as normal glucose metabolism, h-NGT should be recognized as a disease state of metabolic syndrome complicated with impaired glucose regulation, including IFG and IGT, and that careful observation of the course is desirable, paying attention to the risks of progression to diabetes or complication by cardiovascular diseases. Moreover, the diversity between the IFG and IGT groups involves both insulin secretion and resistance, although it is not clear whether IFG and IGT differ with

respect to insulin secretion or sensitivity [16]. The present data demonstrated that there was no significant difference in AFI between IFG and IGT. Thus the pathophysiology of abnormal glucose metabolism in each group is still unclear. There is general agreement that subjects with type 2 DM have both beta-cell dysfunction and insulin resistance [5, 17]. However, the progression stage of glucose intolerance during which these metabolic abnormalities develop remains a matter of debate. Defective insulin action is the major identifiable defect in subjects at risk for type 2 DM [9, 17], whereas beta-cell dysfunction appears to become abnormal only when FPG is elevated [5, 18]. Nevertheless, defective insulin secretion may be present before the onset of overt diabetes [7, 19]. The present findings demonstrated that insulin sensitivity assessed by HOMA-IR tended to be lower in IFG rather than IGT. The present data also demonstrated that acute insulin secretion estimated by I.I. and reduced and total insulin secretion assessed by AUCins increased in IFG as well as in IGT. Thus, it is suggested that the ability of insulin secretion in IFG, showing stronger insulin resistance than IGT, appears to be similar to that of IGT.

It was reported from Taiwan that IFG is a strong predictor of diabetes [20]. The high rate of conversion from IFG to diabetes suggests the future high prevalence rates of diabetes in Taiwan. Moreover, 82.6% subjects of IFG could revert to NGT by controlling their life-style [20]. On the other hand, several long follow-up studies have reported that IGT rather than IFG progressed to overt diabetes. Thus, we should perform further prospective studies to clarify whether or not IGT or IFG is predictive of overt diabetes.

In conclusion, the present findings clearly demonstrated that HOMA-IR was significantly and positively correlated with Smin and Pmax, suggesting that Smin and Pmax are good markers indicating insulin sensitivity.

h-NGT subjects showed slightly lower acute insulin secretion and higher amounts of total insulin secretion, compared with IGT. Moreover, abdominal obesity showing high value of AFI as assessed by ultrasonography was also observed in h-NGT, suggesting that h-NGT belongs to the clinical entity of metabolic syndrome. Thus, h-NGT should be recognized as a disease state of impaired glucose regulation, including IFG and IGT, and careful observation of the course is desirable, paying attention to the risks of progression to diabetes or complication by cardiovascular diseases.

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