Asymmetry in CT Scan Measures of Thigh Muscle 2 Months After Hip Fracture: The Baltimore Hip Studies

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Abstract

Background. Hip fracture is an important problem for older adults with significant functional consequences. After hip fracture, reduced muscle loading can result in muscle atrophy.

Methods. We compared thigh muscle characteristics in the fractured leg with those in the nonfractured leg in participants from the Baltimore Hip Studies 7th cohort using computed tomography (CT) scan imaging.

Results. At 2 months postfracture, a single 10-mm axial CT scan was obtained at the midthigh level in 47 participants (26 men and 21 women) with a mean age of 80.4 years (range 65–96), and thigh muscle cross-sectional area (CSA), CSA of intermuscular adipose tissue (IMAT), as well as mean radiological attenuation were measured. Total thigh muscle CSA was less on the side of the fracture by 9.2 cm² (95% CI: 5.9, 12.4 cm²), whereas the CSA of IMAT was greater by 2.8 cm² (95% CI: 1.9, 3.8 cm²) on the fractured side. Mean muscle attenuation was lower on the side of the fracture by 3.61 HU (95% CI: 2.99, 4.24 HU).

Conclusions. The observed asymmetry is consistent with the effect of disuse and inflammation in the affected limb along with training effects in the unaffected limb due to the favoring of this leg with ambulation during the postfracture period.

Key Words: Hip fracture—Muscle composition—Computed tomography—aged.

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Hip fracture is a major public health problem that results in significant burden to the health care system. More than 340,000 persons aged older than 65 years fracture a hip in the United States annually (1), and this number is expected to double by 2040 (2). Therefore, hip fracture is and will continue to be a significant burden on the health care system (3). A hip fracture event also has significant
consequences for older patients and their families and often heralds a period of increased functional decline and disability (4,5).

Following a hip fracture, there is a sudden loss of physical function (as measured by ability to walk independently and walking speed) followed by a period of recovery that can continue for a year or more depending on the area of function examined (4). By the end of a year, half of those who were able to walk independently before their fracture are still not able to walk independently (4,6). The duration of disability extends beyond that required for fracture healing, implying that the hip fracture event may trigger other adverse consequences that result in disability.

After hip fracture, reduced muscle loading secondary to pain and functional loss can result in muscle atrophy. Additionally, the increased energy demand due to the stress of surgery and healing, coupled with catabolism caused by the postinjury pro-inflammatory state, further increases the risk of muscle protein loss (7–9). Loss of muscle mass and declines in muscle quality may be important mechanisms that impede functional recovery after hip fracture and negatively affect function long after the fracture event. One study found that total body lean mass decreased by 6% in the first 2 months after a hip fracture, whereas fat mass increased by 3.6% in the year following fracture (10). However, little research has examined how specific muscles are affected. Recent work has suggested that loss of muscle mass does not fully explain the decreased muscle strength seen with advanced age (11), with disproportionately larger declines seen in muscle strength than in loss of muscle mass (12). Measures of lower extremity muscle composition may provide greater insights into the pathways through which hip fracture results in functional decline.

Computed tomography (CT) has been used extensively to characterize both the size and composition of skeletal muscle. The extent of radiological attenuation or “radiodensity” is generally considered to result from lipid accumulation and has been extensively used as a radiological proxy for muscle composition characteristics, including intramuscular fat infiltration (13,14). Indeed, higher muscle attenuation on CT scan imaging correlates with lower intramuscular fat content and greater muscle strength, independent of muscle mass (13).

We compared thigh muscle characteristics in the fractured leg with those in the nonfractured leg in older men and women, 2 months following hip fracture, in a cohort from the Baltimore Hip Studies (BHS). We hypothesized that compared with the nonfractured leg, there would be lower muscle cross-sectional area (CSA) and greater fat infiltration in the thigh musculature on the side of the fracture.

**Methods**

**Parent Study**

Study data were obtained from the BHS 7th cohort (BHS-7), a prospective cohort study that is being carried out in eight hospitals that participate in the BHS hospital network. Details of this study can be found elsewhere (15). Briefly, the goal of the parent BHS-7 study is to examine the metabolic, physiological, neuromuscular, functional, and clinical consequences of hip fracture in both men and women.

Patients were eligible if they were ≥65 years and admitted to one of the study hospitals during the study period with a diagnosis of hip fracture (ICD-9 codes 820.00–820.9). Patients were excluded if they had a pathological fracture, were not community dwelling at the time of the fracture, were non-English speaking, were bedbound during the 6 months prior to the fracture, required human assistance with ambulation prior to the fracture, resided more than 70 miles from the hospital, weighed more than 300 pounds, did not undergo surgical repair, or had any hardware in the contralateral hip (either due to hip fracture or hip replacement), thereby leaving no unaffected hip for bone density scanning purposes. Participants were assessed at baseline (within 22 days of hospital admission) and 2 months postadmission. The study protocol was approved by the Institutional Review Board (IRB) at the University of Maryland, Baltimore, as well as by each of the study hospitals’ respective IRBs.

**Baseline Measures**

Information regarding prefracture medical comorbidities, fracture type, and surgical repair was obtained by review of medical charts. Prefracture comorbid disease information was used to calculate the Charlson comorbidity index (16).

At the baseline visit, weight was measured using the same standard scale in all participants. Knee height was measured to the nearest 0.1 cm in the left leg using a sliding caliper, and stature was estimated from the knee height measurement using the method of Chumlea and colleagues (17). Information on participant demographics was obtained at the baseline evaluation by patient self-report or proxy interviews.

**CT Scan Measures**

As part of an ancillary study to BHS-7, CT scans of the midthigh are being obtained at 2 months postfracture. All participants who were enrolled in the parent study and who had not died, dropped out, or been lost to follow-up by the 2-month follow-up visit were eligible for enrollment in the ancillary study. Participants were excluded if they were unable to lie supine for the CT scan or had cognitive impairment preventing them from being left alone during the CT scan. One hundred and thirty five participants in the BHS-7 study were screened for participation in the ancillary study; of these, 67 (49.6%) were determined to be eligible and 50 of whom (74.6% of eligible participants) agreed to participate in the ancillary study. Two participants later withdrew from the ancillary study, and one participant withdrew from both the parent and the ancillary study, leaving the final sample of 47 participants who provided CT scan data.

A single 10-mm axial CT scan (Philips Brilliance 64 CT scanner, Philips Electronics N.V. Eindhoven, The Netherlands) was obtained at the midthigh level on each participant at the time of the 2-month evaluation (18). All images were analyzed by one person. Thigh muscle CSA was quantified using SliceOmatic software version 3 (Tomovision, Montréal, Canada). Intramuscular adipose tissue (IMAT) was distinguished from the subcutaneous adipose tissue by manually drawing a line along the deep fascial plane surrounding the thigh muscles. Once the adipose tissue was segmented from the images, individual muscles were identified. Skeletal muscle attenuation was measured for each muscle as the mean attenuation value between 0 and 100 HU as a marker of skeletal muscle lipid content (13,18). Muscle CSA and muscle attenuation were quantified for all the muscles of the thigh, a majority of which are the quadriceps and hamstring muscles.

**Analyses**

Study participant data are presented as the mean and range. Paired sample t tests were performed to compare the fractured to the nonfractured legs. All analyses were performed using the statistical package SAS (SAS Institute, Cary, NC).
Results

Data on 47 participants (26 men and 21 women) at 2 months after hip fracture are presented. Participant characteristics are presented in Table 1. Mean age was 80.4 years (range 65–96). The majority of participants (n = 37) were either married or widowed. Seventeen participants (37.0%) had a high school diploma, whereas 20 (43.5%) had more than 12 years of formal education, and 9 individuals (19.6%) had less. Mean prefracture Charlson comorbidity index score was 2.4 (range 0.0–8.0), suggesting a moderate comorbid disease burden.

At 2 months postfracture (Table 2), on the side of the fracture, the thigh CSA was smaller by 9.2 cm² (95% CI: 5.9, 12.4 cm²), the CSA of IMAT was greater by 2.8 cm² (95% CI: 1.9, 3.8 cm²), and the overall muscle attenuation was lower by 3.61 HU (95% CI: 2.99, 4.24 HU).

Discussion

Atrophy and replacement of muscle with adipose tissue is a well-described phenomenon of aging, and CT scan–based measures of thigh muscle composition have previously been examined in non–disabled older men and women (19,20). Compared with the data from these studies in nondisabled elderly patients, hip fracture patients appear to have lower mean thigh muscle CSA, in either leg, than nondisabled elderly patients, with similar muscle attenuation (19,20). Although muscle atrophy and replacement of muscle by adipose tissue may occur with aging, such changes may be accelerated by the decreased loading of thigh muscles resulting from pain and disability that occurs early on in hip fracture recovery. Results of the current analysis demonstrate lower muscle area, lower mean muscle attenuation, and greater intermuscular fat in the fractured compared with the nonfractured legs. To our knowledge, this is the first study to examine thigh muscle composition in hip fracture patients using CT scanning and the first study to demonstrate asymmetry in measures of thigh muscle between the fractured and nonfractured leg.

In addition to decline in the lean mass that has been seen following hip fracture (10), changes in muscle composition may also have important functional consequences in this frail population of older adults and may help to further explain the profound functional declines seen following hip fracture (5). Greater muscle attenuation on CT scan imaging reflects lower intramuscular fat content and is positively associated with muscle strength, independent of muscle mass (13). It is muscle strength rather than muscle mass that is believed to be important for function in older adults, including those recovering from hip fracture (20–22). Thus, the changes in muscle composition observed here of decreased lean muscle mass and increased fat in and around the muscle in the fractured leg may explain some of these adverse functional consequences in this population.

The differences in the fractured and nonfractured legs may be explained by the physiological response to the initial injury of hip fracture and surgical repair, as well as postfracture disuse of the affected leg due to functional loss and pain (23,24). Following trauma such as hip fracture and hip fracture surgery, there is an inflammatory response in order to initiate healing through the recruitment of immune and inflammatory cells to the site of injury (25). These cells are instrumental in the orchestration of cell movement necessary for wound repair. Tumor necrosis factor alpha, a key cytokine in this process (26), also induces muscle catabolism and cachexia (8). The inflammatory response following injury may therefore contribute to the observed asymmetry between the affected and the unaffected limbs (27). Inflammation following surgical trauma and hip fracture has been observed to be associated with an adverse effect on recovery (7,28). Pain, which is also mediated by inflammatory cytokines, is an important aspect of postinjury recovery (29).

The decreased weight bearing resulting from favoring the unaffected leg in ambulation during the post–hip fracture period may also explain the differences between the affected and the unaffected leg that we observed at 2 months post–hip fracture repair because muscle disuse resulting from the removal of weight bearing can lead to decreased protein synthesis and increased protein degradation (30). In contrast, the favoring of the unaffected leg in ambulation could lead to an increase in muscle volume and a decrease in adipose tissue content, due to a training effect, further increasing the asymmetry between the two limbs (31). Asymmetrical lower limb loading may persist beyond the 2-month time point examined here. In one cross-sectional study, distal leg loading, knee extension strength, and calf muscle CSA were found to be lower on the fractured leg in older adults who were on average 3.5 years post–hip fracture in one cross-sectional study (32). If measures of lower extremity muscle composition are associated with function in older adults, then this persistent asymmetry in lower limb musculature may help to explain the functional declines seen in hip fracture patients (5). A longitudinal analysis of thigh musculature using the CT scan data from the BHS-7 cohort may help identify factors associated with a persistence of thigh muscle asymmetry in hip fracture patients and the importance of this asymmetry to postfracture recovery.

Table 1. Baseline Characteristics of the Study Sample (N = 47)

| Age       | Mean (range) or N (%) |
|-----------|-----------------------|
| Male      | 26 (55.3)             |
| N (%)     |                       |
| BMI (Kg/m²)| 26.0 (20.4 – 38.2)    |
| Charlson Comorbidity Index | 2.4 (0.0 – 8.0) |
| Marital status |                   |
| Never married | 5 (10.9)              |
| Married    | 21 (45.7)             |
| Widowed    | 16 (34.8)             |
| Divorced   | 4 (8.7)               |
| Ethnicity  |                       |
| White      | 41 (89.1)             |
| African American | 4 (8.7)         |
| Other      | 2 (4.3)               |
| Education* |                       |
| ≤12 years  | 9 (19.6)              |
| 12 years   | 17 (37.0)             |
| >12 years  | 20 (43.5)             |
| Fracture type* |                  |
| Subcapital | 14 (29.8)             |
| Trochanter | 27 (57.5)             |
| Surgical repair* |                |
| Hemiarthroplasty/arthroplasty | 17 (36.2) |
| Internal fixation | 29 (61.7)           |

* Totals may be less than 47 due to the missing data.
Table 2. Thigh Muscle Characteristics (N = 47)*

|           | Fractured Leg | Nonfractured Leg | Difference† |
|-----------|---------------|-----------------|-------------|
| CSA (cm²) | 74.45 (69.18, 79.73) | 83.61 (77.14, 90.07) | -9.15 (-12.37, -5.93) |
| IMAT (cm²) | 11.95 (10.66, 13.24) | 11.95 (10.66, 13.24) | 2.84 (1.86, 3.81) |
| Attenuation (HU) | 36.08 (34.80, 37.37) | 39.70 (38.35, 41.04) | -3.61 (-4.24, -2.99) |

*Mean (95% CI). CSA – total thigh cross sectional area, IMAT – cross sectional area of intermuscular adipose tissue.
†Values in the fractured leg minus those in the non-fractured leg.

the affected limb following hip fracture may explain the observed association, due to the cross-sectional nature of the analyses, we are unable to exclude that the observed asymmetry did not exist prior to the fracture, perhaps resulting from gait asymmetry that may have contributed to a fall and hip fracture.

In conclusion, at 2 months post–hip fracture repair, older men and women demonstrated lower muscle attenuation and greater intermuscular fat in the fractured compared with the nonfractured legs, on CT scan imaging. These changes are consistent with atrophy and replacement of muscle with fatty tissue and may be a result of decreased muscle use, inflammation, or both in the year postfracture. Future studies will better evaluate the processes that explain these changes and their influence on recovery of lower extremity function in the year following hip fracture. A better understanding of these processes may have implications not only for the care of hip fracture patients but may also aid in the understanding of the processes that underlie functional decline in frail and sarcopenic older adults in general.

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