A 6-WEEK TREATMENT WITH SEMAGLUTIDE IMPROVES BOTH KIDNEY DYSFUNCTION AND HEART FAILURE WITH PRESERVED EJECTION FRACTION IN THE SDT FATTY RAT MODEL

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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 heart failure with preserved ejection fraction (HFpEF) in the Spontaneously Diabetic Torii (SDT) fatty, as a type 2 diabetic rat 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 6 weeks. At the end of the treatment, glomerular filtration rate (GFR) was measured using transdermal fluorescence measurement after FITC-sinistrin i.v. injection and cardiac function was investigated by echocardiography.

Male, 4-week-old
SDT fatty rats from CLEA Japan, Japan

2-week acclimation with 5-day sham dosing

body weight/food and water intake weekly

6-week treatment period on Purina 5008 chow diet

Randomization procedure (body weight)

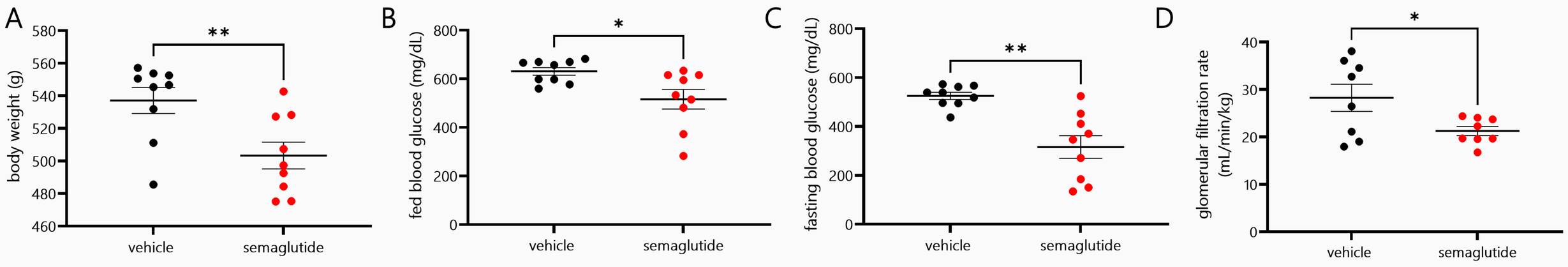
Week 3 of treatment: fed blood glucose

Week 6 of treatment: 6-hour fasting glucose, GFR (FITC-sinistrin), Echocardiography

Treatment groups (n=10 per group, 2 rats per cage):
- group 1: vehicle s.c. Q3D
- group 2: semaglutide s.c. Q3D

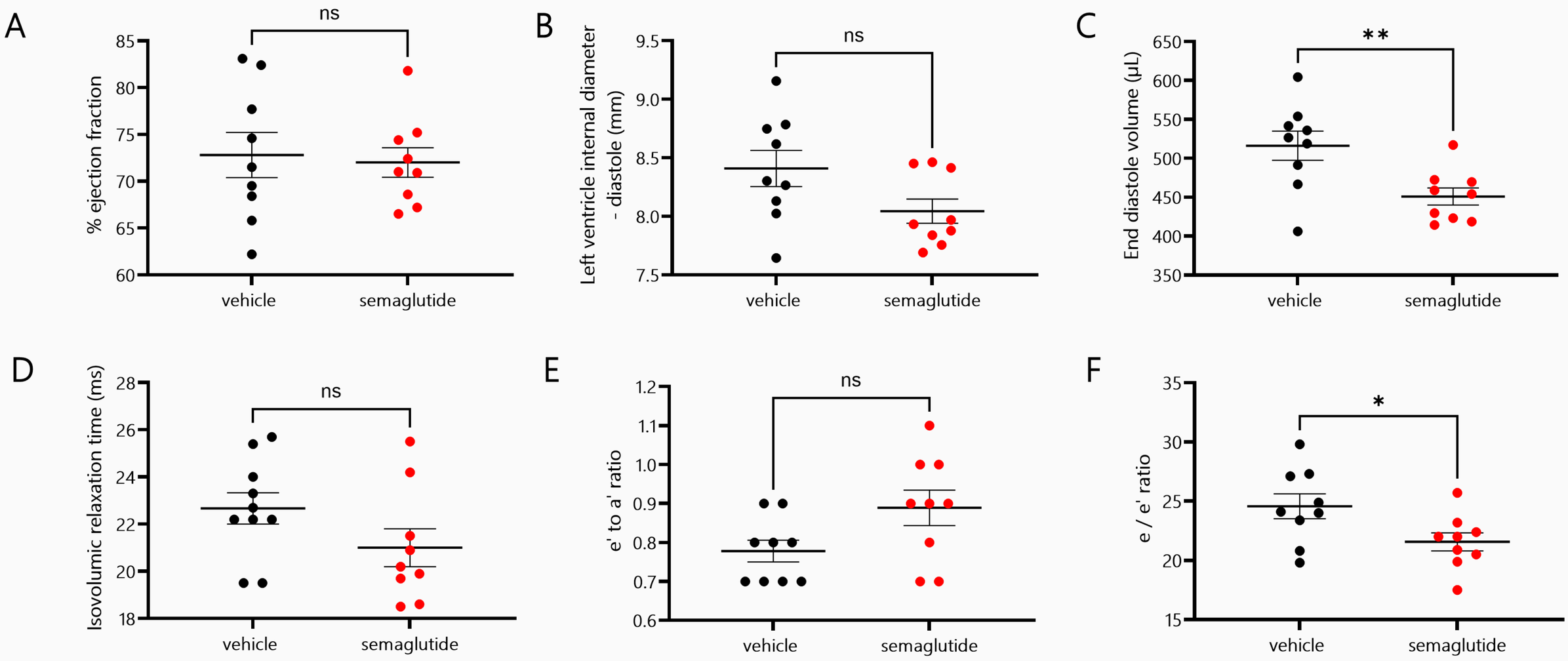
RESULTS:

1 Semaglutide treatment reduces body weight, hyperglycemia and glomerular hyperfiltration



Body weight (A), fed blood glucose (B), fasting blood glucose (C), and glomerular filtration rate (D) in SDT fatty rats treated with vehicle or semaglutide 15nmol/kg s.c. Q3D for 6 weeks.
**p<0.05 and **p<0.01 vs. vehicle.*

2 Semaglutide does not alter left ventricle ejection fraction but improves diastolic function



Left ventricle ejection fraction (A), internal diameter in diastole (B), end diastole volume (C), isovolumic relaxation time (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 6 weeks.
**p<0.05 and **p<0.01 vs. vehicle.*

CONCLUSION

- Our data indicate that a 6-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.

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