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CHRONIC VAGAL NERVE STIMULATION IMPACTS BIOMARKERS OF HEART FAILURE IN CANINES

ACC Oral Contributions
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Background: Vagus nerve stimulation (VS) can attenuate cardiac remodeling and improve left ventricular (LV) function in heart failure (HF), presumably by restoring sympathetic-parasympathetic balance. This study examined protein expression and levels of circulating biomarkers in LV tissue and plasma of dogs with chronic HF treated with VS.

Methods: Dogs with microembolization-induced HF (LV ejection fraction <35%) were implanted with a VS cuff electrode and neurostimulator (Boston Scientific Corporation) and randomized to no therapy (control, n=4) or to VS therapy (n=3) for 3 months. LV tissue and plasma from normal dogs (n=4) was used for comparisons. Protein expression of interlukin-6 (IL-6), SERCA-2a, caspase-3, phosphorylated AKT, tumor necrosis factor (TNF)-alpha, and beta-adrenergic receptor kinase (BARK)-1 was measured in LV tissue with Western blots and quantified in densitometric units (du). NT-pro brain natriuretic peptide (BNP) in plasma and tissue levels of norepinephrine (NE) were measured using commercial enzyme immunoassay kits.

Results: VNS treatment improved expression of all LV proteins, increased tissue NE and reduced plasma nt-pro BNP (Table).

Conclusions: VS produced directionally favorable changes in tissue and plasma biomarkers suggestive of improvement in major pathways that govern progression of HF including apoptosis, inflammation, chamber remodeling, and calcium cycling. The findings provide additional support for VS as a promising therapy for chronic HF.

Biomarker	Normal (n=4)	Control (n=4)	VS (n=3)
IL-6 (du)	37 ± 3	57 ± 3	48 ± 1
SERCA-2a (du)	101 ± 11	47 ± 3	85 ± 12
Caspase-3, P-17 (du)	53 ± 3	66 ± 4	44 ± 7
Phosphorylated AKT (du)	78 ± 2	69 ± 1	81 ± 8
TNF-alpha (du)	47 ± 4	68 ± 3	55 ± 4
BARK-1 (du)	72 ± 4	85 ± 4	70 ± 2
NE (pg/mg of LV tissue)	1236 ± 36	722 ± 55	1009 ± 77
	Baseline	Pre-Treatment	Post-Treatment
Plasma Nt-Pro-BNP (fmols/ml)	154 ± 14	399 ± 28	133 ± 16