DESPITE SARCOPENIA, AGING DOES NOT AFFECT MYOFIBER REGENERATIVE CAPACITY IN MICE

Heather M Hancock, Matthew McHale, Laurel Porter, Zaheer Sarwar, Linda M McManus, and Paula K Shireman

Departments of Surgery and Pathology, The University of Texas Health Science Center at San Antonio, San Antonio, TX
South Texas Veterans Health Care System, San Antonio, TX 78229

Introduction: Muscle maintenance is a lifelong process in which myofibers are removed and replaced, a response that is increased after muscle injury. Sarcopenia or the loss of muscle mass occurs with aging. One theory suggests that muscle regenerative capacity declines with age to the point that muscle regeneration cannot keep pace with injury that occurs through daily living activities. While multiple studies have quantitated sarcopenia in animal models of aging, few reports document recovery from injury in aged animals. We hypothesized that aged mice would exhibit impaired muscle regeneration defined as smaller fiber size and increased adipocyte accumulation as compared to young mice. Thus, the present study examined myofiber size and adipocyte accumulation within regenerated muscle in a murine model of aging.

Methods: Three age groups of wild type mice (C57Bl/6J) were studied: young (4-6 months old), middle (12-14 months), and old (25+ months) and included males and females (n=5-13/group). Mice were obtained at 8 weeks of age from Jackson Laboratories. Cardiotoxin (CTX) was injected into the right hind limb muscles to cause muscle injury. After fourteen days, the hind limb anterior muscle compartment was harvested, formalin fixed, paraffin embedded, sectioned and stained with H & E. Untreated animals (baseline) served as a control. Light microscopic histomorphometry was used to quantitate tibialis anterior myofiber size (cross-sectional area, μm^2) and intramuscular adipocyte content (% of regenerated muscle area).

Results: At baseline, female mice had smaller myofiber size at all ages as compared to male mice of the corresponding age (see Table). Although young and middle aged mice had similar baseline myofiber size, myofibers were considerably smaller in old animals of both sexes. After injury, regenerated myofiber size was proportionally comparable to that of baseline myofibers in male mice at all ages. Note that at 14 days post injury, myofiber size was not yet returned to baseline size. Similar patterns of myofiber regeneration were observed in female mice following CTX-induced injury.

Effect of Aging on Myofiber Size Before and After Injury

	Myofiber Cross-Sectional Area (μm^2)*			
	Male		Female	
	Baseline	14D post-CTX	Baseline	14D post-CTX
Young	2628 ± 52.1	1632 ± 101.6	2115 ± 68.4	1624 ± 81.5
Middle	2797 ± 62.7	1523 ± 43.6	2077 ± 60.7	1423 ± 36.9
Old	2090 ± 124.9	1402 ± 75.1	1499 ± 206.5	1326 ± 68.4

* values expressed as mean ± SE (n= 5 – 13/group)

Regardless of age, no intramuscular adipocytes were present at baseline in either male or female mice. Following injury, young, middle and old male mice had comparable increases of adipocyte accumulation within the areas of regenerated muscle (0.99 ± 0.24%, 1.1 ± 0.34% and 0.95 ± 0.38% respectively). Females shared a similar pattern of fat accumulation with increased fat as compared to corresponding aged males, *i.e.*, 2.9 ± 0.65%, 4.4 ± 0.49% and 2.1 ± 0.54%, respectively.

Conclusion: In an age-independent manner, female mice accumulated more adipose tissue within the area of muscle regeneration as compared to males. Nevertheless and despite sarcopenia, aging did not have a significant impact on myofiber regenerative capacity in either male or female mice.

Acknowledgements: Research supported in part by the Veterans Administration (Merit Review Grant), the National Institutes of Health (HL074236), and the United States Air Force.