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Associations between changes in leg extensor muscle power and physical function after supervised exercise in patients with hip osteoarthritis. Secondary analysis from the hip booster trial

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ABSTRACT

Objective: To investigate associations between changes in leg extensor muscle power of the affected limb (ΔLEP) and changes in physical function after 12 weeks of progressive resistance training (PRT) or neuromuscular exercise (NEMEX) in patients with hip osteoarthritis.
Design: Secondary analyses of a randomized controlled trial. From 160 participants enrolled in the clinical trial and cluster randomized to PRT (n = 82) or NEMEX (n = 78), a total of 147 (92%) had complete follow-up data and were included in the analyses. Simple linear and multivariate linear regression models estimated the crude and adjusted associations between ΔLEP normalized to body weight (watt/kg) and changes in performance-based and patient-reported measures of physical function.
Results: Adjusted estimates [95% confidence intervals] showed associations between ΔLEP (watt/kg) and changes in 30-s chair stand test (β: 2.34 [1.33; 3.35], R^2: 0.13), 9-step timed stair climb test (β: −1.47 [-2.09; −0.85], R^2: 0.38), 40-m fast paced walking test (β: −2.20 [-3.30; −1.11], R^2: 0.09), Activities of Daily Life function (β: 8.63 [3.16; 14.10], R^2: 0.23) and Sport and Recreation function (β: 10.57 [2.32; 18.82], R^2: 0.21) subscales from the Hip disability and Osteoarthritis Outcomes Score. Group allocation to PRT did not lead to greater regression coefficients than in NEMEX.
Conclusions: Changes in leg extensor muscle power after supervised exercise are consistently associated with changes in physical function across performance-based and patient-reported measures in patients with hip osteoarthritis. These associations seem to be independent of allocation to PRT or NEMEX.

1. Introduction

Clinical guidelines recommend exercise therapy as first-line treatment for hip OA because of its effectiveness for improving physical function and reducing pain [1,2]. Physical function, and the ability to participate in daily activities have been identified as key clinical outcomes in recommendations by Osteoarthritis Research Society International [3,4]. Moreover, OARSI has recommended a core set of three performance-based tests to assess physical function consisting of the 30-s chair stand test (30s-CST), the 40-m fast paced walking test (40m-FPWT) and a stair climb test [5]. To optimize the effect of exercise therapy on physical function in hip OA, it is important to identify and understand the underlying mechanisms of that effect. Patients with hip OA have substantial deficits in leg extensor power (LEP) of the affected limb compared with the non-affected limb and compared to healthy older adults [6,7]. This impairment is associated with reductions in performance-based and patient-reported measures of physical function [6]. Of note, LEP appears to be a stronger determinant of physical

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function in hip OA compared to muscle strength [8], which is also observed in the general population [9]. However, there seems to be no longitudinal studies on the relationship between changes in LEP and changes in physical function in patients with hip OA [6,8].

Specifically for improving muscle power in older adults, the American College of Sports Medicine recommends progressive resistance training (PRT) [10]. High-velocity is superior to traditional PRT for improving muscle power in mobility-limited older adults [11]. The proposed specific adaptations include type-II muscle fiber hypertrophy, changes in tendon properties, increased neural firing frequency and motor unit recruitment [12]. A randomized controlled trial tested high-velocity PRT in patients with hip OA [13], and found a substantial increase in mean LEP of 27% and concomitant improvements in patient-reported physical function [13]. The clinical trial providing data for the present study, compared a similar high-velocity PRT intervention to neuromuscular exercise (NEMEX) in hip OA and found no difference in improvements in physical function, pain or quality of life but a potential advantage of PRT regarding muscle power [14]. However, results from another trial in hip OA, comparing PRT with Nordic walking and home-based exercise, suggested that Nordic Walking was superior and that improvements in patient-reported physical function were not dependent on changes in LEP [15,16]. As such, the importance of LEP in relation to exercise-induced improvements in physical function is unclear. Potentially, exercise interventions that increase LEP may be superior for improving physical function, whereby LEP could represent a key target mechanism for optimizing exercise therapy effects in hip OA.

The aim of this secondary analysis was to investigate whether changes in LEP (ΔLEP) of the affected limb are associated with changes in objectively measured physical function assessed with the Osteoarthritis Research Society International recommended core set of performance-based tests, i.e., 30s-CST, 40m-FPWT, and 9-step timed stair climb test (9step-TSCT), in patients with hip OA. Other aims were to investigate, if (1) ΔLEP of the affected limb is associated with changes in patient-reported measures of physical function; (2) associations between ΔLEP and changes in physical function are dependent on the type of exercise performed.

We hypothesized, that (1) ΔLEP is associated with changes in performance-based physical function (30s-CST, 9step-TSCT and 40m-FPWT); (2) changes in ΔLEP are associated with changes in patient-reported measures of physical function (Activities of Daily Life (ADL) Function and Sport and Recreation function subscales of the Hip disability and Osteoarthritis Outcomes Score (HOOS) questionnaire); (3) ΔLEP will explain a larger part of the differences observed in physical function after PRT compared to after NEMEX defined by greater regression coefficients.

2. Methods

2.1. Study design

This is a secondary analysis of results from a 12-week multicenter cluster-randomized controlled trial, The Hip Booster Trial, in which 160 patients with clinically diagnosed hip OA were enrolled from January 2021 to April 2023 [14]. The trial compared the effectiveness of 12 weeks of PRT or NEMEX on functional performance, pain and quality of life in patients with hip OA [17]. The trial was approved by the Central Denmark Region Committee on Health Research Ethics (1-10-72-267-20) and registered with the Danish Data Protection Agency (1-16-02-11-21) and ClinicalTrials.gov (NCT04714047) prior to enrollment of patients. The reporting of this study conforms to guidelines described in the Strengthening the Reporting of Observational Studies in Epidemiology guidelines [18].

2.2. Participants

The patients were screened for eligibility, asked to provide written informed consent, and enrolled at orthopedic departments (n = 48) or physiotherapy clinics (n = 112) across Denmark by orthopedic surgeons or physiotherapists. Inclusion criteria were: (1) Clinically diagnosed OA of the hip joint according to the National Institute for Health and Care Excellence criteria [19]; (2) An event of pain during activity of at least 3 out of 10 on a Numerical Rating Scale in the index hip within the previous 2 weeks; (3) Age ≥45 years; (4) No morning hip stiffness or less than 30 min; (5) No lower extremity surgery 6 months prior to inclusion; (6) No comorbidity markedly affecting hip function; (7) Adequate written and spoken Danish, and (8) not a candidate for total hip arthroplasty. Exclusion criteria were: (1) Body mass index >40; (2) Pregnancy; (3) PRT or NEMEX for the lower extremities exceeding 12 sessions over the last 6 months or 6 sessions over the last 3 months, and (4) planned vacation of more than 14 days within the initial 12-week intervention period without the possibility of extending the intervention accordingly.

2.3. Data collection

At baseline and 12-week follow-up, outcome measures were assessed by a physiotherapist at one of the participating orthopedic departments. These assessments included LEP measured by the Nottingham Leg Extensor Power Rig and physical function measures consisting of 30s-CST, 9step-TSCT, 40m-FPWT and the HOOS questionnaire [17]. In addition, body weight, height, age, and sex were recorded.

2.4. Leg extensor muscle power

Leg extensor muscle power (watt) was measured using the Nottingham Leg Extensor Power Rig as described in the trial protocol paper [17], which is a reliable measure in patients with symptomatic hip OA [20,21]. For each leg, participants performed two warm-up trials followed by a minimum of five trials with 30 s rest between trials. The test was terminated when the participant did not improve on two successive trials, or after having performed a maximum of 10 trials. The test with the greatest power output (watt) was used for analyses.

2.5. Performance-based physical function

The 30s-CST assesses sit-to-stand function (number of repetitions) and is a valid, reliable, and responsive measure [5,22,23]. The 9-step timed stair climb test measures the time (seconds) spent to ascend and descend nine steps and is a reliable measure [20]. The 40 m fast-paced walk test measures the total time (seconds) it takes to walk 4 × 10 m excluding turns. It is a valid, reliable and responsive measure of short distance maximum walking speed [24].

2.6. Patient-reported measures of physical function

The HOOS is a 40-item patient-reported questionnaire consisting of five subscales. Each subscale gives a score ranging from 0 (worst) to 100 (best) [25]. HOOS is a valid, reliable and responsive measure in patients with hip OA [26]. The HOOS subscales for ADL function and Sport and Recreation function are included in the present study.

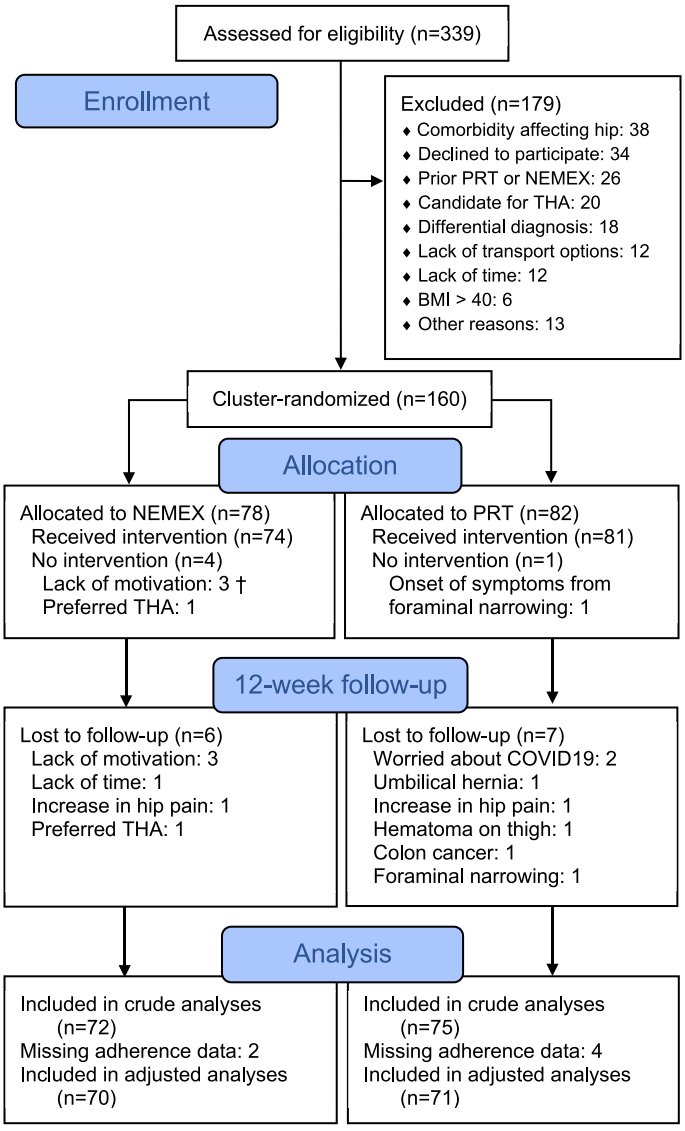
2.7. Statistical analysis

Data from participants in The Hip Booster trial who had completed the baseline and follow-up assessments of LEP of the affected limb were included, resulting in a sample size of 147 participants [14]. Continuous variables were assessed for normality using histograms and QQ plots while the assumption of equal distributions throughout the line was assessed by plotting the residuals against each of the independent variables. Paired t-tests were used to assess differences in change scores.

Simple (Model 1) and multivariate linear regression (Model 2 and 3) models were used to estimate the crude and adjusted associations between the independent variable of ΔLEP normalized to body weight (watt/kg) and changes in each of the physical function outcomes as the

dependent variable. ΔLEP normalized to bodyweight (watt/kg) was chosen as the independent variable rather than absolute ΔLEP, because body weight is a critical component of the influence that LEP has on physical function. Body weight determines the gravitational forces that must be overcome by LEP to perform ADL functions, such as climbing a flight of stairs. Additionally, LEP is usually reported normalized to body weight in the literature [6,8,13,17]. To assess if there was a difference (i.e., effect modification) in the association between ΔLEP and change in physical function depending on the allocation to PRT or NEMEX, an interaction term was included between ΔLEP and allocation (Model 3).

Prior to performing adjusted analyses, potential confounders were selected based on existing evidence and included as covariates. The number of covariates was limited to eight, to have a reasonable number of degrees of freedom based on our sample size of 147 patients [27]. In the adjusted analysis (Model 2 and 3), the following covariates were included: Age, sex, baseline value of the independent variable (LEP, watt/kg), baseline value of the dependent variable (*e.g.*, 30-s chair stand test), baseline hip pain measured by the HOOS questionnaire, adherence to the exercise interventions, and allocation to PRT or NEMEX intervention. In deciding which covariates to include, existing literature was taken into account, showing that baseline physical function is associated with lower limb muscle power [6], which is negatively influenced by pain and age, but positively associated to male sex [21,28]. Some evidence suggests that the magnitude of the effect on physical function depends on the type of exercise being performed [16,29] and on the adherence to the interventions [30]. Lastly, regression toward the mean may result in a negative correlation between baseline scores and change scores [31]. Therefore, baseline levels of the dependent (i.e. LEP) and independent variable (*e.g.*, 30-s chair stand test) were included as covariates.



Participants who discontinued intervention and may or may not be lost to follow-up are; NEMEX: n=4 (Lack of time: 2, Lack of motivation: 1, Increase in hip pain: 1), PRT: n=7 (Worried about COVID19: 2, Lack of time: 1, Back pain: 1, Increase in hip pain: 1, Hematoma on thigh: 1, Colon cancer: 1). †: One participant did not receive any intervention but agreed to perform 12-week follow-up as per the intention to treat approach. PRT: Progressive resistance training, NEMEX: Neuromuscular exercise, THA: Total hip arthroplasty, BMI: Body mass index.

Fig. 1. Flowchart including all patients screened for participation in the Hip Booster trial.

To assess the clinical relevance of the associations, the minimally important differences (MID) estimated in the primary paper were used to estimate the difference in ΔLEP that would be associated with a MID in change in that measure of physical function. This difference in ΔLEP was estimated by interpolation using beta-coefficients derived from Model 2. These MID were calculated using an anchor-based approach and interpreted as the minimal important difference in change between individuals [32].

Sensitivity analyses were performed for Model 1, 2 and 3 by removing observations with extreme leverages or residuals which resulted in comparable or slightly smaller regression coefficients (appendix Table 1). However, these differences were small and would not change the overall interpretation of the analyses, indicating robustness of the associations.

Associations are presented as crude and adjusted regression coefficients with 95% confidence intervals. The level of significance was set at 0.05. Statistical software, Stata 17 (Statacorp, College Station, Texas, USA) was used for the analyses.

3. Results

3.1. Participants

Of 339 patients assessed for eligibility, 160 were enrolled in the clinical trial and cluster randomized to PRT (n = 82) or NEMEX (n = 78) (Fig. 1). Baseline characteristics were comparable between PRT and NEMEX (Table 1). At the 12-week follow-up, 13 participants were lost to follow-up and the remaining 147 were included in the crude analyses (Table 2). Because 6 patients had missing adherence data (lost exercise records) only 141 participants could be included in the adjusted analyses.

Both PRT and NEMEX appeared to improve all included outcome measures (Table 3). Point estimates suggest that in the study population of 147 participants, PRT led to slightly larger improvements in LEP compared to NEMEX (difference: 0.06 [−0.07; 0.19] watt/kg), and that NEMEX led to slightly larger improvements in HOOS Sport and Recreation function subscale compared with PRT (difference: 5.7 [−1.1; 12.6] points). However, these differences were small, and have wide confidence intervals.

3.2. Performance-based physical function

ΔLEP was associated with changes in the 30s-CST, 9step-TSCT and 40m-FPWT (Table 2 and Fig. 2) for crude estimates (Model 1, R^2: 0.05–0.10) and after adjustment for potential confounders (Model 2, R^2: 0.09–0.38). Associations were also observed for LEP and the performance-based measures of physical function at baseline (Appendix, Table 2, adjusted R^2: 0.24–0.51).

To reach a MID for change in 30s-CST of 0.5 repetitions, one patient would need to improve ΔLEP by 0.21 W/kg more than another patient (Table 3). To reach a MID for change in 9step-TSCT of −0.4 s, one patient would need to improve ΔLEP by 0.27 W/kg more than another patient. To reach a MID for change in 40m-FPWT of −0.4 s, one patient would need to improve ΔLEP by 0.18 W/kg more than another patient.

3.3. Patient-reported measures of physical function

ΔLEP was positively associated with changes in the ADL function and Sport and Recreation function subscales of the HOOS questionnaire (Table 2 and Fig. 2) for crude estimates (Model 1, R^2: 0.05 and 0.06) and after adjustment for potential confounders (Model 2, R^2: 0.21 and 0.23). Associations were also observed for LEP and the patient-reported measures of physical function at baseline (Appendix, Table 2, adjusted R^2: 0.56 and 0.68).

To reach a MID for change in ADL function of 8.6 points, one patient would need to improve ΔLEP by 1.0 W/kg more than another patient.

Table 1
Characteristics of included participants at baseline.

Characteristics	Neuromuscular exercise (n = 72)	Progressive resistance training (n = 75)	Total cohort (n = 147)
Female	44 (61)	52 (69)	96 (65)
Age – years, mean (sd)	64.3 (9.2)	65.6 (7.3)	65.0 (8.3)
BMI - kg/m^2, mean (sd)	27.9 (4.7)	27.9 (4.2)	27.9 (4.4)
Hip osteoarthritis			
Unilateral	49 (68)	58 (77)	107 (73)
Bilateral	23 (32)	17 (23)	40 (27)
Duration of symptoms			
0–1 years	14 (19)	16 (21)	30 (20)
>1–2 years	17 (24)	21 (28)	38 (26)
>2–5 years	31 (43)	23 (31)	54 (37)
>5 years	10 (14)	15 (20)	25 (17)
Previous treatment			
Exercise	9 (13)	12 (16)	21 (14)
Physiotherapy	15 (21)	24 (32)	39 (27)
Chiropractor	4 (6)	8 (11)	12 (8)
Corticosteroid injection	5 (7)	5 (7)	10 (7)
Previous surgery			
Contralateral THA	3 (4)	2 (3)	5 (3)
Hip arthroscopy	3 (4)	0 (0)	3 (2)
Use of analgesics			
Acetaminophen	38 (53)	48 (64)	86 (59)
NSAIDS	22 (31)	22 (29)	44 (30)
Morphine or opioids	2 (3)	1 (1)	3 (2)
Other analgesics	5 (7)	6 (8)	11 (7)
Physical activity (weekly)			
≥150 min moderate intensity	31 (43)	28 (37)	59 (40)
≥60 min vigorous intensity	24 (33)	15 (20)	39 (27)
≥90 min vigorous intensity	13 (18)	9 (12)	22 (15)
Functional performance			
LEP aff, watt/kg, mean (sd)	1.67 (0.7)	1.50 (0.6)	1.58 (0.7)
LEP non, watt/kg, mean (sd)	1.85 (0.7)	1.69 (0.7)	1.77 (0.7)
30s-CST, repetitions, mean (sd)	11.6 (4.1)	11.4 (3.2)	11.5 (3.6)
9-step TSCT, s, median (IQR)	10.1 (4.6)	10.1 (4.0)	10.1 (4.1)
40m-FPWT, s, median (IQR)	24.0 (7.5)	24.6 (5.2)	24.2 (6.5)
HOOS (0–100 points)			
ADL function, mean (sd)	65.0 (17.0)	63.3 (18.0)	64.1 (17.5)
Sport/Recreation, mean (sd)	48.4 (22.5)	48.5 (22.9)	48.5 (22.7)
Pain, mean (sd)	59.8 (16.9)	57.0 (14.2)	58.4 (15.6)
Adherence to sessions, mean %	86	85	86
Participants with ≥80%	53 (74)	52 (69)	105 (71)
Participants with ≥50%	67 (93)	68 (91)	135 (92)

Values are presented as numbers (%) if not stated otherwise. Sd: standard deviation, IQR: interquartile range, s: seconds, kg: kilogram, min: minutes, THA: Total hip alloplasty, NSAIDS: Nonsteroidal anti-inflammatory drugs, LEP: Leg extensor muscle power, aff: most affected limb, non: least affected limb, 30s-CST: 30 s chair stand test, 9-step TSCT: 9-step timed stair climb test, 40m-FPWT: 40 m fast-paced walk test, HOOS: Hip disability and Osteoarthritis Outcomes Score questionnaire, ADL: Activities of daily life.

To reach a MID for change in Sport and Recreation function of 8.0 points, one patient would need to improve ΔLEP by 0.76 W/kg more than another patient.

3.4. Difference in associations depending on exercise type

There were no statistically significant differences in the association between ΔLEP and any measure of physical function depending on whether participants performed PRT or NEMEX (Table 2, Model 3). However, moderate-to-large differences in regression coefficients were observed for the changes in 30s-CST in favor of NEMEX and for 40m-FPWT in favor of PRT.

Table 2
Associations between changes in leg extension power (ΔLEP) of the affected limb normalized to bodyweight (watt/kg) and changes in the dependent variables of physical function after 12 weeks of progressive resistance training or neuromuscular exercise in participants with hip osteoarthritis.

Model	β ΔLEP	R^2	P-value	β ΔLEP (PRT)	β ΔLEP (NEMEX)	β ΔLEP(PRT) - β ΔLEP(NEMEX)	P-value
Dependent variable: Δ 30 s chair stand test (number of repetitions)							
Model 1	1.97 [0.99; 2.96]	0.10	<0.001				
Model 2	2.34 [1.33; 3.35]	†.13	<0.001				
Model 3				1.63 [0.26; 3.01]	3.10 [1.68; 4.53]	−1.47 [-3.41; 0.47]	0.14
Dependent variable: Δ 9-step timed stair climb test (seconds to complete)							
Model 1	−0.94 [-1.65; −0.24]	0.05	0.01				
Model 2	−1.47 [-2.09; −0.85]	†.38	<0.001				
Model 3				−1.60 [-2.46; −0.74]	−1.34 [-2.20; −0.48]	−0.26 [-1.44; 0.93]	0.67
Dependent variable: Δ 40 m fast paced walking test (seconds to complete)							
Model 1	−1.81 [-2.82; −0.80]	0.08	0.001				
Model 2	−2.20 [-3.30; −1.11]	†.09	<0.001				
Model 3				−2.71 [-4.20; −1.21]	−1.67 [-3.21; −0.12]	−1.04 [-3.14; 1.05]	0.33
Dependent variable: Δ HOOS ADL (0–100 points)							
Model 1	8.63 [3.02; 14.25]	0.06	0.003				
Model 2	8.63 [3.16; 14.10]	†.23	0.002				
Model 3				8.72 [1.16; 16.29]	8.53 [0.83; 16.24]	0.19 [-10.80; 10.42]	0.97
Dependent variable: Δ HOOS Sport and Recreation function (0–100 points)							
Model 1	11.34 [2.78; 19.90]	0.05	0.01				
Model 2	10.57 [2.32; 18.82]	†.21	0.01				
Model 3				10.49 [-0.94; 21.92]	10.66 [-1.00; 22.33]	−0.18 [-16.27; 15.91]	0.98

Results are presented as regression coefficients of the slope with 95% confidence intervals. †: R-squared estimates are adjusted for multiple independent variables, β: Beta regression coefficients describing the difference in the dependent variable expected with a 1 W/kg difference ΔLEP, Δ: change from baseline to 12-week follow-up, LEP: Leg extensor power normalized to bodyweight (watt/kg), R^2: R-squared estimate, PRT: Progressive resistance training, NEMEX: Neuromuscular exercise, HOOS: Hip disability and Osteoarthritis Outcomes Score questionnaire.
Model 1. Crude estimates from simple linear regression analysis: Dependent variable (e.g., Δ30s-CST) = ΔLEP.
Model 2. Adjusted estimates from multivariate linear regression analysis: Dependent variable (e.g., Δ30s-CST) = ΔLEP + Age + Sex + Baseline 30s-CST + Baseline LEP + Baseline HOOS Pain + Adherence + Allocation to PRT or NEMEX.
Model 3. Adjusted estimates from multivariate linear regression analysis with an interaction term between ΔLEP and Group Allocation (PRT or NEMEX): Dependent variable (e.g., Δ30s-CST) = ΔLEP + Age + BMI + Sex + Baseline 30s-CST + Baseline LEP + Baseline Pain + Adherence + Allocation + ΔLEP# Allocation to PRT or NEMEX.

4. Discussion

ΔLEP was positively associated with improvements in all measures of performance-based or patient-reported physical function, indicating a robust and consistent relationship between ΔLEP and physical function. The crude and adjusted models suggest that a linear relationship is a good approximation of the observed relationship by which patients who attain a larger ΔLEP also experience a larger improvement in all measures of physical function considered in these analyses. These associations suggest that LEP is a potential physiological target mechanism for exercise therapy in hip OA, because of its role in improving physical function and the ability to participate in ADL which are critical clinical outcomes [3,4]. Furthermore, baseline levels of LEP were associated with baseline levels of all measures of physical function, as reported in previous studies [6,8], further supporting the importance of LEP for physical function (Appendix, Table 2).

Given the moderate mean effects on physical function observed after NEMEX and PRT and the relatively small regression coefficients of the associations with ΔLEP, it appears that factors other than ΔLEP make substantial contributions to the improvements in physical function observed after exercise. Additionally, the R^2 estimates of the associations would suggest that only a small-to-moderate amount of the variation in the measures of physical function can be explained by the variation in ΔLEP. However, as physical function is a complex domain with large variation, it is unlikely that a single variable will explain much of this variation. Previous studies have found that improvements in physical

Table 3
Changes in leg extensor muscle power and physical function for participants included in crude analyses after 12 weeks of progressive resistance training or neuromuscular exercise. On the right is the minimal difference in leg extensor muscle power that is associated with a minimal important difference in the measure of physical function. Minimal important differences were estimated as part of the primary paper by an anchor-based method.

Outcome measure	**Mean change [95% CI]** NEMEX (n = 72)	PRT (n = 75)	Total cohort (n = 147)	Difference in ΔLEP = MID †
Leg extensor muscle power (watt/kg)	0.19 [0.09; 0.28]	0.25 [0.16; 0.34]	0.22 [0.15; 0.28]	
Affected limb	0.13 [0.04; 0.22]	0.17 [0.08; 0.26]	0.15 [0.09; 0.21]	
Non-affected limb				
Functional performance tests				
30s chair stand test (reps)	1.5 [0.9; 2.1]	1.5 [0.9; 2.0]	1.5 [1.1; 1.9]	0.21
9-step timed stair climb test (s)	−1.0 [-1.4; −0.5]	−0.9 [-1.3; −0.6]	−1.0 [-1.2; −0.7]	0.27
40 m fast-paced walk test (s)	−1.1 [-1.7; −0.6]	−1.0 [-1.7; −0.4]	−1.1 [-1.5; −0.7]	0.18
Patient-reported outcomes (0–100)				
HOOS ADL function	9.5 [6.4; 12.7]	7.9 [4.6; 11.2]	8.7 [6.4; 11.0]	1.00
HOOS Sport/recreation	14.1 [9.2; 19.1]	8.4 [3.6; 13.2]	11.2 [7.8; 14.6]	0.76

Analyses are performed as paired t-tests. †: Model 2 was used to estimate thresholds for difference in change in LEP (watt/kg) between two patients that can be considered clinically relevant for the specific physical function outcome, as it corresponds to the minimal important difference estimated as part of the clinical trial for that outcome [12]. CI: confidence interval, NEMEX: Neuromuscular exercise group, PRT: Progressive resistance training group, kg: kilogram, s: seconds, reps: repetitions completed, HOOS: Hip disability and Osteoarthritis Outcomes Score questionnaire, ADL: Activities of daily life.

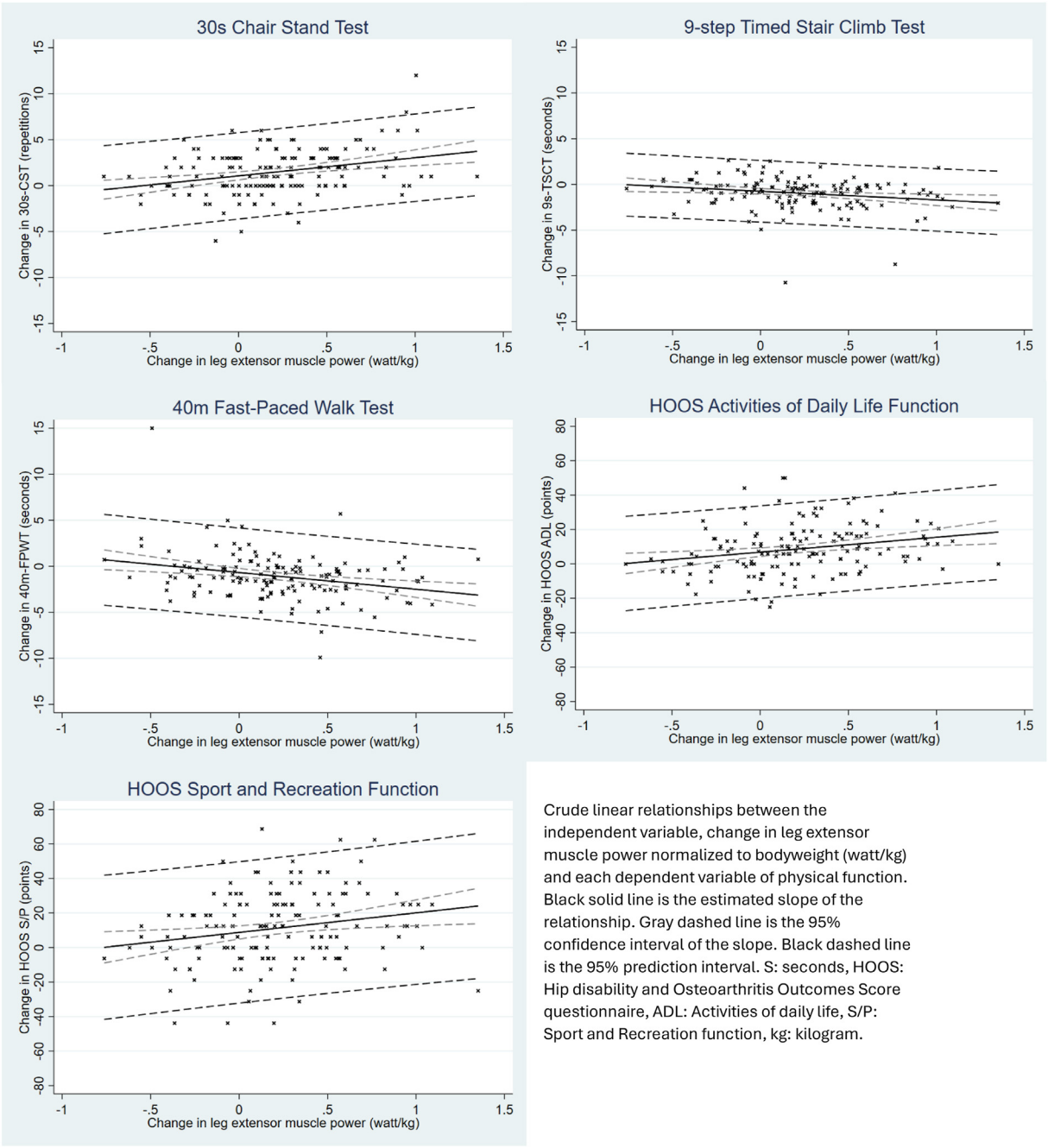


Fig. 2. Scatter plots showing crude linear relationship between changes in leg extensor muscle power (watt/kg) and changes in physical function after twelve weeks of PRT or NEMEX in patients with hip osteoarthritis.

function after exercise interventions in knee OA are mediated by psychological factors such as mobility-related self-efficacy [33] and biological factors such as inflammatory cytokines [34] which may play a similar mediating role in hip OA.

The differences in ΔLEP required to observe a MID on the physical function measures were substantial, particularly for the patient-reported measures, since only few participants in this cohort differ in ΔLEP by 0.78 or 1.00 W/kg. However, for the performance-based measures of physical function, it is likely that differences in ΔLEP as small as 0.27 W/kg, would be associated with a clinically relevant greater increase in the ability to rise from a chair, negotiate stairs and walk at a fast pace. The seemingly weaker association between ΔLEP and patient-reported measures could be attributed to patient-reported measures representing the patients perceived physical function, which is different from an objective test of physical capability, such as LEP or 30s-CST.

A recent individual patient data mediation study with data from four RCTs (294 participants) comparing therapeutic exercise therapy to non-exercise controls found no evidence that increases in knee extensor muscle strength mediated the improvements in physical function or pain in hip OA [35]. Furthermore, an increase in knee extensor muscle strength mediated only 2% of the improvements in physical function and pain [35]. From the present secondary analyses, it seems that there may be a closer relationship between ΔLEP and changes in physical function. This is in line with previous cross-sectional studies showing that muscle power is a stronger determinant of physical function than muscle strength in hip OA and in the general population of older adults [8,9].

Moreover, knee extension performance may be less affected and less important for physical function in hip OA compared to leg extension performance.

When comparing the association of ΔLEP and physical function based on whether the participants had performed PRT or NEMEX, there were some moderate-to-large differences in the regression coefficients estimated. However, it is important to consider that the statistical power was markedly reduced when including an interaction term in the model, resulting in large standard errors and wide confidence intervals. Additionally, these differences between PRT and NEMEX seemed to decrease when outliers were removed in the sensitivity analyses. Taken together, these estimates seem very uncertain and should be interpreted with caution.

4.1. Strengths and limitations

The key strengths of the study include the comprehensive supervision and quantification of exercises performed by participants, alongside the use of blinded outcome assessors, which enhances internal validity. Additionally, a consistent relationship was found between changes in LEP and all included measures of physical function. There are some limitations to the interpretation of these results. The proposed linear regression models are only approximations of the true relationship between ΔLEP and changes in physical function and can only describe differences between patients who are otherwise identical. Furthermore, as these secondary analyses are performed on a cohort of participants, it is not possible to infer causality from the associations found. However, the linear relationships and positive association observed for all performance-based and patient-reported measures of physical function suggest that ΔLEP is a plausible mechanism for the improvement of physical function observed after exercise in hip OA.

4.2. Clinical interpretation

The consistent associations found between ΔLEP and changes in physical function, add to the existing literature, and suggest that muscle power is an important component of physical function in hip OA. High-velocity resistance exercises (exercises involving concentric muscle contractions with the intention of moving as-fast-*as*-possible) may result in greater improvements in LEP and should be considered when designing exercise programs as part of the first-line treatment for hip OA. When designing exercise programs where muscle power is one of the goals, one could consider the general recommendations by the American College of Sports Medicine of exercises with heavy loads (85–100% of 1 RM) to increase the force component of the power equation, and light to moderate loads (0–60% of 1 RM) to improve the velocity component [36]. However, both exercise programs investigated in this cohort, PRT and NEMEX, seem sufficient for attaining small-to-moderate increases in muscle power and equally effective for improving physical function.

This study indicates that muscle power is only one of many important factors to consider when designing and implementing exercise therapy for hip OA. As such, a predominant focus on improving muscle power seems inappropriate in clinical practice. Clinicians should consider patient preferences when designing exercise programs and tend to other physiological or psychological issues as well.

5. Conclusion

Changes in leg extensor muscle power after supervised exercise are consistently associated with changes in physical function across performance-based and patient-reported measures in patients with hip OA. These associations appear to be independent of the type of exercise performed.

Author contributions

The majority of authors (TK, UD, STS, BMB, IM) took part in planning and conducting the clinical trial where the results for these secondary analyses were generated. TK, IM, UD and STS were grant holders for this work. FNF provided expertise for the analyses and collected data on adherence. TK conducted statistical analyses and data management. BMB supervised the statistical analyses. All authors contributed to decisions on the approach for the statistical analyses, assisted in writing the manuscript and approved this final version. TK takes responsibility for the integrity of the work as a whole, from inception to finished article.

Role of the funding source

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Declaration of competing interest

TK, UD and IM have worked extensively with PRT. STS is co-lead of the Danish initiative, Good Life with osteoArthritis in Danmark (GLA:D), which entails NEMEX and has received personal fees from Munksgaard, TrustMe-Ed, and Nestlé Health Science, outside the submitted work.

APPENDIX

Table 1
Results from sensitivity analyses of the crude and adjusted relationship between changes in leg extensor muscle power and measures of physical function using Model 2 and removing observations with extreme leverages or residuals.

Model	β ΔLEP	R^2	P-value	β ΔLEP (PRT)	β ΔLEP (NEMEX)	β ΔLEP(PRT) - β ΔLEP(NEMEX)	P-value
Dependent variable: Δ 30 s chair stand test (number of repetitions) N=143 for model 1, N=137 for model 2 and 3							
Model 1	1.61 [0.69; 2.53]	0.08	0.001				
Model 2	1.95 [1.00; 2.90]	†.11	<0.001				
Model 3				1.53 [0.21; 2.85]	2.36 [1.05; 3.66]	−0.82 [-2.63; 0.99]	0.37
Dependent variable: Δ 9-step timed stair climb test (seconds to complete) N=145 for model 1, N=139 for model 2 and 3							
Model 1	−0.80 [-1.37; −0.22]	0.05	0.01				
Model 2	−1.19 [-1.75; −0.63]	†.25	<0.001				
Model 3				−1.14 [-1.91; −0.36]	−1.25 [-2.00; −0.48]	−0.11 [-1.16; 0.94]	0.84
Dependent variable: Δ 40 m fast paced walking test (seconds to complete) N=143 for model 1, N=137 for model 2 and 3							
Model 1	−1.56 [-2.37; −0.74]	0.09	<0.001				
Model 2	−1.91 [-2.72; −1.10]	†.25	<0.001				
Model 3				−2.43 [-3.58; −1.29]	−1.45 [-2.53; −0.37]	−0.98 [-2.52; 0.54]	0.21

(*continued on next page*)

Table 1 (*continued*)

Model	**β** ΔLEP	R^2	P-value	**β** ΔLEP (PRT)	**β** ΔLEP (NEMEX)	**β** ΔLEP(PRT) - **β** ΔLEP(NEMEX)	P-value
Dependent variable: Δ HOOS ADL (0–100 points) N=144 for model 1, N=138 for model 2 and 3							
Model 1	9.48 [4.36; 14.59]	0.09	<0.001				
Model 2	9.10 [3.88; 14.33]	†.18	0.001				
Model 3				9.38 [2.13; 16.63]	8.82 [1.46; 16.18]	0.56 [-9.61; 10.72]	0.91
Dependent variable: Δ HOOS Sport and Recreation (0–100 points) N=135 for model 1, N=129 for model 2 and 3							
Model 1	7.88 [2.61; 13.15]	0.06	0.004				
Model 2	9.51 [2.39; 16.63]	†.16	0.009				
Model 3				8.63 [-1.77; 19.03]	10.28 [-0.59; 19.96]	−1.64 [-15.74; 12.45]	0.82

Results are presented as regression coefficients of the slope with 95% confidence intervals. †: R-squared estimates are adjusted for multiple independent variables, β: Beta regression coefficients describing the difference in the dependent variable expected with a 1 W/kg difference ΔLEP, Δ: change from baseline to twelve-week follow-up, LEP: Leg extensor power normalized to bodyweight (watt/kg), R^2: R-squared estimate, PRT: Progressive resistance training, NEMEX: Neuromuscular exercise, HOOS: Hip disability and Osteoarthritis Outcomes Score questionnaire.

Model 1. Crude estimates from simple linear regression analysis: Dependent variable (e.g., Δ30s-CST) = ΔLEP.

Model 2. Adjusted estimates from multivariate linear regression analysis: Dependent variable (e.g., Δ30s-CST) = ΔLEP + Age + Sex + Baseline 30s-CST + Baseline LEP + Baseline HOOS Pain + Adherence + Allocation to PRT or NEMEX.

Model 3. Adjusted estimates from multivariate linear regression analysis with an interaction term between ΔLEP and Group Allocation (PRT or NEMEX): Dependent variable (e.g., Δ30s-CST) = ΔLEP + Age + BMI + Sex + Baseline 30s-CST + Baseline LEP + Baseline Pain + Adherence + Allocation + ΔLEP# Allocation to PRT or NEMEX.

Table 2

Associations between baseline leg extension power of the affected limb (LEP) normalized to bodyweight (watt/kg) and baseline values for the dependent variables of physical function in participants with hip osteoarthritis.

Model	**β** LEP	R^2	P-value
Dependent variable: 30 s chair stand test (number of repetitions)			
Model 4	1.99 [1.17; 2.81]	0.14	<0.001
Model 5	2.02 [1.05; 2.99]	†.24	<0.001
Dependent variable: *9-step timed stair climb test (% time to complete)*			
Model 4	−26 [-21; −30]	0.42	<0.001
Model 5	−21 [-16; −26]	†.51	<0.001
Dependent variable: 40 m fast paced walking test (% time to complete)			
Model 4	−16 [-13; −19]	0.36	<0.001
Model 5	−14 [-10; −17]	†.45	<0.001
Dependent variable: *HOOS ADL (0–100 points)*			
Model 4	7.68 [3.64; 11.73]	0.09	<0.001
Model 5	2.88 [-0.17; 5.93]	†.68	0.06
Dependent variable: *HOOS Sport and Recreation function (0–100 points)*			
Model 4	8.82 [3.52; 14.13]	0.07	0.001
Model 5	3.76 [-0.83; 8.35]	†.56	0.11

Results are presented as regression coefficients of the slope or median ratios (as percentages) with 95% confidence intervals. The 9-step timed stair climb test and 40 m fast paced walking test were analysed on the logarithmic scale since residuals of baseline data were not normally distributed on the original scale. **Model 4** (Simple linear regression analysis. Crude estimate): Dependent variable (e.g., baseline 30s-CST) = baseline LEP. **Model 5** (Multiple linear regression analysis. Adjusted estimate): Dependent variable (e.g., baseline 30s-CST) = baseline LEP + Age + Sex + Baseline HOOS Pain. †: R-squared estimates are adjusted for multiple independent variables, β: Beta regression coefficients describing the difference in the dependent variable expected with a 1 W/kg difference in LEP, LEP: Leg extensor power normalized to bodyweight (watt/kg), R^2: R-squared estimate, HOOS: Hip disability and Osteoarthritis Outcomes Score questionnaire, ADL: Activities of daily life function.

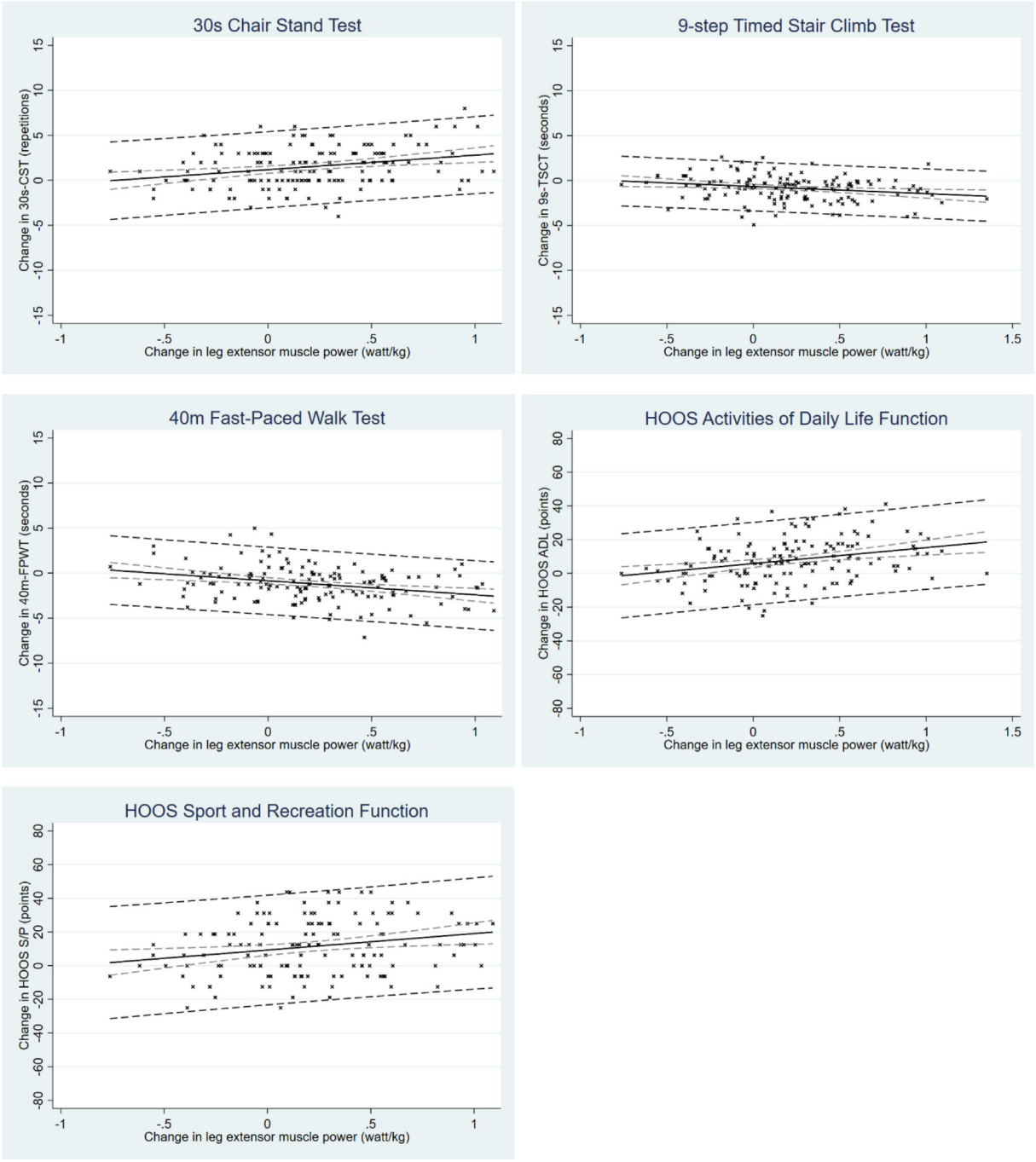

Fig. 1. Scatter plots including only observations included in the sensitivity analyses showing crude linear relationship between changes in leg extensor muscle power (watt/kg) and changes in physical function after 12 weeks of progressive resistance training or neuromuscular exercise in patients with hip osteoarthritis.

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