The Lipid Accumulation Product Is Better Than BMI for Identifying Diabetes

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Gaining weight is associated with diabetes risk (1–3). It may be, however, that gaining lipid is associated more specifically with the development of insulin resistance, pancreatic exhaustion, and diabetes. According to a current pathophysiological model, when available fuels exceed the adipose tissue’s capacity for buffering and safe storage, lipid will be ectopically deposited in nonadipose tissues such as liver, skeletal muscle, and the pancreatic β-cell (4–6). These ectopic lipid deposits are associated with lipotoxicities that in turn lead to insulin resistance and the eventual decline of β-cell function (7,8). To simplify the recognition of lipid overaccumulation, researchers have devised dichotomous risk markers based on waist circumference and fasting triglyceride concentration (9–11). However, lipid accumulation, like body weight, may not be adequately described by a dichotomous index. This report explores whether a continuous “lipid accumulation product” (LAP) performs better than the continuous BMI (in kilograms divided by the square of height in meters) for identifying adults with insulin resistance, elevated glucose, and diabetes.

RESEARCH DESIGN AND METHODS — The LAP was developed from population-based frequency plots of adult waist circumferences and circulating triglyceride concentrations (10,12). With aging, the waist circumference increasingly moves away from its minimal adult value (empirically 65 cm for men and 58 cm for women) and the fasting triglyceride concentration likewise departs from its minimal value (theoretically 0 mmol/l). The following simple definitions attempt to describe total-body lipid accumulation (12): LAP for men = (waist circumference [cm] – 65) × (triglyceride concentration [mmol/l]); LAP for women = (waist circumference [cm] – 58) × (triglyceride concentration [mmol/l]).

Representative data were obtained from the NHANES III (Third National Health and Nutrition Examination Survey), a probability sample of the U.S. civilian, noninstitutionalized population in 1988–1994 (13). The analytic sample included 4,447 men and 4,733 women who were aged ≥18 years, were not pregnant, had fasted 8–19 h before their laboratory examination, and had data available on basic anthropometry and fasting serum triglycerides (excluding three subjects with a triglyceride concentration >15 mmol/l). Participants completed a household interview and an examination including measurement of standing waist circumference (in the horizontal plane at the level just above the iliac crest, at minimal respiration) (14,15).

Serum triglyceride, insulin, plasma glucose, and whole-blood HbA1c (A1C) were measured by standardized methods described elsewhere (16). Insulin resistance was estimated by the homeostasis model assessment (HOMA-IR) formula (17), defined as fasting insulin × fasting glucose/22.5. Diabetes was defined by report of a physician diagnosis or by fasting glucose ≥7.0 mmol/l. The skewed variables (LAP, BMI, and HOMA-IR) were logarithmically (ln) transformed.

Sampling weights from NHANES III were used to describe population distributions of risk factors associated with LAP and BMI and to construct multivariable linear regression models adjusted for race/ethnicity. The analyses thus incorporated sampling weights that accounted for unequal selection probabilities (18). For each continuous outcome variable (analyzed separately by sex and by age-groups 18–49 or ≥50 years), (ln)LAP and (ln)BMI were evaluated by comparing the proportion of the total variation that either index could explain, that is, the R² for the entire regression model minus the R² for a base model that excluded (ln)LAP and (ln)BMI.

RESULTS — The models with LAP were consistently, but weakly, superior to those with BMI for predicting the risk variables HOMA-IR, fasting glucose, and A1C in competing regression models with up to 8,823 participants (representing 98,015,695 adults) who were not using insulin or hypoglycemic medication. For HOMA-IR, the difference in R² was greatest among older (≥50 years) women [R² 0.363 for (ln)LAP vs. 0.318 for (ln)BMI] and smallest among younger (18–49 years) women (R² 0.372 vs. 0.371). For fasting glucose, the difference was greatest among older men (0.080 vs. 0.033) and smallest among younger men (0.069 vs. 0.044). For A1C, the difference was greatest among older women (0.051 vs. 0.019) and smallest among young men (0.035 vs. 0.020). In these competing models, the β coefficients on standardized (ln)LAP were consistently larger than those on standardized (ln)BMI, but the differences in slope were usually not significant. However, a significant difference was found comparing models that predicted A1C in the older population [sex-adjusted β ± SE, 0.186 ± 0.029 for (ln)LAP vs. 0.112 ± 0.021 for (ln)BMI; P = 0.04].

Based on 8,767 survey participants who were tested for diabetes or reported the diagnosis (including users of insulin...
CONCLUSIONS — LAP is modestly superior to BMI for predicting glucometabolic variables but much superior for identifying adults with diabetes. The transition to diabetes (i.e., loss of adequate insulin response) may be linked more closely to lipid accumulation than to increased relative weight. Although diabetes risk is associated continuously with abdominal adiposity (19–26) and circulating triglycerides (25–30), combining these two variables in a single continuous index (LAP) may better summarize how lipid accumulation and lipotoxicities lead to disease.

In place of sophisticated imaging methods for estimating the lipid burden or uptake in isolated tissues (31–33), LAP offers an inexpensive research tool to estimate and monitor total-body lipid accumulation. From a clinical perspective, LAP might also serve to predict the risk of future diabetes, but cross-sectional data cannot prove this point. Prospective data will be needed to establish the association of LAP with diabetes incidence.

References
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