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

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Running title: Muscle architecture and morphology in the elderly

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ABSTRACT

Although the negative effects of bed-rest on muscle strength and muscle mass are well established, it still remains a challenge to identify effective methods to restore physical capacity of elderly patients recovering from hospitalization. The present study compared different training regimes with respect to muscle strength, muscle fiber size, muscle architecture and stair walking power in elderly postoperative patients. Methods: Thirty-six patients (60-86 yrs) scheduled for unilateral hip-replacement surgery due to hip-osteoarthritis (OA) were randomized to either; 1) Resistance Training [RT: 3/wk·12wks], 2) Electrical Stimulation [ES: 1h/day·12wks] or 3) Standard Rehabilitation [SR: 1h/day·12wks]. All measurements were performed at baseline, 5 and 12 wks post-surgery. Results: After 12 wks of RT maximal dynamic muscle strength increased by 30% at 60°/s (p<0.05) and by 29% at 180°/s (p<0.05), muscle fiber area increased for type I (+17%, p<0.05), type IIa (+37%, p<0.05) and type IIx muscle fibers (+51%, p<0.05) while, muscle fiber pennation angle increased by 22% and muscle thickness increased by 15% (p<0.05). Furthermore, stair-walking power increased by 35% (p<0.05) and was related to the increase in type II fiber area (r=0.729, p<0.05). In contrast, there was no increase in any measurement outcomes with ES and SR. Discussion: The present study is the first to demonstrate the effectiveness of resistance training to induce beneficial qualitative changes in muscle fiber morphology and muscle architecture in elderly postoperative patients. In contrast, rehabilitation regimes based on functional exercises and neuromuscular electrical stimulation had no effect. The present data emphasizes the importance of resistance training in future rehabilitation programs for elderly individuals.
INTRODUCTION

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 few studies have examined changes in muscle architecture and muscle fiber morphology in response to aging and physical training, and while the results suggests that a significant plasticity exists, there is generally a lack of data as to which 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 and forth, which is partly due 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 approximately 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 approximately 1.5 % per year from the sixth decade (45).

In addition to the muscular changes pertaining to muscle fiber area, ageing 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 to young individuals has been demonstrated by Narici et al, suggesting that a significant part of the decrease in muscle function with aging may be related to changes in muscle architecture (39). 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 in order to determine effective intervention programs to improve muscle function after chronic disuse 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 (NMES) 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), in patients with chronic diseases (10; 23; 26) and 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 of this, resistance training is still rarely used in the rehabilitation of elderly patients and especially in the elderly who have been hospitalized.

Previously, we have studied the neuromuscular and functional changes, before and after unilateral resistance training (RT), Neuromuscular Electrical Stimulation (ES) and a Standard Rehabilitation (SR) 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 (RFD) 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 has previously investigated the changes in muscle fiber morphology and muscle architecture with different types of intervention in the elderly.
In order 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 muscle before and after the three intervention regimes; Resistance Training (RT), Neuromuscular Electrical Stimulation (ES) and a Standard Rehabilitation (SR).

It was hypothesized, that RT would be more effective to increase muscle fiber pennation angle and muscle fiber area than SR and ES, 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, eighteen women (W; age range 60-86 yrs) and eighteen men (M; age range 60-79 yrs) 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], 3) Standard Rehabilitation [SR, n=12]. Randomization was performed by a computer program (Minimize version 2.1) and patients were stratified by age and gender. All three training regimes have been described in detail elsewhere (47). In brief, resistance training consisted of a 12 week (3/wk) unilateral progressive training-program (Wk 1-2: 3x10 [20 RM], Wk 3-4: 3x12 [15 RM], Wk 5-6: 4x10 [12 RM], Wk 7-8: 5x8 [8 RM], Wk 9-10: 4x8 [8 RM], Wk 11-12:3x8 [8
with focus on knee-extension and leg-press exercises. The ES-group performed Neuromuscular Electrical Stimulation (NMES) of the quadriceps muscle of the operated limb 1h/day (40 Hz). The SR-group performed a standard rehabilitation program consisting of functional exercises with focus on improving mobility and strength without external loading. Measurements were performed 1 week (± 2-3 days) before the operation, 5 and 12 weeks post-surgery and the muscle biopsies were taken 2 days after surgery. The local Ethics Committee approved the conditions of the study and the experimental procedures were performed in accordance with the Declaration of Helsinki.

**Maximal quadriceps muscle strength**

Muscle strength was measured as the maximal voluntary knee extension (peak moment, Nm) 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 non-affected 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 7-9 attempts at each velocity (2).

**Muscle biopsy sampling and analyses**

Bilateral muscle samples were obtained from the middle portion of m. vastus lateralis 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 dissecting the muscle samples of all visible blood, adipose and connective tissue, the muscle samples were oriented in embedding medium (Tissue Tec) frozen in isopentane cooled with liquid
nitrogen and stored at -80º C. Subsequently serial transverse sections (10 µm) were cut in a cryotome at -20º 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 CSA analyses were conducted in a blinded fashion and an average of 397 ± 22 fibers were analyzed in each biopsy. Based on the ATPase staining pattern muscle fibers were characterized as type I, I/IIa, IIa, IIax and IIx (3). Due to a low number of type I/IIa and IIax 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 = I + ½ I/IIa; type IIa = ½I/IIa + IIa + ½IIax and type IIx = ½IIax + 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 videoscope consisting of a microscope (Olympus BX 50) and color video camera (Sanyo high resolution CCD) in combination with Tema Image-analyses System (Scanbeam Denmark) were used to calculate the mean fiber area values of each fiber type.

Muscle fiber pennation angle and muscle thickness

Sagital ultrasound 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 deg. flexion in the hip and knee joint) at 50 % of femur length over the midbelly of VL (1). To ensure the same scan position traces were drawn on acetate paper, which was aligned relative to skin marks and anatomical landmarks. Vastus lateralis (VL) fiber pennation angle (θp) was measured as the angle between VL muscle fiber fascicles and the deep aponeurosis of the insertion (1) (Figure 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 kg body mass (watt/kg) was calculated as the distance of vertical displacement of the body center mass (BCM) 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**

Non-parametric 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 test. Any between group differences were analysed with Kruskall-Wallis tests and subsequent Mann-Whitney U test. Spearman's Rho was used for the correlation analysis on a limited number of data. Analysis were performed on collapsed data for all three groups, except for the relation between the delta change in type II muscle fiber area and stair walking power after 12 weeks of RT. Data are presented as mean values ± SEM. A p-value of less than 0.05 were considered significant.

**RESULTS**

Twenty-eight of the thirty-six included patients completed the study: two withdrew immediately from the SR-group because they were unsatisfied with the randomization, two became ill for reasons unrelated to the study, two persons refused to have taken muscle biopsies and two withdrew because of personal problems. There was no difference between the three groups with respect to anthropometric data (Table 1), maximal muscle strength (Table 2) or muscle fiber CSA (Figure 4) at the inclusion of the study. No training related complications were seen in any of the three groups.
Changes in maximal muscle strength

Muscle strength remained unchanged on the operated side in SR and ES, as well as in the non-operated control-leg (CO) in all three intervention groups (Table 2). Knee extensor peak torque increased by 30% at 60°/s (p<0.05) and by 29% at 180°/s (p<0.05) after 12 weeks of resistance training (RT). Furthermore, the increase in peak torque at 60°/s with RT was significantly different compared to SR at 5 wks (p<0.05), and compared to SR (p<0.05) and ES (p<0.05) at 12 weeks. At the faster contraction velocity (180°/s) the increase with RT was significantly greater compared to SR at 12 wks (p<0.05), but not compared to the ES.

Changes in muscle fiber area

All three fiber types increased following the 12 weeks of RT (Figure 4). Type I muscle fiber area increased by 17% (p<0.05), type IIa fibers increased by 37% (p<0.05) and type IIx fibers increased by 51% (p<0.05) after 12 weeks of RT (Figure 4). The corresponding increase in total mean fiber area was 32% (p<0.05). In contrast, there was no increase in the mean fiber area for any of the examined fiber types with ES and SR. In addition, there was a significant difference in myofiber CSA (type 1, type 2a but not type 2x) at baseline (Pre) in all three groups, however, after 12 weeks of RT this asymmetry was eliminated, in contrast to SR and ES. Muscle fiber CSA in the control leg (CO) did not change in any of the intervention groups (p>0.05). At baseline, there was no difference between groups, however, the delta changes in type 1 muscle fiber CSA observed with 12 weeks of RT and ES were greater than after 12 weeks of SR (RT>SR and ES>SR, p<0.05) as well as the increase in type 2a muscle fiber CSA with 12 weeks of RT were greater than after 12 weeks of ES and SR (RT>ES and RT >SR, p<0.05).
Changes in muscle fiber pennation angles and muscle thickness

Muscle architecture was altered following 12 weeks 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 training (Figure 2). At baseline, there was no difference between groups, however the delta changes with RT was greater than those observed with SR and ES both at 5 weeks (RT>ES, p<0.05 and RT>SR, p<0.05) and at 12 weeks (RT>ES and RT>SR, p<0.05). Muscle thickness of the VL-muscle increased by 14.8% after 12 weeks of RT (15.3 ± 1.3 mm to 17.5 ± 1.6 mm, p<0.05), whereas there was no increase with ES or SR (Figure 3). Moreover, the delta changes with 12 weeks of RT was greater than those observed with SR (RT>SR, p<0.05).

Stair walking power

Maximum stair walking power (watt/kg) increased after 12 weeks of RT (2.6 ± 0.4 watt/kg to 3.5 ± 0.4 watt/kg, p<0.05) and 12 weeks of ES (2.6 ± 0.3 watt/kg to 3.4 ± 0.4 watt/kg, p<0.05), but not after 12 weeks of SR (2.2 ± 0.3 watt/kg to 2.5 ± 0.2 w/kg). Furthermore, the delta changes with RT were greater than those observed with SR at 12 weeks (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°/sec: r=0.619; 180°/sec: 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 weeks 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 weeks of RT was strongly related to the increase in muscle thickness \( r=0.733, \ p<0.05 \).

**DISCUSSION**

Although immobilization and hospitalization is more frequent in old age and leads 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 simultaneous 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 (RT), electrical stimulation (ES), or standard rehabilitation (SR)) in elderly individuals recovering from hip-surgery. The main finding was that 12 weeks 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 RT, no changes occurred in these parameters following the most commonly employed types of training to elderly patients, i.e. a standard rehabilitation program based on functional exercises (SR) or neuromuscular electrical stimulation (ES).

Although the subjects in the present study were rather frail, especially the first 4-6 weeks after surgery, maximal dynamic muscle strength increased by about 30% (Table 2) in response to 12 weeks of resistance training. Similar gains in muscle strength has 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 ACL-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.

While average muscle fiber area increased by 32% following 12 weeks of RT, more pronounced gains in fiber CSA were seen for the type IIa (+37%) and IIx (+51%) fibers compared to 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 pre-operative 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 1 muscle fiber CSA were significantly larger after both RT and ES than SR (RT>SR and ES>SR, p<0.05), whereas RT was the most effective intervention to induce changes in type 2a 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 1 fibers (15; 20) whereas RT effectively induce hypertrophy of type 2 fibers (1; 27). Furthermore, the present data demonstrate that the pre-operative side-to-side difference in muscle fiber CSA (type 1 and type 2a) was eliminated after 12 weeks of RT, in contrast to ES and SR.

Both in sarcopenia and disuse atrophy, muscle fiber fascicles seem to have a reduced pennation angle compared to healthy young individuals, likely due to decreased amounts of contractile tissue (35; 37). In agreement with these findings, muscle fiber pennation angles on the osteoarthritic side (OP) were significantly smaller compared to the healthy side (CO) in the present study. However, the muscle tissue of old individuals also shows a remarkable plasticity with resistance training.
After 12 weeks of RT there was a 22% increase in VL muscle fiber pennation angle (Figure 2), 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 electrical stimulation training (ES) or standard physical rehabilitation (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 (60º/sec: \( r=0.619; \) 180º/sec: \( r=0.530, p<0.05 \)), 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 changes in VL muscle thickness \( (r=0.479, p<0.05) \), which was further emphasized looking separately at the resistance training group \( (r=0.733, p<0.05) \). Notably, there was no relation between the changes in muscle thickness and the anatomical CSA (ACSA) measured by ct-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 1 muscle fiber CSA \( (r=0.528, p<0.05) \) and type 2 muscle fiber CSA \( (r=0.476, p<0.05) \) (1).

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 previous reported in ACSA \( (+ 12\%) \) after 12 weeks of RT (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 indicate the importance of muscle architecture to explain for 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 anatomical CSA 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 post-operative patients. Importantly, the increase in muscle function was accompanied by gains in muscle fiber size and pennation angle that resemble that 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 emphasizes the importance of using resistive exercises in future rehabilitation programs for elderly individuals.
Figure legends

Table 1. Anthropometric data
Data are presented as means ± SEM (range). No significant differences were observed between groups at inclusion time (ns). Resistance training (RT); Electrical stimulation (ES); Standard rehabilitation (SR). W denotes women, M denotes men. BMI denotes Body Mass Index.

Table 2. Changes in dynamic muscle strength normalized to bodyweight
Isokinetic quadriceps strength measurements normalized to bodyweight. Data are presented from both sides, the operated-side (OP) and the control-side (CO) from all three intervention groups at baseline (pre), 5 weeks after the operation (5w) and 12 weeks after the operation (12w). The three intervention groups are resistance training (RT), electrical stimulation (ES) and standard rehabilitation (SR). Data are presented as means ± SE, * p< 0.05 significantly different from baseline. § p< 0.05 refers to intergroup differences, resistance training being significantly different from standard rehabilitation and electrical stimulation.

Figure 1. Measurement of muscle fiber pennation angle and muscle thickness
Sagital ultrasound image obtained in the quadriceps femoris muscle at 50 % femur length. Muscle fiber pennation angle of the vastus lateralis muscle (θp) was determined as the angle between vastus lateralis muscle fiber fascicles and the deep aponeurosis separating vastus lateralis and vastus intermedius. Muscle thickness (red dotted line) was measured as the distance between the superficial and deep aponeurosis of the VL muscle.
Figure 2. Changes in muscle fiber pennation angles

Muscle fiber pennation angles of m. vastus lateralis from both limbs (OP, operated leg; CO, control-leg) in all three intervention groups (Standard Rehabilitation, SR; Electrical Stimulation, ES and Resistance Training, RT) at three time points (Pre, baseline values; 5wk, after five weeks of training; 12wk, after twelve weeks of training). Data are presented as means ± SE, * p< 0.05 significantly different from baseline, # p< 0.05 RT significantly different from SR and ES. CO was significant different from OP in all three intervention before surgery (Pre). After 12 weeks of RT there was no side difference, in contrast to SR and ES.

Figure 3. Changes in VL muscle thickness

Muscle thickness of m. vastus lateralis from both limbs (OP, operated leg; CO, control-leg) in all three intervention groups (Standard Rehabilitation, SR; Electrical Stimulation, ES and Resistance Training, RT) at three time points (Pre, baseline values; 5wk, after five weeks of training; 12wk, after twelve weeks of training). Data are presented as means ± SE, * p< 0.05 significantly different from baseline, # p< 0.05 RT significantly different from SR. CO was significant different from OP in all three intervention before surgery (Pre). After 12 weeks of RT there was no side difference, in contrast to SR and ES.

Figure 4. Changes in VL muscle fiber CSA

Muscle fiber cross sectional area of type 1, type 2a and 2x fibers from both limbs (OP, operated leg; CO, control-leg) in all three intervention groups (Standard Rehabilitation, SR; Electrical Stimulation, ES and Resistance Training, RT) at three timepoints (Pre, baseline values; 5wk, after five weeks of training and 12wk, after twelve weeks of training). Data are presented as means ± SE, * p< 0.05 significantly different from baseline, # p< 0.05 RT significantly different from SR. CO
was significant different from OP in all three intervention before surgery (Pre). After 12 weeks of RT there was no side difference, in contrast to SR and ES.
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Table 1. Anthropometric data

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Data are presented as means ± SEM (range). No significant differences were observed between groups at inclusion time (ns). Resistance training (RT); Electrical stimulation (ES); Standard rehabilitation (SR). W denotes women, M denotes men. BMI denotes Body Mass Index.
Table 2. Changes in dynamic muscle strength normalised to bodyweight

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</tbody>
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Isokinetic quadriceps strength measurements normalised to bodyweight. Data are presented from both sides, the operated-side (OP) and the control-side (CO) from all three intervention groups at baseline (pre), 5 wks after the operation (5w) and 12 wks after the operation (12w). The three intervention groups are resistance training (RT), electrical stimulation (ES) and standard rehabilitation (SR). Data are presented as means ± SE, * p< 0.05 significantly different from baseline, § p< 0.05 refers to intergroup differences, resistance training being significantly different from standard rehabilitation and electrical stimulation.
Figure 1. Measurement of muscle fiber pennation angle and muscle thickness
Figure 2. Changes in muscle fiber pennation angles
Figure 3. Changes in VL muscle thickness

[Graph showing changes in VL muscle thickness across different conditions and time points]

VL muscle thickness (mm)

Pre 5wk 12 wk

CO OP CO OP CO OP
SR ES RT

# *
Figure 4. Changes in muscle fiber CSA

Type I muscle fiber CSA

Type IIa muscle fiber CSA

Type IIx muscle fiber CSA

Pre 5wk 12wk

CO OP CO OP CO OP

SR ES RT

SR ES RT

SR ES RT

SR ES RT