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Heart Failure

GENE EXPRESSION OF THE UBIQUITIN-PROTEASOME PATHWAY IS REFLECTED BY VENTILATORY EXPIRED GAS ANALYSIS INDICES AT PEAK EXERCISE IN HEART FAILURE

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Background: While atrogene expression has been demonstrated to determine key aspects of skeletal muscle atrophy and physiology in animal heart failure (HF) models, effects in humans are less well-explored.

Methods: Male systolic HF patients and age-matched controls were assessed. Real-time polymerase chain reaction was used to measure gene expression in vastus lateralis skeletal muscle biopsies. Cardiopulmonary exercise testing (CPX) was used to quantify aerobic capacity (peak oxygen consumption [VO2], ventilatory efficiency [VE/VCO2] slope, and peak partial pressure of end-tidal carbon dioxide [peak PETCO2]).

Results: 51 adults (23 HF age 67.3 ± 9.5 and 28 controls age 66.9 ± 10.3) were assessed. Peak VO2 (14.9±3.4 vs. 22.8±6.5; p<0.0001), VE/VCO2 (34.5±9.4 vs. 28.9±5.2; p<0.01), and PETCO2 (33.7±6.3 vs. 39.2±5.3; p<0.0001) were reduced in HF, yet atrogene expression was similar. Correlations between atrophy-related gene expression and peak exercise indices were significant in controls, but not in HF patients (Table).

Conclusion: While skeletal muscle atrogene expression is associated with lower aerobic performance in adults with normal cardiac function, low cardiac output may overpower these relationships in HF patients.

Table

	Peak VO_2		Peak VE/VCO_2		Peak $P_{ET}CO_2$	
	HF	Control	HF	Control	HF	Control
Atrogin-1	0.41	-0.37	-0.16	0.29	0.36	-0.42*
MuRF-1	-0.16	-0.46*	-0.01	0.14	0.20	-0.34
UBB	0.12	-0.41*	-0.11	0.12	0.28	-0.34
UBC	0.48*	-0.41*	-0.35	0.16	0.55**	-0.29
FOXO1	-0.14	-0.52**	-0.07	0.07	0.14	-0.17
FOXO3	-0.04	-0.58**	0.11	0.15	0.17	-0.31

*p<0.05, **p<0.01