COMMENTS AND RESPONSES

Pancreatic Fat Content and β-Cell Function in Men With and Without Type 2 Diabetes

Response to Tushuizen et al.

We read the recent paper by Tushuizen et al. (1) with interest. In that study, the authors measured pancreatic fat content by use of proton magnetic resonance spectroscopy in 12 type 2 diabetic and 24 nondiabetic men and examined the relationship between pancreatic fat content and β-cell function. They report a negative correlation between pancreatic fat and a measure of β-cell function in nondiabetic control-subjects (but not individuals with type 2 diabetes) and conclude that "pancreatic lipid content may contribute to β-cell dysfunction and possibly to the subsequent development of type 2 diabetes in susceptible humans." We respectfully suggest that the report contains insufficient evidence to support that conclusion.

We also quantitatively measured total pancreatic fat content (i.e., fat volume within the whole pancreas) by use of computed tomography in 165 type 2 diabetic and 660 age-, sex-, and BMI-matched nondiabetic subjects (2). We reported that pancreatic fat content increases with obesity (BMI) in both nondiabetic and type 2 diabetic humans but that, in this much larger cohort, there was no difference in pancreatic fat content between individuals with type 2 diabetes and BMI-matched nondiabetic control subjects. Moreover, we also examined pancreatic fat histologically in pancreas of 24 nondiabetic and 23 type 2 diabetic subjects across a wide BMI range and, again, noted that pancreatic fat increased with BMI in both groups, but that there was no difference in this relationship based on diabetes status alone. Histological analysis of the pancreas reveals that most pancreatic fat in humans is present in adipocytes within the exocrine tissue or in adipose tissue in the interlobular space (the latter the majority). There is a considerable variation in pancreatic fat content within as well as between pancreata, so measurement of pancreatic fat content in a small portion of pancreas as employed in the study of Tushuizenet et al. may yield flawed data. Also, unlike data regarding ZDF rats, there are not, to our knowledge, data available showing accumulation of fat in islets in humans.

In the study of Tushuizen et al., subjects are neither large in number nor well matched, with a greater waist circumference in type 2 diabetic case subjects than in control subjects and a BMI almost significantly greater in type 2 diabetic case subjects than in control subjects despite small numbers (31.3 ± 1 vs. 29.1 ± 1 kg/m, $P = 0.07$). There was considerable overlap in pancreatic fat content between type 2 diabetic and nondiabetic case subjects, with the proposed difference in pancreatic fat between groups skewed by two nondiabetic individuals with much lower pancreatic fat than the other case subjects in either group. These outliers then heavily influence the regression analysis purporting to show that β-cell function is inversely related to pancreatic fat in nondiabetic control subjects. Indeed, if these two outliers are excluded, it is clear from Fig. 2*B* in the article by Tushuizen et al. that there would be no relationship between glucose-stimulated insulin secretion and pancreatic fat. Since pancreatic fat increases proportionately with BMI (2) and glucose-stimulated insulin secretion increases adaptively in obese nondiabetic individuals (3), we respectfully disagree that pancreatic fat in humans is proven to be deleterious to β-cell function.

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