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

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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

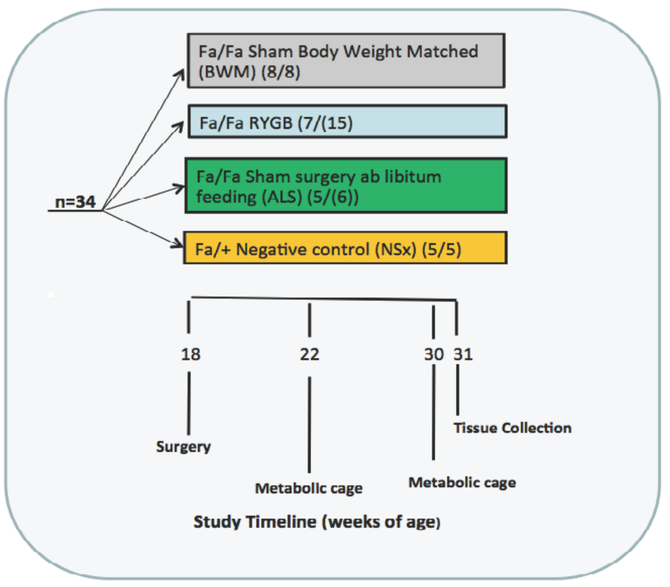
METHODS

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)

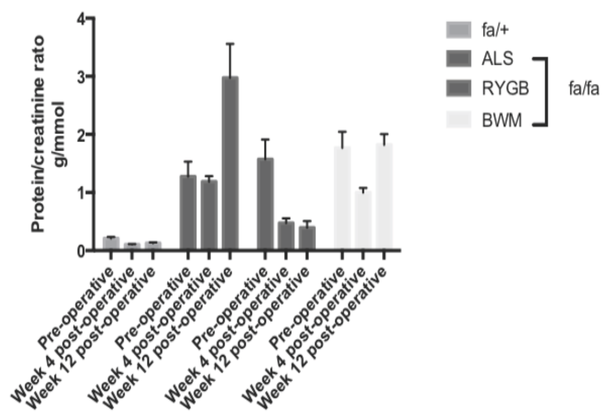


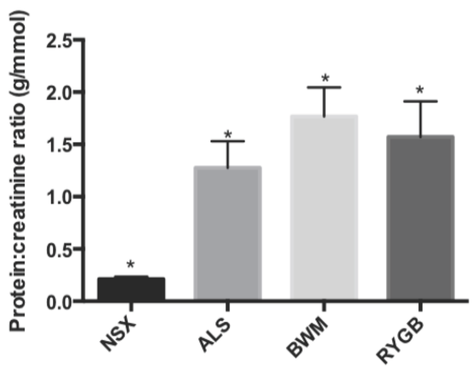
RESULTS

Proteinuria

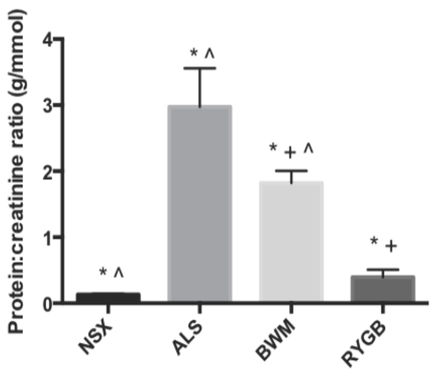
Protein:creatinine ratio during the study at:
a) Baseline (17 weeks of age)
b) 4 weeks post-operative
c) 12 week post-operative

p<0.001 on two-way ANOVA for time and group.





Protein:creatinine ratio at 17 weeks of age (pre-operative)
p=0.006 on ANOVA
*p<0.05



Protein:creatinine ratio at 30 weeks of age (end of study)
p=0.03 on ANOVA.
*p<0.05
+p<0.001 between BWM and RYGB groups
^p<0.05 BWM vs. NSX, BWM vs. ALS.

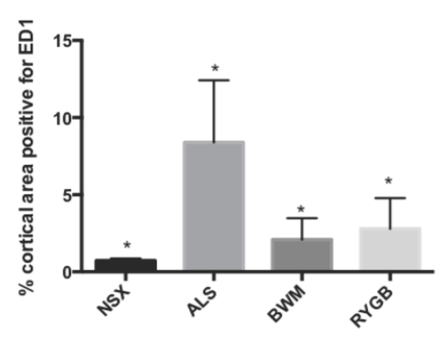
By 4 weeks post-operative, both RYGB and BWM had reduced proteinuria

At 12 weeks only RYGB was reduced from baseline

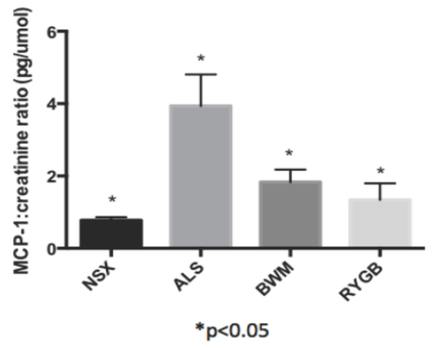
RYGB had a greater effect on reducing proteinuria as compared to the BWM group and the ALS group (p=0.01)

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)

Renal inflammation

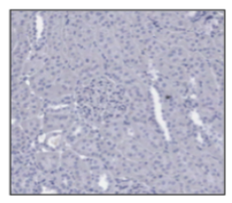


p<0.001 on ANOVA
*p<0.05

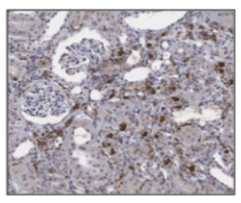


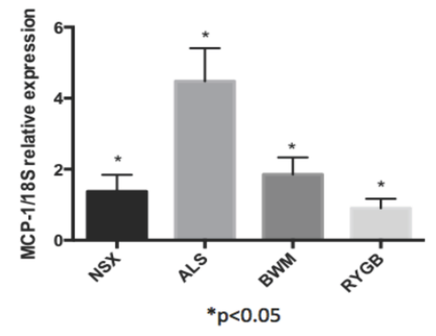
*p<0.05

NSX



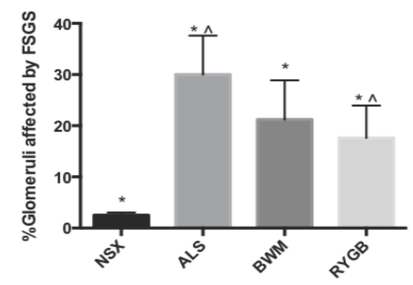
ALS



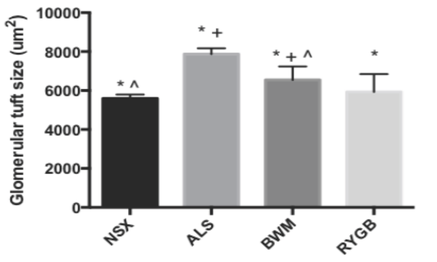


*p<0.05

Glomerulosclerosis

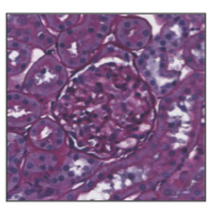


*p<0.05 on ANOVA
^p=0.01 ALS vs. RYGB

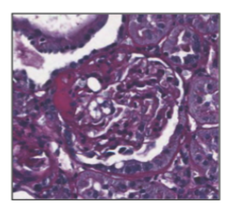


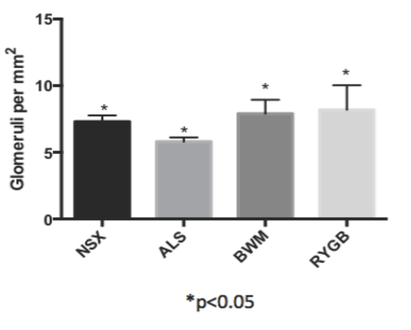
+p=0.002 between BWM and ALS group
^p=0.02 BWM vs. NSX

NSX



ALS





*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)

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