Resistance training induces qualitative changes in muscle morphology, muscle architecture, and muscle function in elderly postoperative patients

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Sarcopenia has long been recognized as a major cause of loss in muscle strength with old age. In fact, aging and disuse are two of the main conditions leading to skeletal muscle atrophy in humans. In both conditions, the loss of muscle mass leads to a decrease in muscle force production, and recent evidence suggests that a significant additional contribution might come from changes in muscle architecture (38, 39). However, only a few studies have examined changes in muscle architecture and muscle fiber morphology in response to aging and physical training, and although the results suggest that a significant plasticity exists, there is generally a lack of data as to what extent different conditioning stimuli may affect muscle architecture in elderly individuals recovering from hospitalization.

The loss of muscle mass with aging accelerates from the sixth decade onward, partly owing to a decreased number of muscle fibers and also as the result of general muscle fiber atrophy (32, 33). Although several cross-sectional studies indicate that type II fibers are more vulnerable to the aging process than type I fibers (4, 27, 29, 32), some find a more marked type I atrophy (13). In essence, the loss of muscle mass with aging is profound and has been estimated to decrease ~30% during the life span (30, 33). Considering these morphological changes, it is not surprising that maximal muscle strength is reduced as a result of aging by ~1.5% per year from the sixth decade (45).

In addition to the muscular changes pertaining to muscle fiber area, aging also leads to marked alterations in muscle architecture that potentially contribute to the loss of muscle strength (39). A reduction of 10–13% in muscle fiber pennation angle in old compared with young individuals has been demonstrated by Narici et al. (39), suggesting that a significant part of the decrease in muscle function with aging may be related to changes in muscle architecture. However, there is a paucity of data describing architectural adaptations to different types of loading, although understanding the impact of different training stimuli on muscle architecture in the elderly seems important to determine effective intervention programs to improve muscle function after chronic disease and/or illness.

The most commonly used rehabilitation regimes for elderly individuals are based on functional types of exercises without external loading, although it has been demonstrated that this type of intervention cannot prevent further muscle atrophy (40) or restore muscle strength and functional performance in elderly postoperative patients (43, 44). Percutaneous neuromuscular electrical stimulation is another method used to restore muscular function after immobilization, although primarily investigated in young individuals (5, 16). During the last decades, resistance training has emerged as an effective method to induce muscle hypertrophy and increase muscle strength and functional performance in frail elderly (12, 21) and in patients with chronic diseases (10, 23, 26). Furthermore there is increasing evidence that resistance training used in the late postoperative phase is an effective method to restore muscle function in elderly patients (22, 34, 42). Despite this, resistance training is still rarely used in the rehabilitation of elderly patients and especially in the elderly who have been hospitalized.

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Previously, we have studied the neuromuscular and functional changes, before and after unilateral resistance training, neuromuscular electrical stimulation, and a standard rehabilitation program in elderly patients recovering from hip replacement surgery (46, 47). These results indicated that resistance training is more effective to restore muscle mass, contractile rate of force development, and functional performance than rehabilitation regimes based on functional exercises and electrical stimulation (46, 47). However, although muscle architecture has been shown to be an important factor for muscle function in young individuals (1), no studies have previously investigated the changes in muscle fiber morphology and muscle architecture with different types of intervention in the elderly.

To describe more closely the potential interaction between muscle morphology, muscle architecture, and contractile capacity, the aim of the present study was therefore, in the same group of patients, to examine the relationship between muscle fiber area and muscle fiber pennation angle of the vastus lateralis (VL) muscle before and after the three intervention regimes: resistance training, electrical stimulation, and standard rehabilitation. It was hypothesized that resistance training would be more effective to increase muscle fiber pennation angle and muscle fiber area than standard rehabilitation and electrical stimulation and furthermore that these changes might be more effective to increase muscle fiber pennation angle and muscle fiber area than standard rehabilitation and electrical stimulation and furthermore that these changes might be related to the potential gains in maximal voluntary contraction capacity and stair-climbing power. The present study is the first in which measurements of muscle fiber pennation angle, muscle fiber area, maximal dynamic strength, and stair-climbing power were combined to examine the specific adaptations to different training regimes in elderly individuals.

METHODS

Subjects and study design. Thirty-six elderly individuals, 18 women (age range 60 – 86 yr) and 18 men (age range 60 – 79 yr) volunteered to participate in the study. The subjects were scheduled for unilateral hip replacement surgery at Bispebjerg University Hospital, Copenhagen, Denmark due to hip osteoarthritis. Before the operation all subjects were randomized to one of three groups: (1) unilateral resistance training (RT; n = 13), (2) unilateral electrical stimulation of the quadriceps muscle (ES; n = 11), and (3) standard rehabilitation (SR; n = 12). Randomization was performed by a computer program (Minimize version 2.1), and patients were stratified by age and sex. All three training regimes have been described in detail elsewhere (47). In brief, RT consisted of a 12-wk (3/wk) unilateral progressive training program [weeks 1–2: 3 × 10 (20 RM, where RM is repetition maximum); weeks 3–4: 3 × 12 (15 RM); weeks 5–6: 4 × 10 (12 RM); weeks 7–8: 5 × 8 (8 RM); weeks 9–10: 4 × 8 (8 RM); weeks 11–12: 3 × 8 (8 RM)] with focus on knee extension and leg press exercises. The ES group performed neuro-muscular electrical stimulation of the quadriceps muscle (ES; n = 11), and (3) standard rehabilitation (SR; n = 12). Randomization was performed by a computer program (Minimize version 2.1), and patients were stratified by age and sex. All three training regimes have been described in detail elsewhere (47).

Maximal quadriceps muscle strength. Muscle strength was measured as the maximal voluntary knee extension (peak moment, N·m) during concentric quadriceps contraction in an isokinetic dynamometer (KinCom) at 60°/s and 180°/s (46). Moment values were corrected for gravity of the lower limb and normalized to body weight. Measurements were performed bilaterally and were preceded by a familiarization trial conducted on a separate day. The nonaffected side was tested first to increase the subject’s comfort with the procedure. Strict care was taken to ensure identical test protocols for all subjects, which included standardized verbal encouragement and visual feedback provided by a real-time display of the force output (25). Successive trials were performed until peak moment could not be improved any further, which typically included seven to nine attempts at each velocity (2).

Muscle biopsy sampling and analyses. Bilateral muscle samples were obtained from the middle portion of the VL utilizing the percutaneous needle biopsy technique of Bergström (7) by the same investigator. Following intervention, efforts were made to extract tissue from the same depth and location (within ~1–2 cm). After being dissected of all visible blood, adipose, and connective tissue, the muscle samples were oriented in embedding medium (Tissue-Tek) frozen in isopentane cooled with liquid nitrogen and stored at −80°C. Subsequently, serial transverse sections (10 μm) were cut in a cryotome at −20°C and stained for myofibrillar ATPase at pH 9.4 after both alkaline (pH 10.3) and acid (pH 4.3 and 4.6) preincubations (9). All samples of each individual person were stained in the same batch to avoid interassay variation. Muscle fiber-type and cross-sectional area (CSA) analyses were conducted in a blinded fashion and an average of 397 ± 22 fibers were analyzed in each biopsy. On the basis of the ATPase staining pattern, muscle fibers were characterized as type I, I/IIa, IIA, IIX, and IIX (3). Because of a low number of type I/IIa and IIX fibers in some individuals, the individual analyses were collapsed into three fiber types, type I, type IIa, and type IIX, before the final statistical analyses were performed (3). The reduction in fiber type was based on the following equations: type I = 1 – I/IIa; type IIa = I/IIa + IIA + IIX; and type IIX = IIX + IIX. For the determination of muscle fiber size, only truly horizontally fibers were used; thus a restricted number of fibers (minimum of 50 fibers) were included for this analysis. A videocscope consisting of a microscope (Olympus BX 50) and color video camera (Sanyo high-resolution charge-coupled device) in combination with Tema Image-analysis System (Scanbeam Denmark) were used to calculate the mean fiber area values of each fiber type.

Muscle fiber pennation angle and muscle thickness. Sagittal ultrasound (UL) images of the quadriceps femoris muscle were recorded with a Siemens real-time scanner with a 7.5-MHz linear array transducer. Images were obtained in the seated position (90° flexion in the hip and knee joint) at 50% of femur length over the midbelly of the VL (1). To ensure the same scan position, traces were drawn on acetate paper, which was aligned relative to skin marks and anatomic landmarks. VL fiber pennation angle was measured as the angle between VL muscle fiber fascicles and the deep aponeurosis of the insertion (1) (Fig. 1). VL muscle thickness was obtained with the UL-transducer in the same position and measured as the distance between the deep and superficial aponeurosis of the VL muscle. Two images from each limb were obtained from each subject. Each image was evaluated three times and the mean value was recorded. The coefficient of variation between two consecutive measurements was <5%.

Stair walking power. Maximum stair walking power per kilogram body mass (W/kg) was calculated as the distance of vertical displacement of the body center mass times g (9.81 m/s²), i.e., the change in potential energy, divided by the fastest time of stair ascent. Each subject performed three trials, and the stairs consisted of 10 steps each with a height of 16.5 cm for a total vertical displacement of 1.65 m.

Statistical analysis. Nonparametric statistics were used for the analyses, since not all data were normally distributed. To evaluate the effect of intervention over time, a Friedman test was used with post hoc Wilcoxon’s test. Any between-group differences were analyzed with Kruskal-Wallis tests and subsequent Mann-Whitney U-test. Spearman’s Rho was used for the correlation analysis on a limited number of patients, to examine the relationship between muscle function in young individuals (1), no studies have previously investigated the changes in muscle fiber morphology and muscle architecture with different types of intervention in the elderly.
Changes in muscle fiber pennation angles and muscle thickness. Muscle architecture was altered following 12 wk of RT training as reflected by a 22% increase in VL muscle fiber pennation angle (7.2 ± 0.5 to 8.6 ± 0.6°, \( P < 0.05 \)), which was contrasted by a 11% decrease following SR (7.6 ± 0.3 to 6.7 ± 0.2°, \( P < 0.05 \)). No change was observed with ES (Fig. 3). At baseline, there was no difference between groups; however, the delta changes with RT were greater than those observed with SR and ES both at 5 wk (RT > ES, \( P < 0.05 \) and RT > SR, \( P < 0.05 \)) and at 12 wk (RT > ES and RT > SR, \( P < 0.05 \)). Muscle thickness of the VL muscle increased by 14.8% after 12 wk of RT (15.3 ± 1.3 to 17.5 ± 1.6 mm, \( P < 0.05 \)), whereas there was no increase with ES or SR (Fig. 4). Moreover, the delta changes with 12 wk of RT was greater than those observed with SR (RT > SR, \( P < 0.05 \)).

Stair walking power. Maximum stair walking power (W/kg) increased after 12 wk of RT (2.6 ± 0.4 W/kg to 3.5 ± 0.4 W/kg, \( P < 0.05 \)) and 12 wk of ES (2.6 ± 0.3 W/kg to 3.4 ± 0.4 W/kg, \( P < 0.05 \)) but not after 12 wk of SR (2.2 ± 0.3 W/kg to 2.5 ± 0.2 W/kg). Furthermore, the delta changes with RT were greater than those observed with SR at 12 wk (RT > SR, \( P < 0.05 \)), but there was no difference between ES and SR (\( P = 0.495 \)).

Correlation analyses. The relative change in VL muscle fiber pennation angle was related to the individual change in dynamic torque at both contraction velocities (60°/s: \( r = 0.619, \) 180°/s: \( r = 0.530, P < 0.05 \)), to the change in total mean fiber area (\( r = 0.429, P < 0.05 \)), and to the change in VL muscle thickness (\( r = 0.479, P < 0.05 \)). The individual delta change in type II muscle fiber area after 12 wk of RT was related to the delta change in stair walking power (\( r = 0.729, P < 0.05 \)). Furthermore, the increase in muscle fiber pennation angle after 12 wk of RT was strongly related to the increase in muscle thickness (\( r = 0.733, P < 0.05 \)).

DISCUSSION

Although immobilization and hospitalization are more frequent in old age and lead to an increased risk of disability (24),
the effects of different types of loading on qualitative changes in muscle architecture and muscle morphology has not previously been investigated in elderly postoperative patients. The present study is the first to simultaneously measure maximal dynamic muscle strength, muscle fiber size, muscle fiber pennation angle, and stair walking power to address the change in muscle contractile function, muscle fiber morphology, muscle architecture, and functional performance with different training modalities (resistance training, electrical stimulation, or standard rehabilitation) in elderly individuals recovering from hip surgery. The main finding was that 12 wk of resistance training led to substantial increases in maximal contractile muscle strength that were accompanied by gains in both type I and II single muscle fiber CSA and gains in VL muscle fiber pennation angle and stair walking power. Notably, in contrast to resistance training, no changes occurred in these parameters following the most commonly employed types of training to elderly patients, i.e., a rehabilitation program based on functional exercises (standard rehabilitation) or neuromuscular electrical stimulation.

Although the subjects in the present study were rather frail, especially the first 4–6 wk after surgery, maximal dynamic muscle strength increased by ~30% (Table 2) in response to 12 wk of resistance training. Similar gains in muscle strength have been demonstrated following resistance training in healthy elderly individuals (18, 31, 41) and recently in frail elderly (8, 27). In contrast, electrical stimulation maintained the preoperative level of muscle strength, which is in line with previous findings in young patients after anterior cruciate ligament reconstruction (5, 16). Notably, the standard rehabilitation regime did not result in any increases in maximal dynamic muscle strength, which is in accordance with studies that have evaluated the effect of physiotherapy exercises after hip surgery (44, 48). Importantly, although all three regimes were commenced already 1–2 days after surgery, there were no training-related complications in any of the groups.

Although average muscle fiber area increased by 32% following 12 wk of RT, more pronounced gains in fiber CSA were seen for the type IIa (+37%) and IIx (+51%) fibers compared with that of the type I fibers (+17%), indicating a more marked hypertrophy of the type II fibers. This is in agreement with previous studies in young (1) and old individuals (27), although not consistently shown (17, 31). Furthermore, the pronounced increase in type II fiber CSA seen with RT compensated for the preoperative difference in type I and II fiber CSA (II < I), which disappeared following RT. In contrast, muscle fiber area remained unaffected by ES or SR. Importantly, the present data demonstrates that changes in type II fiber CSA with RT translated into an improved stair walking power, which is an important functional adaptation (6, 28).

Interestingly, the delta changes in type I muscle fiber CSA were significantly larger after both RT and ES than after SR (RT > SR and ES > SR, P > 0.05), whereas RT was the most effective intervention to induce changes in type Ila muscle fiber CSA (RT > ES and RT > SR, P > 0.05). These findings are in line with previous studies indicating that ES mainly leads to hypertrophy of type I fibers (15, 20) whereas RT effectively induce hypertrophy of type II fibers (1, 27). Furthermore, the present data demonstrate that the preoperative side-to-side difference in muscle fiber CSA (type I and type IIa) was eliminated after 12 wk of RT, in contrast to ES and SR.

In both sarcopenia and disuseatrophy, muscle fiber fascicles seem to have a reduced pennation angle compared with healthy young individuals, likely because of decreased amounts of contractile tissue (35, 37). In agreement with these findings, muscle fiber pennation angles on the osteoarthritic side were significantly smaller compared with the healthy side (control leg) in the present study. However, the muscle tissue of old individuals also shows a remarkable plasticity with resistance training. After 12 wk of RT there was a 22% increase in VL muscle fiber pennation angle (Fig. 3), which was comparable to that seen in both young and old individuals after a period of resistance training (1, 36). That is contrasted by the lack of change in muscle fiber pennation angle for the elderly individuals subjected to ES training or SR. Interestingly, there was a positive relationship between the training-induced change in VL muscle fiber pennation angle and the corresponding changes in dynamic torque at slow-to-fast contraction velocities (60°/s: r = 0.619, 180°/s: r = 0.530, P < 0.05), emphasizing the importance of muscle architecture for the contractile function of the muscle. Moreover, the individual delta changes in muscle fiber pennation angle was positive related to the

### Table 2. Changes in dynamic muscle strength normalized to body weight

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<tr>
<th></th>
<th>OP Pre 60°/s</th>
<th>CO Pre 60°/s</th>
<th>OP 12 wk 60°/s</th>
<th>CO 12 wk 60°/s</th>
<th>OP Pre 180°/s</th>
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<th>OP 12 wk 180°/s</th>
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<tr>
<td>Pre, 60°/s</td>
<td>1.31±0.15</td>
<td>1.64±0.11</td>
<td>1.28±0.12</td>
<td>1.48±0.10</td>
<td>1.22±0.11</td>
<td>1.70±0.13</td>
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<tr>
<td>5 wk, N·m·kg⁻¹</td>
<td>1.34±0.14†</td>
<td>1.67±0.12</td>
<td>1.16±0.13</td>
<td>1.42±0.10</td>
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<td>1.16±0.10</td>
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<tr>
<td>12 wk, N·m·kg⁻¹</td>
<td>1.64±0.15‡</td>
<td>1.64±0.12</td>
<td>1.25±0.13</td>
<td>1.42±0.11</td>
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<td>Peak torque</td>
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<td>Pre, 180°/s</td>
<td>0.88±0.10</td>
<td>1.08±0.09</td>
<td>0.84±0.09</td>
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<td>0.96±0.07</td>
<td>1.14±0.09</td>
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<tr>
<td>5 wk, N·m·kg⁻¹</td>
<td>0.89±0.08</td>
<td>1.09±0.09</td>
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<td>0.98±0.08</td>
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<tr>
<td>12 wk, N·m·kg⁻¹</td>
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<td>1.08±0.09</td>
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<td>0.97±0.08</td>
<td>0.93±0.07</td>
<td>1.16±0.09</td>
<td>0.93±0.07</td>
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Isokinetic quadriceps strength measurements normalized to body weight. Data are presented from both sides, the operated side (OP) and the control side (CO), from all three intervention groups at baseline (Pre), 5 wk after the operation (5 wk), and 12 wk after the operation (12 wk). The 3 intervention groups are RT, ES, and SR. Values are means ± SE. *P < 0.05 significantly different from baseline. †P < 0.05 refers to intergroup differences, RT being significantly different from SR and ES.
changes in VL muscle thickness ($r = 0.479$, $P < 0.05$), which was further emphasized looking separately at the RT group ($r = 0.733$, $P < 0.05$). Notably, there was no relation between the changes in muscle thickness and the anatomic CSA (ACSA) measured by computed tomography scan ($P > 0.05$), yet, the changes in ACSA was positively related to the delta changes in muscle fiber pennation angle ($r = 0.600$, $P < 0.05$).

In line with previous data in young individuals a positive relationship was observed between the changes in ACSA and the individual changes in type I muscle fiber CSA ($r = \ldots$)
In the present study, we found a mismatch between the increase in muscle fiber CSA (+32%) and the gain in muscle thickness (+14%) or as previously reported in ACSA (+12%) after 12 wk of resistance training (47). Similar findings of a mismatch between the gains in ACSA and muscle fiber CSA after a period of resistance training has previously been found in both young (1) and old individuals (11, 14, 19). The observed increase in muscle fiber pennation angle (+22%) in the present study indicates the importance of muscle architecture to explain some of this mismatch, since a steeper muscle fiber pennation angle allows for a larger physiological fiber area for a given muscle volume and it should therefore be recognized that ACSA may not be a very representative measure of changes in the physiological CSA (1).

In conclusion, the present study demonstrated that resistance training offers an effective way of increasing maximal muscle strength in elderly postoperative patients. Importantly, the increase in muscle function was accompanied by gains in muscle fiber size and pennation angle that resemble those typically seen in young healthy individuals. In contrast, these positive adaptations were not achieved by daily neuromuscular electrical stimulation (ES) or standard physiotherapy exercises (SR). Thus, the present data emphasize the importance of using resistive exercises in future rehabilitation programs for elderly individuals.

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