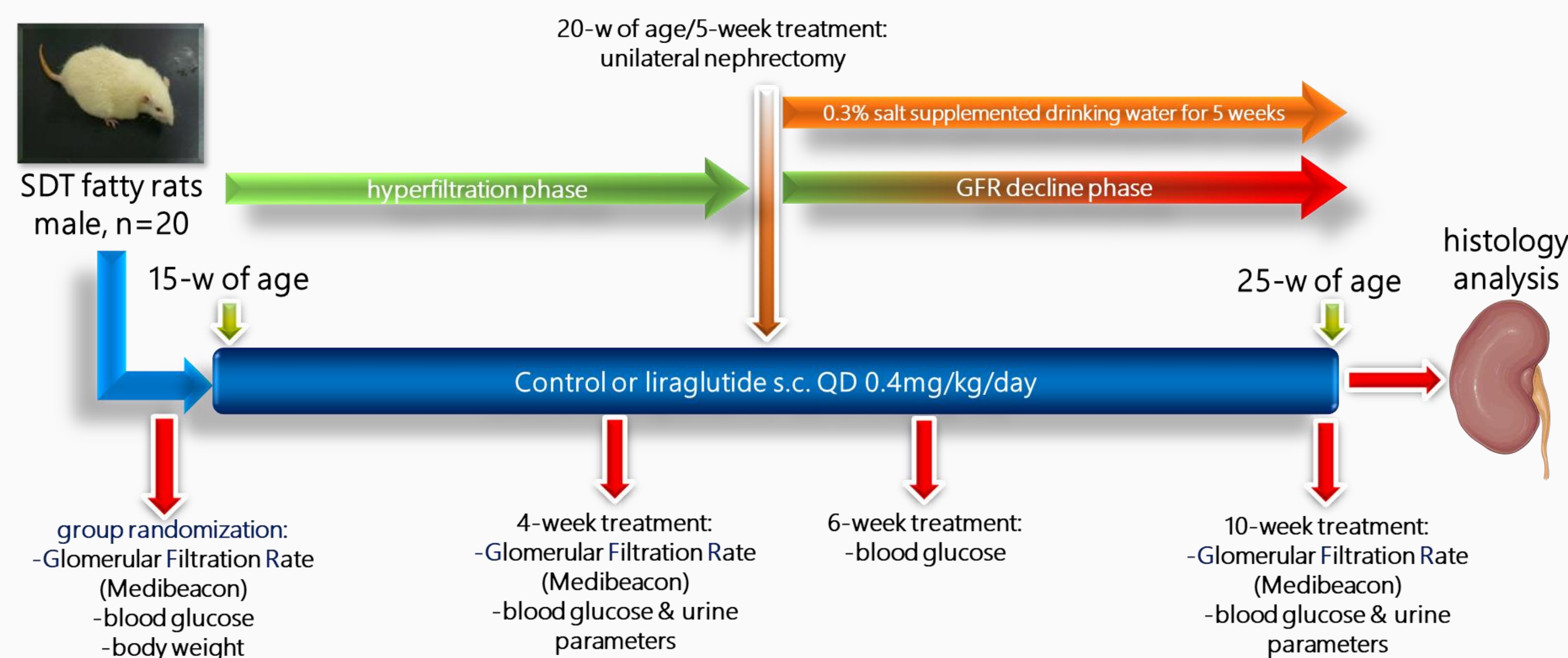


## OBJECTIVES & METHODS

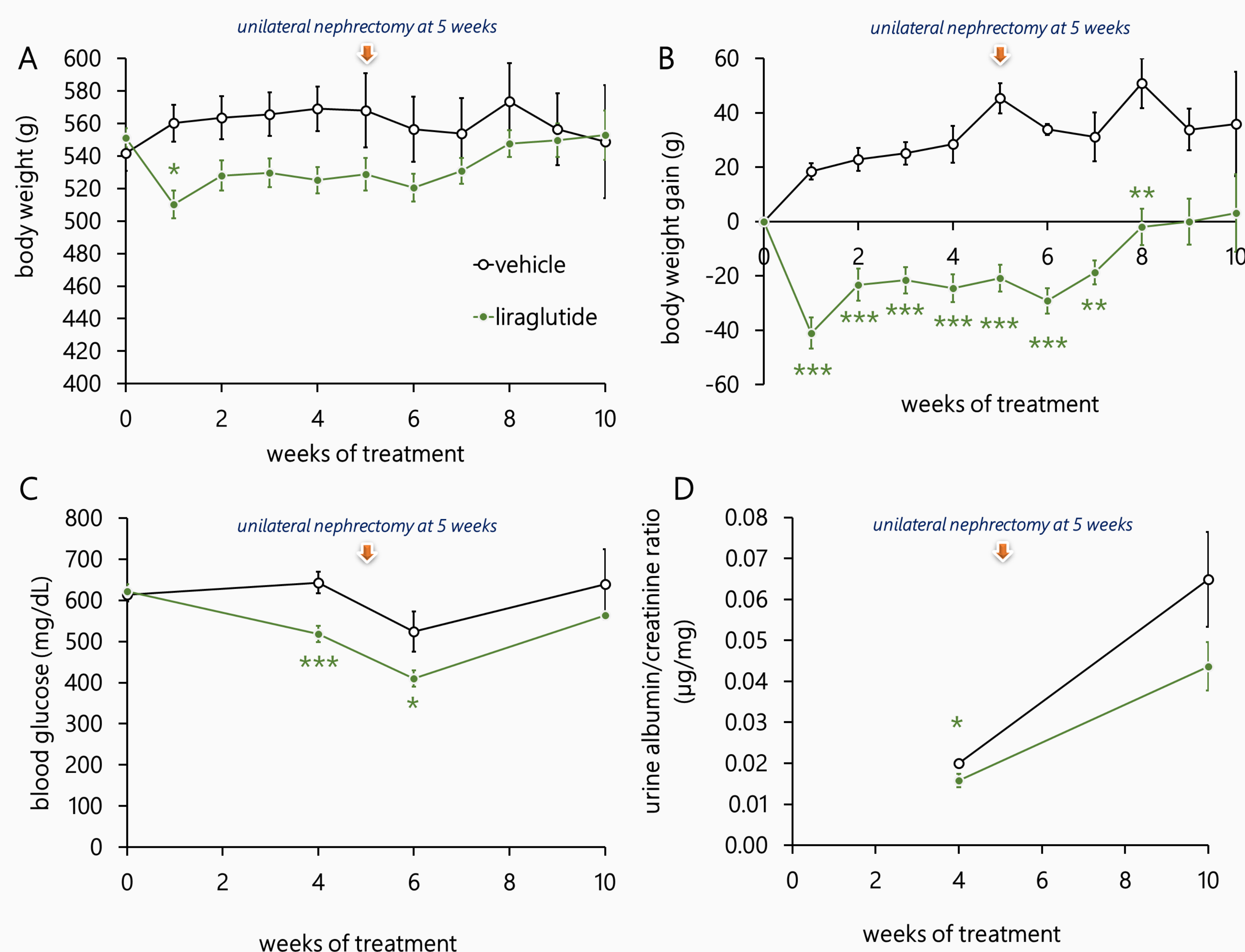
The Glucagon-Like Peptide 1 (GLP-1) receptor agonist liraglutide (LIRA) may reduce the rate of development and progression of diabetic kidney disease in type 2 diabetic patients. To evaluate its impact on kidney function, we evaluated the effects of LIRA on glomerular filtration rate (GFR), in both the hyperfiltration and GFR decline phases in the Spontaneously Diabetic Torii (SDT) fatty rat, a preclinical model of type 2 diabetes.

SDT fatty male rats were treated subcutaneously, once daily with vehicle or LIRA 0.4mg/kg for 10 weeks (n=10/group). To measure the effects of LIRA on glomerular hyperfiltration, rats were injected with FITC-sinistrin at 4 weeks of treatment to measure GFR. After 5 weeks of treatment, rats underwent unilateral nephrectomy and were put on a 0.3% salt diet to induce a GFR decline for the last weeks of treatment, then GFR was measured at 10 weeks of treatment. Urine biochemistry and kidney histology analysis were also performed to evaluate the effects of LIRA treatment.



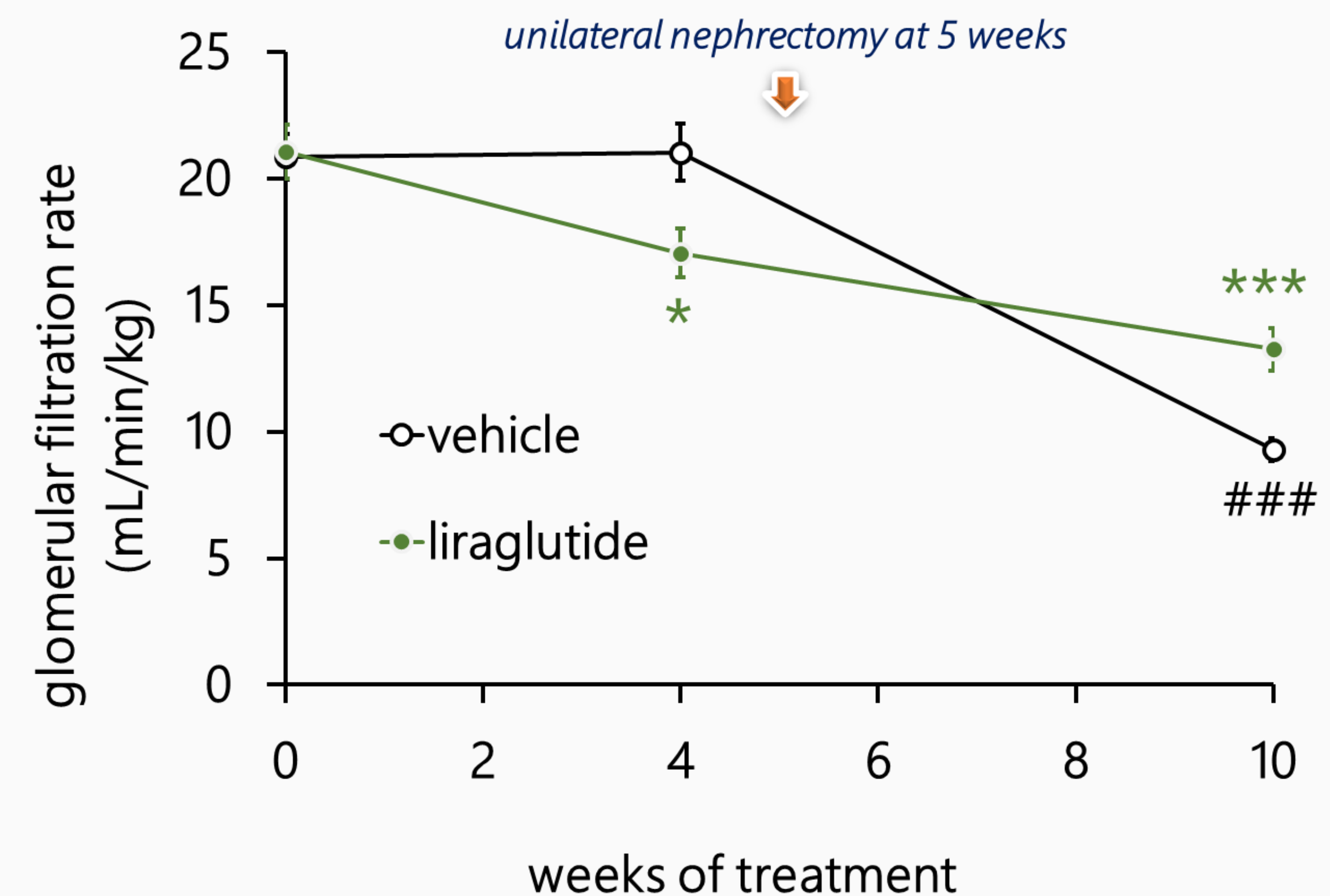
## RESULTS

### 1 Liraglutide reduces body weight, blood glucose and urine albumin/creatinine ratio in SDT fatty rats



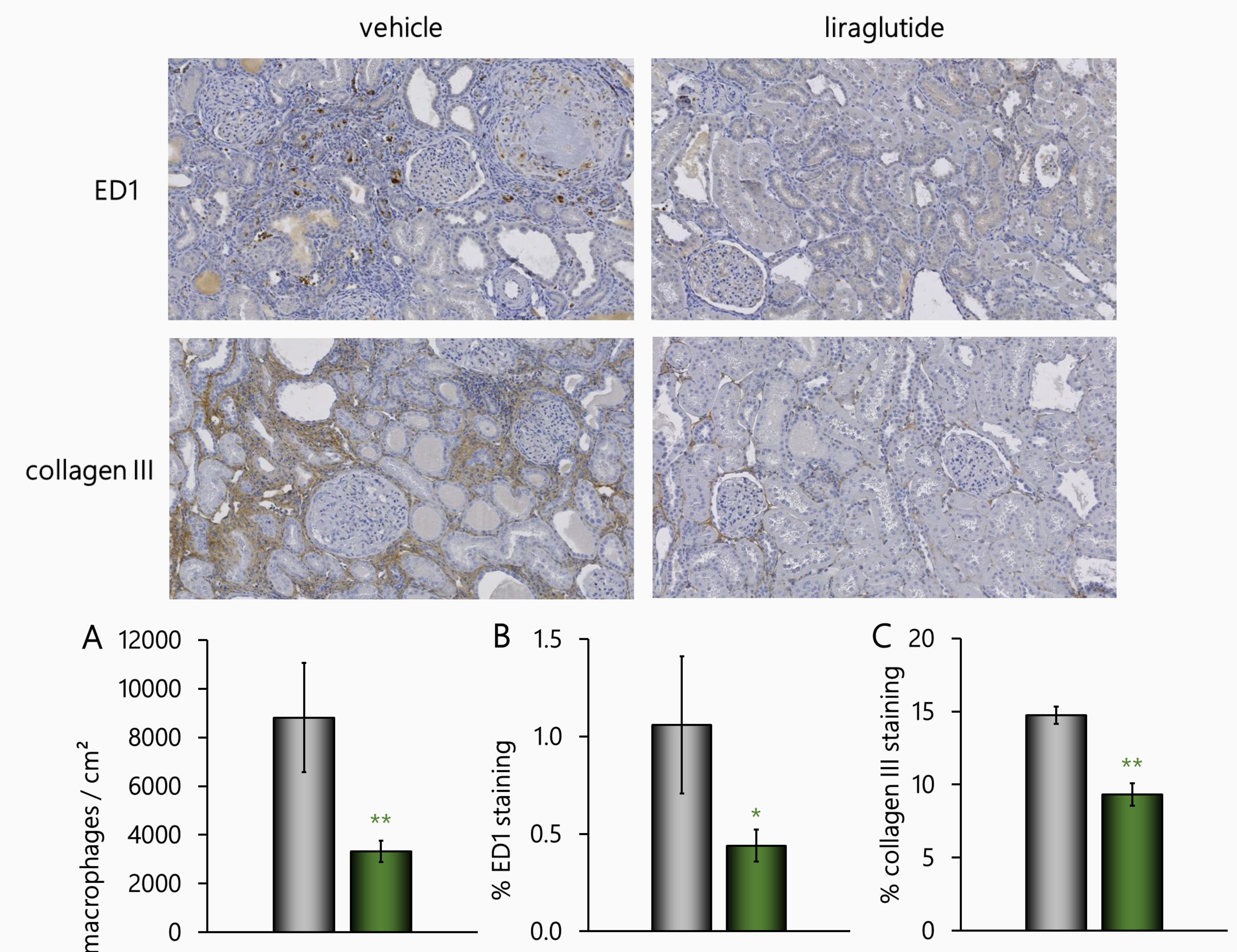
Body weight (A), body weight gain (B), fed blood glucose follow-up (C) and urine albumin/creatinine ratio (D) in SDT fatty rats treated with vehicle or liraglutide 0.4mg/kg QD s.c. for 10 weeks, with unilateral nephrectomy at 5 weeks of treatment. Data are shown as mean ± SEM. \* $p < 0.05$ , \*\* $p < 0.01$  and \*\*\* $p < 0.001$  vs. *chow*.

### 2 Liraglutide significantly reduces glomerular hyperfiltration and glomerular filtration rate decline in SDT fatty rats



Glomerular filtration rate follow-up in SDT fatty rats treated with vehicle or liraglutide 0.4mg/kg QD s.c. for 10 weeks, with unilateral nephrectomy at 5 weeks of treatment. Data are shown as mean ± SEM. \* $p < 0.05$  and \*\*\* $p < 0.01$  vs. *vehicle*. ### $p < 0.001$  *vehicle* at 10 weeks vs. 4 weeks of treatment.

### 3 Liraglutide significantly reduces renal inflammation and fibrosis in SDT fatty rats



Representative ED1 and collagen III immunostaining (upper panel), macrophages density (A), % ED1 staining (B) and % collagen III staining (C) in vehicle or liraglutide 0.4mg/kg QD s.c. for 10 weeks. Data are shown as mean ± SEM. \* $p < 0.05$  and \*\* $p < 0.01$  vs. *vehicle*.

## CONCLUSION

The GLP-1 receptor agonist LIRA induces significant benefits on kidney dysfunction by reducing hyperfiltration and preventing GFR decline, and improves renal inflammation and fibrosis, in the uni-nephrectomized SDT fatty rat.