International Journal of Obesity (2002) 26, 193–199

0307–0565/02 $25.00
www.nature.com/ijo

PAPER

A pilot study of long-term effects of a novel obesity treatment: omentectomy in connection with adjustable gastric banding

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AIM: To determine whether visceral fat reduction in connection with bariatric surgery could improve weight loss and metabolic profile of obese subjects.
PATIENTS AND METHODS: In a one-center, randomized and controlled pilot trial we assigned 50 subjects with severe obesity (body mass index $>35\,kg/m^2$) to either adjustable gastric banding (AGB) alone (11 men and 14 women), or AGB plus surgical removal of the total greater omentum (11 men and 14 women). The patients were followed at regular intervals for 2 y and examined at 0 and 24 months with respect to body composition and metabolic profile.
RESULTS: No significant differences between control and omentectomized patients were observed at baseline. The removed greater omentum constituted $0.8\pm0.4\%$ (mean ± s.d.) of total body fat. At 2 y follow-up there was an expected decrease in body weight and an improvement in metabolic profile in both groups. Although omentectomized subjects tended to lose more weight than control subjects the difference was not statistically significant and changes in waist-to-hip ratio and saggital diameter did not differ between groups. However, the improvements in oral glucose tolerance, insulin sensitivity and fasting plasma glucose and insulin were 2–3 times greater in omentectomized as compared to control subjects (*P* from 0.009 to 0.04), which was statistically independent of the loss in body mass index. No differences in blood lipids between the groups were recorded. No adverse effects related to omentectomy were observed.
CONCLUSIONS: Omentectomy, when performed together with AGB, has significant positive and long-term effects on the glucose and insulin metabolic profiles in obese subjects.
International Journal of Obesity (2002) **26,** 193–199. DOI: 10.1038/sj/ijo/0801871

Keywords: gender; glucose; insulin; insulin resistance; bariatric surgery

Introduction

Obesity is a major health problem in many countries. In the United States, for example, the prevalence of obesity has increased by 50% during the last decade.[1] Obesity has a number of adverse effects on the health outcome, including an increased risk of various atherosclerosis-promoting disorders. However, it is not only the increase in total fat mass that predicts an adverse health profile. A number of epidemiological observations suggest that accumulation of visceral adipose tissue is an independent risk factor for the adverse outcomes of obesity, in particular dyslipidemia, hyperinsulinemia, glucose intolerance, insulin resistance and coagulation abnormalities.[2–4] Furthermore, there is some indirect evidence suggesting that a selective reduction in visceral fat improves the metabolic profile.[5,6] It is likely that some of the intrinsic properties of visceral adipose tissue make this fat depot particularly pernicious.[7] Visceral fat as distinct from other adipose regions is drained by the portal vein and therefore has a unique direct connection with the liver. The lipolytic activity is higher in visceral fat than in other adipose regions, which results in an elevation of 'portal' fatty acids (an end-product of lipolysis). Fatty acids influence liver production of glucose and triglycerides and the clearance of insulin by the liver. So, in obesity there is an

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Received 22 March 2001; accepted 31 July 2001

increased delivery of fatty acids to the liver due to a combination of high lipolytic activity in visceral fat and an expansion of this adipose depot. This in turn has a number of adverse consequences for the liver resulting in hyperglycemia, hyperinsulinemia, insulin resistance and dyslipidemia.[8] Furthermore, the recently discovered and potentially important protein secretory function of adipose tissue, such as the release of leptin and plasminogen activator inhibitor-1 (PAI-1), is subject to regional variations.[7,9] It is possible that visceral fat produces yet undiscovered proteins that might disturb the liver when the visceral fat depot expands during development of obesity.

We undertook a pilot study, which was performed in a randomized, controlled, long-term fashion to investigate the effects of visceral fat resection in obese subjects when performed in connection with bariatric surgery. Our hypothesis was that, under such conditions, removal of visceral fat might have additional important effects on metabolic profile and body weight. Visceral fat is made up of both the greater omentum and the mesenteric fat depot. The latter adipose region cannot be surgically removed without the risk of major peri- and post-operative complications. In contrast, because of its anatomical localization, the whole greater omentum can easily be removed surgically. No data on omentectomy have been reported previously. We obtained ethical permission to perform omentectomy in connection with adjustable gastric binding (AGB) on a limited number of severely obese patients of both gender. They and their obese controls (only treated with AGB) were followed for 2 y and the body composition and metabolic profile were assessed.

Methods

Study design

The patients (age 23 – 57 y) were admitted to our department for surgical treatment of severe obesity (body mass index, BMI $>35\,kg/m^2$). We excluded patients who were treated for diabetes mellitus. Patients who had a suspected (untreated) diabetes on the basis of results from baseline examinations remained in the study but they received no specific antidiabetic therapy. Hypertensive patients on metabolically active drugs (ie beta-blockers or saluretics) were also excluded. All hypertensive patients included remained on their initial pharmacotherapy throughout the study. The women enrolled who were receiving sex hormone therapy did not change their therapy during the study.

After eligibility was evaluated, the patients were stratified according to gender, BMI and age and then randomly assigned to one of two groups. Control patients underwent only AGB while omentectomized patients underwent AGB plus surgical removal of as much as possible of the greater omentum. Eleven men and 14 women constituted the former group and 11 men and 14 women constituted the latter. All patients were stratified, randomized and operated on by AT or GH. None of the subjects refused randomization. The abdomen was entered through an upper midline incision during general anesthesia. A 32F gastric tube was placed along the lesser curvature of the stomach and a channel was developed by blind finger dissection behind the gastric cardiac. The lesser abdominal sac was never entered and an adjustable gastric band (Swedish Adjustable Gastric Band®, Obtech AB, Stockholm, Sweden) was placed in the channel. It was locked around the uppermost part of the stomach with non-absorbable sutures. The anterior gastric wall, distal to the band, was folded over the band and sutured to the upper gastric pouch. This pouch thus became very small and in no case exceeded 20 ml. A subcutaneous injection-port was placed on the lower sternum, sutured to the periosternum and connected to the adjustable band. The gastric tube was removed at the end of the operation. Prophylatic antibiotics and low-molecular weight heparin were always given. The band was left empty during the first month after surgery. The patients were put on liquid diet for one month followed by gradual introduction of solid food. It was technically possible to resect essentially all of the greater omentum in all assigned subjects. Omentectomy was performed immediately after the abdomen was entered.

All patients were followed at the out-patient department according to the clinical routine 1, 2, 3, 6, 9, 12, 18 and 24 months post-operatively by a trained obesity nurse (who was blind to the surgical procedure) in addition to their visits at the research laboratory where they were examined by a research nurse. The routine follow-ups included regular controls of body weight, blood chemistry and clinical examination. These controls usually included gradual filling of the adjustable band with a radiology contrast medium (Iopamiro®, Astra Zeneca AB, Södertälje, Sweden) through the presternal injection-port. The filling volume was dependent on weight changes and clinical factors relating to food intake. The filling volume was recorded at each investigation.

The study was approved by the Huddinge Hospital committee on ethics. Because the long- and short-terms side effects of selective omentectomy were unknown before the study, the ethical committee only allowed the inclusion of a limited number of subjects and it also allowed us to perform omentectomy only in addition to bariatric surgery.

Clinical parameters

All patients were examined at the research laboratory before and at 3, 6, 12 and 24 months following surgery. The investigations were performed at about 8 am following an overnight fast. Body weight, saggital diameter and waist-to-hip ratio (WHR) were determined. WHR was measured in the supine position. The saggital diameter was obtained by measuring the distance from the examination table to a horizontal crossbar placed over the abdomen of the recumbent subject at the crista level. Waist circumference was measured in the middle between the lower costal rib and the upper pelvis rim. The largest hip circumference was used. At all visits an antecubital venous blood sample was obtained for analysis of plasma levels of glucose, insulin, leptin and lipids.

The following examinations were made before and at 24 months following surgery: leptin (on plasma frozen at $-70\,^{\circ}C$) and PAI-1 enzymatic activity (on fresh plasma) were measured using the venous blood sample. On separate occasions they underwent a 75 g oral glucose load and an intravenous insulin tolerance test. The insulin tolerance test was performed as described earlier.[10] Crystalline insulin (Actrapid®, Novo Nordisk, Gentofte, Denmark) was rapidly injected intravenously (0.1 units/kg body weight) and plasma glucose determined at 0, 2, 4, 6, 8, 10, 12, 14 and 16 min. Thereafter, intravenous glucose was given. Plasma catecholamines were determined at 0 and 16 min. In no situation was there a significant difference (>20%) in catecholamine levels at these two time points. Insulin sensitivity was measured as the slope (K_{itt}) of the fall in plasma glucose from 4 to 16 min. Several studies have shown that K_{itt} is reproducible and has a close correlation with other tests of insulin sensitivity in lean, obese, diabetic or non-diabetic subjects.[11–15]

Laboratory procedures

Plasma noradrenaline, adrenaline, glucose, total cholesterol, HDL-cholesterol and triglycerides were measured by the Huddinge Hospital routine chemistry accredited laboratory. Plasma insulin was measured by a radioimmunoassay kit (Amersham-Pharmacia, Uppsala, Sweden). Plasma leptin was measured with a radioimmuno assay and PAI-1 as enzyme activity as described.[16,17]

Statistical analysis

Values are expressed as means±s.d. except for±s.e. in figures. Values for plasma triglycerides were log-transformed before statistical comparison. Student's unpaired *t*-test, analysis of variance (co-variance analysis and repeated measure analysis) and chi-square analysis were used to compare values between groups. All tests were two-sided. $P\leq 0.05$ was considered to be statistically significant. Intention-to-treat analysis was performed according to the method of last-value-recorded carried forward.

Results

Drop-out of study patients and complications

There were no perioperative or post-operative complications related to omentectomy, such as local bleeding or thrombo-embolism. Thirteen patients (26%) discontinued at various times during the study either due to refusal to continue to participate, or not showing up on planned visits. Because oral glucose tolerance, K_{itt}, PAI-1 and leptin were only measured before and 24 months after surgery it was not possible to perform intention to treat analysis on these values. Subjects remaining in or dropping out from the study were equally distributed among the omentectomy ($n=6$) and control ($n=7$) groups. Late complications occurred in three subjects (infection or re-operation because of band dysfunction). One woman became pregnant during the course of investigation. There was no evidence of disturbances related to omentectomy such as bleeding, infection or intestinal obstruction. This is also true for 11 subjects who have now been followed by us for as long as 4 y. Thirty-seven patients completed the study and could be investigated at the 2 y follow-up. Of these remaining subjects, 18 were controls and 19 had undergone omentectomy.

Baseline characteristics

The baseline characteristics of all subjects and those completing the study are shown in Table 1. No significant

Table 1 Baseline characteristics of the patients

	All subjects		*Subjects completing the study*	
Variable	*Control*	*Omentectomy*	*Control*	*Omentectomy*
Gender (F/M)	14/11	14/11	9/9	12/7
Age (y)	38±10	38±10	39±11	36±9
Body mass index (kg/m^2)	43±4	44±6	43±5	44±5
Waist-to-hip ratio	0.97±0.07	0.97±0.10	0.97±0.08	0.95±0.01
Saggital measure (cm)	33±3	33±3	33±4	33±3
pl-glucose (mmol/l)	5.6±0.7	6.0±1.6	5.8±0.8	6.2±1.2
pl-insulin (mU/l)	19.4±9.4	23.7±11.0	20.5±10.4	23.7±12.7
pl-triglycerides (mmol/l)	2.2±1.2	2.8±0.8	2.4±1.6	2.9±1.6
pl-cholesterol (mmol/l)	5.7±0.9	5.4±1.0	5.8±1.0	5.4±1.8
pl-HDL cholesterol (mmol/l)	1.15±0.32	1.13±0.24	1.11±0.31	1.15±0.21
pl-plasmin activator inhibitor I (U/ml)	39.6±19.5	46.5±26.6	43.7±21.0	46.9±29.3
pl-leptin (ng/ml)	44.8±20.9	46.1±26.6	42.1±18.7	48.1±24.3
Intravenous insulin tolerance (%/min)	2.8±0.9	2.7±1.0	2.6±0.9	2.7±1.0
Oral glucose tolerance (mmol/l)	7.5±2.4	8.2±3.5	7.7±2.6	8.5±3.9
Abnormal oral glucose tolerance (yes/no)	10/15	10/15	6/12	8/11

Plus–minus values are means±s.d. They were compared using Student's unpaired *t*-test. No significant differences between control and omentectomy subjects were noted. pl=fasting plasma.

differences between the groups were observed at baseline. Nineteen patients had pathological glucose tolerance at the start of the study (plasma glucose value >7.8 mmol/l at 2 h). These patients were evenly distributed among the groups and three control subjects and four omentectomized subjects had a diabetic glucose value (>11.1 mmol/l). Four patients (two controls and two omentectomized patients) had essential hypertension (treated with calcium blockers or angiotensin converting enzyme inhibitors). One woman in the omentectomy group and one in the control group were postmenopausal.

We also made a separate analysis of the baseline characteristics of the 13 subjects who dropped out of the study. This cohort showed the same pattern of baseline characteristics as the 37 subjects who completed the study.

In all cases more than 90% of the visible omentum majus was resected and the weight of the removed omentum was 0.6±0.3 kg. It constituted 0.8±0.4% of the total fat mass.

Anthropometric measurements

In the two study groups AGB was followed-up by a decline in BMI. However, at 2 y follow-up the net fall in BMI in the omentectomized group was almost 4 kg/m^2 larger than in the control group ($P<0.05$, Table 2). However, intention-to-treat analysis showed no significant difference between groups in loss of BMI (Table 3).

As regards body weight it tended to decrease more in the omentectomy group but the difference from the control group was only of border-line significance when analyzed on those completing the study (Table 2) or according to intention-to-treat (Table 3). WHR decreased following surgery but there was no significant effect of omentectomy when data obtained at 2 y follow-up (Table 2) or when intention-to-treat analysis was performed (values not shown). The same was true for saggital diameter.

We also analyzed the time courses of changes in BMI at 0, 3, 6, 12 and 24 months by repeated measure analysis of variance. There was no significant deviation between omentectomized subjects and controls in BMI ($P=0.18$).

Table 2 Changes from baseline to 24 months

Variable	*Control*	*Omentectomy*	*P-value*
n	18	19	
Body mass index (kg/m^2)	9±6	13±5	0.049
Body weight (kg)	27±17	36±14	0.07
Waist-to-hip ratio	0.04±0.07	0.03±0.06	0.70
Saggital measure (cm)	8±3	9±3	0.12
pl-glucose (mmol/l)	0.7±0.7	1.8±0.8	0.04
pl-insulin (mU/l)	9.8±6.8	17.3±9.3	0.009
pl-triglyceride (mmol/l)	1.2±0.9	1.8±0.8	0.64
pl-cholesterol (mmol/l)	0.9±0.8	0.2±1.4	0.07
pl-HDL cholesterol (mmol/l)	−0.13±0.29	−0.24±0.29	0.26
pl-plasmin activator inhibitor-1 (U/ml)	23.3±22.7	36.1±32.4	0.18
pl-leptin (ng/ml)	19.2±14.5	24.8±18.8	0.32
Intravenous insulin tolerance (%/min)	−0.6±0.7	−1.3±1.0	0.02
Oral glucose tolerance (mmol/l at 2 h)	1.2±1.0	3.2±4.1	0.10

Plus–minus values are baseline minus 24 months and expressed as means±s.d. They were compared between control and omentectomy subjects using Student's unpaired *t*-test. pl=fasting plasma.

Table 3 Intention-to-treat analysis of changes in BMI, body weight and fasting plasma levels of insulin and glucose

Measure	*Omentectomy*	*Control*	*P*
Body weight (kg)	33±16	26±18	0.11
BMI (kg/m^2)	11±1	9±6	0.21
Insulin (mU/l)	16.1±9.0	7.8±7.1	0.001
Glucose (mmol/l)	1.6±2.0	0.6±0.7	0.03

Values are mean±s.d. They were calculated as value at 0 months minus last recorded values (3, 6, 12 or 24 months). Student's unpaired *t*-test was used.

Metabolic profiles

Values at the 2 y follow-up (change from baseline) are shown in Table 2. In both groups the plasma levels of glucose, insulin, triglycerides, PAI-1 and leptin had decreased and that of HDL-cholesterol had increased at the 2 y follow-up. No additional effects of omentectomy were observed in the changes in plasma lipids, leptin and PAI-1. However, the fall in plasma insulin ($P<0.01$) and plasma glucose ($P<0.05$) was about two-fold greater in omentectomized subjects than in control patients. This difference between control and omentectomized patients remained statistically significant in the intention-to-treat analysis (Table 3).

In both groups there was a decline in the 2 h plasma glucose value following an oral glucose load at the 2 y follow-up. The almost three-fold difference between the groups regarding the absolute values for decrease in 2 h plasma glucose only reached a borderline significant level.

Insulin tolerance had improved significantly in both groups at the 2 y follow-up. The improvement in insulin tolerance was two-fold greater in the omentectomy group compared with the control group ($P=0.02$).

In order to co-investigate the changes in BMI and metabolic profiles at 2 y follow-up an analysis of co-variance was performed. When corrected for changes in BMI the effect of omentectomy on insulin tolerance and fasting plasma glucose and insulin remained significant (P from 0.01 to 0.04). Furthermore, the difference between the groups in the decline of 2 h plasma glucose became significant after correction for BMI changes ($P=0.045$).

We also analyzed the time-course of the changes in plasma glucose and insulin (Figure 1). For both parameters there was a significant effect over time induced by omentectomy. The more marked decrease of glucose and insulin in the omentectomy group was already apparent at 6 months following surgery.

Filling of the gastric band

As regards filling volume of the adjustable band, the values did not at any time differ significantly between the two groups. At 2 y follow-up the total filling volume (ml) was 9.2±1.7 in the control and 9.3±1.9 m in omentectomized patients.

Blood pressure

Since patients treated for hypertension were included in the study we were unable to perform detailed analysis of blood pressure. However, in the whole material systolic and diastolic blood pressures were 139±19 and 83±10 mmHg, respectively, at baseline. At the 2 y follow-up the values had decreased by 10 and 2 mmHg, respectively, ($P=0.002$ and $P=0.02$, respectively) by Student's paired *t*-test.

Discussion

Omentectomy is a novel additional treatment to the conventional bariatric obesity surgery. This prospective, gender stratified and randomized pilot study shows significant long-term effects of omentectomy on metabolic profile, when performed in combination with AGB in severely obese patients. About 25% of the patients did not complete the study and could therefore not be used in the 2 y follow-up analysis. However, all available patients were used in the analysis of body composition and plasma insulin and glucose (ie intention-to-treat). The present drop-out frequency was similar to values reported in other Scandinavian long-term studies on bariatric surgery where a less complicated experimental protocol was used. Between approximately 20 and 40% of patients had been lost at the 2 y follow-up.[18,19] We do not believe that the lack of data from patients dropping out had an important bearing on our findings. There were no important initial differences between those patients who remained in or left the study and patients dropping out were equally distributed between the two groups.

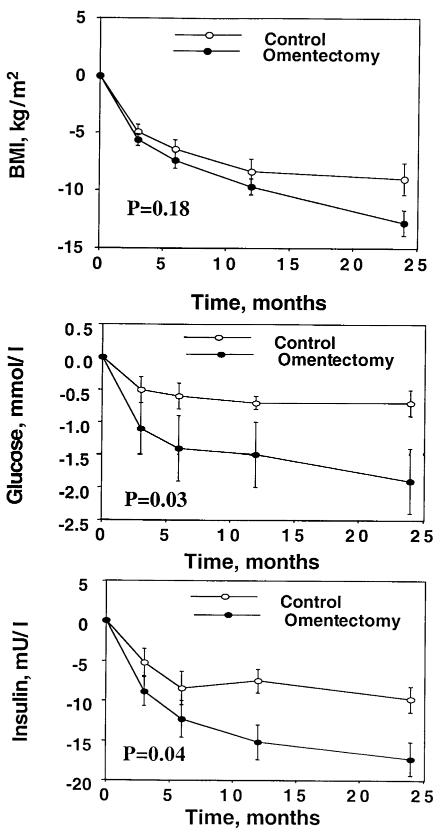

Figure 1 Changes from baseline over time in BMI and fasting plasma glucose and insulin. Omentectomy and control groups were compared by analysis of variance, repeated measure.

The fall in body weight was of the expected order of magnitude as judged by earlier results of bariatric surgery.[18,19] Although, those undergoing AGB and omentectomy tended to lose more in BMI and body weight than those treated with AGB alone, the difference was not significant when intention-to-treat analysis was performed or when the time course of the changes were compared. There was also no difference between groups in changes of body fat distribution following surgery as judged by the results with WHR and saggital diameter. It is unlikely that the omentectomized patients tended to lose more weight than the controls because of differences in post-operative procedures. The filling of the adjustable band was almost identical in the two groups.

A striking finding seen in the current study was the effect on metabolic profile. It is well established that insulin resistance, glucose intolerance and hyperinsulinemia are often observed in obese subjects.[20–22] The relationship between impaired metabolic profile and overweight appears particularly strong in visceral obesity.[20,21] We used a simple test of insulin sensitivity, the intravenous insulin tolerance test. However, it correlates well with the 'gold standard' test, which is hyperinsulinemic euglycemic clamp, and can be used on diabetic and obese subjects.[14,15,23] Insulin sensitivity improved in both groups at the 2 y follow-up but the change was two-fold greater in the omentectomized compared with the control patients. In the whole material we also observed a decline in fasting plasma levels of glucose and insulin and oral glucose tolerance. However, these improvements were two to three times greater in omentectomized patients than in controls. On the other hand, there was no apparent effect of omentectomy on blood lipids or PAI-1. So when omentectomy is performed together with AGB it seems above all to improve the glucose–insulin profile.

Could removal of the greater omentum have long-term undesirable effects? The tissue may have many other functions including preventing intra-abdominal infection. In order to answer this question in full it is probably necessary to have clinical experience from a large group of patients.

However, no peri-operative or post-operative problems related to omentectomy were recorded such as local bleeding or thromboembolism. Furthermore, there was no evidence of late complications such as infection, intestinal obstruction or other problems related to intra-abdominal tissue adhesions during the study. This is true for 11 of the omentectomized subjects who have been followed for 4 y.

It remains to be established how a removal of a small fat depot (on average <1 kg) can cause a marked additional improvement of the metabolic profile. However, it is possible that factors related to the unique anatomy and function of visceral fat could be of importance.[7,24] In particular, a decreased delivery of fatty acids to the liver through the portal vein caused by omentectomy could be beneficial for circulating glucose and insulin. In this respect it is relevant to note that selective reduction of the visceral fat depot improves metabolism and liver function of male rats.[25] It is also possible that synergistic effects between omentectomy and weight loss induced by AGB can occur. It is possible, though, that omentectomy has effects independent of weight loss. Plasma insulin and glucose started to fall more rapidly in omenectomized subjects at 6 months following surgery, whereas the time course of the drop in BMI and body weight did not differ significantly between the groups. This question can only be fully answered if omentectomy is done without weight reduction surgery. In a recent study it was found that liposuction of subcutaneous fat, without a change in diet or lifestyle, improves insulin sensitivity.[26] Unfortunately, it was not for ethical reasons possible to just perform omentectomy on our obese subjects. Nevertheless, it is a major clinical advantage that omentectomy not only may cause some additional weight loss to AGB but also leads to improvement of metabolic profile.

In this study both men and women were included and it has been suggested that men and women may respond differently to weight reduction.[27] However, the number of subjects was too small to allow a reliable comparison of male and female subgroups. Furthermore, we had no prior hypothesis that omentectomy would have a different effect on women compared with men and the proportion of men *vs* women was similar among the initially recruited and those who remaining at 2 y follow-up.

The procedure for surgical removal of the greater omentum was by open surgery. Most gastric banding is currently performed laparoscopically. Since the greater omentum is relatively small, even in obese subjects, it might in the future be possible to use modified laparoscopic procedures to remove this tissue. Because the procedure is easy and appears to be very effective in selected cases we suggest that omentectomy should be further evaluated as an additional therapy to weight reduction surgery in obese subjects, particularly in those who are insulin resistant. We admit that this recommendation is based on a first pilot study.

In summary, this pilot study demonstrates the benefit of omentectomy to add to weight reduction surgery in obese subjects. This procedure improves the long-term insulin-glucose profile and may also cause some additional weight loss.

Acknowledgements

The invaluable help of research nurse Britt Marie Leijonhufvud is greatly appreciated. We are grateful for statistical advise from Anna Hagman.

This study was supported by grants from the Swedish Medical Research Council, the Swedish Diabetes Foundation, the Söderberg Foundation, the Novo Nordic Foundation and the Swedish Heart and Lung Association.

References

1 Modkad AH, Serdula MK, Dietz WH, Boeman BA, Marks JS, Koplan JP. The spread of the obesity epidemic in the United States, 1991–1998. *JAMA* 1999; **282**: 1519–1522.
2 Björntorp P. 'Portal' adipose tissue as a generator of risk factors for cardiovascular disease and diabetes. *Atherosclerosis* 1990; **10**: 493–496.
3 Kissebah AH, Krakower GR. Regional adiposity and morbidity. *Physiol Rev* 1994; **74**: 761–811.
4 Lemieux S, Després JP. Metabolic complications of visceral obesity: contribution of the aetiology of type 2 diabetes and implications for prevention and treatment. *Diabetes Metab* 1994; **20**: 375–393.
5 Fujioka S, Matsuzawa Y, Tokunaga K *et al*. Improvement of glucose and lipid metabolism associated with selective reduction of intra-abdominal visceral fat in premenopausal women with visceral fat obesity. *Int J Obes* 1990; **15**: 853–859.
6 Riches FM, Watts GF, Hua J, Stewart GR, Naoumova RP, Barrett PHR. Reduction in visceral adipose tissue is associated with improvement in apolipoprotein B-100 metabolism in obese men. *J Clin Endocrinol Metab* 1999; **84**: 2854–2861.
7 Arner P. All fat is not alike. *Lancet* 1998; **351**: 1301–1302.
8 Frayn KN, Williams CM, Arner P. Are increased plasma non-esterified fatty acid concentrations a risk marker for coronary heart disease and other chronic diseases? *Clin Sci* 1996; **90**: 243–253.
9 Mohamed-Ali V, Pinkney JH, Coppack SW. Adipose tissue as an endocrine and paracrine organ. *Int J Obes Relat Metab Disord* 1998; **22**: 1145–1158.
10 Bolinder J, Lithell H, Skarfors E, Arner P. Effects of obesity, hyperinsulinemia, and glucose intolerance on insulin action in adipose tissue of sixty-year-old men. *Diabetes* 1986; **35**: 282–290.
11 Hirst S, Phillips DI, Vines SK, Clark M, Hales CN. Reproducibility of the short insulin tolerance test. *Diabetes Med* 1993; **10**: 839–842.
12 Lindheim SR, Buchanan TA, Duffy DM, Vijod MA, Kojima T, Stanczyk FZ, Lobo RA. Comparison of estimates of insulin sensitivity in pre- and postmenopausal women using the insulin tolerance test and the frequently sampled intravenous glucose tolerance test. *J Soc Gynecol Invest* 1994; **1**: 150–154.
13 Gelding SV, Robinson S, Lowe S, Niththyananthan R, Johnston DG. Validation of the low dose short insulin tolerance test for evaluation of insulin sensitivity. *J Clin Endocrinol* 1994; **40**: 611–615.
14 Bonora E, Moghetti P, Zancanaro C, Cigolini M, Querena M, Cacciatori V, Corgnati A, Muggeo M. Estimates of in vivo insulin action in man: comparison of insulin tolerance tests with euglycemic and hyperglycemic glucose clamp studies. *J Clin Endocrinol Metab* 1989; **68**: 374–378.
15 Graci S, Baratta R, Degano C, Luppa A, Vigneri R, Frittittta L, Trischitta V. The intravenous insulin tolerance test is an accurate method for screening a general population for insulin resistance and related abnormalities. *J Endocrinol Invest* 1999; **22**: 472–475.

16 Lönnqvist F, Nordfors L, Jansson M, Thörne A, Schalling M, Arner P. Leptin secretion from adipose tissue in women. Relationship to plasma levels and gene expression. *J Clin Invest* 1997; **99**: 2398–2404.
17 Eriksson P, Reynisdottir S, Lönnqvist F, Stemme V, Hamsten A, Arner P. Adipose tissue secretion of plasminogen activator inhibitor-I in non-obese and obese individuals. *Diabetologia* 1998; **41**: 65–71.
18 Lövig T, Haffner JFW, Kaaresen R, Nygaard K, Stadaas JO. Gastric banding for morbid obesity: five years follow up. *Int J Obes Relat Metab Disord* 1993; **17**: 453–457.
19 Näslund E, Backman L, Granström L, Stockeld D. Seven year results of vertical banded gastroplasty for morbid obesity. *Eur J Surg* 1997; **163**: 281–286.
20 DeFronzo RA, Bonadonna RC, Ferrannini L. Pathogenesis of NIDDM. A balanced overview. *Diabetes Care* 1992; **15**: 318–368.
21 Kissebah AH. Insulin resistance in visceral obesity. *Int J Obes* 1991; **15**: 109–115.
22 Despres JP. Abdominal obesity as important component of insulin-resistance syndrome. *Nutrition* 1993; **9**: 452–459.
23 Del Prato S. Measurement of insulin resistance *in vivo*. *Drugs* 1999; **58**: S3–S6.
24 Bujalska IJ, Kumar S, Stewart PM. Does central obesity reflect 'Cushing's disease of the omentum'? *Lancet* 1997; **349**: 1210–1213.
25 Barzilai N, She L, Liu B-Q *et al*. Surgical removal of visceral fat reverses hepatic insulin resistance. *Diabetes* 1999; **48**: 94–98.
26 Berntorp E, Berntorp K, Brorson H, Frick K. Liposuction in Dercum's disease: impact on haemostatis factors associated with cardiovascular disease and insulin sensitivity. *J Intern Med* 1998; **243**: 197–201.
27 Legato MJ. Gender-specific aspects of obesity. *Int J Fertil Women Med* 1997; **42**: 184–197.