Muscle function tests as supportive outcome measures for performance-based and self-reported physical function in patients with knee osteoarthritis:

Exploratory analysis of baseline data from a randomized trial
ABSTRACT

Uncertainty on the role of muscle function in relation to physical function in knee osteoarthritis (KOA) persists. This study aimed to assess the associations between muscle function and performance-based and self-reported physical function in patients with KOA.

Physical function in 80 subjects with symptomatic and radiographic KOA was assessed using 40m fast-paced walk, 30s chair stand, nine-step stair climb tests, and the subscale activities of daily living from Knee injury and Osteoarthritis Outcome Score (KOOS-ADL). Measurements of muscle function included leg extension (LE) power, knee extension (KE) torque, and estimated leg press one-repetition maximum (LP RM). Associations were investigated using multivariable hierarchical linear regressions adjusted for age, gender, body mass index (BMI), self-reported physical activity, and thigh muscle lean area.

LE power was significantly associated with 40m walk, stair climb, and 30s chair stand, explaining 18%, 8%, and 3% of additional variance, respectively. KE torque explained 13%, 7%, 17% and 7% of additional variance in the 40m walk, stair climb, 30s chair stand, and KOOS-ADL, respectively. LP RM explained 11% of additional variance in the 30s chair stand.

In conclusion, LE power was the best explanatory variable for performance on the 40m walk and stair climb tests, while KE torque best explained chair stand performance. Only KE torque was associated with KOOS-ADL.

Our results highlight the importance of selecting supportive muscle function tests based on the specific physical function and suggest that other factors may be more important for certain physical function outcomes.

Level of significance
P<0.05.

**Keywords:** Osteoarthritis; Knee; Strength; Power; Physical function

Trial identifier: NCT03215602
INTRODUCTION

Knee osteoarthritis (KOA) is one of the most prevalent musculoskeletal conditions worldwide, with pain and functional disability as the hallmark symptoms. Functional disability in KOA manifests in difficulties with daily functions, such as walking, climbing on stairs, and rising from a chair. Accordingly, International guidelines from the leading medical society within osteoarthritis research; the Osteoarthritis Research Society International (OARSI) recommend the use of a minimal core set of performance-based tests (fast-paced walk, stair climb, and chair stand) in knee and hip osteoarthritis to monitor the disease in both research and in the clinic. These performance-based tests are typically performed together with self-reported assessments of disability to obtain a complete assessment of physical function in KOA patients.

In addition, performance-based and self-reported disability measures are often supported by muscle function tests, which represent a measure of the muscle performance, underlying variations to physical function. Since muscle function deficits are associated with an increased risk of functional decline and progression of symptomatic KOA, muscle function tests can be considered a highly relevant component of the physical function evaluation in KOA. Previously, muscle power (the product of force and velocity) has demonstrated a stronger association with performance-based and self-reported physical function in KOA compared to maximal strength tests (e.g. peak torque and repetition maximum (RM) assessments).

However, the different methods used to assess muscle function across previous studies make it somewhat difficult to obtain a clear picture of the relative contribution of muscle strength and power to physical function in KOA. Leg extension explosive power, expressed in watts (W), has been used as a measure of the ability of the muscles to perform work during
contractions of half a second or less. Muscle power seems to have the strongest relation to physical function when assessed in a dynamic closed kinetic chain test. On the other hand, peak torque outputs, typically expressed in newton meters, provide information about the maximum contractile capacity of the muscle. High torque outputs are only possible during eccentric contractions, isometric conditions, and low-velocity concentric contractions.

Hence, different tests are needed to assess maximum muscle power and strength, respectively.

As a clinically applicable alternative to the two standardized tests of muscle power and strength, the RM test is a commonly applied strength assessment method in KOA due to its applicability on any exercise machine with adjustable load systems. The RM test refers to the maximum load that the subject is able to lift for a set number of repetitions (e.g. 1RM, 3RM or 5RM). However, the dynamic properties of the RM test does not necessarily provide optimal conditions for assessing peak muscle strength throughout the range of motion. For example, high quadriceps muscle activity has been reported in the squat and leg press exercises at flexed knee angles but not at more extended knee angles, indicating that the contractile capacity of the quadriceps is tested only at flexed knee angles in these exercises.

The RM test may also be limited by muscular fatigue as well as pain and/or discomfort during maximal load testing of the lower limbs in KOA patients.

Due to non-uniformity of applied test conditions, there is still some uncertainty regarding the respective roles of muscle power, torque, and RM strength in explaining variations to performance-based and self-reported physical function in KOA. Considering the important role of muscle function as a determinant of physical function in KOA, a better understanding of the relative contributions of different muscle function entities to physical function is needed and achieving this will help guide the development of effective therapeutic interventions to combat muscle function impairments in KOA.
Therefore, the aim of this study was to assess the associations between muscle power, peak torque and RM strength, and performance-based and self-reported physical function in patients with KOA. We hypothesized that the measurement of muscle power, due to the dynamic and explosive nature of the test, would demonstrate the greatest association to physical function in KOA patients.

**METHODS**

**Experimental approach to the problem**

**Study design**

This was a cross-sectional study using baseline data from a randomized controlled trial (The EXTRA trial; ClinicalTrials.gov. NCT03215602). Specifically, this study included both performance-based and self-reported physical function assessments at baseline (dependent variables) together with various muscle function assessments (independent variables) to explore the relative contribution to physical function provided by the muscle function assessments. This study did not interfere with any aspects of the study protocol for the randomized controlled trial. The current study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for reporting cross-sectional studies.

**Subjects**

Patients with symptomatic and radiographically confirmed KOA deemed ineligible for knee replacement surgery by an orthopedic surgeon in the outpatient clinic at Næstved Hospital in Region Zealand, Denmark.

**Ethics**
The randomized controlled trial has obtained approval by the Danish Data Protection Agency (REG-061-2016) as well as the Danish Scientific Ethical committee (SJ-517) and all participants signed an informed consent form for participation; hence, no further approval was required for this study.

Exclusion criteria:

- Radiographically assessed Kellgren & Lawrence score of <2
- Less than “mild” symptoms (score >75 in 0-100 Knee Injury and Osteoarthritis Outcome Score, subscale Activities of Daily Living (KOOS-ADL))
- Morphine usage for pain other than knee-joint pain
- Previous ipsilateral knee arthroplasty
- Rheumatoid arthritis
- Inability to comply with the protocol
- Inadequacy in written and spoken Danish

Procedures

Data collection

All performance-based and muscle function data were collected by the same trained physiotherapist. The performance-based and muscle function tests were performed at the Department of Physiotherapy and Occupational Therapy, Slagelse Hospital. Self-reported physical function was assessed as part of the baseline online questionnaire. All assessments were performed between August 2017 and October 2018.

Physical function outcome variables

The selected outcome variables represent the common and recommended outcomes for assessing performance-based and self-reported physical function in KOA in both research
and clinical practice. Despite some concerns about the construct validity of the included performance-based physical function tests\textsuperscript{42}, they arguably still constitute the best available and recommended constructs of performance-based functional status in KOA.

**Performance-based physical function**

- **40m walk**

  The 40m walk test was performed on a 20-meter course, requiring a turn and return to start for test completion. A cone was placed two meters beyond the 20-meter course for turning to ensure that the test time was not influenced by turning time. The subject was instructed to walk as fast as possible without compromising safety. Patients were allowed to use walking aids if necessary. The use and type of aid was recorded for each patient. Time to complete the course in seconds was recorded with a stopwatch and used for later analysis. The 40m walk has demonstrated good reliability in the assessment of fast-paced walking ability in knee and hip OA patients\textsuperscript{26}.

- **Stair climb**

  The stair climb test was performed on a 9-step stairway. The subject was instructed to descend nine steps down to the stairway landing, make a quick turn and ascend the same nine steps up to finish. The subject could use arm rails for help. The use of arm rails was recorded. The time used to complete the full course (18 steps) was recorded and used for later analysis. Stair climb activities are reliable as outcome measurements in KOA\textsuperscript{42}.

- **30second chair stand**

  The 30s chair stand test was performed using a standard height chair (43 cm.) without armrests and placed against a wall. On the assessor’s command, the subject rose from the chair to a full standing position and sat down again and repeated for as many times as
possible in 30 seconds. If the patient was unable to rise independently from the chair, a cushion (6 cm) was placed on the chair to decrease knee flexion. The use of cushion was recorded. The assessor first demonstrated the test and then the subject would perform 1-2 chair-rises for familiarization before the actual test commenced. The number of repetitions in 30 seconds was recorded and used for later analysis.

The 30s chair-stand test is a valid\textsuperscript{22} and reliable\textsuperscript{42} measurement of lower body function.

\textit{Self-reported physical function}

KOOS-ADL was completed as part of the baseline questionnaire. KOOS-ADL consists of 17 questions regarding knee symptoms during various forms of daily living activities. Symptoms were scored on a Likert-type scale from zero (no symptoms) to four (extreme symptoms) for each activity. A normalized score for the full subscale was calculated, ranging from zero (extreme symptoms) to 100 (no symptoms). The reliability and divergent and construct validity of KOOS in evaluating symptom state in knee osteoarthritis has been extensively demonstrated in recent years\textsuperscript{12}.

\textit{Explanatory variables}

The selected muscle function tests represent commonly used tests in both research and clinical practice\textsuperscript{11,35}.

\textit{Muscle function tests}

- Leg extension power

Leg extension (LE) power was assessed using a Nottingham Power Rig (NPR) (University of Nottingham Medical School, Queen’s Medical Centre, Nottingham NG7 2UH, United Kingdom). After being weighed, the subjects were seated in the rig, with the test leg in 15° knee flexion when fully depressing the footplate, which was used for the leg extension
movement. On the assessor’s command, the subject pushed the footplate as forcefully and explosively as possible. The assessor gave strong and standardized verbal encouragement during each attempt. The subject was given two familiarization attempts and a minimum of five recorded attempts. The test was stopped when the subject had two successive recorded attempts below their maximal power output. The acceleration from the push was transmitted to a flywheel. Average power was derived from the final velocity of the flywheel and displayed as watts and watts pr. kilo bodyweight. Maximal power output in watt pr. kilo bodyweight for the symptomatic leg was derived and used for later analysis.

The NPR has previously been demonstrated as a feasible, valid and reliable method for assessing explosive leg extension power across all age groups and levels of physical activity.

- Knee extension torque

Knee extension (KE) torque was assessed during isometric contractions using a dynamometer (Hoggan Health Industries, Inc. 8020 South 1300 West, West Jordan, USA), which was fixed by a strap to a test chair, custom-built for the purpose of isometric dynamometer testing. The subjects were seated in the test chair with the hips and knees in 90° flexion. To avoid excessive hip movement during the contractions, the thighs were stabilized at mid-thigh using a belt attached to the test chair. The force transducer was placed on the front of the distal shin, with the center 7 cm proximal to the apex of the lateral malleolus, and was attached by a strap that was fixed to the rear end of the test chair, perpendicular to the transducer. For better comfort, a foam pad was placed between the transducer and the shin. The lever arm length (in meters) was measured from the center of the transducer to the knee joint axis of rotation (lateral femoral condyle) in order to convert the force (newtons) to torque (newton meters).

After two familiarization attempts, the subjects were instructed to press as forcefully as possible against the transducer for 5 seconds, increasing the force gradually throughout the 5
seconds. The assessor gave strong and standardized verbal encouragement during each attempt. The test was repeated after a one-minute break and performed a minimum of three times for each subject. Additional attempts were performed if the third attempt produced the highest force output. Peak torque output of the symptomatic leg was calculated in newton meters (Nm) and used for later analysis.

Hand-held dynamometry has demonstrated good reliability in the assessment of isometric torque outputs in older adults\(^4\).

- Leg press RM

The estimated 1RM strength was assessed during a submaximal test (5RM), using a 1RM prediction method in a horizontal leg press, hereafter termed LP RM. Initially, the assessor loaded the leg press with a load that the patient was assumed to be able to lift for no more than five repetitions. The initial load was based on the patient’s estimation of his or her lifting capacity and a qualified estimate from the assessor\(^1^1\). If the patient was able to lift the load more than five times, a break ranging from one to three minutes (depending on the level of effort) was afforded, after which the assessor increased the load with up to 20%, again depending on the level of effort in the previous attempt. The assessor gave strong and standardized verbal encouragement during each attempt. The test continued until the patient could lift the load a maximum of five times. To convert the submaximal load to 1RM (maximal load), the Adams prediction equation was used \[ \text{1RM} = \frac{\text{load}}{1 - 0.02 \times \text{repetitions}} \]\(^3^0\). The Adams prediction equation has demonstrated the greatest level of predictive accuracy compared to other prediction equations when assessing maximal leg press load capacity from submaximal loads in a KOA population\(^3^0\). The converted maximal load (1RM) was derived and used for later analysis.

Covariates
A number of covariates, known to be associated with physical function outcomes were added to the analysis in addition to relevant demographic variables (age, gender and body mass index (BMI)) in order to adjust the explained variance provided by the muscle function tests. The covariates were included based on the assumption that muscle structure and physical activity levels act as confounders on muscle function and physical function in KOA (see directed acyclic diagram (DAG) in appendix).

- **Thigh muscle lean area**

Thigh cross-sectional area (CSA) was measured in eleven axial slice-images centered at 50% femur length, using Magnetic Resonance Imaging (MRI) (1.5 T Siemens Magnetom Avanto Fit) and a semi-automated segmentation algorithm. In the next step, segmentation masks were transferred to a corresponding DIXON water and fat suppressed imaging sequence in order to localize intramuscular fat. Thigh CSA (cm²) and thigh inter- and intramuscular fat (cm²) at 50% femur length were derived with the fat area being subtracted from the thigh muscle area to create the variable thigh muscle lean area.

- **Self-reported physical activity**

As part of the baseline questionnaire, the patients were asked to rate their current physical activity levels, using the University of California, Los Angeles, activity score (UCLA score). Physical activity levels were scored from one (physically inactive – dependent on others) to 10 (regular physical activity at very high intensities). The UCLA score has been found to be valid as a measure of physical activity in orthopedic patients.

**Statistical analysis**

The study sample consisted of a convenience sample derived from the RCT, including only subjects with complete baseline assessments. Data were analyzed through multivariable linear regression models.
Analyses were performed as hierarchical regressions, i.e. the explanatory variable was included after modeling one outcome variable (40m walk, stair climb, 30s chair stand, or KOOS-ADL) with all covariates. The stepwise approach included an initial model with one outcome variable and age, gender, BMI, physical activity and thigh lean muscle area. Subsequently, in order to assess adjusted associations and explanatory capabilities for LE power, KE torque and LP RM, the explanatory variables were added to each model separately. Beta (β) regression coefficients and explained proportional variance (adjusted $r^2$) were reported with changes to adjusted $r^2$ after inclusion of the explanatory variable as a measure of the explanatory capacity of the individual muscle function test. The presence of multicollinearity was checked through variance inflation factor (VIF) estimations. Thresholds for excessive correlation between variables were set at ≥4 (individual variables) and >1 (mean of all variables). Assumption of normality and linearity of the data were checked by visual inspection of quantile-quantile (Q-Q) plots and distribution of residual plots around the regression line.

All analyses were performed using STATA 15.0 (StataCorp, College Station, TX, USA) and significance level for independent contribution to the regression model was set at $p<0.05$.

**RESULTS**

80 patients were included in this study. Descriptive statistics are summarized in table 1. All patients had a radiographic Kellgren & Lawrence score of ≥2 (range from 2-4 on a 0-4 scale), consistent with the presence of definite radiographic KOA as well as a clinical verification of KOA according to International guidelines. Four patients used a cane for aid when performing the 40m walk test, 29 patients used arm rails for aid when performing the stair climb test, and three patients used a cushion for aid when performing the 30s chair stand.
Assumptions of normality and linearity of data were confirmed. Multicollinearity testing indicated no excessive collinearity between variables (variance inflation factor <4). Finally, the scatter plots showed an even distribution of the residual plots on either side of the regression line, confirming homoscedasticity.

Leg extension power and physical function

LE power was significantly associated with 40m walk, stair climb, and 30s chair-stand, contributing with 18% (40m walk), 8% (stair climb), and 3% (30 s chair stand) of explained variance to the regression model after controlling for demographic factors, physical activity and thigh muscle lean area. LE power was not significantly associated with self-reported physical function (table 2).

Knee extension torque and physical function

KE torque was significantly associated with all outcomes, adding 13% (40m walk), 7% (stair climb), 17% (30s chair stand), and 7% (self-reported physical function) of explained variance after controlling for demographic factors, physical activity and thigh muscle lean area (table 2).

Leg press RM and physical function

LP RM strength was significantly associated with 30s chair stand, adding 11% of explained variance after controlling for demographic factors, physical activity and thigh muscle lean area. LP RM was not significantly associated with 40m walk, stair climb or self-reported physical function (table 2).

DISCUSSION
This is the first study to compare the association between three common muscle function tests and performance-based and self-reported physical function in KOA. Contrary to our hypothesis, we were unable to demonstrate an overall superior association between LE power and physical function. Instead, the level of explained variance provided by the muscle function tests to physical function varied throughout the tests. We found that LE power best explained level walking and stair climb performance, although the difference between LE power and KE torque in explaining variations to stair climb performance may be negligible. KE torque was significantly associated with all physical function outcomes, demonstrating the strongest association with chair stand performance and the only muscle function test associated with self-reported physical function. LP RM was only associated with repeated sit-to-stand performance. Finally, the total variance explained by the regression models was low compared to previous literature. Our study highlights the importance of choosing a supportive measure of muscle function depending on the physical function in focus and underlines that physical function is dependent on more than just muscle function.

Muscle function and performance-based physical function

The association between LE power and the 40m walk test demonstrated the greatest explained variance provided by any of the muscle function tests on physical function (18% of explained variance). Confirming previous reports, this indicates that the contraction velocity produced during explosive-type movements (e.g. maximal power) is a better determinant of walking speed compared to e.g. the slow ramp-type contractions performed during isometric peak torque testing. Surprisingly, the difference in contributions from LE power and KE torque in the stair climb test was minor (8% and 7% of explained variance, respectively). This is surprising since the travel of the pedal in the leg extension rig used in our study (the NPR) is designed to match the height of a stair-riser and thus creates more favorable test conditions to mimic stair climbing compared to the test conditions applied in the KE torque
test\textsuperscript{7}. The low explained variance provided by either muscle function test to stair climb performance might also reflect that stair climbing is a more demanding task compared to level walking\textsuperscript{47}. Stair climbing is also influenced by other factors such as knee range of motion, cardiorespiratory capacity, and self-efficacy\textsuperscript{46} - these factors may be at least as important as muscle function during a stair climbing task. Importantly, 29 patients used the arm rails for aid when performing the stair climb test. Previously, even light handrail use seems to alter the distribution of joint moments between the knee and ankle and improve dynamic balance in older adults\textsuperscript{34}. From our findings, it seems plausible that the frequent use of arm rails (more than one-third of patients) has improved dynamic balance and thereby performance irrespective of muscle function levels. This may have confounded the total association between muscle function and stair climb performance and is important to consider when interpreting our findings from the stair climb test.

For the chair-stand test, the most explained variance was provided by KE torque (17% of explained variance). The association between KE torque and chair stand performance is consistent with recent findings from a large cohort showing an association between improvements in quadriceps strength and improved chair-stand performance in women with KOA (Odds Ratio (OR): 2.27\textsuperscript{5}). Our findings seem to indicate that the KE torque test is a more sensitive determinant of variations to chair-stand performance than both LE power and LP RM. This is somewhat in contrast to previous findings in patients with mild to moderate KOA, where leg press power derived using linear encoders explained the most variance in a five-time chair stand test compared to both 1RM in the leg press and 1RM and power in a knee extension machine\textsuperscript{40}. The different methods used to assess both muscle strength and muscle power may play a role in these contrasting findings; for example, the aforementioned study used linear encoders to determine maximal power output on a load range of 40, 50, 60, 70, 80, and 90% of 1RM – this is distinctly different from the test conditions used in the
NPR. Currently, there is contradictory evidence regarding optimal test conditions for measuring muscle power\textsuperscript{9,32} and further studies are needed to clarify and possibly resolve these discrepancies.

Taken together, our findings are not entirely consistent with prior literature, which has consistently shown the strongest association between leg extension power and functional impairments in both KOA patients and in older adults\textsuperscript{2,8,39,40}. Rather, our findings reveal varying associations between different tests of muscle function and different performance-based physical function tests in patients with KOA.

**Muscle function and self-reported physical function**

Only KE torque was associated with KOOS-ADL, adding 7\% of explained variance to the regression model. This association is supported by a recent meta-analysis, showing higher odds (Odds Ratio (OR): 1.38) of self-reported functional decline with low knee extension strength\textsuperscript{15}. However, this meta-analysis did not discriminate between different forms of muscle function tests. In a previous investigation comparing associations between self-reported physical function and 1RM leg press strength and power, respectively, only power demonstrated a significant association with self-reported physical function in mild to moderate KOA\textsuperscript{36}. Since KOOS-ADL addresses limitations during mainly dynamic tasks, one would expect greater associations with one or both of the two dynamic strength tests (muscle power & 1RM) and only to a lesser extent association with the isometric strength test (KE torque) in our study. Perhaps importantly, unlike the multiple-joint LE power and LP RM, which involve co-contractions of the hip extensors, the hamstrings and the plantar flexors, only the KE torque output is able to isolate the muscle work produced to the quadriceps. It has been suggested that increased quadriceps strength may result in lower impact and impulsive loads being transmitted through the knee joint, manifesting in less limitations
during daily weight bearing activities 21,28; this may be one reason for our findings, although clear evidence is lacking. Still, in patients 4 weeks post knee replacement surgery for KOA, Aalund and colleagues found that LE power consistently showed better associations with self-reported physical function and symptom scales compared to KE torque using a similar test-setup for power and torque as in our study1. Importantly, patients with KOA, not eligible for knee replacement surgery, may perceive limitations to physical function in a different way than patients in the early stages after knee replacement surgery. These contrasting findings call for a better understanding of muscle function and self-reported physical function across different KOA disease stages.

**Limitations**

There are some important limitations of this study. First, we chose to obtain the most functionally relevant measurement of maximal power and create the best physiological basis for assessing peak torque while also trying to mimic clinical assessments of 1RM strength. To achieve this, we had to use three different test-setups, and this will invariably limit the comparison between the different strength and power outputs. Second, although we avoided multiplicity of testing by including all variables together and retaining them regardless of p values in step 1, we still increased the risk of spurious findings by adding the muscle function tests separately to the regression models in step 2. However, considering the explorative study design, coherent multiplicity corrections are not possible and are therefore not expected for these types of studies33. Third, the regression models in this study displayed somewhat lower explained variance than comparable studies. This can potentially be explained by different statistical approaches (i.e. types of regression models and choice of adjustment variables), but it also highlights the fact that other factors than those included in the current study are important for physical function. The frequent use of arm rails during the stair climb test (more than one-third of patients) may be another important confounding factor,
attenuating the association between stair climb performance and muscle function. Fourth, other than knowing that included patients had definite radiographic KOA (K&L≥2), we were unable to derive specific K&L grades of the included patients (potential range of 2 to 4). Since there seems to be differences in both physical function and muscle function across different levels of radiographic KOA severity\textsuperscript{19}, the lack of information on specific K&L grades is a limitation to this study.

Conclusion
This study demonstrated that the strength of the association between muscle function and recommended performance-based and self-reported physical function measures in patients with KOA depends somewhat on the applied muscle function test. Importantly, a large degree of the variance was not accounted for by the included variables, suggesting that other factors may be more important for certain physical function outcomes. For fast-paced level walking and stair climb performance, leg extension power is the most sensitive determinant of variance, although for stair climb performance in particular, the differences between LE power and KE torque may be negligible. For chair stand performance and self-reported physical function, KE torque may provide the most explained variance in this specific group of patients with KOA.

PRACTICAL APPLICATIONS
If using a muscle function test to support the assessment of physical function, the trainer or therapist needs to carefully define the nature of the physical function task that the particular patient wants to improve before deciding which muscle function measure to use. To probe the factors at the muscle function level which underpin level walking and stair climb ability, the trainer/therapist may want to choose LE power, whereas for chair stand ability and self-reported physical function, KE torque might be the test of choice.
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