Effects of sex on the change in visceral, subcutaneous adipose tissue and skeletal muscle in response to weight loss

by

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SCHOOL OF GRADUATE STUDIES AND RESEARCH

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Abstract

The influence of sex on whole body and regional subcutaneous, visceral, total adipose tissue (AT), lean tissue, and skeletal muscle in response to weight loss induced by diet alone (DO) or the combination of diet and aerobic (DA) or resistance exercise (DR) was studied. The subjects consisted of 60 upper-body obese men and women. All tissues were measured using a whole body, multislice magnetic resonance imaging protocol. Within each group significant ($P<0.01$) reductions were observed for body mass (~11 kg), subcutaneous (~25%) and visceral (~35%) AT. The relative reduction in total AT was greater ($P<0.05$) in men (~27%) than women (~22%). This observation was explained by a greater mobilization of lower-body subcutaneous AT in men ($P<0.05$). In addition, the reduction in abdominal subcutaneous AT was greater in men than women at the 0.06 level. The relative reduction in visceral AT was not different between sexes ($P>0.05$). Independent of sex there was a preferential mobilization of visceral in comparison to subcutaneous AT ($P < 0.05$). With the exception of DA women, the reduction in abdominal subcutaneous AT was greater ($P < 0.05$) than lower-body subcutaneous AT in response to diet and exercise, but not diet alone, in both sexes ($P >0.05$). Skeletal muscle was preserved within the DA and DR groups ($P>0.05$), and reduced (~6%) in the DO groups ($P < 0.05$) independent of sex. Peak $\dot{V}O_2$ (L/min) improved in the DA groups as did muscular strength in the DR groups ($P<0.01$). These findings indicate that in response to equivalent weight loss, the relative reduction in total adiposity is greater in men than women, with this difference being explained in large measure by a decreased mobilization of lower-body subcutaneous AT in women. Reductions in visceral AT are not influenced by sex or treatment. Independent of sex, the combination of diet and exercise results in a preservation of skeletal muscle, a preferential reduction of abdominal subcutaneous AT, and improved functional capacity by comparison to diet alone.

Keywords: weight loss, magnetic resonance imaging, sex difference, obesity, visceral adipose tissue, subcutaneous adipose tissue, skeletal muscle

Co-Authorship

This study was funded by a Natural Sciences and Engineering Research Council of Canada (NSERC) grant. Dr. Robert Ross is the co-author of the manuscript portion of this thesis. He has contributed valuable time and expertise towards the completion of the manuscript.

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List of Abbreviations

AT	Adipose tissue
BMI	Body mass index
CT	Computerized tomography
CVD	Cardiovascular disease
DO	Diet only
DA	Diet in combination with aerobic exercise
DR	Diet in combination with resistance exercise
LT	Lean tissue
L4-L5	Forth to fifth lumbar vertebrae
MRI	Magnetic resonance imaging
NIDDM	Non-insulin dependent diabetes mellitus
RM	Repetition maximum
SAT	Subcutaneous Adipose Tissue
SM	Skeletal muscle
VAT	Visceral Adipose Tissue
VO_{2peak}	Peak oxygen uptake
WC	Waist circumference
WHR	Waist-to-hip circumference ratio

1.0.0 INTRODUCTION

Human adipose tissue is heterogenous with respect to free fatty acid uptake and mobilization (1). In situ (2) and in vivo (3) evidence suggests that catecholamine-stimulated lipolysis differs substantially between intra-abdominal, lower-body, and abdominal subcutaneous adipose tissue (AT) (1). In response to caloric restriction, or the combination of caloric restriction and exercise, the relative reduction in visceral AT is greater than the reduction in subcutaneous AT (4). However, the reductions in abdominal subcutaneous AT are greater than the corresponding reductions in leg subcutaneous AT in response to the combination of diet and exercise but not in response to diet alone (4). These findings demonstrate that weight loss influences AT distribution, and that the combination of diet and exercise may lead to different changes than diet alone.

Although there is evidence which suggests that sex influences the regional differences in catecholamine-stimulated lipolysis (1), it is unknown whether sex affects the changes in AT distribution with weight loss. A recent study has shown that basal free fatty acid release is greater in upper- compared to lower-body subcutaneous AT in both sexes, but that lower-body adipocytes in women are resistant to catecholamine stimulation in comparison to men of a similar phenotype (3). These observations suggest that sex may influence the effects of diet- and exercise-induced weight loss on AT distribution. Indeed, that gluteal/femoral adipocytes are resistant to catecholamine stimulation suggest that women would preferentially mobilize abdominal subcutaneous AT. Accordingly, by comparison to men, women would ne expected to mobilize less lower-body subcutaneous AT. Given the established relationship between AT distribution and cardiovascular disease and non-insulin dependent risk factors in both sexes (5), knowledge of how men and women mobilize free fatty acids from different depots (i.e., visceral and subcutaneous AT) during weight loss is important. Doing so may improve our understanding of acknowledged sex differences in weight loss-mediated improvements as they relate to metabolic risk factors (6).

The fact that no published reports have compared the effects of different treatments on AT or lean tissue distribution in men and women likely reflects difficulty in accessing the imaging techniques required to pursue such studies. We have recently employed a whole-body magnetic resonance imaging (MRI) model to study the effects of diet and/or exercise on AT and lean tissue distribution in men (4). In this study we have used the same model to determine whether sex influences these variables in moderately obese men and premenopausal obese women. In so doing we tested the following hypotheses: 1) That sex influences the reductions in subcutaneous AT, but not visceral AT, independent of treatment, 2) That independent of sex, the combination of diet and exercise induces a preferential reduction in abdominal compared to leg subcutaneous AT, 3) That independent of sex and treatment, a preferential reduction in visceral AT compared to subcutaneous AT will occur. 4) That the combination of diet and exercise would preserve skeletal muscle in comparison to diet alone in both sexes.

2.0.0 REVIEW OF THE LITERATURE

2.1.0 Association between obesity, adipose tissue distribution, visceral adipose tissue, and disease

It is well established that obesity is a major risk factor for cardiovascular disease (CVD) and non-insulin dependent diabetes mellitus (NIDDM) (Figure 1). In 1956 it was first noted that the location of the excess body fat may play an important role in determining health risk. Vague (8) observed that there was an increased prevalence of metabolic disturbances such as diabetes, atherosclerosis, gout, and uric calculous disease in upper-body, but not in lower-body obese individuals (8). Thirty years after these initial clinical observations, a number of cross-sectional studies demonstrated that upper-body obesity, as measured by the waist-to-hip circumference ratio (WHR), was a stronger correlate of metabolic variables than is the degree of obesity per se (9-14). More recently, epidemiological studies have confirmed that upper-body obesity is associated with CVD and NIDDM in both men and women (15-19).

The location of the adipose tissue (AT) within the abdominal region is also of critical importance when relating upper-body obesity to metabolic risk factors. The application of computerized tomography (CT) and magnetic resonance imaging (MRI) for studying human body composition in the late 1980's and early 1990's provided researchers with the opportunity to divide abdominal AT into two separate compartments: subcutaneous AT, and intra-abdominal, or visceral AT. It is now well established that visceral AT is an independent predictor of plasma

1930's: Initial observations that obesity is related to metabolic risk factors
(Reference 7)

1950's: Clinical observation that upper-body obese individuals had a greater prevelance of diabetes and atherosclerosis compared to lower-body obese persons
(Reference 8)

Early 1980's: Epidemiological and cross-sectional studies reported that WHR is associated with insulin sensitivity, NIDDM, plasma lipids, and CVD
(References 9-19)

Late 1980's & 1990's: The advent of CT and MRI enabled researchers to separate abdominal AT into VAT and abdominal SAT to study the effects of each depot on plasma lipids, lipoproteins, insulin and glucose
(References 20-29)

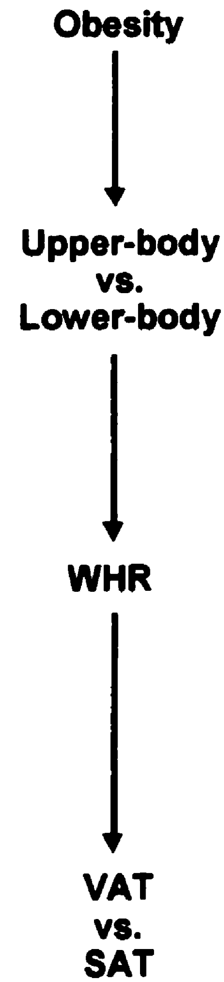

Figure 1. A time line outlining the progression in research on the association between obesity, insulin resistance, non-insulin diabetes mellitus (NIDDM), hyperlipidemia, and cardiovascular disease (CVD). WHR, waist-to-hip circumference ratio; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue.

glucose, insulin, lipid, and lipoprotein concentrations in obese men and women (20-29). In addition, recent reports have shown that abdominal subcutaneous AT is independently related to insulin metabolism in both sexes (27-29)

2.1.1 Mechanisms associating upper-body obesity with metabolic risk

The metabolic risk factors associated with obesity are caused from the excessive release of free fatty acids into the circulation observed in the obese state (30-34). As upper-body obese individuals high a higher prevalence of CVD and NIDDM in comparison to lower-body obese individuals (15-19), it seems reasonable to believe that free fatty acid release is elevated in abdominal AT. Indeed, Jensen et al. (35) observed that obese women with a high WHR had higher free fatty acid levels and turnover rates than obese women with a low WHR.

The visceral AT depot may be the AT depot which conveys the greatest influence on metabolic variables. Omental and mesenteric adipocytes, which comprise ~80% of the visceral depot (36-38), have a uniquely rapid turnover due to increased rates of triglyceride storage (39) and breakdown (39-43) in comparison to subcutaneous adipocytes. In addition, metabolites from omental and mesenteric adipocytes go directly to the liver through the portal circulation. Taken together, these observations suggest that the accumulation of visceral AT increases the exposure of the liver to free fatty acids (Figure 2). Increased delivery of free fatty acids to the liver is believed to affect hepatic production of lipoproteins, hepatic clearance of insulin, and hepatic gluconeogenesis (32-34). Thus, the accumulation of visceral AT has the potential to alter the concentration of plasma lipids,

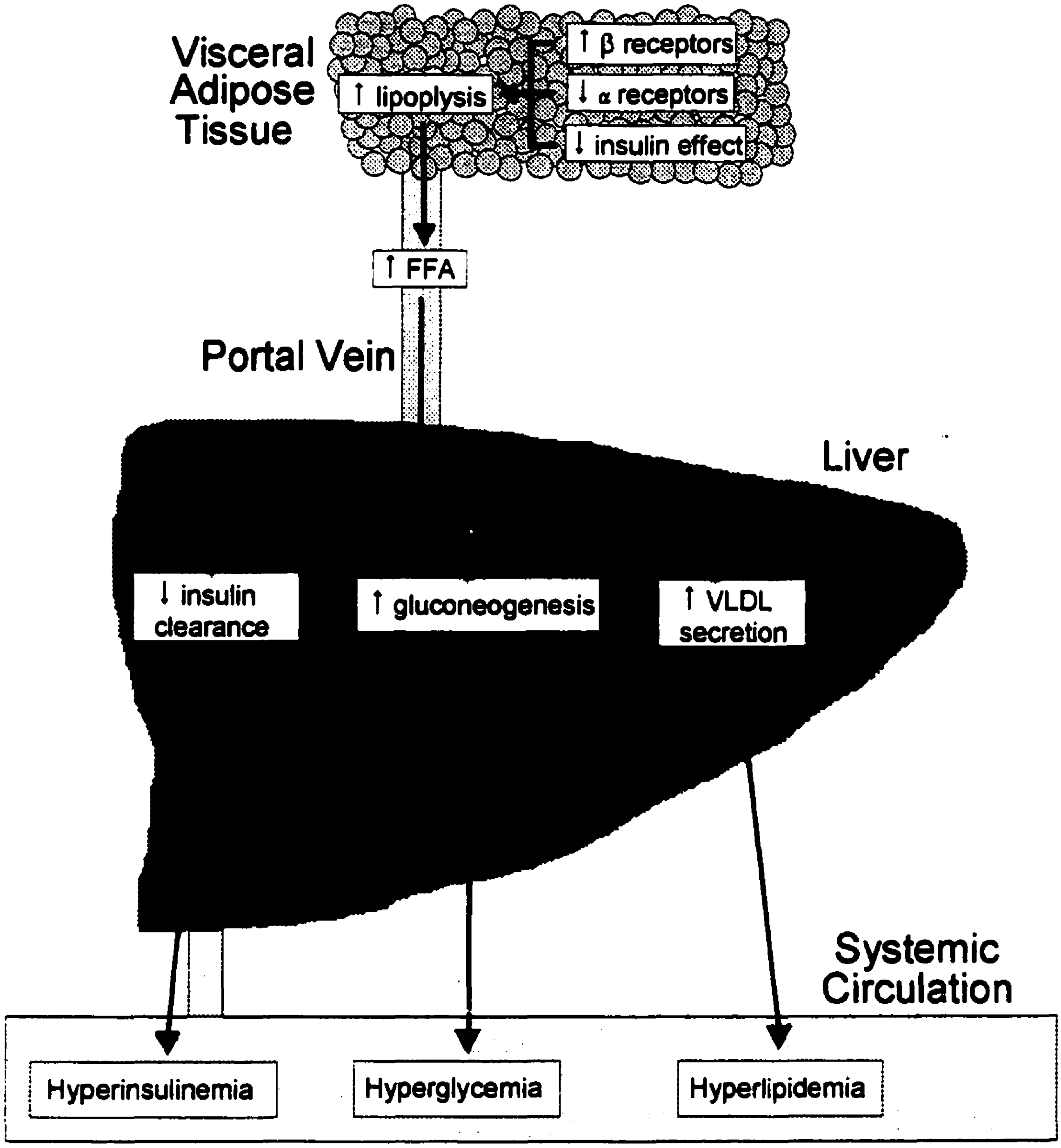

Figure 2. Mechanisms associating visceral adipose tissue (VAT) with metabolic risk. Visceral adipocytes have a preponderance of β-adrenergic receptors, as well as diminished α-adrenergic receptors, and decreased insulin binding in comparison to subcutaneous adipocytes. Therefore, there is a high lipolytic rate in VAT. This causes a high delivery of free fatty acids (FFA) to the portal vein. Portal FFA are thought to stimulate secretion of very low density lipoproteins (VLDL), glucose, and insulin, which will tend to create hyperlipidemia, hyperglycemia, and hyperinsulinemia, all of which are established risk factors for cardiovascular disease and non-insulin dependent diabetes mellitus.

lipoproteins, insulin, and glucose; all of which are putative markers for CVD and/or NIDDM (Figure 2).

In addition to visceral AT, abdominal subcutaneous AT is also independently related to metabolic risk factors such as insulin sensitivity (28, 29). Abdominal subcutaneous AT is more sensitive to the lipolytic action of catecholamines than gluteal-femoral subcutaneous AT both at rest and during exercise (2). These findings indicate that the accumulation of abdominal subcutaneous AT increases in the release of free fatty acids into the systemic circulation. It has been proposed that free fatty acids mobilized from subcutaneous adipocytes induce peripheral insulin insensitivity by suppressing glucose uptake in the muscle (30).

2.1.2 Circumstances to consider in weight loss studies

Composition/location of weight loss. The above observations suggest that if weight loss is used to control the metabolic complications associated with obesity, there must be reductions in both total adiposity and upper-body obesity. Although a wide variety of weight loss programs are being used to combat obesity, many of these programs are only concerned with the total weight loss and not with the composition and/or location of the weight loss. As upper-body obesity, and in particular visceral and abdominal subcutaneous AT, are important factors contributing to the metabolic complications associated with obesity, preferential reductions in these depots should have a high priority in treatment programs aimed at preventing CVD and NIDDM. The maintenance of skeletal muscle and the total lean tissue mass concurrent with reductions in AT is also important, as the preservation of these tissues also have specific health implications. The resting energy expenditure is highly related to the lean tissue mass, especially that of the visceral organs, and is an important determinant of our daily energy needs (44). The preservation of skeletal muscle mass is also vital as it is needed to perform everyday activities that require muscular strength and/or endurance.

Measurement of body composition. Although it is clear that it is important to look at both the composition and location of the weight loss, the changes in body composition have traditionally been measured using two-compartment models (i.e., hydrostatic weighing) which can only measure the changes in the total fat mass and lean body mass. The recent application of MRI and CT for measuring human body composition has made it possible to examine the changes within the different AT (i.e., visceral and subcutaneous AT) and lean tissue (i.e., skeletal muscle, organ) compartments. With a whole body MRI or CT protocol it is also possible to measure both total (i.e., whole body subcutaneous AT) and regional (i.e., abdominal and leg subcutaneous AT) effects of a given intervention.

Although some studies have utilized a whole body CT model to measure AT distribution and the changes in AT distribution with weight loss (45, 46), such studies are by many standards unethical as multiple CT scans expose the subjects to significant levels of ionizing radiation. MRI is better suited for obtaining multiple images as this technique does not result in any radiation exposure. A multiple slice MRI protocol has been developed in which regional and whole body measurements of the different AT and lean tissue constituents can be made (47). Using this model, a number of recent studies has reported for the first time the changes in whole body and regional visceral AT, subcutaneous AT, lean tissue, and skeletal muscle in response to exercise- and/or diet-induced weight loss (4, 47-50). However, as such techniques are new, expensive, and time consuming, their use has been limited to only a few studies.

Sex. To date, it is not known whether sex influences the changes in AT and lean tissue distribution with weight loss. However, as gender influences the regional differences in catecholamine stimulated lipolysis (1), the changes in body composition with weight loss may be different in men and women. Furthermore, as the AT and lean tissue distribution is different in obese men and women, even when matched for obesity phenotype (51, 52), and as the composition and location of the weight loss is an important factor in determining the success of a weight loss program, the influence of sex on changes in body composition should be given careful consideration.

2.2.0 Effects of exercise- and/or diet-induced weight loss on body composition

2.2.1 Diet only

Total fat mass and lean body mass. It is well established that diet-induced weight loss is associated with large reductions in total adiposity in both men and women (Table 1). The average weight loss observed in response to diet alone in the reviewed studies was ~ 8 kg (1.7 kg/week). In addition, more than half of these studies observed significant reductions in lean body mass. In fact, a summary of

Table 1. Studies which have examined the effect of energy restriction and/or exercise on changes in body composition

Reference	Subjects	Treatment	Duration	Exercise Type, Duration, & Intensity	Energy Intake/ Deficit (kcal/day)	Weight Loss (kg)	Fat Loss (kg)	ΔLBM (kg)	LBM ÷ weight loss (%)	Body Comp Method
Ballor et al. (53)	10♀ 10♀	Diet Only Diet + Resistance	8 wk	3 d/wk, 8 exercises, 2 sets of 10 + 1 set of max number of lifts	D = 1000	4.5 3.9	3.6 4.3	-0.9 +0.4[1]	20% 0%	HW
Belko et al. (54)	6♀ 6♀	Diet Only Diet + Aerobic	6 wk	Daily walking, increase daily energy expenditure by 25%	D = 50% D = 25%	7.8[1] 5.7	5.1 6.7	-2.7[1] -1.0	35% 17%	HW
Dengel et al. (55)	15♂ 15♂	Diet Only Diet + Aerobic	~10 mo	Walk/jog/cycle, 3 d/wk, progress to 45 min at 75-85% VO_{2max}	I/D prescribed to lose 0.25-0.5 kg/week	8.0 7.6	6.0 6.1	-2.0 -1.5	25% 20%	HW
Donnelly et al. (56)	26♀ 16♀ 18♀ 9♀	Diet Only Diet + Aerobic Diet + Resistance Diet + A + R	90 d	A = Various forms, 4 d/wk, progress 60 min at 70% HR reserve. R = 4 d/wk, 4 exercises, progress to 3 sets of 6-8 reps at 80% I RM	I = 520	20.4 21.4 20.9 21.9	16.1 16.6 16.1 18.0	-4.7 -4.8 -4.7 -4.1	22% 23% 23% 21%	HW
Donnelly et al. (57)	7♀ 7♀	Diet Only Diet + Resistance	90 d	3 d/wk, 8 exercises, 3 sets of 8-6-6 reps, progress from 70-80% 1 RM	I = 800	17.1 15.1	13.0 11.3	-4.1 -3.8	24% 25%	HW
Hagan et al. (58)	12♂ 12♂ 12♀ 12♀	Diet Only Diet + Aerobic Diet Only Diet + Aerobic	12 wk	Walk/jog, 5 d/wk, 30 min, ~2 miles	I = 1200	8.4 11.3[2] 5.5 7.5[2]	5.8 7.8[2] 5.0 5.9[2]	-2.6 -3.5 -0.5 -1.6	31% 31% 9% 21%	HW
Hammer et al. (59)	8♀ 6♀	Diet Only Diet + Aerobic	16 wk	Walk/jog, 5 d/wk, 70-85% HR max, progress to 4.8 km/session	I = 800 d	9.5 12.5	7.9 9.4	-1.6 -3.1	17% 24%	HW
Heymsfield et al. (60)	6♀ 6♀	Diet Only Diet + Aerobic	4 wk	Daily walking, progress distance to 5.6 km (~350 kcal/day)	I = 900	7.0 7.5	4.4 5.3[2]	-2.6[1] -2.2	37% 29%	HW
Hill et al. (61)	5♀ 3♀	Diet Only Diet + Aerobic	5 wk	Daily walking, progress to 5.6 km	I = 800	8.1 8.2	4.7 6.1[2]	3.4[1] -2.1	43% 26%	HW
Marks et al. (62)	8♀ 10♀ 11♀ 10♀	Diet Only Diet + Aerobic Diet + Resistance Diet + A + R	20 wk	A = cycling, 3 d/wk, 70-85% of HR max, 3 d/wk, progress to 36 min for D+A and 24 min for D+A+R, R = 3 d/wk, 7 exercises, sets of 12 reps, 2 sets for D+R, 1 for D+A+R	I/D prescribed to lose < 0.9 kg/week	3.7 4.5 3.5 5.5	3.5 4.7 4.2 5.8	-0.2 +0.2 +0.7 +0.3	5% 0% 0% 0%	HW
Pavlou et al. (63)	41♂ 31♂	Diet Only Diet + A + R	8 wk	Walk/jog for ~45 min at 85% HR max + callisthenics, 3 d/wk	I = 800-1000	9.2 11.8	5.9 11.2[3]	-3.3 -0.6[5]	36% 6%	^{40}K

Table 1. Studies which have examined the effect of energy restriction and/or exercise on changes in body composition (Continued)

Reference	Subjects	Treatment	Duration	Exercise Type, Duration, & Intensity	Energy Intake/ Deficit (kcal/day)	Weight Loss (kg)	Fat Loss (kg)	ΔLBM (kg)	LBM ÷ weight loss (%)	Body Comp Method
Pavlou et al. (64)	16♀ 15♀	Diet Only Diet + A + R	8 wk	Walk/jog, 3 d/wk, 30-40 min, 60-85% of HR max	I = 1000 d	6.3 8.2[3]	5.5 6.9[3]	-0.8 -1.3	13% 16%	BIA
Svendsen et al. (65)	21♀ 51♀ 49♀	Control Diet Only Diet + A + R	12 wk	A = cycle/stepping/running, 3 d/wk, increase to 30-55 min, 70% VO_{2max} R = 8-10 exercises, 7-15 reps at 65% I RM, 3 d/wk	I = ad lib (Control) I = 380 d (Diet only, D + A + R)	+0.5 9.5 10.3	+0.2 7.8 9.6[3]	+0.3 -1.2 0.0	— 13% 0%	DEXA
Van Dale et al. (66)	6♀ 6♀	Diet Only Diet + A + R	12 wk	2 d/wk of aerobic dancing and 2 d/wk of callisthenics, 1 hr/session at 50-60% VO_{2max}	I = 400 d (4 wk) I = 810 d (8 wk)	12.2 13.2	9.4 10.9	-2.8 -2.3	23% 17%	HW
Weltman et al. (67)	11♂ 23♂	Diet Only Diet + Aerobic	10 wk	Walking, 4 d/wk, progress to 45 min	D = 500	5.6 5.4	3.7 4.3	-1.9 -1.1	32% 21%	HW
Whatley et al. (68)	7♀ 8♀ 8♀	Diet Only Diet + Mod A + R Diet + Int A + R	12 wk	A = Walk, 3/d/wk for Mod. and 5 d/wk for Int., 50-65% HR reserve, ~50 min. R = 3 d/wk, 4 exercises, 3 sets of 8 at 80% 1RM	I = 800 d	13.1 15.8 19.6[4]	9.3 12.9 15.7[4]	-3.8 -2.9 -3.9	30% 18% 20%	HW
Wood et al. (69)	31♂ 42♂ 40♀ 39♀	Diet Only Diet + Aerobic Diet Only Diet + Aerobic	1 yr	Walk/jog, 3 d/wk, progress to >45 min, 60-80% HR max	National Cholesterol Education Program Step 1 diet	5.1 8.7[2] 4.1 5.1	4.3 7.8[2] 4.0 4.7	-0.8 -0.9 -0.1 -0.4	16% 10% 2% 8%	HW

Abbreviations: ♀, women; ♂, men; I, intake; D, deficit; A, aerobic; R, resistance; Mod, moderate; Int, intense; HR, heart rate; d, day; wk, week; mo, month; HW, hydrostatic weighing; ^{40}K, total body potassium; BIA, bioelectrical impedance analysis; DEXA, dual energy x-ray absorptiometery;

[1]Diet Only > Diet + Aerobic
[2]Diet + Aerobic > Diet Only
[3]Diet + Aerobic + Resistance > Diet Only
[4]Diet + Intense Aerobic + Resistance > Diet Only
[5]Diet Only > Diet + Aerobic + Resistance

the results listed in Table 1 suggests that ~25% of the weight loss was comprised of lean body mass in diet only treatments. The average weight loss was ~11 kg in the studies in which significant reductions in lean body mass were observed, whereas the average weight loss was only ~7 kg in the studies in which lean body mass was preserved. This suggests that with a large diet-induced weight loss there will be significant reductions in both the fat mass and lean body mass.

Regional adipose tissue. Several recent studies have examined the influence of caloric restriction on changes in AT distribution (Table 2). All of these studies reported large reductions in visceral AT in response to caloric restriction (Table 2). Figure 3, which plots the reductions in weight against the reductions in visceral AT for each of the diet-induced weight loss studies listed in Table 2, demonstrates that the reductions in visceral AT vary according to the reductions in weight. The greater the weight loss, the greater the reduction in visceral AT. A recent review has suggested that for every 1 kg of weight loss there is a corresponding 2-3% reduction in visceral AT (76). Thus, a diet-induced weight loss of 10 kg corresponds to a ~25% reduction in visceral AT.

In addition to the reductions in visceral AT, most of the reviewed studies also observed reductions in abdominal subcutaneous AT in response to caloric restriction (Table 2). As with visceral AT, the larger the weight loss the larger the reduction in subcutaneous AT (Figure 3). A summary of these results suggests that for a 10 kg weight loss there is an ~18% reduction in SAT. Therefore, with weight loss there is a preferential reduction of visceral in comparison to subcutaneous AT

Table 2. Studies which have examined the effect of weight loss on visceral adipose tissue.

Reference	Subjects	Treatment	Duration	Energy Intake/ Deficit (kcal/day)	Wt Loss (kg)	VAT Loss (%)	SAT Loss (%)	Method (Location)
Bosello et al. (70)	19♀	Diet Only	15-20 d	I = 320	6.1	20	6	CT (L4)
Armellini et al. (71)	26♀	Diet Only	15 d	I = 329	6.0	15	1	CT (L4)
Chowdhury et al. (45)	9♂	Diet Only	7 d	I = 350	4.4	9	5	CT (whole body, 22 images)
Fujioka et al. (46)	14♀ (VFO) 26♀ (SFO)	Diet Only	8 wk	I = gradual reduction to 800 d	12.0 12.3	38 33	25 23	CT (umbilicus)
Stallone et al. (72)	11♀	Diet Only	6 mo	I = ~600 d (3 mo) refeed (2 mo) I = ~1360 (1 mo)	18.8	38	33	CT (L4)
Gray et al. (73)	10♀	Diet Only	10 wk	I = 650	10.5	27	13	MRI (umbilicus)
Leenen et al. (6)	40♀ 38♂	Diet Only	13 wk	D = 1000	11.7 12.6	33 39	30 36	MRI (mid-way between iliac crest & rib margin)
Zamboni et al. (74)	16♀	Diet Only	16 wk	I = 300 d (2 wk) I = 1000 d (14 wk)	16.2	44	25	CT (L4)
Ross & Rissanen (49)	10♀ 14♀	Diet + Aerobic Diet + Resistance	16 wk	D = 1000	10.9 10.1	34 30	23 23	MRI (whole body, 41 images)
Ross et al. (4)	11♂ 11♂ 11♂	Diet Only Diet + Aerobic Diet + Resistance	16 wk	D = 1000	11.5 11.4 12.3	32 39 40	24 22 26	MRI (whole body, 41 images)
Conway et al. (75)	10♀ (white) 8♀ (black)	Diet + Aerobic	6 mo	I = 800 d (12 wk) I = increase to 1200-1500 d (12 wk)	17.2 17.2	27 29	20 27	CT (L4-L5)

Abbreviations: ♀, women; ♂, men; I, intake; D, deficit; d, day; wk, week; mo, month; CT, computerized tomography; MRI, magnetic resonance imaging; VFO, visceral fat obesity; SFO, subcutaneous fat obesity

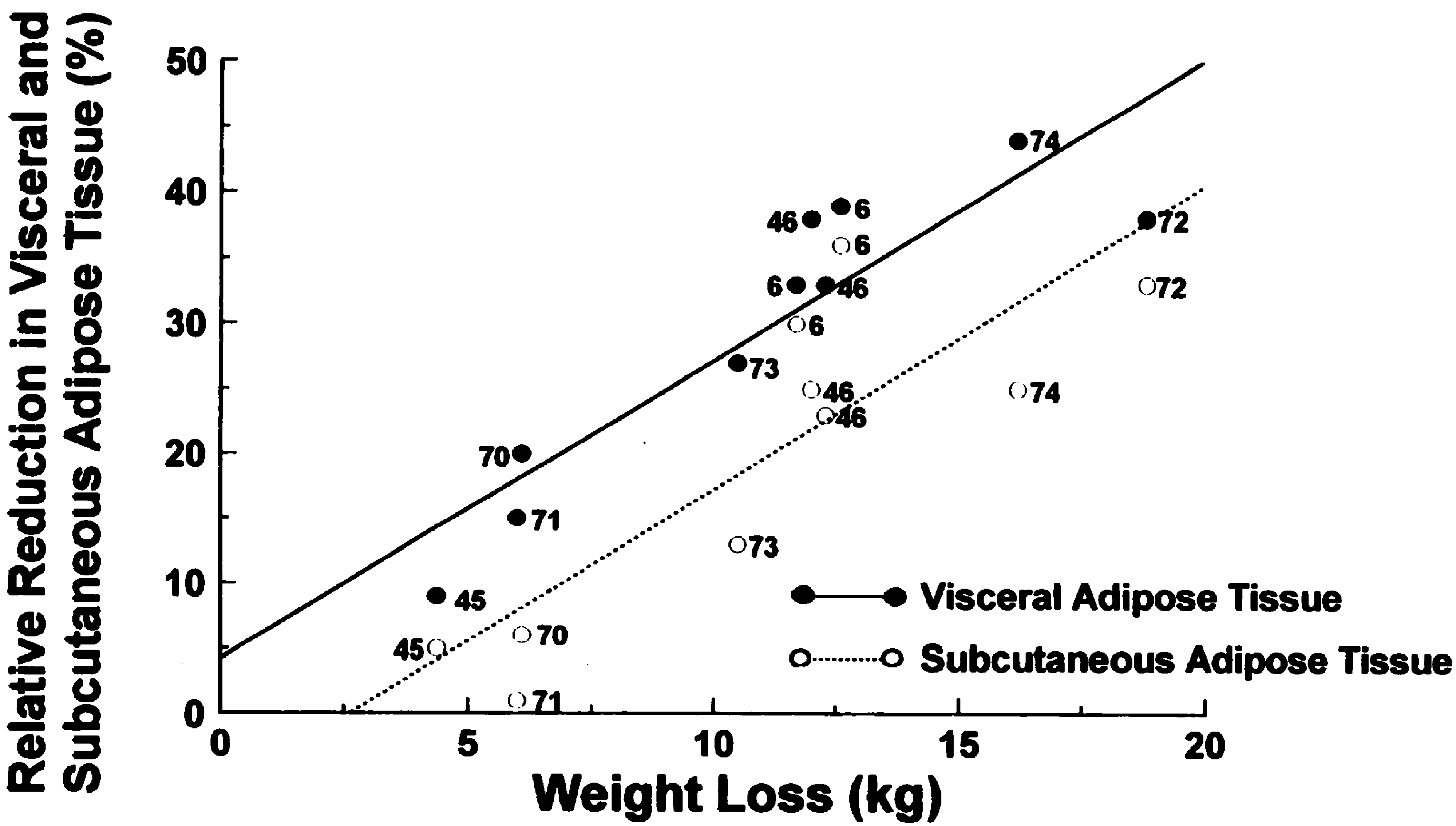

Figure 3. Relationship between the diet-induced weight loss and the reductios in visceral and subcutaneous adipose tissue. The correlation was obtained by regressing the mean values form each study shown for weight loss (kg) and relative reduction in visceral and subcutaneous adipose tissue (%). The data in all studies was derived from diet-induced weight loss. The numbers beside each point refer to reference numbers.

(Table 2). The preferential reduction of visceral AT is supported by in vitro evidence which has demonstrated that omental and mesenteric adipocytes are more sensitive to lipolytic stimulation in comparison to abdominal and femoral subcutaneous adipocytes (39-42).

Few studies have examined whether there are regional differences in the reductions in subcutaneous AT in response to caloric restriction. In two studies there were no differences between the relative reductions in abdominal and leg subcutaneous AT in response to diet alone (4, 45). However, in two other studies abdominal subcutaneous AT was reduced to a greater extent than thigh (72) and hip (77) subcutaneous AT in response to a diet induced weight loss. These findings of these studies, although not conclusive, suggest that with weight loss there may be a preferential reduction of subcutaneous AT in the abdominal area.

Regional lean tissue. Only two studies have examined the effects of diet-induced weight loss on changes in lean tissue and skeletal muscle distribution (4, 49). Using a whole body MRI protocol, Ross et al. (4) reported that there is a ~7% (~2.3 kg) reduction in whole body skeletal muscle in response to an ~11 kg weight loss induced through diet alone in obese men. The reduction in whole body skeletal muscle is accounted for by reductions in both leg, upper-body, and arm skeletal muscle (4, 49), therefore, there is not an increase in skeletal muscle in one region that was masked by concurrent reductions in another region. These authors also observed that there was a preservation of intra-abdominal lean tissue (i.e., liver, kidney) which indicates that the losses of lean tissue in response to caloric restriction may be limited to skeletal muscle in the appendicular regions (4).

2.2.2 Diet and exercise

Weight loss. Whether the addition of exercise to a program of caloric restriction provides additional benefits with respect to weight loss and/or changes in body composition beyond those of diet alone has been a topic of considerable debate. A review of the studies in Table 1 and 2 suggests that in response to the combination of diet and exercise the average weight loss was ~9 kg (~1.8 kg/week), which was only marginally greater than the average weight loss of ~8 kg (~1.7 kg/week) observed in response to diet alone. Indeed, only 4 out of 19 studies examined in this review observed a greater weight loss in response to the combination of diet and exercise than diet alone (Tables 1 and 2).

Several explanations have been given to account for the similar weight loss between the diet only and combined diet and exercise programs. First, it is possible that there is a decrease in the non-structured physical activity in the exercise groups. One study has shown that endurance training does not increase the total energy expenditure in healthy older adults because of a decline in the spontaneous physical activity during the remainder of the day (78). It has also been speculated that the subjects in diet plus exercise groups under reported their food intake, which resulted in the caloric deficits being smaller than calculated (59). However, as the accuracy of diet records is related to the level of obesity (79), and as the subjects in the diet only groups and diet combined with exercise groups were usually matched for the degree of adiposity, it can be assumed that the under recording of calories would be similar in both groups. Other authors have suggested that the increased muscle glycogen and water content with training would induce a modest increase in weight and make the overall reductions in body mass in the combined diet and exercising groups smaller (60, 61). Finally, some of the studies utilized exercise programs that may not have elicited a large enough energy expenditure to burn ample amounts of fat. Ballor et al. (53) have shown that only ~120 kcal are expended during one session of resistance training. Even with aerobic exercise the amount of exercise may not have been sufficient to elicit a significantly greater weight loss. For example, in one study the addition of exercise resulted in an increased caloric expenditure of ~12,000 kcal, which is only equivalent to ~1.5 kg (60).

When observing the differences in weight loss between diet alone and combined diet and exercise treatments, it is somewhat misleading to only examine the changes in body mass. If the combination of diet and exercising results in larger reductions in fat mass and a greater preservation of lean body mass in comparison to diet alone, it would require a greater energy loss to lose equivalent amounts of weight, as fat (9000 kcal/kg) is more calorically dense than lean body mass (4000 kcal/kg). For example, Hill et al. (61) observed a 0.1 kg difference in weight loss between a diet alone group and a diet plus exercise group (Table 1). As the exercise group lost more calorically dense fat and less lean body mass, they on average lost a further 10,296 kcal of body energy than the diet only group, which compares very closely with the energy that was expended during the exercise

(10,101 kcal).

Total fat mass. A summary of the references listed in Table 1 suggests that although the combined diet and exercise groups only lost an additional ~1.1 kg of body mass, they lost an extra ~1.7 kg of fat mass in comparison to the diet alone groups. This suggests two things. First, the addition of exercise to a program of caloric restriction may lead to an increased mobilization of fat mass. Indeed, ~50% of the studies in this review reported this (Table 1). Second, the energy required to reduce body weight was greater in response to the combination of diet and exercise, which may in part explain the similar weight loss to diet alone.

Regional adipose tissue. Only one study has examined whether or not the addition of exercise would have an increased effect on visceral AT and AT distribution with weight loss (4). This study reported that the addition of aerobic or resistance exercise had no effect on the reduction in body weight, visceral AT, or total subcutaneous AT (4). It was, however, observed that the combination of diet and exercise resulted in a preferential mobilization of abdominal compared to leg subcutaneous AT, which was not observed in response to diet alone. These findings are supported by in vivo (3) and in situ (2) evidence which suggests that upper-body subcutaneous adipocytes are more sensitive to catecholamine stimulation than femoral adipocytes. This is an important observation given that abdominal subcutaneous AT is a strong correlate of CVD and NIDDM risk factors (27-29) and that reductions in this depot are correlated with concurrent reductions in metabolic risk factors (6, 74, 80).

Total lean body mass. Although ~50% of the studies examined in this review observed reductions in lean body mass in response to the combination of diet and exercise (Table 1), it still appears that exercise may help to preserve lean body mass. A summary of the results in Table 1 suggests that the percent contribution of lean body mass to the total weight loss decreased from ~25% in diet only programs to ~15% in combined diet and exercise programs. These results concur with those of Ballor & Poehlman (81) who, in a meta-analytical study, reported that exercise training reduced by ~50% the percent contribution of lean body mass to the weight loss.

Regional lean tissue. Recent studies have found no changes in either regional or whole body lean tissue and skeletal muscle in response to the combination of diet and aerobic or resistance exercise, whereas reductions in these tissues occurred in response to diet alone (4, 49). An interesting observation in these studies was that muscular strength increased in response to the combination of diet and resistance training despite any increase in MRI-measured skeletal muscle volume. As the increases in strength were calculated starting the fourth week of training to control for neural adaptations in the muscle, these results suggest that there was an increase in the muscle fiber contractile protein that was masked by concurrent reductions in one of the other skeletal muscle constituents (i.e., lipid, water, non-contractile protein). This observation can be supported by the findings of Donnelly et al. (56), who observed an increase in the fast twitch muscle fiber size after caloric restriction and resistance training in the presence of a 3.4 kg decline in hydrostatically weighed lean body mass.

2.3.0 Possible explanations for the discrepant findings

The observations in the present review clearly demonstrate that study differences exist with respect to the added benefits of exercise in weight loss programs. For example, ~50% of the studies found that the combination of diet and exercise increased the fat loss and decreased the lean body mass loss, whereas the other 50% found that exercise had no effect on changes in fat mass or lean body mass in comparison to diet alone. Furthermore, differences exist across studies in which a similar treatment was employed. For example, Hammer et al. (59) observed that 17% of the weight loss was comprised of lean body mass in response to a ~9 kg diet-induced weight loss. In response to a similar treatment and weight loss, Pavlou et al. (63) observed that 36% of the weight loss was comprised of lean body mass. Unfortunately there is no simple answer to explain the variations in these findings, however, differences in the study design likely play a role. This section will consider differences in methodologies used in the studies examined in this review.

2.3.1 Subject characterization

Degree of adiposity. The available evidence suggests that individuals with a high degree of adiposity will loose more weight than individuals who are only slightly obese in response to a similar exercise and/or diet program. For example, highly obese women (~45% body fat) had a weight loss of 13.1 kg after a 12 week diet (68). In response to a similar caloric intake, moderately obese women (~38%

body fat) had a smaller weight loss of 9.5 kg, even though the treatment period lasted for 16 weeks (59). In addition to the greater weight loss, it is also clear that the subjects who start with the most AT will loose the most AT in response to weight loss. Studies have shown strong relationships between the amount of visceral AT and subcutaneous AT before weight loss and the changes in these tissue with weight loss (6, 77), even after adjusting for the changes in body weight.

The results of the studies in Table 1 suggests that the absolute change in lean body mass is greater in severely obese individuals (56, 57, 61, 68). This would be expected as they normally had a large weight loss, which would in turn result in sizable changes in lean body mass. However, even when the changes in lean body mass were calculated as a percentage of the total weight loss, the highly obese still appeared to have marked reductions in lean body mass (Table 1, references 56, 57, 61, 68). These observations were unanticipated, as it has been speculated that as severely obese subjects have more fat to burn they should be able to preferentially burn fat, and consequentially preserve lean body mass during weight loss, (82). Perhaps the degree of the caloric restriction may explain these findings. The studies conducted on the highly obese subjects all used very low calorie diets. Larger reductions in lean body mass occur in response to very low calorie diets than moderate caloric restriction (83), which was frequently used with the moderately overweight subjects in the studies examined in this review (Table 1).

Sex. One factor that has been given relatively little consideration in weight loss studies is sex. When men and women were used in the same study and exposed to a similar treatment, the men lost more weight and fat mass than the women in response to diet alone or the combination of diet and exercise (Table 3). In these two studies the women also showed noticeably smaller changes in fat free mass, both absolute and as a percentage of weight loss. In response to a diet-induced weight loss, Leenen et al. (6) observed that men lose more visceral AT than women, but that the changes in abdominal subcutaneous AT are similar across sex.

When comparing the changes in body composition between men and women, it may be misleading to examine the absolute changes in body size, fat mass, lean body mass, and the different AT depots, as there are pretreatment sex differences in these variables. To control for these differences it is perhaps better to examine the relative (percent) change. Based on the data in Table 3 (58, 69), the relative changes in body mass, fat mass and lean body mass were calculated (Table 3). Although not statistically compared in these studies, these results suggest that there are no sex differences for the relative reductions in body weight in response to diet alone or the combination of diet and exercise. However, it does appear that the men had larger relative reductions in fat mass in comparison to women (Table 3). Also, as shown in Table 2 (reference 5), the relative reductions in visceral and abdominal subcutaneous AT appear to be slightly greater in men than women in response to a diet-induced weight loss.

Other variables. In addition to sex and the degree of adiposity, variables such as menopausal status, age, and the obesity phenotype may also partially explain the discrepant findings in the literature. The changes in body composition with

Table 3. Studies which have examined the effect of exercise and/or energy restriction on changes in body composition in men and women

Reference	Subjects	Treatment	Weight Loss (kg)	Weight Loss (%)	Fat Loss (kg)	Fat Loss (%)	LBM Loss (kg)	LBM Loss (%)	LBM Loss / Weight Loss (%)
Hagan et al. (58)	12♂	Diet Only	8.4	9	5.8	25	2.6	4	31%
	12♂	Diet + Aerobic	11.3	12	7.8	31	3.5	5	31%
	12♀	Diet Only	5.5	8	5.0	20	0.6	1	9%
	12♀	Diet + Aerobic	7.5	10	5.9	24	1.6	3	21%
Wood et al. (69)	31♂	Diet Only	5.1	5	4.3	16	0.8	1	16%
	42♂	Diet + Aerobic	8.7	9	7.8	28	0.9	1	10%
	40♀	Diet Only	4.1	5	4.0	15	0.1	0	2%
	39♀	Diet + Aerobic	5.1	7	4.7	17	0.4	1	8%

Abbreviations: ♀, women; ♂, men; LBM, lean body mass weight loss have been shown to be different in premenopausal and postmenopausal women (84). Studies conduced on old and young men have also shown that age can affect the changes in AT distribution with exercise and a small weight loss (85). In addition, the obesity phenotype influences the changes in body composition with weight loss (86). Taken together, these results suggest that the subjects must be carefully characterized in future weight loss studies, as this will influence the changes in weight loss and/or body composition in response to the imposed treatments.

2.3.2 Exercise

Amount/duration of exercise. Whatley et al. (Table 1, reference 68) reported that moderate amounts of exercise (3 days/week) were not associated with larger reductions in body weight or adiposity in comparison to diet alone. However, large amounts of exercise (5 days/week) were associated with a 33% larger reduction in weight and a 41% larger reduction in fat mass in comparison to diet alone. These authors also observed that significant differences in the weight loss between diet only compared to the combined diet and exercise group was only found during the second half of the 12 week study (68). These results suggest that in many of the studies examined in this review, the amount (i.e., 3 days/week) and/or duration (i.e., $\leq$ 8 weeks) of exercise may not have been sufficient to elicit an effect beyond that of diet alone.

Other exercise variables. As opposed to the study duration and amount of exercise, the type of exercise and exercise intensity do not appear to affect the changes in weight or body composition with caloric restriction. A number of studies have shown that the changes in weight and body composition are similar when either aerobic or resistance exercise is used in combination with caloric restriction (4, 57, 62). In addition, it has been demonstrated that the intensity of exercise does not influence the changes in body composition with weight loss (87, 88).

2.3.3 Diet

Although it has been observed that the dietary composition (i.e., percentage of calories derived from fat) plays an important role in the regulation of body weight and body composition during weight maintenance (89), it appears as if the diet composition has no significant effect on the amount, rate, or composition of the weight loss under conditions of a negative energy balance (90). The most important factor determining the extent of weight loss with caloric restriction is the degree of negative energy balance (90). The extent of the caloric deficit also affects the changes in body composition, as the contribution of lean body mass to the total weight loss is greater with severe energy restriction (91). It is believed that very low calorie diets (i.e., intake $\leq$ 800 kcal/day) result in protein metabolism and/or water loss that can be avoided to a greater extent with moderate caloric restriction (i.e., intake $\geq$ 1000 kcal/day) (62). The extent of the energy deficit may also affect the ability of exercise to facilitate weight loss and preserve lean body mass loss. The combination of diet and exercise resulted in a greater weight loss in comparison to diet alone in some of the studies where moderate energy restriction was used (58, 64, 69), but not in any of the studies where very low calorie diets were used (see Table 1). In other words, the magnitude of the exercise effect becomes smaller as the dietary restriction is increased.

Although it is clear that the weight loss is related to the magnitude of the caloric deficit created, the optimal energy intake which maximizes weight and fat loss while maintaining lean body mass is unknown. To determine the effectiveness of caloric restriction on body composition, the caloric intake required to maintain a stable body weight should be determined before initiating a weight reduction program. Subsequently, the caloric deficit prescribed should be based on individual requirements for weight maintenance. If the prescribed caloric intake is the same for all subjects, variable caloric deficits are created which may result in large variations in weight loss and subsequent changes in body composition. Thus, it is important to determine the caloric deficit based on individual weight maintenance values. Only a small percentage of the studies examined in this review prescribed a caloric deficit based on energy requirements for weight maintenance (see Tables 1 and 2).

2.3.4 Measurement of body composition.

Hydrostatic weighing. The most commonly used method (~90%) for measuring changes in body composition has been hydrostatic weighing (Table 1). The validity of this technique rests on the many inherent assumptions of the body density equation, which are not met in obese individuals before or after weight loss. Firstly, estimations of fat mass and lean body mass from body density use equations that are based on the chemical composition of lean, young, adult male cadavers. These formulas have been applied to obese men and women of all ages, who differ markedly from reference man, without direct proof of their application (92, 93). Second, these formulas assume that the lean body mass density is constant at 1.1 g/cm^2, which means that there are constant ratios of lean body mass as water, protein, and mineral content (94, 95). Caloric restriction can dehydrate the body (83, 96), diet-induced weight loss decreases muscle mass (4), and training increases bone mineral content (65). These three factors taken individually or together would increase the lean body mass density, leading to an overestimation of fat loss based on the body density equation.

Magnetic resonance imaging and computerized tomography. In recent years MRI and CT have proven to be accurate techniques for measuring body composition in comparison with cadaver (36, 97, 98) and animal (99, 100) data. MRI is particularly useful as it does not expose the subject to ionizing radiation and allows for the measurement of whole body and regional body composition. MRI measurements are not subject to the inherent assumptions of two-compartment methods, as its measurements are not based on assumptions regarding stable relationships among tissue constituents, but rather the contrast between tissues on MRI images. As the contrast between tissues on MRI images does not change with exercise and/or weight loss, this makes MRI particularly suitable for measuring changes in body composition.

2.4.0 Predicting changes in visceral adipose tissue and adipose tissue distribution

Given the clinical importance of visceral AT and AT distribution, and as routine access to MRI and CT is not possible, attempts have been made to determine whether external anthropometry can be used to follow changes in visceral AT and AT distribution. Several studies have used the WHR as an indication of the reduction in upper-body obesity. However, although these studies reported large reductions in both abdominal subcutaneous AT and visceral AT with weight loss, the reductions in the WHR were very small or non-existent (4, 37, 45, 72). The WHR is a ratio score, and the numerator (waist) and the denominator (hip) may both change with weight loss, disguising any changes in upper-body obesity because the ratio score remains the same. Therefore, although the WHR may be a good indicator of upper-body obesity, it is a poor indicator of changes in upper-body obesity and visceral AT with weight loss. The waist circumference itself has proven to be a better predictor of both visceral AT and the changes in visceral AT with weight loss (45, 101, 102). A recent study has reported that a 1 cm reduction in the waist circumference is associated with a 4% reduction in visceral AT mass (102). Unfortunately, even with the waist circumference the contribution of visceral AT and abdominal subcutaneous AT to a change in upper-body obesity can not be identified. Nevertheless, if a simple anthropometric technique is used to measure reductions in upper-body obesity, the waist circumference appears to be the measurement of choice.

2.5.0 Summary

Weight loss is associated with reductions in total adiposity as well as improvements in AT distribution. The combination of diet and exercise increased the reductions in total adiposity in comparison to diet alone is some, but not all studies. Although the addition of exercise does not increase the reduction of visceral AT in comparison to diet alone, it is associated with a preferential reduction of abdominal subcutaneous AT. In addition, the combination of diet and exercise plays an important role in preserving the total lean tissue and skeletal muscle mass.

From the present review it is apparent that there is a lack of studies examining the influence of diet and exercise induced weight loss on AT and lean tissue distribution. In particular, to our knowledge no published reports have compared the effects of different treatments on AT or lean tissue distribution in men and women. This is surprising given the well documented differences in AT and distribution between the sexes (51, 52), the importance that AT distribution plays in determining health risk, and that catecholamine-stimulated lipolysis differs substantially between the different AT depots (2, 3); with gender influencing these regional differences (1). Therefore, the purpose of this study was to determine whether sex influences the changes in these variables in response to weight loss induced by diet alone or the combination of diet and aerobic or resistance exercise. In so doing we tested the following hypotheses: 1) That the reductions in subcutaneous AT will be greater men than women, but that sex does not influence the reductions in visceral AT, independent of treatment, 2) That, independent of sex, the combination of diet and exercise induces a preferential reduction in abdominal compared to leg subcutaneous AT, 3) That independent of sex and treatment, a preferential reduction in visceral AT compared to subcutaneous AT will occur, and 4) That the combination of diet and exercise would preserve skeletal muscle in comparison to diet alone in both sexes.

3.0.0 MANUSCRIPT

The following chapter of this thesis has been submitted for publication to the American Journal of Clinical Nutrition and is presented in a format consistent with that required by the journal. For simplicity the references for the manuscript are included in Chapter 5.0.0.

Effects of sex on the change in visceral, subcutaneous adipose tissue and skeletal muscle in response to weight loss

Introduction

Human adipose tissue is heterogenous with respect to free fatty acid uptake and mobilization (1). In situ (2) and in vivo (3) evidence suggests that catecholamine-stimulated lipolysis differs substantially between intra-abdominal, lower-body, and abdominal subcutaneous adipose tissue (AT), and that sex appears to influence these regional differences (1). Whereas basal free fatty acid release in greater in upper- compared to lower-body subcutaneous AT in both sexes, lower-body adipocytes in women are resistant to catecholamine stimulation in comparison to men of a similar phenotype (3). These observations suggest that sex may influence the effects of diet- and exercise-induced weight loss on AT distribution. Indeed, that gluteal/femoral adipocytes are resistant to catecholamine stimulation suggest that women would preferentially mobilize abdominal subcutaneous AT. Accordingly, by comparison to men, women would mobilize less lower-body subcutaneous AT. Given the established relationship between AT distribution and health risk in both sexes (5), knowledge of how men and women mobilize free fatty acids from different depots (i.e., visceral and subcutaneous AT) during weight loss is important. Doing so may improve our understanding of the acknowledged sex difference for weight loss-mediated improvements in metabolic risk factors (6).

To our knowledge no published reports have compared the effects of different treatments on AT or lean tissue (LT) distribution in men and women. This likely reflects difficulty in accessing the imaging techniques required to pursue such studies. We have recently employed a whole-body magnetic resonance imaging

(MRI) model to study the effects of diet and/or exercise on AT and LT distribution in men (4). In this study we have used the same model to determine whether sex influences these variables in moderately obese men and moderately obese premenopausal women. In so doing we tested the following hypotheses: 1) That the reductions in subcutaneous AT will be greater men than women, but that sex does not influence the reductions in visceral AT, independent of treatment, 2) That independent of sex, the combination of diet and exercise induces a preferential reduction in abdominal compared to leg subcutaneous AT, 3) That independent of sex and treatment, a preferential reduction in visceral AT compared to subcutaneous AT will occur. 4) That the combination of diet and exercise would preserve skeletal muscle (SM) in comparison to diet alone in both sexes.

Subjects and methods

Subjects

Subjects were recruited from the general population through the local media. Inclusion criterion required that the subjects were upper body obese [body mass index (BMI, kg/m^2) > 27; waist-to-hip ratio (WHR) $\geq$ 0.95 in men and $\geq$ 0.85 in women, derived using the umbilicus waist circumference], weight stable ($\pm$ 2kg) in the six months prior to the study, taking no medications known to affect the study variables (i.e., oral contraceptives), consumed on average no more than two alcoholic beverages per day, and that the women were premenopausal. Those subjects meeting the study criteria were randomly assigned to one of three treatments; diet alone (DO), diet and aerobic exercise (DA), or diet and resistance exercise (DR). Due to limitations within our laboratory it was not possible to study both sexes concurrently, thus the women were studied prior to the men. Seventy-one subjects completed the study, 11 were excluded from data analysis in order to ensure that the groups were matched for age and BMI. The descriptive characteristics for all groups are presented in Table 1. The men were slightly older (~ 5 yrs) and had larger WHR's and visceral AT depots compared to the women, while the women had more subcutaneous and total AT compared to the men ($P < 0.05$). There were no differences across treatment for any of the anthropometric or MRI variables ($P > 0.05$). All subjects gave their fully informed and written consent to participate in the study, which was conducted in accordance with the ethical guidelines as set by Queen's University.

Tissue measurement by MRI

For all women the MRI images were obtained with a Siemens 1.5-tesla scanner (Erlangen, Germany) while for the men the MRI images were obtained with a General Electric Signa Advantage 1.5-tesla scanner (Wisconsin). A T1-weighted, spin-echo sequence with a 210-ms repetition time and a 17-ms echo time was used to obtain the MRI data. The MRI protocol is described in detail elsewhere (4). Briefly, the subjects lay in the magnet in a prone position with their arms placed strait overhead. Using the intervertebral space between the fourth and fifth lumbar vertebrae (L4-L5) as the point of origin, transverse images (10 mm slice thickness) were obtained every 40 mm from hand to foot resulting in a total of ~41 images for each subject (six data sets of seven images). The total time required to acquire all of the MRI data for each subject was ~25 min. All MRI data was transferred to a computer workstation (Silicon Graphics Inc., Mountain View, CA) for analysis using specially designed image analysis software (Tomovision Inc., Montreal, PQ).

Segmentation and calculation of tissue areas and volumes

The model used to segment the various tissues is fully described and illustrated elsewhere (4). A multiple step procedure was used to identify tissue area (cm^2) for a given MRI image. In the first step a threshold was selected for AT and LT based on the analysis of a sample of typical images and their respective grey level-histograms. Each image was then reviewed by an interactive slice editor program which allowed for verification, and where necessary, correction of the segmented results. The original grey level image was superimposed on the binary segmented image using a transparency mode to facilitate the corrections. In the final step, the observer labeled the different tissues by assigning them different codes (Figure 1).

The areas (cm^2) of the respective tissues in each image were computed automatically by summing the given tissues' pixels and multiplying by the individual pixel surface area. The volume (cm^3) of the different tissues in each slice was calculated by multiplying the tissue area (cm^2) by the slice thickness (10 mm). The volume of the tissues for the space between two consecutive slices were calculated by using a mathematical algorithm given elsewhere (4).

Whole body subcutaneous AT, total AT (subcutaneous + visceral + intrapelvic + intrathoracic + interstitial AT), LT (SM + organ + bone + connective tissue), and adipose-tissue free SM (SM - interstitial AT) volumes were determined using all 41 images. To determine if regional differences existed with respect to the effect of sex and/or treatment on the various tissues, the body was divided into different sections (Figure 1). Visceral AT and abdominal subcutaneous AT were calculated using the five images extending from 5 cm below L4-L5 to 15 cm above L4-L5. Lower-body LT, SAT, and SM were calculated using the images extending from one image below L4-L5 to the foot, while upper-body LT and SM were calculated using the images extending from L4-L5 to the hand. Intra-abdominal LT (i.e., liver, kidney, spleen, etc.) was determined using the images extending from L4-L5 to four images above L4-L5 (i.e., level of the lung). Regional effects of weight loss on subcutaneous AT were determined by comparing the lower-body and abdominal regions; the effects of weight loss on LT distribution were determined by examining the upper-body, lower-body, and intra-abdominal regions; the effects of weight loss on regional changes in SM were determined by examining the lower-body and upper-body regions.

Determination of tissue mass

For AT and SM, volume units (liters) were converted to mass units (kg) by multiplying the volumes by the assumed constant density for AT (0.92 kg/L) and adipose-tissue free SM (1.04 kg/L) (103). The density for whole body adipose-tissue free LT has never been reported. Using data from the only two overweight human cadavers (> 20% body fat) in which both the chemical composition and individual tissue weights of the entire body have been reported (104, 105), a value of 1.08 kg/L was used to estimate adipose-tissue free LT density.

Reliability of MRI measurements

We have previously reported that the mean difference for repeat measurements of whole body LT and AT is < 2% and < 3% respectively. For repeat AT measurements at the L4-L5 level, we report that the mean difference for subcutaneous and visceral AT is 1.1% and 5.5% respectively (47). A recent study has determined the reproducibility of MRI-SM and -subcutaneous AT volume measurements by comparing the intra- and inter-observer estimates for MRI measurements (one series of seven images taken in the legs) obtained in three male and three female subjects (98). The inter-observer difference was 1.8 ± 0.6% for SM and -2.9 ± 1.2% for subcutaneous AT and the intra-observer difference was 0.34 ± 1.1% for SM and 1.5 ± 1.5% for subcutaneous AT (98). For both studies the intra-observer differences was calculated by comparing the analysis of two separate MRI acquisitions in a single observer. The inter-observer difference was determined by comparing two observers' analysis of the same images.

Anthropometric variables

Body mass was measured on a balance scaled calibrated to the nearest 0.1 kg with the subjects dressed in a t-shirt and shorts. Barefoot standing height was measured to the nearest 0.1 cm using a wall-mounted stadiometer. Circumference measurements were taken with the subjects in a standing position at the level of the umbilicus, last rib, and hip using standard procedures (106). The circumference measurements were taken by the same observer pre- and post-treatment. As upper body obesity is typically determined using the umbilicus waist circumference (WC), the descriptive WHR and WC measurements were derived using the umbilicus WC. However, as the level of the umbilicus may change with weight loss, the pre- to post-treatment changes in the WHR and WC were measured using the last rib WC.

Diet and exercise regimens

Dietary protocol. The subjects' energy requirements were determined by multiplying the Harris-Benedict equation (107) by a factor of 1.5, which has been reported to be within ~8% of actual energy requirements in healthy subjects (108). During the pre- and post-treatment testing periods (~ one week), a weight maintenance diet was followed at the prescribed energy intake. For the 16 week treatment period the weight maintenance energy intake was reduced by 4.19

MJ/day (1000 kcal/day) in all groups. All foods were self selected and no supplements were prescribed. All subjects were required to keep daily diet records for the duration of the study and to limit their dietary fat intake to less than 30% of the total energy intake. The diet records were reviewed on a weekly basis using standard food tables (109) to ensure compliance to the prescribed diet and that proper nutrition was maintained. All subjects were requested to attend weekly meetings to discuss individual success strategies and obtain dietary counsel.

Aerobic exercise protocol. Ten men and 10 women performed aerobic exercise 5 d/wk in addition to the energy restriction. The exercise sessions lasted for ~15 min at the beginning and progressed to a maximum of 60 min based on the subjects' capabilities. The mode of aerobic exercise was determined by the subject and consisted of either brisk walking on a motorized treadmill (Quinton Instruments, Seattle, WA), stationary cycling on a cycle ergometer (Monark, Stockholm, Sweden), or stair stepping on an electronic stairmaster (StairMaster 4000, Tri-Tech Inc., Tulsa, OK). Exercise intensity was monitored using an automated heart rate monitor (Polar USA, Stanford, CT). The intensity of the exercise progressed from 50% to 85% of the maximal heart rate that was achieved during a peak oxygen uptake test ($\dot{V}O_{2peak}$). All of the exercise sessions were by appointment and supervised by a physical educator to ensure compliance with the prescribed program.

Resistance training protocol. In addition to the energy deficient diet, 10 men and 10 women also performed resistance exercise 3 d/wk using Nautilus weight-training equipment (Nautilus, Deland, FL). Training sessions began with a 5-10 min warm-up of low intensity stationary cycling and 5 min of static stretching. Following the warm-up, seven exercises were performed in each session: leg extension, leg flexion, super pullover (latissimus dorsi), bench press, shoulder press, triceps extension, and biceps curl. One set of 8 to 12 repetitions were performed to the point of volitional fatigue. For each repetition, the concentric contraction phase was performed in ~2 s and the eccentric contraction phase in ~4 s. As soon as 12 repetitions could be performed at a given weight, the weight was increased by an amount (i.e., one plate) that permitted ~8 repetitions to be performed. Large increases in strength [one repetition maximum (RM)] of 30-45% have been observed in both men and women using a similar training protocol with the same equipment (110). Sit-ups (curl-ups) were performed for the abdominal muscles in addition to the other seven exercises. Each resistance exercise session lasted ~30 min. All of the exercise sessions were by appointment and supervised by a physical educator. The exercise monitor provided verbal encouragement to help ensure that physiological failure was reached and that proper lifting techniques were employed.

Evaluation of training performance

Aerobic capacity ($\dot{V}O_{2peak}$). $\dot{V}O_{2peak}$ was determined using a graded treadmill test that employed a constant walking speed of 4.8 to 5.6 km/h. For the initial two minutes the grade was set at 0%, after which time it was increased to 2% for the third minute and by 1% every minute thereafter. Standard open-circuit spirometry techniques using a Beckman metabolic measurement cart (Sensormedics, Fullerton, CA) were used to determine oxygen uptake ($\dot{V}O_2$). It was assumed that $\dot{V}O_{2peak}$ was obtained when at least two of the following three criterion were achieved: no increases in $\dot{V}O_2$ despite further increases in treadmill grade, a heart rate at or above age predicted maximum (220-age), and a respiratory exchange ratio above 1.0.

Muscular strength. Increases in strength were determined using the following formula: [(a-b)/a]X100, where *a* equals the number of weight plates (10 lbs per plate) lifted at the beginning of *week 4*, and *b* equals the number of weight plates lifted at the completion of the 16 week program. Week 4 was chosen as the initial week in an attempt to represent changes in muscular strength that were primarily due to SM hypertrophy, thereby omitting initial increases in strength that were predominately attributable to neuromuscular factors (111). A linear relationship between the 7-10 RM and the 1 RM both pre (r=0.94) and post-training (r=0.95) have been shown with the use of a Nautilus training program similar to ours (110). Increases in upper-body strength were calculated using the bench press and super pullover exercises, whereas lower-body strength changes were determined using the leg extension and leg curl exercises.

Energy cost of exercise.

Aerobic exercise. The oxygen cost of both treadmill walking and stationary cycling were determined using the equations given by the American College of Sports Medicine (112). Howley et al. (113) have previously reported that direct measurement of metabolic equivalent (MET) values with the use of a StairMaster 4000 were ~20% lower that those determined using the equation provided by the equipment manufacturer. Therefore the MET values obtained when using the stair stepper were reduced by 20% before estimation of the oxygen cost. Energy expenditure for all three modes of exercise was subsequently determined by multiplying the oxygen cost by 21.1 kJ/L (5.04 kcal/l).

Resistance exercise. On the basis of data reported by Ballor et al. (53), the energy expenditure of the resistance exercise program was estimated to be 28 kJ (120 kcal) per session.

Statistical analysis

Data are presented as group means ± SD. A three (treatment) by two (sex) way analysis of variance (ANOVA), with the pre-treatment score acting as the dependent variable, was performed to examine differences between the groups, sexes, and treatments prior to the intervention. Paired student *t*-tests were used to assess within group changes (pre- to post-treatment) for all dependent variables. Bonferonni adjustments ($P < 0.008$, 0.05/number of groups) were used to interpret all *t*-test results. A three (treatment) by two (sex) way ANOVA, with the relative change score [(pre-treatment - post-treatment) / pre-treatment * 100] acting as the dependent variable, was used to evaluate main treatment effects and interactions on all dependent variables. A two way repeated measures multiple analysis of variance (MANOVA), with the relative change in the different AT depots acting as the dependent variables (i.e., dependent variables = change in visceral AT and change in subcutaneous AT), was used to assess the within group differences between the change in subcutaneous and visceral AT (Figure 7), abdominal subcutaneous and lower-body subcutaneous AT (Figure 5), and between the relative change in the visceral AT area at different levels of the abdomen. To control for sex differences in AT and LT (Table 1), the relative change score rather than the absolute change was employed in the ANOVA and MANOVA tests. When the ANOVA or MANOVA P-value was < 0.05, a Scheffé post hoc comparison test was used to locate specific pre-treatment differences and main treatment effects. Pearson-product moment correlations and linear regression analysis were used to determine the simple relationship between different dependent variables within each sex. An analysis of covariance (ANCOVA) was used to determine if the y intercepts and/or slopes of the regression lines (Figure 3) were different across sex using the procedures described by Kleinbaum and Kupper (114). Statistical procedures were performed using SYSTAT (SYSTAT Inc., Evanston, IL).

Determination of sample size and statistical power

The sample size required to observe a significant difference in MRI measurements within each group was determined using a t-test (single tailed) (115). For MRI-visceral AT volume the precision (SD) in our laboratory is 10% and the expected difference is 35% (4, 48). The corresponding numbers for MRI-subcutaneous AT volume are 3% and 25% respectively (4, 48). For MRI-SM volume we have recently reported that the precision is 1.5% (98) and an expected difference of 7% (4). On the basis of these data and with an α of 0.05, a sample size of 10 subjects provides a power of 90% to detect a difference of <6% for visceral AT, <3% for subcutaneous AT, and ~1% for SM in both sexes.

Results

Adherence to diet and exercise

With few exceptions, complete dietary-intake records were submitted as required by all subjects. Analysis of the diet records indicated that the mean dietary-induced energy deficit for the male DO, DA, and DR groups were 255 ± 30 kJ/day (1065 ± 127 kcal/day), 232 ± 53 kJ/day (968 ± 222 kcal/day), and 271 ± 62 kJ./day (1132 ± 261 kcal/day) respectively. The corresponding fat intakes were 20.0 ± 4.5%, 22.1 ± 6.9%, and 22.9 ± 3.7%. The mean dietary-induced energy deficit for the female DO, DA, and DR groups were 302 ± 64 kJ/day (1264 ± 266 kcal/day), 356 ± 125 kJ/day (1488 ± 524 kcal/day), and 288 ± 48 kJ/day (1203 ± 199 kcal/day. The corresponding fat intakes were 20.6 ± 4.2%, 23.3 ± 4.3%, and 23.4 ± 5.7%. Analysis indicated that there was no sex by treatment interaction for the mean dietary-induced energy deficit ($P > 0.1$). Furthermore, there were no differences across sex or treatment for either the energy deficit or the intake ($P > 0.05$)

For the DA groups, attendance for the exercise sessions averaged 89% (range 74-98%) and 92% (range 85-98%) for the men and women respectively. The duration of the exercise sessions for the men (38.6 ± 6.9 min) was not different from that of the women (33.7 ± 5.9 min) ($P > 0.1$). For the DA groups the average exercise intensity was 79.2 ± 6.6% of the maximal predicted heart rate (220 - age) for the men and 78.0 ± 4.4% of the maximal heart rate for the women ($P > 0.1$). For the men ~50% of the aerobic exercise was performed on the treadmill, 25% stair stepping, and 25% on the stationary bicycle. For the women ~27% of the exercise was performed on the treadmill, 68% stair stepping, and 5% on the stationary bicycle. The corresponding energy expenditures values for the DA men [6.4 ± 2.9 MJ (26,649 ± 12,148 kcal)] and DA women [4.6 ± 1.0 MJ (19,246 ± 4,373 kcal)] were not different ($P > 0.05$).

For the DR groups, attendance for the exercise sessions averaged 95% (range 81-100%) and 94% (85-98%) for the men and women respectively. Assuming an energy cost of 28 kJ (120 kcal) per session, it was estimated that the mean energy expenditure for the DR men (1.3 ± 0.1 MJ, 5,388 ± 302 kcal) was not different compared to DR women (1.3 ± 0.1 MJ, 5,424 ± 224 kcal) ($P > 0.1$). However, these values were significantly lower than the mean energy expenditure observed in the DA groups ($P < 0.05$).

Peak $\dot{V}O_2$

In response to the aerobic exercise program, $\dot{V}O_{2peak}$ increased ($P < 0.01$) by 17% within the male DA group (0.47 ± 0.39 L/min) and 9% within the female DA group (0.20 ± 0.16 L/min). The relative improvement in $\dot{V}O_{2peak}$ for the DA men was greater compared to the DA women ($P < 0.01$). $\dot{V}O_{2peak}$ did not change within any DO or DR group ($P > 0.01$).

Strength-training performance

Improvements in strength were determined using four (two upper- and two lower-body) of the eight resistance training exercises. The mean increase for the two lower-body exercises was 19% within the DR men ($P < 0.01$) and 23% within the

DR women ($P < 0.01$). The mean increase in the two upper-body exercises was 12% within the DR men ($P < 0.01$) and 42% within the DR women ($P < 0.01$). No differences were observed between the DR men and women for the changes in lower-body strength ($P > 0.01$), however, the women improved to a greater extent than men in upper-body strength ($P < 0.01$).

Effects of weight loss on anthropometric variables

With the exception of WHR in both DO groups and the DA women; significant ($P < 0.008$) reductions were observed for all anthropometric variables within all groups (Table 2). There were no significant treatment by sex interactions, or difference across sex or treatment, for the changes in any of the anthropometric variables ($P > 0.05$).

Effects of weight loss on total and regional AT distribution

Total adipose tissue

As indicated in Table 2, a significant reduction in the total adipose tissue (visceral + subcutaneous AT + intrapelvic + intrathoracic + interstitial AT) (~25%) was observed within each group ($P < 0.008$). Analysis revealed that there were no sex by treatment interactions for the reductions in total AT ($P > 0.1$). However, it was found that there was a difference across sex as the relative reduction in total adiposity for the men (~27%) was greater than the corresponding reduction for women (~22%) ($P < 0.05$). There were no differences across treatment for the reductions in the total AT ($P > 0.05$).

Subcutaneous adipose tissue

Whole body subcutaneous AT. Significant reductions were observed for total subcutaneous AT(~25%) within each group ($P < 0.008$) (Figure 2). There was no significant sex by treatment interaction when comparing the relative reduction in subcutaneous AT ($P > 0.1$). However, a difference was noted across sex as the men (~26%) had a greater reduction compared to women (~22%) ($P < 0.05$) (Figure 2). Although no significant differences were observed across treatment for the reduction in subcutaneous AT ($P > 0.05$), the results illustrated in Figure 2 clearly indicate a trend towards an increased reduction in response to the combination of diet and exercise. Indeed, when the DR and DA subjects were combined, the reduction in subcutaneous AT was greater in response to the combination of diet and exercise (~25%) in comparison to diet alone (~21%) ($P < 0.05$).

To determine whether a systematic variation existed in the subcutaneous AT reduction between sexes, we examined the reduction in subcutaneous AT over the range of weight loss obtained for both men and women (Figure 3). ANCOVA revealed that there were no differences across sex for either the slope or intercept of the regression lines ($P > 0.1$).

Regional subcutaneous AT. To determine the effects of weight loss on the regional mobilization of subcutaneous AT, the changes within both lower-body and abdominal subcutaneous AT were examined independently. Significant reductions were observed in both depots for all groups ($P < 0.008$). There was no significant sex by treatment interaction when the reductions in abdominal and lower-body subcutaneous AT were analyzed independently ($P > 0.1$). However, for lower-body subcutaneous AT (i.e., MRI images 1 to 20, Figure 1), the reduction was greater in men than women ($P < 0.05$). Inspection of Figure 4, which illustrates the reduction in subcutaneous AT area (cm^2) for each of the 41 images in both sexes, confirms that the sex differences observed for SAT reduction can be accounted for by a resistance in the lower-body adipose tissue reduction in women. In addition, a trend suggested that the men had a greater reduction in abdominal ($P = 0.06$) subcutaneous AT in comparison to women. There was also a difference across treatment for abdominal subcutaneous AT as the DR subjects had a larger reduction compared to DO subjects ($P < 0.01$).

Abdominal vs lower-body subcutaneous AT. To determine if there was a preferential reduction of abdominal subcutaneous AT, the relative reduction for the abdomen was compared to the lower-body. Figure 5 shows that with the exception of DA women, the relative reduction in abdominal subcutaneous AT was greater compared to lower-body subcutaneous AT within all exercise groups ($P < 0.01$). Reductions in abdominal and lower-body subcutaneous AT were not different in response to diet alone ($P > 0.05$).

Visceral adipose tissue

Total visceral AT. Significant reductions in visceral AT (~35%) were observed within each group independent of treatment and sex ($P < 0.008$) (Figure 6). There was no significant sex by treatment interaction when comparing the relative reduction in visceral AT ($P > 0.1$). Furthermore, no differences were seen across sex (Figure 6) or treatment for the reduction in visceral AT (P > 0.1). No systematic variation in visceral AT reduction was observed between sexes as the slope and intercept of the regression lines were not different (P > 0.1) (Figure 3).

Regional visceral AT. The effects of weight loss on the regional mobilization of visceral AT was determined by examining the change in visceral AT area (cm^2) for the five images extending from one below (-5 cm) L4-L5 to three above (+15 cm). Independent of sex, within each group the relative reduction in visceral AT area was not different between the five images (P > 0.05). Thus, the reduction in visceral AT was uniform throughout the abdomen for both the men and women. Furthermore, when each abdominal image was analyzed independently, there was no significant sex by treatment interaction, difference across sex, or difference across treatment for the reduction in visceral AT (P > 0.05).

Visceral vs subcutaneous adipose tissue.

To compare the effects of weight loss on the relationship between visceral AT and subcutaneous AT, the relative change in whole body subcutaneous AT was compared to the change in visceral AT (Figure 7). Within each group the relative reduction in visceral AT was greater than the reduction in subcutaneous AT (P < 0.05). Further analysis revealed that there was no significant sex by treatment interaction, difference across sex, or difference across treatment when the difference between the reduction in visceral AT and subcutaneous AT was analyzed (P > 0.1). Thus, visceral AT was preferentially mobilized by comparison to subcutaneous AT to a similar extent in both sexes.

Effects of weight loss on total and regional SM and LT distribution

Skeletal muscle

Whole body SM. The effects of weight loss on the relative change in whole body SM is illustrated in Figure 8. Independent of sex, whole body SM was maintained within the diet and exercise groups ($P > 0.008$). However, significant reductions in SM were observed in response to diet alone ($P < 0.008$). There was no significant sex by treatment interaction for the change in SM. It was also noted that there was no difference across sex for the change in SM ($P > 0.1$), however, there were differences across treatment as the DO subjects lost more SM than both the DA and DR subjects ($P < 0.01$).

Regional SM. To determine whether regional differences existed in response to weight loss, the change in lower- and upper-body SM were examined independently. As illustrated in Figure 9, significant decreases in both lower- and upper-body SM were observed within the DO groups, independent of sex ($P < 0.008$). There was no significant sex by treatment interaction or difference across sex for the relative change in lower- or upper-body SM ($P > 0.1$). There were, however, differences across treatment for the reduction in upper-body SM (but not lower-body SM), as the DO subjects lost more upper-body SM than both the DA and DR subjects ($P < 0.05$).

Total lean tissue

Whole body LT. Significant reductions in whole body LT (SM + organ + bone + connective tissue) were observed within the DO groups alone ($P < 0.008$) (Table 2). There was no significant sex by treatment interaction, difference across sex, or difference across treatment for the changes in whole body LT ($P > 0.05$).

Regional LT. No changes were observed in the intra-abdominal LT (i.e., kidney, liver) within any group ($P > 0.05$). Within the DO groups, reductions ($P < 0.008$) were observed for both lower-body (men and women) and upper-body (men only) LT, indicating that the loss of LT in response to diet alone was limited to SM in the appendicular regions.

Discussion

The influence of sex on adipose and lean tissue distribution in response to exercise and/or diet induced weight loss in upper-body obese men and women was examined. The findings demonstrate for the first time that, in response to equivalent weight loss (~11 kg): 1) Reductions in total adipose tissue are greater in men (~26%) compared to women (~22%). The difference is explained by a decreased mobilization of lower-body subcutaneous adipose tissue in women. 2) Visceral adipose tissue is substantially and uniformly reduced (~35%) independent of sex and treatment. 3) Visceral adipose tissue is preferentially reduced in comparison to subcutaneous adipose tissue independent of sex and treatment. 4) Independent of sex, the combination of diet and exercise results in a preservation of lean tissue and its principle constituent skeletal muscle, whereas diet alone is associated with modest but significant reductions in skeletal muscle.

Although no other study has rigorously investigated whether sex influences the composition of weight loss, our finding that the relative reduction in total adiposity is greater in men than women is at odds with the conclusion of a recently performed meta-analysis suggesting that sex does not influence the changes in total fat loss (81). In that study the reductions in fat loss were expressed as a percentage of weight loss. As such, in response to diet or the combination of diet and exercise, fat represented ~75% and 85% of the weight loss respectively in both sexes. However, using their data (Tables 1 and 2) we calculated that, had the authors expressed the reductions in fat mass as a percentage of initial values, the reductions in fat mass would be greater in males (~28%) than females (~24%). These sex differences (~4%) are similar to those reported in this study (~5%) for total adiposity.

That the relative reduction in total adiposity was greater in obese men is explained in large measure by a decreased mobilization of lower-body subcutaneous AT in women (i.e., the gluteal-femoral region, images 1-20, Figure 1). This observation is consistent with in vivo evidence which demonstrates that lower-body adipocytes are resistant to catecholamine stimulation in women, but not in men (3). Because two thirds of the subjects in this study participated in regular exercise at intensities known to increase plasma epinephrine concentrations in both sexes (116), the failure of lower-body subcutaneous AT to respond to catecholamine stimulation in women may partially explain the sex difference in AT reduction. In addition to the sex differences observed for lower-body adipose tissue reduction, the relative reduction in abdominal subcutaneous AT in men (30%) was greater than women (25%) at the 0.06 level. Inspection of Figure 4 confirms that for 2 of the 5 MRI images we employed to calculate abdominal subcutaneous AT volume, the reduction in subcutaneous adipose tissue area (cm^2) was greater in men. Given that this depot is a strong correlate of metabolic risk factors (27-29), diet and exercise-induced weight loss may confer an added benefit in men through an greater reduction in abdominal subcutaneous AT.

Consistent with the observation that upper-body adipocytes are more sensitive to catecholamine stimulation than femoral adipocytes in both sexes (2,3), with the exception of DA women, within both sexes we observed a preferential reduction of abdominal versus lower-body subcutaneous AT in response to diet and exercise, but not diet alone. As stated above, that this depot is preferentially reduced in response to diet and exercise may convey a health risk benefit as abdominal subcutaneous AT is an independent predictor of metabolic risk factors in both sexes (27-29). Accordingly, it is reported that reductions in this depot are correlated with concurrent reductions metabolic risk factors in men and women (80, 72, 74).

In this study, no differences were observed across sex for reductions in visceral adiposity. These findings agree with a previous study in which no sex differences were observed in basal or epinephrine stimulated lipolysis in omental and mesenteric adipocytes in vitro (40). The data presented here also demonstrate that regardless of sex, the mobilization of visceral AT was uniform throughout the abdominal region. In other words, within each group the relative reduction in visceral AT area for any given abdominal image was not different from the reduction in visceral AT observed in any other abdominal image. Furthermore, regardless of the abdominal image used, no differences were seen across sex or treatment for the reduction in visceral AT. This implies that a single computerized tomography or MRI image is appropriate for assessing the influence of weight loss on the change in visceral AT within both obese men and women, and that a single image can be used to compare the visceral AT reduction between sexes.

The 35% reduction in visceral AT may be of particular importance to men, as for a given level of adiposity, men accumulate greater quantities of visceral AT compared to women (51, 52). Thus, although we report that sex does not influence the relative reduction in visceral adiposity, on an absolute basis the men lost more visceral AT (1.3 kg) than women (0.6 kg). Because visceral adiposity is an independent correlate of metabolic risk factors in both men and women (5), our finding that men lose more visceral AT on an absolute basis may partially explain why reductions in cardiovascular risk factors are greater in men than women despite a similar decrease in relative visceral AT (6).

It is well documented that within both sexes there is a preferential reduction of visceral AT in response to diet alone, or the combination of diet and exercise (4, 70, 74). It is reported here for the first time that there is a preferential reduction of visceral AT independent of sex and treatment as the relative reduction in visceral AT was ~10% greater than subcutaneous AT within both sexes. The preferential reduction of visceral adiposity may be explained by a decreased sensitivity of visceral adipocytes to α_2-adrenergic stimulants in upper-body obese men and women in comparison to non-obese controls (117). Furthermore, an increased sensitivity of omental adipocytes to β-adrenergic stimulants in comparison to abdominal subcutaneous adipocytes has been shown in obese men (40) and in obese women (42).

In this study the combination of diet and exercise was associated with a preservation of whole body and regional skeletal muscle independent of sex. This is consistent with the observation of an increase in muscular strength and peak $\dot{V}O_2$ within the DR groups and DA groups respectively. As expected diet alone was associated with a similar reduction in skeletal muscle within both genders. This is consistent with our previous observation in men (4) and reaffirms the utility of diet and exercise as a means of reducing adiposity concurrent with a preservation of muscle mass and improvements in functional capacity.

Summary

The findings of this study demonstrate that in response to equivalent weight loss the relative reduction in total adiposity is greater in obese men than premenopausal women of similar phenotype. This observation was explained in part by a reduced mobilization of lower-body subcutaneous adipose tissue in women. Sex did not influence the reduction in visceral adipose tissue. Our findings reaffirm the importance of exercise as a means of preserving skeletal muscle, improving functional capacity, and reducing abdominal subcutaneous adipose tissue in both sexes. Because both obesity phenotype (86) and menopausal status (84) are known to influence the change in body composition with weight loss, the findings of this study are restricted to upper-body obese men and upper-body obese premenopausal obese women.

TABLE 1.
Descriptive characteristics of subjects[1]

Variable	MEN DO (*n* = 10)	MEN DA (*n* = 10)	MEN DR (*n* = 10)	WOMEN DO (*n* = 10)	WOMEN DA (*n* = 10)	WOMEN DR (*n* = 10)
Anthropometric						
Age (yr)[2]	45.6 ± 6.8	47.5 ± 6.7	37.9 ± 13.3	39.6 ± 7.5	39.0 ± 6.2	37.3 ± 4.4
BMI[3]	31.6 ± 2.8	33.0 ± 3.4	33.6 ± 4.3	34.5 ± 4.4	35.5 ± 6.6	32.5 ± 4.6
WC (cm)[4]	109.7 ± 7.4	115.0 ± 8.0	117.5 ± 10.8	113.9 ± 15.6	114.4 ± 19.8	111.5 ± 11.1
WHR[5]	0.99 ± 0.04	1.01 ± 0.05	1.01 ± 0.4	0.93 ± 0.04	0.92 ± 0.07	0.93 ± 0.05
MRI						
Total AT (kg)[6]	31.0 ± 7.2	33.7 ± 6.5	37.5 ± 10.1	42.8 ± 12.4	46.5 ± 15.3	38.8 ± 9.8
Subcutaneous AT (kg)[6]	23.7 ± 6.4	25.2 ± 6.2	30.6 ± 8.2	38.5 ± 10.7	40.7 ± 14.6	34.8 ± 9.4
Visceral AT (kg)[2]	3.7 ± 1.3	4.0 ± 1.2	3.2 ± 2.1	2.3 ± 1.2	2.0 ± 0.8	1.6 ± 0.6
Lean Tissue (kg)[2]	65.7 ± 5.3	64.6 ± 7.2	67.4 ± 7.0	46.9 ± 5.5	48.4 ± 4.2	45.4 ± 2.6
Skeletal Muscle (kg)[2]	34.1 ± 3.9	33.4 ± 5.3	35.2 ± 4.8	23.1 ± 3.7	23.6 ± 2.6	21.5 ± 2.3

[1] $\bar{x}$ ± SD. DO, diet only; DA, diet and aerobic exercise; DR, diet and resistance exercise; BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; AT, adipose tissue; MRI, magnetic resonance imaging; AT, adipose tissue.

[2] men > women, $P < 0.05$ (ANOVA)

[3] In kg/m^2.

[4] Obtained at the umbilicus level.

[5] Calculated by using the umbilicus waist circumference; men > women, $P < 0.05$ (ANOVA)

[6] women > men, $P < 0.05$ (ANOVA)

TABLE 2.
Effects of weight-loss on anthropometric and whole body MRI variables[1]

	DO		DA		DR	
	Abs	%	Abs	%	Abs	%
Men						
Anthropometric						
Weight (kg)	-11.7 ± 3.5[2]	-11.5	-11.4 ± 3.9[2]	-11.1	-12.7 ± 3.9[2]	-11.9
WC (cm)[3]	-8.4 ± 4.0[2]	-7.7	-13.2 ± 4.1[2]	-11.6	-11.8 ± 4.1[2]	-10.5
WHR[4]	-0.02 ± 0.03	-1.9	-0.02 ± 0.05[2]	-2.2	-0.05 ± 0.02[2]	-4.7
MRI						
Total AT (kg)[5]	-7.5 ± 2.7[2]	-24.3	-9.4 ± 3.9[2]	-28.0	-10.3 ± 3.6[2]	-27.5
Subcutaneous AT[5]	-5.5 ± 2.3[2]	-22.9	-6.5 ± 2.6[2]	-25.9	-8.6 ± 2.6[2]	-29.8
Visceral AT (kg)	-1.2 ± 0.7[2]	-31.1	-1.6 ± 0.9[2]	-40.4	-1.1 ± 0.7[2]	-38.2
Lean Tissue (kg)	-2.9 ± 1.9[2]	-4.3	-1.6 ± 2.0	-2.4	-1.8 ± 1.8	-2.6
Skeletal Muscle[6]	-2.6 ± 1.2[2]	-7.6	-0.9 ± 1.0	-2.9	-1.0 ± 1.0	-3.1
Women						
Anthropometric						
Weight (kg)	-10.7 ± 4.0[2]	-11.4	-11.5 ± 3.2[2]	-11.8	-10.0 ± 2.7[2]	-11.8
WC (cm)[3]	-7.3 ± 5.1[2]	-7.2	-9.0 ± 3.6[2]	-8.8	-10.6 ± 6.6[2]	-11.2
WHR[4]	-0.00 ± 0.05	-0.6	-0.02 ± 0.02	-1.5	-0.03 ± 0.06[2]	-3.9
MRI						
Total AT (kg)[5]	-8.2 ± 3.4[2]	-19.1	-10.5 ± 3.7[2]	-22.6	-8.7 ± 2.3[2]	-22.4
Subcutaneous AT[5]	-7.1 ± 2.9[2]	-18.3	-8.7 ± 3.2[2]	-22.1	-8.0 ± 1.7[2]	-24.2
Visceral AT (kg)	-0.7 ± 0.4[2]	-30.7	-0.7 ± 0.4[2]	-35.1	-0.4 ± 0.2[2]	-29.8
Lean Tissue (kg)	-1.5 ± 1.3[2]	-3.0	-0.5 ± 1.6	-1.1	-0.2 ± 1.8	-0.4
Skeletal Muscle[6]	-1.2 ± 0.7[2]	-5.2	-0.5 ± 0.9	-1.9	-0.7 ± 1.0	-3.5

[1] $\bar{x}$ ± SD. DO, diet only; DA, diet and aerobic exercise; DR, diet and resistance exercise; Abs, absolute change; %, % change; WC, waist circumference; WHR, waist-to-hip ratio; MRI, magnetic resonance imaging; AT, adipose tissue.

[2] Significant within-group difference, $P < 0.008$ (paired *t*-test)

[3] Obtained at the last rib.

[4] Calculated by using the last rib waist circumference

[5] men > women, $P < 0.05$ (ANOVA)

[6] DO > DA, DO > DR, $P < 0.01$ (ANOVA)

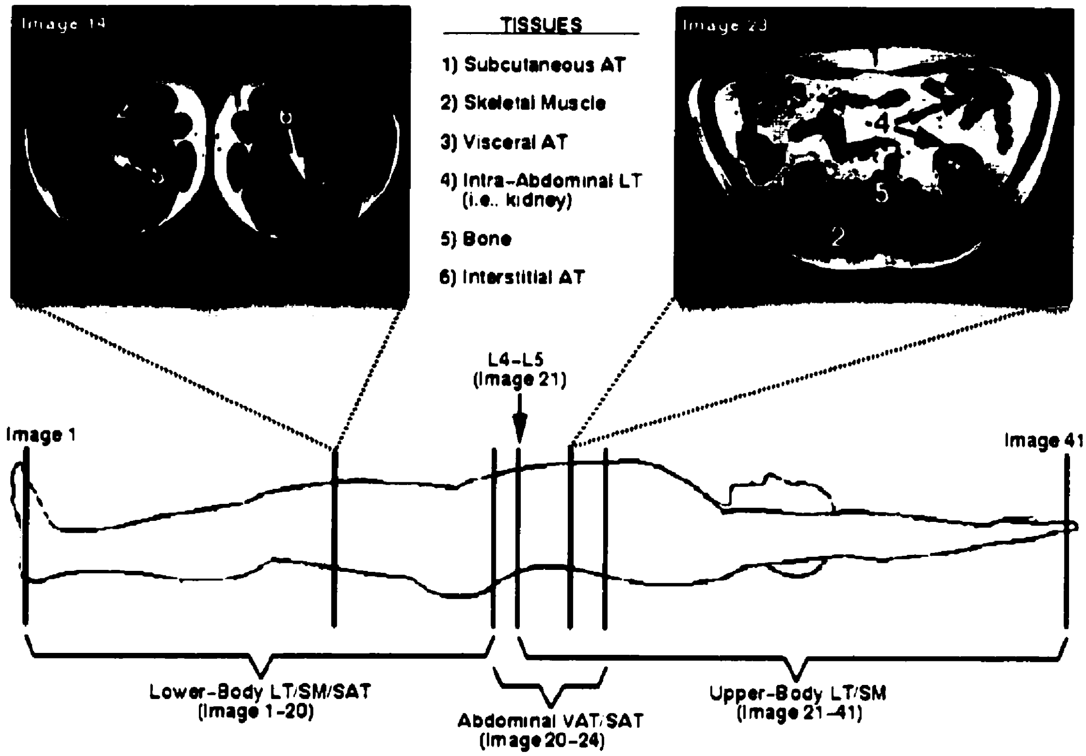

Figure 1.

Protocol used to: 1) Label the various tissues, and 2) To determine regional measurements of body composition. AT, adipose tissue; LT, lean tissue; SAT, subcutanious adipose tissue; SM, skeletal muscle; VAT, visceral adipose tissue; L4-L5, 4th to 5th lumbar vertebrae.

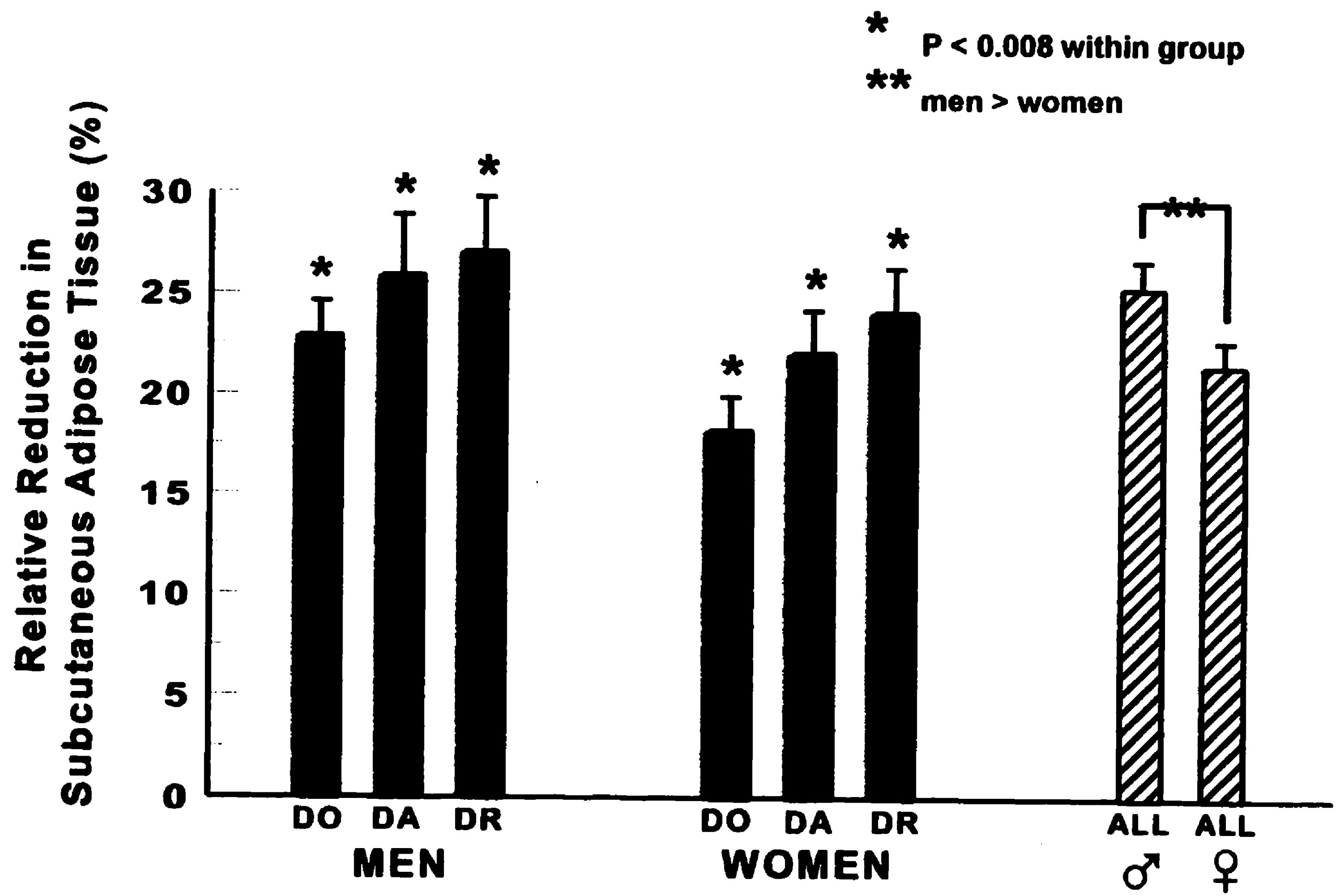

Figure 2. Relative reduction in whole body subcutaneous adipose tissue mass. * significant within group reduction ($P < 0.008$), ** relative reduction in men is greater than reduction in women ($P < 0.05$). Values are means ± standard error of estimate.

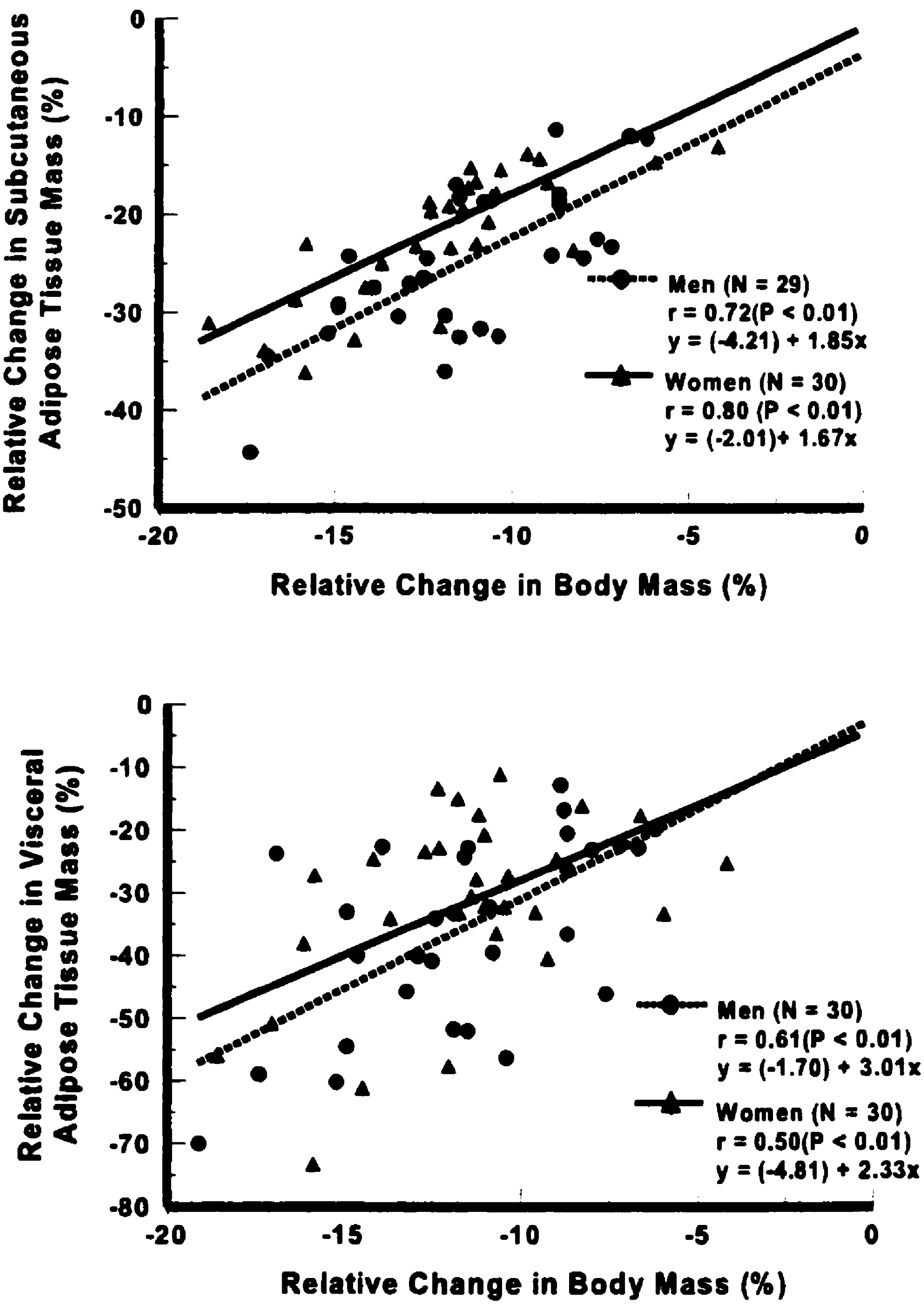

Figure 3. Relationship between the relative reduction in body mass with the relative reduction in subcutaneous adipose tissue mass and visceral adipose tissue mass. One outlier was removed for subcutaneous adipose tissue, therefore, the results for only 29 men were included.

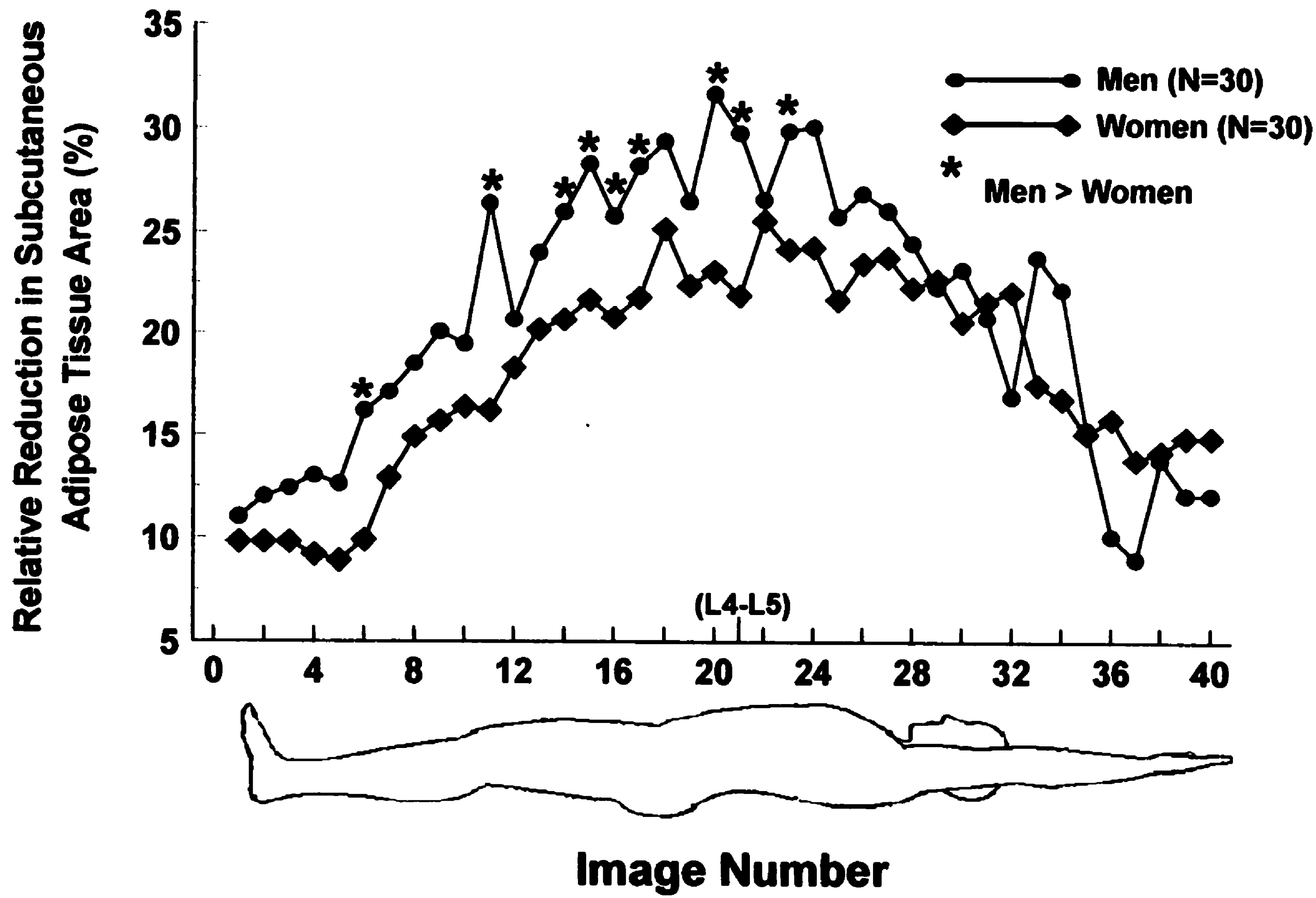

Figure 4. Relative reduction in subcutaneous adipose tissue for each of the 41 images in the men and women. * relative reduction in men is greater than reduction in women ($P < 0.05$). Data are expressed as mean values.

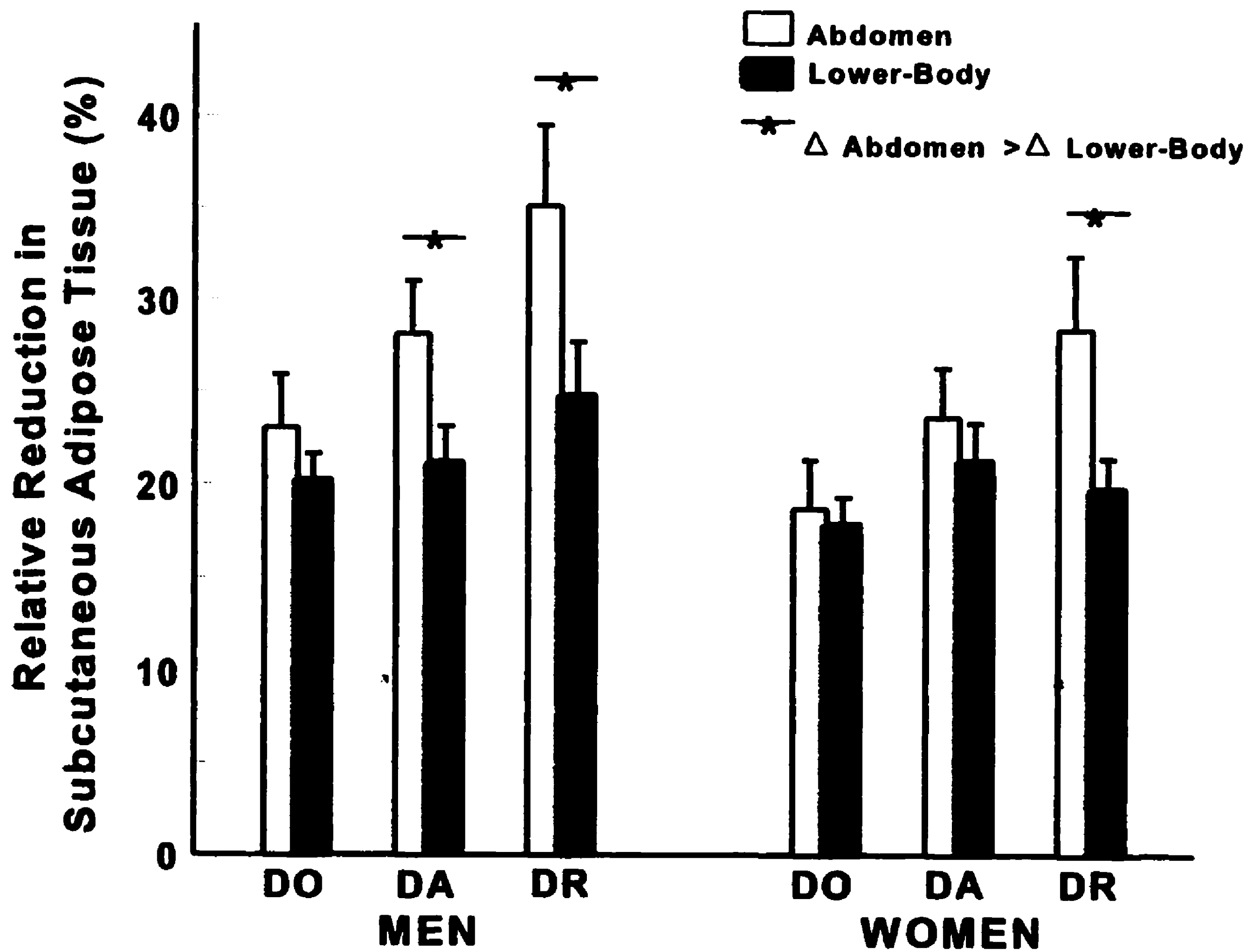

Figure 5. Relative reduction in subcutaneous adipose tissue mass in the lower-body and abdominal regions. * relative reduction in abdomen is greater than reduction in lower-body within group ($P < 0.05$). Values are means ± standard error of estimate.

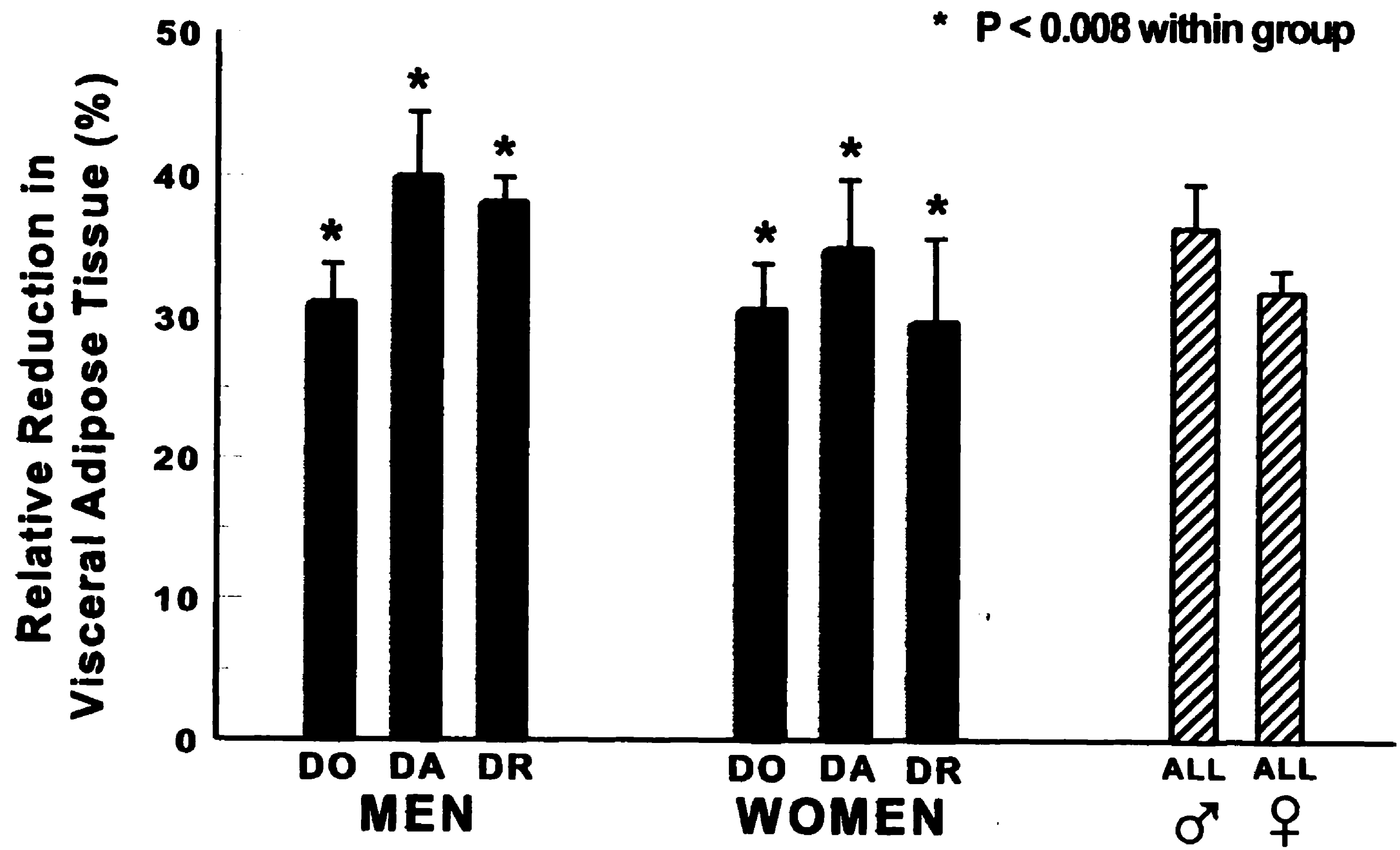

Figure 6. Relative reduction in visceral adipose tissue mass. * significant within group reduction ($P < 0.008$). Values are means ± standard error of estimate.

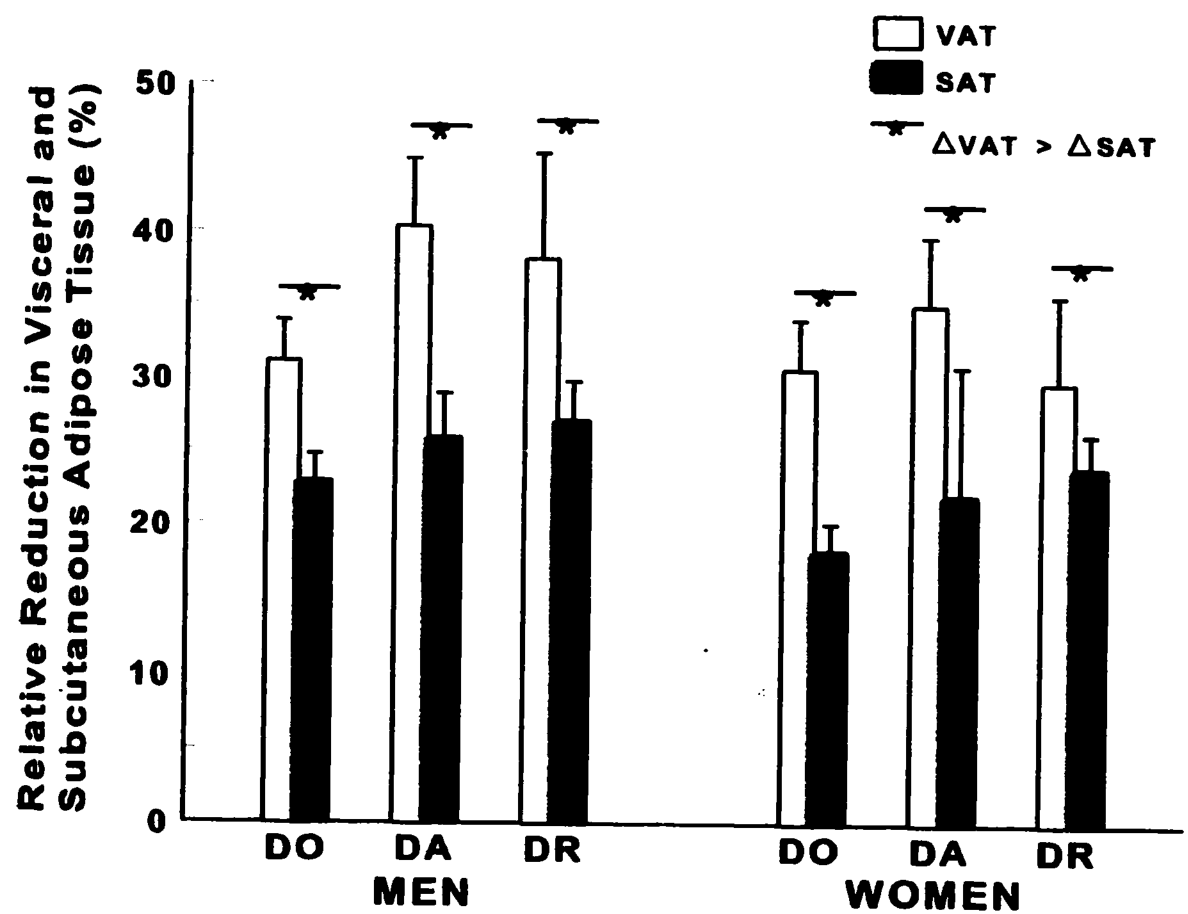

Figure 7. Relative reduction in whole body subcutaneous adiopse tissue and visceral adipose tissue mass. VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue. * relative reduction in visceral adipose tissue greater than reduction in subcutaneous adipose tissue within group ($P < 0.05$). Values are means ± standard error of estimate.

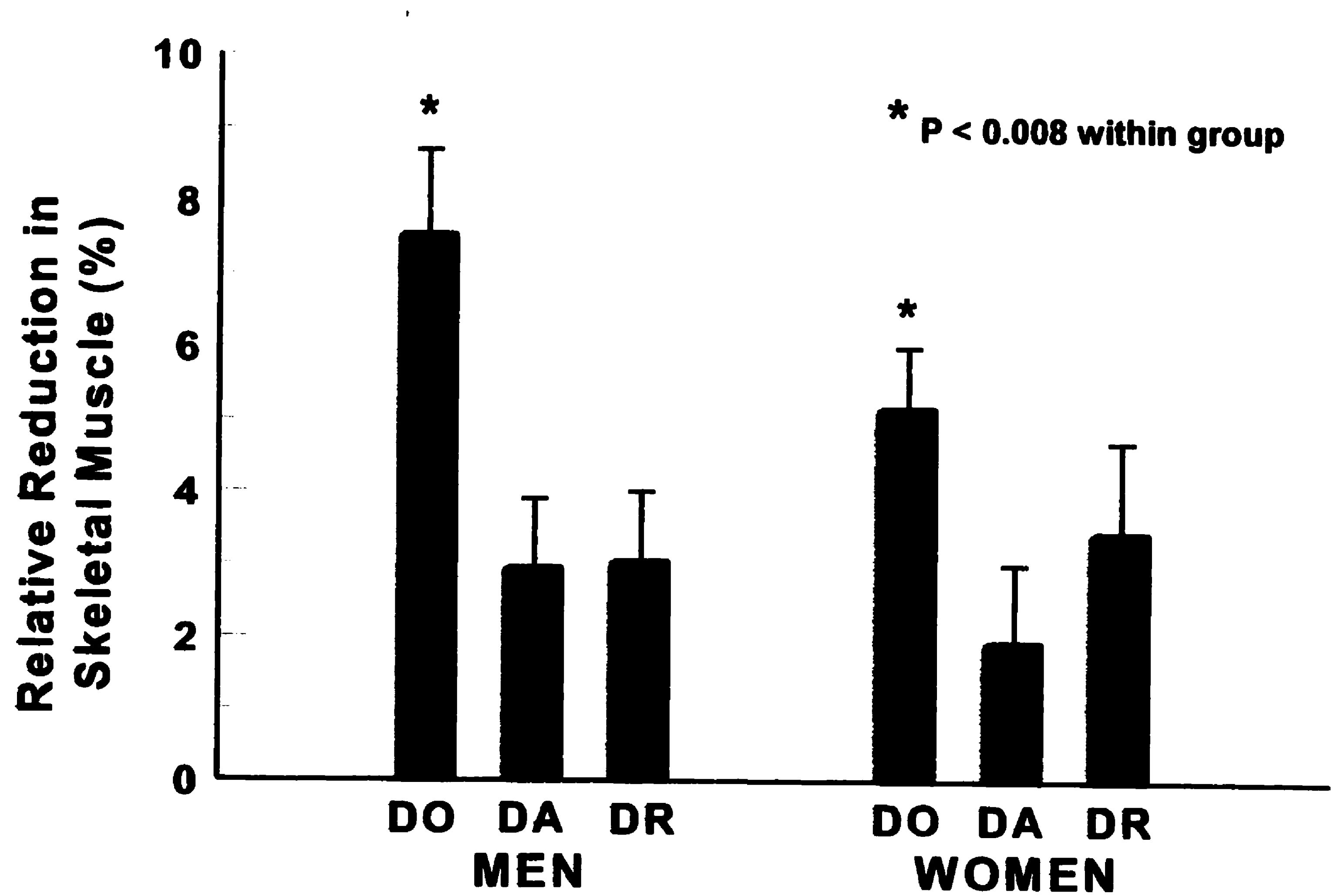

Figure 8. Relative reduction in whole body skeletal muscle mass. * significant within group reduction ($P < 0.008$). Values are means ± standard error of estimate.

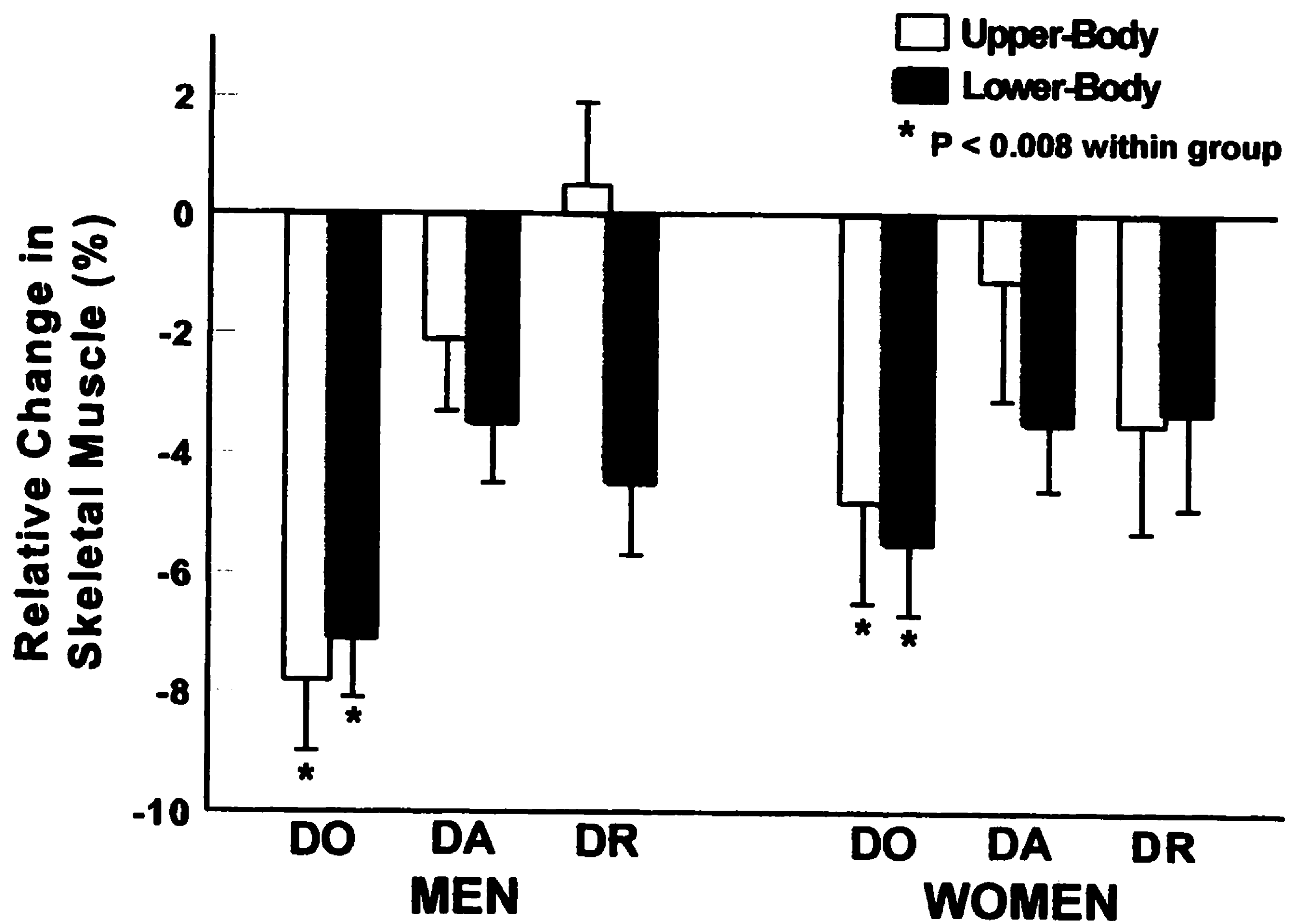

Figure 9. Relative reduction in lower-body and upper-body skeletal muscle mass. * significant within group reduction ($P < 0.008$). Values are means ± standard error of estimate.

4.0.0 CONCLUSIONS

Within this laboratory we have observed that there a large reductions in total and regional AT in response to a moderate weight loss in both genders. These observations provide support for a modest approach to obesity reduction and suggest that in both men and women the caloric restriction and subsequent weight loss should approximate 1000 kcal/day and 1.5 lbs per week respectively. Our findings reaffirm the importance of combining low intensity aerobic (~35 min 5 times per week) or resistance exercise (~25 min 3 times per week) with the caloric restriction, as the addition of exercise preserves skeletal muscle, preferentially mobilizes abdominal subcutaneous AT, and improves functional capacity.

The underlying goal of any weight reduction program should be to not only decrease total adiposity and improve AT distribution, but also to improve the metabolic risk profile. We have recently investigated the effects of diet- and exercise-induced with loss on metabolic variables in men (118). These results suggest that the combination of diet and exercise has a greater influence on insulin metabolism than diet alone. Although not considered in this study, the measurement of metabolic variables such as plasma lipids, lipoproteins, insulin, and glucose in response to exercise and/or diet in both sexes may provide valuable information regarding sex differences in improvements in metabolic variables.

The current literature examining the influence of exercise during weight loss is based on studies which have compared diet alone to combined diet and exercise programs. Studies of this design do not allow for the comparison of the separate effects of exercise and diet on body composition. Is equivalent weight loss, induced by diet alone or exercise alone, associated with equivalent reductions in total adiposity, AT distribution, and visceral AT? Furthermore, the effects of exercise *per se* on the changes in AT and lean tissue distribution are unknown. Is exercise, in the absence of weight loss, associated with reductions in visceral and/or subcutaneous AT? Answers to these questions would provide practitioners with valuable information regarding the beneficial effects of exercise, with or without weight loss, on improvements in body composition.

An experimental design to investigate these questions would include four groups: a control group, a group that would loose weight through increased caloric expenditure (exercise-induced weight loss), a group that would loose weight by decreasing their caloric intake (diet-induced weight loss), and an exercise group that is refed after each session (exercise weight stable). Such a study would require strict control of both the caloric intake and the daily activity levels. Doubly-labeled water, a technique used to measure 24-hour energy expenditure, could be employed to provide information on energy expended outside of supervised exercise sessions (119).

In our laboratory we are currently undertaking a study as described above. Preliminary observations from this study are shown in Appendix A (120). These observations suggest that similar reductions in visceral and subcutaneous AT occur in response to equivalent diet- or exercise-induced weight loss, however, exercise alone preserves skeletal muscle and improves functional capacity. In addition, although aerobic exercise in the absence of weight loss is not associated with significant reductions in total adiposity, it is associated with reductions in the two most critical AT depots, visceral and abdominal subcutaneous AT.

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Appendix A: Independent Influence of Diet- or Exercise-Induced Weight Loss on Visceral Adipose Tissue and Skeletal Muscle in Obese Men

Independent Influence of Diet- or Exercise-Induced Weight Loss on Visceral Adipose Tissue and Skeletal Muscle in Obese Men

I Janssen, R Hudson, P Jones, and R Ross

OBJECTIVE: We evaluated the effects of equivalent diet- or exercise-induced weight loss on visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), and skeletal muscle (SM) in twenty-four obese men.

MATERIALS AND METHODS: Subjects were randomly assigned to four groups (N=6 in each): control (C), diet induced weight loss (DWL), exercise (aerobic) induced weight loss (EWL), and exercise weight stable (EWS). The groups were not different for age, body mass index (kg/m^2), total adiposity, VAT, and SAT. VAT, SAT, and SM were measured by magnetic resonance imaging (MRI). The treatment period for all groups was 12 weeks.

RESULTS: Weight loss in the DWL (7.4 $\pm$ 0.8 kg) and EWL (7.1 $\pm$ 1.7 kg) was not different ($P > 0.1$). Significant improvements in peak $\dot{V}O_2$ were observed in the EWL and EWS groups only ($P < 0.05$). The significant reductions in VAT and SAT within the DWL and EWL groups was not different ($P > 0.1$). Significant ($P < 0.05$) reductions in VAT and abdominal SAT were also observed in the EWS group. SM was preserved within EWL and EWS groups, but not in the DWL. No changes in VAT, SAT, or SM were observed in the C group ($P > 0.1$).

CONCLUSIONS: The principle finding is twofold. First, that similar reductions in VAT and SAT are observed in response to equivalent diet- or exercise-induced weight loss, however, exercise alone preserved SM and improved functional capacity. Second, aerobic exercise in the absence of weight loss is associated with concomitant reductions in both VAT and SAT.

Appendix B: Informed Consent

QUEEN'S UNIVERSITY

DIET AND EXERCISE STUDY

INFORMED CONSENT

The following brief is intended to provide you with the details you should be aware of prior to your consent as a participant in this research project. Please read the following information carefully and feel free to ask any question that you may have.

Objective of the study

In recent years a number of studies have clearly shown that a relationship exists between obesity and the development of numerous health problems including cardiovascular disease and diabetes. In fact, the relationship is strengthened if one considers the regional distribution of body fat (i.e where your body fat is located). Given the relationship between obesity with ill health, and the fact that obesity is a condition characterized by large amounts of body fat, it follows that an important component of an effective prevention program would be the ability to lose body fat. Hence the purpose of this research project will be to investigate different methods of changing body composition through diet and or exercise.

EXPLANATION OF PROCEDURES

Pre-participation screening

Prior to participation in this study you will be required to have a medical exam. The exam will be conducted by a medical doctor at the Kingston General Hospital. The examination will include a fasting blood sample that will be used to measure your glucose and fat levels, and the levels of certain hormones that may be related to fat metabolism. This procedure is explained in further detail on the last page of this form.

Diet and Exercise Protocol

The study will be 18 weeks in duration. The low calorie diet and exercise part of the study will last 16 weeks. The 16 week treatment period will be prefaced and followed by a 1 week weight maintenace period - hence 18 weeks in total. By volunteering to participate in this study, your name will be selected by chance and placed into one of the following five groups: control (no diet or exercise program), diet (diet only), diet plus aerobic exercise, diet plus strength training exercise and diet plus both aerobic and strength training exercises.

Diet Procedure

The diet will consist of regular foods that you will buy and prepare yourself. After a 1 week weight-maintenance period, the diet you follow will total approximately 1000 calories less than the amount you need to maintain your present weight. You will follow that diet for 16 weeks. After the 16 week period, you will be given a diet that will increase your total caloric intake to a level that will maintain your new weight. All aspects of the diet plan will be explained to you in detail. The session will take place at the beginning of the study, with several additional sessions planned throughout to help you follow the diet plan. If someone else shops for your food or prepares your meals, or if you share those tasks with someone else, that person is invited to meet with the dietitian as well. You will be required to record the food you eat each day for one week, 5 times during the the 18 week study. All of your meetings with the dietitian will be at the Fitness Center in the Physical Education building at Queen's.

Exercise Procedure - Aerobic Group

If you are a participant in this group, in *addition* to following the same diet procedures described above, you will be required to perform aerobic exercise (walk/run type exercise) 5 times per week. The aerobic exercise program will be designed to meet your abilities. The duration of the sessions will range from approximately 15 minutes at the beginning of the program to a maximum of 60 minutes by the end. Each exercise session will be supervised by a trained physical educator.

Exercise Procedure - Strength Training Group

If you are a participant in this group, in *addition* to following the same diet procedures described above, you will be required to perform strength training exercises using Nautilus equipment 3 times per week. As with the aerobic exercise group, the strength training exercises will begin at a very easy level and progress slowly. A total of 8 exercises will be performed each session assuring that all the major muscles of the body are used. Each exercise session will be supervised by a physical educator.

Although as a participant in this study you will follow all the appropriate safety precautions including a pre-participation medical exam, there are risks associated with exercise. These risks include a slight chance of fainting and a remote chance of heart attack. As indicated, all your exercise sessions will be supervised by a masters level physical educator. This person will be trained in emergency procedures including cardio-pulmonary resusitation (CPR).

Assessment of Body Composition

Magnetic Resonance Imaging

Magnetic resonance imaging is a new technique for imaging or creating pictures of body structures or organs. Magnetic resonance (MR) gives images in slices comparable to those produced by x-ray tomography or CT (CAT) scan. One of the primary advantages of MR is that it does not employ x-rays or other potentially harmful forms of radiation, contrary to ordinary radiography or nuclear medicine. Instead, a large magnet, a radio transmitter/receiver and a computer are used to gather chemical information from the body, and to produce images or pictures of internal anatomy. No harmful effects have been associated with MR under existing conditions of use.

It is important that you fill out the enclosed questionnaire. The purpose of the questionnaire is to identify any metallic pieces which would have been implanted during a surgery or would have been lodged in your body during an accident.

As mentioned, the MR procedure is very similar to a scanner examination. You will be placed on a table and you will be moved smoothly into the scanner. A loud-speaker within the magnet makes it possible for you to keep in constant contact with the staff. At all times the operator can see and hear you if you need help or have questions, and you can be removed from the machine if necessary. The scanning procedure takes 45 to 60 minutes. All MR images will be obtained at the Kingston General Hospital.

Bioelectrical Impedance

This is a very simple and safe procedure requiring no more than 5 minutes to complete. Laying on your back, 2 electrodes will be placed on the surface of your right hand and foot. Two of the electrodes will introduce an alternating current that you can't feel into the body, while the other 2 record the resistance. In order to obtain accurate results with this technique it is very important that you follow the following procedure prior to your assessment. Prior to the test you should not:

1) have eaten or consumed caffeine for the 4 to 5 hours immediately preceding the test,

2) have exercised or consumed alcohol for 24 hours.

Anthropometry/Summation of skinfolds

Many circumference and diameter measurements will be taken at numerous sites on the body. These measure can be used to derive estimates of body composition. In addition, through the use of skinfold callipers, skinfold thickness will be measured at 10 different sites on your body. This is a simple procedure requiring no special preparation on your part.

Underwater weighing

Recognized by many researchers as the best method of measuring body composition (i.e. percent body fat), the intent of the procedure is to weigh you while you are submerged in water. In a seated position, you will be submerged in water (comfortable temperature) to the shoulder level. Approximately 10 times during the test you will be asked to put your head in the water, exhale completely, and hold your breath for 5 to 10 seconds while your body weight is measured. At any time during the procedure you can come out of the water by simply lifting your head.

With the exception of the MRI measurements, the anthropometric measurements (bioelectrical impedance, skinfolds and underwater weighing) will be obtained at the School of Physical and Health Education, Queen's University.

Assessment of Cardiovascular Fitness

In addition to body composition measurements we will measure your cardiovascular fitness by using either a stationary bicycle or a treadmill procedure. The work level will begin at a level you can easily accomplish and will be advanced in stages, depending on your capacity to do so. We may stop the test at any time because of signs of fatigue or you may stop when you wish to because of persinal feelings of fatigue or discomfort.

Risks and Discomforts

The treadmill or bicycle test will involve risks comparable to any strenuous exercise situation. They include very rare instances of abnormal blood pressure, faintings, disorders of the heart beat, and heart attack. Every effort will be made to minimize them by preliminary medical examination and observation during the test.

Benefits to be expected

These test results will be used to help us give you the proper amount of aerobic exercise that is right for you, and, to check for any possible reasons why you should not participate in an exercise program. Quantification of your fitness level will also enable us to follow your improvement throughout the study.

Blood Chemistry Analysis

Fasting Blood Samples

At the beginning, after 8 weeks, and at the end of the 16 week study, you will have a fasting blood test in order to measure blood sugar, blood fats and hormones (including adrenal, thyroid and pancreatic hormones). This procedure will involve a venepuncture with a needle and the removal of about 30 ml (3 tablespoons) of blood. The only risk from this is possible local pain and bruising at the time of the blood test. In addition, at the beginning and end of the study, you will be given a glucose tolerance test. The purpose of this test is to determine your bodie's response to sugar.

Subject's Name: ______________________________

I have been given an opportunity to ask any questions concerning the procedures. All of my questions regarding the research project have been satisfactorily answered. I understand that my test results will be considered confidential and will never be released in a form traceable to me, except to my family physician or myself. I do understand that I am free to deny consent if I so desire, and that I may withdraw from the study at any time. I understand that I may contact Dr. Robert Ross, 545-6583, or the head of the School of Physical and Health Education, Dr. Gavin Reid 545-2666, should I have any questions about the study. In addition, I release the principals and Queen's University from all claims arising out of my participation in this study that do not arise due to negligence.

Signature of Subject: ______________________________

Witness: ______________________________

Date: ______________________________

Appendix C: Medical Questionnaire

Please follow the instructions for each section carefully, and answer every question unless otherwise indicated, or unless you choose not to.

1. **PERSONAL DATA (Please print)**

Name:	______________	Date:	______________
Home Address:	______________	Home Tel:	______________
City:	______________	Postal Code:	______________
Position:	______________		
Business Address:	______________	Business Tel:	______________
City:	______________	Province:	______________
Birth Date:	______________	Age:	______________

2. **MEDICAL HISTORY**

***N.B. There are two parts to medical and health history. Please complete your parts on page 1 and 2, and have your physician fill out pages 3, 4 and half of page 5.**

		Yes	No
1.	Has your doctor ever said that you have heart trouble?	___	___
2.	Do you have pains in your chest?	___	___
3.	Do you often feel faint, or experience severe dizziness?	___	___
4.	Has your doctor told you that you have high blood pressure?	___	___
5.	Has your doctor ever told you that you have a bone or joint problem (arthritis) that might be made worse by exercise?	___	___
6.	Is there a good reason, not mentioned here, why you should not follow an exercise program, even if you'd like to?	___	___

7. Do you have, or have you had any of the following health problems or diseases?

		Yes	No	Comment
1)	Heart, Cardiovascular	___	___	______________
2)	Neurological	___	___	______________
3)	Respiratory (asthma, etc.)	___	___	______________
4)	Gastrointestinal (ulcers, etc.)	___	___	______________
5)	Genito-urinary	___	___	______________
6)	Endocrine (glandular)	___	___	______________
7)	Musculoskeletal (low back pain, etc)	___	___	______________

	Yes	No	Comment
8) Skin	___	___	______________________
9) Gynaecological	___	___	______________________
10) Other (Women - are you pregnant?)	___	___	______________________

8. Please list any serious injuries suffered, or surgery undergone:

___________________________________ Date:______________________

___________________________________ Date:______________________

9. If you have undergone surgery, was any metal (ie. pins or screws to repair broken bones) left in your body?

____

____

10. Are you presently taking any medication including vitamin or mineral supplements? If yes, please specify what type, and reasons:

____

9. If you have undergone surgery, was any metal (i.e. pins or screws used to repair bone fractures) left in your body?

____

____

10. Are you presently taking any medication including vitamin or mineral supplements? If yes, please specify what type, and reasons:

____

11. Are you presently undergoing any physiotherapy, or any other sort of treatment? If yes, please specify:

____

12. Are you presently under the care of a physician? If so for what?

____

3. **MEDICAL REFERRAL**

To The Physician:

The applicant is considering participation in a research project that intends to investigate the effects of different methods of exercise, in combination with caloric restriction, on body composition. A brief that describes the details of the study is appended to the Medical Questionnaire. Should you have any questions regarding the participation of your patient in this project, please contact Robert Ross Ph.D., School of Physical and Health Education, Queen's University (545-6583/2666), or Robert Hudson M.D., Department of Endocrinology, Kingston General Hospital.

ACSM - Contraindications to Exercise Testing

Absolute Contraindications

1. A recent significant change in the resting ECG suggesting infarction or other acute cardiac events
2. Recent complicated myocardial infarction
3. Unstable angina
4. Uncontrolled ventricular dysrhythmia
5. Uncontrolled atrial dysrhythmia that compromises cardiac function
6. Third-degree A-V block
7. Acute congestive heart failure
8. Severe aortic stenosis
9. Suspected or known dissecting aneurysm
10. Active or suspected myocarditis or pericarditis
11. Thrombophlebitis or intracardiac thrombi
12. Recent systemic or pulmonary embolus
13. Acute infection
14. Significant emotional distress (psychosis)

Relative Contraindications

1. Resting diastolic blood pressure >120 mm Hg or resting systolic blood pressure >200 mm Hg
2. Moderate valvular heart disease
3. Known electrolyte abnormalities (hypokalemia, hypomagnesemia)
4. Fixed-rate pacemaker (rarely used)
5. Frequent or complex ventricular ectopy
6. Ventricular aneurysm
7. Cardiomyopathy, including hypertrophic cardiomyopathy
8. Uncontrolled metabolic disease (e.g., diabetes, thyrotoxicosis, or myxoedema)
9. Chronic infectious disease (e.g., mononucleosis, hepatitis, AIDS)
10. Neuromuscular, musculoskeletal, or rheumatoid disorders that are exacerbated by exercise
11. Advanced or complicated pregnancy

I **REVIEW OF SYSTEMS**

a) Cardiovascular ______________________
b) Respiratory ______________________
c) Neurological ______________________
d) Gastrointestinal ______________________
e) Genitourinary ______________________
f) Endocrine ______________________
g) Musculoskeletal ______________________
h) Skin ______________________
i) Gynaecological ______________________

II. **PHYSICAL EXAMINATION**

Blood Pressure Supine ___RA___LA Bruits ______________________
Standing ___RA___LA Pulses ______________________

Evidence of chronic Lung Disease ____________

Heart rate ______________________ ______________________

Heart sounds ______________________ Bone or Joint Abnormalities ______________

____

EKG interpretation, 12 lead, resting. **Enclose copy if available**

____

III. **LABORATORY FINDINGS (NOT MANDATORY)** Date of Test(s): ______________

Hb ____________ Hct ____________ RBC ____________ WBC ____________

Total Cholesterol ____________ HDL ____________ LDL ____________

Triglycerides ____________ Uric acid ____________

Glucose ____________ post dexicola 30 min ________ 1 hr ________ 2 hr ________
3 hr ________ 4 hr ________

IV. Additional Abnormalities you are aware of ______________________

____

____

V. Current medications and dosages ______________________

____

____

VI. Impression of above information ______________________________

____

____

On the basis of your knowledge and medical evaluation of the applicant, you would recommend:

- participation in a fitness appraisal with supervision by physical education graduate __________
- participation only with physician in attendance ______________________
- participation not recommended ______________________

Signed______________________________M.D.

Name of Physician______________________________
(Please print or type)

Address______________________________

Telephone______________________________

Date______________________________

4. FAMILY MEDICAL HISTORY (Should be filled out by participant)

Have either of your parents or any brothers or sisters ever suffered from any cardiovascular disease (heart attack, high blood pressure, stroke, angina, etc.) or diabetes? If yes, please describe which relative, the type of problem, and the approximate age of the relative at the first diagnosis of the disease.

____

____

____

5. SMOKING

Are you a: smoker ______________________

ex-smoker (stopped) ______________________

non-smoker (never smoked) ______________________

Enter average amount smoked per day in the last five years, or in the last five years prior to quitting:

cigarettes per day ______________________

pipes/cigars inhaled per day ______________________

pipes/cigars not inhaled per day ______________________

If you are an ex-smoker, how many years ago did you start? ________ quit? ____________

6. **DIET**

Weight now: ______________ 1 year ago: ______________ at age 21: ______________

What do you consider a good weight for you? ______________________

What is the most you've ever weighed? ____________________ at age? ____________________

Do you regularly eat: Are these meals:

	yes	no	light	moderate	heavy
Breakfast	____	____	____	____	____
Lunch	____	____	____	____	____
Dinner	____	____	____	____	____
Snacks	____	____	____	____	____

Have you ever dieted? ____________________ If yes, for what reasons? ______________

____

Are you presently on a diet? _______________ If yes, what kind? ____________________

____

Do you have any special dietary needs, e.g., vegetarian? ________________________________

Do you drink alcoholic beverages? _______________ If yes, how much?:

	none	occasional	often	drinks per week
Wine (4 oz.)	________	________	________	________
Hard Liquor (1 - 1¼ oz.)	________	________	________	________
Beer (12 oz.)	________	________	________	________

7. **EXERCISE**

Are you currently involved in a regular exercise program? ______________________________

Physical activity in your present occupation is:

none __________ light __________ moderate __________ heavy __________

How many hours per day are you presently active? (at work and play/or exercise)

none __________ 0 - ½ ______ ½ - 1 ________ 1 - 2 ________ 2 or more ________

Please list the moderate to vigorous activities (such as brisk walking, jogging, aerobics) that you are presently involved in and the # of times per week that you participate.

____

____

Please list the recreational or leisure activities (such as casual walking, etc.) you are presently involved in and the # of times per week.

____

____

What activity or activities would you prefer to be included for you in an exercise program (if you are not presently involved)?

____

____

If you have been involved in an exercise program in the past, and quit, or had difficulty participating regularly, what were the reasons?

____

____

8. **PERSONAL INTERESTS**

Please list in order of importance to you, what you would like to change in terms of your present lifestyle?

1. ____
2. ____
3. ____

What areas of health or fitness would you like to learn more about?

____

____

Volunteer Name: ______________________
Date of Birth: ______________________
Weight: __________

MRI RESEARCH SCREENING FORM

To ensure patient safety, this form MUST BE completed.

I have been informed how the MR examination is performed. I have answered the following questions.

I have:	Yes	No
surgical aneurysm clips	___	___
a cardiac Pacemaker	___	___
a cochlear implant	___	___
a prosthetic heart valve replacement	___	___
a neurostimulator device	___	___
metal fragments (in or around eyes in particular?)	___	___
a hearing aid	___	___
an implanted insulin/chemotherapy pump	___	___
an IUD	___	___
shrapnel	___	___
dentures	___	___
metal rods, plates, screws, or nails	___	___
claustrophobia/vertigo	___	___
removed my eye makeup	___	___
I am pregnant	___	___
had previous surgery	___	___

If yes, explain: ____

____

Volunteer
Signature: ______________________ Date: ______________________

Witnessed by: ______________________ Date: ______________________

Body Part: ______________________ Research Physician: ______________________

Appendix D: Anthropometric Data Collection Form

MRI DIET AND EXERCISE
ANTHROPOMETRIC DATA COLLECTION FORM

NAME:_______________________ **M F DATE:**_________________ **TIME:**_____

WEIGHT:___________**kg AGE (yr.mo):**_________ **TEST #:**________________

ARM LENGTH:________________**(cm) STANDING HEIGHT:**____________**(cm)**

ACROMION HEIGHT:______________**(cm) SITTING HEIGHT:**____________**(cm)**

IMPEDANCE (ohms)	**R:**	Arm ___	Torso ___	Leg ___	Whole L___	R___
	Xc:	___	___	___	___	___

SKINFOLDS (mm)

	1	2	3	$\bar{X}$
Chest	___	___	___	___
Tricep	___	___	___	___
Bicep	___	___	___	___
Mid-Axillary	___	___	___	___
Subscapular	___	___	___	___
Iliac	___	___	___	___
Abdomen	___	___	___	___
Thigh	___	___	___	___
Suprapatellar	___	___	___	___
Calf	___	___	___	___

NAME:______________________ DATE:________________ TIME:_______

CIRCUMFERENCE MEASURES (cm):

Chest:___________ Hip:____________

Waist (standing): ____________(L) ____________Last Rib___________(U)

Waist (supine): ____________Last Rib___________(U)

Bicep: ______(R) ______(L) Thigh: ______(PR) ______(PL)

Forearm: ______(R) ______(L) ______(MR) ______(ML)

Calf: ______(R) ______(L) ______(DR) ______(DL)

Appendix E: Diet Record

Name: ______________________

Date: ______________

Target kcal	Max. fat(g)

	Source (SEE BELOW)	Amount	Food	Calories	Fat (g)
Breakfast					
			Breakfast Subtotals:		
Lunch					
			Lunch Subtotals:		
Dinner					
			Dinner Subtotals:		
Snacks					
			Snacks Subtotals:		
			Totals:	A	B

Please include source book and page or reference number (eg. T-5 = T-factor, page 5)

T = T-factor

P = Photocopied book

*= Food label

? = Best guess

Fat calories: (B) x 9 kcal/g fat ______ **C**

% kcal from fa '(C / A) X 100 = ______ **%**

Appendix F: Aerobic Exercise Recording Sheet

AEROBIC TRAINING PROGRAM

Name: ______________________

Week	1					2					3					4					5					6				
Date																														
Activity																														
Duration																														
Intensity/Workrate																														
Mean Heart Rate																														

Week	7					8					9					10					11					12				
Date																														
Activity																														
Duration																														
Intensity/Workrate																														
Mean Heart Rate																														

Week	13					14					15					16				
Date																				
Activity																				
Duration																				
Intensity/Workrate																				
Mean Heart Rate																				

Appendix F: Resistance Exercise Recording Sheet

NAUTILUS TRAINING PROGRAM

TECHNIQUE: Select a weight with which you can obtain total momentary failure in between 8 and 12 repetitions. One repetition should take approximately 7 seconds.

POSITIVE – 2 seconds lifting / PAUSE – 1 second hold / NEGATIVE – 4 seconds lowering.

Perform each repetition smoothly and with good form.

Legend: Total Repetitions → 12 / 4 ← Exercise Weight

Name: ______________________

RECORD EXERCISE WEIGHTS AND TOTAL REPETITIONS FOR EACH EXERCISE (See Legend)

Exercise		Seat Pos.	R	Week	Week		Week	Week	Week	Week	Week	Week
LOWER BODY												
Hip and Back						*						
Compound Leg	Extension											
	Press											
Leg Curl												
UPPER BODY						S						
Super Pullover						E						
Rowing						E						
Double Chest	Cross											
	Press					I						
HIP	Abduction ← →					N						
	Adduction → ←					S						
Torso Arm						T						
Double Shoulder	Lateral					R						
	Overhead					U						
Bicep						C						
Tricep						T						
Rotary Torso						O						
Abdominal						R						
4-way Neck	Lateral											
	Anterior											
	Posterior											
Neck and Shoulder												
Multi-Exercise	Heel Raises					*						
	Wrist Rollers											
SIT UPS	TOTAL REPETITIONS											

TEST TARGET (QA-3)

150mm

6"