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Age-related structural changes in upper extremity muscle tissue in a nonhuman primate model

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Background: Longitudinal studies of upper extremity aging in humans include logistical concerns that animal models can overcome. The vervet is a promising species with which to study aging-related processes. However, age-related changes in upper extremity muscle structure have not been quantified in this species. This study measured age-related changes to muscle structure, examined relationships between muscle structure and measures of physical performance, and evaluated the presence of rotator cuff tears.

Methods: Muscle structure (volume, optimal fiber length, and physiologic cross-sectional area (PCSA)) of 10 upper extremity muscles was quantified from the right upper limb of 5 middle-aged and 6 older adult female vervets.

Results: Total measured PCSA was smaller ($P = .001$) in the older adult vervets than in the middle-aged vervets. Muscle volume reduction predominate the age-related reductions in PCSA. Total measured PCSA was not correlated to any measures of physical performance. No rotator cuff tears were observed. Supraspinatus volume was relatively larger and deltoid volume relatively smaller in the vervet compared with a human.

Conclusions: The vervet is an appropriate translational model for age-related upper extremity muscle volume loss. Functional measures were not correlated to PCSA, suggesting the vervets may have enough strength for normal function despite loss of muscle tissue. Reduced relative demand on the supraspinatus may be responsible for the lack of naturally occurring rotator cuff tears.

Level of evidence: Basic Science Study, Anatomy, Animal Model.

Keywords: Aging; muscle; volume loss; function; primate

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Age-related changes to muscle structure and function in the upper limb are thought to be associated with progression to disability in humans, and thus, quantifying these features is important for providing context for healthy aging and also for other musculoskeletal disorders of the upper limb when they occur in an older patient group. Age-related changes to skeletal muscle are well known but have largely been evaluated in cross-sectional studies.[28] In the upper limb specifically, declines in muscle volume[1,36,43] and increased levels of fat and connective tissue[36] have been reported. Further, relationships between structural and functional changes are limited; longitudinal studies of the upper limb have primarily measured grip[8,16,26,35,41] or elbow strength,[3,10,15,34] but not more complex tasks, and corresponding measurements of skeletal muscle mass were not consistently measured or were not specific to the upper limb.[15,26]

Understanding longitudinal changes to muscle structure, function, and the interplay between the two would lend insight into early predictive factors for future disability that are difficult to assess in a cross-sectional study design. However high cost, long life span, and the need for invasive measurements to fully characterize skeletal muscle make longitudinal studies of the musculoskeletal system difficult to perform in humans. An animal model of upper extremity aging would more easily allow for longitudinal studies by limiting many of the logistical concerns associated with human subjects. Unfortunately, data regarding musculoskeletal degeneration in animals resulting strictly from normal aging are limited,[7,12,24,31,32] and many of the animal models are small, quadrupedal, or have bony geometry that is substantially different from that of a human.[9,22,31] A nonhuman primate model may offer a solution that mitigates many of these problems.[31]

Previous data suggest that the African vervet monkey (*Chlorocebus pygerythrus*) may be a promising species to use as a human surrogate to study age-related changes in physical function and in the upper extremity. Reductions in muscle fiber force in the vastus lateralis were present in older vervets,[7] although whether the upper extremity musculature experiences the same decline is unclear. Older vervets demonstrated age-related deteriorations of the shoulder similar to reports in older adult humans, including degeneration of the glenoid, increased glenoid retroversion, and decreased supraspinatus superficial cross-sectional area.[31] Similarly, measures of physical performance that incorporate the upper extremity were diminished in older vervets.[7,31,39] However, within this vervet species, age-related changes to the upper extremity musculature have not been evaluated, and degenerative rotator cuff tears, a common age-related injury affecting older adult humans,[44] have not been described.[31]

Quantifying age-related changes in the upper extremity musculature is necessary before the vervet can be appropriately evaluated as a human surrogate for longitudinal studies on upper extremity aging. To this end, we sought to expand upon the findings of age-related bony degeneration and decreased fiber cross-sectional area in the superficial portion of the supraspinatus in this vervet species by measuring the physiologic cross-sectional area (PCSA) of 10 upper extremity muscles important for upper limb function. PCSA combines measurements of volume and fiber length and is proportional to force-generating capacity. We also sought to determine how PCSA affects physical performance and the presence of rotator cuff tears.

Materials and methods

The right upper limbs of 5 middle-aged and 6 older adult female African vervets were obtained from a previously studied population of vervets (Table I). The current reports list vervets aged older than 20 years as elderly, with the 26.4-year-old in the current study the oldest known female vervet in captivity originating from the original colony.[31] Briefly, all animals were housed in social groups at the Wake Forest Primate Center and were allowed to traverse the inside/outside pens at their own leisure. Feeding was ad libitum. Physical performance (walking speed, percentage of time hanging, and percentage of time climbing) was measured for the animals as described previously.[7,31,39] Euthanasia was performed as part of a larger experiment exploring immunologic and physiologic parameters and their relationship to aging. All procedures were conducted in compliance with state and federal laws, standards of the U.S. Department of Health, and Human Services, and regulations and guidelines established by the Institutional Animal Care and Use Committee. After euthanasia, the right upper extremity was removed from the torso and frozen.

Each limb was thawed over a period of 24 hours, skinned, and fixed in 10% phosphate-buffered formalin for 24 hours. Before fixation, the limb was placed in a neutral shoulder and wrist posture with 90° of elbow flexion and attached to an aluminum plate via the spine. Each limb was removed from the formalin and placed in a 70% ethanol solution for a minimum of 24 hours to preserve the fixation and rinse any excess formalin. Measurements of arm length (acromion to lateral epicondyle) and forearm length (lateral epicondyle to ulnar styloid) were made using digital calipers.

The muscle-tendon unit of the 4 rotator cuff muscles (subscapularis, infraspinatus, supraspinatus, and teres minor), teres major, deltoid, biceps, triceps, coracobrachialis, and brachialis were dissected from the skeleton. Care was taken to ensure the entire muscle-tendon unit was removed from the skeleton. Before dissection, rotator cuff tendons were visually inspected for tears. Subscapularis, infraspinatus, deltoid, triceps, and biceps were divided into subsections according to previous descriptions of muscle architecture[13,42] for a total of 18 muscle-tendon units (Table II). After dissection, excess connective tissue and fat was removed from the muscle-tendon unit, and each muscle-tendon unit was stored in a 70% ethanol solution.

Measurements of muscle length and volume were made for each of the 18 muscle-tendon units. The tendon was removed at the muscle-tendon junction and the muscle belly length was measured using digital calipers and defined as the distance from the most proximal point to the most distal point. The 70% ethanol solution was placed in a graduated cylinder, and muscle volume was determined as the difference in volume with and without the muscle. Location of the meniscus was determined from high-