Roux-en-Y gastric bypass reduces proteinuria in diabetic kidney disease to a greater extent than weight loss alone in the Zucker Diabetic Fatty rat without a greater improvement in renal inflammation

Karl J Neff1, Jessie Elliott1, Caroline Corteville2, Kathrin Abegg3,4, Neil G Docherty1, Roderigo Muñoz5, Thomas Lutz2,4, Carel le Roux1

1. Diabetes Complications Research Centre, Conway Institute, School of Medicine, University College Dublin, Ireland
2. Institute of Veterinary Physiology, Vetsuisse Faculty, University of Zurich, Switzerland
3. Zurich Center for Integrative Human Physiology, University of Zurich, Switzerland
4. Institute of Laboratory Animal Sciences, University of Zurich, Switzerland
5. Department of Digestive Surgery, School of Medicine Santiago, Pontificia Universidad Católica, Santiago, Chile

OBJECTIVES
1. Determine the effect of RYGB and equivalent diet-induced weight loss on diabetic kidney disease (DKD) in the Zucker Diabetic Fatty (ZDF) rat
2. Evaluate the effect of RYGB and equivalent diet-induced weight loss on renal inflammation in the ZDF rat

METHODS
Homozygous ZDF rats (fa/fa) develop obesity, insulin resistance and hyperglycaemia. At age 18 weeks they have diabetic kidney disease. ZDF fa/fa rats underwent RYGB (n=15) or sham surgery (n=14). Sham operated animals were food restricted to match the weight loss of the RYGB group: body-weight matched group (BWM, n=8). Other sham operated animals were untreated and acted as positive controls: Ad libitum sham group (ALS, n=6). Heterozygotes are non-diabetic non-obese rats and acted as negative controls: fa/+ (NSX, n=5).

RESULTS

Proteinuria

By 4 weeks post-operative, both RYGB and BWM had reduced proteinuria. At 12 weeks only RYGB was reduced from baseline. RYGB had a greater effect on reducing proteinuria as compared to the BWM group and the ALS group (p=0.01).

Renal inflammation

Macrophage infiltration (ED1 staining), urinary MCP-1:creatinine ratio and MCP-1 expression in kidney tissue was reduced by in both RYGB and BWM groups (p<0.05).

CONCLUSIONS
1. RYGB has a greater effect on reducing proteinuria in DKD in the ZDF rat than weight loss alone
2. This may be due to other mechanisms such as greater reductions in hyperglycaemia or enhanced GLP-1 secretion

RYGB had a greater effect in improving glomerular appearance as compared to ALS and BWM (p<0.05)