Effect of weight loss on muscle lipid content in morbidly obese subjects

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Gray, Robert E., Charles J. Tanner, Walter J. Pories, Kenneth G. MacDonald, and Joseph A. Houmard. Effect of weight loss on muscle lipid content in morbidly obese subjects. *Am J Physiol Endocrinol Metab* 284: E726–E732, 2003. First published December 17, 2002; 10.1152/ajpendo.00371.2002.—The purpose of this study was to test the hypothesis that weight loss results in a reduction in intramuscular lipid (IMCL) content that is concomitant with enhanced insulin action. Muscle biopsies were obtained from morbidly obese individuals [body mass index (BMI) 52.2 ± 2.5 kg/m²; n = 6] before and after gastric bypass surgery, an intervention that improves insulin action. With intervention, there was a 47% reduction (P < 0.01) in BMI and a 93% decrease in homeostasis model assessment, or HOMA (7.0 ± 1.9 vs. 0.5 ± 0.1). Histochemically determined IMCL content decreased (P < 0.05) by ~30%. In relation to fiber type, IMCL was significantly higher in type I vs. type II fibers. In both fiber types, there were reductions in IMCL and trends for muscle atrophy. Despite these two negating factors, the IMCL-to-fiber area ratio still decreased by ~44% with weight loss. In conclusion, despite differing initial levels and possible atrophy, weight loss appears to decrease IMCL deposition to a similar relative extent in type I and II muscle fibers. This reduction in intramuscular triglyceride may contribute to enhanced insulin action seen with weight loss.

Recent evidence indicates that the accumulation of triglyceride within skeletal muscle is related to insulin resistance. In humans, a negative association between whole-body insulin action and intramuscular lipid (IMCL) content has been observed (5, 7, 11, 17, 23, 25, 31, 33). An elevated IMCL deposition has also been reported in obese individuals (6, 7, 18), obese individuals with type 2 diabetes (6), and the insulin resistant relatives of type 2 diabetics (11, 24). It is hypothesized that intermediates derived from IMCL sources such as triglyceride, i.e., long-chain acyl-CoAs and/or ceramide, directly induce insulin resistance by impeding insulin signal transduction (30). This type of mechanism would explain the negative relationship between IMCL accumulation and insulin action.

Although an elevated IMCL content has been documented in a variety of insulin-resistant populations, information on the ability to reduce IMCL and concomitantly enhance insulin action with intervention, such as weight loss, is sparse and controversial. Either a reduction (6, 7) or no change (7, 19) in muscle triglyceride deposition with weight loss has been reported. However, in some of these studies, insulin action was either not measured (6) or did not improve (7, 19), making it difficult to elucidate the interaction between IMCL and insulin action. The purpose of the present study was to test the hypothesis that weight loss results in a reduction in IMCL content that is concomitant with enhanced insulin action. This was accomplished by examining IMCL deposition before and after a weight loss intervention (gastric bypass surgery) known to normalize insulin action in insulin-resistant, morbidly obese individuals (26).

Although IMCL content is related to insulin action, a measurement of overall muscle triglyceride content may not be indicative of what is occurring in specific muscle fibers. Skeletal muscle is a heterogenous tissue consisting of distinct muscle fiber phenotypes. The type I (red) fibers are more oxidative, more insulin sensitive, and contain more intramuscular triglyceride than the type II (white) fibers (2, 9, 12, 22, 29). Given these differences, it is feasible to hypothesize that a reduction in IMCL content with weight loss could be limited to a distinct muscle fiber type. For example, IMCL loss may be selective for the type I fibers due to their high initial intramuscular triglyceride content and elevated ability to oxidize lipids; changes in IMCL content in type I fibers would also affect whole body insulin action more profoundly due to their insulin-sensitive nature. Thus a second purpose of the present study was to specifically examine IMCL content in type I and type II fibers before and after weight loss. As a potential mechanism explaining changes in IMCL, we determined whether indexes of muscle oxidative capacity were altered with the intervention.

RESEARCH DESIGN AND METHODS

Subjects and study design. Morbidly obese [body mass index (BMI) > 40 kg/m² and/or ≥45 kg over ideal body weight] subjects (5 female, 1 male, all Caucasian) were ex-
amined before and 1 year after elective gastric bypass surgery to induce weight loss (26). Descriptive data for the subjects are presented in Table 1. We have previously characterized responses to gastric bypass surgery in morbidly obese subjects; the 12-mo postsurgery time was selected because body mass stabilizes and remains significantly depressed and there is a dramatic improvement in insulin action (26). All subjects had normal fasting glucose concentrations.

Subjects reported to the laboratory at ~0800 after a 12-h fast. For the 3 days before the study, subjects were instructed to consume ≥250 g of carbohydrate per day. Body mass and stature were measured upon subject’s arrival at the laboratory. A fasting blood sample was obtained for the measurement of plasma glucose and insulin to calculate a homeostasis model assessment (HOMA) value (20). A muscle sample was obtained from the vastus lateralis muscle with the needle biopsy technique. Tissue was subsequently treated histochemically and analyzed for fiber type distribution (myosin-ATPase), neutral lipid content [oil-red-O (ORO)], and glycolytic capacity (NADH-tetrazolium reductase), and glycolytic capacity (α-glycerophosphate dehydrogenase (α-GPDH)). All procedures were approved by the East Carolina University Institutional Review Board, and informed consent was obtained before any experimental procedures were performed.

Insulin action. A fasting blood sample was obtained via venipuncture, and plasma was frozen at –80°C for the subsequent determination of insulin and glucose. Insulin was measured with immunoassay (Access Immunoassay System; Beckman Coulter, Fullerton, CA) and glucose with an oxidation reaction (YSI model 2300 Stat Plus, Yellow Springs Instrument, Yellow Springs, OH). Insulin action was determined by HOMA (fasting glucose (mg/dl) × 0.05551 × fasting insulin (μU/ml)/22.1 (20). The HOMA determination correlates highly with insulin action determined with a euglycemic hyperinsulinemic clamp (1).

Muscle biopsies. Muscle samples were obtained from the vastus lateralis with the percutaneous needle biopsy technique (3). After removal from the biopsy needle, the sample was mounted and frozen in isopentane cooled over liquid nitrogen and subsequently stored in liquid nitrogen. Before histochemical staining, samples were placed in a cryostat/microtome (Tissue-Tek; Miles, Elkhart, IN) at −20°C. Serial, transverse sections 12 μm thick were cut from each sample. To minimize variability, pre- and postweight loss sections for each subject were placed on the same slides and stained in the same solutions.

Lipid staining. Lipid content was determined using the ORO staining procedure, modified from Goodpaster et al. (6). The ORO stock solution was composed of 300 mg of ORO and 100 ml of 2-propanol (99%) and stored at room temperature. An ORO working solution comprised of 24 ml of ORO stock mixed with 16 ml of distilled water was prepared immediately before staining. After a 10-min standing period, the working solution was filtered by aspiration (no. 42 Whatman paper) to separate undissolved ORO. The sections were placed in a Columbia jar containing the working solution and, after a 12-min incubation period at room temperature, were rinsed twice with distilled water (2 × 20 s). Sections were rinsed in cold, running tap water for 10 min and allowed to dry at room temperature; a coverslip was applied using glycerol jelly. ORO stains neutral lipid (mainly triglyceride) with an orange-red tint.

Fiber typing. Myosin-ATPase staining method was used for fiber type determination, as previously described (9, 10, 34). An alkaline preincubation solution of pH 10.3 was used to clearly delineate between types I and II fibers. Under light microscopy, stained fibers appeared as light (type I) or dark and heavily stained (type II).

Oxidative capacity. The oxidative capacity of individual muscle fibers was assessed using the NADH-tetrazolium reductase (NADH) stain (21). A working solution was prepared by mixing 6 mg of nitroblue tetrazolium (NBT) and 24 mg of NADH in 30 ml of Trizma buffer solution (pH 7.4 at 25°C). After mixing, the solution was placed in a 37°C water bath and allowed to warm for 20–30 min. Sections were incubated in the working solution for 30 min at 37°C. The 37°C incubation solution-stained regions. For each image, sections were lightly rinsed three times (15 s each rinse) with distilled water and allowed to air dry at room temperature, and a coverslip was applied. Fibers appeared as dark blue, indicating a high oxidative capacity or light blue, indicating a low oxidative capacity.

Glycolytic capacity. α-GPDH staining was used to determine glycolytic capacity (35). A working solution was prepared by mixing 6 mg of NBT, 120 mg of glyceral 3-phosphate, and 6 mg of menadione in 30 ml of Trizma buffer solution (pH 7.4 at 25°C). The solution was poured into a Columbia jar and allowed to warm to 37°C in a water bath for 20–30 min. Sections were incubated in the working solution for 45 min. The solution was poured off, and the sections were gently rinsed three times with distilled water and allowed to air dry. Highly glycolytic fibers stained dark blue, and fibers with a low glycolytic capacity stained light blue. Fiber area was calculated from the α-GPDH stain.

Microscopy and imaging. Stained sections were viewed under light microscopy using a Nikon Microphot FX microscope (Diagnostic Instruments, Sterling Heights, MI) at a magnification of ×10. When the desired field of view was obtained, software (Spot Advanced 3.2.4; Diagnostic Instruments) was used to generate a live image. The image was digitally captured, stamped with a calibration mark, and saved as a 32-bit tagged image format file (TIFF).

Image analysis. Sigma Scan Pro 5.0 (SPSS Science, Chicago, IL) software was used to perform image analysis. The technician (R. E. Gray) was blinded to the subject and pre- or postweight loss condition. Images were initially converted to grayscale, 8-bit images. By use of the image analysis software, at least three fields were selected from each image, and each field was saved as a new image with the original calibration. The fields chosen comprised the majority of the sample and were free from artifacts. The width and height of the new image were used to calculate area.

The determination of lipid from the ORO staining was performed with two methods. The first was based on the lipid accumulation index described by Goodpaster et al. (6). Intensity thresholding was performed to determine the number and area of ORO-stained regions. For each image, a histogram was plotted on an intensity scale of 0–255 arbitrary units (AU) and the peak recorded. The image with the lowest peak on the 0–255 scale was used to determine the high end of the intensity threshold. The low end of the intensity threshold was the peak minus 10 AU. This was evaluated for

Table 1. Descriptive data before and after weight loss

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Preweight Loss</th>
<th>Postweight Loss</th>
<th>%Change</th>
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<tbody>
<tr>
<td>Ages, yr</td>
<td>36.8 ± 4.6</td>
<td>27.9 ± 4.8</td>
<td>-47</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.7 ± 0.1</td>
<td>1.7 ± 0.1</td>
<td>0</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>148 ± 9.9</td>
<td>79.1 ± 4.4*</td>
<td>-47</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>52.2 ± 2.5</td>
<td>27.9 ± 0.8*</td>
<td>-47</td>
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</table>

Values are means ± SE. BMI, body mass index. *P < 0.01 vs. preweight loss.
each subject and held constant for pre- and postanalysis of the images. We found that this thresholding method effectively isolated ORO-stained intramuscular regions, as have similar thresholding techniques utilized by others (6). To test reliability, two researchers (R. E. Gray, C. J. Tanner) determined ORO fraction in the same samples (n = 5) and obtained a correlation coefficient of r = 0.98. To quantify the amount of IMCL present, an ORO fraction was calculated for each new image as ORO fraction = (no. of stained areas × area of each stained area)/area of the measured field. A high ORO fraction is an indication of elevated neutral lipid (triacylglycerol) content within the field of view.

To determine the relationship between muscle fiber type and IMCL content, two images representing each stain (myosin-ATPase, ORO) were viewed simultaneously. From the myosin-ATPase stain, fibers were classified as either type I or type II. Fibers from the fiber type image were identified and matched to the ORO images. By use of the image analysis software, individual fibers were selected and analyzed for fiber area and average intensity of staining within the fiber (optical transmittance). To assess IMCL content per fiber type, optical transmittance (AU) was determined from the ORO image on a 0–1,000 intensity scale with 0 representing completely dark (i.e., maximum amount of lipid) and 1,000 representing completely light (i.e., no visibly stained lipid). To simplify interpretation (i.e., higher AU values indicate increased lipid) the data are expressed as 1/transmittance. An ORO composite value, weighted by fiber type proportion, was calculated as the second index of overall lipid content. The formula for ORO composite was ORO composite = 1/(type I ORO optical transmittance × fractional type I fiber proportion) + (type II ORO optical transmittance × fractional type II fiber proportion). A higher ORO composite corresponded to increased lipid content.

Optical transmittance was determined using similar methods to quantify oxidative and glycolytic capacity (NADH and α-GPDH images, respectively). Transmittance was determined as the mean light intensity on a 0–255 scale (0 representing completely dark and 255 representing completely light). To simplify interpretation, data are expressed as 1/transmittance.

Statistics. Data are presented as means ± SE. Repeated-measures analysis of variance (ANOVA) was used to compare data before and after weight loss. Statistical significance was denoted at P < 0.05.

RESULTS

Adiposity and insulin action. Body mass and BMI significantly decreased with intervention by 47%, as presented in Table 1. There was a significant (P < 0.01) decrease (−89%) in fasting insulin concentration following weight loss (25.4 ± 7.4 vs. 2.8 ± 0.3 μU/ml; Fig. 1). Fasting glucose was lower after weight loss (114.0 ± 18.0 vs. 76.8 ± 2.8 mg/dl), but this change did not attain statistical significance (P = 0.12; Fig. 1). There was a significant (P < 0.01) 92% improvement in insulin sensitivity as measured by HOMA (7.0 ± 1.9 vs. 0.5 ± 0.1; Fig. 1).

Fiber type distribution and fiber area. Fiber type and area are presented in Table 2. No significant changes were found in fiber type distribution with weight loss. There were statistically insignificant trends for reductions in fiber area in both fiber types, with type I fiber area reduced by 14% and type II fiber area by 25% (P = 0.10). The relative percentage of type II fibers (~60%) was similar to what we have previously reported in morbidly obese individuals (9, 34).

Effects of weight loss on IMCL. Weight loss resulted in significant changes in all measures pertaining to neutral IMCL content. With the intervention, there was a statistically significant (P < 0.05) 30% reduction in ORO fraction (0.31 ± 0.06 vs. 0.22 ± 0.04; Fig. 2), indicating reduced IMCL with weight loss.

Table 2. Fiber type distribution and fiber area

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Preweight Loss</th>
<th>Postweight Loss</th>
<th>%Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I fibers, %</td>
<td>38.3 ± 5.2</td>
<td>38.9± 3.5</td>
<td>1.6</td>
</tr>
<tr>
<td>Type II fibers, %</td>
<td>61.7 ± 5.2</td>
<td>61.6 ± 3.5</td>
<td>0</td>
</tr>
<tr>
<td>Type I fiber area, μm²</td>
<td>4,163 ± 340</td>
<td>3,583 ± 307</td>
<td>−14</td>
</tr>
<tr>
<td>Type II fiber area, μm²</td>
<td>4,155 ± 393</td>
<td>3,111 ± 296</td>
<td>−25</td>
</tr>
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</table>

Values are means ± SE.
To assess lipid content relative to fiber type, 1/optical transmittance (AU), was determined in the type I and II fibers; a reduction in this variable was indicative of less ORO staining per fiber and thus a lower IMCL content. Type I fibers were found to have significantly ($P < 0.01$) more neutral lipid than type II fibers both before (+36%) and after (+15%) weight loss (Fig. 3). Weight loss resulted in a significant reduction of ORO content in both the type I (−45%; $3.7 \pm 0.8$ vs. $2.0 \pm 0.3$ AU) and the type II fibers (−29%; $2.4 \pm 0.3$ vs. $1.7 \pm 0.2$ AU, for before vs. after weight loss, respectively, $P < 0.05$). There was no statistically significant inter-

Effects of weight loss on muscle oxidative and glycolytic capacity. The effects of weight loss on oxidative (NADH) and glycolytic ($\alpha$-GPDH) staining parameters are presented in Fig. 5. The type I fibers had an elevated oxidative capacity compared with the type II fibers both before and after weight loss (Fig. 5). There were no changes in oxidative capacity with weight loss in either the type I ($10.6 \pm 0.6$ vs. $11.3 \pm 1.0$ AU) or type II fibers ($6.5 \pm 0.3$ vs. $7.2 \pm 0.5$ AU). As determined by $\alpha$-GPDH staining, significant differences in glycolytic capacity were found between fiber types before and after weight loss ($P < 0.01$; Fig. 5), with the type II fibers being more glycolytic. Weight loss did not change glycolytic capacity in either the type I ($6.0 \pm 0.2$ vs. $5.9 \pm 0.2$ AU) or type II fibers ($8.0 \pm 0.7$ vs. $8.0 \pm 0.2$ AU for before vs. after weight loss, respectively; Fig. 5). The glycolytic-to-oxidative ratio was significantly higher in type II compared with type I fibers ($P < 0.01$), and weight loss did not significantly alter this ratio in either the type I ($5.7 \pm 0.3$ vs. $5.3 \pm 0.6$ AU).
version surgery that induced weight loss (in morbidly obese individuals after biliopancreatic deposition occurs with weight loss, which in turn may other data (6, 7) suggest that a reduction in IMCL improved insulin action. Together, the current and reported a more substantial reduction (‡) in IMCL content accompanied by atrophy may be indicative of the relative lipid content within an individual fiber, a reduction in IMCL deposition occurs with weight loss, which in turn may be related to an improvement in insulin action. Such findings are relevant to the insulin-resistant state, as IMCL appears to be a useful index for intermediates of lipid metabolism that induce insulin resistance, such as long-chain acyl-CoA derivatives and/or ceramide (30).

It is important to consider that skeletal muscle is a heterogeneous tissue consisting of two distinct phenotypes, the type I and type II fibers. We have reported a positive relationship between the relative percentage of type I fibers and insulin action both in vitro (9) and in vivo (10). A negative relationship between adiposity and type I fiber expression is also evident (9, 34). In terms of fiber type and intramuscular triglyceride, Perseghin et al. (24) demonstrated that IMCL content in the soleus (type I) but not the tibialis anterior (type II) predicted insulin resistance in the lean offspring of type 2 diabetics. The data of Perseghin et al. suggest an interaction between fiber type and triglyceride deposition, with IMCL content in the type I fibers being more influential in relation to whole body insulin action. However, little is known concerning the impact of weight loss on IMCL content in the respective muscle fiber types. Our working hypothesis was that IMCL content would be reduced more substantially in the type I fibers due to the high oxidative capacity of these fibers and their initially greater intramuscular triglyceride content (Figs. 3 and 5). A selective reduction of IMCL in the insulin-sensitive type I fibers could also offer an explanation of why HOMA was dramatically improved with weight loss (Fig. 1).

A novel finding of the present study was that IMCL content was reduced with weight loss to a similar relative extent in the type I and type II fibers in morbidly obese individuals. This conclusion is based on virtually identical reductions (−44%) in the ORO/fiber area ratio for both fiber types (Fig. 3). These data indicate that weight loss intervention induces similar relative changes in IMCL in both fiber types despite the elevated oxidative capacity (Fig. 5) and muscle IMCL content (Fig. 3) in the type I fibers. A reduction of IMCL in both fiber types may be particularly vital in the morbidly obese, as we have previously reported that this group of individuals expresses predominantly more type II fibers than nonobese controls (9, 34). The present data suggest that a reduction in IMCL in both fiber types can contribute to the enhanced whole body insulin action seen with weight loss in the morbidly obese (Fig. 1).

Muscle fiber atrophy has been reported with weight loss, which may be a function of either the catabolic state and/or a reduction in the load-bearing stimulus (27, 28). Theoretically, if muscle atrophy is present, then overall indexes of IMCL deposition, such as the ORO fraction used in the present study (Fig. 2) may not be indicative of the relative lipid content within an individual fiber. For example, in a given fiber, a reduction in IMCL content accompanied by atrophy may maintain the IMCL/fiber area ratio, which would likely minimize any potential effect on insulin action. The current findings suggest that, despite evidence for atrophy, particularly in the type II fibers (Table 2),
IMCL deposition per fiber area for both fiber types still decreased by ~45% with weight loss. Data obtained with the ORO method (4, 6) indicate that, in obese skeletal muscle, lipid occupies ~3–4% of total fiber area, whereas in lean individuals this value declines to ~1–2%. These findings (4, 6) suggest that, in the present study, the decline in IMCL content contributed to the reduction in muscle fiber area with weight loss; however, it is likely that other elements linked with muscle atrophy (i.e., contractile proteins) also declined substantially, leading to the reduction in cross-sectional area observed (14–25%). Regardless, the reduction in IMCL content was still evident despite any atrophy linked with weight loss, resulting in a lower lipid content per fiber. This finding indicates the robust nature of the reduction in IMCL with the intervention utilized and perhaps why weight loss is effective in treating insulin resistance.

It is difficult to reconcile what aspect of weight loss contributes to the reduction in IMCL in obese and morbidly obese subjects. Greco et al. (7) observed a decrease in IMCL with bariatric surgery (biliopancreatic diversion) but not with caloric restriction and hypothesized that a marked reduction in lipid absorption is the primary means by which IMCL is reduced. In the present experiment, it is difficult to discern the relative fat intake of the morbidly obese subjects before vs. after weight loss. In a previous study (8), we observed that morbidly obese subjects 1-yr postweight loss greatly underreport energy intake, making an evaluation of total fat intake speculative. Due to the magnitude of the weight loss (~69 kg or ~50% of initial body mass; Table 1), it is logical to assume that fat intake, and thus lipid exposure to the skeletal muscle fibers, was substantially reduced in our morbidly obese subjects with intervention, which may have contributed to the reduction in IMCL observed.

The role of dietary lipid restriction in reducing IMCL during weight loss is, however, difficult to reconcile when other findings are considered. Two studies (7, 19) reported that IMCL deposition was not reduced in obese individuals with weight loss (means of ~11 to ~14 kg) via caloric and dietary fat restriction (intake of 1,200 kcal/day). This is in conflict with the findings of Goodpaster et al. (6), who reported a significant reduction in IMCL (~31%) with the use of a virtually identical caloric restriction regimen (intake of 800–1,200 kcal/day, weight loss ~15 kg). With consistent reductions in IMCL after pronounced weight loss (i.e., >30 kg) in morbidly obese patients (Fig. 3 and Ref. 7), it is tempting to hypothesize that a threshold of weight loss must be achieved for IMCL to exhibit a significant decrement. However, the discrepant findings concerning either no change (7, 18) or a decrease (6) in IMCL with weight loss of 11–15 kg makes such a hypothesis suspect. These contradictory data (6, 7, 18) make it difficult to determine what aspect of weight loss intervention contributes to reducing IMCL. It may also be overly simplistic to infer a relationship between IMCL and weight loss; interventions such as bariatric surgery may specifically target IMCL stores compared with other fat depots, as after the surgery patients remain overweight/obese despite normalized insulin action (7, 20). Regardless, weight loss that reduces IMCL also consistently improves insulin action (Ref. 7 and current findings); weight loss studies with no reduction in IMCL reported no concomitant improvement in insulin action (7, 18) supporting the IMCL-insulin action relationship.

Several research groups have reported that the oxidative capacity of skeletal muscle is reduced with obesity (13, 16). This observation has led to the hypothesis that lipid is selectively partitioned toward storage rather than oxidation within the muscle cell of obese individuals, which contributes to elevated IMCL stores and subsequent insulin resistance (13, 14). In the current study, despite a reduction in IMCL with weight loss, we observed no changes in the oxidative capacity of the type I or type II muscle fibers (Fig. 5). Others (14, 15, 18, 32) have also reported no changes in muscle indexes of lipid oxidation with weight loss in obese individuals but have not studied specific fiber types. Together, these data indicate that weight loss intervention does not alter muscle oxidative capacity despite reduced IMCL stores and enhanced insulin action. The absence of an increase in muscle oxidative capacity (Fig. 5) also provides evidence that the improvements in insulin action and reduction in IMCL were likely not due to increased physical activity after the weight loss.

In the present study, IMCL declined in conjunction with an improvement in HOMA; others (5, 7, 11, 17, 23, 25, 31, 33) have reported a negative relationship between IMCL content and insulin action. However, in contrast to the negative relationship between IMCL and insulin action, insulin-sensitive, endurance-trained individuals possess elevated IMCL concentrations that are virtually equivalent to those reported in sedentary, insulin-resistant obese individuals and patients with type 2 diabetes (4). These latter findings (4) suggest that intramuscular triglyceride alone is not responsible for inducing insulin resistance but rather acts as a proxy measure for other lipid products that are directly detrimental to insulin action.

In conclusion, IMCL content was determined in morbidly obese subjects before and after weight loss intervention that improved an index of insulin action (HOMA). Histochemically determined overall IMCL content decreased (P < 0.05) by ~30%. With regard to fiber type, lipid was significantly higher in the type I vs. type II fibers before and after weight loss. The reduction in the lipid content-to-fiber area ratio with weight loss was similar for each fiber type (~44%) despite a trend for muscle atrophy. There were no changes in the relative percentages of fiber types or glycolytic and oxidative capacity with weight loss. Therefore, despite differing initial levels and possible atrophy, weight loss appears to decrease IMCL deposition to a similar relative extent in type I and II muscle fibers; these changes may contribute to enhanced insulin action.
REFERENCES


