Gait & Posture 74 (2019) 20–26

Contents lists available at ScienceDirect

Gait & Posture

journal homepage: www.elsevier.com/locate/gaitpost

Full length article

Measures of knee and gait function and radiographic severity of knee osteoarthritis – A cross-sectional study

J.E. Naili[a,*], E.W. Broström[a], B. Clausen[b,c], A. Holsgaard-Larsen[a,d]

[a] Department of Women's and Children's Health, Karolinska Institutet, Q2:07, Karolinska University Hospital, 171 76, Stockholm, Sweden
[b] Research Unit for Musculoskeletal Function and Physiotherapy, Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Campusvej 55, 5230, Odense M, Denmark
[c] Department of Physiotherapy and Occupational Therapy, Næstved-Slagelse-Ringsted Hospitals, Region Zealand, Fælledvej 7, 4200 Slagelse, Denmark
[d] Orthopaedic Research Unit, Department of Clinical Research, University of Southern Denmark & Odense University Hospital, Heden 18, 5000 Odense C, Denmark

ARTICLE INFO

Keywords:
Osteoarthritis
Function
Performance
Biomechanics
Patient-reported outcome
Radiography

ABSTRACT

Background: Pain reports show at most weak to moderate relationship with structural findings of knee osteoarthritis (OA). Less is known about the relationship between measures of knee and gait function and structural findings of knee OA.

Research question: To test the hypothesis that patient-reported, performance-based and three-dimensional knee and gait measures can distinguish between individuals with varying degrees of radiographic knee OA severity.

Methods: To increase the spectrum of radiographic severity baseline data of individuals included in a cohort study and in a randomized controlled trial respectively were included in this cross-sectional study. Individuals completed the Knee injury and Osteoarthritis Outcome Score (KOOS), Single Limb Mini Squat (SLMS) test, and three-dimensional gait analysis. Radiographic severity was dichotomized into mild (Kellgren Lawrence (KL) 1-2) or severe (KL 3-4) knee OA. Proxies for medial knee joint loading were peak knee adduction moment (KAM) and KAM impulse, and summary measures of overall gait function were the Gait Deviation Index for kinematics (GDI) and kinetics (GDI-kinetic). Area under the receiver operating characteristic curves (AUC) and logistic regressions were used to evaluate whether KOOS-scores, SLMS test, peak KAM, KAM impulse, and GDI-scores could discriminate radiographic severity of knee OA.

Results: The sample (n = 115) consisted of 60% women, mean age 61 years (SD 8). Good discriminating abilities (AUC > 0.7) were demonstrated for all measures of knee function and gait, except for GDI and GDI-kinetic (0.62 and 0.36, respectively). Odds ratios from logistic regressions largely supported the AUC findings.

Significance: With the exception of gait summary measures, discriminating abilities were demonstrated by all measures of knee and gait function. Given the interest in interpreting OA as a multi-factorial disease, this information may assist researchers in selecting the most appropriate outcomes for biomechanical studies.

1. Introduction

Knee osteoarthritis (OA) is a multi-factorial condition but is at least in part considered a mechanically driven disease where higher abnormally distributed forces are thought to play a role [1]. OA disease severity is often evaluated by plain radiographs [2], but doubts have been expressed about the validity of radiographic classification criteria [3]. Consequently, reliable and valid outcome measures of physical function, may provide additional biomechanical and functional information that is not provided by plain radiographs. However, assessment of physical function in OA is complex [4], and patient reported outcome measures (PROM) of knee function and pain, in addition to performance-based measures, are recommended since they represent different and complementary constructs of physical functioning [4–8]. The Knee injury and Osteoarthritis Outcome Score (KOOS) is a reliable and valid PROM that has been developed to assess patients' opinion about their knee and associated problems [9] and has been showed to be associated with radiographic severity defined by the Kellgren and Lawrence (KL) radiological classification system in a general Japanese population [10]. Improvements in KOOS-scores, beyond the minimal detectable change, following total knee arthroplasty have been shown to be accompanied by several changes in sagittal and frontal plane knee

* Corresponding author.
E-mail addresses: josefine.naili@ki.se (J.E. Naili), eva.brostrom@ki.se (E.W. Broström), brian_clausen@hotmail.com (B. Clausen), AHLarsen@health.sdu.dk (A. Holsgaard-Larsen).

https://doi.org/10.1016/j.gaitpost.2019.08.003
Received 19 November 2018; Received in revised form 14 June 2019; Accepted 6 August 2019
0966-6362/

Table 1
Inclusion and exclusion criteria for the Swedish cohort and Danish randomized controlled trial.

Inclusion criteria	
Swedish cohort [Reference no 13]	**Danish randomized controlled trial** [Reference no 15]
Physician diagnosed primary knee OA	Persistent knee pain
Scheduled for a TKA within one month	Diagnosis of knee OA in accordance with the ACR
Understand verbal and written Swedish	No leg surgery/trauma within the last 6 months.
Ability to walk 10 m repeatedly without use of a walking aid	No contraindication for exercise, non-steroidal anti-inflammatory drugs, or X-ray
Exclusion criteria	
Swedish cohort [Reference no 13]	**Danish randomized controlled trial** [Reference no 15]
BMI > 35	BMI > 32
Previous major orthopedic surgery in the lower extremities	Previous major orthopedic surgery in the lower extremities
Diabetes mellitus	Known ACL deficiency
Neurologic disorder	Steroid injection within the past 6 months
Other condition affective walking ability	Medial knee OA of KL grade 4
Rheumatoid arthritis	Radiographic signs of lateral compartment OA worse than medial compartment OA
Additional exclusion criteria applied for the present sequel analysis	
Medial knee OA of KL grade 0	

ACL, Anterior Cruciate Ligament; ACR, American College of Rheumatology; BMI, body mass index; KL, Kellgren and Lawrence radiological classification system; OA, osteoarthritis; TKA, total knee arthroplasty.

kinetics and kinematics, in addition to increased walking speed [11]. These biomechanical changes were however not observed for patients reporting change in KOOS-scores below the minimal detectable change [11]. A reliable performance-based test that has been applied to evaluate knee function in knee OA patients is the 30 s maximal Single Limb Mini Squat (SLMS) [12]. SLMS has been used to investigate the impact of the disease prior to surgery [13], and the effect of exercise [14,15]. However, KOOS and SLMS test do not provide explanatory information regarding the underlying biomechanical mechanisms of the observed symptoms, which may be provided by objective outcomes from a three-dimensional gait analysis.

Despite the exact pathogenesis of OA still remains unknown, mechanistic variables of knee joint loading are thought to play a role [1]. Explanatory research of isolated knee joint loading derived from three-dimensional gait analysis suggest that the peak knee adduction moment (KAM) and positive KAM impulse are valid and reliable proxies for the load of the medial knee compartment [16,17]. Furthermore, peak KAM and positive KAM impulse have displayed the ability to distinguish between different degrees of radiographic severity of knee OA, which facilitate understanding of the, at least in part, biomechanical role in the pathogenesis of knee OA [18,19]. Beside interest in specific outcomes of knee function, the past decade has focused on overall gait function that may be more related to activity and participation in everyday life [13,20,21]. The Gait Deviation Index for kinematics (GDI) and kinetics (GDI-kinetic) are summary measures of gait function that quantify overall 'gait quality' into a single score by means of kinematic or kinetic data from a three-dimensional gait analysis, respectively [22,23]. The GDI and GDI-kinetic have been reported to identify deviant gait patterns in individuals scheduled for total knee arthroplasty [13,24]. However, the responsiveness of GDI-scores in patients undergoing total hip arthroplasty has been questioned [21,25], and it is unknown if GDI and GDI-kinetic scores are influenced by different degrees of radiographic knee OA severity.

This study aimed to investigate whether varying degrees of radiographic knee OA severity is related with differences in patient-reported knee function and pain, performance-based function and three-dimensional knee and gait summary measures. Thus, we tested the hypothesis that KOOS, SLMS, KAM, KAM impulse, GDI, and GDI-kinetic can distinguish between individuals with varying degrees of radiographic knee OA severity.

2. Methods

2.1. Study design

This is a cross-sectional analysis of baseline data from individuals included in a cohort study (n = 40) conducted at Karolinska University Hospital, Solna, Sweden [13], and individuals from a randomized controlled trial (n = 93) conducted at University of Southern Denmark, Odense, Denmark [15]. The current cross-sectional study is reported following the "Strengthening the Reporting of Observational Studies in Epidemiology" (STROBE) [26].

2.2. Participants

Individuals in Sweden were recruited from two orthopedic departments in Stockholm (Ortho Center, Löwenströmska Hospital, and Karolinska University Hospital) between November 2010 and November 2012. Individuals in Denmark were recruited via general practitioners in the communities of Odense and Middelfart, and from advertisements in local clubs, libraries, print media, and Facebook from October 2012 to May 2015. Inclusion criteria were age 40–70 years, clinical diagnosis of knee OA in accordance with the American College of Rheumatology [27], and persistent knee pain. For all study participants in the current analysis, exclusion criteria included any previous joint replacement or other major surgery, BMI > 35, KL score of 0, and systemic arthritis. Prior to inclusion, all participants provided a signed informed consent. Detailed inclusion and exclusion criteria for the Swedish cohort [13] and Danish randomized controlled trial [15], respectively, are presented in Table 1.

2.3. Patient-reported knee function and pain

Participants completed the KOOS [9]. The KOOS is reported as five separate subscales addressing Symptoms, Pain, Function in Activities of Daily Living (ADL), Function in Sport and Recreation, and Knee-related quality of life (QoL). Each subscale generates a final score ranging from 0 to 100, where 0 represents "worst" and 100 represents "best" [9].

2.4. Performance-based function

The 30 s maximal SLMS test, examines unilateral neuromuscular control, the ability to quickly change between concentric and eccentric muscle work of the hip and knee extensors [28]. Participants stood on one leg on a well-defined area shaped like the letter "T" with the long axes of the foot on the "stem", and toes placed on the "arm" of the T. Fingertip support for balance was provided. Participants were instructed to flex the knee (on the standing leg) until toes were no longer visible and then fully extend the knee. The test has demonstrated to be valid and reliable in individuals with knee OA [12,28]. In this study, the number of repetitions performed on the most affected leg was used for further analysis.

2.5. Three-dimensional gait analysis

Three-dimensional gait analyses were conducted at the Motion Analysis Laboratory at Karolinska University Hospital, Stockholm, Sweden, and at Odense University Hospital, Odense, Denmark, respectively, using identical laboratory protocols. Data were recorded using an 8 camera system (Vicon Motion Systems Ltd, Oxford, UK), and a conventional biomechanical model, the Plug-In-Gait model [29]. All study participants were instructed to walk at a self-selected walking-speed. The outcome measures derived from the gait analyses (i.e. peak KAM, positive KAM impulse, GDI and GDI-kinetic scores) were calculated based on approximately five (and no less than three) gait strides per person and subsequently averaged to obtain a single value. Peak KAM and positive KAM impulse were calculated using inverse dynamics (Vicon Plug-in-Gait version 1.9). Peak KAM was defined as the highest external knee adduction moment throughout the stance phase and KAM impulse was calculated by integrating the positive section of the curve between heel strike and toe-off [30]. Subsequently both outcome measures were normalized to body weight and height (Peak KAM; Nm/BW*HT%, KAM-impulse; Nm*s/BW*HT%). The GDI and GDI-kinetic scores were, as described in the original papers [23,31], calculated based on a reference-set consisting of healthy individuals (n = 59 for GDI, n = 56 for GDI-kinetic) which was selected from the control database at the Motion Analysis Laboratory at Karolinska University Hospital, Stockholm, Sweden. For outcome measures derived from the three-dimensional analysis, values of the most affected leg were used for further analysis.

2.6. Radiographic classification of knee osteoarthritis

At each health care site, pre-operative standing anterior-posterior radiographs were collected according to standard procedures. Two experienced senior orthopedic surgeons and three chiropractors assessed the radiographs for the Swedish and Danish participants, respectively, according to the KL classification ranging from grade 1–4 [32]. Subsequently, to allow an analysis on the discriminating ability of various outcome measures on radiographic severity, the present sample was dichotomized, as also done in similar studies [19,33], according to the most affected knee, into mild knee OA (KL 1–2) and severe knee OA (KL 3–4).

2.7. Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics version 23 (Chicago, IL, USA). Normality of data was assessed using Shapiro-Wilks test and Q-Q plots. Independent sample t-tests were used to compare differences between OA groups (mild and severe). Receiver operating characteristic (ROC) curves were calculated to evaluate whether number of KOOS subscale scores, SLMS test repetitions, magnitude of peak KAM and positive KAM impulse, and finally GDI and GDI-kinetic scores could discriminate between mild and severe radiographic knee OA. The area under the ROC curve (AUC) and 95% confidence intervals (CI) were calculated for each outcome measure, and an AUC of at least 0.70 was considered to be appropriate [34]. The ROC-analyses provide information on sensitivity/specificity corresponding to a specific threshold. The area under the ROC curve (AUC) provides a measure of how well a specific measure can distinguish between two groups (Mild/Severe knee OA). Using logistic regression, unstandardized and standardized odds ratios of severe knee OA, along with 95% CI and *p*-values, were estimated to provide information for the impact of each outcome measure on the specific scale (unstandardized odds ratio). Unit-less odds ratios (standardized odds ratios) were estimated to allow for comparisons between the different outcome measures represented by dissimilar scales. In addition, odds ratios were adjusted for age and BMI as the two groups (Mild and Severe) presented with significant differences in these parameters. A *p*-value below 0.05 was considered statistically significant.

2.8. Ethical approval

This study is compliant with the Helsinki Declaration and was approved by the regional ethical board in Stockholm, Sweden, DNR: 2010/1014-31/1 and by the Regional Scientific Committee for Southern Denmark (identifier: S-20110153).

3. Results

In total, 133 individuals (n = 40 from the Swedish cohort study and n = 93 from the Danish trial) with knee OA were included in this cross-sectional sequel analysis. Fifteen individuals were excluded during the analysis of GDI and GDI-kinetic due to limitations of the available capturing volume (i.e. the analysis require two complete strides and double force plate strikes), and three individuals were excluded due to no radiographic signs of knee OA (KL score of 0). Consequently, analyzes were performed on 115 individuals (n = 63 with mild knee OA, and n = 52 with severe knee OA) (Table 2). The characteristics of study participants demonstrated that individuals categorized with severe knee OA (KL 3–4) were significantly older, had significantly higher weight, and higher BMI compared to the mild knee OA (KL 1–2) group (Table 2). Furthermore, all outcome measures (i.e. KOOS, SLMS test, and measures derived from three-dimensional gait analysis) were significantly worse among individuals with severe knee OA as compared to individuals with mild knee OA (Table 2).

3.1. Ability to discriminate between mild and severe knee osteoarthritis

All KOOS subscale scores displayed good ability to discriminate between individuals with mild and severe knee OA, with the Symptoms subscale demonstrating the highest discriminating ability (AUC 0.80, 95% CI 0.70 – 0.89) and the ADL subscale the lowest ability (AUC 0.73, 95% CI 0.63–0.83) (Fig. 1, Table 3). Performance on the SLMS test displayed a good discriminating ability (AUC 0.83, 95% CI 0.76 – 0.91), which peak KAM, and positive KAM impulse also did (AUC 0.73, 95% CI 0.64 – 0.83, and AUC 0.81, 95% CI 0.73 – 0.89, respectively). Finally, the discriminating ability of GDI-score was moderate (AUC 0.62, 95% CI 0.52 – 0.73), and GDI-kinetic score poor (AUC 0.36, 95% CI 0.26–0.47) (Fig. 1, Table 3).

3.2. Odds ratio

The unstandardized and standardized odds ratios of severe knee OA for the evaluated variables are presented in Table 4. Among the examined variables, performance on the SLMS test displayed the highest standardized odds ratio of 6.06 with a corresponding un-standardized odds ratio of 1.17, indicating that participants who perform one less repetition are 1.17 times more likely to have severe OA (Table 4). Finally, age and BMI did not have any substantial impact on the ability of any of the studied variables to discriminate between mild and severe knee OA (Table 4).

Table 2
Characteristics of study participants, including patient-reported knee function and pain, performance-based function, and results of three-dimensional gait analysis at baseline.

	Total sample n = 115	Mild knee OA n = 63	Severe knee OA n = 52	Δ between Mild and Severe knee OA	
	Mean (SD)			p-value	95% CI
Participant characteristics					
Age	60.6 (8.5)	56.9 (8.0)	65.2 (6.7	< 0.001	[−11.1 to −5.5]
BMI	27.6 (3.8)	26.6 (2.9)	28.8 (4.3)	0.001	[−3.6 to −0.9]
Weight	80.5 (12.4)	78.3 (11.2)	83.3 (13.4)	0.032	[−9.5 to −0.4]
Female, n (%)	69 (60)	37 (59)	32 (61)		
KL Score					
1, n (%)	36 (31)	36 (57)	–		
2, n (%)	27 (24)	27 (43)	–		
3, n (%)	21 (18)	–	21 (40)		
4, n (%)	31 (27)	–	31 (60)		
Knee Injury and Osteoarthritis Outcome Score (0-100)					
Symptoms	58.1 (20.9)	68.3 (14.4)	45.7 (21.0)	< 0.0001	[16.0 - 29.2]
Pain	54.9 (16.6)	62.1 (13.6)	46.6 (15.9)	< 0.0001	[9.9 - 21.0]
ADL	63.2 (17.4)	69.1 (16.3)	56.3 (16.3)	< 0.0001	[6.7 - 19.0]
Sport and Recreation	31.3 (24.5)	40.6 (23.6)	20.3 (20.9)	< 0.0001	[11.9 - 28.7]
Knee-related QoL	39.3 (17.7)	47.3 (16.6)	29.9 (14.1)	< 0.0001	[11.6 - 23.2]
Performance-based knee function					
SLMS repetitions	20.2 (11.7)	26.1 (11.1)	13.2 (8.1)	< 0.0001	[9.2 - 16.6]
Three-dimensional gait analysis variables					
Normalized peak KAM (Nm/BW*HT%)	1.3 (0.7)	1.0 (0.4)	1.7 (0.8)	< 0.0001	[−0.9 to −0.5]
Positive KAM impulse (Nm*s/BW*HT%)	3.2 (1.0)	2.8 (0.8)	3.6 (1.1)	< 0.0001	[−1.2 to −0.5]
GDI kinematics	90.8 (11.7)	93.3 (12.3)	87.9 (10.4)	0.015	[1.1 to 9.7]
GDI-kinetic	85.9 (8.9)	84.1 (9.0)	88.1 (8.3)	0.014	[−7.3 to −0.8]
Walking speed (m/s)	1.2 (0.2)	1.2 (0.2)	1.1 (0.2)	< 0.001	[0.05–0.18]

ADL, Activities of Daily Living; BMI, Body Mass Index; GDI, Gait Deviation Index; KAM, Knee Adduction Moment; OA, Osteoarthritis; SLMS, Single Limb Mini Squat test; QoL, Quality of Life. Independent samples t-tests were used to calculate differences between study participants with Mild and Severe knee OA.

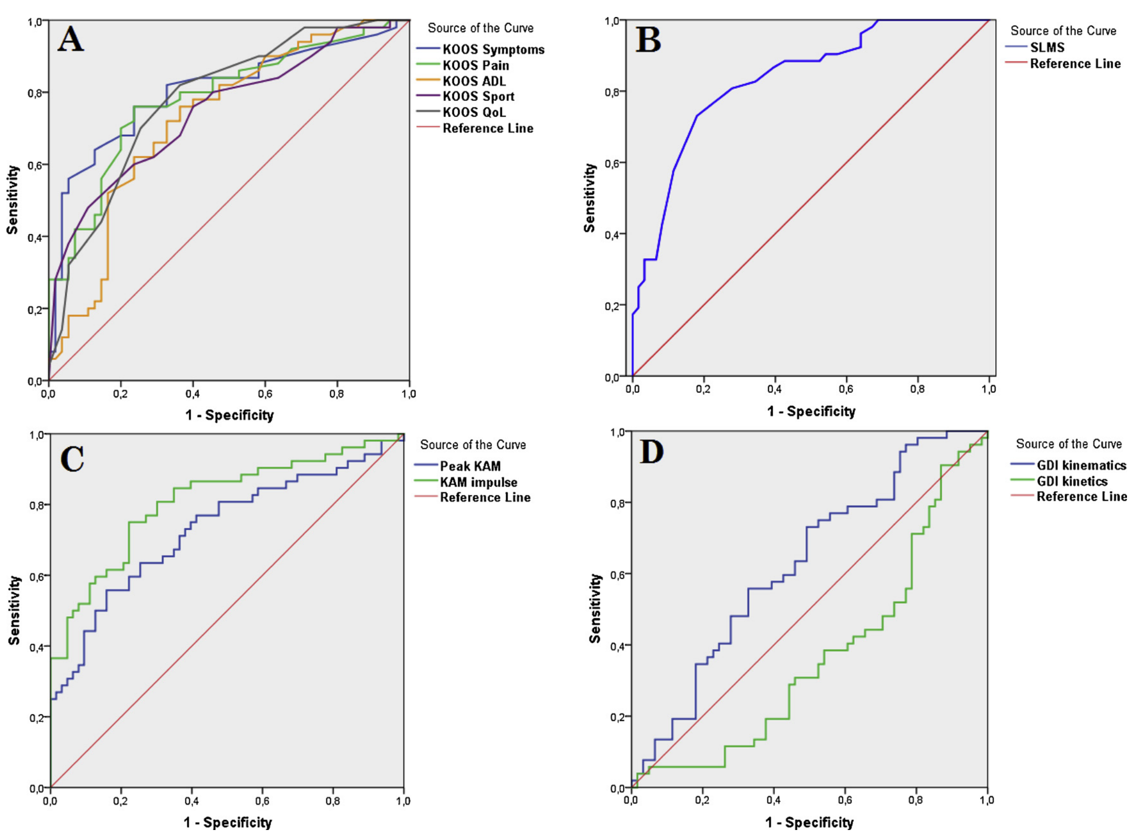

Fig. 1. Receiver operating characteristic curves of A) patient-reported knee function and pain represented by all subscales of the Knee Injury and Osteoarthritis Outcome Score (KOOS), B) performance-based function represented by the Single Limb Mini Squat (SLMS) test, C) three-dimensional gait analysis variables represented by peak knee adduction moment (KAM) and positive KAM impulse, and D) gait summary measures represented by the Gait Deviation Index for kinematics (GDI) and kinetics (GDI-kinetics).

Table 3
Area under the receiver operating characteristic curves and 95% confidence intervals.

	Area under the curve	95% CI
Knee Injury and Osteoarthritis outcome score		
Symptoms	0.80	[0.72–0.89]
Pain	0.78	[0.70–0.87]
ADL	0.73	[0.63–0.83]
Sport and Recreation	0.75	[0.66–0.84]
Knee-related QoL	0.78	[0.69–0.87]
Performance-based knee function		
SLMS test	0.83	[0.76–0.91]
Three-dimensional gait analysis variables		
Normalized peak KAM	0.73	[0.64–0.83]
Positive KAM impulse	0.81	[0.73–0.89]
GDI kinematics	0.62	[0.52–0.73]
GDI-kinetic	0.36	[0.26–0.47]

ADL, Activities of Daily Living; GDI, CI, confidence interval; Gait Deviation Index; KAM, Knee Adduction Moment; SLMS, Single Limb Mini Squat test; QoL, Quality of Life.

4. Discussion

4.1. Major findings

The present analyses demonstrate that KOOS subscale scores, SLMS test, peak KAM, and positive KAM impulse are more sensitive at discriminating between OA disease severities when defined by KL grade than gait summary measures (GDI and GDI-kinetic scores). Consequently, these outcome measures may be implemented in research to contribute additional information on knee function and underlying biomechanics of the disease that radiographs alone cannot provide. The present findings are not meant to imply that KOOS, SLMS test, or KAM impulse can or should be used to replace radiographic examination for grading disease severity, diagnostics and/or surgery. Rather, our findings suggest that these measures representing different constructs may assist as an adjunct to traditional measures of radiographic knee OA severity.

4.2. Patient-reported knee function

The current study confirms the findings by Oishi et al., 2016 that all KOOS subscale scores demonstrate good discriminating abilities of radiographic knee OA [10]. While the AUC analysis indicates that KOOS Symptoms subscale is a more sensitive measure (AUC 0.80, [0.72 - 0.89]) than the KOOS ADL (AUC 0.73, [0.63 - 0.83]), the magnitude of the difference is small with overlapping 95% CI, and thus the present results do not allow to differentiate between the discriminating abilities of the five KOOS subscale scores.

4.3. Performance-based function

Despite being considered a gold standard in research and implemented as a regular evaluation for the severity of knee OA, the KL classification system is based on plain radiographs that are static in nature [2]. Consequently, radiographs do not reflect the dynamic aspects of knee function and locomotion, which the SLMS test and three-dimensional gait analysis aim to provide. The SLMS test was chosen since it is simple, feasible, and examines the unilateral knee extensor muscle strength, during concentric and eccentric coupled muscle work. However, the SLMS test is not one of the recommended performance-based tests to assess physical function in individuals diagnosed with knee or hip OA that following the start of the current two studies was published by the Osteoarthritis Research Society International (OARSI) [4]. Still, SLMS has shown to be reliable and responsive [12,14] and the current results demonstrate that the SLMS test has the highest discriminating magnitude among the investigated outcome measures. Moreover, the SLMS test demonstrated the highest standardized odds ratio (6.06) among examined variables, which allows for direct comparisons between variables using dissimilar scales. However, as also stated above for the AUC, the magnitude of the difference in odds ratios are small and consequently differentiating between the outcome measures should be done with caution. Nevertheless, due to its discriminating, clinometric characteristics and feasible nature, we suggest the implementation of the SLMS test in knee OA research and potentially also in the clinic to provide additional diagnostic information on knee function.

Table 4
Odds ratios (unstandardized and standardized) for all KOOS subscale scores, SLMS test, normalized peak KAM, and positive KAM impulse.

	Odds ratio	Standardized odds ratio	p-value	95% CI for odds ratio
Knee Injury and Osteoarthritis Outcome Score				
Symptoms	1.07	3.89	< 0.0001	[1.04–1.09]
Adjusted for age and BMI	1.08	4.90	< 0.0001	[1.05–1.12]
Pain	1.07	3.08	< 0.0001	[1.04–1.10]
Adjusted for age and BMI	1.07	3.25	< 0.0001	[1.04–1.11]
ADL	1.05	2.32	< 0.001	[1.02–1.08]
Adjusted for age and BMI	1.04	1.86	0.019	[1.01–1.07]
Sport and Recreation	1.04	2.70	< 0.0001	[1.02–1.06]
Adjusted for age and BMI	1.04	2.79	< 0.001	[1.02–1.08]
Knee-related QoL	1.08	3.61	< 0.0001	[1.04–1.11]
Adjusted for age and BMI	1.07	3.53	< 0.0001	[1.04–1.11]
Performance-based knee function				
SLMS test	1.17	6.06	< 0.0001	[1.09–1.24]
Adjusted for age and BMI	1.16	5.95	< 0.0001	[1.08–1.25]
Three-dimensional gait analysis variables				
Normalized peak KAM	2.43	2.53	< 0.0001	[1.57–3.77]
Adjusted for age	2.42	2.32	< 0.001	[1.38–3.65]
Positive KAM impulse	13.62	5.94	< 0.0001	[4.49–41.27]
Adjusted for age	12.50	5.60	< 0.0001	[3.74–41.89]

For performance on SLMS test and all subscales of KOOS the unstandardized odds ratios represents a one-unit *decrease*, and for peak KAM and KAM impulse the odds ratios represents a one-unit *increase*. Standardized odds ratio is a unit-less ratio that allows for comparison between the different outcome measures irrespectively their dissimilar scales. Adjustments were made for age and BMI for all outcome measures, except for peak KAM and KAM-impulse that already are normalized for body weight and height. ADL, Activities of Daily Living; BMI, Body Mass Index; KAM, Knee Adduction Moment; SLMS, Single Limb Mini Squat test; QoL, Quality of Life.

4.4. Three-dimensional knee and gait summary measures

Peak KAM and positive KAM impulse are commonly used as proxy variables of medial joint loading [16,17,19,35]. Despite disputed theories of the mechanistic role of KAM and KAM impulse on knee OA [36,37], peak KAM and KAM impulse have displayed the ability to distinguish between different degrees of radiographic severity of knee OA, which facilitate understanding of the biomechanical role in the pathogenesis of knee OA [18,19]. This is in agreement with the present findings since peak KAM and KAM impulse demonstrated good discriminating abilities. Furthermore, our results also support the findings of Kean et al., 2012 that KAM impulse provides more comprehensive information than peak KAM as it demonstrates superior discriminatory ability [19]. Opposed to KAM and KAM impulse, the current results show that summary measures of overall gait function as measured by the GDI and GDI-kinetic are not able to discriminate radiographic OA severity. It should be noted that the current analyses do not exclude GDI and GDI-kinetic as potential index variables for the evaluation of overall gait function and/or improvement following different interventions in individuals with OA. Nevertheless, the responsiveness of GDI has been questioned in end-stage hip OA patients since no or only minor changes were observed following total hip arthroplasty [20,21,25]. Finally, the feasibility of the apparatus-dependent three-dimensional motion analyses excludes these outcome measures from standardized examinations of individuals with knee OA.

4.5. Limitations and strengths

The current study is not without limitations, and these should be acknowledged. The limitations include the use of a cross-sectional design to infer superiority of a measure to detect disease stage. Furthermore, it should be acknowledged that the present ancillary analysis is based on a case-mix of individuals with OA sampled at two different institutions, with the majority of individuals classified as having mild radiographic OA from the Danish trial and the majority of individuals with severe knee OA from the Swedish cohort, which may be viewed as a confounder. Differences between participants from the Danish trial and the Swedish cohort were similar to those between the Mild and Severe knee OA group, and included age, walking-speed, KOOS subscale-scores, GDI-kinetic, KAM-impulse and peak KAM (data not shown). In addition, classification of radiographic severity has not been “cross-checked” between the two study sites to ensure comparable classification. However, prior to inclusion of study participants the specific protocols for conducting tests were coordinated, and for the three-dimensional gait analyses identical apparatus and marker protocols were used making a direct comparison possible. In addition, to avoid potential bias, the data processing of GDI and GDI-kinetic was performed using the same reference data set. Thus, the likelihood of systematic bias from pooling the present data is considered negligible. Fifteen individuals were excluded during the analysis of GDI and GDI-kinetic due to restrictions in the capturing volume of the motion capturing system. Nevertheless, dropout analyses revealed that the excluded individuals did not differ statistically from the included sample with regards to age, BMI, and gender, and therefore selection bias cannot be attributed to this. The strengths of this study includes using a case-mix of individuals with KL scores ranging from 1 to 4, and the use of several measurements of knee and gait function representing multiple constructs including PROM, a performance-based test of knee function, specific proxy measures of medial knee compartment loading and measures of overall gait function derived from three-dimensional gait analysis.

5. Conclusion

In this study of measures of knee and gait function, representing different constructs, it was shown that KOOS subscale scores, SLMS test, peak KAM, and KAM impulse, in contrast to gait summary measures, were able to distinguish between individuals with varying degrees of radiographic knee OA severity. Given the interest in interpreting OA as a multi-factorial disease this information may assist researchers and clinicians in selecting the most appropriate outcomes and help our understanding of the role of different factors in the pathogenesis of knee OA. Future, longitudinally studies on the cause-relationship between structural changes and different constructs on knee and gait function will help to determine the clinical impact of the current results.

Author contributions

JEN, AHL: Conception and design, data analysis, and drafting the article. JEN, BC: Acquisition of data. All authors have made substantial contributions in the interpretation of data, revising the article critically and all approved of the final version for submission.

Declaration of Competing Interest

None to declare.

Acknowledgements

The authors would like to acknowledge Prof. Ewa Roos and Prof. Michael Schwartz for useful discussions. This research was financially supported by grants from Karolinska Institutet, Stiftelsen Promobilia, the Swedish Rheumatism Foundation, Stiftelsen Skobranschens utvecklingsfond, the Region of Southern Denmark PhD Fund, the Region of Southern Denmark Research Fund, the Danish Rheumatism Association, the Danish Rheumatism Association Ryholts grant, the University of Southern Denmark Scholarship, the Association of Danish Physiotherapists, Odense University Hospitalfree research funds, and Family Hede Nielsens Fund. Study sponsors had no involvement in study design, collection, analysis and interpretation of data; in the writing of the manuscript; or in the decision to submit the manuscript for publication.

References

[1] D.T. Felson, Osteoarthritis as a disease of mechanics, Osteoarthrit. Cartil. OARS 21 (2013) 10–15 Osteoarthritis Research Society.
[2] O. Robertsson, S. Bizjajeva, A.M. Fenstad, O. Furnes, L. Lidgren, F. Mehnert, et al., Knee arthroplasty in Denmark, Norway and Sweden. A pilot study from the Nordic Arthroplasty Register Association, Acta Orthop. 81 (2010) 82–89.
[3] M.D. Kohn, A.A. Sassoon, N.D. Fernando, Classifications in brief: Kellgren-Lawrence classification of osteoarthritis, Clin. Orthop. Relat. Res. 474 (2016) 1886–1893.
[4] F. Dobson, R.S. Hinman, E.M. Roos, J.H. Abbott, P. Stratford, A.M. Davis, et al., OARSI recommended performance-based tests to assess physical function in people diagnosed with hip or knee osteoarthritis, Osteoarthrit. Cartil. OARS 21 (2013) 1042–1052 Osteoarthritis Research Society.
[5] A.A. Wright, E.J. Hegedus, G.D. Baxter, J.H. Abbott, Measurement of function in hip osteoarthritis: developing a standardized approach for physical performance measures, Physiother. Theory Pract. 27 (2011) 253–262.
[6] P.W. Stratford, D.M. Kennedy, Performance measures were necessary to obtain a complete picture of osteoarthritic patients, J. Clin. Epidemiol. 59 (2006) 160–167.
[7] K.P. Jordan, R. Wilkie, S. Muller, H. Myers, E. Nicholls, Arthritis Research Campaign National Primary Care C, Measurement of change in function and disability in osteoarthritis: current approaches and future challenges, Curr. Opin. Rheumatol. 21 (2009) 525–530.
[8] C.B. Terwee, L.B. Mokkink, M.P. Steultjens, J. Dekker, Performance-based methods for measuring the physical function of patients with osteoarthritis of the hip or knee: a systematic review of measurement properties, Rheumatology (Oxford) 45 (2006) 890–902.
[9] E. Roos, H. Roos, L. Lohmander, C. Ekdahl, B. Beynnon, Knee Injury and Osteoarthritis Outcome Score (KOOS)–development of a self-administered outcome measure, J. Orthop. Sports Phys. Ther. 28 (1998) 88–96.
[10] K. Oishi, E. Tsuda, Y. Yamamoto, S. Maeda, E. Sasaki, D. Chiba, et al., The Knee injury and Osteoarthritis Outcome Score reflects the severity of knee osteoarthritis better than the revised Knee Society Score in a general Japanese population, Knee 23 (2016) 35–42.
[11] J.E. Naili, P. Wretenberg, V. Lindgren, M.D. Iversen, M. Hedstrom, E.W. Brostrom, Improved knee biomechanics among patients reporting a good outcome in knee-related quality of life one year after total knee arthroplasty, BMC Musculoskelet. Disord. 18 (2017) 122.

[12] A. Villadsen, E.M. Roos, S. Overgaard, A. Holsgaard-Larsen, Agreement and reliability of functional performance and muscle power in patients with advanced osteoarthritis of the hip or knee, Am. J. Phys. Med. Rehabil./Assoc. Acad. Physiatrists 91 (2012) 401–410.
[13] J.E. Naili, A.C. Esbjornsson, M.D. Iversen, M.H. Schwartz, M. Hedstrom, C.K. Hager, et al., The impact of symptomatic knee osteoarthritis on overall gait pattern deviations and its association with performance-based measures and patient-reported outcomes, Knee (2017).
[14] A. Villadsen, S. Overgaard, A. Holsgaard-Larsen, R. Christensen, E.M. Roos, Immediate efficacy of neuromuscular exercise in patients with severe osteoarthritis of the hip or knee: a secondary analysis from a randomized controlled trial, J. Rheumatol. 41 (2014) 1385–1394.
[15] A. Holsgaard-Larsen, B. Clausen, J. Sondergaard, R. Christensen, T.P. Andriacchi, E.M. Roos, The effect of instruction in analgesic use compared with neuromuscular exercise on knee-joint load in patients with knee osteoarthritis: a randomized, single-blind, controlled trial, Osteoarthrit. Cartil. OARS 25 (2017) 470–480 Osteoarthritis Research Society.
[16] T.B. Birmingham, M.A. Hunt, I.C. Jones, T.R. Jenkyn, J.R. Giffin, Test-retest reliability of the peak knee adduction moment during walking in patients with medial compartment knee osteoarthritis, Arthritis Rheum. 57 (2007) 1012–1017.
[17] D. Zhao, S.A. Banks, K.H. Mitchell, D.D. D'Lima, C.W. Colwell Jr, B.J. Fregly, Correlation between the knee adduction torque and medial contact force for a variety of gait patterns, J. Orthop. Res. 25 (2007) 789–797.
[18] S.M. Robbins, T.B. Birmingham, M.R. Maly, B.M. Chesworth, J.R. Giffin, Comparative diagnostic accuracy of knee adduction moments in knee osteoarthritis: a case for not normalizing to body size, J. Biomech. 44 (2011) 968–971.
[19] C.O. Kean, R.S. Hinman, K.A. Bowles, F. Cicuttini, M. Davies-Tuck, K.L. Bennell, Comparison of peak knee adduction moment and knee adduction moment impulse in distinguishing between severities of knee osteoarthritis, Clin. Biomech. (Bristol, Avon). 27 (2012) 520–523.
[20] C. Jensen, J.O. Penny, D.B. Nielsen, S. Overgaard, A. Holsgaard-Larsen, Quantifying gait quality in patients with large-head and conventional total hip arthroplasty–a prospective cohort study, J. Arthroplasty 30 (2015) 2343-8 e1.
[21] C. Jensen, S. Rosenlund, D.B. Nielsen, S. Overgaard, A. Holsgaard-Larsen, The use of the Gait Deviation Index for the evaluation of participants following total hip arthroplasty: An explorative randomized trial, Gait Posture 42 (2015) 36–41.
[22] M.H. Schwartz, A. Rozumalski, The gait deviation index: a new comprehensive index of gait pathology, Gait Posture 28 (2008) 351–357.
[23] A. Rozumalski, M.H. Schwartz, The GDI-Kinetic: a new index for quantifying kinetic deviations from normal gait, Gait Posture 33 (2011) 730–732.
[24] J.E. Naili, M.D. Iversen, A.C. Esbjornsson, M. Hedstrom, M.H. Schwartz, C.K. Hager, et al., Deficits in functional performance and gait one year after total knee arthroplasty despite improved self-reported function, Knee Surg. Sports Traumatol. Arthrosc. 25 (2017) 3378–3386.
[25] S. Rosenlund, L. Broeng, S. Overgaard, C. Jensen, A. Holsgaard-Larsen, The efficacy of modified direct lateral versus posterior approach on gait function and hip muscle strength after primary total hip arthroplasty at 12months follow-up. An explorative randomised controlled trial, Clin. Biomech. (Bristol, Avon 39 (2016) 91–99.
[26] E. von Elm, D.G. Altman, M. Egger, S.J. Pocock, P.C. Gotzsche, J.P. Vandenbroucke, et al., The strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies, J. Clin. Epidemiol. 61 (2008) 344–349.
[27] R. Altman, E. Asch, D. Bloch, G. Bole, D. Borenstein, K. Brandt, et al., Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association, Arthritis Rheum. 29 (1986) 1039–1049.
[28] A. Bremander, L. Dahl, E. Roos, Validity and reliability of functional performance tests in meniscectomized patients with or without knee osteoarthritis, Scand. J. Med. Sci. Sports 17 (2007) 120–127.
[29] R. Davis, S. Ounpuu, D. Tyburski, J. Gage, A gait analysis data collection and reduction technique, Hum. Mov. Sci. 10 (1991) 575.
[30] K.L. Bennell, M.W. Creaby, T.V. Wrigley, K.A. Bowles, R.S. Hinman, F. Cicuttini, et al., Bone marrow lesions are related to dynamic knee loading in medial knee osteoarthritis, Ann. Rheum. Dis. 69 (2010) 1151–1154.
[31] M.H. Schwartz, A. Rozumalski, The Gait Deviation Index: a new comprehensive index of gait pathology, Gait Posture 28 (2008) 351–357.
[32] J.H. Kellgren, J.S. Lawrence, Radiological assessment of osteo-arthrosis, Ann. Rheum. Dis. 16 (1957) 494–502.
[33] M. Henriksen, J. Aaboe, H. Bliddal, The relationship between pain and dynamic knee joint loading in knee osteoarthritis varies with radiographic disease severity. A cross sectional study, Knee 19 (2012) 392–398.
[34] H.C.W. de Vet, C.B. Terwee, L.B. Mokkink, D.L. Knol, Measurement in Medicine: A Practical Guide, Cambridge University Press, Cambridge, 2011.
[35] M. Hall, K.L. Bennell, T.V. Wrigley, B.R. Metcalf, P.K. Campbell, J. Kasza, et al., The knee adduction moment and knee osteoarthritis symptoms: relationships according to radiographic disease severity, Osteoarthrit. Cartil. OARS 25 (2017) 34–41 Osteoarthritis Research Society.
[36] J.P. Walter, D.D. D'Lima, C.W. Colwell Jr, B.J. Fregly, Decreased knee adduction moment does not guarantee decreased medial contact force during gait, J. Orthop. Res. 28 (2010) 1348–1354.
[37] M. Henriksen, M.W. Creaby, H. Lund, C. Juhl, R. Christensen, Is there a causal link between knee loading and knee osteoarthritis progression? A systematic review and meta-analysis of cohort studies and randomised trials, BMJ Open 4 (2014) e005368.