Body Composition and Fat Distribution Measured by Dual-Energy x-Ray Absorptiometry in Premenopausal and Postmenopausal Insulin-Dependent and Non–Insulin-Dependent Diabetes Mellitus Patients

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The study aim was to measure body composition and fat distribution in premenopausal and postmenopausal women with insulin-dependent ([IDDM] n = 53) and non–insulin-dependent ([NIDDM] n = 32) diabetes mellitus by dual-energy x-ray absorptiometry. IDDM and NIDDM patients had similar, normal lean tissue mass (LTM) and 24-hour urinary excretion of creatinine. Total body and abdominal fat percentages were higher in the NIDDM group (~40%) than in the IDDM group (~27%, $P < .001$) and were constant with age and menopausal status in both groups. In postmenopausal patients with IDDM, total body and abdominal fat values were less than in postmenopausal healthy women (~27% *v* ~37%, $P < .001$). In premenopausal patients with NIDDM, total body and abdominal fat were higher than in premenopausal healthy women (~42% *v* ~25%, $P < .001$). In conclusion, women with IDDM or NIDDM have a normal LTM and probably a normal muscle mass. Total body and abdominal fat were higher for women with NIDDM than for those with IDDM.

MOST PATIENTS WITH non–insulin-dependent diabetes mellitus (NIDDM) are overweight, whereas those with insulin-dependent diabetes mellitus (IDDM) are generally more normal in weight. However, little is known about the body composition of diabetic patients. Some[1-4] but not all[5-8] studies indicate that in uncontrolled diabetes the nitrogen balance is negative and lean body mass is low, but these seem to normalize when the diabetes is treated.[9,10] However, there are methodological drawbacks to most of the previous studies: determination of total body ^{40}K or 24-hour urinary excretion of creatinine has been used in non–steady-state settings, and study samples involved selected or unspecified subpopulations of diabetic patients and unmatched controls. Dual-energy x-ray absorptiometry (DXA) is a relatively new, accurate, and precise method of measuring body composition, ie, lean (LTM) and fat (FTM) soft tissue mass, bone mineral, content, and fat distribution.[11-12]

Increased abdominal fat is associated with NIDDM and cardiovascular disease.[13] Reports on fat distribution in patients with IDDM are sparse, but show less abdominal fat than in patients with NIDDM.[14] Fat distribution has mostly been assessed by anthropometric measurements such as the skinfold thickness and waist to hip ratio.

In healthy women, LTM decreases, FTM increases, and fat distribution becomes more abdominal with age and probably with menopause,[15-17] whereas the variation with age and menopausal status in women with IDDM and NIDDM is unknown.

The aim of the present study was thus to assess the variation with menopausal status in LTM, FTM, and fat distribution, as measured by DXA, and 24-hour urinary excretion of creatinine in women with IDDM and NIDDM. Furthermore, we compared these body composition parameters with those in control groups of healthy women matched for age and menopausal status.

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SUBJECTS AND METHODS

Female diabetic patients were recruited after examining the records of women attending the Steno Diabetes Center (Gentofte, Denmark) outpatient clinic during a 6-month period in 1993. The patients were sampled with the purpose of obtaining a representative subpopulation of relatively healthy premenopausal and postmenopausal women with IDDM and NIDDM and a wide age range. Exclusion criteria were a random blood glucose greater than 20 mmol/L, ketonuria, pregnancy, age less than 18 years, nephropathy (albuminuria >300 mg/d and serum creatinine >0.15 mmol/L), hysterectomy, major diseases, surgery, and current medication other than antidiabetics with known effects on body composition, fat distribution, and bone other than those caused by diabetes. A questionnaire was sent to 215 potentially eligible patients with an invitation to participate in the study. Of these, 11 were excluded (use of diuretics [n = 2], current use of hormone replacement therapy [n = 3], hysterectomy [n = 2], breast tumor [n = 1], artificial hip joint [n = 1], lower-leg amputation [n = 1], and withdrawal of the diabetes diagnosis [n = 1]; 15 could not be contacted; 85 declined to participate; and 19 who had consented failed to keep the appointment. Hence, 85 female diabetic patients consented to participate and completed the study.

The study was performed in accordance with the Declaration of Helsinki II and with the approval of the ethical committee of Copenhagen County.

Methods

With the women wearing light indoor clothing and no shoes, weight was measured to the nearest 0.1 kg and height to the nearest 0.5 cm. Waist and hip circumferences were measured to the nearest 0.5 cm at the smallest standing horizontal circumference below the ribs and at the largest standing horizontal circumference at the buttocks.

Body composition, total and abdominal (from the first to the fourth lumbar intervertebral disk), was measured[11,12] with a total-body DXA scanner (DPX, software version 3.6y; Lunar Radiation, Madision, WI). FTM, LTM, and bone mineral content were measured. FTM as measured by DXA does not consist solely of adipose tissue, but is the sum of the fatty elements of the soft tissue. Similarly, LTM is not an anatomical entity; it represents the sum of the chemical fat-free elements of soft tissue.

Creatinine excretion was assessed on samples from 24-hour collections of urine. The hemoglobin A_{1c} (HbA_{1c}) value was the last one registered on the patient record.

Calculations and Statistical Analysis

The ratio of abdominal to total body fat measured by DXA and the waist to hip ratio were calculated as indicators of fat distribution.

The diabetic patients were divided into premenopausal and postmenopausal IDDM and NIDDM groups. Postmenopausal status was defined as an elapsed time of more than 6 months since the last menstrual bleeding. Comparisons were made with values obtained by DXA (Lunar) in control groups matched for age and menopausal status. These control groups derive from a reference population of healthy Danish women.[16]

Comparisons between groups were made by Student's unpaired *t* test or by the nonparametric chi-square test. Pearson's or nonparametric Spearman's rank correlation coefficients were calculated. The significance and independence of predictive variables (age, menopausal status [pre/post; dummy code, 0/1], and years since menopause) were assessed by stepwise multiple linear regression analyses. The Statistical Analysis System (SAS Institute, Cary, NC) was used for all analyses.

RESULTS

Fifty-three subjects had IDDM: mean age, 49.9 years (range, 24 to 80); duration of diabetes, 20.5 years (range, 0.6 to 58); HbA_{1c}, 8.5% (range, 4.4% to 11.8%); and prevalence of retinopathy, 42%; microalbuminuria, 8%; macroangiopathy, 9%; and neuropathy, 8%. Thirty-two subjects had NIDDM: age, 56.8 years (range, 35 to 81); duration of diabetes, 5.6 years (range, 0.1 to 21); HbA_{1c}, 9.0% (range, 5.5% to 13.7%); treated with insulin, 16%; metformin, 31%, sulfonylurea, 47%; and prevalence of retinopathy, 19%; microalbuminuria, 6%; macroangiopathy, 31%; and neuropathy, 22%. Of the eligible female diabetic patients who were not examined (nonresponders, n = 119), 75 had IDDM and 44 had NIDDM. Nonresponders with NIDDM were older (63.5 ± 2.1 years) and had a higher prevalence of retinopathy (36%) ($P < .05$) than the NIDDM patients examined. Otherwise, no significant differences were found for age, duration of diabetes, HbA_{1c}, or prevalence of diabetic complications between the subjects who were examined and those not examined.

Table 1 shows anthropometric variables for the groups divided according to menopausal status and IDDM and NIDDM. In the premenopausal and postmenopausal IDDM and NIDDM patients, there were no significant differences in age or years since menopause. However, patients with NIDDM had a shorter duration of known diabetes, a higher body mass index (BMI), and a higher waist to hip ratio (only the postmenopausal patients) than those with IDDM.

Table 1. Anthropometric Characteristics According to Menopausal Status in Female Diabetic Patients

Characteristic	IDDM	NIDDM	*P*
Premenopausal			
No. of subjects	31	11	
Age (yr)	39.6 ± 1.3	44.1 ± 1.9	NS
Diabetes duration (yr)	15.3 ± 1.7	3.0 ± 1.2	<.001
Weight (kg)	66.4 ± 2.1	79.0 ± 6.6	NS
Height (cm)	167.8 ± 1.3	164.8 ± 1.9	NS
BMI (kg/m²)	23.5 ± 0.6	28.9 ± 2.2	<.05
Waist to hip ratio	0.85 ± 0.03	0.92 ± 0.05	NS
Postmenopausal			
No. of subjects	22	21	
Age (yr)	64.5 ± 1.9	63.4 ± 1.7	NS
Diabetes duration (yr)	27.8 ± 3.6	7.0 ± 1.2	<.001
Time since menopause (yr)	13.9 ± 2.0	13.6 ± 1.7	NS
Weight (kg)	61.5 ± 1.6	74.4 ± 3.4	<.01
Height (cm)	164.5 ± 1.4	159.9 ± 1.5	<.05
BMI (kg/m²)	22.7 ± 0.5	28.9 ± 1.1	<.001
Waist to hip ratio	0.79 ± 0.028	0.90 ± 0.022	<.01

NOTE. Results are the mean ± SEM.

Table 2. 24-Hour Urinary Creatinine Excretion According to Menopausal Status in Female Diabetic Patients

Parameter	IDDM	NIDDM	*P*
Premenopausal			
No. of subjects	31	11	
24-h creatinine (mmol/d)	11.1 ± 0.6	10.1 ± 0.9	NS
% of expected for height*	118 ± 6§	112 ± 10	NS
% of expected for weight†	109 ± 6	86 ± 8	<.05
Postmenopausal			
No. of subjects	22	21	
24-h creatinine (mmol/d)	8.9 ± 0.5‖	10.7 ± 0.9	NS
% of expected for height*	120 ± 7‡	144 ± 12§	NS
% of expected for weight†	114 ± 6	111 ± 10	NS

NOTE. Results are the mean ± SEM.

*Expected 24-h urinary excretion of creatinine in normal adult women with similar height, with ideal body weight, and within the same age decade,[18] or † in normal adult women with similar age and weight[18]: creatinine excretion (mmol/d) = [(21.9 − 0.115 · age) · weight]/113.

‡$P < .05$, §$P < .01$: *v* expected value (100%).

‖$P < .01$, premenopausal *v* postmenopausal.

LTM was similar in the two diabetic groups, and was not significantly different from the LTM in the control group (Figs 1 and 2). Similarly, 24-hour urinary excretion of creatinine was not different in the two diabetic groups, either premenopausal or postmenopausal (Table 2). However, after correction for age and weight, it was lower in premenopausal women with NIDDM than in those with IDDM. When adjusted for age and height, 24-hour excretion of creatinine was higher than expected in patients with IDDM, but when adjusted for age and weight, it was not different from the expected value in either of the diabetic groups (Table 2).

In women with IDDM, LTM (44.5 *v* 41.4 kg, $P < .05$; Fig 1) and creatinine excretion (Table 2) were significantly lower in postmenopausal patients, and both were negatively correlated with age and years since menopause ($r = .3$ to $.4$, $P < .05$) but not with diabetes duration or HbA_{1c}. In a stepwise multiple linear regression analysis with age, years since menopause, and menopausal status as independent variables, only menopausal status was associated with LTM ($P < .05$) and only age was associated with creatinine excretion ($P < .01$). FTM was significantly higher in patients with NIDDM than in those with IDDM, both premenopausally and postmenopausally (Figs 1 and 2), and in premenopausal patients, it was significantly higher than in the control groups matched for age and menopausal status. When FTM in the IDDM groups was compared with FTM in the control groups, it was found to be similar in premenopausal women and lower in postmenopausal women. The same pattern was seen for total body fat percent (Fig 2), abdominal fat percent, and the ratio of abdominal to total body FTM (Figs 1 and 2). In a multiple regression with abdominal FTM or the ratio of abdominal to total body FTM as dependent

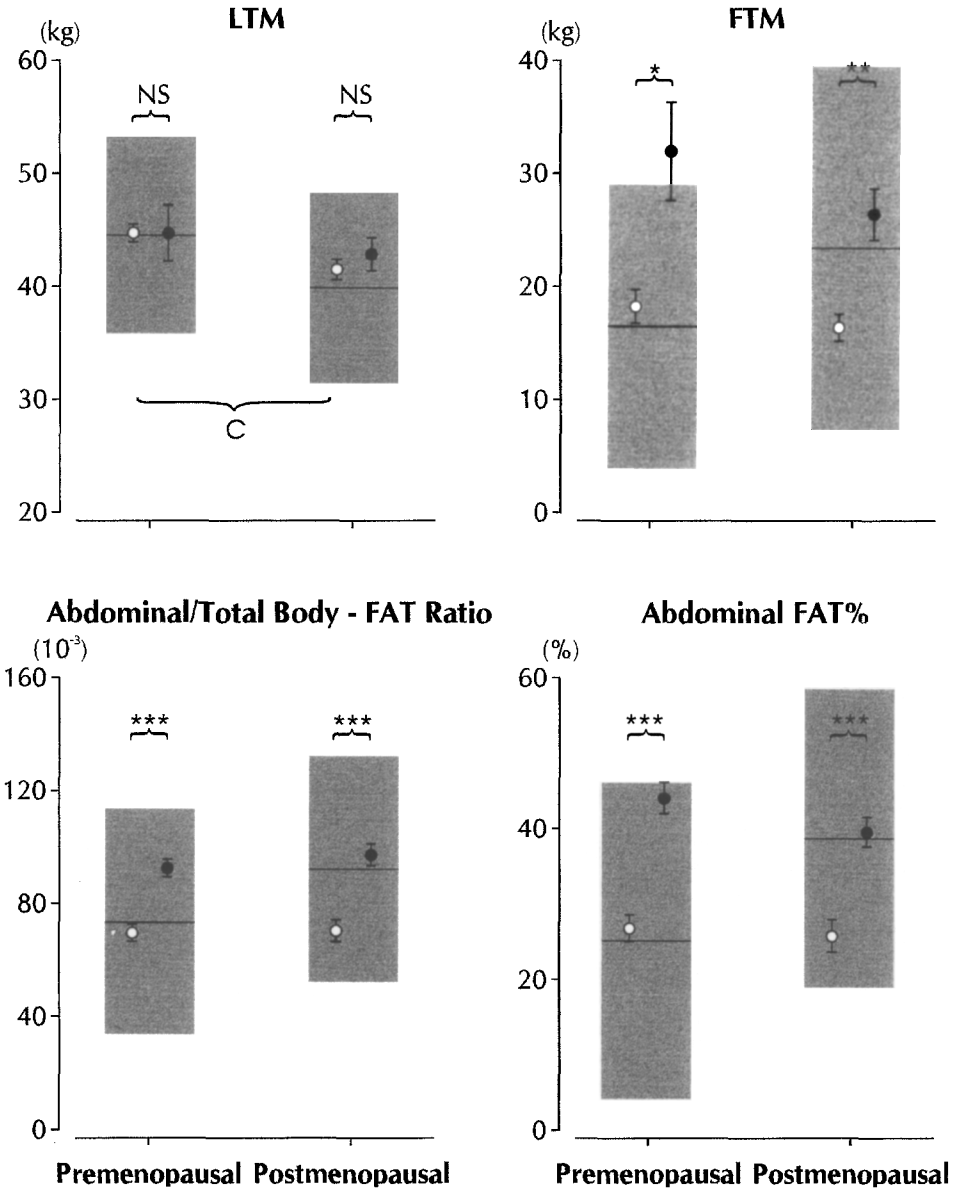

Fig 1. Body composition and fat distribution measured by DXA in premenopausal and postmenopausal women with (○) IDDM and (●) NIDDM (mean ± SEM). Horizontal lines and gray areas indicate the mean ± 2 SD for control groups of healthy women matched for age and menopausal status.[16] ***$P < .001$, **$P < .01$; IDDM *v* NIDDM. c: $P < .05$, premenopausal *v* postmenopausal IDDM. NS, $P > .05$.

variables and total body FTM and type of diabetes (IDDM, 0; NIDDM, 1) as independent variables, both the total body FTM and type of diabetes were positively associated with the abdominal FTM or ratio of abdominal to total body FTM ($P < .001$).

In neither the IDDM nor the NIDDM group were FTM or fat distribution parameters associated with menopausal status (Fig 1), age, years since menopause, duration of diabetes, HbA_{1c}, or blood glucose ($P > .05$).

DISCUSSION

Poor control of glycemia may be associated with protein catabolism and low lean body mass in uncontrolled diabetes.[1-4] However, we were unable to find an association between the duration of diabetes or recent glycemic control and any of the body composition and fat distribution parameters in either the IDDM or NIDDM group, consistent with other studies.[5-8]

Little, if anything, is known about the effect of menopause on body composition and fat distribution in women with IDDM and NIDDM. The present study comprises a relatively healthy sample of women with IDDM and NIDDM with a wide age range divided into subgroups of premenopausal and postmenopausal IDDM and NIDDM patients matched for age and years since menopause. Furthermore, body composition parameters were compared with those of healthy controls matched for age and menopausal status.

We found that LTM was similar in IDDM, NIDDM, and the control groups. Furthermore, in the IDDM group, postmenopausal women had a lower LTM than premenopausal women, as is the case in healthy women.[15-17] LTM as measured by DXA is not an anatomical entity, but consists of the chemical fat-free soft tissue of organs, muscles, body fluids, and connective tissue. The 24-hour urinary excretion of creatinine, which can be used as an estimate of muscle mass during the steady state and with an ordinary diet,[19] was similar in patients with IDDM and NIDDM. In healthy women, creatinine excretion decreases

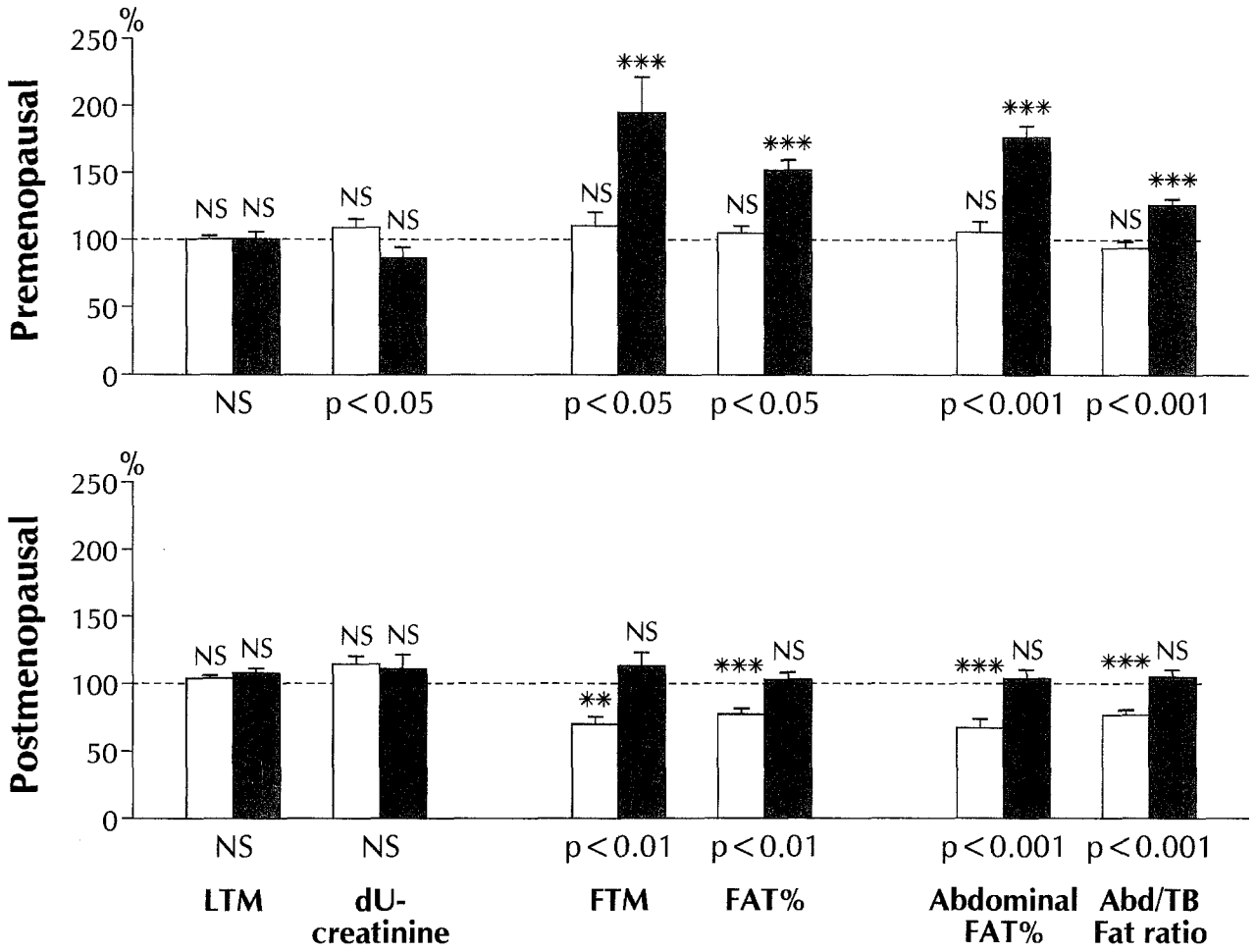

Fig 2. Body composition and fat distribution in premenopausal and postmenopausal women with (□) IDDM and (▩) NIDDM as a % of the mean values for control groups of healthy women matched for age and menopausal status.[16,18] ***$P < .001$, **$P < .01$, *$P < .05$: *v* control group (100%). *P* values below the bars, IDDM *v* NIDDM. NS, $P > .05$.

with age.[18,19] This evidence of a normal muscle mass and a decrease with menopause was also found for women with IDDM but not for those with NIDDM in the present study. When creatinine excretion was adjusted for age and weight or age and height in the two diabetic groups, it was generally similar to or higher than the value expected for healthy women. The reference values we used are from the United States,[18] but they have been found valid for Danes, as well.[8] Thus, in general, it seems that LTM and muscle mass in healthy women and women with IDDM and NIDDM are similar irrespective of menopausal status, and that, except in more acute, uncontrolled or untreated diabetes, women with IDDM or NIDDM do not have increased protein catabolism with low LTM or muscle mass as the outcome.

Compston et al[5] have previously shown in postmenopausal women with IDDM that FTM (and LTM) as measured by DXA was not different from that of controls matched for age and weight. However, when matching control subjects with IDDM patients according to weight, the controls may not be representative of healthy subjects in general. In the present study, we found that total body fat and abdominal fat in women with IDDM were constant with age and menopause. This is in contrast to normal women, in whom total body and abdominal fat increase with age and menopause,[16] probably because of a deficiency in endogenous estrogen or decreased physical activity.[15-17,20] Total body fat and abdominal fat in premenopausal women with IDDM were thus similar to the levels in healthy women, but were significantly less in postmenopausal women with IDDM. The leanness of postmenopausal IDDM patients is thus due to low total body and abdominal fat but normal LTM. Whether a lean body composition constitutes a potential health risk or benefit is uncertain, but it is probably more healthy than if the LTM had been decreased.

One report found that the waist to hip or thigh ratio was significantly lower in women with IDDM as compared with NIDDM,[14] which is consistent with our finding that the ratio of abdominal to total body fat was smaller in patients with IDDM than in patients with NIDDM, even after adjustment for differences in total body FTM.

NIDDM patients are generally overweight or obese, and we found that the FTM was higher in NIDDM versus IDDM irrespective of menopausal status. As in IDDM patients, FTM was constant with age in subjects with NIDDM unlike in healthy women. Therefore, FTM in patients with NIDDM was

higher than normal only in the premenopausal women. This could be interpreted as follows. Genetic susceptibility may result in NIDDM if the subject is overweight or obese. Young healthy Danish women have a relatively low frequency of obesity and NIDDM. With age and menopause, the frequency of overweight and obesity increases (up to 50% with BMI > 25 kg/m_2), and consequently, the frequency of NIDDM also increases. Thus, in postmenopausal women, the difference in FTM for women with NIDDM and age-matched healthy women diminishes.

Besides being overweight or obese, patients with NIDDM may have a greater degree of abdominal fat distribution. Fat distribution has mostly been assessed by the waist to hip ratio, but NIDDM patients may also have relatively more visceral than subcutaneous adipose tissue, as measured by computed tomographic or magnetic resonance imaging scanning.[13,21] We found that, as with FTM, fat distribution in these patients was constant with age and menopause, which contrasts with the FTM in healthy women, in whom it becomes more abdominal after the menopause. Thus, fat distribution was significantly more abdominal in premenopausal women, but in postmenopausal women it was similar to that of healthy women. The interpretation for this is analogous to that for total body fat as already described.

In conclusion, no differences were found for LTM or 24-hour urinary creatinine excretion in IDDM, NIDDM, and healthy women irrespective of age or menopausal status. In the IDDM group, LTM and 24-hour creatinine excretion were lower in postmenopausal than in premenopausal women. Patients with IDDM had significantly less total body and abdominal fat than those with NIDDM irrespective of age and menopausal status. In postmenopausal patients with IDDM, total body fat and abdominal fat were less than normal, whereas these were higher than normal in premenopausal patients with NIDDM.

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