Obesity and Albuminuria Among Adults With Type 2 Diabetes

The Look AHEAD (Action for Health in Diabetes) Study

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OBJECTIVE — To determine the association between obesity measures and albuminuria in adults with type 2 diabetes.

RESEARCH DESIGN AND METHODS — In the Look AHEAD (Action for Health in Diabetes) Study, BMI and waist circumference were measured among 4,985 participants while total percent body fat was measured by whole-body DEXA scans among 1,351 participants. Odds of albuminuria by quartiles of BMI, waist circumference, and percent total body fat were calculated using logistic regression analysis while adjusting for covariates.

RESULTS — The highest quartile of BMI (odds ratio [OR] 1.72 [95% CI 1.40–2.11]) and waist circumference (OR 1.75 [95% CI 1.42–2.15]) was significantly associated with albuminuria compared with the lowest quartile after adjustment for covariates. No associations were noted between quartiles of percent total body fat and albuminuria in any model.

CONCLUSIONS — Increased BMI and abdominal obesity are associated with albuminuria in overweight and obese adults with type 2 diabetes.

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Despite substantial improvements in blood pressure and glucose control, ~2% of adults develop microalbuminuria per year after type 2 diabetes diagnosis (1). Lifestyle factors remain an integral component of cardiovascular risk reduction, yet treatment and prevention of albuminuria (micro- or macroalbuminuria) have primarily focused on pharmacologic agents, specifically those which block the renin angiotensin system. This study examined the association between measures of obesity and albuminuria among adults who participated in the Look AHEAD (Action for Health in Diabetes) Study. We hypothesized that obesity is positively associated with albuminuria.

RESEARCH DESIGN AND METHODS

— The Look AHEAD Study is a randomized clinical trial conducted in 16 centers in the U.S., and the design and methods of this trial have previously been described (2). The purpose of the Look AHEAD Study is to determine whether cardiovascular morbidity and mortality in those with type 2 diabetes can be reduced through an intensive lifestyle intervention aimed at producing and maintaining weight loss. To address this, participants are randomized to an intensive lifestyle intervention, which includes moderate-intensity physical activity and a calorie-reduced diet, or to a support and education control group. The present manuscript is based on data collected in the full cohort before randomization. A total of 5,145 adults were enrolled; BMI of 5,144 participants was measured, and 4,985 (97%) participants provided a spot urine sample. A subset of 1,372 participants underwent baseline whole-body dual energy X-ray absorptiometry (DEXA) scans at one of five clinical study sites, (3) and albuminuria data were available for 1,351 participants. Sex-specific urine albumin (micrograms per milliliter) to creatinine (milligrams per milliliter) ratios (ACRs) were used to define albuminuria, including both microalbuminuria (ACR ≥17–249 and ≥25–354 mg/g for men and women, respectively) and macroalbuminuria (ACR ≥250 mg/g in men and ≥355 mg/g in women) (4).

Weight was measured in duplicate on a digital scale. Standing height was determined in duplicate with a standard stadiometer. Waist circumference was measured with subjects in light clothing with a nonmetallic, constant tension tape placed around the body at the midpoint between the highest point of the iliac crest and the lowest part of the costal margin in the mid-axillary line. Whole-body DEXA scans were completed using Hologic QDR4500A densitometers except for the Boston site (Hologic Delphi A). Cross-calibration on a standard phantom was used to determine percent total body fat. Scans were read and monitored for quality by the Prevention Sciences Group, University of California at San Francisco. Participants weighing greater than 300 lbs were not included in this subset.

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Standardized interviewer-administered questionnaires were used to obtain self-reported data on personal medical history and prescription medications. Seated blood pressure was measured in duplicate with an automated device and blood was drawn after an 8-h fast. A1C was measured by a dedicated ion-exchange high-performance liquid chromatography instrument (Biorad Variant II).

Statistical analysis. Quartiles of BMI, waist circumference, and percent total body fat were determined after stratifying by sex. Multivariate-adjusted odds ratios [ORs] for albuminuria by quartiles of BMI, waist circumference, and percent total body fat were calculated using logistic regression analysis. Several different logistic regression analyses were performed so that changes in parameter estimates with the addition of selected covariates could be examined. Model 1 adjusted for age, sex, and race/ethnicity, model 2 added duration of diabetes and A1C, and model 3 added hypertension and use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. Effect modification by sex was explored by fitting interaction terms into the full model.

Table 1—*Model comparison of adjusted ORs of albuminuria*

	Model 1	Model 2	Model 3
BMI quartiles (n = 4,985)			
1	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
2 vs. 1	1.38 (1.13–1.68)	1.35 (1.10–1.65)	1.25 (1.02–1.54)
3 vs. 1	1.43 (1.17–1.75)	1.40 (1.13–1.72)	1.28 (1.04–1.58)
4 vs. 1	1.98 (1.63–2.42)	1.93 (1.58–2.36)	1.72 (1.40–2.11)
Waist circumference quartiles (n = 4,985)			
1	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
2 vs. 1	1.30 (1.06–1.59)	1.25 (1.02–1.55)	1.22 (0.99–1.51)
3 vs. 1	1.61 (1.32–1.97)	1.56 (1.27–1.91)	1.47 (1.19–1.81)
4 vs. 1	2.04 (1.67–2.48)	1.92 (1.57–2.40)	1.75 (1.42–2.15)
% body fat quartiles (n = 1,351)			
1	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
2 vs. 1	1.08 (0.75–1.54)	0.97 (0.67–1.40)	0.94 (0.65–1.37)
3 vs. 1	1.01 (0.70–1.45)	0.93 (0.64–1.35)	0.90 (0.62–1.31)
4 vs. 1	1.07 (0.75–1.54)	1.05 (0.72–1.52)	0.97 (0.67–1.42)

Data are OR (95% CI). Model 1 adjusts for age, sex, and race/ethnicity. Model 2 adjusts for covariates in model 1, diabetes duration, and A1C. Model 3 adjusts for covariates in models 1 and 2, and presence of hypertension, systolic blood pressure, and use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers.

RESULTS — Baseline characteristics of the total Look AHEAD participants (5) and DEXA substudy participants have been previously described (3). Among all participants, 19.2% had microalbuminuria and 2.7% had macroalbuminuria. Substantial overlap existed between the BMI and waist circumference quartiles, with 72% of participants in the highest BMI quartile (>38.4 kg/m^2 in men and >40.1 kg/m^2 in women) also included in the highest quartile of waist circumference (>127.0 cm in men and >119.0 cm women). In the subgroup with DEXA scans, total percent body fat ranged from ≤27.6% in men and ≤39.3% in women in the lowest quartile to >34.5% in men and >45.4% in women in the highest quartile. Among participants in the highest quartile of total percent body fat, 59 and 47% were included in the highest quartile of BMI and waist circumference, respectively.

Table 1 shows the multivariate-adjusted ORs of albuminuria by quartiles of obesity measures. In Model 1, the highest quartile of both BMI and waist circumference was associated with an approximate twofold increased odds of albuminuria compared with the lowest quartile. These associations were reduced after further adjustment for hypertension and use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers medication. In contrast, no significant association was noted between quartiles of percent total body fat and albuminuria. Interaction terms for measures of obesity and sex were not significant in any of the models.

CONCLUSIONS — Abdominal obesity is associated with albuminuria in obese adults with type 2 diabetes, but percent total body fat does not appear to be associated with albuminuria. The majority of Look AHEAD participants had a BMI ≥30 kg/m^2, and 72% of participants in the highest BMI quartile were also in the highest waist circumference quartile. This may explain the similar associations noted in this study between albuminuria and BMI and waist circumference. Regression of albuminuria has been associated with use of renin-angiotensin system–blocking drugs and tight glycemic control (6). However, moderate weight loss reduces the metabolic demands on the kidney and may lead to substantial regression of urine albumin excretion (7).

The study was limited by the smaller sample size for total body fat and the lack of a direct measure of visceral fat. Nonetheless, these findings contribute to existing data that demonstrate an urgent need to determine whether behavioral interventions that reduce abdominal obesity retard the development and progression of albuminuria. The Look AHEAD Study provides an excellent opportunity to quantify the effects of weight loss and exercise on measures of obesity and albuminuria. Such information may have a substantial impact for the prevention and treatment of kidney disease.

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