

Genotype May Help Predict Best Diet Response

BY ROBERT FINN

SAN FRANCISCO — Genotypes may identify women likely to lose weight on a low-carbohydrate diet and those likely to do better on a low-fat diet, based on data from 133 participants in the A TO Z Weight Loss Study.

Women who have one pattern of single nucleotide polymorphisms (SNPs) lost five times as much weight on the Atkins diet, compared with those who did not have that pattern.

Similarly, women with a different SNP genotype lost five times as much weight on the Ornish diet, Mindy Dopler Nelson, Ph.D., of Stanford (Calif.) University, said at a conference sponsored by the American Heart Association.

In the original A TO Z study, 311 women were randomized to one of four popular diets. Ranging on a continuum from low carbohydrate to low fat, they were the Atkins diet, the Zone diet, the LEARN diet, and the Ornish diet.

On average, the women lost weight on all four diets; the only significant difference was that

they tended to lose somewhat more weight on the Atkins diet than on the Ornish diet (JAMA 2007;297:969-77).

“Within each of the diet groups, there are women who had lost over 15 kg ... as well as people who gained 5 kg,” Dr. Nelson said in an interview.

The interaction between genotype and diet was statistically significant, with striking differences among the women in the lowest-carb and lowest-fat diets.

“When you look at the averages you don’t see the differences, but when you look at each individual participant you see some variability.”

Some time after the conclusion of that trial, Interleukin Genetics approached Stanford researchers and suggested they use the company’s proprietary SNP test to assess responders and nonresponders to particular diets.

In previous studies, the company had found polymorphisms in three genes—fatty acid binding protein, PPAR-gamma, and the beta-2 adrenergic receptor—that appeared to predict a person’s response to diets.

Among the 133 women from the original study who agreed to provide DNA samples from swabs of the inner cheek, 31 had been in the Atkins group, 32 in the Zone group, 34 in the LEARN group, and 36 in the Ornish group.

There were no statistically significant baseline differences among the groups in measures such as body mass index, blood pressure, or levels of cholesterol, insulin, and glucose.

The company’s test showed that 79 of the women had genotypes designated as low-carb appropriate, and 54 had genotypes designated as low-fat appropriate.

The interaction between genotype and diet was statistically significant, with striking differences among the women in the lowest-carb and lowest-fat diets.

Among the women on the Atkins diet, those designated as low-carb appropriate lost an average of just under 6 kg during 12 months, while those designated as low-carb inappropriate lost about 1 kg.

Among the women on the Ornish diet, those designated as

VITALS

Major Finding: Women randomized to a low-fat or a low-carbohydrate diet considered appropriate (based on a pattern of three single nucleotide polymorphisms) lost about 6 kg, compared with about 1-1.5 kg among women randomized to diets judged as inappropriate.

Data Source: Data from 133 participants in the A TO Z Weight Loss Study.

Disclosures: Research support was provided by Interleukin Genetics. Dr. Nelson had no financial conflicts.

low-fat appropriate lost an average of more than 6 kg during 12 months, while those designated as low-fat inappropriate lost an average of about 1.5 kg.

Thus, in each of those groups, women who had been randomized to what was designated as the appropriate diet lost about five times as much weight as those randomized to the apparently inappropriate diet.

Among women on the Zone or LEARN diets, which involve intermediate levels of carbohydrates and fat, women with low-carb and low-fat genotypes did not have statistically significant differences in weight loss.

Dr. Nelson acknowledged that the trial was relatively small, and that the findings need to be confirmed in a larger trial in a more heterogeneous population.

Nevertheless, the results do

provide some guidance to people who are trying to lose weight, she said.

“I would suggest that if somebody is discouraged by the weight loss that they’re having on whatever particular diet they’re following, they may just want to consider changing the distribution of their macronutrients,” Dr. Nelson said.

“So maybe if you’re doing a higher-carbohydrate diet and you’re not seeing your weight loss, give up some of the more processed carbohydrates, keep the healthier ones in there, and see if shifting to the lower-carbohydrate diet will help with weight loss,” she added.

Dr. Nelson said that Interleukin Genetics supported her study, but neither she nor Stanford University has any financial involvement in the company’s products. ■

Intra-Abdominal Fat Better Predictor of Liver Injury

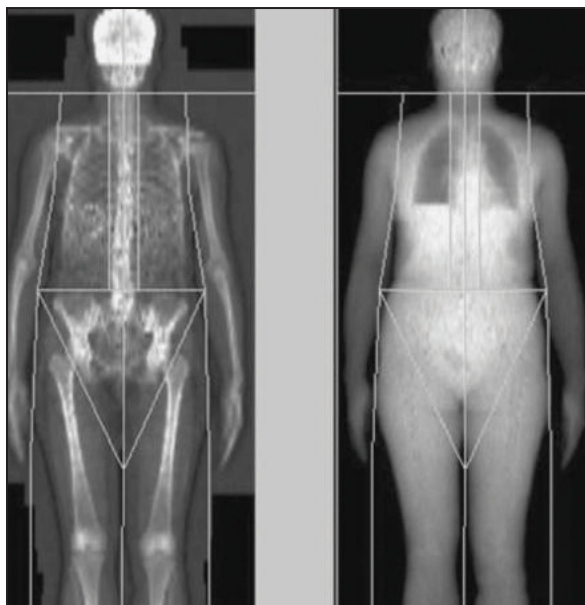
BY DENISE NAPOLI

Increased trunk fat on dual-energy x-ray absorptiometry was independently associated with elevated serum alanine aminotransferase levels, a measure of liver injury—more so than was extremity fat, body mass index, or waist circumference, according to an analysis of the National Health and Nutrition Examination Survey.

The findings “support the hypothesis that liver injury can be induced by metabolically active intra-abdominal fat,” wrote Dr. Constance E. Ruhl and Dr. James E. Everhart, noting that “obesity is an important risk factor for liver injury.”

Dr. Ruhl of Social & Scientific Systems Inc., a research support company, and Dr. Everhart of the National Institute of Diabetes and Digestive and Kidney Diseases studied data from patients in the National Health and Nutrition Examination Survey (NHANES). Pregnant women and survey participants who were positive for serum hepatitis B surface antigen or were positive or indeterminate for hepatitis C antibody were excluded, as were patients whose hepatitis status could not be determined. Patients were aged 20 years and older.

In all, 11,821 participants (5,918 men and 5,903 women) who participated in NHANES between 1999 and 2004 were ultimately included in the analysis. Study participants had dual-energy x-ray absorptiometry (DXA) measurements to determine trunk fat, trunk lean mass, extremity fat, and extremity lean mass, and were then divided into quintiles within each category. Missing DXA measurements were imputed by the National Center for Health Statistics. Serum alanine aminotransferase (ALT) levels, a marker of liver dam-



Trunk fat, as measured by DXA (right image), was significantly associated with elevated ALT levels.

age, were considered elevated above 44 U/L in men and above 31 U/L in women.

“The prevalence of elevated ALT was 11.1% among men and 10.1% among women,” wrote the authors.

Among men, each step up in trunk fat quintile conferred a 1.7 increased odds ratio for elevated ALT (P less than .001). In women, each step up in trunk fat quintile was associated with a 1.4 increased OR (P less than .001). The results were adjusted for ethnicity, age, glucose status, serum total cholesterol, cigarette smoking, and alcohol consumption.

In contrast, having an increased amount of extremity fat actually was protective against elevated ALT. Among men, every increased quintile conferred a 0.87 OR of elevated ALT ($P = .002$), and for women, each increasing quintile conferred a 0.86 OR ($P = .001$).

Trunk lean mass and extremity lean mass, however, showed no significant relationship with ALT level.

“Having established that elevated ALT was most strongly associated with trunk fat, we considered its effect on the association of BMI and waist circumference with elevated ALT,” wrote the authors. “When trunk fat, BMI, and waist circumference were included together in multivariate-adjusted models, higher trunk fat remained independently associated with elevated ALT among both men [$P = .002$] and women [$P = .011$], but BMI and waist circumference were not.”

Regarding the “unexpected” finding that extremity fat was protective against elevated ALT, the researchers postulated that the “uptake and storage of free fatty acids by femoral adipose tissue could lead to protection of other organs such as the liver from exposure to fatty acids and ectopic fat deposition.”

The authors conceded several limitations to their study. First, DXA measurements of abdominal fat are not as accurate as CT or MRI, although the technology “is still considered a relatively accurate and precise method to estimate body fat and lean soft tissue mass components.” Second, the use of ALT levels alone as a marker of liver damage cannot be entirely accurate. “Inevitably, participants were included in the elevated ALT group who would not have been had repeat ALT measurements been available.”

Dr. Ruhl and Dr. Everhart reported having no conflicts of interest. The study was supported by NIDDK. ■