Original Article

The hypertriglyceridaemic waist in New Zealand **Maori**

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The objective of this study was to find a simple practical method of predicting insulin resistance in New Zealand Maori. Thirty-six Maori participants had insulin sensitivity measured using a euglycaemic insulin clamp. Several clinical and easily measured laboratory variables were compared, singly and in combination, with this measure of insulin sensitivity usually regarded as the gold standard. The combination of either fasting insulin and triglycerides or waist circumference and triglycerides, were the best simple methods for predicting insulin resistance in Maori. As insulin assays are not always available and are often not standardised, measurement of waist circumference and triglycerides provides a practical method for predicting insulin sensitivity in New Zealand Maori.

Keywords: **insulin resistance, fasting insulin, triglycerides, waist circumference, abdominal obesity, Maori, New Zealand**

Introduction

Diabetes is a major health problem among New Zealand Maori as it is among other indigenous people worldwide. Adult prevalence may be as high as 20% (Cooper - unpublished data). Type 2 diabetes accounts for more than 95% of diabetes in Maori.

Insulin resistance is considered to be the underlying abnormality in the majority of cases of type 2 diabetes.[1] There is increasing evidence that appreciable β cell damage has occurred by the time glucose levels become impaired,[2] and cardiovascular risk may already have increased. Thus, attempts to prevent diabetes and its complications are more appropriately made at the stage of insulin resistance, before impaired fasting glucose, or impaired glucose tolerance develops. The euglycaemic insulin clamp and Intravenous Glucose Tolerance Test (IVGTT) are standard methods of assessing insulin sensitivity[3], but are both invasive tests and are impractical for community based surveys and interventions. Several other less invasive tests have been used to measure insulin sensitivity in glucose intolerant individuals. However, there have been relatively few studies which have examined the extent to which simple clinical and laboratory measures predict insulin resistance using the euglycaemic insulin clamp as the gold standard in individuals not known to be diabetic. Lemieux *et al.,*[4] have recently shown that measurement of waist circumference and triglyceride level predicts the atherogenic metabolic triad (elevated insulin, apolipoprotein B and small dense LDL particles) in men. These are also features of the insulin resistance syndrome, so that insulin resistance may be expected to be predicted by similar clinical and laboratory measurements.[4]

Studies have not been performed in New Zealand Maori, who, because of their higher prevalence and complication rates, might be expected to benefit more from an early intervention than people of European descent. The aim of this study was to compare insulin sensitivity measured using the euglycaemic clamp with other standard techniques of predicting insulin resistance, as well as simple clinical and metabolic variables, to evaluate the best method of predicting insulin resistance in Maori.

Methods

Approval for the study was gained after consultation with local Maori, this process was performed under kaupapa Maori (Maori protocol) which ensured that the research was performed in a culturally appropriate manner. Key people in the community were approached and invited to participate, they in turn encouraged the participation of friends. Those with diagnosed diabetes were excluded, but it was deemed culturally inappropriate to exclude participants found to be diabetic or with impaired fasting glucose after they had volunteered. This study was approved by the Otago Ethics Committee. Clinical and anthropometric data on the 36 participants were obtained at their first visit. Family history was recorded, with a positive family history of Type 2 diabetes being defined as having a first degree relative with diabetes diagnosed

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after the age of 30 years and not requiring insulin in the first six months. Height and weight were measured, and blood pressure was measured in a sitting position after a ten minute rest. Waist girth was measured in a standing position half way between the iliac crest and the rib cage, and the hip measurement taken at the level of the greater trochanters. Waist hip ratio (WHR) and body mass index (BMI) were calculated.

All participants agreed to have a euglycaemic clamp test.[5] An intravenous cannula was inserted into the cubital vein for delivery of insulin and 25% dextrose, another was inserted into a vein in the dorsum of the hand in order to sample arterialised blood (using the heated hand technique). Basal blood samples were obtained prior to starting the test for measurement of fasting lipids, insulin and glucose. Insulin (Actrapid) was infused at 40U/m2/minute to achieve hyperinsulinaemia. Arterialised samples were obtained every ten minutes for immediate glucose measurements using a YSI Sidekick Glucose Analyser, which was calibrated before and during testing. A variable rate glucose infusion was given and adjusted every ten minutes.[6] Blood glucose levels were kept as close as possible to 4.5mmol/L. Plasma insulin levels were measured at 0, 60, 90 and 120 minutes. The glucose infused (G, measured in mg/kg/min) was calculated from measurements made during the final hour of the clamp. Insulin sensitivity using total body weight (Gbw) was calculated by dividing the average G value by the average plasma insulin concentration over the last 60 minutes (Gbw/I, G/mIU/L). Insulin sensitivity corrected for fat free mass was also calculated (Gffm/I), using Humes equation.[7] Insulin resistance was defined as an Gffm/I of <6.3 G/mIU/L, which corresponded to the lowest quartile for a lean population (BMI <27). Insulin sensitivity using the Homeostasis Model Assessment (HOMA) was calculated using Mathews *et al*.,[8] methods.

Plasma insulin was measured using the Coat-A-Count125I radioimmunoassay (Diagnostics Products Corporation, Los Angeles, CA, USA). Triglycerides were measured enzymatically using Roche kits on a Cobas Fara analyser. HDL was measured in supernatant after precipitation of apo B containing lipoproteins with phosphotungstate/magnesium chloride solution.

Statistical analysis

Product moment correlations after using a natural log transformation on the variable were used to describe the associations of interest. Regression analysis was then used to estimate the multiple correlations between insulin sensitivity and combinations of variables. A boot-strap procedure was used to assess the statistical benefit of adding fasting insulin to the combination of waist circumference and triglyceride, this was performed using 1000 samples with replacement.

Results

Clinical and metabolic descriptors of the population are given in Table 1. Of the 36 participants none were known to have diabetes, but 5 (13%) were found to meet the criteria for diabetes (fasting glucose >7.0mmol/L) and 4 11%) had impaired fasting glucose (fasting glucose 6.1-6.9 mmol/L).

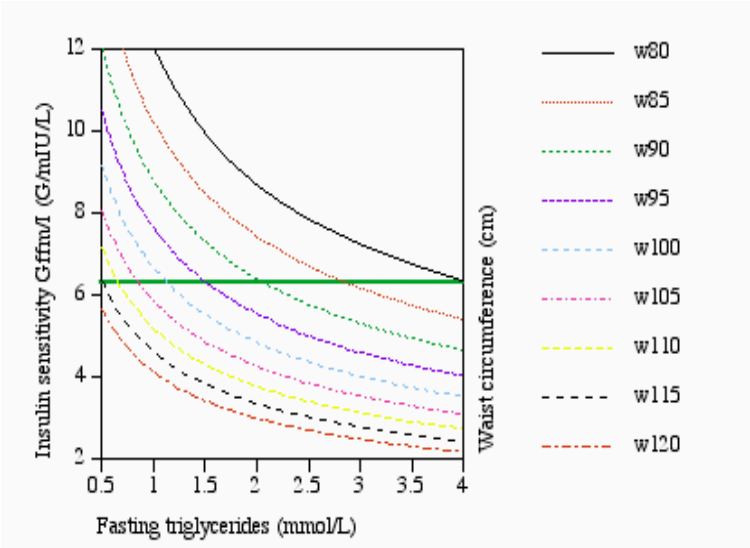

Figure 1. The relationship between insulin sensitivity, fasting triglycerides and waist circumference in study participants

Table 1. Clinical and metabolic descriptors of the study population

	Male (*N* = 8)			Female (*N* = 28)		
	Mean	S.D	Range	Mean	S.D	Range
Age (Years	40.4	11.1	24.2 - 60.2	40.8	8.6	25 - 54
Weight (kg)	107.7	19.1	87.3 - 145.2	94.9	20.3	64 - 136
BMI (m2/kg)	33.3	4.6	26.3 - 41.5	34.6	6.3	25 - 46
Waist (cm)	108.8	11.6	94 - 130.5	106.6	16.0	82 - 133
WHR	0.98	0.03	0.93 - 1.04	0.89	0.06	0.75 - 1.02
Systolic BP (mmHg)	146	20	107 - 172	133	22	101 - 189
Diastolic BP (mmHg)	87	10	74 - 105	84	12	69 - 120
TAG (mmol/L)	1.3	0.44	0.76 - 2.12	1.7	.73	0.54 - 3.6
HDL (mmol/L)	0.89	0.22	0.6 - 1.14	1.1	0.32	0.42 - 1.89
Insulin (mIU/L)	21.3	14.8	9.7 - 52.7	25.1	14.7	5.2 - 64
Glucose (mmol/L)	5.2	0.45	4.6 - 5.7	57	1.28	4.2 - 9.2
Gbw/I (G/mIU/L)	3.4	2.0	1.2 - 7.0	3.06	1.8	0.9 - 7.7
Gffm/I (G/mIU/L)	5.4	3.0	1.9 - 11.5	5.1	2.8	1.7 - 11.7

BMI = body mass index; WHR = waist to hip ratio; TAG = triglycerides; HDL = high density lipoprotein; Gbw/I = glucose infused for body weight/average plasma insulin; Gffm/I = glucose infused for fat free mass/average plasma insulin

The correlation coefficients between insulin sensitivity (Gffm/I) and the investigated clinical and metabolic parameters believed to be associated with insulin resistance are presented in Table 2. The variables most strongly associated with insulin resistance were fasting insulin and waist circumference.

In order to determine the most powerful method for predicting insulin resistance, the individual variables were entered into several predictive equations based on different combinations of variables. R^2 values are shown in Table 3. A number of combinations appeared to be powerful predictors of insulin resistance, namely: insulin, triglyceride and waist circumference ($R^2 = 0.68$), insulin, triglyceride and body mass index ($R^2 = 0.65$), triglyceride, body mass index and waist circumference, ($R^2 = 0.65$), triglyceride and waist circumference ($R^2 = 0.65$).

Sixty-seven percent of our population met the criteria for insulin resistance, an Gffm/I of less than 6.3. Figure 1 shows the relationship between insulin sensitivity and waist, and triglyceride levels. It appears that individuals with a triglyceride level of less than 2 mmol/l are at risk of insulin resistance if waist circumference is above 90cm. Individuals with a triglyceride level greater than 4 mmol/l appear to be insulin resistant regardless of their waist circumference.

Discussion

Prediction of insulin resistance in normoglycaemic people is important as diabetes prevention programmes may be more successful at this stage than they are once glucose intolerance has developed. Insulin resistance is most accurately measured by the euglycaemic insulin clamp technique.[5] This test is invasive, expensive and time consuming and hence unsuitable for community based intervention programmes. Several studies have investigated predictors of insulin resistance, but they have usually been in people with impaired glucose tolerance, or diabetes. Our intention was to examine predictors of insulin resistance in a Maori population not known to be diabetic. Our sample of 36 did, however, identify five people with diabetes, and four with impaired fasting glucose levels, which was not surprising given the high prevalence of diabetes amongst Maori.

This study investigated the prediction of insulin resistance using several previously described methods including the HOMA and insulin to glucose ratio. It appears that in the Maori population the prediction of insulin resistance using the HOMA or insulin to glucose ratio is no better than fasting insulin alone. This is comparable to the findings of Laakso *et al.*,[9] who demonstrated that there was a strong positive correlation between fasting insulin levels and insulin resistance, although the association was weaker in those individuals with impaired glucose tolerance and Type 2 diabetes.[9] Howard *et al.*,[10] confirmed that the best method of predicting insulin sensitivity depended on the glucose status of the individual. Their data suggested that the HOMA and the Galvin model were the most appropriate method when considering individuals with a wide range of glucose levels. We did not examine the Galvin method,

Table 2. Product moment correlations coefficients between insulin sensitivity reported for total body weight (Gbw/I), and for fat free mass (Gffm/I) using the euglycaemic insulin clamp and the examined variables

	Sample size	Gbw/I	Log(Gbw/I)G	Gffm/I	Log(Gffm/I)G
Insulin (mIU/L)	36	-0.65	-0.74	-0.64	-0.73
HOMA	36	0.64	0.74	0.60	0.73
I/G	36	0.72	0.95	0.55	0.63
BMI (m^2kg)	36	0.64	-0.64	0.55	0.59
Waist (cm)	36	0.72	0.75	0.68	0.70
WHR	36	0.26*	0.32*	0.30*	0.36
TAG (mmol/L)	36	0.39	0.41	0.43	0.46
HDL (mmol/L)	36	0.47	0.49	0.49	0.49
Family History	36	0.17*	0.07*	0.17*	0.07*
Systolic BP (mmHg)	36	0.51	0.47	0.49	0.44
Diastolic BP (mmHg)	36	0.37	0.40	0.36	0.37

* not significant; HOMA = homeostasis model assessment; I/G = insulin to glucose ratio; WHR waist to hip ratio; TAG = triglycerides; HDL = high density lipoprotein; BP = blood pressure

Table 3. R^2 values for predictors of insulin resistance

	R^2	*Adjusted R^2
Waist	0.49	0.47
Insulin + TAG	0.57	0.55
Insulin + BMI	0.56	0.53
Insulin + Waist	0.60	0.57
TAG + Waist	0.65	0.62
TAG + BMI	0.60	0.57
Insulin + TAG + Waist	0.68	0.65
Insulin + TAG + BMI	0.65	0.62
TAG + BMI + Waist	0.65	0.62

TAG = triglycerides; BMI = body mass index ;waist = waist circumference; * adjusted R^2 provides an indication of how much the score would shrink if it were used on a new sample.

other frequently sampled intravenous glucose tolerance tests or the oral glucose tolerance test (OGTT), since these are less suited to population based intervention. However, it is interesting that Strumvoll *et al*.,[11] found the correlation between fasting insulin and insulin sensitivity (-0.59) was remarkably similar to that between a 120 minute insulin post OGTT (-0.62) and insulin sensitivity. This suggests there is little difference between using fasting or two hour post glucose load insulin to predict insulin sensitivity.

When carrying out screening in the community measurement of fasting insulin may be impractical. Therefore, it is of particular interest to examine whether routine clinical and laboratory measurements can be used to predict insulin resistance and the range of metabolic abnormalities associated with the insulin resistance or metabolic syndrome. Lemieux *et al.*,[4] have found that a combination of waist circumference and triglyceride levels accurately predicts the atherogenic metabolic triad (hyperinsulinaemia, elevated apo B and small dense LDL) in normoglycaemic men, thus providing a useful, inexpensive screening tool.[4]

We too have found that insulin resistance measured by the euglycaemic clamp can be predicted with a reasonable degree of accuracy by measurement of waist circumference and triglyceride in Maori men and women. Our data suggests that risk of insulin resistance increases dramatically once waist circumference is greater than or equal to 90cm and triglyceride greater than or equal to 2 mmol/l. Once waist circumference is greater than 100 cm individuals are likely to have insulin resistance irrespective of triglycerides. The comparable figure for triglycerides appears to be 4 mmol/l. It has previously been suggested that BMI cut-offs should be modified for Maori and other Polynesian people since they appear to have more lean mass than Europeans at a given BMI. However, this does not appear to apply to waist circumference, where a relatively low measurement of 90 cm implies a considerable degree of risk of type 2 diabetes, one of the most important conditions effecting the health of Maori people. While larger studies may permit more precise cut-offs to be defined according to gender the present findings suggest that a simple clinical measurement combined with an easily performed laboratory measurement may help to identify high risk individuals who will benefit from lifestyle intervention programmes.

Acknowledgement

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