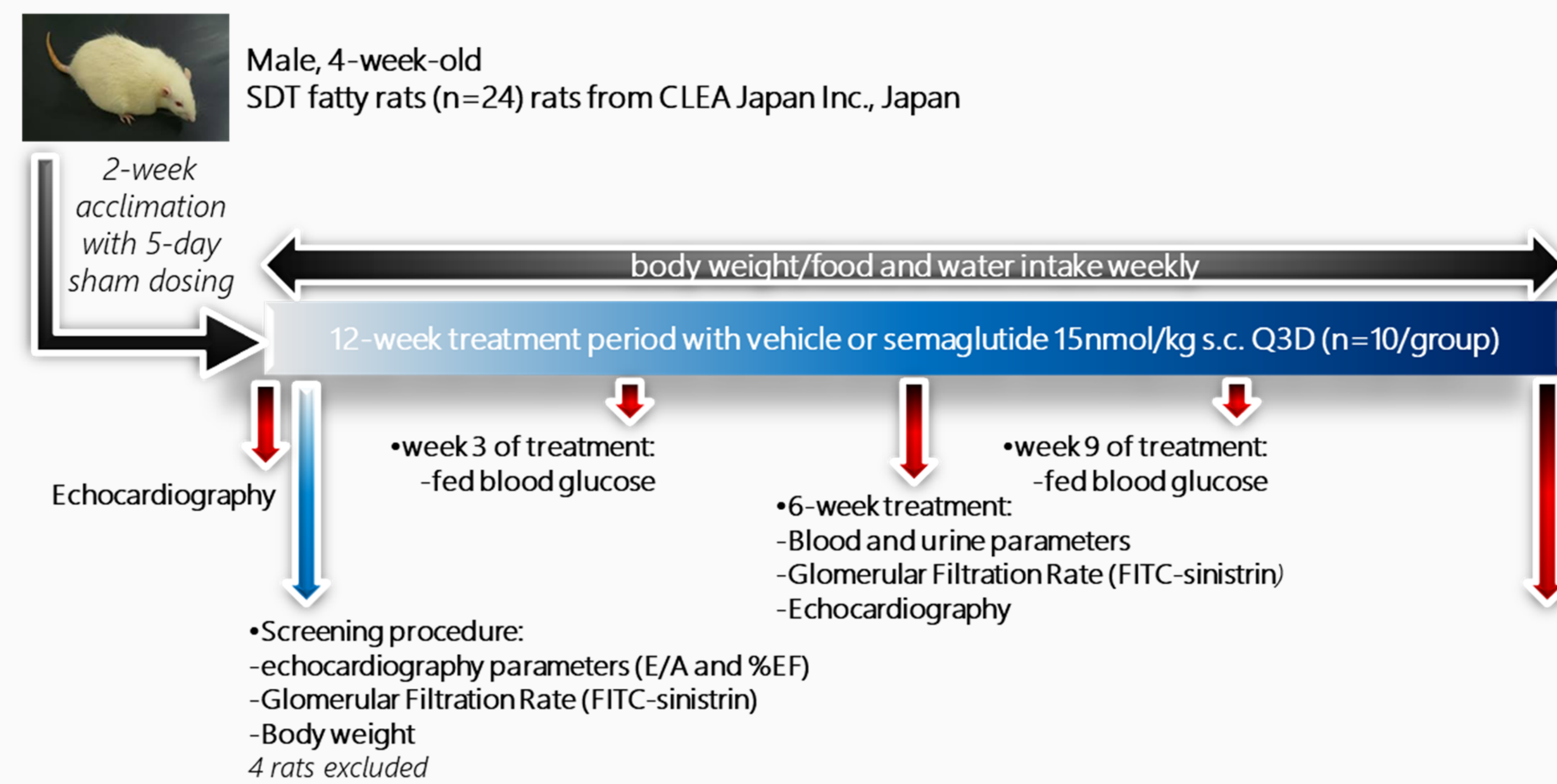


## BACKGROUND:

The high prevalence of cardiovascular-kidney-metabolic (CKM) syndrome in the population requires novel therapeutics to reduce cardiovascular death, and to this aim, predictive animal models are needed. Here we evaluated the effects of the GLP-1 receptor agonist semaglutide on kidney dysfunction and left ventricle diastolic dysfunction in the Spontaneously Diabetic Torii (SDT) fatty rat, a new type 2 diabetic animal model of CKM syndrome.

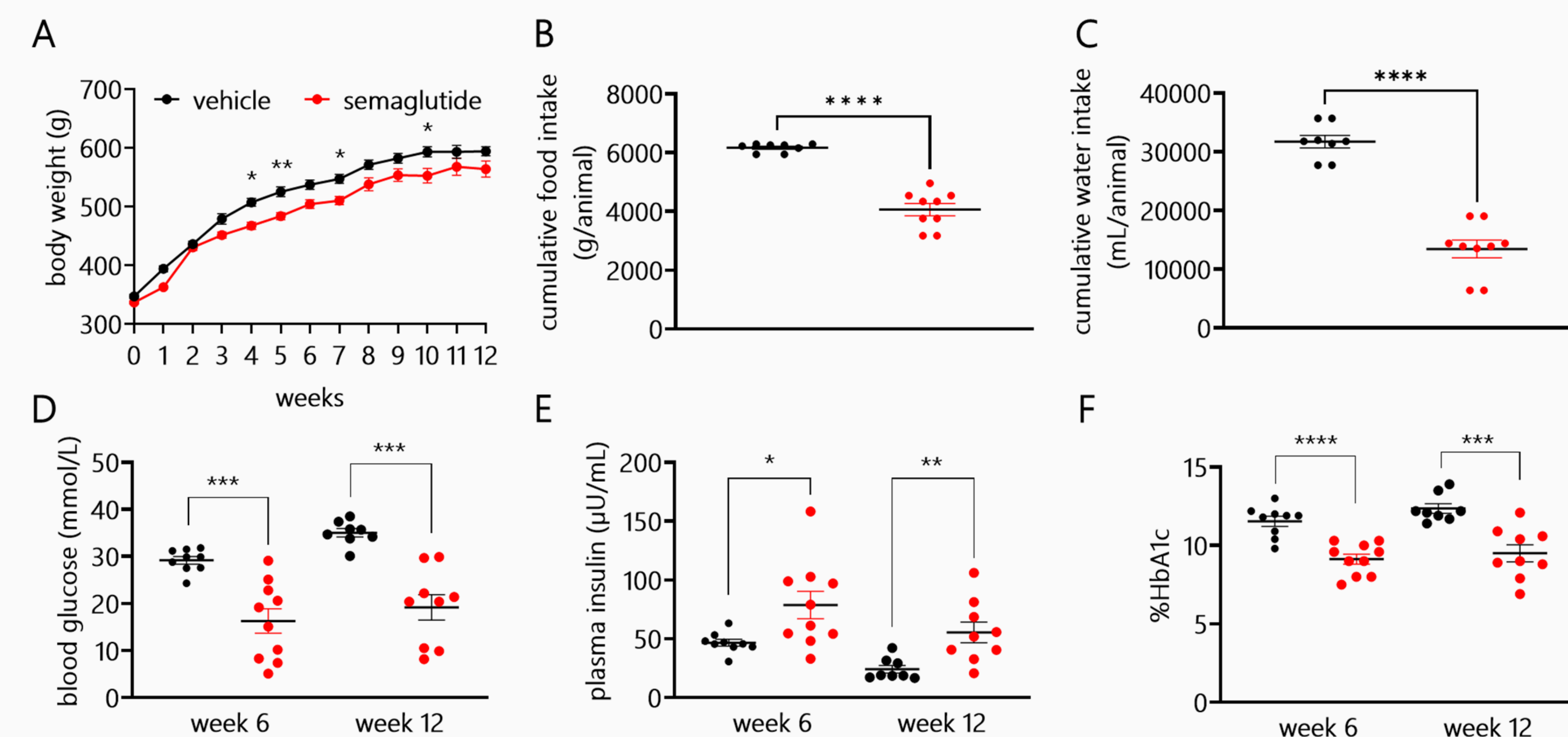
## METHODS:



Male, 6-week-old SDT fatty rats were treated with vehicle or semaglutide 15 nmol/kg s.c. Q3D for 12 weeks. At 6 weeks and 12 weeks of treatment, urine parameters and glomerular filtration rate (GFR) were measured, and cardiac function was investigated by echocardiography.

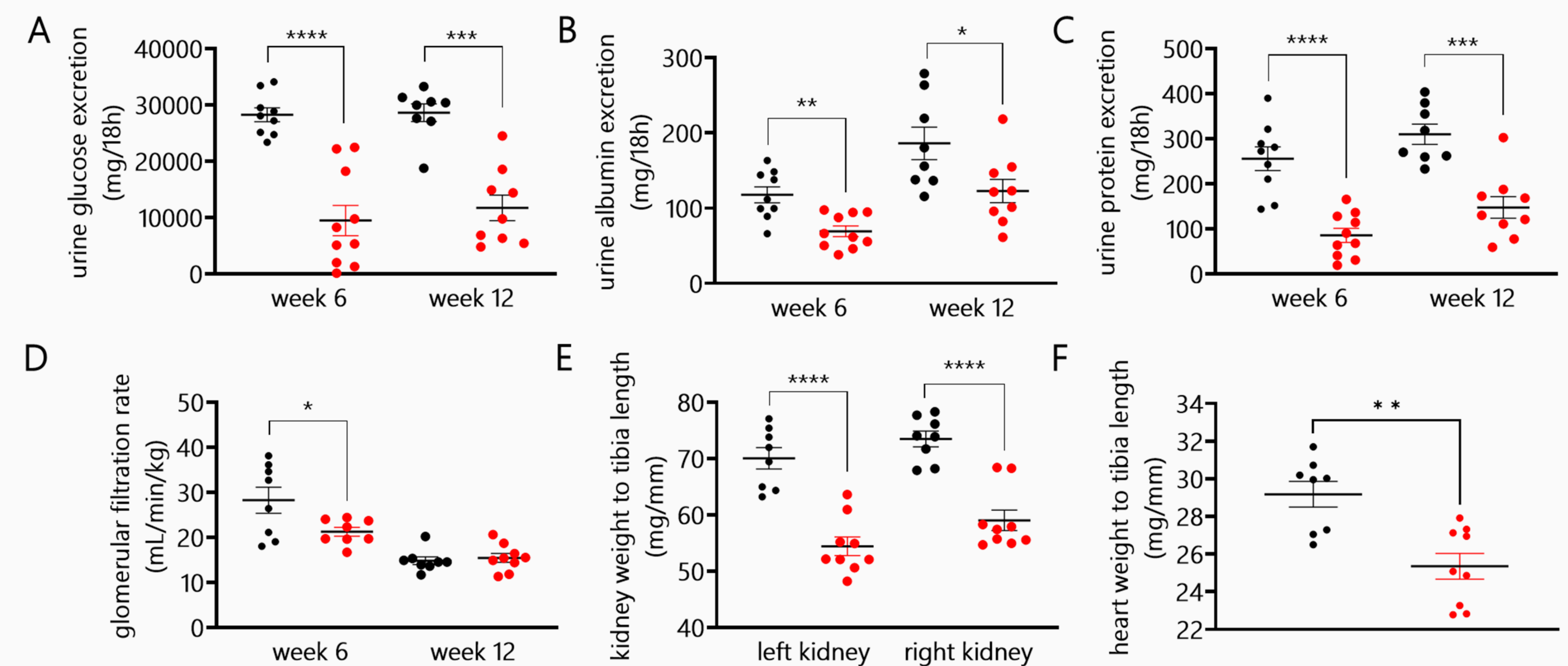
## RESULTS:

### 1 Semaglutide reduces body weight and improves glycemic control in SDT fatty rats.



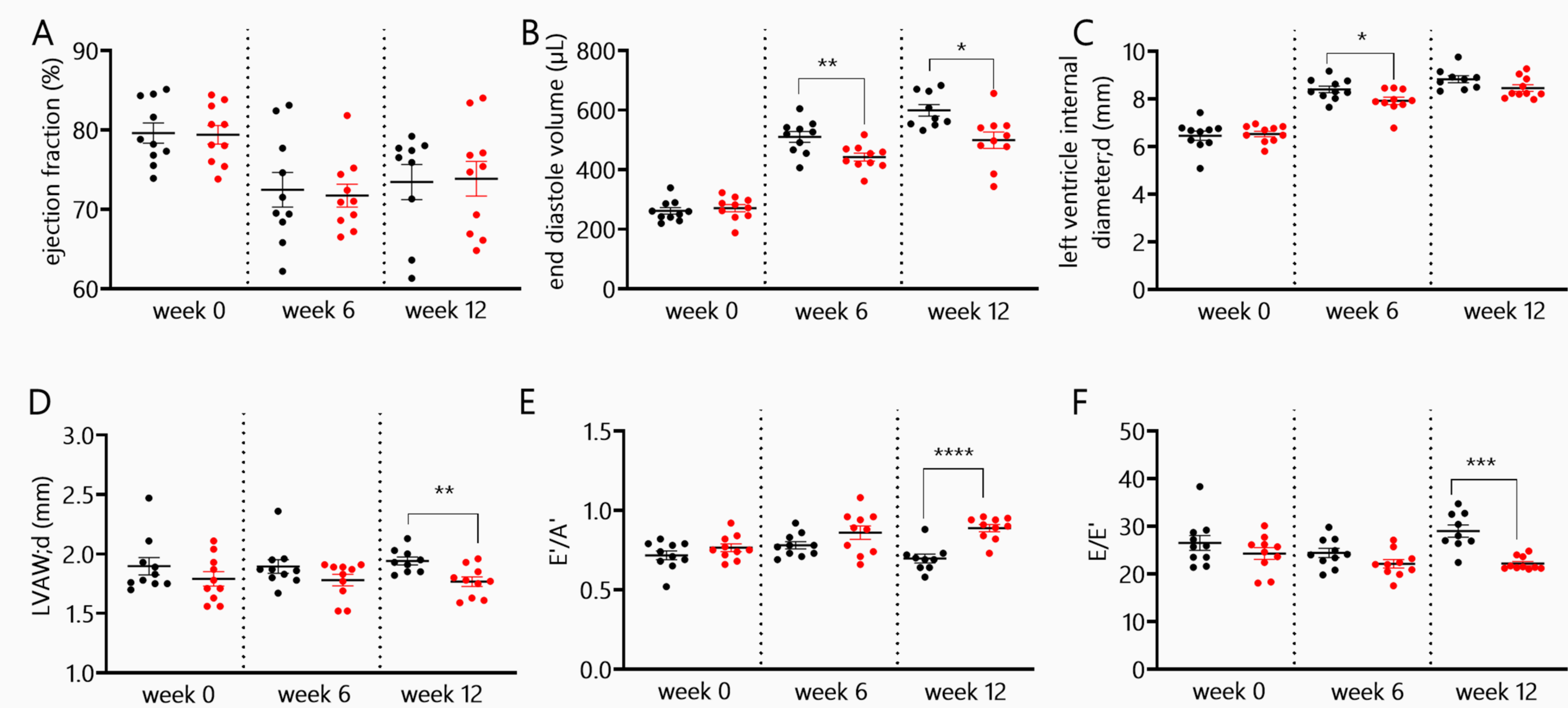
Body weight (A), cumulative food intake (B) and water intake (C), fasting blood glucose (D), plasma insulin (E) and %HbA1c (F) in SDT fatty rats treated with vehicle or semaglutide 15nmol/kg s.c. Q3D for 12 weeks. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$  and \*\*\*\* $p < 0.0001$

### 2 Semaglutide improves kidney function and reduces kidney and heart hypertrophy in SDT fatty rats.



Urine glucose (A), albumin (B) and protein (C) excretion, glomerular filtration rate (D) kidney (E) and heart (F) weight in SDT fatty rats treated with vehicle or semaglutide 15nmol/kg s.c. Q3D for 12 weeks. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$  and \*\*\*\* $p < 0.0001$

### 3 Semaglutide does not alter ejection fraction but significantly improves diastolic dysfunction in SDT fatty rats.



Left ventricle ejection fraction (A), end diastole volume (B) internal diameter (C) and arterial wall (D), e' to a' ratio (E) and e to e' ratio (F) measured by echocardiography in SDT fatty rats treated with vehicle or semaglutide 15nmol/kg s.c. Q3D for 12 weeks. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$  and \*\*\*\* $p < 0.0001$

## CONCLUSION

- Our data indicate that a 12-week treatment with semaglutide improved both kidney dysfunction and HFpEF in the SDT fatty rat.
- The SDT fatty rat represents a translational model for evaluating therapies targeting CKM syndrome versus the standard of care semaglutide.