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DOES GROWTH HORMONE DEFICIENCY ASSOCIATED WITH AGE HAVE A ROLE IN DIASTOLIC DYSFUNCTION?

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Introduction: Delayed ventricular relaxation has been identified as a major component in the development of diastolic dysfunction specifically associated with cardiac aging. Impairment of ventricular relaxation often heralds a predictable decline in cardiac performance which may ultimately lead to congestive heart failure.¹ The pathophysiologic mechanisms responsible for this age-related diastolic dysfunction are likely related to alterations in high-amplitude growth hormone (GH) secretion and reduced concentrations of its circulating mediator, Insulin-like Growth Factor 1 (IGF-1). Administration of low-dose GH to aged animals improves myocardial structure and function.² We hypothesized that GH repletion would attenuate the decline in diastolic dysfunction of aging, thus we compared Doppler diastolic indices in GH-replete aged rats to age-matched saline-treated rats.

Methods: After ACUC approval, 10 old (24 mo) BN x F344 rats were randomized to receive either GH replacement (200 µg) (OGH) or saline (OSal) subcutaneously, twice daily. Three young (5 mo) rats treated with saline (YSal) were included as owing 6 months of GH or saline treatment, transthoracic echocardiographic examinations were performed under ketamine (60 mg/kg)/xylazine (5 mg/kg) anesthesia (im) using a 12 MHz probe and 4500 Philips scanner. 2D images were used to measure left ventricular (LV) dimen-

sions and wall thickness and M-mode was used to evaluate systolic function by % fractional shortening (FS). Transmittal Doppler flow indices including peak early (E_{max}) and late (A_{max}) filling velocities, E to A ratio, E wave deceleration time (E_{dec} t) and the rate of E wave decline (E_{dec} slope) were used to evaluate diastolic function. Differences among groups were determined by ANOVA ($p < 0.05$ was considered significant).

Results: Body weight and LV thickness were significantly greater in old vs. young rats, independent of GH replacement. Systolic function was unaffected by age or treatment (%FS: YSal=44 ± 1, OSal=47 ± 2, OGH=44 ± 2). In contrast, there was an age-associated decline in diastolic function and a strong tendency for GH-repletion to attenuate this effect. See Table 1.

Conclusions: We believe this data suggests that long-term GH replacement in aged rats may attenuate the diastolic impairment associated with normal aging independent of changes in systolic parameters. Ongoing research will determine whether the GH-induced functional improvement results from alterations in cardiac structure, microvascular flow, or neuroendocrine responses.

References:

1. *Ann Intern Med* 2002;137(8):631-9
2. *Cardiovasc Res* 2002;54:25-35

Table 1. Diastolic Indices

	HR (b/m)	E_{max} (cm/s)	A_{max} (cm/s)	E_{dec} t (sec)	E_{dec} slope (cm/s ²)	E/A
YSal (n=3)	281 ± 21	65 ± 2	30 ± 3	0.043 ± .001	14.6 ± 0.8	2.2 ± 0.1
OSal (n=5)	211 ± 9	52 ± 4	35 ± 4	0.057 ± .001	8.6 ± 0.6	1.5 ± 0.1
OGH (n=5)	189 ± 5	56 ± 4	26 ± 2	0.056 ± .009	10.5 ± 1.3	2.2 ± 0.3
	P<0.001		P=.14	P=0.06	P=0.01	P=0.07