



Liraglutide improves both diabetic nephropathy and cardiomyopathy in the SDT Fatty rat, a cardiorenal model of Type 2 diabetes



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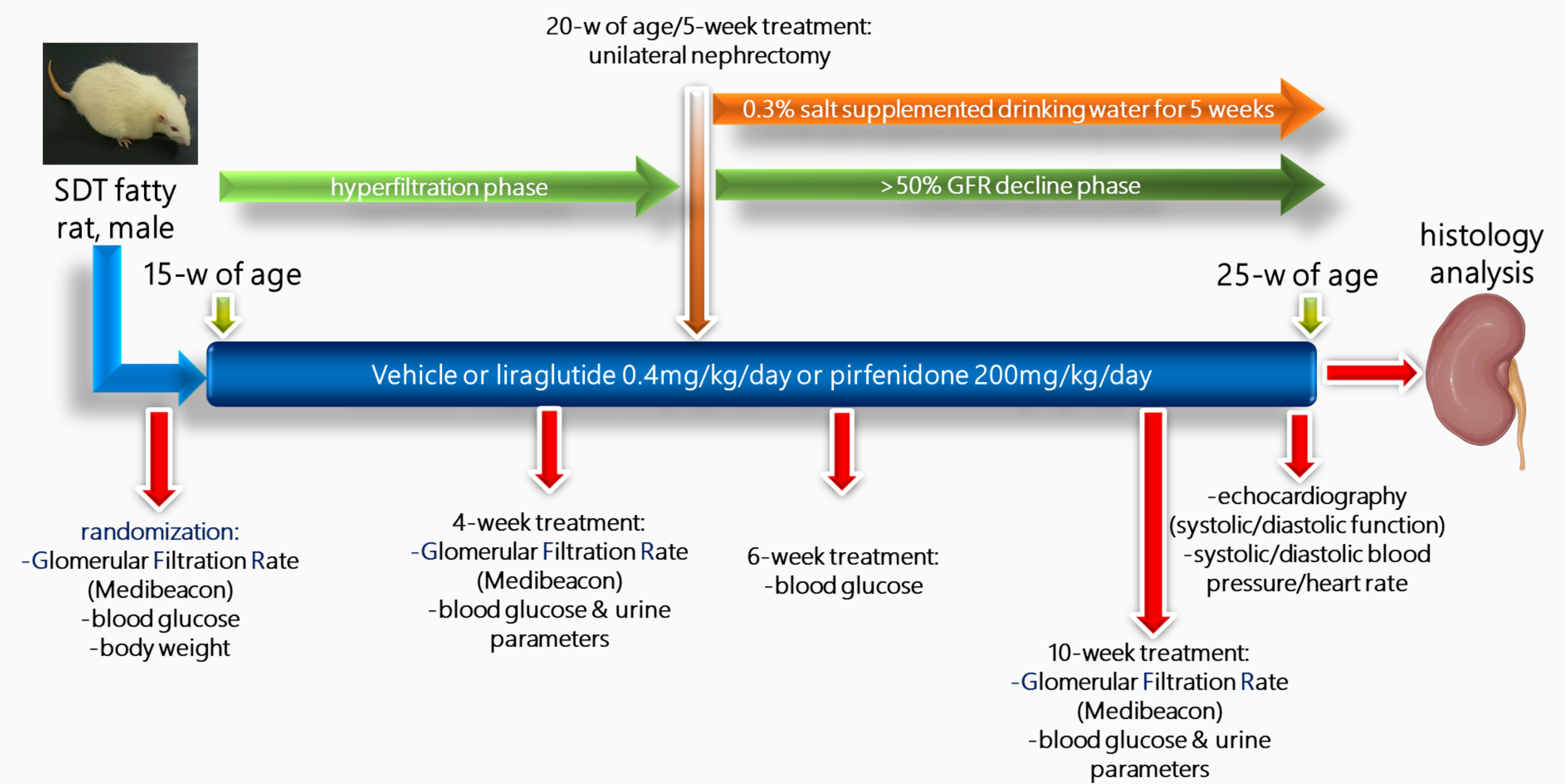
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BACKGROUND:

The Glucagon-Like Peptide 1 (GLP-1) receptor agonist liraglutide (LIRA) has cardioprotective effects and may reduce the development of kidney disease in type 2 diabetic patients. We here evaluated the effects of LIRA on both kidney and heart function in the Spontaneously Diabetic Torii (SDT) fatty rat, a type 2 diabetic cardiorenal model.

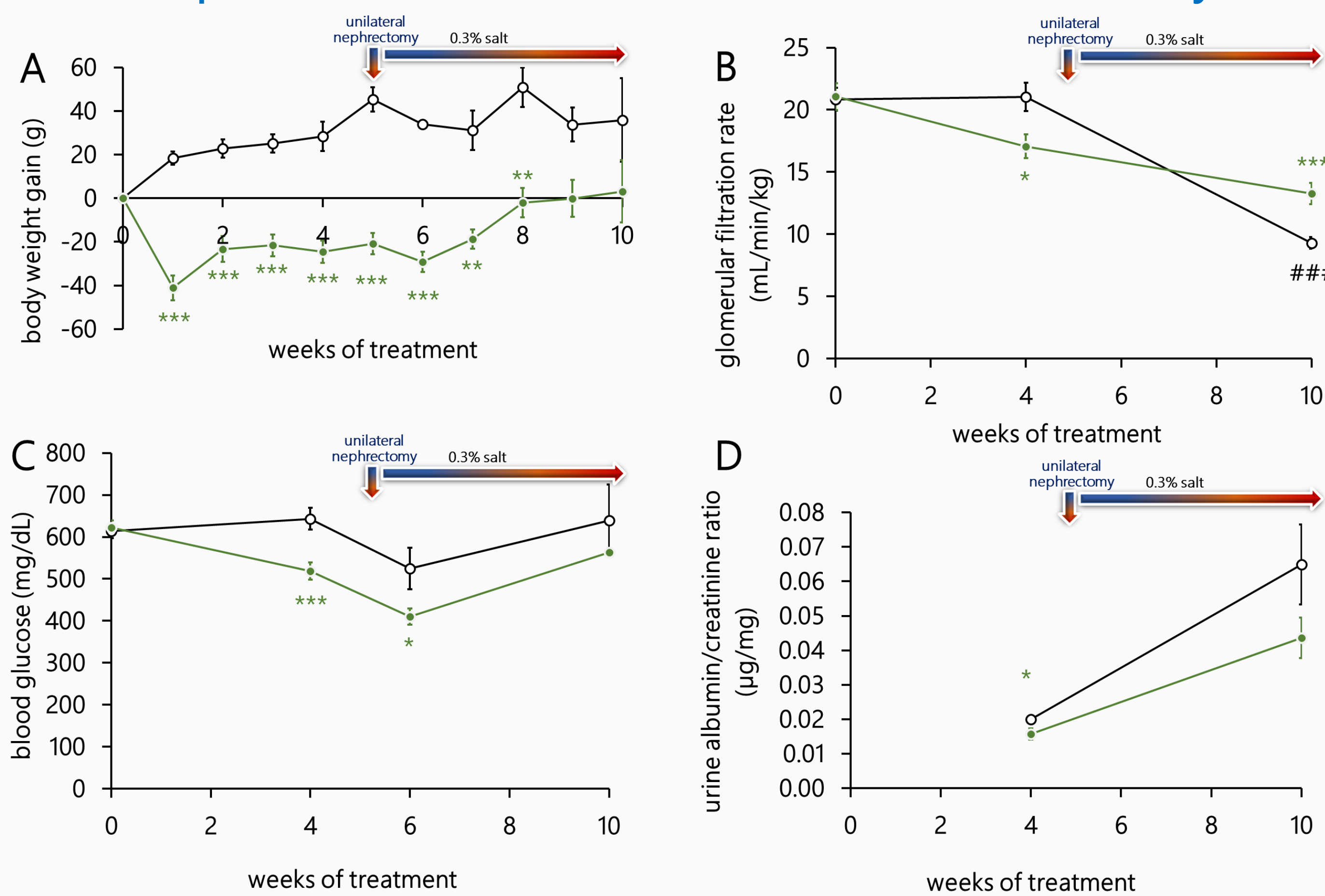
METHODS:

SDT fatty male rats were treated subcutaneously with vehicle or LIRA 0.4mg/kg QD for 10 weeks. To measure the effects of LIRA on glomerular hyperfiltration, rats were injected with FITC-sinistrin to measure glomerular filtration rate (GFR) at 4 weeks of treatment. At 5 weeks of treatment, rats underwent unilateral nephrectomy and were put on a 0.3% salt diet to induce a GFR decline. GFR was then measured at 10 weeks of treatment, before hemodynamics measurement and echocardiography.



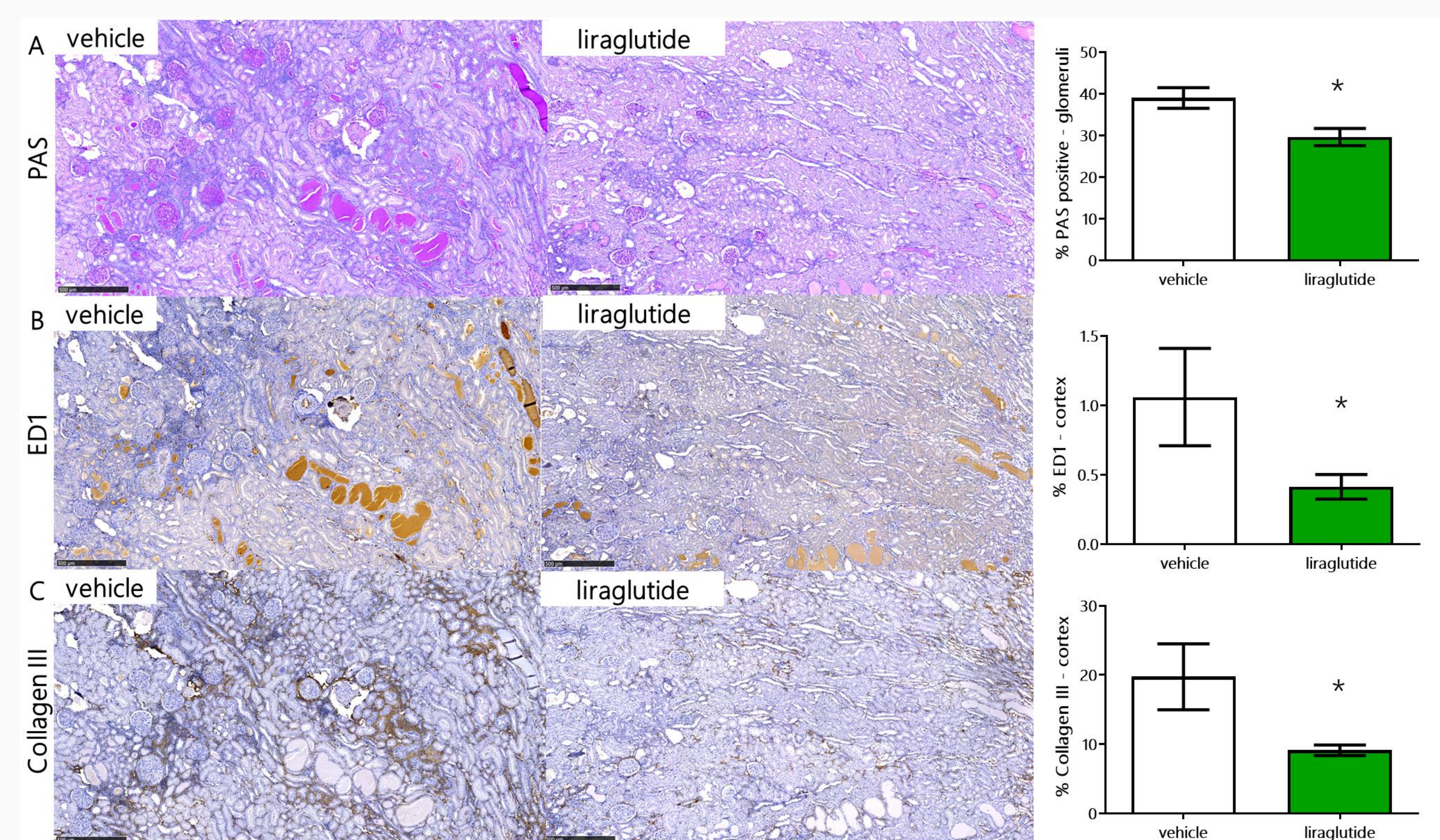
RESULTS:

1 Liraglutide prevents body weight gain, reduces fed glycemia, and improves alterations in GFR and ACR in SDT fatty rats.



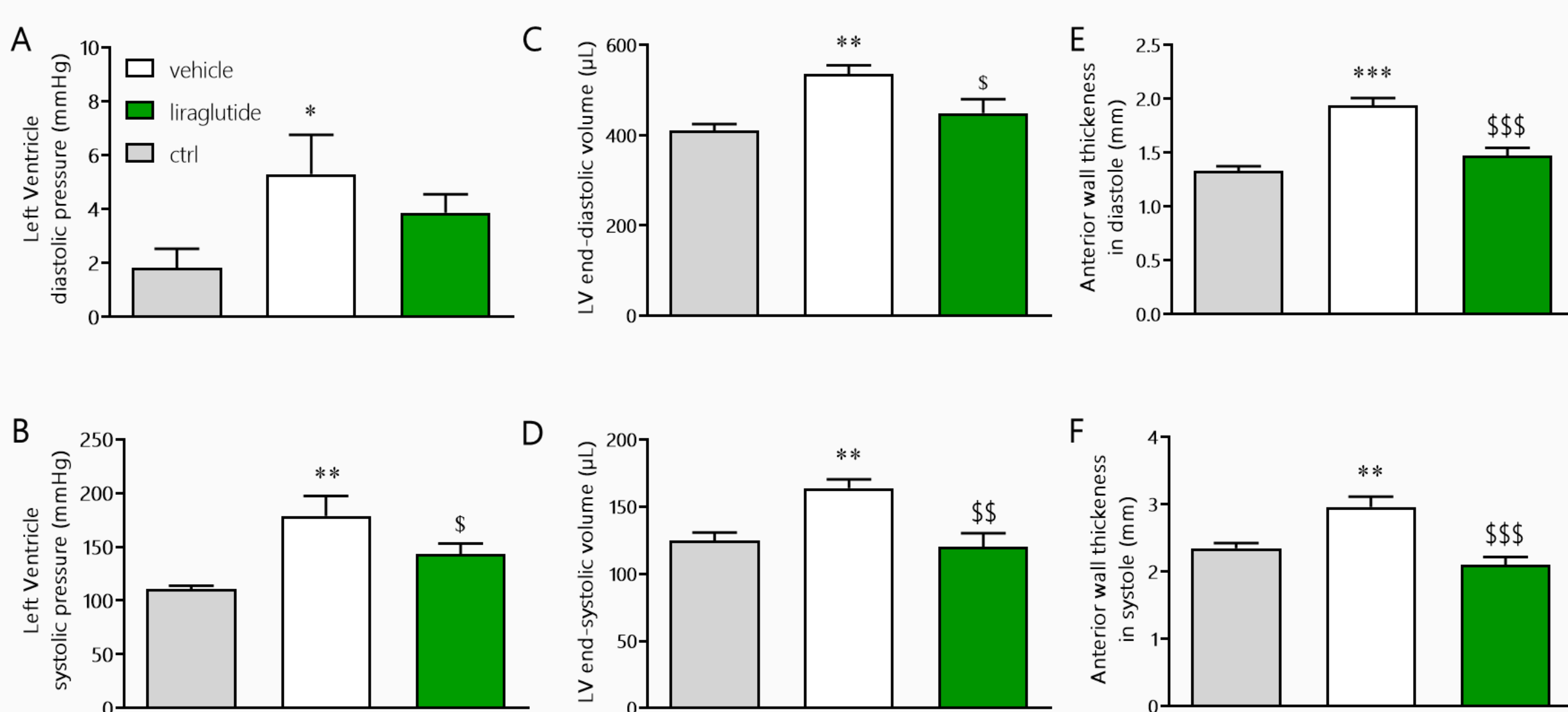
Body weight gain (A), glomerular filtration rate (B), fed blood glucose levels (C), and urine albumin/creatinine ratio in SDT fatty rats treated for 10 weeks with vehicle or liraglutide s.c. QD. **p*<0.05, ***p*<0.01 and ****p*<0.001 vehicle vs. liraglutide

2 Liraglutide improves kidney lesions in SDT fatty rats



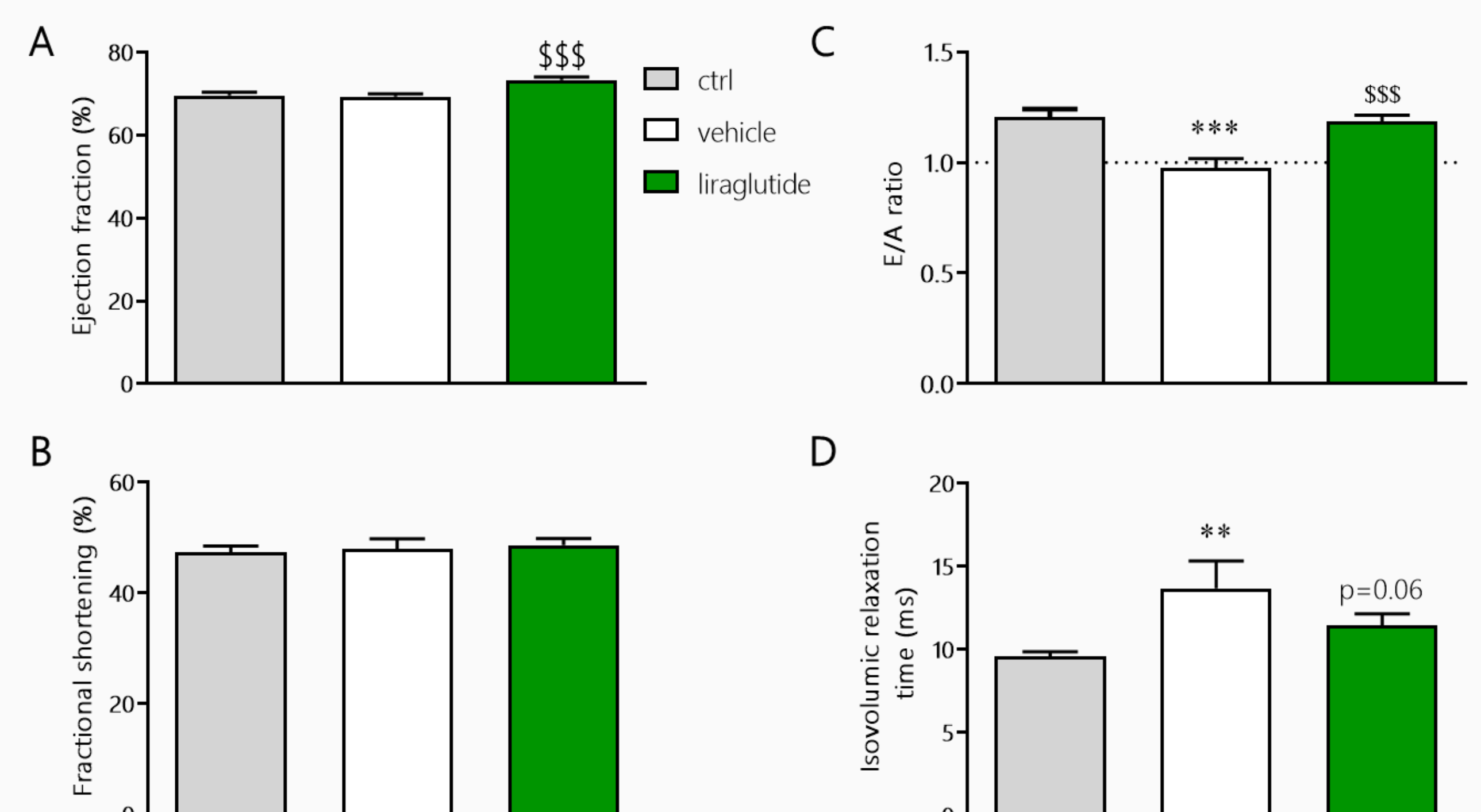
Representative pictures and % labelling for Periodic Acid Schiff (PAS) staining (A), ED1 (B) and Collagen III (C) immunostaining in SDT fatty rats treated for 10 weeks with vehicle or liraglutide s.c. QD. **p*<0.05 vehicle vs. liraglutide

3 Liraglutide reduces left ventricle end-systolic pressure and cardiac hypertrophy in SDT fatty rats



Left ventricle pressure (A-B), left ventricle volume (C-D) and left ventricle anterior wall thickness (E-F)- in diastole and systole in SDT fatty rats treated with vehicle or liraglutide for 10 weeks. Values from normal rats (ctrl) are shown for baseline values. **p*<0.05, ***p*<0.01, ****p*<0.001 ctrl vs. vehicle. \$*p*<0.05, \$\$*p*<0.01, \$\$\$*p*<0.001 vehicle vs. liraglutide

4 Liraglutide improves heart failure with preserved ejection fraction observed in SDT fatty rats



Left ventricle ejection fraction (A) and fractional shortening (B), E/A ratio (C) and isovolumic relaxation time (D) in SDT fatty rats treated with vehicle or liraglutide for 10 weeks. Values from normal rats (ctrl) are shown for baseline values. ***p*<0.01, ****p*<0.001 ctrl vs. vehicle. \$*p*<0.05, \$\$*p*<0.01, \$\$\$*p*<0.001 vehicle vs. liraglutide

CONCLUSION

In the SDT fatty rat, LIRA shows significant benefits by reducing renal hyperfiltration, preventing GFR decline, and improving cardiac hypertrophy, blood pressure and diastolic dysfunction. This preclinical model will be useful to evaluate drugs targeting the cardiorenal axis in type 2 diabetes.