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The Impact of Roux-en-Y Gastric Bypass on Biochemical and Morphological Correlates of Glomerular Injury in an Animal Model of Type 2 Diabetes

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Purpose of the Study:

The Zucker Diabetic Fatty (ZDF) rat is extensively used as a model of Diabetic Kidney Disease (DKD) associated with obesity and progressive insulin resistance ('diabetes'). This study aimed to validate qualitative ultrastructural parameters of glomerular injury in the ZDF animal model and apply these criteria to an interventional study investigating the effects of Roux-en-Y gastric bypass (RYGB) on DKD.

Methods:

Superficial renal cortices were immersion-fixed in 2.5% glutaraldehyde, post-fixed in 1% osmium tetroxide, processed and embedded in epoxy resin prior viewing under a Technai 12 transmission electron microscope. Glomerular basement membrane (GBM) thickness, podocyte foot process diameter (PFPD) and podocyte foot process frequency (PFPF) per unit length of GBM were determined for each group (Sham and RYGB operated ZDF fa/fa diabetic animals vs non-operated non-diabetic ZDF fa/+ lean controls). Statistical analysis was performed using a Mann Whitney U test and an unpaired t-test where appropriate.

Summary of Results:

Selected TEM parameters (GBM thickness, PFPD and PFPF) demonstrated significant differences between specified Sham-operated ZDF fa/fa vs fa/+ samples, $p=0.017$. *Analysis of RYGB interventional study samples still in progress.* Early post-operative glucose measurements showed a significant improvement in glucose homeostasis in the RYGB group (RYGB vs SHAM, $P=0.0001$) occurring independently of weight loss. Urinary albumin:creatinine ratios were lower in the RYGB group vs Sham operated positive controls ($P=0.0079$) and were comparable with age-matched lean control fa/+ samples.

Conclusions:

Preliminary findings support a beneficial role for RYGB in an animal model of 'Diabetes'. Validated ultrastructural parameters should assist in elucidating changes in podocyte activation and differentiation as mediators of the observed remission of albuminuria following RYGB surgery.