Three Months of Progressive High-Load Versus Traditional Low-Load Strength Training Among Patients With Rotator Cuff Tendinopathy

Primary Results From the Double-Blind Randomized Controlled RoCTEx Trial

Kim Gordon Ingwersen,*†‡ PT, PhD, Steen Lund Jensen,§ MD, PhD,
Lilli Sørensen,‖ MD, Hans Ri Jørgensen,¶ MD, PhD, Robin Christensen,# Prof.,
Karen Søgaard,** Prof., and Birgit Juul-Kristensen,††† Assoc. Prof.
*Investigation performed at Hospital Lillebaelt, Vejle Hospital, Vejle, Denmark,
and University of Southern Denmark, Odense M, Denmark*

Background: Progressive high-load exercise (PHLE) has led to positive clinical results in patients with patellar and Achilles tendinopathy. However, its effects on rotator cuff tendinopathy still need to be investigated.

Purpose: To assess the clinical effects of PHLE versus low-load exercise (LLE) among patients with rotator cuff tendinopathy.

Study Design: Randomized controlled trial; Level of evidence, 1.

Methods: Patients with rotator cuff tendinopathy were recruited and randomized to 12 weeks of PHLE or LLE, stratified for concomitant administration of corticosteroid injection. The primary outcome measure was change from baseline to 12 weeks in the Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire, assessed in the intention-to-treat population.

Results: A total of 100 patients were randomized to PHLE (n = 49) or LLE (n = 51). Mean changes in the DASH questionnaire were 7.11 points (95% CI, 3.07-11.16) and 8.39 points (95% CI, 4.35-12.44) in the PHLE and LLE groups, respectively; this corresponded to a statistically nonsignificant adjusted mean group difference of −1.37 points (95% CI, −6.72 to 3.99; P = .61). Similar nonsignificant results were seen for pain, range of motion, and strength. However, a significant interaction effect was found between the 2 groups and concomitant corticosteroid use (P = .028), with the largest positive change in DASH in favor of PHLE for the group receiving concomitant corticosteroid.

Conclusion: The study results showed no superior benefit from PHLE over traditional LLE among patients with rotator cuff tendinopathy. Further investigation of the possible interaction between exercise type and corticosteroid injection is needed to establish optimal and potentially synergistic combinations of these 2 factors.

Registration: NCT01984203 (ClinicalTrials.gov identifier): Rotator Cuff Tendinopathy Exercise Trial (RoCTEx).

Keywords: shoulder; rotator cuff; tendinopathy; exercise; physical therapy

Shoulder pain is a frequent complaint in primary and secondary care.[23,39,43] Subacromial impingement syndrome (SIS) is estimated to account for one-third of all shoulder-related health care contacts.[13,56] The definition of SIS covers an umbrella of different underlying pathological disorders, such as rotator cuff syndrome, tendinitis, and bursitis, rather than a specific diagnosis.[22,36] Consequently, some authors avoid the term SIS.[34,35,47] The diagnosis of rotator cuff tendinopathy is often used synonymously with SIS, but rotator cuff tendinopathy should be confined to tendon-related pain with weakness, especially during elevation and external rotation, largely preserved range of motion, and minimal resting pain.[34,36,37] These clinical signs and symptoms roughly differentiate patients with rotator cuff tendinopathy from those having signs of bursitis, which include more constant

pain and, often, more pronounced decreased range of motion.[36] The diagnostic accuracy of existing orthopaedic tests are too low to clinically differentiate rotator cuff tendinopathy from other shoulder disorders.[19,47] However, ultrasound may be used to increase the diagnostic accuracy of patients with shoulder pain.[47] Ultrasound has high specificity in diagnosing changes related to tendinopathy,[41,45,47] and it is reliable when performed in a standardized manner.[25] High specificity is especially important when allocating patients to treatment strategies in a randomized controlled study.

Danish national guidelines recommend a minimum of 3 months of physical therapy before surgery is considered.[53] However, methodologically rigorous studies are necessary to evaluate the effectiveness of specific exercise regimens for rotator cuff tendinopathy.[36] These studies should focus on strengthening exercises of different intensity and frequency, as compared with an active control group.[36]

Eccentric/progressive heavy slow-resistance training has shown positive results on tendinopathy in the knee and ankle, with clinically relevant improvement in pain and function, as well as structural changes verified by ultrasound.[2,31,32] For rotator cuff tendinopathy, loaded eccentric exercises have proved superior to unloaded exercises[20] and equal to traditional rotator cuff training[40] in reducing pain and improving function. The superiority of progressive high-load exercise (PHLE) has been demonstrated only when compared with passive controls.[38]

Concomitant corticosteroid injection has frequently been administered to enhance the beneficial effects of exercise.[53] Corticosteroids decrease inflammation and edema in the surrounding tissue, thereby decreasing pain in these structures. The precise mechanism of action of corticosteroids in rotator cuff tendinopathy is not entirely clear,[6] and the influence of corticosteroid injection on exercise is unknown.

The primary aim of this study was to evaluate whether PHLE is superior to traditional low-load exercise (LLE) among patients with rotator cuff tendinopathy. We hypothesized that after 12 weeks of exercise, the intervention group would have a significant improvement in the primary outcome measure (Disabilities of the Arm, Shoulder, and Hand [DASH] questionnaire score),[21] with a decrease in shoulder pain and an increase in shoulder strength. The secondary aim was to evaluate the interaction of a concomitant corticosteroid injection in both PHLE and LLE exercise programs.

METHODS

Trial Design

The multicenter RoCTEx (Rotator Cuff Tendinopathy Exercise) trial was a randomized controlled superiority trial stratified by corticosteroid injection (yes/no), with observers and patients blinded. The primary endpoint was 12 weeks after baseline. Details on the trial are published in Ingwersen et al.[24]

Participants, Settings, and Locations

Between November 2013 and June 2015, participants with rotator cuff tendinopathy were recruited from 3 orthopaedic shoulder clinics at hospitals in western Denmark, supplemented by advertisements in local newspapers and sports/fitness clubs. Patients were seen at the nearest shoulder clinic for a standard clinical examination and assessment. Eligible participants were adults aged 18 to 65 years with shoulder symptoms lasting for a minimum of 3 months, in addition to pain in the proximal lateral aspect of the upper arm, aggravated by abduction. Further eligibility criteria were signs of rotator cuff tendinopathy verified by ultrasound, including at least 1 of the following: tendon swelling, presence of hypoechoic areas, calcification, fibrillar disruption, or neovascularization in the supraspinatus tendon. The

*Address correspondence to Kim Gordon Ingwersen, PT, PhD, Department of Physiotherapy, Hospital Lillebaelt, Vejle Hospital, Beriderbakken 4, DK-7100 Vejle, Denmark (email: kim.ingwersen@rsyd.dk).

†Research Unit of Musculoskeletal Function and Physiotherapy, Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense M, Denmark.

‡Department of Physiotherapy, Hospital Lillebaelt, Vejle Hospital, Vejle, Denmark.

§Department of Orthopaedic Surgery, Shoulder Clinic, Aalborg University Hospital, Farsø Hospital, Farsø, Denmark.

‖Department of Orthopaedic Surgery, Shoulder Clinic, Hospital Lillebaelt, Vejle Hospital, Vejle, Denmark.

¶Department of Orthopaedic Surgery, Shoulder Clinic, Odense University Hospital, Svendborg Hospital, Svendborg, Denmark.

#Musculoskeletal Statistics Unit, Parker Institute, Copenhagen University Hospital, Bispebjerg and Frederiksberg, Copenhagen, Denmark.

**Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense M, Denmark.

††Department of Health Sciences, Institute of Occupational Therapy, Physiotherapy and Radiography, Bergen University College, Bergen, Norway.

primary investigator performed all ultrasound measurements, in a standardized manner, which has shown good to excellent reliability for detecting pathological changes of rotator cuff tendinopathy.[25] Additionally, participants had to have a positive full can,[28] Jobe,[26] or resisted external rotation test[29] as well as a positive Hawkins-Kennedy[18] or Neer test.[46]

Patients were excluded if they had resting pain >40 mm on a visual analog scale (VAS; range, 0-100; 0 = no pain),[5] <90° active elevation of the arm, a full-thickness rotator cuff tear (verified by ultrasound), a corticosteroid injection within the previous 6 weeks, or competing diagnoses.[24]

Exercise Programs

Patients were randomized to the PHLE (intervention) or LLE (comparator) group. Both groups received the same exercises, attention, and basic information. Patients were seen by a physical therapist for initial exercise instruction (60 minutes) in week 1 and for supervised exercise sessions (30 minutes) in weeks 2-4, 6, and 9 and were instructed to perform home-based exercises 3 times per week.

The exercise program consisted of 2 exercises for the scapula-stabilizing muscles, 2 for the rotator cuff muscles, and 2 mobility exercises for the rotator cuff and scapulothoracic complex. The specific rotator cuff exercises were chosen according to studies showing the highest amount of activation in relation to the deltoid and taking the risk of impingement into consideration.[12,49-51] The only between-group difference was progression of load for the rotator cuff exercises. The PHLE group gradually increased its load from a 15-repetition maximum in week 1 to a 6-repetition maximum in weeks 9 to 12, allowing patients to perform isometric exercises if pain exceeded 50 mm on VAS. The control group performed a 20- to 25-repetition maximum from weeks 1 to 12 (for further description, see Appendices A and B).

Orthopaedic specialists, in accordance with the local standard procedures and in collaboration with the patients, based a potential concomitant administration of corticosteroid injection on their clinical evaluation. In general, a corticosteroid injection was considered applicable in patients with increased pain at night or with active movements of the arm, presence of inflamed bursa (verified on ultrasound), or signs of Doppler activity around calcifications. The corticosteroid injection was administered to patients after baseline assessment but before randomization.

Outcomes

The primary outcome was a change in DASH score (primary/activities of daily living = 0-100, 0 = no problems) from baseline to week 12.[21] Secondary outcomes included DASH scores at weeks 1-4, 6, and 9; perceived pain at rest, during general activities, and at night and maximum pain during the previous 24 hours (on VAS)[5]; and maximum isometric voluntary contraction (IsoForce Dynometer EVO2; Medical Device Solutions AG) and active/passive

range of motion (ROM) (HALO digital goniometer; HALO Medical Devices) for scaption and external/internal rotation (see Appendix C). Pilot studies of strength (intraclass correlations = 0.84-0.92) and ROM measurements (intraclass correlations = 0.75-0.96) have shown excellent[14] interrater reliability. Furthermore, explorative measurements included standardized ultrasound measurements obtained to verify changes consistent with tendinopathy, including tendon thickening versus the contralateral nonaffected tendon, signs of fibrillar disruption, presence of calcification, and neovascularization (dichotomized: yes/no).[25,48] These ultrasound changes are associated with tendinopathy.[54,57]

Patients were instructed to complete an exercise diary. Good compliance was defined as attending at least 4 of 6 visits to the physical therapist and completing >80% of the exercises at home (reported in the diary).[24]

Data Collection

The primary investigator performed all baseline and follow-up assessments. Fifteen pilot patients were assessed for adjustment and training of inclusion and baseline/follow-up procedures. The treating physical therapists were trained to teach patients how to perform the exercise programs and administer the DASH questionnaire.

Sample Size and Power Calculations

Given studies on patients with SIS,[4,8,20,27,33,42,55] we expected a mean baseline of 40 ± 17 points in the DASH questionnaire, 50% change in the PHLE group, and a 25% change in the LLE group. For a 2-sample pooled t test of a normal mean difference (2-sided significance level of 0.05, $P \leq .05$), 100 patients per group were required to obtain a power of at least 98.5% for detecting a mean difference of 10 DASH points between the 2 groups. For the second study objective of examining the interaction between corticosteroid use and exercise group, 260 patients in total were required to achieve 90% power.

A priori, the final deadline for inclusion for this study was March 2015.[24] However, this was postponed to June 2015. From November 2013 to June 2015, 100 participants were included; a substantially lower inclusion rate than expected resulted in a power of 0.84 for the primary aim.

Randomization and Allocation Concealment

Patients were randomly assigned to PHLE or LLE with a 1:1 allocation per center, stratified by administration of concomitant corticosteroid injection. A computer-generated randomization schedule with permuted blocks of random sizes (2-6) was used to prepare opaque, sealed, sequentially numbered envelopes placed in 2 separate ring binders (corticosteroid: yes/no) for each center. A university secretary prepared the envelopes for each center, while local secretaries performed the

allocation procedure by taking the next prepared and sealed envelope.

Blinding

Baseline measurements were performed before group allocation. At follow-up, the primary investigator strongly encouraged patients not to disclose their allocated exercise program. Patients were informed that 2 active exercise strategies were compared, but they were blinded regarding group differences and the hypotheses.

Statistical Analysis

For primary efficacy analysis in the intention-to-treat (ITT) population (all randomized patients independent of compliance and withdrawals), the between-group difference in DASH change (baseline to 12 weeks) was calculated, with baseline observation carried forward used for missing data. Analysis of covariance was used to compare mean changes from baseline in DASH scores, as well as the secondary continuous outcomes. The primary model included change from baseline as the dependent variable, with treatment group (PHLE or LLE), corticosteroid status (yes or no), and center site (Nos. 1-3) as the main effects and with baseline score as additional covariate. In the analysis of the secondary aim, the interaction for group and corticosteroid was added to the primary model. Results are expressed as the difference between group means (95% CIs) with associated *P* values.

To analyze the longitudinal element of time effects on the DASH score (repeated measures at 1-4, 6, 9, and 12 weeks), a mixed linear model approach was used, based on restricted maximum likelihood estimates of the parameters, with treatment group (PHLE or LLE), corticosteroid status (yes or no), and center site (Nos. 1-3) as main effects and with baseline score as an additional covariate.

For the effect on ultrasound-verified structural changes, differences in change between groups were analyzed by a chi-square test.

All ITT analyses were performed blinded to group allocation (groups were named A and B in the data set). Sensitivity analyses for missing values were performed on the ITT population, first with imputation of the mean change value of group A as a positive value and group B as a negative value, and then combined oppositely. All ITT data analyses were carried out according to the pre-established analysis plan.[24] An external statistical consultant performed analyses on the primary outcomes. Before group allocation was unblinded, the primary conclusion was approved by all authors. Analyses were performed with Stata/IC 14 (2015; StataCorp), with *P* < .05 considered statistically significant.

Ethics and Registration

The Regional Scientific Ethics Committee of Southern Denmark approved the trial on June 27, 2013 (project S-20130071). The trial was registered with the Danish Data

Protection Agency and approved on May 30, 2013 (registration 2008-58-0035). The trial is registered at Clinical-trials.gov (NCT01984203). The study followed the principles of the Declaration of Helsinki,[58] and informed consent was obtained from all participants before participation.

RESULTS

A total of 103 patients from hospitals and 47 patients from external recruitments were assessed for eligibility. Of these, 100 patients who fulfilled the eligibility criteria and signed informed consent to participate constituted the ITT population; 49 patients were randomized to PHLE and 51 to LLE (Figure 1). A total of 93 patients (PHLE, n = 44, 90%; LLE, n = 49, 96%) participated in the follow-up assessment and constituted the "as observed" population. Fifty-nine patients (PHLE, n = 28, 57%; LLE, n = 31, 61%) were compliant with the exercise protocol and constituted the "per protocol" population.

At baseline, demographic and clinical characteristics were not different between groups, except for a statistically significantly higher Hospital Anxiety and Depression score[60] in the PHLE group (Table 1). Furthermore, the DASH baseline score was significantly higher in patients receiving concomitant corticosteroid injection (mean ± SD, 27.64 ± 10.75) than in those not receiving (22.83 ± 11.70, P = .048). Demographic and clinical characteristics of the participants who did not complete the follow-up tests were not different from those with a complete data set (data not shown).

Efficacy Analysis

In the ITT population, there was no significant group difference in the adjusted change in DASH score, with robust results in sensitivity analyses. Furthermore, no significant between-group differences were found in any secondary outcomes (pain, strength, ROM). Both groups had, in general, significant improvements in DASH, pain, and strength, except for pain at rest. ROM significantly changed for only some of the movements (Tables 2 and 3).

Analysis of Secondary Aim

A significant interaction was found between the exercise type/groups and concomitant corticosteroid injection (P = .028) on DASH. However, there was no significant main effect of group (P = .82) or concomitant corticosteroid injection (P = .62). The effect of PHLE was higher than that of LLE, although not significantly, among those receiving concomitant corticosteroids (adjusted between-group difference: 6.92 DASH points; 95% CI, −2.11 to 15.96). The effect of PHLE was lower than that of LLE, although not significantly, among those not receiving concomitant corticosteroids (adjusted between-group difference: −5.63 DASH points; 95% CI, −12.10 to 0.83) (Table 4, Figure 2).
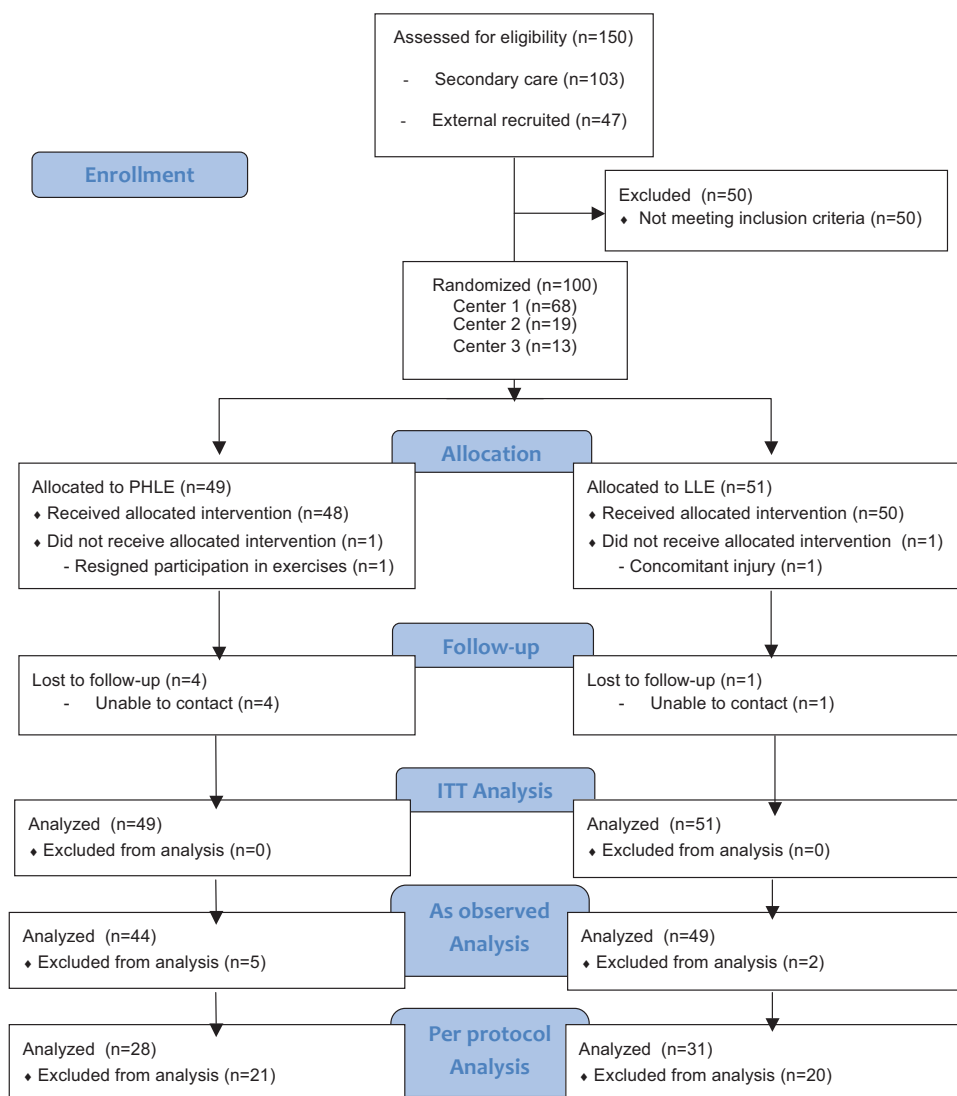
Figure 1. Flowchart of participants with rotator cuff tendinopathy in the RoCTEx trial intention-to-treat (ITT) population. Two patients did not receive allocated intervention: 1 had complications after knee surgery (progressive high-load exercise [PHLE]), and 1 resigned from participation before starting physical therapy (low-load exercise [LLE]). Five patients (4 in the PHLE group and 1 in the LLE group) could not be reached for follow-up appointments. Therefore, the baseline observation carried forward technique was performed on these 7 patients, corresponding to an ITT population of 100 patients. A total of 93 patients (PHLE, n = 44, 90%; LLE, n = 49, 96%) constituted the "as observed" population for the primary outcome. These included 14 patients who discontinued the assigned intervention (PHLE, n = 9, 18%; LLE, n = 5, 10%) because of increased shoulder pain (PHLE, n = 1; LLE, n = 1), referral for a shoulder operation (PHLE, n = 1; LLE, n = 1), other concomitant sickness (PHLE, n = 5; LLE, n = 3), or increased burdens at work (PHLE, n = 2). However, they completed the DASH questionnaire at 12 weeks. From these 14 participants, 10 were not willing or able to participate in the physical follow-up tests assessing ultrasound, visual analog scale, strength, and range of motion, resulting in 83 patients (PHLE, n = 39, 80%; LLE, n = 44, 86%) in the "as observed" population for these measurements. A total of 59 patients (PHLE, n = 28, 57%; LLE, n = 31, 61%) were compliant with the exercise protocol and were included in the per-protocol analysis.

Secondary Analyses

Repeated measures of DASH showed no between-group difference, as was the case with the as-observed (DASH, −1.19; 95% CI, −6.88 to 4.51) and per-protocol (DASH, −0.14 [95% CI: −6.20 to 5.92]) analyses, in the primary outcomes and with the secondary outcomes (pain, strength, and ROM; $P > .30$) (Appendix D).

A significant effect ($P = .039$) on ultrasound-verified neovascularity was observed in the per-protocol analysis in favor of PHLE, resulting in a 28.6% decrease in the number of patients presenting with neovascularity in the PHLE

TABLE 1
Demographic and Baseline Values for PHLE and LLE (N = 100)[a]

Variable	PHLE (n = 49)	LLE (n = 51)	Variable	PHLE (n = 49)	LLE (n = 51)
Sociodemographic measurements, compliance and adverse advents			Patient-reported and physiologic measurements		
Age, y	45.7 ± 10.6	46.5 ± 10.1	DASH		
Women	19 (38.9)	27 (52.9)	Primary (ADL)	24.3 ± 11.2	24.6 ± 12.0
BMI	26.5 ± 3.5	25.3 ± 3.6	Hobby	42.2 ± 28.0	37.5 ± 24.7
Duration of symptoms, mo, median (range)	12.0 (3-180)	12.0 (3-180)	Work	19.5 ± 21.0	18.0 ± 22.2
Symptom history[b]			HAD		
Accident or acute incidence	14 (29.8)	17 (33.3)	Depression	2.7 ± 3.1	1.4 ± 2.4
Slow consistent development (overload)	13 (27.7)	18 (35.3)	Anxiety	5.0 ± 3.6	3.3 ± 3.2
			VAS[f]		
Unknown	20 (42.6)	16 (31.4)	Rest	10.7 ± 10.6	7.7 ± 8.8
Dominant side affected[c]	29 (59.2)	34 (66.7)	Activity	37.1 ± 18.3	37.9 ± 17.1
On sick leave at baseline	2 (4.1)	0 (0)	Night	38.4 ± 23.8	34.3 ± 24.0
Workload, present occupation (0-10; 10, very physically heavy)[d]	3.8 ± 2.4	2.8 ± 1.9	Maximum	71.0 ± 15.0	71.9 ± 13.2
			Isometric strength, N/BW[b]		
			Scaption	0.42 ± 0.20	0.42 ± 0.21
			External rotation	0.23 ± 0.09	0.23 ± 0.10
Heavy workload (entire work history)[e]	9 (20.0)	9 (17.7)	Internal rotation	0.32 ± 0.14	0.31 ± 0.15
			Passive ROM[b]		
Corticosteroid injection at baseline	17 (34.7)	17 (33.3)	Scaption	149.1 ± 16.9	152.1 ± 15.5
			External rotation	92.1 ± 26.4	88.9 ± 24.6
Compliance with exercise protocol	28 (57)	31 (61)	Internal rotation	52.0 ± 14.4	50.9 ± 15.4
			Active ROM[b]		
Use of analgesics, No. per exercise session, median (range)	0.0 (0.0-4.5)	0.0 (0.0-0.3)	Scaption	136.9 ± 19.4	143.4 ± 17.1
			External rotation	77.5 ± 24.1	75.2 ± 24.0
			Internal rotation	44.6 ± 13.3	44.2 ± 14.4
Corticosteroid injection after baseline	0 (0.0)	1 (2.0)	Ultrasound measurements		
			Fibrillar disruption	44 (89.8)	46 (90.2)
Referred to surgery after baseline	2 (4.1)	1 (2.0)	Neovascularity	24 (49.0)	21 (41.2)
			Tendon swelling	16 (32.7)	12 (23.5)
Adverse events[c]			Calcification	18 (36.7)	21 (41.2)
At least 1 episode with increased pain (>1 h) vs pain before exercise because of exercise performance	13 (30.2)	18 (36.7)			
At least 1 episode with decreased strength (>1 h) vs strength before exercise because of exercise performance	11 (25.6)	12 (24.5)			

[a]Values are presented as mean ± SD and No. (%) unless otherwise noted. ADL, activities of daily living; BMI, body mass index; BW, body weight (kg); DASH, Disabilities of the Arm, Shoulder, and Hand (range, 0-100); HAD, Hospital Anxiety and Depression (range, 0-21); LLE, low-load exercise; N, newton; PHLE, progressive high-load exercise; ROM, range of motion; VAS, visual analog scale (range, 0-100).
[b]n = 98 (LLE = 51, PHLE = 47).
[c]n = 93 (LLE = 49, PHLE = 44).
[d]n = 85 (LLE = 45, PHLE = 40).
[e]n = 96 (LLE = 51, PHLE = 45).
[f]n = 99 (LLE = 51, PHLE = 48).

group, in contrast to only a 9.7% decrease in the LLE group, at 12-week follow-up.

Adherence to the Exercise Protocol

There was no between-group difference in compliance, corresponding to 28 (57%) being compliant in the PHLE group and 31 (61%) being compliant in the LLE group.

Adverse Events

Three patients were referred for operation within the study period because of worsening of symptoms, and 1 patient received a corticosteroid injection after randomization because of increased pain. There was no significant between-group difference in episodes of increased pain or loss of strength after training (Table 1).

TABLE 2
Analysis of Changes in Intention-to-Treat Population (N = 100)
for Primary and Secondary Outcomes 12 Weeks After Baseline for PHLE and LLE[a]

| | Within-Group Change | | | |
	PHLE	LLE	Adjusted Between-Group Difference on Change[b]	P Value
DASH				
Primary[c]	7.11 (3.07 to 11.16)	8.39 (4.35 to 12.44)	−1.37 (−6.72 to 3.99)	.61
Hobby[d]	9.38 (1.31 to 17.44)	9.47 (−1.45 to 20.38)	−2.13 (−14.43 to 10.17)	.73
Work[e]	3.20 (−2.83 to 9.23)	3.49 (−1.32 to 8.30)	−1.00 (−7.78 to 5.79)	.77
VAS[c]				
Rest	1.55 (−2.16 to 5.26)	1.02 (−1.66 to 3.70)	−1.05 (−5.07 to 2.97)	.61
Activity	11.14 (5.42 to 16.86)	14.07 (8.83 to 19.33)	−2.65 (−9.69 to 4.38)	.46
Night	12.57 (5.67 to 19.48)	15.75 (8.93 to 22.56)	−5.01 (−13.30 to 3.28)	.23
Maximum	15.14 (7.63 to 22.66)	17.14 (10.68 to 23.59)	−2.04 (−11.97 to 7.89)	.69
Isometric strength (N/BW)[f]				
Scaption	0.07 (0.03 to 0.11)	0.07 (0.03 to 0.10)	0.00 (−0.05 to 0.06)	.95
External rotation	0.03 (0.02 to 0.05)	0.04 (0.02 to 0.06)	0.00 (−0.02 to 0.02)	.85
Internal rotation	0.07 (0.04 to 0.09)	0.07 (0.05 to 0.10)	−0.01 (−0.05 to 0.03)	.71
Passive ROM[f]				
Scaption	2.84 (−0.92 to 6.60)	3.86 (0.62 to 7.09)	−1.93 (−6.53 to 2.68)	.41
External rotation	3.84 (0.32 to 7.35)	4.94 (0.01 to 9.88)	−0.51 (−6.48 to 5.47)	.87
Internal rotation	−0.10 (−2.60 to 2.40)	−0.12 (−3.60 to 3.36)	0.35 (−3.68 to 4.38)	.86
Active ROM[f]				
Scaption	7.38 (2.16 to 12.61)	3.50 (−0.89 to 7.88)	0.66 (−5.25 to 6.56)	.83
External rotation	5.38 (1.11 to 9.66)	5.23 (−0.54 to 10.99)	1.04 (−5.49 to 7.58)	.75
Internal rotation	1.68 (−1.16 to 4.52)	0.61 (−2.62 to 3.85)	1.20 (−2.81 to 5.21)	.55

[a]Values are presented as mean (95% CI). BW, body weight (kg); DASH, Disabilities of the Arm, Shoulder, and Hand (range, 0-100); LLE, low-load exercise; N, newton; PHLE, progressive high-load exercise; ROM, range of motion; VAS, visual analog scale (range, 0-100).
[b]Adjusted for baseline value, location (3 centers), and corticosteroid (yes/no).
[c]n = 100 (LLE = 51, PHLE = 49).
[d]n = 69 (LLE = 36, PHLE = 33).
[e]n = 86 (LLE = 43, PHLE = 43).
[f]n = 98 (LLE = 51, PHLE = 47).

DISCUSSION

No superior benefit of PHLE was seen when compared with LLE in primary or secondary outcomes. In both groups, significant within-group improvements were found in primary and secondary outcomes of pain with activity, pain at night, maximum pain, strength, and passive external ROM. A significant interaction was found between concomitant administration of corticosteroid injection and the type of exercise. This interaction resulted in an increased, although not significant, effect in favor of PHLE for patients receiving corticosteroid injection. The interpretation of the results based on the interaction of exercise and cortisone injection should be considered in relation to the lack of power necessary to prove this secondary aim.

Explanation of Results

This study did not find a significant effect of PHLE in comparison with LLE. In contrast, Lombardi et al[38] and Holmgren et al[20] evaluated the effect of PHLE and eccentric exercises in comparison with a waiting list (passive control) or an unloaded movement exercise program with no progression (active control). Both studies showed a

significant difference in the between-group analyses on DASH. However, it is questionable whether Holmgren et al (active control) defined the control exercise program sufficiently to conclude a significant effect of eccentric exercises over general exercises. In comparison, Maenhout et al[40] also evaluated the effect of eccentric exercises, in comparison with an active general exercise program, and they found no between-group differences.

The current lack of effect between exercise groups could arise from several reasons, such as the intervention length, diagnostic criteria, compensation strategies, and equal workload. First, in relation to the length of the intervention, 12 weeks of PHLE exercise may not be long enough to improve the patient's tendon health, as tendon healing may take a longer time. Therefore, a longer exercise period may have been preferable to evaluate the efficacy of PHLE. Second, as the biomechanics of the shoulder girdle are complex and the differential diagnosis between SIS and rotator cuff tendinopathy is challenging, it remains unknown whether the absence of between-group differences is due to a proportion of patients not having rotator cuff tendinopathy as their main source of pain. The results of this study should be interpreted with this in mind. However, we did follow thorough inclusion procedures to ensure the presence of

TABLE 3
Proportion of Participants With Structural Changes Verified by Ultrasound at 12 Weeks
in Intention-to-Treat Population (N = 100)[a]

	Change From Baseline to 12 wk, No. (%)		
Ultrasound Measurement	PHLE (n = 49)	LLE (n = 51)	P Value
Fibrillar disruption	40 (81.6)	42 (82.4)	
Negative change	1 (2.0)	3 (5.9)	.511
No change	43 (87.8)	41 (80.4)	
Positive change	5 (10.2)	7 (13.7)	
Neovascularity	15 (30.6)	20 (39.2)	
Negative change	1 (2.0)	4 (7.8)	.163
No change	38 (77.6)	42 (82.4)	
Positive change	10 (20.4)	5 (9.8)	
Tendon thickness	10 (20.4)	11 (21.6)	
Negative change	2 (4.1)	8 (15.7)	.138
No change	39 (79.6)	34 (66.7)	
Positive change	8 (16.3)	9 (17.6)	
Calcification	17 (34.7)	20 (39.2)	
Negative change	1 (2.0)	1 (2.0)	.999
No change	46 (93.9)	48 (94.1)	
Positive change	2 (4.1)	2 (3.9)	

[a]With analysis of changes in ultrasound measurements 12 weeks after baseline for PHLE and LLE. LLE, low-load exercise; PHLE, progressive high-load exercise.

TABLE 4
Analysis of the Interaction Between the Exercise Groups and Concomitant Administration
of Corticosteroid for PHLE and LLE in the Intention-to-Treat Population (N = 100)[a]

	CS−			CS+			
	Within-Group Change		Adjusted Between-Group Difference in Change[b]	Within-Group Change		Adjusted Between-Group Difference in Change[b]	P Value
DASH	PHLE	LLE		PHLE	LLE		
Main[c]	4.49 (−0.74 to 9.72)	9.13 (4.32 to 13.93)	−5.63 (−12.10 to 0.83)	12.05 (5.78 to 18.31)	6.92 (−1.23 to 15.06)	6.92 (−2.11 to 15.96)	.028
Hobby[d]	5.21 (−3.86 to 14.27)	9.38 (−3.56 to 22.31)	−4.55 (−19.72 to 10.62)	17.71 (0.54 to 34.88)	9.66 (−14.05 to 33.36)	2.66 (−18.67 to 24.00)	.584
Work[e]	2.78 (−5.93 to 11.49)	6.25 (−0.20 to 12.70)	−6.21 (−14.50 to 2.08)	3.91 (−4.24 to 12.05)	−2.23 (−8.50 to 4.04)	8.59 (−2.69 to 19.87)	.039

[a]Values are presented as mean (95% CI). CS−, no concomitant administration of corticosteroid injection; CS+, concomitant administration of corticosteroid injection; DASH, Disabilities of the Arm, Shoulder, and Hand (range, 0-100); LLE, low-load exercise; PHLE, progressive high-load exercise.
[b]Adjusted for baseline value and location (3 centers).
[c]n = 100 (LLE = 51, PHLE = 49).
[d]n = 69 (LLE = 36, PHLE = 33).
[e]n = 86 (LLE = 43, PHLE = 43).

tendinopathy in the rotator cuff. Based on these methods—consisting of a general assessment performed by experienced orthopaedic specialists to exclude differential diagnoses, a combination of orthopaedic clinical tests to confirm pain arising from the subacromial structures, and a standardized ultrasound procedure[25]—the risk of a heterogeneous study population was considered to be small. Third, the absence of between-group differences may also be explained by the fact that tendon loading is biomechanically different in the complex shoulder joint, as compared with patellar and Achilles tendon loading, where PHLE has shown equal or superior

effects versus eccentric exercises in treatment of tendinopathy.[2,7,31,32] Although rotator cuff tendinopathy shows similarities with patellar and Achilles tendinopathy,[3,9,30,36] the tendon loading on painful rotator cuff muscles may evoke inhibition of rotator cuff muscle activity.[11,44] As compensation, the deltoid muscle may increase its activity to perform the required task.[1,44] Consequently, the absorbed load of the rotator cuff tendon may be less than expected in a pain-free shoulder. As loading of the tendon appears important,[7] this potential protection/compensation mechanism may explain why the present study and others of eccentric/PHLE in

Primary Objective
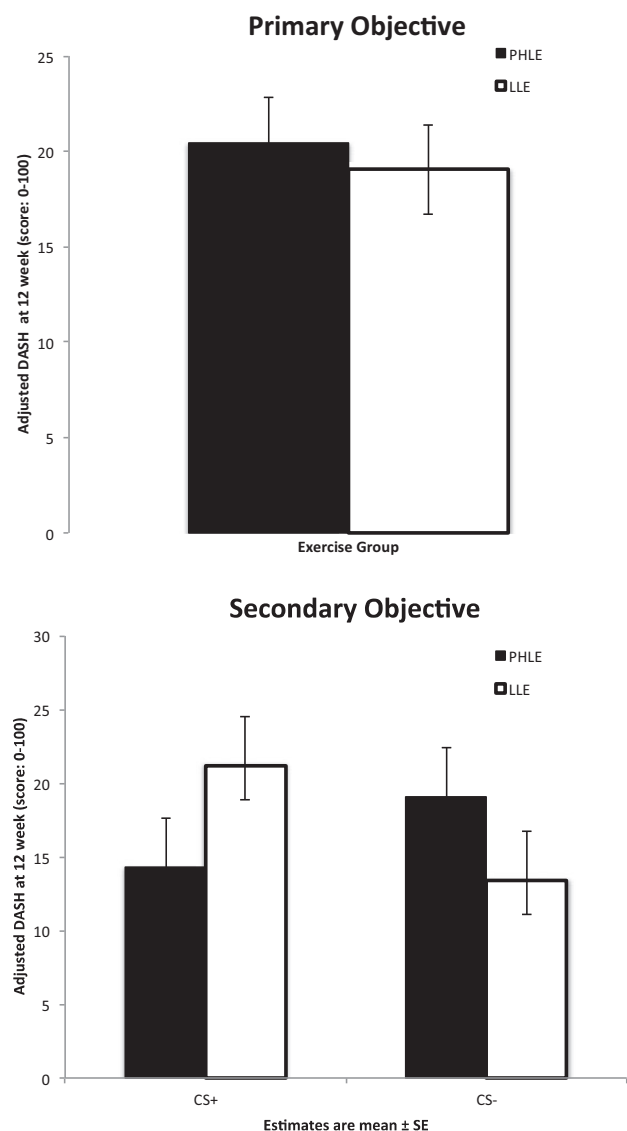

Secondary Objective

Figure 2. Main outcome: primary and secondary objectives in intention-to-treat analysis (N = 100). Primary objective: illustration of Disabilities of the Arm, Shoulder, and Hand (DASH) score at 12 weeks. Secondary objective: DASH score at 12 weeks stratified for concomitant corticosteroid injection. Estimates are mean ± standard error. CS+, concomitant corticosteroid; CS−, no concomitant corticosteroid; LLE, low-load exercise; PHLE, progressive high-load exercise.

rotator cuff tendinopathy[40] generally do not result in superior effects when compared with LLE. Fourth, another question may be whether the groups trained with different loads. According to exercise diaries from the per-protocol population, the PHLE group actually exercised with twice the amount of load (normalized to 1-repetition maximum at baseline) of the LLE group in the 2 rotator cuff exercises (data not shown).

This study found a significant interaction effect of corticosteroid injection and exercise type, which resulted in a higher effect of PHLE versus LLE in those patients who had a corticosteroid injection, while the opposite effect was present for those who did not have an injection. This may indicate that concomitant use of corticosteroid injection opens a "window of opportunity," resulting in decreased pain inhibition in the rotator cuff muscles. This window may ensure that the rotator cuff muscles receive optimal stimulation, resulting in clearer changes, as those previously found in patellar and Achilles tendinopathy.[2,31,32] The role of inflammation within tendinopathy is controversial,[7] but recent evidence supports the occurrence of active inflammation.[10,52] Conversely, the addition of corticosteroids in relation to degenerative tendons is reported to negatively influence regenerative processes in tendons.[16,17,59] The combined risk and benefit must therefore be assessed when administering corticosteroid injection. However, a recent systematic review found that tendon rupture in relation to corticosteroid injections was uncommon, occurring in only 0.1% of tendons in general.[6] To confirm the current results and eventually evaluate the underlying mechanisms, further research of the interaction between exercise type and concomitant corticosteroid injection must be performed.

We found a positive effect of PHLE on structural changes verified by ultrasound among the patients who were compliant with the assigned intervention (per-protocol analyses). The signs of neovascularity disappeared in significantly more patients after the PHLE intervention versus LLE. Furthermore, more patients had decreased tendon thickness in the PHLE group (increased tendon thickness: 33% at baseline and 20% at follow-up in the PHLE group vs 24% and 22%, respectively, in the LLE group), although this difference was not statistically significant. Reduced tendon thickness is anticipated to be a strong indicator of improved function and diminished pain because of the reduced volume occupied by nonedematous tendon in the subacromial space.[34] However, per-protocol analyses are prone to bias, and results should be investigated further before accepting these conclusions.

The current within-group change in DASH score of 7.1 to 8.4 points (29% to 34%) is below the minimal clinically important difference (MCID), which for the DASH has been suggested to be 10.5 points for patients with general shoulder disorders.[15] However, the MCID should generally be considered in relation to the specific population, the specific intervention, and the baseline value.[42]

The current baseline DASH was lower than in previous studies of patients with SIS,[4,8,20,27,33,42,55] indicating less discomfort in the current population at inclusion. The addition of recruitment by external advertisements did not appear to cause lower baseline scores, since exploratory analyses (data not shown) showed no differences in baseline scores between recruitment types. Another reason for the low baseline DASH score may be the minimal resting pain and largely preserved ROM often seen in patients with rotator cuff tendinopathy,[36,37] in contrast to higher DASH scores in SIS patients being attributed to a greater variety of symptoms. Camargo et al[4] evaluated the effect of eccentric exercises in a cohort study with similar inclusion criteria, including ultrasound, as in the current trial. They found equally low baseline DASH values. Since none of the previous randomized controlled

studies[20,38,40] evaluating eccentric/PHLE used ultrasound measurements to confirm structural abnormalities in the rotator cuff tendon at inclusion, comparisons between the present and previous studies are difficult to perform. In the Holmgren et al[20] study, only clinical signs were used as inclusion criteria. After inclusion, ultrasound measurements of the rotator cuff showed 31% of patients having either partial- or full-thickness rotator cuff tear, which may be the reason for a more heterogenic population and higher baseline score on the DASH. Also, Lombardi et al[38] used only clinical tests to include patients, with equally high levels of DASH baseline results as in the Holmgren et al[20] study. Since no further evaluations of potential differential diagnoses were presented in these studies, the specific differentiation among tendinopathy, bursitis, and rotator cuff tears remains uncertain. Furthermore, the current within-group change of 29% to 34% in PHLE and LLE, respectively, is larger than or similar to the percentage change in the intervention group from Lombardi et al[38] and Camargo et al,[4] indicating that the MCID change in relation to baseline values is similar across studies for rotator cuff tendinopathy, and the results of these studies may therefore seem more consistent.

Strengths and Limitations

A major limitation is the clinical criteria for rotator cuff tendinopathy, which could explain some of the reasons for the lack of between-group differences. However, as described, this problem was approached by strict inclusion procedures, including ultrasound-confirmed structural changes. Another limitation was the inability of blinding the treating physical therapists to the primary hypothesis, which could have influenced administration of exercise. However, because several physical therapists were involved and standardized information for patients was provided through written material and as an exercise DVD describing exercises and progression, this potential bias was minimized. Additionally, the number of compliant participants (60%) was relatively low. However, given that the requirement for being compliant was 80% completion of the exercise sessions, in addition to a high total number of visits to the physical therapists, the current compliance rate is acceptable. Other studies (eg, Holmgren et al[20]) found approximately 85% compliance on number of days trained, but completion of exercise sessions was not recorded, making comparisons difficult.

A significant interaction occurred between exercise and concomitant administration of corticosteroid injection. However, the current study did not achieve sufficient power to detect a significant between-group difference in the area of concomitant corticosteroid injection. Therefore, further investigation of this interaction is warranted.

The strengths of the current study are the inclusion of an active control group and the blinding of patients. Furthermore, vital methodological strengths of the current study include blinding of the primary examiner, a blinded outcome analysis performed by an external statistician, interpretation of the results prior to unblinding, publication of a detailed study protocol, and a standardized public exercise protocol (Appendices A and B).

Deviations From Protocol

See Appendix E: "Deviations From Protocol."

CONCLUSION

Our results showed there was no superior benefit of PHLE over traditional LLE in patients with rotator cuff tendinopathy. Further investigation of the possible interaction between exercise type and corticosteroid injection is needed to establish optimal and potentially synergistic combinations of these 2 factors. This finding suggests that shared decision making between patients and therapists, based on individual preferences, can safely be performed to secure optimal compliance.

ACKNOWLEDGMENT

REFERENCES

1. Bandholm T, Rasmussen L, Aagaard P, Diederichsen L, Jensen BR. Effects of experimental muscle pain on shoulder-abduction force steadiness and muscle activity in healthy subjects. *Eur J Appl Physiol*. 2008;102(6):643-650.
2. Beyer R, Kongsgaard M, Hougs Kjaer B, Ohlenschlaeger T, Kjaer M, Magnusson SP. Heavy slow resistance versus eccentric training as treatment for achilles tendinopathy: a randomized controlled trial. *Am J Sports Med*. 2015;43(7):1704-1711.
3. Camargo PR, Alburquerque-Sendin F, Salvini TF. Eccentric training as a new approach for rotator cuff tendinopathy: review and perspectives. *World J Orthop*. 2014;5(5):634-644.
4. Camargo PR, Avila MA, Alburquerque-Sendin F, Asso NA, Hashimoto LH, Salvini TF. Eccentric training for shoulder abductors improves pain, function and isokinetic performance in subjects with shoulder impingement syndrome: a case series. *Rev Bras Fisioter*. 2012;16(1):74-83.
5. Carlsson AM. Assessment of chronic pain: I. Aspects of the reliability and validity of the visual analogue scale. *Pain*. 1983;16(1):87-101.
6. Coombes BK, Bisset L, Vicenzino B. Efficacy and safety of corticosteroid injections and other injections for management of tendinopathy: a systematic review of randomised controlled trials. *Lancet*. 2010;376(9754):1751-1767.
7. Couppe C, Svensson RB, Silbernagel KG, Langberg H, Magnusson SP. Eccentric or concentric exercises for the treatment of tendinopathies? *J Orthop Sports Phys Ther*. 2015;45(11):853-863.
8. de Witte PB, Henseler JF, Nagels J, Vliet Vlieland TP, Nelissen RG. The Western Ontario rotator cuff index in rotator cuff disease patients: a comprehensive reliability and responsiveness validation study. *Am J Sports Med*. 2012;40(7):1611-1619.
9. Dean BJ, Franklin SL, Carr AJ. A systematic review of the histological and molecular changes in rotator cuff disease. *Bone Joint Res*. 2012;1(7):158-166.
10. Dean BJ, Gettings P, Dakin SG, Carr AJ. Are inflammatory cells increased in painful human tendinopathy? A systematic review. *Br J Sports Med*. 2016;50(4):216-220.
11. Diederichsen LP, Winther A, Dyhre-Poulsen P, Krogsgaard MR, Norregaard J. The influence of experimentally induced pain on shoulder muscle activity. *Exp Brain Res*. 2009;194(3):329-337.
12. Escamilla RF, Yamashiro K, Paulos L, Andrews JR. Shoulder muscle activity and function in common shoulder rehabilitation exercises. *Sports Med*. 2009;39(8):663-685.

13. Feleus A, Bierma-Zeinstra SM, Miedema HS, Verhaar JA, Koes BW. Management in non-traumatic arm, neck and shoulder complaints: differences between diagnostic groups. *Eur Spine J*. 2008;17(9): 1218-1229.

14. Fleiss JL. Reliability of measurement: *The Design and Analysis of Clinical Experiments*. Hoboken, NJ: John Wiley & Sons Inc; 1999.

15. Franchignoni F, Vercelli S, Giordano A, Sartorio F, Bravini E, Ferriero G. Minimal clinically important difference of the Disabilities of the Arm, Shoulder and Hand outcome measure (DASH) and its shortened version (QuickDASH). *J Orthop Sports Phys Ther*. 2014;44(1):30-39.

16. Haraldsson BT, Aagaard P, Crafoord-Larsen D, Kjaer M, Magnusson SP. Corticosteroid administration alters the mechanical properties of isolated collagen fascicles in rat-tail tendon. *Scand J Med Sci Sports*. 2009;19(5):621-626.

17. Haraldsson BT, Langberg H, Aagaard P, et al. Corticosteroids reduce the tensile strength of isolated collagen fascicles. *Am J Sports Med*. 2006;34(12):1992-1997.

18. Hawkins RJ, Kennedy JC. Impingement syndrome in athletes. *Am J Sports Med*. 1980;8(3):151-158.

19. Hegedus EJ, Goode AP, Cook CE, et al. Which physical examination tests provide clinicians with the most value when examining the shoulder? Update of a systematic review with meta-analysis of individual tests. *Br J Sports Med*. 2012;46(14):964-978.

20. Holmgren T, Bjornsson Hallgren H, Oberg B, Adolfsson L, Johansson K. Effect of specific exercise strategy on need for surgery in patients with subacromial impingement syndrome: randomised controlled study. *BMJ*. 2012;344:e787.

21. Hudak PL, Amadio PC, Bombardier C; Upper Extremity Collaborative Group. Development of an upper extremity outcome measure: the DASH (Disabilities of the Arm, Shoulder and Hand) [corrected]. *Am J Ind Med*. 1996;29(6):602-608.

22. Huisstede BM, Miedema HS, Verhagen AP, Koes BW, Verhaar JA. Multidisciplinary consensus on the terminology and classification of complaints of the arm, neck and/or shoulder. *Occup Environ Med*. 2007;64(5):313-319.

23. Huisstede BM, Wijnhoven HA, Bierma-Zeinstra SM, Koes BW, Verhaar JA, Picavet S. Prevalence and characteristics of complaints of the arm, neck, and/or shoulder (CANS) in the open population. *Clin J Pain*. 2008;24(3):253-259.

24. Ingwersen KG, Christensen R, Sorensen L, et al. Progressive high-load strength training compared with general low-load exercises in patients with rotator cuff tendinopathy: study protocol for a randomised controlled trial. *Trials*. 2015;16:27.

25. Ingwersen KG, Hjarbaek J, Eshoej H, Larsen CM, Vobbe J, Juul-Kristensen B. Ultrasound assessment for grading structural tendon changes in supraspinatus tendinopathy: an inter-rater reliability study. *BMJ Open*. 2016;6(5):e011746.

26. Jobe FW, Jobe CM. Painful athletic injuries of the shoulder. *Clin Orthop Relat Res*. 1983;173:117-124.

27. Karthikeyan S, Kwong HT, Upadhyay PK, Parsons N, Drew SJ, Griffin D. A double-blind randomised controlled study comparing subacromial injection of tenoxicam or methylprednisolone in patients with subacromial impingement. *J Bone Joint Surg Br*. 2010;92(1):77-82.

28. Kelly BT, Kadrmas WR, Speer KP. The manual muscle examination for rotator cuff strength: an electromyographic investigation. *Am J Sports Med*. 1996;24(5):581-588.

29. Kelly SM, Brittle N, Allen GM. The value of physical tests for subacromial impingement syndrome: a study of diagnostic accuracy. *Clin Rehabil*. 2010;24(2):149-158.

30. Khan KM, Cook JL, Bonar F, Harcourt P, Astrom M. Histopathology of common tendinopathies: update and implications for clinical management. *Sports Med*. 1999;27(6):393-408.

31. Kongsgaard M, Kovanen V, Aagaard P, et al. Corticosteroid injections, eccentric decline squat training and heavy slow resistance training in patellar tendinopathy. *Scand J Med Sci Sports*. 2009; 19(6):790-802.

32. Kongsgaard M, Qvortrup K, Larsen J, et al. Fibril morphology and tendon mechanical properties in patellar tendinopathy: effects of heavy slow resistance training. *Am J Sports Med*. 2010;38(4): 749-756.

33. Lee JH, Lee SH, Song SH. Clinical effectiveness of botulinum toxin type B in the treatment of subacromial bursitis or shoulder impingement syndrome. *Clin J Pain*. 2011;27(6):523-528.

34. Lewis J, McCreesh K, Roy JS, Ginn K. Rotator cuff tendinopathy: navigating the diagnosis-management conundrum. *J Orthop Sports Phys Ther*. 2015;45(11):923-937.

35. Lewis JS. Subacromial impingement syndrome: a musculoskeletal condition or a clinical illusion? *Phys Ther Rev*. 2011;16(5): 388-398.

36. Littlewood C, Ashton J, Chance-Larsen K, May S, Sturrock B. Exercise for rotator cuff tendinopathy: a systematic review. *Physiotherapy*. 2012;98(2):101-109.

37. Littlewood C, May S. A contractile dysfunction of the shoulder. *Man Ther*. 2007;12(1):80-83.

38. Lombardi I, Jr, Magri AG, Fleury AM, Da Silva AC, Natour J. Progressive resistance training in patients with shoulder impingement syndrome: a randomized controlled trial. *Arthritis Rheum*. 2008;59(5): 615-622.

39. Luime JJ, Koes BW, Hendriksen IJ, et al. Prevalence and incidence of shoulder pain in the general population: a systematic review. *Scand J Rheumatol*. 2004;33(2):73-81.

40. Maenhout AG, Mahieu NN, De Muynck M, De Wilde LF, Cools AM. Does adding heavy load eccentric training to rehabilitation of patients with unilateral subacromial impingement result in better outcome? A randomized, clinical trial. *Knee Surg Sports Traumatol Arthrosc*. 2013; 21(5):1158-1167.

41. Martin-Hervas C, Romero J, Navas-Acien A, Reboiras JJ, Munuera L. Ultrasonographic and magnetic resonance images of rotator cuff lesions compared with arthroscopy or open surgery findings. *J Shoulder Elbow Surg*. 2001;10(5):410-415.

42. Michener LA, Snyder Valier AR, McClure PW. Defining substantial clinical benefit for patient-rated outcome tools for shoulder impingement syndrome. *Arch Phys Med Rehabil*. 2013;94(4):725-730.

43. Miranda H, Viikari-Juntura E, Heistaro S, Heliovaara M, Riihimaki H. A population study on differences in the determinants of a specific shoulder disorder versus nonspecific shoulder pain without clinical findings. *Am J Epidemiol*. 2005;161(9):847-855.

44. Myers JB, Hwang JH, Pasquale MR, Blackburn JT, Lephart SM. Rotator cuff coactivation ratios in participants with subacromial impingement syndrome. *J Sci Med Sport*. 2009;12(6):603-608.

45. Naredo AE, Aguado P, Padron M, et al. A comparative study of ultrasonography with magnetic resonance imaging in patients with painful shoulder. *J Clin Rheumatol*. 1999;5(4):184-192.

46. Neer CS, 2nd, Welsh RP. The shoulder in sports. *Orthop Clin North Am*. 1977;8(3):583-591.

47. Papadonikolakis A, McKenna M, Warme W, Martin BI, Matsen FA 3rd. Published evidence relevant to the diagnosis of impingement syndrome of the shoulder. *J Bone Joint Surg Am*. 2011;93(19):1827-1832.

48. Poltawski L, Ali S, Jayaram V, Watson T. Reliability of sonographic assessment of tendinopathy in tennis elbow. *Skeletal Radiol*. 2012; 41(1):83-89.

49. Reinold MM, Escamilla RF, Wilk KE. Current concepts in the scientific and clinical rationale behind exercises for glenohumeral and scapulothoracic musculature. *J Orthop Sports Phys Ther*. 2009;39(2):105-117.

50. Reinold MM, Macrina LC, Wilk KE, et al. Electromyographic analysis of the supraspinatus and deltoid muscles during 3 common rehabilitation exercises. *J Athl Train*. 2007;42(4):464-469.

51. Reinold MM, Wilk KE, Fleisig GS, et al. Electromyographic analysis of the rotator cuff and deltoid musculature during common shoulder external rotation exercises. *J Orthop Sports Phys Ther*. 2004;34(7):385-394.

52. Scott A, Backman L, Speed C. Tendinopathy—update on pathophysiology. *J Orthop Sports Phys Ther*. 2015;45(11):833-841.

53. Sundhedsstyrelsen. *National klinisk retningslinje for diagnostik og behandling af patienter med udvalgte skulderlidelser* [National clinical guidelines for diagnostic and treatment of patients with selected shoulder impairments]. Copenhagen, Denmark: Sundhedsstyrelsen (Danish Health Authority); 2013.

54. Sunding K, Fahlstrom M, Werner S, Forssblad M, Willberg L. Evaluation of Achilles and patellar tendinopathy with greyscale ultrasound and colour Doppler: using a four-grade scale. *Knee Surg Sports Traumatol Arthrosc*. 2016;24(6):1988-1996.
55. Tate AR, McClure PW, Young IA, Salvatori R, Michener LA. Comprehensive impairment-based exercise and manual therapy intervention for patients with subacromial impingement syndrome: a case series. *J Orthop Sports Phys Ther*. 2010;40(8):474-493.
56. van der Windt DA, Koes BW, de Jong BA, Bouter LM. Shoulder disorders in general practice: incidence, patient characteristics, and management. *Ann Rheum Dis*. 1995;54(12):959-964.
57. Venu KM, Howlett DC, Garikipati R, Anderson HJ, Bonnici AV. Evaluation of the symptomatic supraspinatus tendon—a comparison of ultrasound and arthroscopy. *Radiography*. 2002;8(4):235-240.
58. Vollmann J, Winau R. Informed consent in human experimentation before the Nuremberg code. *BMJ*. 1996;313(7070):1445-1449.
59. Wong MW, Tang YN, Fu SC, Lee KM, Chan KM. Triamcinolone suppresses human tenocyte cellular activity and collagen synthesis. *Clin Orthop Relat Res*. 2004;(421):277-281.
60. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67(6):361-370.

APPENDIX A: LLE EXERCISE PROGRAM

General Information About the Training

Slow-Controlled Movements. All exercises are to be performed slowly and with controlled movements. Be careful to keep focus on the quality of the exercise to achieve the expected effect. Perform the workout at a time of the day where you can perform the exercises undisturbed.

Customize the Load to the Planned Number of Repetitions. As part of the training, you need to continuously adjust the load in the exercises so that you cannot perform more repetitions than planned. It is important that you follow the instructions given by the therapist upon the load of the exercises and continuously adjust the load according to the program.

The physiotherapist will help you find the appropriate load when seen for the control sessions at the rehabilitation department.

Pain During Exercise. When you exercise, you may experience slight increased pain in the shoulder. This is normal and OK. What you must be aware of is how high the pain is. That is, if the pain rises >5 on a scale of 0 to 10 (VAS: 0 = no pain, 10 = worst pain imaginable), it should not be any higher. Five on the scale corresponds approximately to a pain that you can tolerate without feeling that it is directly harmful.

In addition, the pain is expected to decrease to about the level that it was before the training within a maximum of 30 minutes. Furthermore, the pain must not be increased the days following training. If pain does not decrease after training or gets worse in the following days, you should approximately reduce the load of your exercises by half and, over 3 or 4 exercise sessions, increase toward the planned load again. If this does not help, please contact the physiotherapist who initially instructed you.

If you take pain medication, the pain may be lower than normal, but you should follow the same guidelines in terms of how long the pain may last and worsen from day to day.

Why We Believe This Training Works. The training is believed to have a positive effect on the muscles called the *rotator cuff*. The exercises work by improving the muscles' ability to stabilize and coordinate the shoulder joint and reduce the undesirable joint forces that may come when the joint is not completely stable and well coordinated. The exercises are believed to awaken the muscles and make them progressively stronger and more enduring, so they can work a entire day without getting overloaded and tired.
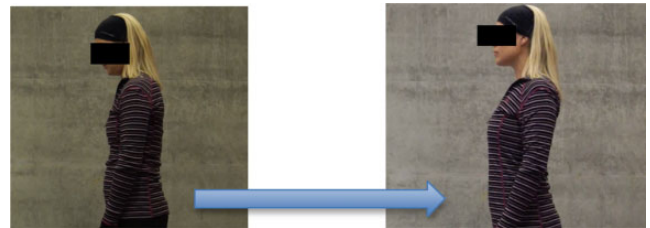
The exercise program is to be performed 3 times per week.

First Exercise. Stand with your back in a stooped position. Now, try to make the distance between your breastbone and navel longer, until you feel you are standing with your back straight.

While holding this position, bring your scapulae slowly together.

The position is maintained for 5 deep breaths (approximately 15 seconds). Then fully relax and let your shoulders/back fall forward into the stooped position.

Repeat the exercise 3 times. Spend about 30 seconds of rest between each repetition.

If you experience pain, adjust the degree of movement, so a light pain occurs (maximum, 5 on VAS) and then diminishes immediately after the exercise.

Second Exercise. Stand with your back straight and scapula (involved side) resting against a wall.

Grasp with your opposite arm the back of your upper arm/elbow, and move the arm toward the chest so that the elbow moves closer the opposite shoulder.

Try to keep the elbow at the height of the shoulder, but adjust in case of pain

The position is then maintained for 5 deep breaths (approximately 15 seconds). Then fully relax and let the arm slowly fall down along the body.

Repeat the exercise 3 times. Spend about 30 seconds of rest between repetitions.

If you experience pain, adjust the degree of movement, so a light pain occurs (maximum, 5 on VAS) and then diminishes immediately after the exercise.
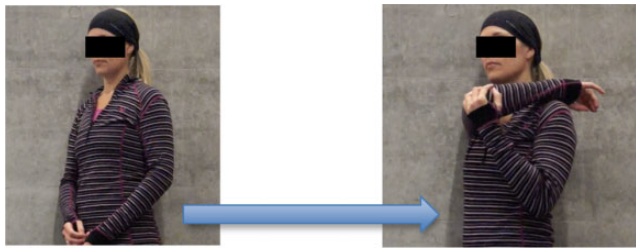
Third Exercise. Stand with your back straight and shoulders slightly held back (same position as in the first exercise). Hold the dumbbell in your hand so that the palm faces slightly forward and the thumb points away from the body.

Lift the dumbbell toward the horizontal plane, at an angle of 45° from the body (midway between flexion and abduction). Attempt to come up to a height where the arm is horizontal. Use about 2 seconds on the movement up.

Next, lower the arm slowly until it is again held down alongside the body. Use about 2 seconds on the down movement. Stop the movement just before you relax completely, and then repeat the exercise 20 to 25 times.

The exercise is carried out for 3 sets. Spend about 30 seconds of rest between sets.

Adjust the load if it is too easy or heavy (±5 than the proposed).

Remember the advice on pain: Pain is OK during exercise but should not exceed 5 on a 0-10 scale. Similarly, increased pain should decrease shortly after the exercise and overall not be elevated >30 minutes after your workout, get worse, or increase in the following days.

If you experience increased pain, adjust the load, so a light pain occurs (maximum, 5 on VAS) and then diminishes immediately after the exercise.
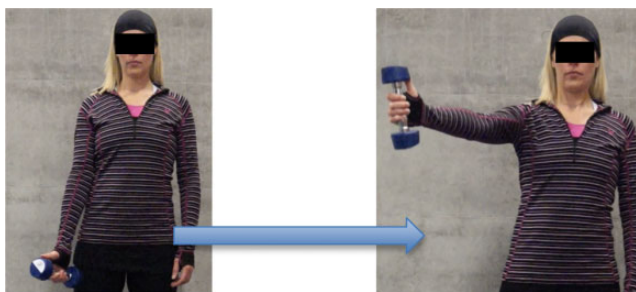
Fourth Exercise. Lie down on your opposite shoulder. Lie with your back straight (do not curve the upper part of your back). Let your legs be slightly bent, so you feel that you have the balance while lying on the side. Let your upper arm of the training arm lie down alongside your body, so the elbow is located between the ribs and hip. The elbow is bent 90° so your hand is placed approximately in front of your navel. The scapula is kept slightly back.

Grasp the dumbbell, and lift it slowly toward the ceiling by making an external rotation in the shoulder. The movement is made as far as you can or maximally until your forearm is held in a vertical position. Use about 2 seconds on the movement up. Keep your elbow at the same point midway between the ribs and hip throughout the exercise. You must keep the rest of your body at rest so that only the arm moves. Keep your scapula slightly back during the entire movement.

Next, lower your hand slowly until the dumbbell approaches the starting point. Use about 2 seconds on the movement down. Stop the movement just before touching the ground, and perform the exercise again.
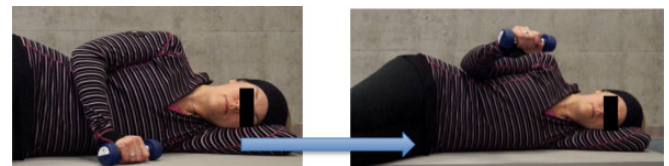
The exercise is repeated 20 to 25 times.

The exercise is carried out for 3 sets. Spend about 30 seconds of rest between sets.

Adjust the load if it is too easy or heavy (±5 than the proposed).

Remember the advice on pain: Pain is OK during exercise but should not exceed 5 on a 0-10 scale. Similarly, increased pain should shortly decrease after the exercise and overall not be elevated >30 minutes after your workout, get worse, or increase in the following days.

If you experience increased pain, adjust the load, so light pain occurs (maximum, 5 on VAS) and then diminishes immediately after the exercise.

Fifth Exercise. Lie flat on your back, with your knees bent approximately 90°. Take the dumbbell in your hand, and lift it toward the ceiling so that the arm is vertical (if necessary, use your contralateral arm to aid you in placing the dumbbell in the starting position). Let the shoulder/scapula rest against the surface.
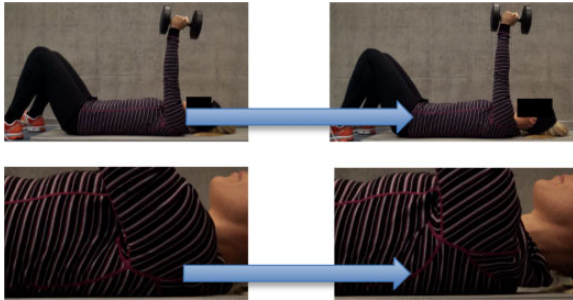
Then perform a push with shoulder/scapula so that the dumbbell is lifted as high toward the ceiling as you feel that you can, without lifting more than your shoulder/scapula from the surface. You should not perform a rotation in the back. Use about 2 seconds on the movement up. Next, gradually lower your shoulder/scapula back to the starting point. Use about 2 seconds on the movement back to the starting point. Stop the movement just before you feel you can relax. The exercise is performed 20 times.

The exercise is carried out for 3 sets. Spend about 30 seconds of rest between sets.

Adjust the load if it is too easy or heavy (±5 than the proposed).

Remember the advice on pain: Pain is OK during exercise but should not exceed 5 on a 0-10 scale. Similarly, increased pain should decrease shortly after the exercise and overall not be elevated >30 minutes after your workout, get worse, or increase in the following days.

If you experience increased pain, adjust the load, so light pain occurs (maximum, 5 on VAS) and then diminishes immediately after the exercise.

Sixth Exercise. Attach the middle of the rubber band to a fixed anchor (handrail at a staircase, radiator piping, or door hinge) approximately at a height equal to your shoulder. Grasp the elastic ends with both hands at the markings set by the physiotherapist. Stand about 1.5 m away from where the rubber band is attached.

Stand with your back straight and your shoulders slightly held back. With straight arms, slowly pull back so that your hands are moved down to the outside of your hip. Keep your back straight and shoulders slightly back during the entire exercise. Use about 2 seconds on the motion.

Slowly move your hands back to the starting point. Remember to keep your back straight and shoulders back slightly during the entire movement—also on the way back. Use about 2 seconds on the movement back to the starting point. Stop the movement just before you feel you can relax. The exercise is performed 20 times.
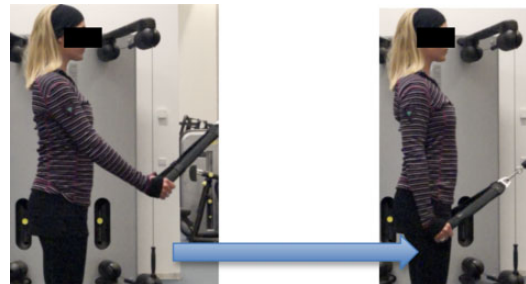
The exercise is carried out for 3 sets. Spend about 30 seconds of rest between sets.

If the load is too heavy (you can do 5 repetitions less than proposed), adjust the load by grasping the rubber band closer to the ends, and make a new mark at this point (longer distance between marks).

If the load is too easy (you can do 5 repetitions over the proposed), adjust the load by grasping the rubber band closer to where it is attached, and make a new mark at this point (shorter distance between marks).

Remember the advice on pain: Pain is OK during exercise but should not exceed 5 on a 0-10 scale. Similarly, increased pain should shortly decrease after the exercise and overall not be elevated >30 minutes after your workout, get worse, or increase in the following days.

If you experience increased pain, adjust the load, so light pain occurs (maximum, 5 on VAS) and then diminishes immediately after the exercise.

APPENDIX B: PHLE EXERCISE PROGRAM

General Information About the Training

Slow-Controlled Movements. All exercises are to be performed slowly and with controlled movements.

Be careful to keep focus on the quality of the exercise to achieve the expected effect.

Perform the workout at a time of the day where you can perform the exercises undisturbed.

Customize the Load to the Planned Number of Repetitions. As part of the training, you need to continuously adjust the load in the exercises so that you cannot perform more repetitions than planned. It is important that you follow the instructions given by the therapist for the load of the exercises and continuously adjust the load according to the program.

The physiotherapist will help you find the appropriate load when seen for the control sessions at the rehabilitation department.

Pain During Exercise. When you exercise, you may experience slight increased pain in the shoulder. This is normal and OK. What you must be aware of is how high the pain is. That is, if the pain rises >5 on a scale of 0 to 10 (VAS: 0 = no pain, 10 = worst pain imaginable), it shall not be any higher. Five on the scale corresponds approximately to a pain that you can tolerate without feeling that it is directly harmful.

In addition, the pain is expected to decrease to about the level that it was before the training within a maximum of 30 minutes. Furthermore, the pain must not increase the days following training.

If pain does not decrease after training or gets worse in the following days, you should reduce the load of your exercises by approximately half and, over 3 to 4 exercise sessions, increase it toward the planned load again. If this does not help, please contact the physiotherapist who initially instructed you.

If you take pain medication, the pain may be lower than normal, but you should follow the same guidelines in terms of how long the pain may last and worsen from day to day.

Why We Believe This Training Works. The training is believed to have a positive effect on the muscles called the *rotator cuff*. The exercises work by improving the muscle's ability to stabilize and coordinate the shoulder joint and reduce the undesirable joint forces that may come when the joint is not completely stable and well coordinated. The exercises are believed to awaken the muscles and make them progressively stronger and more enduring, so they can work a entire day without getting overloaded and tired.

The difficulties that you are experiencing in the shoulder are partly due to one of the tendons of the rotator cuff, called the *supraspinatus tendon*, not being as functional as it used to be—there are signs that the tissue in the tendon is worn and needs to be reinforced. In the third and

fourth exercises, you must gradually train with heavier and heavier loads over the 12 weeks. The heavy load is expected to help reinforcement of the tendon by actively stimulating tissue in the tendon to make it stronger.

In performing the heavy loaded exercises, it is not necessarily how much movement you can perform but, more so, the load on the muscle that is considered to be important. Therefore, it may be enough just to perform a small movement and hold this position static to apply load on the muscle/tendon. But if possible, you should of course make the whole movement.

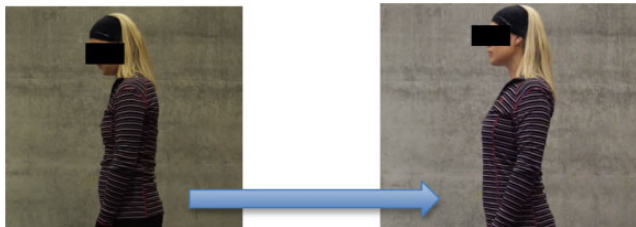The exercise program is to be performed 3 times per week.

First Exercise. Stand with your back in a stooped position. Now, try to make the distance between your breastbone and navel longer until you feel that you are standing with your back straight.

While holding this position, bring your scapulae slowly together.

The position is maintained for 5 deep breaths (approximately 15 seconds). Then fully relax and let your shoulders/back fall forward into the stooped position.

Repeat the exercise 3 times. Spend about 30 seconds of rest between sets.

If you experience pain, adjust the degree of movement, so a light pain occurs (maximum, 5 on VAS) and then diminishes immediately after the exercise.

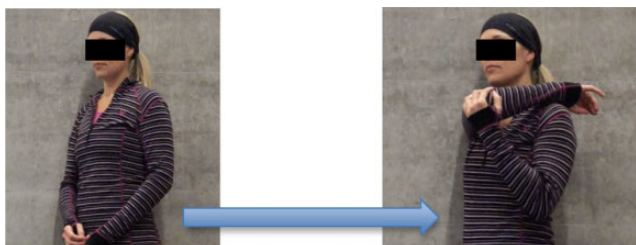*Second Exercise.* Stand with your back straight and scapula (involved side) resting against a wall.

Grasp with your opposite arm the back of your upper arm/elbow, and move the arm toward the chest so that the elbow moves closer the opposite shoulder.

Try to keep the elbow at the height of the shoulder, but adjust in case of pain.

The position is then maintained for 5 deep breaths (approximately 15 seconds). Then fully relax, and let the arm slowly fall down along the body.

Repeat the exercise 3 times. Spend about 30 seconds of rest between sets.

If you experience pain, adjust the degree of movement, so a light pain occurs (maximum, 5 on VAS) and then diminishes immediately after the exercise.

Third Exercise. Stand with your back straight and shoulders slightly held back (same position as in the first exercise). Hold the dumbbell in your hand so that the palm faces slightly forward with the thumb pointing away from the body.

Lift the dumbbell toward the horizontal plane at an angle of 45° from the body (midway between flexion and abduction). Attempt to come up to a height where the arm is horizontal. Use about 3 to 4 seconds on the movement up.

Remember: In performing the heavy loaded exercises, it is not how much movement you can perform but, more so, that you load the muscle with high load, which is important. So, it may be enough just to perform strong static pressure so that the dumbbell is moved only a little and then held static. But move the weight as far as you can and of course make the whole movement, if you can.

Next, lower the arm slowly until the arm again is held down alongside the body. Use about 3 to 4 seconds on the down movement. Stop the movement just before you relax completely, and then repeat the exercise again.
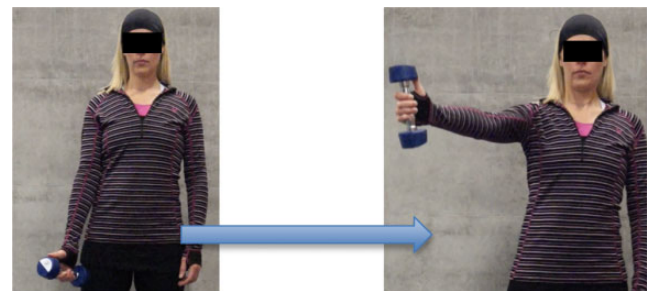
The exercise is performed as follows:

15 repetitions in week 1
12 repetitions in weeks 2 + 3
10 repetitions in weeks 4 + 5
8 repetitions in weeks 6 + 7 + 8
6 repetitions in weeks 9 + 10 + 11 + 12

The exercise is carried out for 4 sets. Spend about 30 seconds of rest between sets.

If the load is too easy (you can make 2 repetitions more than the proposed), increase the load.

Remember the advice on pain: Pain is OK during exercise, but it must not exceed 5 on a 0-10 scale. Similarly, the increased pain should shortly begin to decrease after the exercise stops and overall not be elevated >30 minutes after your workout, get worse, or increase in the following days.

If you experience pain, first adjust the degree of movement so that maximum a light pain occurs (maximum, 5 on VAS) and then diminishes immediately after the exercise. If this does not help, adjust the load.

Fourth Exercise. Lie down on your opposite shoulder. Lie with your back straight (do not curve in the upper part of your back). Let your legs be slightly bent, so you feel that you have the balance while lying on the side. Let your upper arm of the training arm lie down alongside your body, so the elbow is located between the ribs and hip. The elbow is bent

90° such that your hand is placed approximately in front of your navel. The scapula is kept slightly back.

Grasp the dumbbell and lift it slowly up toward the ceiling by making a external rotation in the shoulder. The movement is made as far as you can or maximally until your forearm is held in a vertical position. Use about 3 to 4 seconds on the movement up. Keep your elbow at the same point midway between the ribs and hip throughout the exercise. You must keep the rest of your body at rest so that only the arm moves. Keep your scapula slightly back during the entire movement.

Remember: While performing the heavy loaded exercises, it is not how much movement you can perform but, more so, that you load the muscle with high load, which is important. So it may be enough just to perform strong static pressure so that the dumbbell is moved only a little and then held static. But move the weight as far as you can and of course make the whole movement, if you can.

Next, lower your hand slowly until the dumbbell approaches the starting point. Use about 3 to 4 seconds on the movement down. Stop the movement just before touching the ground and perform the exercise again.

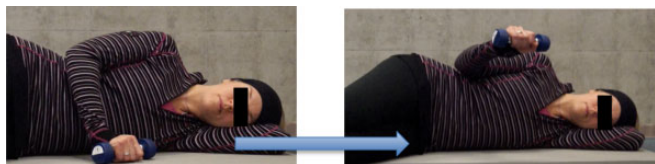The exercise is performed as follows:

15 repetitions in week 1
12 repetitions in weeks 2 + 3
10 repetitions in weeks 4 + 5
8 repetitions in weeks 6 + 7 + 8
6 repetitions in weeks 9 + 10 + 11 + 12

The exercise is carried out for 4 sets. Spend about 30 seconds of rest between sets.

If the load is too easy (you can make 2 repetitions more than the proposed), increase the load.

Remember the advice on pain: Pain is OK during exercise, but it must not exceed 5 on a 0-10 scale. Similarly, the increased pain should shortly begin to decrease after the exercise stops and overall not be elevated >30 minutes after your workout, get worse, or increase in the following days.

If you experience pain, first adjust the degree of movement so that maximum a light pain occurs (maximum, 5 on VAS) and then diminishes immediately after the exercise. If this does not help, adjust the load.

Fifth Exercise. Lie flat on your back, with your knees bent approximately 90°. Take the dumbbell in your hand and lift it toward the ceiling, so the arm is vertical (if necessary, use your contralateral arm to aid you in placing the dumbbell in the starting position). Let the shoulder/scapula rest against the surface.

Then perform a push with your shoulder/scapula so that the dumbbell is lifted as high toward the ceiling as you feel you can, without lifting more than your shoulder/scapula from the surface. You should not perform a rotation in the back. Use about 2 seconds on the movement up.
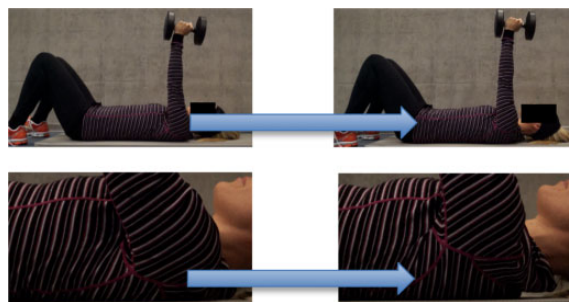
Next, gradually lower your shoulder/scapula back to the starting point (use about 2 seconds). Stop the movement just before you feel that you can relax. The exercise is performed 20 times.

The exercise is carried out for 3 sets. Spend about 30 seconds of rest between sets.

Adjust the load if it is too easy or heavy (±5 than the proposed).

Remember the advice on pain: Pain is OK during exercise but should not exceed 5 on a 0-10 scale. Similarly, increased pain should shortly decrease after the exercise and overall not be elevated >30 minutes after your workout, get worse, or increase in the following days.

If you experience increased pain, adjust the load, so light pain occurs (maximum, 5 on VAS) and then diminishes immediately after the exercise.

Sixth Exercise. Attach the middle of the rubber band to a fixed anchor (handrail at a staircase, radiator piping, or door hinge) approximately at a height equal to your shoulder. Grasp the elastic ends with both hands at the markings set by the physiotherapist. Stand about 1.5 m away from where the rubber band is attached.

Stand with your back straight and your shoulders slightly held back. With straight arms, slowly pull back so that your hands are moved down to the outside of your hip. Keep your back straight and shoulders slightly back during the entire exercise. Use about 2 seconds on the motion.

Slowly move your hands back to the starting point. Remember to keep your back straight and shoulders back slightly during the entire movement—also on the way back. Use about 2 seconds on the movement back to the starting point. Stop the movement just before you feel that you can relax. The exercise is performed 20 times.
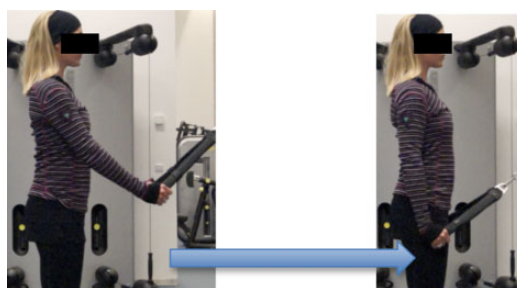
The exercise is carried out for 3 sets. Spend about 30 seconds of rest between sets.

If the load is too heavy (you can do 5 repetitions less than proposed), adjust the load by grasping the rubber band closer to the ends, and make a new mark at this point (longer distance between marks).

If the load is too easy (you can do 5 repetitions over the proposed), adjust the load by grasping the rubber band closer to where it is attached, and make a new mark at this point (shorter distance between marks).

Remember the advice on pain: Pain is OK during exercise but should not exceed 5 on a 0-10 scale. Similarly, increased pain should shortly decrease after the exercise and overall not be elevated >30 minutes after your workout, get worse, or increase in the following days.

If you experience increased pain, adjust the load, so light pain occurs (maximum, 5 on VAS) and then diminishes immediately after the exercise.

APPENDIX C: MEASUREMENT OF STRENGTH AND RANGE OF MOTION

Maximum Isometric Voluntary Contraction

A dynamometer (IsoForce Dynometer EVO2; Medical Device Solutions AG) was used to measure maximum isometric voluntary contraction for external rotation, internal rotation, and scaption. Before measurements, patients were seated with the back against a wall for support. For external rotation and internal rotation, the upper arm was placed vertically in the frontal and sagittal planes, supported by a foam rubber wedge, and the elbow was flexed to 90°. For scaption, participants were placed with the arm straight and shoulder flexed to 45° in the scapular plane. For all 3 measurements, the dynamometer was placed at the distal forearm. After a warm-up trial, patients were instructed to push as hard as they could against the dynamometer for 5 seconds. The mean of 3 approved maximal contractions was used. A pilot study of the method showed excellent[1] interrater reliability (ICC: 0.84-0.92).

Active and Passive ROM

A goniometer (HALO digital goniometer; HALO Medical Devices) was used to assess active and passive ROM in external rotation, internal rotation, and scaption. Active and passive ROM in scaption was assessed with the participant standing with his or her back tight against a wall with a small pillow supporting the lumbar spine. The participant was instructed to keep constant pressure on the pillow. The participant's arm was straight and moved in the scaption plane. The goniometer was placed just proximal to the elbow in the scapular plane. Patients were instructed to keep the arm straight while the movement was performed (active and passive) and to stop when they could not keep the lumbar spine fixed against the pillow or they reached the wall with the hand. Internal and external rotation was performed with the participant in the supine position; the shoulder was abducted and the elbow flexed to 90° with the forearm placed vertically. The goniometer was placed just proximal to the wrist in the sagittal plane. In internal rotation, participants were instructed to keep the scapulae against the surface during the entire movement. After a test trial, the mean of 3 measurements was taken. A pilot study of the method showed excellent[1] interrater reliability (intraclass correlation: 0.75-0.96).

REFERENCE

1. Fleiss JL. Reliability of measurement. In: *The Design and Analysis of Clinical Experiments*. Hoboken, NJ: John Wiley & Sons Inc; 1999.

APPENDIX D

TABLE A1
"As Observed" Population: Primary and Secondary Outcomes 12 Weeks After Baseline for PHLE and LLE[a]

| | Within-Group Change | | | |
	PHLE	LLE	Adjusted Between-Group Difference on Change[b]	P Value
DASH				
Main[c]	7.92 (3.46 to 12.38)	8.73 (4.55 to 12.92)	−1.19 (−6.88 to 4.51)	.68
Hobby[d]	12.5 (1.85 to 23.15)	13.0 (−2.02 to 28.07)	1.27 (−14.77 to 17.32)	.87
Work[e]	3.7 (−3.32 to 10.76)	3.9 (−1.51 to 9.40)	−3.75 (−1.95 to 3.45)	.30
VAS[f]				
Rest	1.95 (−2.75 to 6.65)	1.18 (−194 to 4.31)	−1.33 (−5.93 to 3.27)	.57
Activity	14.00 (7.05 to 20.95)	16.32 (10.49 to 22.15)	−2.65 (−1.34 to 5.05)	.50
Night	15.80 (7.36 to 24.23)	18.25 (10.58 to 25.92)	−4.37 (−13.61 to 4.87)	.35
Maximum	19.03 (9.92 to 28.13)	19.86 (12.69 to 27.04)	−.81 (−12.31 to 1.70)	.89

(continued)

TABLE A1 (continued)

| | Within-Group Change | | | |
	PHLE	LLE	Adjusted Between-Group Difference on Change[b]	P Value
Isometric strength, N/BW[g]				
Scaption	0.09 (0.05 to 0.11)	0.08 (0.03 to 0.12)	0.01 (–0.05 to 0.08)	.71
External rotation	0.04 (0.02 to 0.06)	0.04 (0.02 to 0.06)	0.00 (–0.02 to 0.03)	.76
Internal rotation	0.08 (0.05 to 0.12)	0.08 (0.06 to 0.11)	0.00 (–0.05 to 0.04)	.92
Passive ROM[g]				
Scaption	3.61 (–1.18 to 8.40)	4.47 (0.73 to 8.21)	–2.11 (–7.62 to 3.41)	.45
External rotation	4.87 (0.43 to 9.32)	5.73 (0.01 to 11.44)	–0.71 (–7.79 to 6.37)	.84
Internal rotation	–0.13 (–3.33 to 3.08)	–0.14 (–4.19 to 3.92)	1.17 (–3.70 to 6.04)	.63
Active ROM[g]				
Scaption	9.38 (2.83 to 15.92)	4.05 (–1.04 to 9.15)	.95 (–6.11 to 8.02)	.79
External rotation	6.84 (1.46 to 12.22)	6.06 (–0.62 to 12.75)	.83 (–6.82 to 8.47)	.83
Internal rotation	2.14 (–1.50 to 5.77)	0.71 (–3.05 to 4.48)	2.35 (–2.44 to 7.15)	.33

[a]Values are presented as mean (95% CI). BW, body weight (kg); DASH, Disabilities of the Arm, Shoulder, and Hand (range, 0-100); LLE, low-load exercise; N, newton; PHLE, progressive high-load exercise; ROM, range of motion; VAS, visual analog scale (range, 0-100).
[b]Adjusted for baseline value, location (3 centers), corticosteroid (yes/no).
[c]n = 93 (LLE = 49, PHLE = 44).
[d]n = 51 (LLE = 24, PHLE = 27).
[e]n = 75 (LLE = 38, PHLE = 37).
[f]n = 83 (LLE = 44, PHLE = 39).
[g]n = 81 (LLE = 44, PHLE = 37).

TABLE A2
"Per Protocol" Population: Primary and Secondary Outcomes 12 Weeks After Baseline for PHLE and LLE[a]

| | Within-Group Change | | | |
Outcome	PHLE	LLE	Adjusted Between-Group Difference on Change[b]	P Value
DASH				
Main[c]	12.59 (7.78 to 17.40)	11.97 (7.53 to 16.41)	–0.14 (–6.20 to 5.92)	.96
Hobby[d]	11.84 (1.71 to 21.98)	12.17 (–4.19 to 28.53)	1.54 (–17.29 to 20.37)	.68
Work[e]	4.5 (–1.39 to 10.39)	6.94 (0.36 to 13.53)	–2.68 (–9.51 to 4.14)	.75
VAS[c]				
Rest	4.68 (–0.52 to 9.88)	1.61 (–2.08 to 5.30)	–0.09 (–5.02 to 4.84)	
Activity	17.89 (9.48 to 26.30)	15.19 (8.80 to 21.58)	0.74 (–8.20 to 9.67)	.87
Night	19.82 (8.42 to 31.22)	15.35 (7.51 to 23.20)	1.51 (–9.79 to 12.80)	.79
Maximum	20.43 (8.44 to 32. 42)	17.84 (10.28 to 25.40)	0.81 (–13.47 to 15.09)	.91
Isometric strength, N/BW[f]				
Scaption	0.09 (0.03 to 0.16)	0.08 (0.03 to 0.14)	0.00 (–0.08 to 0.08)	.99
External rotation	0.05 (0.02 to 0.07)	0.05 (0.03 to 0.08)	0.00 (–0.03 to 0.03)	.92
Internal rotation	0.09 (0.04 to 0.13)	0.09 (0.06 to 0.13)	–0.01 (–0.07 to 0.05)	.73
Passive ROM[f]				
Scaption	5.01 (–1.20 to 11.23)	6.12 (1.48 to 10.76)	–3.47 (–10.96 to 4.03)	.36
External rotation	3.78 (–1.81 to 9.36)	4.30 (–2.97 to 11.58)	–3.56 (–12.66 to 5.54)	.44
Internal rotation	0.43 (–3.45 to 4.32)	0.33 (–3.01 to 3.68)	0.41 (–3.96 to 4.78)	.85
Active ROM[f]				
Scaption	11.51 (2.99 to 20.02)	7.79 (2.45 to 13.12)	–3.00 (–11.20 to 5.20)	.47
External rotation	8.00 (1.21 to 14.80)	4.12 (–4.60 to 12.83)	0.14 (–10.17 to 10.45)	.98
Internal rotation	2.67 (–2.18 to 7.51)	0.91 (–2.21 to 4.04)	1.82 (–3.05 to 6.69)	.46

[a]Values are presented as mean (95% CI). BW, body weight (kg); DASH, Disabilities of the Arm, Shoulder, and Hand (range, 0-100); LLE, low-load exercise; N, newton; PHLE, progressive high-load exercise; ROM, range of motion; VAS, visual analog scale (range, 0-100).
[b]Adjusted for baseline value, location (categorical: 3 centers), corticosteroid (yes/no).
[c]n = 59 (LLE = 31, PHLE = 28).
[d]n = 38 (LLE = 19, PHLE = 19).
[e]n = 52 (LLE = 27, PHLE = 25).
[f]n = 58 (LLE = 31, PHLE = 27).

APPENDIX E: DEVIATIONS FROM PROTOCOL

The following deviations from the protocol to the RoCTEx trial[1] were made.

Participants, Settings, and Locations

To obtain an acceptable number of participants before the prespecified deadline for final inclusion, the inclusion criterion on maximum age was increased from <60 to <65 years, and recruitment from outside the secondary sector was added.

Outcomes

In the trial protocol, the Shoulder injury and Osteoarthritis Outcome Score (scores = 0-100, 100 = no problems)[2] was listed as a secondary outcome. However, the Shoulder injury and Osteoarthritis Outcome Score was not finally developed and validated in time to be included in the present publication. Evaluation for ultrasound changes was assessed through dichotomized variables because the method for grading structural changes on ordinal scales was not finally developed and tested at the time of initial inclusion of patients.

REFERENCES

1. Ingwersen KG, Christensen R, Sorensen L, et al. Progressive high-load strength training compared with general low-load exercises in patients with rotator cuff tendinopathy: study protocol for a randomised controlled trial. *Trials*. 2015;16:27.
2. Shoulder injury and Osteoarthritis Outcome Score (SOOS)—reliability and validity of a new patient reported outcome measure. Paper presented at: Sports Medicine Congress; February 2-4, 2012; Kolding, Denmark.