

Could Obesity Possibly be harmless

L. S. Szczepaniak¹, J. L. Legendre², E. W. Szczepaniak¹, A. L. Price², and I. Lingvay²

¹The Heart Institute, Cedars-Sinai Medical Center, Los Angeles, California, United States, ²Endocrinology, UT Southwestern Medical Center, Dallas, Texas, United States

Abstract: There is no doubt that obesity is associated with diabetes, increased cardiovascular risk factors, not to mention arthritis and cancers. Sixty to 90% of patients with diabetes are obese but not all obese individuals present metabolic and cardiovascular diseases. This leads to a notion that certain individuals tolerate obesity well and without metabolic consequences. We present clinical evidence that given enough time the so called "healthy obesity" eventually becomes harmful with full spectrum of metabolic consequences.

Methods and study population: In 209 individuals we evaluated glycemic control status using 2 Hrs oral glucose tolerance test. In addition to traditional vital signs we measured abdominal subcutaneous and visceral fat mass by abdominal MRI, as well as ectopic fat deposition in forms of fat droplets in heart and liver (N=134) and in pancreas (N=75) using localized proton MRS. MRS of myocardial and pancreatic fat was performed with compensation of respiratory and cardiac motion. Weight 1, 5, and 10 years prior to the study was obtained by self report. Study subjects were divided into 4 groups based on their body mass index (BMI) and glucose control: (1) L (Lean)-BMI<25 kg/m² and normal glucose tolerance (2hrs glu<140 mg/dL); (2) O (Obese)-BMI>25 kg/m² and normal glucose tolerance; (3) IGT (Impaired glucose tolerance) regardless of BMI (2hrs glu>140 mg/dL and <200 mg/dL); (4) T2D (newly diagnosed diabetes) – 2 hrs glu > 200 mg/dL.

Results & Discussion: As illustrated in Figure 1, subcutaneous fat mass was doubled in obese state compared to lean and did not increase in IGT or T2D states. Visceral fat mass continuously increased across all groups. Ectopic fat levels experienced the most dramatic increase in obese state but there was no difference in ectopic fat levels between IGT and T2D states in all studied organs. These observations demonstrate that when the subcutaneous fat reservoir fills up fat accumulates in other compartments.

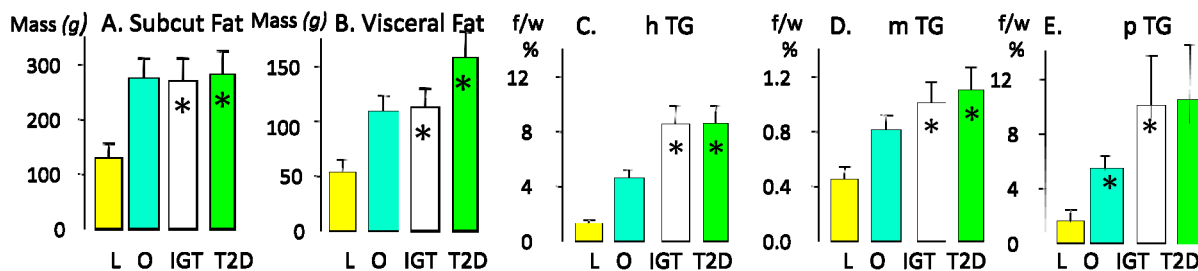


Figure 1. A. Subcutaneous fat mass, B. Visceral fat mass, C. intra-hepatic TG, D. intra-myocardial TG, and E. intra-pancreatic TG

Figure 2 illustrates how duration of obesity matters. The levels of pancreatic TG elevate dramatically with duration of obesity being highest for longest duration of obesity. Interestingly lean and obese individuals were in average 13 years younger than individuals with IGT or with T2D suggesting that obesity without complication may last 10 to 15 years and after that period complications develop. We postulate that duration of obesity is a significant determinant of ectopic fat accumulation and ultimately onset of metabolic abnormalities. We propose that the concept of "healthy obesity" is a mere matter of time. Persistent over

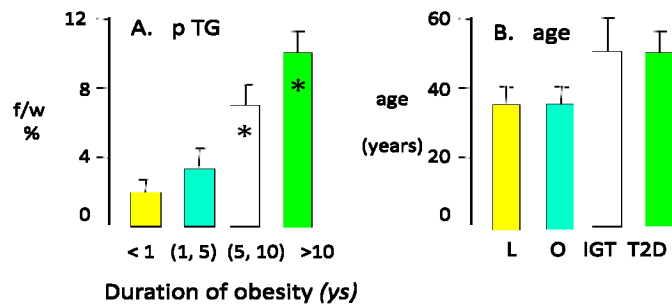


Figure 2. A. Pancreatic TG levels and duration of obesity B. Age of individuals in studied groups.

nutrition will eventually over-ride the protective capacity of adipose tissue to store excessive fat. This fat excess will consequently spill over to ectopic sites and lead to lipotoxic organs dysfunction such as non-alcoholic fatty liver disease, insulin resistance, beta cell failure, and myocardial dysfunction. This is of a special concern given that population of obese children expands fast. Unlike obese adults, obese children will live long enough to outgrow their period of benign obesity and will face adulthood with metabolic complications.