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Heart Failure

A CANINE MODEL OF CHRONIC HEART FAILURE AND RENAL INSUFFICIENCY (CARDIORENAL SYNDROME)

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Authors: *Robert Brewer, Mengjun Wang, Keife Zhang, Ramesh Gupta, Sharad Rastogi, Gaetano Paone, Hani N. Sabbah, Henry Ford Hospital, Detroit, MI, USA*

Background: Renal insufficiency (RI) in patients with heart failure (HF) often referred to as "cardiorenal syndrome" (CRS), carries a poor prognosis. The development of new drugs to treat this complex syndrome is hindered by lack of animal models of CRS. We tested the hypothesis that a unilateral nephrectomy with increase in contralateral renal vein pressure in dogs with established HF would lead to RI with a rise in serum creatinine (sCr) and blood urea nitrogen (BUN) and development of proteinuria (PTN) and serve as a model of CRS.

Methods: Six dogs with coronary microembolization-induced HF (LV ejection fraction, EF <30%) were studied. A right nephrectomy was performed and the distal left renal vein was banded to increase proximal renal vein pressure from ~10 to ~35 mmHg. sCr and BUN were measured preoperatively (week 0) and at 1, 2, 3, 4, 7, and 8 weeks thereafter. A diuretic challenge (DC) was administered (furosemide 80 mg IV) to all dogs 3-4 weeks after surgery and sCr and BUN measured before and 5 hrs after DC. Protein level in urine was measured at weeks 0 and 8.

Results: All dogs developed RI evidenced by a rise in sCr and BUN that persisted for 8 weeks and rise in urine protein levels from 37±7 to 83±12 mg/dL ($p<0.001$). DC increased sCr from 1.3±0.1 to 1.6±0.1 mg/dL ($p<0.003$) and BUN from 24±1.8 to 33±1.8 mg/dL ($p<0.001$).

Conclusions: The results describe a dog model of chronic HF and RI (model of CRS) that manifest chronic kidney injury and responds to DC in a manner consistent with the response of CRS patients to IV diuretics.

Temporal Changes in sCr and BUN

Week	Baseline	1	2	3	4	7	8
sCr (mg/dL)*	0.9±0.1	1.8±0.3	1.5±0.1	1.4±0.1	1.3±0.1	1.4±0.1	1.4±0.1
BUN (mg/dL)*	13±1.5	26±1.7	22±4.2	25±1.9	22±2.3	21±1.6	27±1.2
*=p<0.001 based on Repeated Measures ANOVA							