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Original Article

Does Muscle Atrophy and Fatty Infiltration Plateau or Persist in Chronic Spinal Cord Injury?

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Abstract

Atrophy and fatty infiltration of lower extremity muscle after spinal cord injury (SCI) predisposes individuals to metabolic syndrome and related diabetes and cardiovascular disease. The objective of this study was to prospectively measure changes in muscle atrophy and fat content of distal lower extremity muscles and explore related factors in a cohort of adults with chronic SCI and diverse impairments. Muscle cross-sectional area and density were calculated from peripheral quantitative computed tomography scans of the 66% site of the calf from 70 participants with chronic SCI (50 male, mean age 49 years, C2-T12, American Spinal Injury Association Impairment Scale A-D) at study enrollment and annually for 2 years. Mixed-model repeated measures analysis of variance (rANOVA) examined longitudinal changes in muscle area and density, and regression analyses explored factors related to muscle changes using 16 potential correlates selected *a priori*. A high degree of individual variation in muscle area and density change was observed over 2 years (range: 8.5 to −22.6 cm^2; 6.4 to −8.6 mg/cm^3). Repeated measures analysis of variance revealed significant reductions in muscle area (estimated mean difference [95% confidence intervals] −1.76 [−3.29 to −0.23]) cm^2, $p = 0.025$) and density (−1.04 [−1.94 to −0.14] mg/cm^3, $p < 0.024$); however, changes in area were not significant with outliers removed. Regression analyses explained a small proportion of the variability in muscle density change; however, none of the preselected variables were significantly related to changes in muscle density after *post hoc* sensitivity analyses. Lower extremity muscle size and fat content may not reach a "steady-state" after chronic SCI. Progressive atrophy and fatty infiltration of lower extremity muscle may have adverse implications for metabolic syndrome and cardiovascular disease risk and related mortality after chronic SCI.

Key Words: Body composition; muscle cross-sectional area; muscle density; peripheral quantitative computed tomography; spinal cord injury.

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Introduction

Individuals with chronic spinal cord injury (SCI) often experience cardiovascular disease, type II diabetes, and osteoporosis at an earlier age compared with their peers who have no SCI *(1)*. Secondary health complications are a major contributor to premature mortality among individuals with SCI and result in disproportionally high health-care resource utilization by individuals with SCI compared with their age- and sex-matched peers without SCI *(2,3)*.

Furthermore, individuals with SCI are living longer than ever before (4), and the number of older adults who experience SCI secondary to falls or myelopathy is increasing. Therefore, it is expected that the prevalence of age-related chronic conditions in the SCI population will increase concurrently (5).

Skeletal muscle is vital for maintaining cardiometabolic and bone health. Lower extremity muscle paralysis and the associated atrophy and changes in muscle fiber type are major contributors to metabolic dysregulation, impaired circulation, and osteoporosis after SCI (6). Furthermore, adipose tissue deposition in and around the skeletal muscle groups of the lower extremities is closely linked to a host of conditions, including chronic inflammation, glucose intolerance, impaired serum lipid and lipoprotein levels, poor bone health, and decreased strength and mobility in many clinical populations including SCI (7). Therefore, an understanding of how muscle health changes while aging with chronic SCI and lower extremity paralysis or paresis is an increasingly important concern among clinicians who desire to prevent and treat metabolic syndrome (8) and related morbidity in the SCI population.

Declines in lower extremity fat-free mass after SCI are well documented, especially in the acute phase after SCI, where adverse changes in muscle are rapid and profound (9). However, examinations of lower extremity muscle size and fat content in individuals with chronic SCI are limited to cross-sectional studies or prospective case series among men with motor complete paraplegia whose impairment is not representative of the diverse impairments within the SCI population. Furthermore, muscle atrophy and fat infiltration are part of the natural aging process (10); however, little is known about how chronic denervation influences age-related declines in muscle size and quality. Currently, the clinical course or trajectory of changes in muscle area and density are not well described in individuals with SCI outside of the subacute period, despite the prevalence of metabolic syndrome among those with chronic SCI.

To date, no study has prospectively examined changes in lower extremity muscle size and fat content in a sample of individuals with chronic SCI and diverse impairments. Therefore, the purpose of this study was twofold. First, it aimed to prospectively measure changes in distal lower extremity muscle size and fat content in a sample of individuals with chronic SCI with diverse demographic and impairment profiles. Second, this study sought to explore correlates of longitudinal changes in muscle size and fatty infiltration to better understand the factors associated with distal lower extremity muscle changes.

Methods

General Design

Seventy adults with chronic SCI were enrolled in a prospective observational cohort study, which required annual assessments of medication profile, medical history, and peripheral quantitative computed tomography (pQCT) scan acquisition and analysis, and twice-annual assessment of physical activity levels and health status, among other assessments (11,12). pQCT images of the 66% site of the calf were collected at enrollment and annually for 2 years. Longitudinal changes in muscle area and density were examined in relation to injury and demographic characteristics.

Study Participants

Participants with SCI were enrolled in a 2-year longitudinal study conducted at the Toronto Rehabilitation Institute, University Health Network, with analyses completed at the University of Waterloo. Study recruitment began in March 2009, and data were collected between April 2009 and June 2014. To establish a representative sample of the SCI population, men and women ≥18 years of age with spinal cord impairment (C1-L2, American Spinal Injury Association Impairment Scale [AIS] A-D) of sudden onset (<24 h) were included in this study. All participants had a SCI for at least 2 years before enrollment. Participants were excluded if they had (a) current or prior known conditions, other than paralysis, that influence bone metabolism; (b) a body weight ≥270 lb; (c) plans of becoming pregnant or pregnancy at enrollment; or (d) contraindications to pQCT, including bilateral lower extremity metal implants or severe hip and knee flexion contractures. All participants provided written informed consent. The project was approved by local research ethics boards.

pQCT Assessments

Muscle cross-sectional area (cm^2) and muscle density (mg/cm^3) were calculated from pQCT scans of the 66% site of the tibia measured from distal to proximal, starting at the inferior border of the medial malleolus. This site was chosen because it is the region of the calf with the largest circumference and muscle cross-sectional area (13). Images were acquired using a Stratec XCT 2000 scanner (Stratec Medizintechnik, Pforzheim, Germany) with Stratec software, version 5.50. The right tibia was scanned, except in cases of severe spasticity, or other contraindications, such as the presence of metal or fracture. Scans had a slice width of 2.2 mm, and a pixel size of 0.5×0.5 mm was used, except in seven instances where a pixel size of 0.4×0.4 mm was used because of a procedural error. A comparison analysis was performed by our group, and the smaller voxel size had no effect on muscle outcomes.

Tissue segmentation was performed using sliceOmatic software, version 4.3 (TomoVision, Magog, Canada). Our group has previously published a detailed description of this technique (12,14). Briefly, muscle was defined as the soft tissue beneath the fascia boarder separating the muscle and subcutaneous fat compartments. Tissue was segmented with the aid of a watershed algorithm and manually corrected for watershed spillover. We found that this method has better precision compared with threshold-based