Waist circumference is a better predictor than body mass index of insulin resistance in type 2 diabetes

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Abstract
Insulin resistance is an important pathogenic factor in type 2 diabetes patents. An easy and efficiency measurement predicting insulin resistance; which can be done easily by type 2 patients is desired. The aim of this study is to examine whether waist circumference is a better predictor of insulin resistance in type 2 diabetes than body mass index (BMI). From a population of 1356 registered diabetic patients, 144 who met (1) aged between 30 and 75 years, (2) being Chinese, (3) having had type 2 diabetes for more than one year, (4) having been taking gliclazide and metformin for more than 6 months were enrolled in this study. The main outcome evaluated is the associations of HOMA insulin resistance index (HOMA index); which were assessed using multiple linear regression analysis. The coefficients of multiple regression analysis with stepwise model showed that waist circumference (β = 0.35, p < 0.001) but not BMI (β = 0.01, p= 0.94), and hemoglobulin A1C% (HbA1C) (β = 0.25, p = 0.01) were the main predictors of HOMA index. These initial findings indicate that waist circumference is a better predictor of insulin resistance in type 2 diabetes than BMI.

Keywords: *type 2 diabetes; waist circumference; insulin resistance; body mass index*

Introduction

Insulin resistance is an important pathogenic factor in type 2 diabetes patents. No easy clinical test exists for predicting the insulin resistance in type 2 diabetes. An easy and efficiency measurement predicting insulin resistance; which can be done easily by type 2 patients is desired.

As we know that poor insulin resistance in type 2 diabetes have high risks to developing cardiovascular disease.[1-3] Many studies also demonstrated that waist circumference is a strong association of cardiovascular disease.[4-7] Many previous studies have been reported that waist circumference is a stronger predictor of insulin resistance in non-type 2 diabetes.[8,9] Several studies have also indicated that waist circumference is superior to BMI as a risk factor maker in non-type 2 diabetes population.[10-12] How the association between waist circumference and insulin resistance in type 2 diabetes is worth to investigate.

The different severity or condition of type 2 diabetes might present as confounding factors of different insulin concentration and resistance. We therefore examined, whether waist circumference is a better predictor than body mass index of insulin resistance risk in type 2 diabetes. In order to avoid the above undetectable confounders and bias, we examined the type 2 diabetes more than one year after the onset of the disease, in patients taking gliclazide and metformin for more than six months, 20-75 years old, Chinese adult homogenous cohort.

We hypothesized there would be strong association between insulin resistance and waist circumference in homogeneous type 2 diabetes after controlling other factors. This study is to examine the regulatory roles of insulin resistance in a cohort of homogenous diabetic patients.

Research design and method

Study population

The trial was conducted from July 2005 through June 2006 in Taipei Hospital, Taiwan. 1356 registered diabetic subjects were screened. 186 subjects met the inclusion criteria/exclusion criteria (Table 1). A letter explaining the purpose of the study were sent to the 186 subjects inviting

Table 1: Inclusion and exclusion criteria.

Inclusion criteria.
(1) Age between 30 and 75 years old
(2) Chinese population
(3) Type 2 diabetes more than one year
(4) Taking gliclazide and metformin more than six months
Exclusion criteria
(1) GOT, GPT＞80 U/L, serum creatinine ＞2.0 mg/dl
(2) Prolaction or pregnancy women
(3) Heart failure, AMI stroke and heavy injury diseases
(4) Any other conditions not suitable for trial as evaluated by the physician.

Received on: 09/03/2010
Accepted on: 11/02/2011

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Table 2: Comparison of characteristics among quartiles of HOMA insulin resistance index

Variable	Quartiles of HOMA insulin resistance index				P for trend
	1	2	3	4	
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Basic data					
HOMA IR*	1.7(0.7)	3.2(0.4)	4.9(0.7)	9.3(3.2)	<0.001
Male/Female	19/17	12/24	19/17	15/21	0.55
Age (year)	60.5(8.9)	60.5(9.3)	56.4(10.0)	54.3(11.8)	0.003
FH* (yes/no)	21/15	19/17	18/18	17/18	0.45
G* (mg/day)	166.9(45.0)	182.2(41.1)	175.6(46.1)	173.7(30.6)	0.66
M*(mg/day)	1648.6(628.9)	1779.2(601.7)	1784.7(611.8)	1577.1(583.8)	0.65
BMI*(kg/m^2)	24.8(2.9)	24.8(2.8)	26.6(5.3)	28.5(4.5)	<0.001
WC* (cm)	83.6(7.6)	83.4(7.8)	87.3(9.1)	93.0(10.4)	<0.001
HC* (cm)	93.8(5.9)	93.9(6.9)	96.2(8.6)	99.8(8.7)	0.002
SBP* (mmHg)	131.9(16.0)	135.9(18.8)	136.3(15.6)	139.3(13.0)	0.07
DBP* (mmHg)	77.4(7.8)	79.5(10.9)	80.8(9.6)	80.5(9.7)	0.002
Fasting serum factors					
Glucose (mg/dl)	169.3(57.2)	184.5(48.6)	198.2(47.5)	223.6(63.0)	<0.001
HbA1c (%)	8.7(1.5)	8.7(1.6)	9.4(1.8)	9.8(1.3)	0.001
Insulin (IU/ml)	4.6(2.5)	7.4(1.9)	10.8(4.0)	17.5(5.9)	<0.001
Adiponectin (μg/ml)	19.1(7.7)	18.0(7.0)	15.3(7.7)	15.0(6.2)	0.006
Fasting lipoproteins					
Triglyceride, (mg/dl)	130.9(85.3)	155.7(95.3)	189.3(223.8)	270.4(404.6)	0.01
Cholesterol, (mg/dl)	172.8(33.9)	174.9(40.1)	171.8(30.3)	194.9(48.4)	0.03
HDL (mg/dl)	43.7(8.9)	45.2(9.8)	41.9(8.3)	42.8(9.6)	0.40
LDL (mg/dl)	111.8(30.8)	108.4(33.2)	106.8(30.9)	121.8(36.6)	0.25

Abbreviation HOMA IR**:** HOMA insulin resistance index; FH: Family history of type 2 diabetes disease; G:Gliclazide; M: Metformin; BMI**:** Body mass index; WC: Waist circumflex; HC: Hip circumflex; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HDL:HDL-cholesterol; LDL:LDL-cholesterol.

them to participate in the study. 144 subjects enrolled after agreeing to a written an informed consent. The protocol was approved by the Human Ethics Committee of Taipei hospital.

Assessment

Homeostasis model assessment for insulin resistance (HOMA index) [fasting glucose (mmol/l) × fasting insulin (UI/l)/22.5] was used as the evaluation of insulin resistance [13-14]. The main outcome evaluated is the associations of HOMA index; which were calculated using multiple linear regression analysis. Anthropometric measurements, blood pressure, fasting glucose, HbA1C, insulin, adiponectin and triglyceride, cholesterol, cholesterol-HDL (HDL) and cholesterol-LDL (LDL) were measured.

Waist circumference was measured mid-way between the lateral lower rib margin and the iliac crest, hip circumference (HC) was measured at the levels of the major trochanters through the pubic symphysis. Height was measured with a wall-mounted stadiometer to the nearest 0.1 cm, weight was measured on a calibrated balance beam scale to the nearest 0.1 kg, and BMI was calculated (BMI= body weight/height (kg/ m^2). A mercury sphygmomanometer with standard cuff was used to measure the indirect auscultatory arterial blood pressure taken from the right arm with subjects in seated position.

All measurements were made at 08:00-09:00h, after an overnight fast, using standardized methods. A sample of whole blood was drawn and centrifuged at 4°C, and a 1.0 ml aliquot of serum was rapidly frozen (-80°C) for subsequent hormone analysis. The plasma adiponectin concentration was measured by a radioimmunoassay kit (Linco Research Inc., St. Charles, MO, USA). This kit employs the double-antibody/polyethylene glycol technique using ^{125}I-lableled adiponectin and a multispecies adiponectin rabbit antiserum. Plasma insulin levels were measured using a commercially available radioimmunoassay (Linco Research Inc.). The intra- and inter-assay coefficients of variation were 3.1% and 4.9%, respectively. The limit of sensitivity is 0.5 ng/ml.

High waist circumference and normal waist circumference defined

With Asia obesity classification, we defined normal waist circumference (NWC) is < 80 cm in female and < 90 cm in

Table 3: Demographic and biochemical characteristics between high waist circumference and normal waist circumference by gender

Variable	WC* of male (cm)			WC* of female (cm)			WC* of all (cm)		
	HWC* (>=90) Mean (SD)	NWC* (<90) Mean (SD)	P	HWC* (>=80) Mean (SD)	NWC* (<80) Mean (SD)	P	HWC* Mean (SD)	NWC* Mean (SD)	P
HOMA IR*	6.1(3.2)	3.6(2.1)	<0.001	6.0(4.3)	3.4(1.5)	<0.001	6.1(3.9)	3.5(1.8)	<0.001
Age (year)	55.2(13.1)	56.9(10.9)	0.59	58.3(8.9)	60.1(8.7)	0.38	57.2(10.6)	58.4(10.0)	0.51
FH* (yes/no)									
G* (mg/day)	166.4(45.7)	180.0(39.5)	0.23	173.9(42.3)	172.1(40.6)	0.85	171.3(43.4)	176.4(39.9)	0.46
M* (mg/day)	1598.0 (619.5)	1702.5 (668.7)	0.52	1732.6 (594.6)	1722.7 (505.6)	0.94	1685.2 (606.6)	1711.6 (596.6)	0.79
BMI* (kg/m^2)	29.8(4.7)	24.0(2.1)	<0.001	28.0(4.2)	23.5(2.2)	<0.001	28.6(4.5)	23.7(2.1)	<0.001
WC*(cm)	99.8(8.9)	83.2(5.5)	<0.001	90.4(8.3)	76.5(3.2)	<0.001	93.7(9.6)	80.6(5.1)	<0.001
HC*(cm)	103.8(9.7)	91.4(4.41)	<0.001	100.2(7.8)	89.6(5.1)	<0.001	101.4(8.6)	90.6(4.8)	<0.001
SBP* (mmHg)	139.7(14.4)	134.1(14.5)	0.13	138.7(16.4)	131.1(17.5)	0.053	139.1(15.6)	132.7(15.9)	0.02
DBP* (mmHg)	83.8(10.0)	79.0(8.2)	0.05	82.9(9.4)	76.7(10.0)	0.06	83.3(9.5)	77.9(9.1)	0.001
Glucose (mg/dl)	177.8(51.3)	181.4(45.2)	0.78	215.7(68.1)	190.5(51.7)	0.07	202.4(64.9)	185.5(48.1)	0.08
HbA1c (%)	8.9(1.8)	9.1(1.4)	0.58	9.5(1.7)	9.0(1.7)	0.25	9.3(1.7)	9.1(1.6)	0.51
Insulin (IU/ml)	14.4(6.9)	8.4(5.6)	0.001	11.1(6.6)	7.4(3.1)	0.01	12.4(6.8)	7.9(4.6)	<0.001
Adiponectin (μ g/ml()	13.0(5.1)	16.7(6.8)	0.02	16.4(7.4)	20.7(7.8)	0.02	15.2(6.8)	18.5(7.5)	0.007
Triglyceride (mg/dl)	225.4(167.4)	122.9(68.3)	0.01	211.9(374.8)	198.5(236.0)	0.84	216.6(295.7)	157.1(169.5)	0.14
Cholesterol (mg/dl)	184.6(45.1)	166.6(28.2)	0.08	180.2(41.5)	182.9(43.4)	0.78	181.8(42.6)	174.0(36.5)	0.24
HDL (mg/dl)	39.2(8.6)	41.5(7.7)	0.30	45.8(10.4)	45.0(8.5)	0.71	43.5(10.2)	43.0(8.2)	0.79
LDL (mg/dl)	118.3(36.5)	110.8(26.5)	0.38	110.0(30.0)	109.2(42.6)	0.92	113.0(32.4)	110.1(34.4)	0.61

Abbreviation WC: Waist circumflex; HWC: High waist circumflex; NWC: normal waist circumflex; HOMA IR**:** HOMA insulin resistance index; FH: Family history of type 2 diabetes disease; G: Gliclazide; M: Metformin; BMI**:** Body mass index; HC: Hip circumflex; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HDL:HDL-cholesterol; LDL:LDL-cholesterol.

male; the high waist circumference (HWC) is ≥ 80 cm in female and ≥ 90 cm in male[15].

Statistical analysis

One-way analysis of variance (ANOVA) and linear trend test were employed to evaluate the trend among the plasma HOMA index quartile groups. The Student *t*-test was employed to analyze the comparisons between HWC and NWC. Chi-square test was used for gender (male/female), family history of type 2 diabetes comparison. Multiple linear regression analysis with stepwise method was applied to HOMA index concentrations. All *p* values were two-tailed and α level of significance was set at 0.05. The data were analyzed with SPSS software (version11.5).

Results

Demographics

Among the 1356 screened patients, 186 met the inclusion criteria, 144 (77.4 %) agreed to participate. There are 79 female (age 59.0 ± 8.7 years) and 65 male (age 56.3. ± 11.7 years). There are no significant difference in means of age, BMI, waist circumference, blood pressure, HbA1C, fasting glucose, cholesterol, triglycerol, insulin, HOMA index, aminotransferases alanine, aminotransferases aspartate and creatinine between male and female.

Measurements among HOMA index quartile categories.

Table 2 shows the comparison of characteristics among quartiles of HOMA index categories. There is a significant difference in BMI (p<0.001), waist circumference (p<0.001), HC (p=0.002), diastolic blood pressure (p=0.002), fasting glucose (p<0.001), $HbA1_C$ (p=0.001), adiponectin level (p=0.006), triglyceride level (p=0.01) and cholesterol level (p=0.03) with linear trend test. Results of linear trend test show no statistically difference in family history of type 2 diabetes, gender ratio and dose of metformin and gliclazide taking among quartiles of HOMA index.

Demographic and biochemical characteristics between HWC and NWC

Table 3 shows the demographic and biochemical characteristics between HWC and NWC. HWC have higher

Table 4: Multiple regression analysis of HOMA insulin resistance index with stepwise method.

	β	p
Factors		
Gender (male=1/female=0)	-0.12	0.06
Family History of type 2 DM (yes=1/no=0)	0.07	0.94
Basic data		
Age	-0.01	0.89
Body mass index	0.01	0.94
Waist circumflence	0.35	<0.001
Hip circumflex	0.30	0.08
Systolic blood pressure	0.10	0.26
Diastolic blood pressure	0.11	0.26
Fasting serum factors		
HbA1c	0.25	0.01
Fasting triglyceride	0.13	0.16
Fasting cholesterol	0.06	0.54
HDL-cholesterol	-0.07	0.42
LDL-cholesterol	0.05	0.59

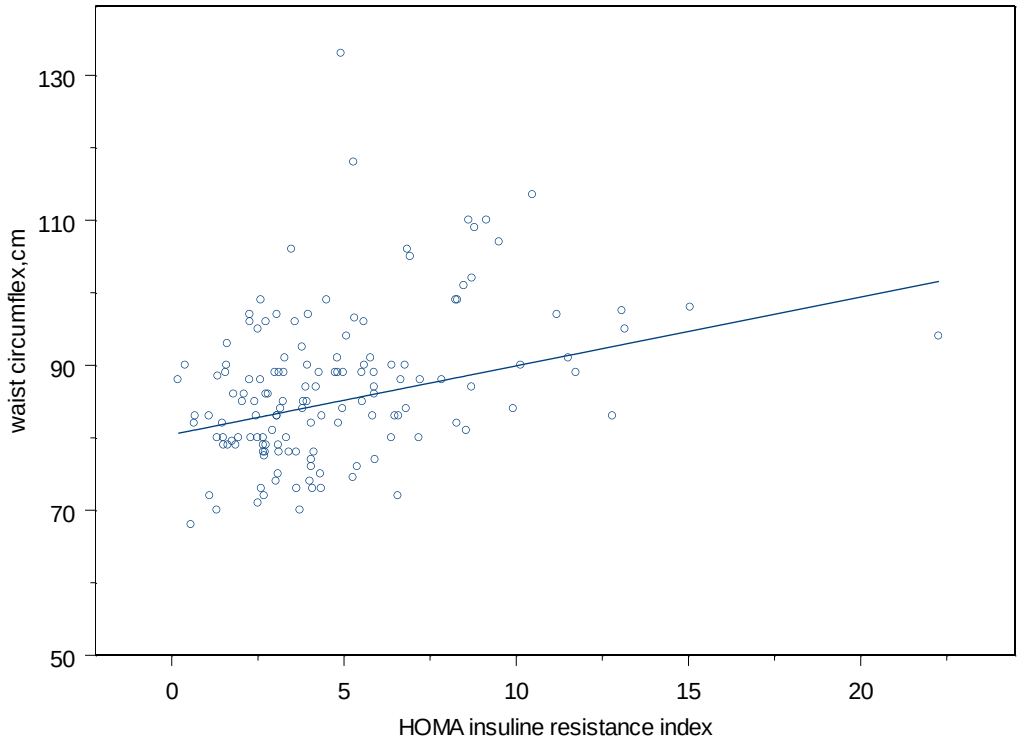

Figure 1: Scatter of HOMA insulin resistance index and waist circumference in type 2 diabetes

mean of HOMA index (p<0.001), HC (p<0.001), BMI (p<0.001), systolic blood pressure (p=0.02), diastolic blood pressure (p=0.001) and insulin level (p<0.001) than NWC; which shows significant difference with student *t* test. There are no significant differences in fasting glucose and HbA1C between HWC and NWC. Subjects with HWC have lower mean of adiponectin level than NWC (p=0.007).

Coefficiences of linear multiple regression on HOMA IR index

Table 4 shows the coefficients of linear multiple regression on HOMA index using stepwise method; Waist circumference (β = 0.35, p < 0.001) and HbA1C (β = 0.25, p= 0.01) was the main predictor on HOMA index in all type 2 diabetic subjects. BMI was not the predictor on the model

analysis (β = 0.01, p = 0.94). Figure 1 shows the relationship (Scatter) of HOMA index and waist circumference in this cohort of type 2 diabetes patients.

Discussion

Many studies have demonstrated that insulin resistance is the main pathogenic factor in type 2 diabetes.[1-2] The poor control of insulin resistance in type 2 diabetes might be the cause of high risk of complications including cardiovascular disease.[4-7] It is therefore of paramount importance to evaluate the pattern of insulin resistance in type 2 diabetes. To our knowledge, there is no available and easy way of self-checking or measuring this parameter by a healthcare worker. The result of this study seemed to indicate that waist circumference is a predictor of insulin resistance in type 2 diabetes, which can be easily measured by the healthcare worker or the patient.

Our results have reconfirmed that HOMA index has a strong positive association with waist circumference, BMI, HC, and the serum levels of glucose, triglyceride and cholesterol. All of the above variables are the risk factors of developing complications in type 2 diabetes. Our data have demonstrated the negative relation between the level of adiponetin and HOMA index in this homogenous cohort of type 2 diabetics. Many studies have demonstrated that adiponectin has both anti-atherogenic and anti-diabetic properties.[18-19] Previous studies show that adiponectin levels are significantly lower in type 2 diabetes.[20] The subjects with hypoadiponectin level might be at high risk for cardiovascular disease.[21-22] Adiponectin levels are positively correlated with insulin sensitivity and negatively correlated with insulin resistance.[18-19,23] The finding in this study support that high HOMA index of type 2 diabetes have lower adionectin level which might be a high risk for developing cardiovascular disease in the future.

Our observation that subjects with HWC have higher mean of HOMA index, BMI, HC, systolic blood pressure, diatolic blood pressure and insulin level.; but lower mean of adiponectin level than those with NWC. Patients with HWC have cetral obesity, which is strongly associated with diabetes, high risk factor of cardiovascular disease, and insuline resistance.[7-11] Our finding in in this cohort of type 2 diabetes corroborates this findings of these reports. There are no significant difference in fasting glucose and $HbA1_C$ levels between between subject with HWC and NWC. This may be attributed to the homogenous nature our type 2 diabetic patients.

We also observed that waist circumference was the main predictor for HOMA index after adjusting other factors for homogeneous type 2 diabetic subjects. In multiple regression analysis with stepwise model, the BMI as a predictor of HOMA index did not reach statistical significance. This may be due to the fact that, BMI can be fully predicted by waist circumference in this cohort of patients.

Previous studies have demonstrated that waist circumference can be used to predict insulin resistance,[24] and some studies showed that waist circumference is a better predictor of risk factors other than BMI.[10-11] BMI change may be attributable to the change of skeletal muscle rather than body fat, whereas waist circumference changes are most of abdominal fat. Tanko LB, *et al.* demonstrated that central abdominal fat is passively associated with insulin resistance.[25] On the other hand, the determination of BMI required the measurement of height and weight, but waist circumference is done once. Besides, patients can easily understand the concept of waist circumference than BMI. Lastly, waist circumference is a predictor of insulin resistance controlling other factors, including BMI, and it can be self-management by patients and health professionals.In conclusion, this study showed that waist circumference is a better predictor of insulin resistance in type 2 diabetes than BMI; which can be done easily by type 2 patients and health professionals.

Acknowledgments

We thank all colleagues in Taipei Hospital, Taiwan for helping with this study. This study was supported by grants from the Taipei Hospital.

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