FGF23 impairs microvascular function and myocardial perfusion in experimental renal failure

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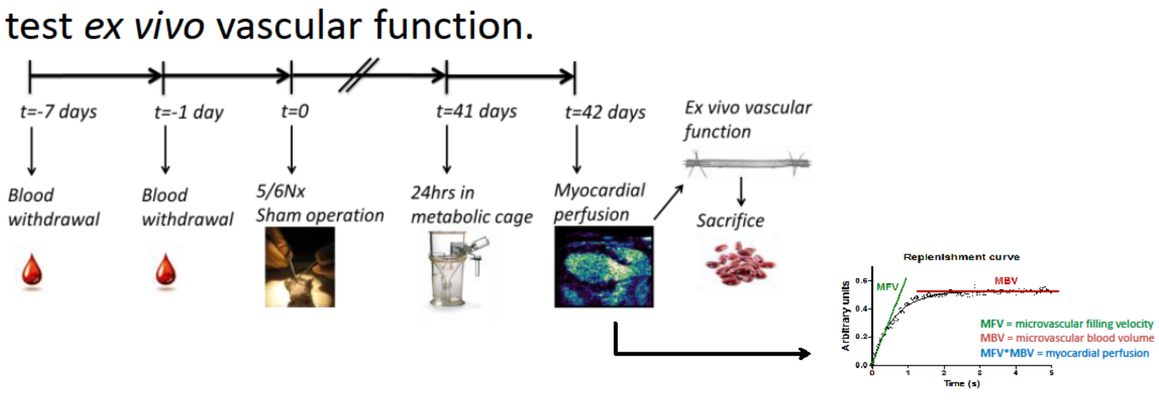
Background and Aim:

- Chronic kidney disease is associated with increased cardiovascular mortality
- FGF23 is a phosphate lowering protein and is highly increased in CKD
- FGF23 is associated with cardiovascular mortality and endothelial dysfunction

We hypothesized that CKD impairs vascular function and myocardial perfusion and that this can be partly attributed to FGF23.

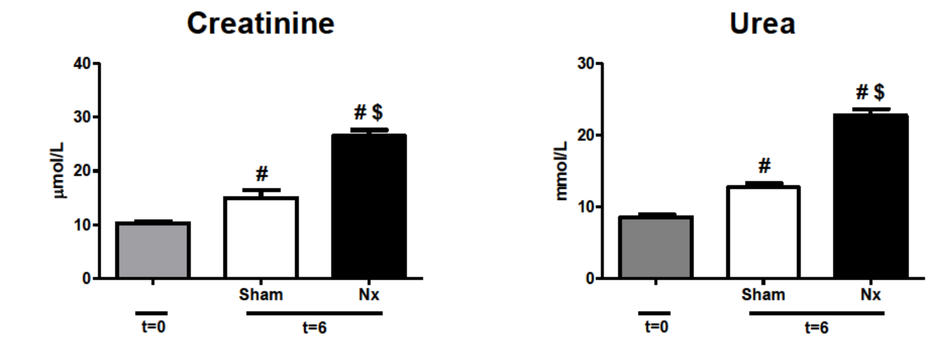
Methods:

Eight week old male wild type C57Bl/6J mice were subjected to partial nephrectomy (5/6Nx) or sham-surgery, and after 42 days mice were placed into a metabolic cage and subjected to myocardial contrast echocardiography (MCE) to test myocardial perfusion and a pressure myograph setup to test *ex vivo* vascular function.



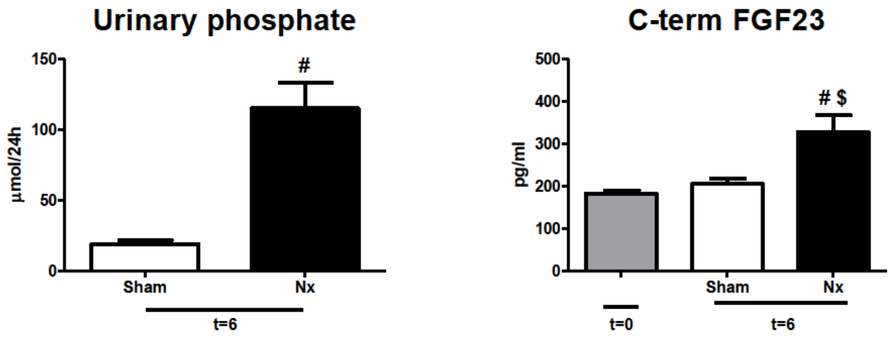
Results:

1) 5/6Nx-subjected mice develop renal failure



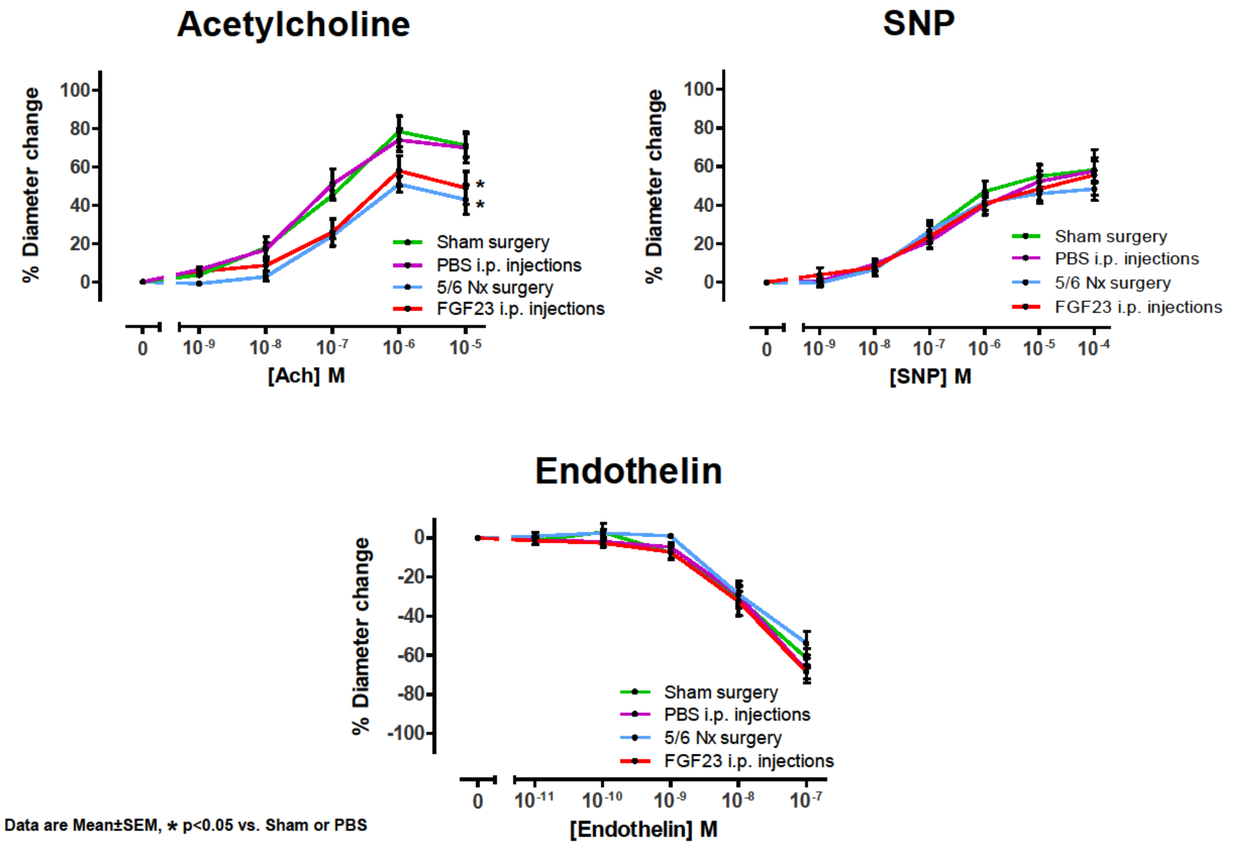
Data are Mean±SEM, # p<0.05 vs. t=0, $ p<0.05 vs. sham

2) 5/6Nx results in increased phosphate excretion through increased plasma FGF23 levels



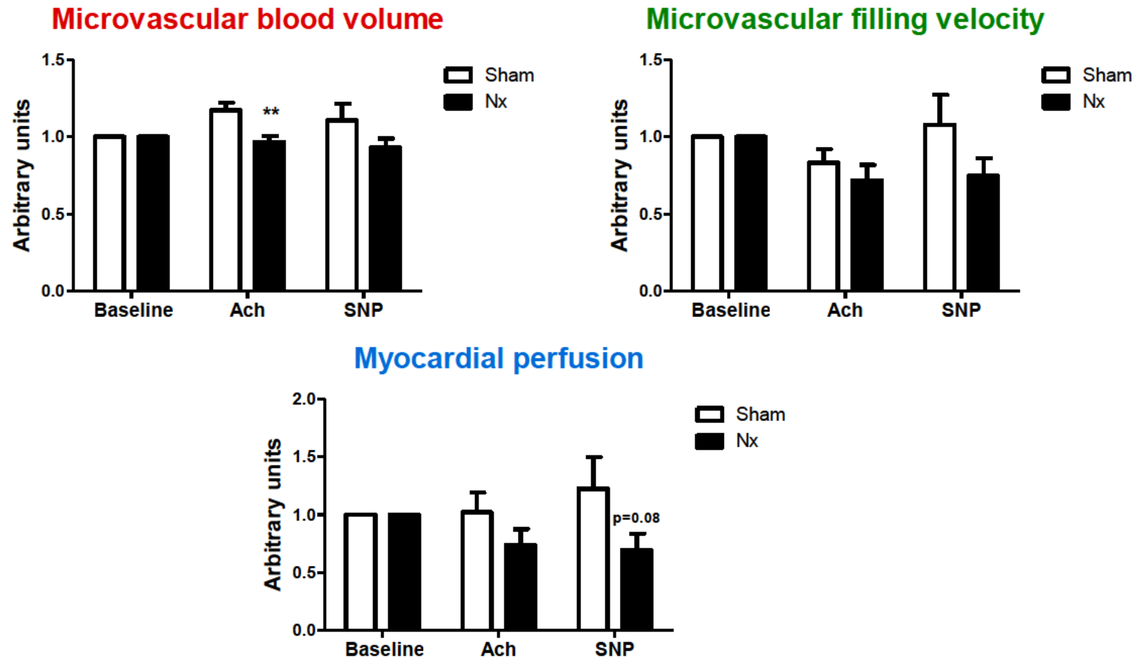
Data are Mean±SEM, # p<0.05 vs. t=0, $ p<0.05 vs. sham

3) FGF23 impairs endothelium-dependent, but not independent vasodilation



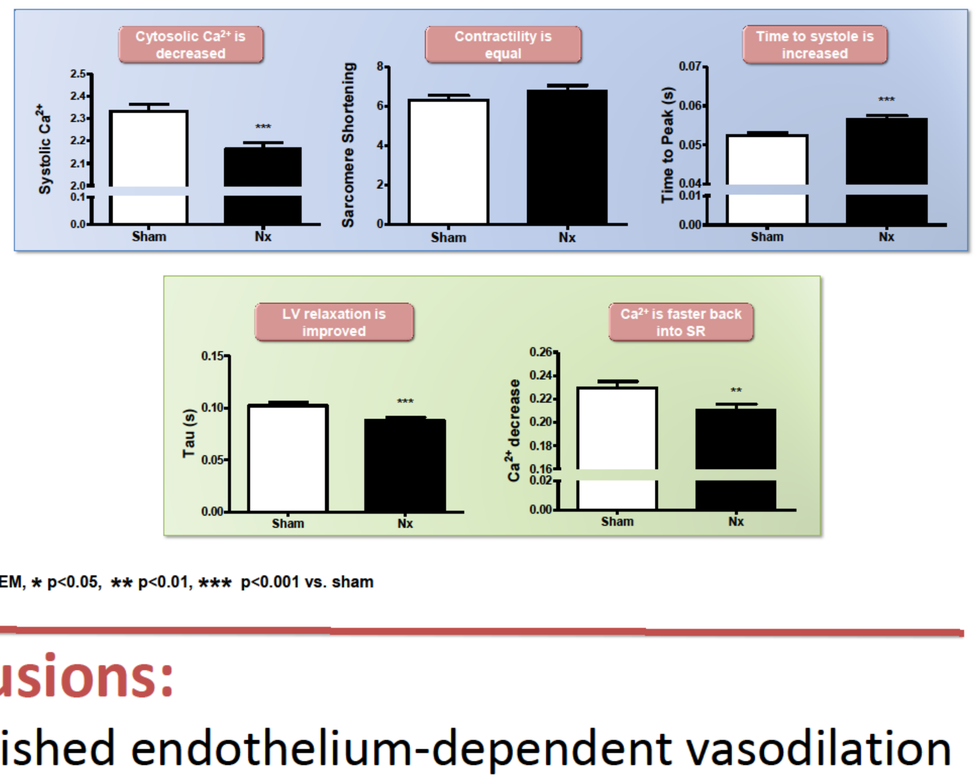
Data are Mean±SEM, * p<0.05 vs. Sham or PBS

4) Experimental renal failure impaires myocardial perfusion reserve



Data are Mean±SEM, * p<0.05, ** p<0.01 vs. sham

5) Experimental renal failure affects calcium channels in cardiomyocytes



Data are Mean±SEM, * p<0.05, ** p<0.01, *** p<0.001 vs. sham

Conclusions:

- Diminished endothelium-dependent vasodilation of renal failure is mimicked by FGF23 injections in non-renal failure mice
- Renal failure compromises myocardial perfusion increments and cardiomyocyte calcium handling
- Currently it is unknown if these myocardial effects are also FGF23 mediated

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