

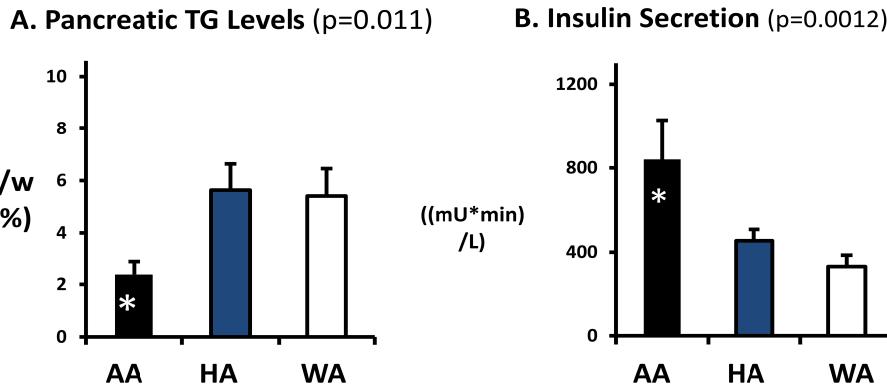
Ethnic Disparity of Pancreatic Triglyceride Levels: Implications for Type 2 Diabetes Development

Lidia S Szczepaniak¹, Ruchi Mathur¹, Edward Szczepaniak¹, Nicole Tyer¹, Michael D Nelson¹, Ida Chen¹, Ronald G Victor¹, and Ildiko Lingvay²
¹Cedars-Sinai Medical Center, Los Angeles, California, United States, ²UT Southwestern Medical Center, Dallas, Texas, United States

Introduction The exact role of pancreatic fat in the development of human impaired glucose tolerance remains unclear (1, 2, 3). Basic research using rodent models of type 2 diabetes has identified pancreatic steatosis and lipotoxicity as a leading cause of beta cell dysfunction (4). We sought to translate these mechanistic studies into the clinical population. Type 2 diabetes and impaired glucose tolerance are especially prevalent in minority populations such as Hispanic and African Americans. Therefore, the purpose of this investigation was two-fold: First, to determine differences in pancreatic fat content by localized ¹H MR Spectroscopy across three major ethnic groups: African American (AA), Hispanic (HA), and White (WA). Secondly, to explore the association between pancreatic fat content and insulin secretion. We hypothesized that pancreatic fat content would be higher in AA and HA compared to WA, and that the high level of pancreatic fat content would be associated with impaired insulin secretion.

Study Population and Experimental Design We studied 100 individuals of both genders, who were relatively young (average age= 39 y) without diabetes (N=50 HA +20 AA +30 WA). Each study participant was tested for glucose tolerance by standard glucose tolerance test; insulin sensitivity and insulin secretion by frequently intravenous sampled glucose tolerance test; abdominal fat distribution by high resolution abdominal MRI; and intra-pancreatic triglyceride (TG) levels by localized ¹H MRS.

Localized ¹H MRS With subjects in the supine position, high-resolution images through the abdomen were collected at end-expiration to locate the pancreas. On three perpendicular images of the pancreas, a testing volume of 2cc was selected within the body of the pancreas. Data were collected as patients breathed freely with MRS signal triggered at exhalation (trigger delay=300 ms, T_R =4s, T_e =40ms, and N_a =32). The figure below summarizes results of our study.



Results and Discussion We found differences in pancreatic fat content between AA, HA and WA (panel A). Contrary to our hypothesis however, pancreatic TG levels were higher in WA and HA, compared to AA. Importantly, the level of pancreatic TG content was significantly inversely associated with insulin secretion (panel B). Our data suggest that pancreatic steatosis may identify a subset of asymptomatic individuals who are at high risk for development of type 2 diabetes. ¹H-MRS and measurement of pancreatic TG content may therefore constitute a new therapeutic target. Our data also highlight a potential need for ethnically appropriate preclinical biomarkers.

References

1 Lingvay et al, JCEM, 2009;10:4070 2 Tushuizen ME et al, 2007;30:2916, 3 Saisho Y et al, Clin Anat 2007;20:933 4 Lee Y et al, PNAC 1994; 91;10878

Support: NIH RO1DK081524, K23RR024470, CTSI Grant UL 1RR033176