



Obesity type and clustering of insulin resistance-associated cardiovascular risk factors in middle-aged men and women

MJ Vanhala¹, TK Pitkääjärvi², EA Kumpusalo³ and JK Takala⁴

¹Pieksämäki District Health Centre, Naarajärvi Health Station, Naarajärvi; ²Community Health Centre of the City of Tampere, Tampere and ³Kuopio University, Department of Public Health and General Practice, Kuopio, Finland

OBJECTIVE: To examine different clusterings of the insulin resistance-associated cardiovascular risk factors with respect to different types of obesity.

DESIGN: A screening programme for obesity (body mass index; BMI ≥ 30 kg/m²) and abdominal adiposity (waist-to-hip ratio; WHR ≥ 1.00 in men and ≥ 0.88 in women).

SETTINGS: Pieksämäki District Health Centre and the Community Health Centre of the City of Tampere, Finland.

SUBJECTS: All volunteers were either aged 36, 41, 46 or 51 y ($n = 1148$) and living in the town of Pieksämäki, with a control population of 162 subjects in the City of Tampere.

MAIN OUTCOME MEASURES: Different clusterings of: 1) hypertension (a systolic blood pressure ≥ 160 mmHg and/or a diastolic blood pressure ≥ 95 mmHg or concurrent drug treatment for hypertension); 2) hypertriglyceridaemia ≥ 1.70 mmol/l; 3) a low level of high-density-lipoprotein (HDL) cholesterol; < 1.00 mmol/l in men, < 1.20 mmol/l in women; 4) abnormal glucose metabolism (impaired glucose tolerance or non-insulin-dependent diabetes) and 5) hyperinsulinaemia with a fasting plasma insulin ≥ 13.0 mU/l.

RESULTS: The prevalence of a cluster consisting of dyslipidaemia (hypertriglyceridaemia and/or low HDL-cholesterol) and insulin resistance (abnormal glucose metabolism and/or hyperinsulinaemia) was found to be 4% in the control subjects, 18% in the abdominal adipose subjects (WHR ≥ 1.00 in men and ≥ 0.88 in women with a BMI < 30 kg/m²), 28% in the 'pure' obese subjects (BMI ≥ 30 kg/m² with WHR < 1.00 in men and < 0.88 in women), and 46% in the central obese subjects (subjects showing both 'pure' obesity and abdominal adiposity). The prevalence rates of the other clusterings of abnormalities varied similarly according to the type of obesity.

CONCLUSION: Clusterings of insulin resistance-associated abnormalities were related to the type of obesity in both middle-aged men and middle-aged women.

Keywords: obesity; abdominal adiposity; central obesity; epidemiology; metabolic syndrome; insulin resistance

Introduction

The most common clinical state characterized by insulin resistance is obesity with a centralized distribution of adipose tissue.¹ This type of obesity has been suggested to be the most distinctive mark of a 'metabolic syndrome', which is characterized by a clustering of many insulin resistant cardiovascular risk factors such as hypertension, hypertriglyceridaemia, low high-density-lipoprotein (HDL) cholesterol, abnormal glucose metabolism and hyperinsulinaemia.^{2–10}

An increase in body-mass index (BMI) is usually associated with an increase in waist-to-hip ratio (WHR), a conventional clinical marker of abdominal adiposity.¹¹ Some studies have suggested that obesity *per se* would be necessary for the expression of metabolic defects associated with centrally distributed fat.^{12–14} Because of this close association between

obesity and abdominal adiposity, it is difficult to differentiate between these two types of obesity, without magnetic resonance imagination (MRI) or computed tomography (CT), neither of which are available in common clinical practice. As obesity is known to be increasing in all Westernized countries, it is of crucial importance that the professional clinician has some simple tools to assist in recognizing harmful types of obesity that may lead to increased risks for cardiovascular disease, stroke and non-insulin-dependent diabetes mellitus (NIDDM).^{3–7,14}

Based on simple measurements of height, weight and circumference of waist and hip, this report describes a classification scheme for the three different types of obesity: 1) 'pure' obesity, 2) abdominal adiposity and 3) central obesity. We screened all 841 volunteers from four age groups aged 36, 41, 46 and 51 y ($n = 1148$) in Pieksämäki, Finland, for these three types of obesity and examined the relationship between different clusterings of insulin resistance-associated cardiovascular risk factors and type of obesity. A randomly selected sample of 162 subjects without any defined type of obesity was used as a control population.

Material and methods

The target population ($n=1172$) in Pieksämäki, a town in Finland, included men and women born in 1942 ($n=164$), 1947 ($n=357$), 1952 ($n=345$) and 1957 ($n=306$). The sample was drawn from an updated census register, and volunteers were invited by a letter for screening. A control population of 162 volunteers, without any defined type of obesity, was randomly selected from participants in health check-ups, which are annually arranged for all inhabitants aged 40 or 45 y in the City of Tampere, Finland. In the examination year, 4386 (80%) out of the 5480 invited inhabitants aged 40 or 45 y participated in the health check-ups. The screening was carried out by trained nurses between March 1993–December 1994.

Blood pressure was measured using a mercury sphygmomanometer after a 15 min rest.¹⁵ An appropriate large size cuff was used for obese subjects. Hypertension was defined as a systolic blood pressure of ≥ 160 mmHg and/or a diastolic pressure of ≥ 95 mmHg, or concurrent drug treatment for hypertension.¹⁶

For anthropometric measurements, subjects were examined while wearing light clothes. Height was measured to the nearest cm and weight to the nearest 0.1 kg. BMI was calculated as weight (kg) divided by height squared (m^2). Waist and hip circumferences were measured to the nearest cm using a calibrated soft tape with the subject standing. Waist circumference was defined as the smallest girth, midway between the lowest rib margin and the iliac crest, hip circumference was measured at the level of greater trochanters, and WHR was calculated.⁷

Serum cholesterol and triglycerides were measured from fresh serum samples, drawn after an overnight fast, by enzymatic colorimeter methods (CHOD-PAP, GPO-PAP, Boehringer Mannheim GmbH, Germany). Serum high-density-lipoprotein (HDL)-cholesterol was measured using the same method, after precipitation of low-density-lipoprotein and very-low-density-lipoprotein cholesterol by phosphotungstic acid and magnesium. Hypercholesterolaemia was defined as a fasting serum cholesterol ≥ 6.50 mmol/l, hypertriglyceridaemia as a fasting serum triglycerides ≥ 1.70 mmol/l, and low level of HDL-cholesterol as a fasting serum HDL-cholesterol < 1.0 mmol/l in men and < 1.2 mmol/l in women.^{17,18}

Plasma, for the determination of fasting insulin, was separated by centrifugation and samples were immediately frozen at $-20^\circ C$. Insulin was determined by Phadeseeph Insulin radio immuno assay (RIA), 100 method (Pharmacia Diagnostics AB, Uppsala, Sweden). Hyperinsulinaemia was defined as a fasting plasma insulin level ≥ 13.0 mU/l.¹⁹ The oral glucose tolerance test (OGTT) was performed according to the WHO protocol using 75 g of glucose. Blood glucose concentrations were measured by automated colorimetric method (Peridochrom Glucose

GOD-PAP, Boehringer). Abnormal glucose metabolism was defined as impaired glucose tolerance or NIDDM, according to the WHO guidelines.²⁰

Definitions for the three types of obesity and clusterings of risk factors

'Pure' obesity was defined as BMI ≥ 30 kg/ m^2 with a WHR < 1.00 in men and a WHR < 0.88 women. These cut-off points for WHR represent the highest quartile in the distribution of subjects aged 41 or 46 y in Pieksämäki. Abdominal adiposity was defined as WHR ≥ 1.00 in men and ≥ 0.88 in women, with a BMI < 30 kg/ m^2 . Central obesity was defined in those subjects simultaneously having both BMI ≥ 30 kg/ m^2 and WHR ≥ 1.00 in men and ≥ 0.88 in women.

Metabolic cluster A consisted of ≥ 2 and metabolic cluster B consisted of ≥ 3 of the following five insulin resistance-associated cardiovascular risk factors examined: 1) hypertension, 2) hypertriglyceridaemia, 3) low HDL-cholesterol, 4) abnormal glucose metabolism and 5) hyperinsulinaemia. A cluster of dyslipidaemia (hypertriglyceridaemia and/or low HDL-cholesterol) and insulin resistance (abnormal glucose metabolism and/or hyperinsulinaemia) was used as a marker for the 'metabolic core' of the metabolic syndrome.^{9,21} A cluster of hypertension, dyslipidaemia and insulin resistance was used as a marker for the conventional metabolic syndrome.²

Statistical methods

Statistical analyses were performed using the SPSS/PC+ statistical software. Variance analysis (ANOVA) was used to analyze the significance of differences of continuous variables, and differences of prevalences of cluster of abnormalities with respect to the different types of obesity. Chi squared method was used to calculate the difference in the prevalence rates of different clusterings of abnormalities in men and women.

Results

After the exclusion of two pregnant women, three foreigners, and 19 other individuals who could not be contacted, the size of the final experimental group was 1148 subjects. Of those, 841 (77%) volunteers participated in the study. The participation rate was 63% for men aged 36 y, 73% for men aged 41 y, 70% for men aged 46 y and 75% for men aged 51 y. For

women, the corresponding participation rates were 72%, 78%, 87% and 90%, respectively.

Obesity, defined as BMI ≥ 30 kg/m², was present in 74 of the 394 (19%) men and in 74 of the 447 (17%) women in the experimental group. The occurrence of 'pure' obesity was 6% for men and 5% for women, the occurrence of abdominal adiposity was 13% for men and 11% for women, and the prevalence of central obesity was 13% for men and 11% for women. Some type of obesity was present in 124 (31%) of the men and in 122 (27%) of the women in the experimental group.

The mean age in the control group of 162 volunteers (77 men and 85 women) without any defined type of obesity was 1.8 y lower than in the experimental group of 246 subjects having some defined type of obesity (42.4 ± 2.5 y vs 44.2 ± 5.0 y). In the experimental cases, 32% of men and 19% of women were smokers. In the control group, the corresponding figures were 25% and 15%. The difference in the prevalence rates was not statistically significant between groups. The levels of triglycerides, 2 h-glucose in OGTT and plasma insulin were all higher, and the level of HDL-cholesterol was lower, in the experimental cases (study subjects with some type of obe-

sity), as compared to controls. The levels of total cholesterol were roughly equivalent in the cases and the controls (Table 1).

Hypertension, and the insulin resistance-associated abnormalities were more often present in the experimental cases than in the controls. The prevalence of hyperinsulinaemia ≥ 13.0 mU/l was four- to nine-fold higher in the experimental cases than in the controls (Table 2).

The prevalence of the 'metabolic core' of the syndrome was 4% for controls, 18% for the abdominal adipose, 28% for the 'pure' obese, and 46% for the central obese volunteers. The corresponding figures for the conventional metabolic syndrome were 3%, 8%, 15% and 22%, respectively. The prevalence rates of the metabolic cluster A and the metabolic cluster B varied similarly according to the type of obesity (Table 3).

In women, unlike men, we could not find any statistically significant difference in the prevalence rates of different clusterings between the control group and abdominal adipose group. In the abdominal adipose men, all examined clusterings were more prevalent than in the abdominal adipose women, this difference between genders being statistically signifi-

Table 1 Basic characteristics of 246 subjects, with some type of obesity, and 162 controls

	Type of obesity			
	Controls	Abdominal adipose	'Pure' obese	Central obese
Men/Women (n)	77/85	50/48	23/24	51/50
Age (y)				
Men	42.4 (2.5)	44.2 (5.5) ^a	43.4 (5.4)	44.7 (4.3) ^a
Women	42.5 (2.5)	43.2 (4.8) ^a	46.4 (5.7) ^a	43.7 (4.9) ^a
Body mass index (kg/m ²)				
Men	24.8 (2.9)	27.6 (1.5) ^a	31.0 (0.8) ^{ab}	32.7 (2.5) ^{abc}
Women	23.7 (2.8)	27.2 (2.0) ^a	34.8 (5.0) ^{ab}	35.1 (4.6) ^{ab}
Waist-to-hip ratio				
Men	0.93 (0.01)	1.02 (0.01) ^{ac}	0.96 (0.01) ^a	1.04 (0.02) ^{abc}
Women	0.78 (0.01)	0.91 (0.01) ^{ac}	0.83 (0.01) ^a	0.92 (0.01) ^{ac}
Systolic blood pressure (mmHg)				
Men	131 (17)	140 (15) ^a	135 (18)	148 (20) ^{ac}
Women	123 (11)	138 (22) ^a	140 (17) ^a	142 (15) ^a
Diastolic blood pressure (mmHg)				
Men	84 (9)	85 (10)	85 (11)	90 (14) ^a
Women	79 (8)	83 (10) ^a	83 (8)	86 (9) ^a
Fasting serum cholesterol (mmol/l)				
Men	5.9 (1.2)	5.9 (0.8)	5.7 (1.0)	5.8 (1.0)
Women	5.3 (1.0)	5.3 (1.0)	5.9 (0.8)	5.4 (0.9)
Fasting serum HDL-cholesterol (mmol/l)				
Men	1.3 (0.5) ^d	1.2 (0.3)	1.2 (0.4)	1.1 (0.3)
Women	1.6 (0.4) ^d	1.5 (0.4)	1.5 (0.4)	1.3 (0.3)
Fasting triglycerides (mmol/l)				
Men	1.5 (0.7)	1.7 (0.7)	2.5 (2.0)	2.6 (3.3) ^a
Women	1.1 (0.5)	1.2 (0.8)	1.5 (0.8) ^a	1.6 (0.9) ^{ab}
2h glucose in OGTT (mmol/l)				
Men	5.1 (1.0)	5.5 (2.2)	5.8 (2.2)	6.2 (3.4) ^a
Women	5.6 (1.7)	5.9 (1.2)	6.6 (2.8)	6.1 (1.6)
Fasting plasma insulin (mU/l)				
Men	9.4 (4.4)	11.6 (4.0)	12.7 (5.5) ^a	17.7 (7.4) ^{abc}
Women	8.1 (2.7)	10.8 (4.5) ^a	13.8 (6.3) ^a	15.5 (7.3) ^{ab}
Smoking prevalence (%)				
Men	25	42	30	24
Women	15	25	4 ^b	20

Values are expressed as means (s.d.). Tukey's highly significant difference (HSD) test for intergroup differences; $P < 0.05$, ^avs controls, ^bvs abdominal adipose, ^cvs 'pure' obese, ^dvs central obese.

Table 2 Prevalence % (*n*) of hypercholesterolaemia and five insulin resistance-associated abnormalities (hypertension, low high-density-lipoprotein (HDL) cholesterol, hypertriglyceridaemia, abnormal glucose metabolism and hyperinsulinaemia) according to type of obesity in 246 middle-aged subjects

	Controls	Type of obesity		
		Abdominal adipose	'Pure' obese	Central obese
Men/Women (<i>n</i>)	77/85	50/48	23/24	51/50
Hypertension				
Men	16 (12)	32 (16) ^a	26 (6)	49 (25) ^{ac}
Women	9 (8)	31 (15) ^a	29 (7) ^a	34 (17) ^a
Total	12 (20)	32 (31) ^a	28 (13) ^a	42 (42) ^a
Hypercholesterolaemia				
Men	29 (22)	26 (13)	17 (4)	24 (12)
Women	15 (13)	11 (5)	25 (6)	14 (7)
Total	22 (35)	19 (18)	21 (10)	19 (19)
Low HDL-cholesterol				
Men	10 (8)	34 (17) ^a	35 (8) ^a	45 (23) ^a
Women	18 (15)	21 (10)	25 (6)	40 (20) ^{ab}
Total	14 (23)	28 (27) ^a	30 (14) ^a	43 (43) ^a
Hypertriglyceridaemia				
Men	30 (23)	44 (22)	57 (13) ^a	55 (28) ^a
Women	8 (7)	10 (5)	33 (8) ^{ab}	36 (18) ^{ab}
Total	19 (30)	28 (27)	45 (21) ^{ab}	46 (46) ^{ab}
Abnormal glucose metabolism				
Men	4 (3)	16 (8)	26 (6) ^a	28 (14) ^a
Women	12 (10)	23 (11)	25 (6)	30 (15) ^a
Total	8 (13)	19 (19) ^a	26 (12) ^a	29 (29) ^a
Hyperinsulinaemia				
Men	8 (6)	40 (20) ^a	39 (9) ^a	69 (35) ^{abc}
Women	6 (5)	25 (12) ^a	38 (9) ^a	48 (24) ^{ab}
Total	7 (11)	33 (32) ^a	38 (18) ^a	58 (59) ^{abc}

Values are expressed as % (*n*). Analysis of variance (ANOVA) for intergroup differences; $P < 0.05$, ^avs controls, ^bvs abdominal adipose, ^cvs 'pure' obese, ^dvs central obese.

Table 3 Prevalence % (*n*) of different clusterings of the five insulin resistance associated abnormalities in different types of obesity in 246 men and women, and in a control population of 162 subjects without any type of obesity

	Controls	Type of obesity		
		Abdominal adipose	'Pure' obese	Central obese
Men/Women (<i>n</i>)	77/85	50/48	23/24	51/50
Cluster A				
Men	12 (9)	54 (27) ^{a**}	57 (13) ^a	78 (40) ^{abc**}
Women	12 (10)	25 (12)	38 (9) ^a	54 (27) ^{ab}
Total	12 (19)	40 (39) ^a	47 (22) ^a	66 (67) ^{abc}
Cluster B				
Men	5 (4)	30 (15) ^{**}	30 (7) ^a	51 (26) ^{abc*}
Women	2 (2)	8 (4)	29 (7) ^{ab}	32 (16) ^{ab}
Total	4 (6)	19 (19) ^a	30 (14) ^a	42 (42) ^{abc}
Clustering of dyslipidaemia and insulin resistance (metabolic 'core')				
Men	7 (5)	28 (14) ^{a**}	30 (7) ^a	51 (26) ^{abc}
Women	2 (2)	8 (4)	25 (6) ^{ab}	40 (20) ^{ab}
Total	4 (7)	18 (18) ^a	28 (13) ^a	46 (46) ^{abc}
Clustering of hypertension, dyslipidaemia and insulin resistance (conventional metabolic syndrome)				
Men	4 (3)	16 (8) ^{a*}	17 (4) ^a	26 (13) ^a
Women	1 (1)	– (–)	13 (3) ^{ab}	18 (9) ^{ab}
Total	3 (4)	8 (8)	15 (7) ^a	22 (22) ^{ab}

Analysis of variance (ANOVA) for intergroup differences; $P < 0.05$, ^avs controls, ^bvs abdominal adipose, ^cvs 'pure' obese, ^dvs central obese. Chi-squared between genders in different types of obesity; * $P < 0.05$, ** $P < 0.01$

cant ($P < 0.05 - P < 0.01$). Also present was a gender difference in the prevalences of cluster 2 and cluster 3 in the central obese individuals. In the controls and in the 'pure obese' subjects, we could not find any gender difference (Table 3).

In both genders, all different clusterings of abnormalities occurred most frequently in the

central obese subjects, as compared to the controls, or in the subjects having any other type of obesity. The difference in the prevalence rates of different clusterings between the defined types of obesity was statistically significant. Adjustment for age and smoking did not change these results (Table 3).

Discussion

Many epidemiological studies have suggested that the localisation of the adipose tissue intra-abdominally is linked to many cardiovascular risk factors^{3–8} and is a more important predictor of cardiovascular disease and death than the total amount of fat.^{22–24} Visceral fat has been shown to be associated with insulin resistance and the compensatory hyperinsulinaemia.^{1–7,14,21} This association results in an increased hormone sensitive lipase (HSL) activity and a decreased lipoprotein lipase (LPL) activity, which leads to high levels of triglycerides, low levels of HDL-cholesterol and high levels of free fatty acids in the blood.^{4,25,26} Increased free fatty acid concentrations may subsequently lead to abnormalities in glucose metabolism.^{1,25,26} Thus, our results are in line with the presented theoretical background, reaffirming the existence of different clusterings of hypertension, hypertriglyceridaemia, low HDL-cholesterol level, abnormal glucose metabolism and hyperinsulinaemia especially in the subjects with central obesity; i.e. a combination of obesity and abdominal adiposity.^{2–6} The ‘metabolic core’ of the metabolic syndrome²¹ was present in only 4%, and the conventionally defined metabolic syndrome in 3%, of the controls. About half the volunteers with central obesity also had the ‘metabolic core’ of the syndrome, and one in five volunteers with central obesity also had the conventionally defined metabolic syndrome with hypertension, dyslipidaemia and insulin resistance. Some type of obesity occurred in one of every three subjects and 66–80% of different clusterings of the insulin resistance related abnormalities were detectable in this subset.

The differing categories of obesity, though arbitrary in definition, are justified. The purpose of this classification was to help to give some indication of the more harmful types of obesity, and thereby increase understanding of the separate role for both obesity and abdominal adiposity on the manifestation of hyperinsulinaemia, dyslipidaemia and abnormal glucose metabolism. We applied accepted criteria (upper 25th percentiles in the distribution of variable concerning WHR in this study, and results from earlier published studies) to define the relevant risk factors.^{15–18} A fasting plasma insulin level ≥ 13.0 mU/l was used as a defining criterion for hyperinsulinaemia and insulin resistance. It has been shown that at this level of fasting plasma insulin, about 75% of the subjects were insulin resistant, as measured by the hyperinsulinaemic clamp technique.¹⁹

The mean level of the fasting plasma insulin, the usual reflector of insulin resistance, was higher in the experimental cases when compared to controls. Also demonstrated, are the prevalence rates of other abnormalities reflecting increased insulin resistance, such as hypertriglyceridaemia, low HDL-cholesterol level and abnormal glucose metabolism, all of which

were higher in the experimental cases than in the controls. Moreover, the rate of prevalence for different clusterings of these insulin resistance-associated risk factors was found to be six- to twelve-fold higher in the experimental cases having some type of obesity, as compared to the controls. Smoking was more prevalent in both men and women of the experimental group, as compared to the control men and women. However, this difference between groups was not statistically significant, and did not explain the discovered difference in the occurrence of abnormalities in the different groups.

Our results are in line with some earlier studies suggesting that abdominal fat distribution may at least partly explain the gender difference in the risk profile of coronary heart disease.^{27,28} In men of our study, abdominal adiposity alone or associating with obesity was a more powerful indicator for different clusterings of the insulin resistance-associated risk factors, compared to women. These findings can be explained at least partly by our relatively young study population, with a mean age of about 43 y, i.e. women had normal estrogen production. It has been shown that in women, estrogen may have a protective effect on the insulin resistance-associated risk factors, and that this advantage is lost after the menopause.^{4,29,30} Another explanation for the gender difference, is that men are known to have twice the proportion of total fat distributed intra-abdominally when compared to women with the same BMI.¹¹ Therefore, in women, a higher BMI than in men may be needed for the metabolic disturbances associating with the obesity and central adiposity.¹²

This study also demonstrates that the rates of prevalence for different clusterings of abnormalities were significantly higher in the experimental men and experimental women having central obesity. This result indicates that any type of obesity may be metabolically harmful, and serves as a signal of a constellation of insulin-resistance related abnormalities in both genders.^{2–6,21} It also provides more evidence to suggest that especially a combination of obesity and abdominal adiposity, i.e. central obesity, may be used as a distinctive marker for the metabolic syndrome, a clustering of many insulin-resistance related risk factors.^{4,14} This conclusion is also in agreement with the findings that implicate central obesity as a powerful risk factor for coronary heart disease (CHD), stroke, and NIDDM,^{3,25,26}

In daily clinical practice, BMI alone is usually used as an indicator for obesity. However, our results like many other epidemiological studies, show that the measurement of WHR could improve our possibilities in the assessment of cardiovascular risk at both individual and population level. Our study demonstrates that most patients at risk of having clusterings of abnormalities consistent with the concept of the metabolic syndrome, and possible candidacy for CHD, stroke and NIDDM, are recognizable by the simple measurements of BMI and WHR.

References

- 1 Beck-Nielsen H. Clinical Disorders of Insulin Resistance. *International Textbook of Diabetes Mellitus*. In: Alberti KGM-M, DeFronzo RA, Keen H, Zimmer P (eds). John Wiley: London, 1992, pp 531–549.
- 2 Reaven GM. Banting lecture 1988: Role of insulin resistance in human disease. *Diabetes* 1988; **37**: 1595–1607.
- 3 DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diab Care* 1991; **14**: 173–194.
- 4 Björntorp P. Abdominal obesity and the metabolic syndrome. *Annals of Medicine* 1992; **24**: 465–468.
- 5 Reaven GM. A syndrome of resistance to insulin stimulated glucose uptake (Syndrome-X): Definitions and implications. *Cardiovascular Risk Factors* 1993; **1**: 2–11.
- 6 Haffner SM, Valdez RA, Hazuda HP, Mitchell BD, Morales PA, Stern MP. Prospective analysis of the insulin-resistance syndrome (Syndrome-X). *Diabetes* 1992; **41**: 715–722.
- 7 McKeigue PM, Shah B, Marmot MG. Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians. *Lancet* 1991; **337**: 382–386.
- 8 Moller DE, Flier JS. Insulin resistance-mechanism, syndromes, and implications. *N Engl J Med* 1991; **325**: 938–948.
- 9 Wajchenberg BL, Malerbi DA, Rocha MS, Lerario AC, Santomauro TMG. Syndrome X: A syndrome of insulin resistance. Epidemiological and clinical evidence. *Diabetes Metab Rev* 1994; **1**: 19–29.
- 10 Laws A, Stefanick ML, Reaven GM. Insulin resistance and hypertriglyceridemia in nondiabetic relatives of patients with non-insulin-dependent diabetes mellitus. *J Clin Endocrinol Metab* 1989; **69**: 343–347.
- 11 Kvist H, Chowhury B, Grangård U, Tylene U, Sjöström L. Predictive equations of total and visceral adipose tissue volumes derived from measurements with computed tomography in adult men and women. *Am J Clin Nutr* 1988; **48**: 1351–1361.
- 12 Landin K, Krotkiewski M, Smith U. Importance of obesity for metabolic abnormalities associated with an abdominal fat distribution. *Metabolism* 1989; **38**: 572–576.
- 13 Shen DC, Shien SM, Fuh MT, Chen YDI. Comparison of the effects of differences in waist to hip girth and body mass index on carbohydrate metabolism in Chinese females. *Horm Metab Res* 1990; **22**: 533–536.
- 14 Björntorp P. “Portal” adipose tissue as a generator of risk factors for cardiovascular disease and diabetes. *Arteriosclerosis* 1990; **10**: 493–496.
- 15 Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure: The Fifth Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNCV). *Arch Intern Med* 1993; **153**: 154–183.
- 16 WHO Expert Committee. *Arterial Hypertension*. Technical Report Series No 628. World Health Organization: Geneva, 1978.
- 17 Prevention of coronary heart disease: Scientific background and new clinical guidelines. Recommendations of the European Atherosclerosis Society prepared by the international task force for the prevention of coronary heart disease. *Nutr Metab Cardiovasc Dis* 1992; **2**: 113–156.
- 18 Castelli WP. Epidemiology of triglycerides: a view of Framingham. *Am J Cardiol* 1992; **70**: 3H–9H.
- 19 Laakso M. How good a marker is insulin level for insulin resistance? *Am J Epidemiol* 1993; **9**: 959–965.
- 20 WHO Expert Committee on Diabetes Mellitus. Technical Reports Series No. 727, World Health Organization: Geneva, 1985.
- 21 Laakso M. The possible pathophysiology of insulin resistance syndrome. *Cardiovascular Risk Factors* 1993; **1**: 55–66.
- 22 Larsson B, Svardsudd K, Welin K, Wilhelmssen L, Björntorp P, Tiddlin G. Abdominal adipose tissue distribution, obesity, and risk of cardiovascular disease and death: 13 year follow up of participants in the study of men born 1913. *BMJ* 1984; **288**: 1401–1404.
- 23 Lapidus L, Bengtsson C, Larsson B, Pennert K, Rybo E, Sjöström L. Distribution of adipose tissue and risk of cardiovascular disease and death: a 13 year follow up of participants in the population study of women in Gothenburg, Sweden. *BMJ* 1984; **289**: 1257–1261.
- 24 Kahn HS, Williamson DF. Abdominal obesity and mortality risk among men in nineteenth-century North America. *Int J Obes* 1994; **18**: 686–691.
- 25 Frayn KN, Coppack SW. Insulin resistance, adipose tissue and coronary heart disease. *Clin Sci (Colch)* 1992; **82**: 1–8.
- 26 Despres J-P, Marette A. Relation of components of insulin resistance syndrome to coronary disease risk. *Curr Opin Lipidol* 1994; **5**: 274–289.
- 27 Wingard DL. Sex difference and coronary heart disease: a case of comparing apples and pears? *Circulation* 1990; **81**: 1710–1712.
- 28 Larsson B, Bengtsson C, Björntorp P, Lapidus L, Sjöström L, Svardsudd K, Tibblin G, Wdel H, Weklin L, Wilhelmsen L. Abdominal body fat distribution: a major explanation for the sex difference in the incidence of myocardial infarction? The study of men born 1913 and the study of women, Göteborg. *Am J Epidemiol* 1992; **3**: 266–273.
- 29 Haarbo J, Marslew U, Gotfredsen A, Christiansen C. Postmenopausal hormone replacement therapy prevents central distribution of body fat after menopause. *Metabolism* 1991; **40**: 1323–1326.
- 30 Manolito TA, Fuhrberg CD, Shemanski L, Psaty BM, O’Leary DH, Tracy RP, Bush TL. Associations of postmenopausal estrogen use with cardiovascular disease and its risk factors in older women. *Circulation* 1993; **88**: 163–171.