Background and Aim
Cardiorenal syndrome (CRS) is an umbrella term covering disorders of the heart and the kidneys whereby dysfunction of the one organ may induce dysfunction of the other. Despite advances in treatment of both (chronic kidney disease (CKD) and cardiovascular disease (CVD), CRS remains a major health problem. The current study aimed at optimizing an animal model mimicking CRS in order to allow experimental evaluation of new treatment strategies.

Materials and Methods
• An adenine (0.25%) supplemented, high phosphate (P) diet was administrated to 56 male Wistar rats, which were sacrificed at different time-points: 3, 4, 5, 6, 7 and 8 weeks (n= 8 or 10/group) after start of adenine treatment. Control animals (n=4) which received standard diet were sacrificed at 8 weeks. Blood samples were taken at 2, 4, 6 and 8 weeks.
• The following aspects of CRS where studied: CKD, mineral-bone disorder (MBD), CVD and (iron deficient) anemia. Hereto the following parameters were followed-up during the study: serum creatinine, serum Ca, serum P, serum FGF-23, dynamic bone parameters, aortic Ca deposits, heart weight, serum NT-proANP, Hct, Hb, reticulocytes, spleen iron and serum hepcidin.

Results
Development of CKD and disturbed mineral balance
Serum creatinine, phosphate and FGF23 showed a statistically significant increase after respectively 2, 4 and 2 weeks and serum calcium significantly decreased after 6 weeks. These parameters became more severe during the course of the study and thus evidenced the development of a severe CKD and disturbed mineral balance.

Development of aortic calcification
Aortic calcification developed simultaneously with bone disease.

Development of iron deficient anemia
Animals promptly (week 2) developed a serious iron deficient anemia as evidenced by significantly steep decreases in Hct, Hb and reticulocyte levels and significant, steep increases in serum hepcidin and spleen iron.

Development of high turn over bone disease
High bone turnover disease developed from week 5 as evidenced by the quantification of static and dynamic bone parameters.

Development of cardiac hypertrophy
Finally the animals developed cardiac hypertrophy as demonstrated by significantly and steadily increasing heart weight (relative to whole body weight) and significantly increased NT-proANP levels.

Conclusions
The proposed animal model will for the first time allow to study the cardiorenal syndrome in all its aspects and will be useful to concomitantly evaluate effects of new treatment strategies on the various aspects of the cardiorenal syndrome.