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# Regional Adiposity and Risk for Coronary Artery Disease in Type 1 Diabetes: Does Having Greater Amounts of Lower Body Adiposity Lower the Risk?

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## Abstract

**AIMS—**Evidence suggests that gluteal-femoral adiposity may be inversely associated with coronary artery disease (CAD) risk; however, this association has not been evaluated in type 1 diabetes (T1D).

**METHODS—**The relationship between regional adiposity, cardiovascular risk factors, and presence of CAD was examined in participants from the Pittsburgh Epidemiology of Diabetes Complications (EDC) study using data collected from the 18-year exam (*n*=163). Total and regional adiposity was assessed by dual x-ray absorptiometry (DEXA).

**RESULTS—**Participants with CAD exhibited lower % leg fat mass (FM) (33.42 vs. 36.96, p=0.006) and higher % trunk FM (48.33 vs. 45.18, p=0.02), respectively, after adjusting for age, sex, height, and total adiposity compared to those without CAD. Multivariate logistic regression analyses revealed that in females, every 1 SD increase in % leg FM was associated with an approximate 60% reduction in CAD risk (OR=0.40, 95% CI 0.16–0.99). Higher % trunk FM was also associated with greater risk of CAD prevalence in females (OR=2.79, 95% CI 1.08–7.20 per SD change). These associations were not observed in males.

**CONCLUSIONS—**This is novel evidence that DEXA-assessed lower body adiposity is inversely associated with CAD in T1D, however, this association seems to only exist in females.

### Keywords

adiposity; type 1 diabetes; coronary artery disease; EDC Study; dual x-ray absorptiometry; gluteal-femoral adiposity



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## INTRODUCTION

Coronary artery disease (CAD) is a major cause of morbidity and mortality in type 1 diabetes (T1D). The development of CAD occurs decades earlier and at a 10-fold magnitude in T1D compared to non-diabetic individuals [1]. While the factors associated with greater CAD risk in this population have been well documented, the pathogenesis is still unclear [2].

Although general obesity is a significant CAD risk factor, recent studies have shown that differences in fat distribution throughout the body have varying effects on CAD risk [3]. Prospective evidence indicates that simple measures of central adiposity (e.g. waist circumference) remain significant predictors of CAD after controlling for other pertinent risk factors [4,5], and measures of abdominal adiposity by various imaging techniques (e.g. CT, MRI, DEXA) have confirmed these results [6,7]. Lower extremity adiposity, on the other hand, has recently been shown to have a protective cardiovascular effect through favorable associations with CAD risk factors, such as insulin sensitivity and lipid profiles [8–10]. Additional evidence suggests that this metabolic protection of lower body fat may intensify at higher levels of obesity [11,12]; therefore, overall level of total adiposity must be accounted for when evaluating associations between cardiovascular risk and regional adiposity.

Using data from a 20-yr prospective study of childhood-onset T1D, the two purposes of this study were: 1) to determine if regional adiposity assessments assist in the characterization of those with both CAD and T1D, and 2) to examine the associations between CAD risk factors and both total adiposity and regional adiposity in individuals with T1D.

## METHODS

All participants came from the Pittsburgh Epidemiology of Diabetes Complications Study (EDC), a 20-year prospective follow-up study of childhood-onset (age < 17 at diagnosis) type 1 diabetes mellitus that began in 1986. EDC participants were diagnosed (or seen within 1 year of diagnosis) between 1950–1980 at the Children's Hospital of Pittsburgh, as previously described [13]. During the 18-year exam cycle (2004–2007), 439 participants were eligible for examination, 72% of whom (*n*=318) took part. A subset of these participants (*n*=185) agreed to also undergo a dual x-ray absorptiometry (DEXA) scan and, of these, 163 had sufficient information on CAD status and body composition for this cross-sectional analysis.

### Clinical Evaluation and Procedures

At the EDC exam, height was measured using a stadiometer and weight was measured on a calibrated balance beam scale. Standardized sitting blood pressures and heart rate were measured after a 5-min rest period. Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg or the reported use of medications for blood pressure control. Total cholesterol was measured enzymatically [14]. High-density lipoprotein cholesterol (HDLc) levels were determined by a precipitation technique (heparin and manganese chloride) with modification of Lipid Research Clinics method [15]. Non-HDLc levels were calculated by subtracting HDLc from total cholesterol. Blood samples were analyzed for hemoglobin $A_{1c}$ ($HbA_{1c}$) using the DCA 2000 analyzer (Bayer Diagnostics, Tarrytown, NY). Coronary artery calcification (CAC) was assessed by electron beam computed tomography (Imatron, San Francisco, CA). Insulin sensitivity was assessed using the estimated glucose disposal rate (eGDR) formula, which was derived from hyperinsulinemic-euglycemic clamp studies in T1D (involving $HbA_1$, waist-hip ratio, and hypertension status) [16]. The median of three timed urine collections (or, if necessary, the

mean of two urine collections) were used to determine albumin excretion rates (AER). Overt nephropathy (ON) was defined as an AER >200 μg/min or, in the absence of urine, a serum creatinine level >2 mg/dl, renal failure or renal transplantation. Medication history included current medication use, dosage, and reason for taking medications.

### Coronary Artery Disease Classification

A standardized medical history and clinical examination were performed by a trained internist to determine CAD status. CAD cases included a positive clinical history (myocardial infarction (either confirmed with hospital records or pathological Q waves (Minnesota codes 1.1, 1.2)), hospital record or validated angiographic evidence of ≥50% stenosis with or without revascularization, EDC physician-diagnosed angina and/or ischemic ECG (Minnesota codes 1.3, 4.1–4.3, 5.1–5.3, 7.1) on exam with CAC ≥ 100), or CAC ≥ 400 without presence of clinical disease.

### Adiposity Assessment

Hip and waist circumference (WC) were assessed as a measure of visceral adiposity, and waist-hip ratio (WHR) was calculated. Adiposity distribution was measured by dual x-ray absorptiometry (DEXA) using a Hologic QDR4500A scanner and Hologic QDR system software version 12.3 (Hologic, Bedford, MA). Total body fat mass (FM) (kg), bone-free lean body mass (LBM) (kg), and percent body FM (% FM) was calculated along with regional measures of arm FM (kg), leg FM (kg), and trunk FM (kg). FM in arms and legs was calculated as the sum of both corresponding appendages. The separation between trunk and leg regions was made by two oblique lines passing through the femoral necks, and the separation between trunk and arm regions was made by two oblique lines passing through the humeral heads. Measures of regional adiposity (legs, arms, and trunk) relative to total body FM were calculated as percentages of total FM (% leg FM, % arm FM, and % trunk FM). Participants were excluded from analysis if any region of the body was amputated (n=3), if any plastic artifacts were scanned that may influence the computation of adipose tissue (n=14), or if any area of the body was excluded from the DEXA scan (n=5). The protocol was approved by the University of Pittsburgh Institutional Review Board.

### Statistical Analyses

Variables lacking a normal distribution were transformed by natural log prior to testing. Non-parametric variables that were not normalized after transformation were analyzed with non-parametric techniques. Group differences were examined using Student's *t*-test and Mann-Whitney-U test, as appropriate. $P < 0.05$ was considered statistically significant. General linear models were used to determine group differences after adjusting for factors known to influence adiposity (e.g. age, sex, and/or height). Multivariate logistic regression models using a forward conditional approach were fit by gender to examine variables most strongly associated with presence of CAD. All variables with a univariate association ($p < 0.25$) with presence of CAD were made available for modeling. A significance of $p < 0.10$ was applied for entry and $p > 0.05$ for exclusion from the models. Variables known to influence risk for CAD or adiposity distribution were also included in models. Because many adiposity measures were inter-correlated, separate models were fit for each individual regional adiposity measure. Also, since WC was a component of eGDR and was highly correlated with all adiposity variables, WC was removed from multivariate analyses. Variance inflation factor (VIF) was calculated as a collinearity diagnostic for the final models and variables were considered to be collinear if VIF ≥ 2.0 Akaike's Information Criteria (AIC), a measure of goodness of fit and a tool for model selection, was computed for the final models, and the model with the lowest AIC was considered to have the best fit. SPSS for Windows version 16.0 was used for all analyses (SPSS, Chicago, IL).

# RESULTS

## Participant Characteristics

Comparisons between the DEXA study population (*n*=163, 52.8%) and the remaining EDC population examined at the 18-year follow-up (*n*=146, 47.2%) are reported in Table 1. The mean (±SD) age and diabetes duration for the DEXA population at the 18-year exam were 45.7 (±7.3) and 36.9 (±6.8) years, respectively, which did not significantly differ from the study participants who refused a DEXA scan. The only significantly different factors were lower BMI ($p<0.01$), lower total cholesterol ($p=0.02$), and lower non-HDL cholesterol ($p=0.01$) in the DEXA participants compared to EDC participants who did not have a DEXA scan. All other key variables did not significantly differ between groups.

Characteristics of the 163 participants with T1D are presented by CAD status in Table 2. Forty-eight (29.4%) of the participants had a history of CAD: 8 had a myocardial infarction (16.7%), 12 had revascularization (25.0%), 6 had confirmed angina (12.5%), 8 had an ischemic ECG (16.7%), 2 had ≥50% stenosis (4.1%), and 12 had CAC > 400 (25.0%). The mean duration between CAD onset and the DEXA scan was 14.7 yrs (range 1.8–19.7 yrs). Participants with CAD were older, had longer diabetes duration, were more frequently on an LDLc medication, and showed a trend toward lower HDLc. AER was lower in CAD cases; however, smoking status, $HbA_{1c}$, total cholesterol, LDLc, non-HDLc, triglycerides, SBP, and eGDR were similar between groups. Body composition characteristics by both CAD status and gender are presented in Table 3. Regardless of CAD status, men exhibited higher weight, WC, WHR, and LBM and lower leg, arm, trunk, and total FM (kg and %) compared to women. Examining adiposity measures by CAD status showed that women with CAD exhibited higher % FM in the trunk and lower % FM in the legs as compared with women without CAD, a finding not seen in men. All other adiposity measures were similar between groups.

## Coronary Artery Disease Risk Factors and Regional Adiposity

When examining CAD risk factors and regional adiposity (Table 4), a striking inverse correlation is readily apparent between % leg FM and % trunk FM (r=.94, $p<.001$), which was also reflected in inverse associations between these measures and other CAD risk factors. Moderately positive correlations existed between % leg FM and both HDLc and eGDR. Conversely, significant inverse correlations between % trunk FM and both HDLc and eGDR were observed, and moderately negative correlations existed between % leg FM and CAC, AER, serum creatinine, SBP, DBP, LDLc, non-HDLc, triglycerides, and BMI. Stronger negative correlations were observed between % leg FM and both WC and WHR. Similar, yet opposite, associations were observed between CAD risk factors and % trunk FM compared to the associations observed with % Leg FM. Positive correlations were observed between % arm FM and diabetes duration, BMI, and WC, while negative correlations existed between % arm FM and both eGDR and DBP. Gender differences in correlates were largely absent, except for significant correlations between serum creatinine and both % trunk FM and % leg FM seen in males but not in females. Also, strong correlations were observed between % arm FM and both % leg FM and % trunk FM in females but not in males.

## Presence of Coronary Artery Disease and Regional Adiposity

Univariate logistic regression revealed that, in females, age and HDLc were the CAD risk factors most strongly associated with presence of CAD, while age and serum creatinine were most strongly associated with presence of CAD in males. Even though not selected in the final models, additional variables were added due to their established associations with CAD and/or regional adiposity (i.e., smoking status, height, eGDR, and FM) (Table 5). After controlling for these risk factors, % leg FM and % trunk FM exhibited independent

associations with presence of CAD in females, while no regional adiposity measure was associated with presence of CAD in males (Table 5, Models 2–4 by gender). In females, every 1% higher leg FM was associated with approximately 12% lower CAD risk (OR=0.89, 95% CI 0.79–0.99), while every 1% higher trunk FM was associated approximately 16% higher CAD risk (OR=1.16, 95% CI 1.01–1.33).

## DISCUSSION

The novel finding from this investigation is that a preference to store body fat in the lower limbs appears to be associated with a lower prevalence of CAD in women but not men with T1D, even after controlling for general obesity and other CAD risk factors. This finding confirms previous observations that leg and trunk adiposity have independent and opposite associations with CAD risk factors [17,18], but this is the first report of these associations using DEXA-assessed adiposity measures in T1D.

There has been great interest in identifying regions of the body that are metabolically “optimal” to store adipose tissue. Recent examinations of gluteal-femoral adiposity using DEXA have shown protective associations between gluteal-femoral adiposity and a variety of CAD risk factors [19–21]. The potential for lower-body adiposity to serve as a marker of anti-atherogenicity has propelled the theory that greater leg fat may reflect ability to “spillover” excess adiposity away from the abdomen, into regions where it is less metabolically active and less detrimental to cardio-metabolic health. Although we report that this association only exists in females with T1D, to our knowledge, this is the first investigation to explore these specific associations in T1D, and further investigation is needed to confirm these sex-specific findings.

The sex-specific protective association between lower body fat storage and CAD deserves further discussion. It is well established that women store more adiposity in the lower limbs than men [22]; thus, gender differences in the association between regional adiposity and CAD risk are plausible. Reports from Aasen et al. suggest that a preference toward leg adiposity attenuates CVD risk in obese individuals, particularly in women, but the associations lessened in overweight individuals [11,23]. Women in the current investigation were found to have a greater proportion of fat stored in the legs compared to men after controlling for total adiposity. Therefore, we hypothesize that the enhanced cardio-protective effect of gluteal-femoral adiposity in women with T1D may be due to both a greater preference to store adiposity in legs as well as higher overall adiposity as compared to males. Also, since individuals with T1D have lower levels of overall adiposity compared to non-diabetic controls [24], it is reasonable to conclude that the cardio-protective effect of lower body adiposity in T1D may actually be present in men but is more robustly expressed in women who have greater levels of adiposity. Although such speculations are plausible, the strength of these hypotheses is limited without the benefit of direct comparison to a non-diabetic control group.

The nearly identical, but inverse, associations with CAD risk factors observed between % leg FM and % trunk FM are quite intriguing (Table 4). Similar associations exist in non-diabetic populations [8]; thus, it is possible that fat storage in the legs is simply an inverse indication of fat storage in the trunk region. However, since DEXA assessments of % leg FM and % trunk FM were strongly and inversely correlated with each other, the independent effect of each measure on CAD risk could not be examined. Additionally, the use of DEXA to examine regional adiposity is limited in that distinction between visceral, subcutaneous, and intramuscular fat depots cannot be made. To properly explore the biological plausibility of the current findings, future investigations should focus on examining the independent metabolic influences of specific leg and trunk fat depots on cardiovascular outcomes.

It is also interesting to note that the proportional DEXA measures of leg and trunk adiposity did not strongly correlate with traditional CAD risk factors, such as age, $HbA_{1c}$, and CAC in this investigation. This finding may be explained by the fact that the regional adiposity measures in this study were proportional, rather than absolute measures. Leg fat (kg) was strongly correlated with overall body fat (kg) (r=0.68, $p<0.001$) in this T1D population. Since overall adiposity is traditionally considered an independent CVD risk factor, this would explain the previous associations reported between leg fat and CVD risk [8,25–27]. However, absolute leg fat (kg) showed a very weak association with proportional leg adiposity (r=0.08, $p=.31$) in this sample, potentially contributing to the lack of association between proportional adiposity and the traditional CVD risk factors. Although measures of proportional adiposity were not strongly associated with traditional CVD risk, % FM in the legs and trunk were independently associated with presence of CAC in women with T1D, suggesting these adiposity measures may influence CAD risk through a mechanism different than that of overall adiposity. Examining whether the proportion of leg adiposity is associated with CAD risk attempts to answer a different question than whether amount of leg fat, per se, is associated with CAD risk. If the propensity to store more adipose tissue in a given region is cardio-protective, regardless of overall adiposity, classifying individuals based on this phenotype may better characterize CAD risk, particularly in high-risk populations (e.g., T1D). As DEXA assessment of body composition provides useful information regarding various adiposity regions associated with CAD risk [28,29], applying the comprehensive DEXA assessments to a T1D population is appealing.

Although the current findings are intriguing, it is important to note the significant differences between study participants who declined the DEXA scan compared to those who agreed to participate. Participants who had a DEXA scan as part of the 18-year study exam exhibited lower BMI, lower total cholesterol, and higher non-HDL cholesterol compared to the EDC participants who did not have a DEXA scan. Since individuals who participated were less likely to be obese and potentially have better blood lipid profiles, it is possible that sampling bias influenced the current findings. Therefore, the possibility that greater % FM in the legs may play a different role in CAD risk in lower weight, healthier T1D individuals than it does among individuals with more adverse CAD risk factors cannot be dismissed.

The cross-sectional design of this study limits causal inference of the observed associations. It is conceivable that greater amounts of leg fat may be associated with a lower risk of developing CAD; however, the duration between CAD onset and the time of the DEXA scan ranged from approximately 2 to 20 years, indicating that CAD diagnosis could have occurred many years prior to the measurement of regional adiposity. It is therefore possible that individuals with T1D and CAD have similar levels of leg fat at the time of CAD diagnosis, but begin to lose lower body fat mass or store more adiposity in the trunk region as the disease progresses. Further investigation of the temporal nature of these associations is warranted to more clearly understand the metabolic implications.

Despite our definition of CAD including a wide variety of `soft' endpoints, (i.e., ECG changes, angina, a high burden of CAC), this study is limited by the small number of CAD cases. Therefore, a sensitivity analysis was performed to examine whether the observed associations would vary if CAD was defined only by “hard” endpoints (i.e., myocardial infarction or revascularization). Although the number of CAD cases was further reduced by this definition (8 women and 12 men), greater % FM in the legs was associated with a borderline lower odds of CAD in women ($p=0.07$) but not in men ($p=0.69$) (data not shown). We thus conclude that including “soft” endpoints in the CAD definition did not strongly influence the overall findings.

Since this cohort consists mainly of middle aged adults (age range = 37–64 years), only 17 women were post-menopausal. Although there was insufficient power to detect any differences by menopausal status, an additional sensitivity analysis of the multivariable linear regression models (Table 5) was performed excluding all post-menopausal women and revealed similar results (data not shown). Despite this limitation, this investigation is the largest study to date using DEXA to explore the associations between regional adiposity and CAD in a T1D population.

In summary, a propensity to store adipose tissue in the lower body was favorably associated with CAD risk factors and negatively associated with presence of CAD in women with T1D, but not in men. This lack of association in men with T1D may be due to lower levels of overall adiposity and proportionally less adipose tissue stored in the legs in men compared to women. Our findings that leg and trunk adipose tissue storage may have independent and opposing effects on CAD risk may reflect the metabolically "protective" ability to store body fat away from the abdomen; however, further investigation into the biological plausibility influencing these anthropomorphic trends is needed.

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## ABBREVIATIONS

| | |
|---|---|
| AIC | Akaike's information criterion |
| AER | albumin excretion rate |
| CAC | coronary artery calcification |
| CAD | coronary artery disease |
| DBP | diastolic blood pressure |
| DEXA | dual x-ray absorptiometry |
| EDC | Epidemiology of Diabetes Complications |
| eGDR | estimated glucose disposal rate |
| FM | fat mass |
| LBM | lean body mass |
| MI | myocardial infarction |
| SBP | systolic blood pressure |
| WC | waist circumference |

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## Table 1

Characteristics of DEXA study population compared to remaining study population at 18-year exam in the Pittsburgh Epidemiology of Diabetes Complications Study

| Characteristics | No DEXA | DEXA | *p*-value |
|---|---|---|---|
| N (% male) | 146 (43.7) | 163 (53.2) | .11 |
| Age (years) | 44.3 (7.72) | 45.7 (7.28) | .12 |
| Diabetes duration (years) | 36.8 (7.46) | 36.9 (6.81) | .86 |
| Ever smoked, *n* (%) | 50 (33.8) | 58 (37.2) | .55 |
| Serum creatinine (mg/dL)[a,b] | 1.00 (.80–1.18) | 1.00 (.83–1.18) | .47 |
| AER (μg/min)[a,b] | 12.9 (4.87–77.4) | 6.91 (4.34–39.0) | .06 |
| $HbA_{1c}$ (%) | 7.61 (1.37) | 7.42 (1.44) | .25 |
| Resting heart rate (bpm)[b] | 75.2 (12.6) | 73.7 (10.9) | .26 |
| eGDR (mg/kg/min) | 7.24 (2.47) | 7.49 (2.23) | .36 |
| Hypertension, *n* (%) | 62 (41.6) | 57 (36.1) | .35 |
| Systolic blood pressure (mmHg) | 114.1 (15.3) | 118.0 (15.9) | .07 |
| Diastolic blood pressure (mmHg) | 66.4 (11.0) | 62.8 (10.8) | .08 |
| Body Mass Index ($kg/m^2$) | 28.1 (4.82) | 26.3 (4.09) | <.01 |
| Waist-Hip Ratio | 0.88 (0.09) | 0.88 (0.09) | .78 |
| Total cholesterol (mg/dL) | 181.1 (43.5) | 170.5 (31.0) | .02 |
| HDLc (mg/dL) | 58.2 (15.9) | 59.2 (16.8) | .61 |
| Non-HDLc (mg/dL) | 122.8 (42.0) | 111.4 (29.0) | .01 |

All values are means (SD) unless otherwise noted.

Abbreviation: AER, albumin excretion rate; eGDR, estimated glucose disposal rate

[a] Data presented as median (interquartile range)

[b] Log-transformed before statistical testing

## Table 2

Characteristics by coronary artery disease (CAD) status in type 1 diabetes at 18-year exam in the Pittsburgh Epidemiology of Diabetes Complications Study

| Characteristics | CAD Negative | CAD Positive | *p*-value |
|---|---|---|---|
| N (% male) | 115 (51.3) | 48 (56.3) | .56 |
| Age (years) | 44.0 (6.78) | 49.4 (6.79) | < .01 |
| Diabetes duration (years) | 35.4 (6.03) | 40.3 (7.13) | < .01 |
| Ever smoked, *n* (%) | 39 (34.5) | 20 (41.7) | .58 |
| Serum creatinine (mg/dL)[a,b] | 1.00 (.80–1.10) | 1.00 (.90–1.28) | .13 |
| AER (μg/min)[a,b] | 5.98 (4.02–26.1) | 5.27 (5.27–59.3) | .03 |
| Overt nephropathy, *n* (%) | 26 (22.6) | 15 (31.9) | .24 |
| $HbA_{1c}$ (%) | 7.52 (1.45) | 7.15 (1.40) | .14 |
| Daily insulin dose (U/kg) | 0.59 (0.22) | 0.63 (0.25) | .36 |
| Resting heart rate (bpm)[b] | 74.0 (10.8) | 73.2 (11.3) | .69 |
| eGDR (mg/kg/min) | 7.66 (2.29) | 7.05 (2.04) | .12 |
| Hypertension, *n* (%) | 30 (27.0) | 18 (37.5) | .19 |
| Systolic blood pressure (mmHg) | 114.1 (15.3) | 118.0 (15.9) | .16 |
| Diastolic blood pressure (mmHg) | 66.4 (11.0) | 62.8 (10.8) | .06 |
| Taking ACE/ARB inhibitors, *n* (%) | 61 (53.0) | 27 (56.3) | .71 |
| Total cholesterol (mg/dL) | 172.4 (30.6) | 165.6 (31.6) | .21 |
| LDLc (mg/dL) | 97.9 (27.7) | 94.5 (27.7) | .51 |
| HDLc (mg/dL) | 60.8 (17.2) | 55.1 (15.4) | .05 |
| Non-HDLc (mg/dL) | 111.6 (28.6) | 110.6 (29.9) | .84 |
| Triglycerides (mg/dL)[b] | 78.5 (36.5) | 91.4 (50.3) | .09 |
| Taking LDL medications, *n* (%) | 41 (36.3) | 26 (54.2) | .04 |

All values are means (SD) unless otherwise noted.

Abbreviation: AER, albumin excretion rate; eGDR, estimated glucose disposal rate

[a] Data presented as median (interquartile range)

[b] Log-transformed before statistical testing

## Table 3

Body composition assessments by CAD status in type 1 diabetes participants at 18-year exam in the Pittsburgh Epidemiology of Diabetes Complications Study (N=163)

| | Females | | Males | |
|---|---|---|---|---|
| | **CAD Negative** | **CAD Positive** | **CAD Negative** | **CAD Positive** |
| N | 54 | 21 | 59 | 27 |
| Weight (kg) | 68.7 (11.6) | 68.4 (10.7) | 80.9 (12.2) | 80.0 (13.6) |
| BMI (kg/m$^2$) | 25.5 (4.3) | 27.1 (4.4) | 26.3 (3.5) | 26.8 (4.5) |
| WC (cm) | 83.1 (10.5) | 87.9 (10.5) | 92.6 (10.5) | 94.9 (12.0) |
| Waist-Hip Ratio | 0.82 (0.07) | 0.86 (0.08)* | 0.92 (0.07) | 0.95 (0.07) |
| LBM (kg) | 44.9 (5.0) | 43.8 (5.3) | 61.8 (7.0) | 58.8 (7.5)* |
| % FM | 32.6 (6.1) | 34.7 (6.2) | 21.8 (5.6) | 23.6 (6.9) |
| FM (kg) | 22.4 (7.1) | 24.0 (7.0) | 17.7 (6.5) | 18.8 (7.5) |
| Leg fat (kg) | 8.88 (2.58) | 8.44 (2.47) | 5.73 (1.83) | 5.73 (2.33) |
| Arm fat (kg) | 2.95 (1.14) | 3.31 (1.14) | 2.23 (0.87) | 2.38 (1.07) |
| Trunk fat (kg) | 9.76 (4.21) | 11.39 (4.35) | 8.81 (4.03) | 9.63 (4.57) |
| % FM in Legs | 40.7 (7.6) | 36.2 (7.2)* | 33.3 (5.1) | 31.3 (5.1) |
| % FM in Arms | 13.0 (2.2) | 13.6 (2.0) | 12.5 (1.7) | 12.5 (2.0) |
| % FM in Trunk | 42.2 (6.8) | 46.4 (6.5)* | 48.0 (6.1) | 49.8 (6.9) |

Values are unadjusted means (SD); *p*-values were adjusted for effects of age, and height, except for weight, BMI, and % FM, which were adjusted only for age

Abbreviations: WC, waist circumference, LBM, lean body mass; FM, fat mass

*Significantly different than CAD Negative within gender, $p<0.05$

## Table 4

Pearson correlations between CAD risk factors and regional adiposity in type 1 diabetes in the Pittsburgh Epidemiology of Diabetes Complications Study (N=163)

| | % FM in Legs | | % FM in Trunk | |
|---|---|---|---|---|
| | **Females (*n*=77)** | **Males (*n*=86)** | **Females (*n*=77)** | **Males (*n*=86)** |
| ***Clinical Characteristics*** | | | | |
| Age (years) | .03 | −.18 | −.06 | .15 |
| Diabetes duration (yrs) | .03 | −.09 | −.08 | −.01 |
| Agatston CAC score[a] | −.24 | −.22 | .24 | .12 |
| AER (μg/min)[b] | −.28[c] | −.31[c] | .30[c] | .23 |
| Serum creatinine (mg/dL)[b] | −.06 | −.30[c] | .10 | .33[c] |
| $HbA1_c$ (%) | −.01 | −.26 | −.03 | −.13 |
| eGDR (mg/kg/min) | .41[c] | .49[d] | −.39[c] | −.42[d] |
| Resting heart rate (bpm) | −.10 | −.23[c] | .10 | .23 |
| Systolic BP (mmHg) | −.26[c] | −.28[c] | .32[c] | .22[c] |
| Diastolic BP (mmHg) | −.16 | −.14 | .24[c] | .13 |
| Total cholesterol (mg/dL) | −.14 | −.14 | .18 | .12 |
| DLc (mg/dL) | −.19 | −.23 | .25 | .20 |
| HDLc (mg/dL) | .15 | .17 | −.11 | −.22 |
| Non-HDLc (mg/dL) | −.25[c] | −.22[c] | .28[c] | .22[c] |
| Triglycerides (mg/dL)[b] | −.31[c] | −.28[c] | .29[c] | .34[c] |
| ***Anthropometry*** | | | | |
| BMI ($kg/m^2$) | −.46[d] | −.43[d] | .57[d] | .55[d] |
| Waist circumference (cm) | −.66[d] | −.50[d] | .74[d] | .62[d] |
| Waist-Hip Ratio | −.57[d] | −.59[d] | .56[d] | .60[d] |
| Total FM (kg) | −.48[d] | −.43[d] | .61[d] | .62[d] |
| %FM | −.48[d] | −.46[d] | .59[d] | .66[d] |
| Arm FM (kg) | −.67[d] | −.38[c] | .69[d] | .48[d] |
| Leg FM (kg) | .19 | −.01 | −.02 | −.24[c] |
| Trunk FM (kg) | −.72[d] | −.60[d] | .82[d] | .77[d] |
| % FM in Arms | −.67[d] | −.12 | .48[d] | -.07 |
| % FM in Legs | -- | -- | −.96[d] | −.92[d] |
| % FM in Trunk | −.96[d] | −.92[d] | -- | -- |

Data presented as correlation coefficients

Abbreviations: CAC, coronary artery calcification; AER, albumin excretion rate; eGDR, estimated glucose disposal rate; FM, fat mass.

[a] Log-transformed +1 before statistical testing

[b] Log-transformed before statistical testing

[c] $p<0.05$

[d] $p<0.01$

**Table 5**

Association of CAD risk factors and regional adiposity measures with CAD status in men and women with type 1 diabetes - The Pittsburgh Epidemiology of Diabetes Complications Study (N=163)

| FEMALES | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Model 1[a] | | | Model 2 | | | Model 3 | | | Model 4 | | |
| Variable | OR | 95% CI | p | OR | 95% CI | p | OR | 95% CI | p | OR | 95% CI | p |
| Age (years) | 1.14 | 1.03–1.25 | .01 | 1.15 | 1.03–1.27 | .01 | 1.13 | 1.03–1.25 | .01 | 1.15 | 1.04–1.29 | .01 |
| HDLc | 0.62 | 0.32–1.20 | .16 | 0.69 | 0.36–1.35 | .28 | 0.62 | 0.32–1.20 | .16 | 0.70 | 0.36–1.35 | .28 |
| History of Smoking | 1.64 | 0.46–5.93 | .45 | 1.99 | 0.51–7.74 | .32 | 1.65 | 0.46–5.92 | .44 | 1.98 | 0.50–7.85 | .33 |
| Height | 0.46 | 0.23–0.90 | .02 | 0.45 | 0.22–0.92 | .03 | 0.45 | 0.23–0.90 | .02 | 0.46 | 0.22–0.94 | .03 |
| eGDR | 1.08 | 0.55–2.12 | .83 | 1.38 | 0.65–2.95 | .40 | 1.10 | 0.56–2.20 | .78 | 1.42 | 0.66–3.06 | .37 |
| Total FM | 1.56 | 0.80–3.01 | .19 | 1.16 | 0.55–2.45 | .69 | 1.50 | 0.77–2.92 | .23 | 0.96 | 0.41–2.21 | .91 |
| % FM in Legs | | | | 0.40 | 0.16–0.99 | .05 | | | | | | |
| % FM in Arms | | | | | | | 1.26 | 0.63–2.50 | .51 | | | |
| % FM in Trunk | | | | | | | | | | 2.79 | 1.08–7.20 | .03 |
| AIC | | 80.5 | | | 77.8 | | | 82.0 | | | 77.2 | |

| MALES | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Model 1 | | | Model 2 | | | Model 3 | | | Model 4 | | |
| **Variable** | **OR** | **95% CI** | **p** | **OR** | **95% CI** | **p** | **OR** | **95% CI** | **p** | **OR** | **95% CI** | **p** |
| Age (years) | 1.15 | 1.04–1.28 | .01 | 1.15 | 1.04–1.28 | .01 | 1.16 | 1.05–1.28 | .01 | 1.15 | 1.04–1.28 | <.01 |
| Serum Creatinine | 1.53 | 0.88–2.65 | .13 | 1.52 | 0.87–2.64 | .14 | 1.53 | 0.88–2.65 | .13 | 1.52 | 0.88–2.64 | .14 |
| History of Smoking | 1.18 | 0.38–3.62 | .77 | 1.20 | 0.39–3.71 | .75 | 1.22 | 0.40–3.77 | .73 | 1.19 | 0.38–3.70 | .76 |
| Height | 0.67 | 0.38–1.16 | .15 | 0.67 | 0.39–1.17 | .16 | 0.65 | 0.37–1.15 | .14 | 0.67 | 0.39–1.17 | .16 |
| eGDR | 0.83 | 0.43–1.57 | .56 | 0.86 | 0.43–1.75 | .68 | 0.83 | 0.44–1.58 | .57 | 0.84 | 0.42–1.68 | .62 |
| Total FM | 1.14 | 0.64–2.05 | .65 | 1.11 | 0.61–2.04 | .73 | 1.17 | 0.65–2.10 | .60 | 1.12 | 0.57–2.18 | .75 |
| % FM in Legs | | | | 0.90 | 0.46–1.78 | .76 | | | | | | |
| % FM in Arms | | | | | | | 0.84 | 0.47–1.51 | .56 | | | |
| % FM in Trunk | | | | | | | | | | 1.06 | 0.49–2.26 | .89 |
| AIC | | 95.2 | | | 97.1 | | | 96.9 | | | 97.2 | |

Model 2: Includes Model 1 variables and % FM in Legs

Model 3: Includes Model 1 variables and % FM in Arms

Model 4: Includes Model 1 variables and % FM in Trunk

Odds ratios are per 1 SD increase, except for age (per 1 yr increase) and history of smoking (yes)

Abbreviations: CAD, coronary artery disease; OR, odds ratio; CI, confidence interval; eGDR, estimated glucose disposal rate; FM, fat mass; AIC, Akaike's Information Criteria

[a]Model 1: Includes significant univariate variables (age and HDLc in women, age and serum creatinine in men) and potential confounders (history of smoking, height, eGDR and Total FM)