One Week of Hospitalization Following Elective Hip Surgery Induces Substantial Muscle Atrophy in Older Patients

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Original Study

One Week of Hospitalization Following Elective Hip Surgery Induces Substantial Muscle Atrophy in Older Patients

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A B S T R A C T

Objectives: Short successive periods of skeletal muscle disuse have been suggested to substantially contribute to the observed loss of skeletal muscle mass over the life span. Hospitalization of older individuals due to acute illness, injury, or major surgery generally results in a mean hospital stay of 5 to 7 days, during which the level of physical activity is strongly reduced. We hypothesized that hospitalization following elective total hip arthroplasty is accompanied by substantial leg muscle atrophy in older men and women.
Design and participants: Twenty-six older patients (75 ± 1 years) undergoing elective total hip arthroplasty participated in this observational study.
Measurements: On hospital admission and on the day of discharge, computed tomographic (CT) scans were performed to assess muscle cross-sectional area (CSA) of both legs. During surgery and on the day of hospital discharge, a skeletal muscle biopsy was taken from the m. vastus lateralis of the operated leg to assess muscle fiber type−specific CSA.
Results: An average of 5.6 ± 0.3 days of hospitalization resulted in a significant decline in quadriceps (−3.4% ± 1.0%) and thigh muscle CSA (−4.2% ± 1.1%) in the nonoperated leg ($P < .05$). Edema resulted in a 10.3% ± 1.7% increase in leg CSA in the operated leg ($P < .05$). At hospital admission, muscle fiber CSA was smaller in the type II vs type I fibers (3326 ± 253 μm^2 vs 4075 ± 279 μm^2, respectively; $P < .05$). During hospitalization, type I and II muscle fiber CSA tended to increase, likely due to edema in the operated leg ($P = .10$).
Conclusions: Six days of hospitalization following elective total hip arthroplasty leads to substantial leg muscle atrophy in older patients. Effective intervention strategies are warranted to prevent the loss of muscle mass induced by short periods of muscle disuse during hospitalization.

Aging is associated with the progressive loss of skeletal muscle mass and function, termed sarcopenia, which is accompanied by a decline in muscle strength and physical capacity, and an increased risk of developing chronic metabolic diseases.[1,2] Various situations such as hospitalization or recovery from illness or injury often necessitate a period of physical inactivity that is accompanied by the accelerated loss of muscle mass and muscle strength.[3–5] Such disuse-induced muscle loss contributes to negative health outcomes, including a reduction in the ability to perform activities of daily living, increased incidence of complications and subsequent need for readmission, decreased quality of life, and an increased risk for permanent institutionalization.[6–8] This is likely associated with the fact that older individuals generally do not regain all muscle tissue that was lost during a period of disuse.[9–11] As such, accumulation of (short) periods

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of muscle disuse that occur throughout the life span may contribute substantially to the etiology of sarcopenia.[3,4,12]

Muscle disuse has been studied in healthy young and older subjects using different lab-based models such as limb immobilization or bed rest. Studies investigating muscle disuse atrophy models in humans generally apply a relatively prolonged period of limb immobilization or bed rest (>10 days) to ensure measurable muscle loss in a research setting.[13–16] Recently, we[17–19] as well as others[20–22] showed that even a few days of disuse already leads to significant losses in muscle mass and strength in both young and older individuals. At present, hospitalization in older patients ranges between 5 and 13 days,[23,24] during which the level of physical activity is strongly reduced.[25,26] As such, short-term hospitalization might be accompanied by a significant loss in skeletal muscle mass and strength in older patients, posing a major threat to fully regaining physical function after discharge. Muscle disuse models are often used to predict changes in muscle mass during hospitalization. However, the impact of surgery, associated physical and mental stress, and reduced food intake during hospitalization are likely to further aggravate skeletal muscle loss in clinical practice. Although hospital-based deconditioning is well recognized as a negative consequence of hospitalization, there is a paucity of data on the actual loss of muscle tissue during the hospitalized period.[27–29] Moreover, studies so far have largely focused on rather severe conditions, such as cancer cachexia and critical illness,[29–35] leaving a gap in knowledge on the negative impact of (planned) short-term hospitalization in relatively healthy older patients.

Elective total hip arthroplasty (THA), a surgical procedure for end-stage osteoarthritis, has evolved into a reliable and suitable surgical procedure to gain pain relief and improve quality of life and function of patients within 3 months up to 2 years after surgery.[36,37] Despite the success in treating the osteoarthritic joint, THA patients suffer from muscle atrophy,[38–40] reduced muscle strength,[40–42] and mobility impairment[40,42,43] in the longer term. This places a huge burden on the health care system, which will take on dramatic proportions given the expected doubling of the number of joint arthroplasties over the coming years.[37,44] To what extent muscle disuse atrophy occurs during short-term hospitalization following elective total hip replacement surgery is currently unknown.

The specific aim of the present study was to quantitatively assess the extent of muscle atrophy in older hospitalized patients during the first (hospital-based) days of recovery from THA, representing a relatively healthy group of older patients entering the hospital for planned surgery. Therefore, in the present study, we selected 26 male and female patients who were scheduled for THA and assessed skeletal muscle mass and muscle fiber characteristics at admission and on subsequent discharge from the hospital.

Methods

Subjects

Twenty-six older patients ($n = 7$ males, $n = 19$ females, aged $\geq$65 years) participated in this observational study during an average length of hospital stay of 5.6 ± 0.3 days. On hospital admission and on the day of discharge, computed tomographic (CT) scans were obtained to assess muscle mass (primary outcome measure); no CT scans were taken in $n = 6$ patients because of conflicting medical appointments, inability to mobilize, or pain. During surgery and on the day of hospital discharge, a skeletal muscle biopsy was taken from the m. vastus lateralis of the (to be) operated leg to assess muscle fiber characteristics (secondary outcome measure). In all 26 patients, skeletal muscle biopsies were taken during surgery; however, no muscle biopsies were taken at hospital discharge in 8 patients because of excessive edema or at the patients' request. A flowchart of patients' enrolment is shown in Figure 1. All participants were recruited via the outpatient clinic of the Department of Orthopedic Surgery after scheduling an elective THA. Subjects were informed about the nature and risks of the experimental procedures before written consent was obtained. The study was part of a larger project on the impact of immobility and nutrition on skeletal muscle adaptation during hospitalization and approved by the Medical Ethical Committee of the Maastricht University Medical Centre+, The Netherlands (registered as NTR3773 at www.trialregister.nl), conformed to the standards for the use of human subjects in research as outlined in the latest version of the Declaration of Helsinki.

Protocol

All eligible subjects were pretested on the day before surgery directly after arrival at the hospital ward. Exclusion criteria included age $\leq$65 years, all comorbidities, and use of medication interacting with muscle metabolism and mobility of the limbs, such as chronic obstructive pulmonary disease, peripheral arterial disease, severe cardiovascular impairment, neurologic disorders, coagulation diseases, and malignant disease. Height and weight were measured and body composition was assessed using dual-energy x-ray absorptiometry (Discovery A; Hologic, Bedford, MA). Thereafter, a single-slice CT scan (Brilliance 64, Philips Medical Systems, Best, the Netherlands) was performed to assess upper leg muscle cross-sectional area (CSA). The scanning characteristics were as follows: 120 kV, 300 mA, rotation time of 0.75 seconds, and a field of view of 500 mm. With subjects lying supine with their legs extended, a 3-mm-thick axial image was taken 15 cm proximal to the top of the patella for both legs. The exact scanning position was measured and marked for replication at the time of discharge from the hospital. Intramuscular adipose tissue was defined using radiation attenuation ranges from −190 to −30 Hounsfield units (HUs), and muscle area of the legs was selected between −29 and + 150 HU,[45] after which the quadriceps muscle was selected by manual tracing using ImageJ software (version 1.45d; National Institute of Health, Bethesda, MD).[46,47] Leg volume measurements were performed using anthropometric measurements on both legs.[48]

Information regarding quality of life, habitual physical activity, and nutritional status were evaluated using several questionnaires: Short Form–36,[49] Physical Activity Scale for the Elderly,[50,51] Mini Nutritional Assessment (MNA),[52] Malnutrition Universal Screening Tool,[53] and Mini-Mental State Examination.[54] Maximal handgrip strength was measured using a JAMAR handheld dynamometer (model BK-7498, Fred Sammons Inc., Burr Ridge, IL). Grip strength was measured 3 times (with a 10-second interval) with each hand, and the highest value for both hands was reported. Measurements of handgrip strength were taken with the patient sitting on a chair with the elbow in 90° flexion and the forearm in the neutral position.

On the day of surgery, a first muscle biopsy was collected from the m. vastus lateralis of the operated leg during the surgical procedure. A second muscle biopsy was taken from the same leg on the day of hospital discharge. In addition, on the day of hospital discharge, a second CT scan was performed, and maximal handgrip strength and leg volume were assessed.

Muscle Biopsy

Skeletal muscle biopsy samples were obtained from the operated leg from the middle region of the m. vastus lateralis 15 cm above the patella and approximately 2 cm away from the fascia by means of the percutaneous needle biopsy technique described by Bergström et al.[55] Biopsies were spaced by 1 to 2 cm, and the order of distal and proximal incision was randomized to minimize any potential systematic effect of the previous biopsy. Muscle biopsies were carefully freed from any

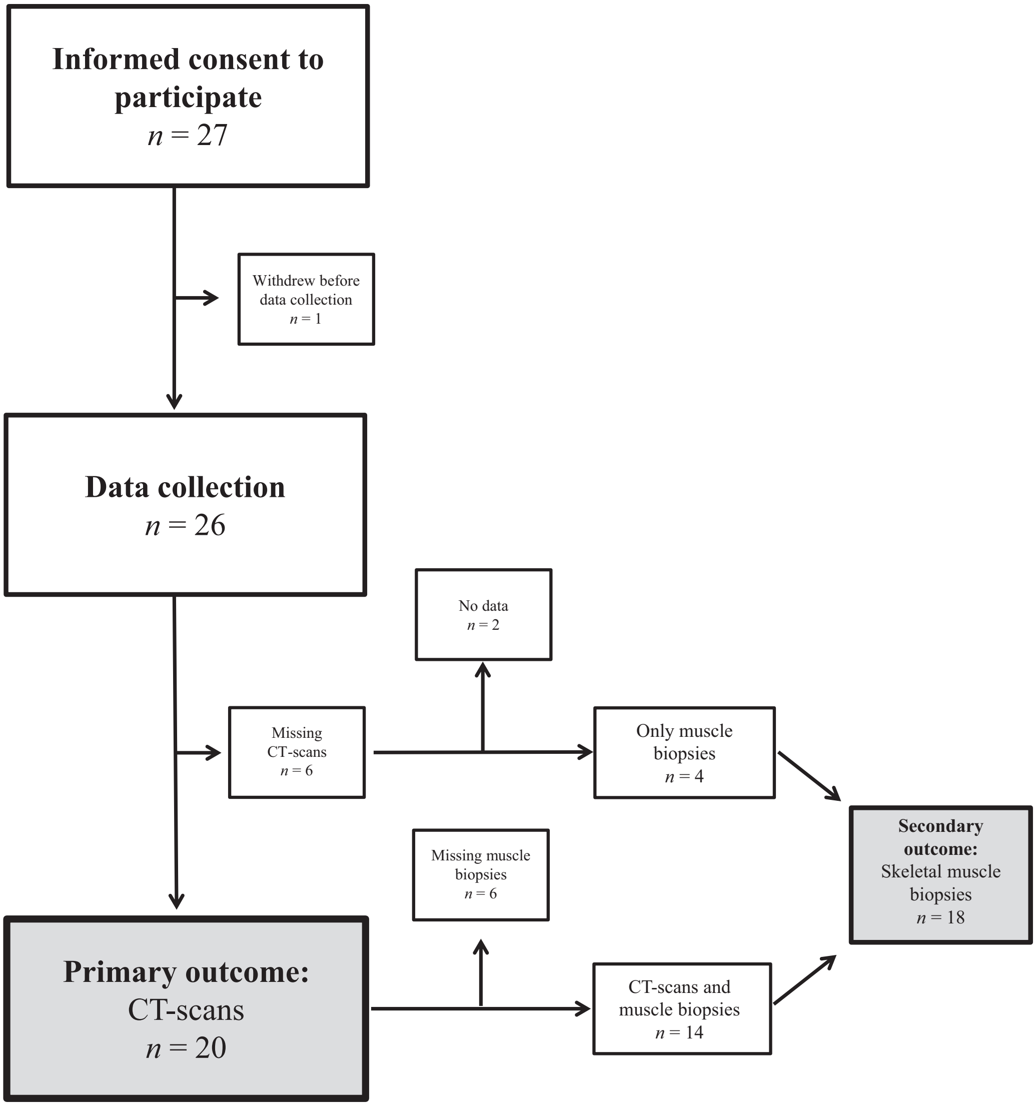

Fig. 1. Flow diagram of patients' enrollment procedure.

visible fat and blood, embedded in Tissue-Tek (Sakura Finetek Europe BV, Zoeterwoude, the Netherlands), and rapidly frozen in liquid nitrogen cooled isopentane and stored at −80°C for subsequent histochemical analysis.

Diet and Physical Activity

Nutritional intake was ad libitum during hospitalization, except from the perioperative period since all patients were operated on in a fasted state. Nutritional intake was monitored during hospitalization on a thrice-daily basis. Hospital meals were provided at 3 strict time slots every day—breakfast, lunch, and dinner. In between the meals, patients were provided with hot and/or cold drinks 3 times a day. On the serving tray, patients received a description of their ordered menu, which was collected for the study. Products that were not consumed were recorded. Total energy [megajoules (MJ)] and protein [grams and energy % (En%)] contents were calculated for all consumed food based on product specifications provided by the food suppliers and the Dutch Food Consumption Database 2016 (NEVO; RIVM, Bilthoven, the Netherlands). Food intake data were available for 23 patients. Dietary intake was only reported when complete data for all 3 main meals was available; separate data were calculated for the day of surgery (n = 13) and combined for the hospitalization days following surgery (n = 23). During hospital stay, patients were encouraged to mobilize as soon as possible and received physiotherapy training twice daily for 20 minutes from the first day after surgery onward. Patients were allowed to also mobilize without supervision from nursing staff or physical therapists from day 1 onward; however, from observations made while being on the nursing ward, patients mainly performed sedentary behavior outside of the therapy sessions (ie, sitting in and around their hospital bed, except for toilet visits and bedside transfers).

Immunohistochemistry

Frozen muscle biopsies were cut into 5-μm-thick cryosections using a cryostat at −20°C, and thaw mounted on uncoated precleaned glass slides. Samples from pre- and postsurgery were mounted together on the same glass slide. Care was taken to properly align the samples for cross-sectional fiber analyses. Muscle biopsies were stained for muscle fiber type determination, that is, type I and type II muscle fibers. Details of the analytical procedures have been described previously.[56] First, antibodies were directed against laminin (polyclonal rabbit anti-laminin, dilution 1:50; Sigma, Zwijndrecht, the Netherlands) and myosin heavy chain-I (A4.840, dilution 1:25;

Developmental Studies Hybridoma Bank, Iowa City, IA). Images were visualized and automatically captured at × 10 magnification with a fluorescent microscope equipped with an automatic stage (IX81 motorized inverted microscope; Olympus, Hamburg, Germany). Quantitative analyses were performed using ImageJ version 1.46d software package (version 1.45d; National Institutes of Health[47]). All image recordings and analyses were performed by an investigator blinded to subject coding. Muscle fiber type (fiber %) and fiber CSA were measured separately for each muscle fiber. As such, mean muscle fiber size was calculated for the type I and type II muscle fibers separately. Mean numbers of 476 ± 72 and 504 ± 70 muscle fibers were analyzed in the biopsy samples collected during surgery and (on average) 5 days following surgery, respectively.

Statistics

All data are expressed as mean ± standard error of the mean. A sample size of n = 16 was calculated assuming a decline of 2% (standard deviation 2%) in muscle CSA based on CT scans, using an α-level of 0.05 and 95% power, based on previous disuse studies.[17,19,22] To err on the side of caution, we aimed to include 20 patients for our primary outcome; 26 patients were finally needed to obtain full data sets (pre and post) for CT scans (Figure 1). Data were analyzed using paired samples *t* tests to assess changes from pre- (hospital admission) to post hospitalization (discharge). Muscle CSA and muscle fiber characteristics were analyzed using repeated measures analysis of variance with time (pre vs post) and leg (nonoperated or operated) or fiber type (type I vs II) as within-subject factors. Because of significant "time × leg" interaction, paired samples *t* tests were used to assess changes for each leg separately. Statistical significance was set at $P < .05$. All calculations were performed using SPSS Statistics (version 24.0; IBM Corp, Armonk, NY).

Results

Patients' Characteristics and Body Composition

Patients' characteristics and body composition data are shown in Table 1. Total lean body mass (presented in absolute and relative numbers) averaged 47.6 ± 1.9 kg (63.0% ± 1.1%), appendicular lean mass: 19.9 ± 1.0 kg (26.2% ± 0.7%), and fat mass: 25.5 ± 1.1 kg (34.0% ± 1.2%). Skeletal muscle mass index (SMMI) was calculated for women (n = 19) and men (n = 7) separately and averaged 7.0 ± 0.2 in women and 9.2 ± 0.4 in men. None of the patients were classified as malnourished based on the Mini Nutritional Assessment (average score 26.2 ± 0.4). However, 4 of the patients were classified as "high risk for malnutrition" (a Malnutrition Universal Screening Tool score of 2 based on recent weight loss) on hospital admission. Scores for the Short Form–36, Physical Activity Scale for the Elderly, and Mini-Mental State Examination are depicted in Table 1. Based on the Mini-Mental State Examination, none of the patients presented cognitive impairments at hospital admission. Handgrip strength before surgery averaged 26.4 ± 1.8 kg and 25.0 ± 1.6 kg in the right and left hand, respectively, and did not change during hospitalization (both $P > .05$).

Table 1
Patients' Baseline Characteristics

	Patients (n = 26)
Age, y	74.7 ± 0.8
Gender: male/female, n	7/19
Hospitalization duration, d	5.6 ± 0.3
Weight, kg	73.9 ± 2.3
BMI	28.0 ± 0.8
Lean body mass, kg (%)	47.6 ± 1.9 (63.0% ± 1.1%)
Fat mass, %	34.0 ± 1.2
SMMI	7.6 ± 0.3
Anesthesia: epidural/general anesthesia, n	12/14
MNA score	26.2 ± 0.4
SF-36 score	
Physical component summary	45.8 ± 3.4
Mental component summary	54.8 ± 4.3
MMSE score	28.4 ± 0.4
PASE	101.7 ± 14.9

BMI, body mass index; MMSE, Mini-Mental State Examination; MNA, Mini Nutritional Assessment; PASE, Physical Activity Scale for the Elderly; SF-36, Short Form–36; SMMI, skeletal muscle mass index.
Values are expressed as mean ± standard error of the mean.

Leg Muscle Mass

In the nonoperated leg, CSA of the thigh muscles declined by 4.2% ± 1.1% (from 11,071 ± 577 to 10,565 ± 528 mm^2) during hospitalization ($P = .001$; Figure 2). In accordance, quadriceps femoris CSA in the nonoperated leg declined by 3.4% ± 1.0% from hospital admission to hospital discharge (from 5285 ± 320 to 5095 ± 303 mm^2, respectively, $P = .004$; Figure 2). Total thigh volume assessed by CT scans decreased by 2.8% ± 1.2% during hospitalization in the nonoperated leg (from 20,477 ± 909 to 19,841 ± 876 mm^2, respectively, $P = .03$). Anthropometric whole leg volume in the nonoperated leg did not change from hospital admission to hospital discharge (7436 ± 386 and 7646 ± 335 cm^3, respectively, $P = .54$). Average muscle radiation attenuation values in the nonoperated leg decreased by 6.4% ± 1.0% in the thigh muscles and by 6.4% ± 1.1% in the quadriceps femoris (from 39.5 ± 1.4 to 37.0 ± 1.5 HU and from 45.0 ± 1.2 to 42.2 ± 1.4 HU, respectively, both $P < .001$).

At hospital admission, both thigh and quadriceps muscles CSA were lower in the operated leg (10,359 ± 599 and 4740 ± 332 mm^2) when compared with the nonoperated leg (11,071 ± 577 and 5285 ± 320 mm^2; both $P < .05$). In the operated leg, thigh muscle CSA increased by 8.0% ± 1.7% during hospitalization (from 10,359 ± 599 to 11,095 ± 584 mm^2, $P < .001$) and quadriceps CSA increased by 12.2% ± 2.9% when compared with baseline values (from 4740 ± 332 to 5209 ± 308 mm^2, $P < .001$). In accordance, total thigh CSA of the operated leg assessed by CT scans increased during hospital stay with 10.3% ± 1.7% (from 20,185 ± 867 mm^2 at hospital admission to 22,154 ± 897 mm^2 at hospital discharge, respectively, $P < .001$). Anthropometric whole leg volume increased by 16.2% ± 4.6% during hospitalization (from 7606 ± 387 to 8715 ± 420 cm^3, respectively, $P < .001$). Average muscle radiation attenuation in the operated leg decreased by 14.1% ± 1.7% in the thigh muscles and 14.5% ± 1.8% in quadriceps femoris CSA (from 37.4 ± 1.5 to 32.3 ± 1.6 HU and from 42.9 ± 1.4 to 37.0 ± 1.7 HU, respectively; both $P < .001$).

Total thigh CSA and anthropometric whole leg volume did not differ between legs at hospital admission (both $P > .05$) but were significantly lower in the nonoperated leg when compared with the operated leg at hospital discharge (both $P < .001$). Moreover, the change in leg volume (both CT and anthropometric measurements) differed between legs (time × leg interaction effect, $P < .001$). This was likely due to swelling of the operated leg following the surgery; therefore, muscle mass changes were only presented graphically for the nonoperated leg (Figure 2). Moreover, a significant time × leg interaction effect was observed for muscle radiation attenuation in thigh muscles and quadriceps CSA (both $P < .05$). HU values in thigh muscles and quadriceps femoris were lower in the operated leg when compared with the nonoperated leg both at hospital admission and hospital discharge (both $P < .05$).

Muscle Fiber Characteristics

Muscle fiber characteristics of skeletal muscle biopsies collected from the operated leg during surgery and on the day of hospital

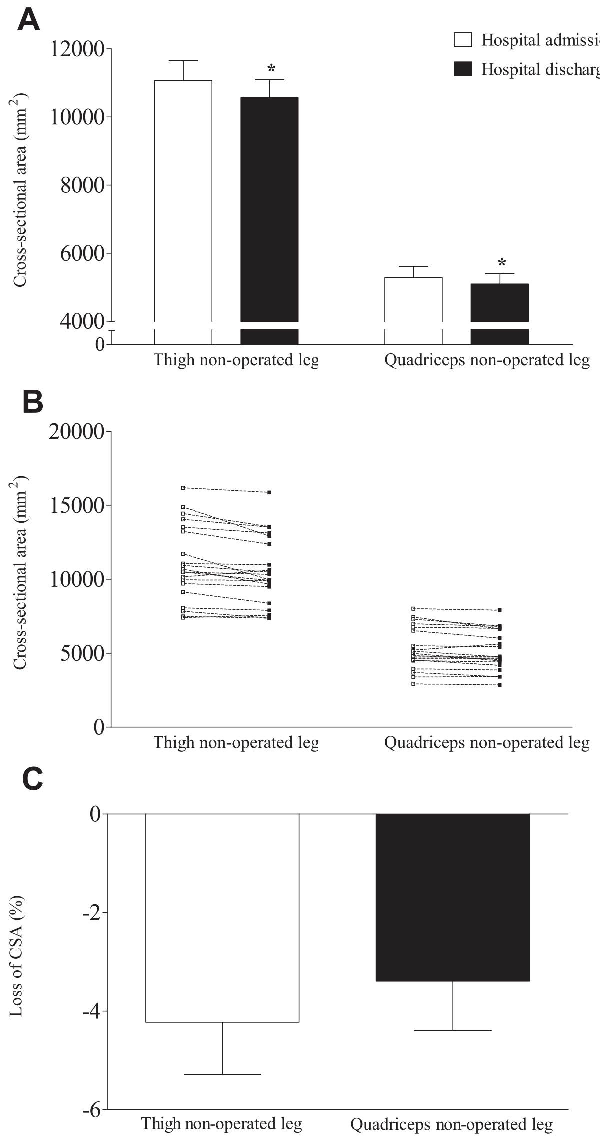

Fig. 2. Muscle cross-sectional area (CSA in millimeters squared) of the quadriceps and thigh muscles of the nonoperated leg in older patients (n = 20) undergoing elective total hip arthroplasty, assessed by single-slice CT scans taken on the day of hospital admission and on the day of discharge. (A) mean ± standard error of the mean; (B) individual data; (C) mean ± standard error of the mean of relative decline CSA (in percentage). *Significantly different from hospital admission.

discharge are displayed in Table 2. At hospital admission and discharge, type II muscle fibers were smaller when compared with type I muscle fibers (3325 ± 253 vs 4075 ± 279 μm^2, respectively, $P = .001$). No significant time × fiber type interaction was observed for muscle fiber size ($P = .37$). Six days of hospitalization tended to increase both type I and II muscle fiber size by 21.9% ± 11.0% and 17.8% ± 9.2%, respectively (main time effect, $P = .10$). Subtle changes in fiber type distribution were observed during hospitalization (Table 2).

Nutritional Intake

On the day of surgery, energy intake averaged 1.32 ± 0.62 MJ, whereas energy intake increased to 4.21 ± 0.38 MJ ($P < .001$) on the hospitalization days following surgery. Protein intake averaged 0.08 ± 0.03 g/kg bodyweight/day on the day of surgery, after which protein intake increased to 0.58 ± 0.04 g/kg bodyweight/day during the following days of hospitalization ($P < .001$).

Table 2
Muscle Fiber Characteristics

	Hospital Admission		Hospital Discharge	
	Type I	Type II	Type I	Type II
No. of fibers	198 ± 32	278 ± 45	175 ± 28	329 ± 48
Muscle fiber CSA, μm^2	4075 ± 279	3326 ± 253*	4881 ± 548	3953 ± 471*
% fiber	42.3 ± 3.4	57.7 ± 3.4	34.7 ± 2.5†	65.3 ± 2.5
% fiber area	47.2 ± 4.1	52.8 ± 4.1	40.1 ± 3.1†	59.9 ± 3.1

Values are expressed as mean ± standard error of the mean. No time × fiber type interaction was observed for any of the outcomes ($P > .05$).
*Main fiber type effect: significantly different from type I.
†Main time effect: significantly different from hospital admission, $P = .01$.

Discussion

Six days of hospitalization leads to a substantial decrease in thigh and quadriceps femoris muscle CSA in the nonoperated leg following elective hip arthroplasty. This reduction in muscle CSA is not observed in the operated leg, showing a ∼10% increase in thigh CSA and ∼16% increase in whole leg volume due to postsurgery edema.

Muscle disuse is associated with a decline in skeletal muscle mass and strength.[4] Experimental models studying muscle disuse have shown a ∼2% to 6% decrease in leg muscle mass and an ∼8 to 22% decrease in leg strength following as little as 4 to 7 days of limb immobilization in both young[17,19,57] and older[18,20] subjects. Moreover, up to 14 days of bed rest typically results in a similar decline in whole-body and appendicular lean body mass in young and older individuals.[11,21,58–62] As the average hospital length of stay in older patients is 5 to 13 days,[23,24] a short period of hospitalization may already induce a substantial decline in skeletal muscle mass and strength. Studies applying muscle disuse models are often used to predict changes in muscle mass during hospitalization; however, only few data are available on actual muscle loss in a clinical setting. Such a period of hospitalization is generally accompanied by general anesthesia, surgery, associated physical and mental stress, a reduced level of physical activity, enforced bedrest, and/or changes in habitual food intake. Therefore, we hypothesized that even a short period of hospitalization is associated with substantial muscle loss.

With the increasing aging population, elective joint replacement surgeries such as THA have increased exponentially over the last decades, with more than 60% of the patients being 65 years and older.[37,44,63] Elective hip replacement surgeries are effective for pain relief and improving quality of life and function in patients with end-stage osteoarthritis[36,37]; however, elective THA in older patients is typically followed by a short hospitalization period of 3 to 4 days.[63] In the present study, we assessed the impact of such a short-term hospitalization period on skeletal muscle mass following elective THA. We performed single-slice CT scans of the upper leg on the day of hospital admission and on the day of discharge to assess muscle CSA of both legs. We show for the first time that 5 days of hospitalization following elective THA is accompanied by a substantial loss of muscle CSA. Thigh muscle CSA significantly declined by 4.2% ± 1.1% and quadriceps femoris CSA by 3.4% ± 1.0% during hospitalization in the nonoperated leg when compared with baseline values (both $P < .001$). In contrast, in the operated leg, we observed a ∼10% increase in total thigh CSA and a ∼16% increase in anthropometrically determined leg volume, probably because of swelling following surgery. In support, muscle radiation attenuation values in the thigh and quadriceps femoris muscle area were substantially decreased in the operated leg when compared with the nonoperated leg ($P < .001$). The pronounced decrease in muscle attenuation in the operated leg may be attributed to edema, fluid retention in the interstitial spaces, and/or fat deposition.[45] For example, reduced muscle attenuation values have been associated with conditions such as obesity, diabetes, physical inactivity, and muscle deconditioning.[38,45,46] Because of the observed swelling and extensive increase in leg volume in the operated leg, we were not able to reliably assess changes in muscle mass in the operated leg. However, the substantial declines in leg muscle mass observed in the nonoperated leg within as little as 5 days of hospital stay clearly indicate the detrimental impact of hospitalization on muscle mass maintenance in older patients. In a recent meta-analysis, it was reported that muscle mass is lost in electively admitted older patients (in line with our findings), whereas generally no decline was observed when patients were admitted acutely.[29] Importantly though, changes in hydration status may strongly influence the assessment of muscle mass, and the methodology used to determine muscle loss likely explains part of the inconsistent findings in literature.[29,35] As such, the CT scans performed on the nonoperated leg in the present study provide a very accurate and sensitive measure, clearly showing substantial reductions in muscle mass during hospitalization.

In addition to performing CT scans, we obtained skeletal muscle biopsies from the vastus lateralis muscle of the operated leg during the surgical procedure and on the day of hospital discharge to assess muscle atrophy–related changes in muscle fiber characteristics. At baseline, type II muscle fibers were smaller than type I muscle fibers ($P < .05$), which is in line with previous research showing substantial type II muscle fiber atrophy with aging,[64,65] type 2 diabetes,[66] and hip fracture patients.[67] Six days of hospitalization tended to increase both type I and II muscle fiber size by ~20% ($P = .10$). The observed swelling and substantial increase in leg volume observed in the operated as opposed to the nonoperated leg was likely not only associated with extracellular edema but also caused a fluid shift into the muscle cells and, as such, intracellular edema, thereby increasing muscle fiber CSA. Therefore, we were unable to adequately assess muscle fiber size and characteristics following surgery in these hospitalized patients. We hypothesized that short-term hospitalization would be characterized by a decline in muscle fiber size in the operated leg, which could explain the observed muscle atrophy in such a clinical setting. For example, substantial decreases in muscle fiber size have been observed during critical illness[68] and bed rest.[62] However, because of the presence of postoperative (intracellular) edema, we could not reliably assess muscle fiber changes in the operated leg. Therefore, future studies should be aware that muscle fiber size loss during hospitalization after orthopedic surgery should not be assessed in the limb in which surgery has been performed.

Short, successive "catabolic crises" have been proposed to contribute to the persistent age-related loss of skeletal muscle mass and strength.[3,12] Assuming the usual age-related decline in muscle mass of 1% to 2% per year above the age of 65,[1,3] the 3% to 4% muscle loss observed during only a few days of hospitalization likely has a dramatic impact on the development of sarcopenia. Moreover, older individuals generally do not regain all muscle tissue that was lost during a period of disuse.[9–11] Therefore, cumulative periods of disuse episodes do not only impact muscle loss during hospitalization but likely also contribute to impaired recovery and physical functioning after hospital discharge. Indeed, it has been well established that hospital-associated deconditioning in the older population contributes to an overall functional decline during and following a period of hospitalization, affecting long-term clinical outcomes after hospitalization.[12,27,28] Although such deconditioning is known to occur in various clinical situations, the actual loss of muscle mass during hospitalization is rarely assessed. Moreover, much of this work so far has focused on severe medical conditions (eg, ICU-acquired weakness, organ failure, and cancer cachexia),[29–35] which may be different from the large group of relatively healthy individuals entering the hospital for planned surgery. In the present study, we quantitatively assessed the extent of skeletal muscle atrophy during short-term hospitalization in older patients who were electively admitted for THA. We observed substantial muscle loss during only several days of hospitalization, although patients were encouraged to mobilize as soon as possible and were provided with daily physical therapy and standard nutritional care. This loss in skeletal muscle mass seems greater when compared to muscle disuse observed in experimental models, which generally report ~0.5% loss of appendicular muscle mass per day during limb immobilization or bedrest.[4,5] In line with the literature on deconditioning, probably the combination of multiple factors such as the impact of surgery, the associated physical and mental stress, reduced food intake during hospitalization, inflammation, medication, type of anesthesia, and medical history could further impact skeletal muscle loss in clinical practice.[27,28] With the relatively low number of patients included here ($n = 26$) we were unable to further study the relative contribution of these factors to the observed muscle loss. Furthermore, although we would expect the substantial loss of muscle mass during hospitalization to also occur in other older patient populations, it is clear that the reason for admission (ie, underlying pathology) and the type of admission (ie, acute vs elective[29]) can affect the extent of muscle loss. Thus, future work is needed to further establish the various factors that affect the extent of muscle atrophy in clinical conditions, and to what extent hospital-associated muscle loss differs between various patient populations.

Apart from the above-mentioned patient-related factors that may affect muscle maintenance, the 2 key anabolic stimuli for skeletal muscle tissue are muscle contraction and food intake.[2] In the present study, daily protein intake was very low on the day of surgery (only ~6 g in total), as well as on the following days of hospitalization (~0.6 g/kg bodyweight/day). As such, daily protein intake remained well below the recommended protein intake guidelines of 1.2 to 1.5 g/kg bodyweight/day for older adults.[69] A protein intake of less than 1.2 g/kg bodyweight/day will likely be insufficient to maintain or regain skeletal muscle mass during postsurgery hospitalization in these patients. Increasing protein intake has been proposed as a nutritional strategy to attenuate the loss of muscle mass during hospitalization. Protein supplementation has been shown to increase muscle mass and function in older adults.[70,71] Moreover, amino acid supplementation (ie, leucine and β-hydroxy β-methylbutyric acid) has been shown to attenuate the loss of muscle mass during a period of bed rest.[14,60,61] However, additional protein supplementation during limb immobilization does not seem to preserve the loss of skeletal muscle mass in healthy older subjects.[18,72] Though it has not been proven whether increasing habitual protein intake during short-term hospitalization can attenuate muscle loss, it has been well established that a decline in protein intake below habitual intake levels aggravates muscle loss during a period of bedrest or immobilization.[3,14,73,74] Therefore, nutritional interventions should focus on maintaining habitual protein intake levels in both the perioperative phase as well as during hospital stay.

Hospitalization is typically a period during which physical activity levels are reduced, and it has been shown that older patients spend >80% of their hospital stay in bed.[25,26] Because muscle contraction directly stimulates muscle protein synthesis,[2] increasing physical activity and/or introducing physical activity mimetics during hospitalization forms an important strategy to reduce muscle loss. In addition, as protein ingestion and exercise have a synergistic effect,[2] physical activity (mimetics) should be combined with nutritional support in clinical practice to minimize muscle and strength loss in older and more clinically compromised patient groups.

Conclusion

We conclude that short-term hospitalization following elective THA leads to substantial muscle loss in older patients. Effective intervention strategies are warranted to prevent the loss of muscle mass induced by short periods of muscle disuse during hospitalization.

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