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Identifying key gait features associated with the radiological grade of knee osteoarthritis

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SUMMARY

Purpose: Knee osteoarthritis (KOA) is characterized by pain and decreased gait function. This study assessed key features that can be used as mechanical biomarkers for KOA severity and progression. The identified features were validated statistically and were further examined by developing a classification model based on a machine-learning algorithm.
Methods: The study included 227 volunteers with various grades of KOA. The severity of KOA was graded using the Kellgren–Lawrence (KL) system. A total of 165 features were extracted from the gait data. The key features were selected using neighborhood component analysis. The selected features were validated using the *t*-test. Then, the features were examined by building a classification model using a random forest algorithm.
Results: Twenty features were identified that could discriminate the grade of KOA, including nine features extracted from the knee joint, seven from the hip, two from the ankle and two from the spatio-temporal gait parameters. The *t*-test showed that some features differed significantly between health and sever group, while some were significantly different among the severe group, and others were significantly different for all KL grades. The areas under the receiver operating characteristic curves for classification were 0.974, 0.992, 0.845, 0.894, and 0.905 for KL grades 0 through 4, respectively.
Conclusion: Key gait features reflecting the grade of KOA were identified. The results of the statistical analysis and machine-learning algorithm show that the features can discriminate the severity of disease according to the KL grade.

Introduction

Osteoarthritis (OA) is a leading cause of disability. More than 250 million people suffer from OA worldwide, and 1–2% of the gross national product is spent on OA[1,2]. With the aging population, the number of knee OA (KOA) patients is expected to grow rapidly and the number of patients requiring Knee osteoarthritis (KOA) surgery is expected to sextuple by 2030[3]. KOA is characterized by pain and gait dysfunction, which worsen as the stage of KOA progresses[4].

As gait function, an overall gait performance, declines with progression of the disease, an objective, comprehensive evaluation of gait function would assist with the prognostic evaluation and treatment decisions. Effort has been made to evaluate gait function using patient-reported outcome measures (PROMs), including the Western Ontario & McMaster Universities Osteoarthritis Index (WOMAC) and Knee Society Function Score (KSFS). Although these well-known indexes are used to measure joint function, these measures have low repeatability and are readily affected by the patient's pain and emotions[5].

Modern gait analysis is a powerful technique that provides biomechanical information about joints and is objective and repeatable compared with other methods. Gait analysis provides multiple temporal waveforms for each joint in the lower limbs. With this method, gait dysfunction can be evaluated objectively in individuals with joint disease, including KOA. However, the large

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volume and high complexity of data are significant barriers to its clinical application[6]. The method most commonly used to resolve this issue involves extracting specific features from the original data.

Several features are correlated with KOA severity[4,7,8]. Kean *et al.*[9] reported that the knee adduction moment (KAM) impulse was positively correlated with the severity of disease. Spatiotemporal gait parameters, including speed, cadence, and duration of the stance phase, differ significantly in KOA patients and asymptomatic groups[10]. However, most previous studies concentrated on specific joints, such as KAM, and features were separated into trends, unsuited for clinical application. To make gait data more applicable clinically, we first sought to extract as many features from various joints as possible and then to identify key features by Kellgren–Lawrence (KL) grade.

This cross-sectional study analyzed the gait data of subjects ranging from no KOA to end-stage KOA. We hypothesized that the patients' gait function would decrease gradually with the stage of KOA and specific features would change with the progression. This study sought key features that can be used as mechanical biomarkers of KOA progression and validated the identified features by developing a classification model based on a machine-learning algorithm.

Materials and methods

Participants

This study was approved by our Institutional Review Board (IRB no. 1810-004-974). Written informed consent was obtained from all participants This study was performed with the database of our gait lab. The database consists of the gait reports of the various degrees of knee OA patients and healthy volunteers from 2012 to 2017. The inclusion criteria of the database were healthy volunteers or knee OA patients who decided to participate the gait analysis and X ray analysis. The subjects' medical records were obtained, and all participants underwent a physical examination and standing, knee-extended position, full-limb radiography of the knee. We excluded 397 subjects based on the following criteria: (1) patients who lacked some data for both legs ($n = 202$); (2) patients aged > 70 or < 20 years ($n = 22$); (3) spine disease, hip, or ankle arthritis on X-ray ($n = 12$); (4) inflammatory or traumatic arthritis of the knee ($n = 6$); (5) any prior bone surgery in the lower extremities ($n = 4$); and (6) All participants with equal KL grades for both knees. ($n = 151$). Consequently, 227 unilateral subjects with KOA participated in this study. The degree of KOA was determined using the KL grading system. Table I summarizes the participants' demographic characteristics and walking speed.

Data collection

All gait analysis data, including kinetic, kinematic and spatial–temporal, were collected at the Human Motion Analysis Laboratory of Seoul National University Hospital. The subjects were asked to walk for a few minutes to get used to the setting. After warming up, an operator with 19 years of experience placed reflective markers on the subjects based on the Helen Hayes set. The subjects were asked to walk along a 9-m track. Motion data were collected using twelve charge-coupled device cameras with a three-dimensional optical motion capture system (Motion Analysis Corp., Santa Rosa, CA, USA) at a sampling frequency of 120 Hz. The kinetic data was obtained with two force plates which is embedded in the floor. The kinetic and kinematic data for each joint were averaged after five or six trials of the 9-m walk and then used as study data.

Radiographic assessment

The entire radiographic evaluation was performed independently by two authors with fellowship training in arthroplasty who were blinded to other information on the study subjects. KOA was graded using the KL scale[11]. The two authors discussed about the grading and made a consensus. The inter-observer reliability of the radiological assessment was satisfactory (Kappa value: 0751). All radiographic images were acquired digitally using a picture archiving and communication system (Maroview 5.4; INFINITT Healthcare, Seoul, Korea).

Statistical analysis

All data analyses and classifications were performed using MATLAB 2017a (MathWorks, Natick, MA, USA). In all, 149 features were extracted from the kinetic and kinematic data for the hip, knee, and ankle in the gait analysis data. These features are extracted by calculating the area under the curve, maximum value during swing phase, Kurtis, area of absolute value of the curve, and other characteristic of the kinetic and kinematic curves. An additional 16 gait characteristics were selected as features for the classification model, such as velocity and cadence. All features were extracted only from the right leg. We analyzed only the right leg to remove statistical dependency from multiple observation from single individuals[12]. Neighborhood component feature selection[13] was performed to reduce the number of features. Neighborhood component feature selection performs regularization to obtain feature weights by minimizing the error for leave-one-out classification. Features with approximately zero feature weight were excluded. The remaining features were identified as key features and were used for the classification model. The student's t-test was performed to identify differences in the features among KL grades.

A random forest algorithm was used to build a classification model using the selected features. Random forest is a type of ensemble learning, constructed with multiple number of decision tree. Random forest was selected as a classifier because have been widely used and validated in various fields[14,15]. To resolve the class imbalance problem, we oversampled the dataset for KL grades 0–3 using adaptive synthetic sampling[16]. A 10-fold cross-validation method was used to validate the models. Each class was divided randomly into ten different subsamples; nine subsamples were used to train the model, and the remaining subsample was used for validation. This process was repeated ten times, using a different subsample for validation each time. The models were further examined using the area under the receiver operating characteristic curve (AUROC).

Table I
Subject characteristics

	KL 0	KL 1	KL 2	KL 3	KL 4	*P*-value
age	59.08 (18.77)	61.69 (6.01)	65.13 (9.23)	63.98 (7.56)	67.14 (10)	0.01
height	158.91 (10.42)	156.87 (6.51)	158.07 (7.88)	156.44 (7.9)	155.14 (8.26)	0.17
weight	64.99 (13.46)	60.02 (8.51)	65.27 (10.58)	63.97 (9.65)	63.5 (10.81)	0.55
BMI	25.59 (3.62)	24.32 (2.31)	26.09 (3.7)	26.08 (2.87)	26.29 (3.3)	0.36
TS	95.52 (26.69)	105.97 (17.11)	93.81 (21.25)	92.78 (22.1)	80.55 (21.74)	<0.01

Results

Among the 165 features extracted from the gait analysis data, 20 features (9 from the knee, seven from the hip, two from the ankle joint, and two spatiotemporal parameters) remained after the neighborhood component analysis (NCA) feature selection and were selected as the final features. The gait parameters included as key features were: knee extension moment, knee abduction moment, knee rotational moment, knee flexion angle, hip abduction moment, hip extension moment, hip extension angle, ankle dorsiflexion moment, cadence and stride length. Figure 1 shows the averaged values of representative parameters for each KL grade. Table II shows the means and standard deviations with the results of the *t*-tests. Table III shows the confusion matrix and AUROC of the classification model, with the receiver operating characteristic (ROC) curve shown in Fig. 2. The respective AUROC values were 0.974, 0.992, 0.845, 0.894, and 0.905 for KL grades 0 to 4. The sensitivity of the model was 73.5% and the specificity was 93.6%. The 95% confidence interval was 0.045 and 0.025 respectively.

Discussion

This study shows that gait function decreased gradually as the severity of KOA increased by identifying key gait features and classifying the patients by their severity of disease using the identified key features and machine algorithms. Our study differs from previous ones in three ways. First, instead of extracting the features with traditional methods, such as peak or minimum values, we used methods that contain overall information on gait data, including the root mean square (RMS) and kurtosis, and selected key features using a validated algorithm. Second, this study identified the statistical significance among all KL grades, whereas previous studies have shown only the difference between control and patient groups. Lastly, we used a machine-learning algorithm to discriminate the severity of KOA for further validation of our features.

The parameters listed in Table II are well-known joint parameters that have significantly different values at each stage of the disease. Kean *et al.*[9] reported that a feature extracted from the KAM during gait can distinguish individuals with different KL grades. Thorp *et al.*[17] reported that the same feature extracted from the KAM differed significantly among the control (KL grade 0 or 1), mild (KL grade 2), and moderate (KL grade 3) groups. Other parameters in Table II have also been reported[18–20]. Weidow *et al.*[21] reported that the maximum hip extension angle was smaller for OA patients compared with controls and that the peak hip flexion moment was also smaller in patients. They also showed that the knee flexion angle decreased in lateral OA patients. Astephen *et al.*[19] reported

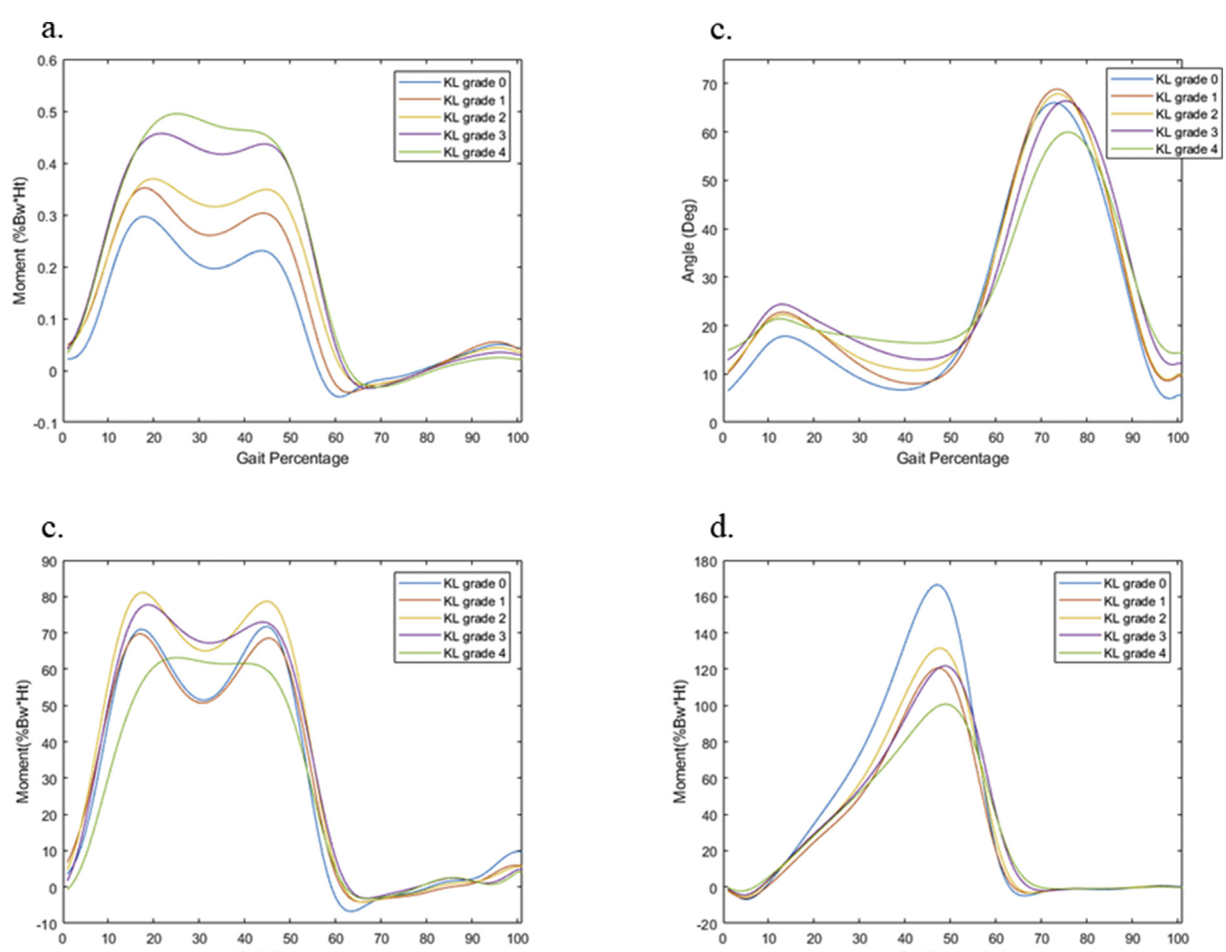

Fig. 1. Mean values of representative gait parameters for each KL grade where features were extracted from the a) knee abduction moment, b) knee flexion angle, c) hip abduction moment, and d) ankle dorsiflexion moment. All three moments were normalized using weight × height.

Table II
Key features selected using NCA

Joint	Parameter	Feature	KL 0	KL 1	KL 2	KL 3	KL 4
Knee	Extension Moment	Variance	4.73 (3.94)	5.14 (3.52)	4.52 (5.11)	4.05 (2.91)	3.65 (3.56)
	Abduction Moment	Area during the stance phase	170.84 (94.28)^{1,4}	134.07 (40.18)^{0,2,3,4}	170.14 (90.26)^{1}	188.14 (107.09)^{1}	217.5 (123.9)^{0,1}
		Area under the curve	172.95 (92.44)^{1,4}	137.48 (39.97)^{0,2,3,4}	172.84 (89.65)^{1}	189.87 (105)^{1}	217.61 (121.13)$^{0.1}$
		Area of the absolute value	183.49 (94.12)^{1,4}	149.36 (36.94)^{0,2,3,4}	183.72 (91.87)^{1,4}	205 (96.73)^{1}	232.85 (116.75)^{0,1,2}
	Rotational Moment	Area during the stance phase	−37.72 (21.27)^{1,4}	−30.97 (12.14)^{0,2,3,4}	−39.56 (22.05)^{1}	−40.8 (24.13)^{1}	−48.28 (27.44)^{0,1}
	Flexion Angle	Area of the absolute value during the stance phase	1142.65 (428.89)^{1}	992.52 (240.7)^{0,3,4}	1099.14 (282.18)^{4}	1202.14 (509.65)^{1}	1348.7 (624.77)^{1,4}
		Area of the absolute value	2624.46 (447.93)	2760.66 (446.49)	2725.03 (375.22)	2762.38 (598.36)	2811 (753.56)
		RMS	1152.65 (409.26)^{1}	992.52 (240.7)^{0,3,4}	1099.4 (281.46)^{2}	1204.97 (504.2)^{1}	1385.88 (542.79)^{1,4}
		Mean	2634.45 (421.86)	2760.66 (446.49)	2725.28 (374.67)	2765.46 (592.17)	2850.24 (676.52)
Hip	Abduction Moment	Area under the curve	301.31 (106.51)	285.52 (36.71)^{2}	325.26 (117.3)^{1,4}	299.05 (98.29)^{4}	255.36 (114.46)^{2,3}
		Area of the absolute value during the stance phase	301.52 (105.7)	283.88 (35.37)^{2}	322.72 (116.18)^{1,4}	298.93 (97.22)	259.13 (113.39)^{2}
		RMS	316.94 (108.69)	300.36 (37.3)^{2}	339.89 (120.93)^{1,4}	313.69 (100.08)	275.23 (114.04)^{2}
	Extension Moment	Area under the curve	−21.23 (92.28)^{1,4}	14.94 (85.67)^{0}	20.33 (91.59)	8.81 (78.8)	18.79 (88.93)^{0}
		Area of the absolute value during the stance phase	−18.73 (87.53)^{1,4}	10.34 (81.48)^{0}	16.86 (88)	7.55 (73.35)	16.18 (83.57)^{0}
	Extension Angle	Maximum value during the late phase	−3.21 (7.17)^{1,4}	−6.85 (4.81)^{0,2,3,4}	−1.58 (8.54)^{1,4}	−2.14 (8.97)^{1}	1.19 (9.09)^{0,1,2}
		Area under the curve	917.43 (395.26)^{4}	832.54 (316.54)^{3,4}	1057.37 (480.62)	1074.9 (536.93)^{1}	1164.82 (552.67)^{0,1}
Ankle	Dorsiflexion Moment	Area during the stance phase	305.76 (109.52)	278.32 (81.44)^{2}	302.08 (115.76)^{1}	276.95 (99.62)	285.22 (115.21)
		Standard deviation	19.36 (14.48)	15.48 (7.4)	17.54 (10.34)	15.1 (10.98)	13.79 (9.41)
Spatial−temporal		Cadence	108.14 (10.97)	111.78 (12.56)	106.69 (11.89)	108.19 (11.32)	101.4 (14.92)
		Stride Length	104.79 (24.36)^{1}	112.96 (12.95)^{0,2,3,4}	104.01 (18.32)^{1,4}	101.42 (18.22)^{1,4}	93.78 (17.4)^{1,2,3}

^{0} Significantly different with KL grade 0^{1}; Significantly different with KL grade 1; ^{2} Significantly different with KL grade 2;^{3} Significantly different with KL grade 3;^{4} Significantly different with KL grade 4.

Table III
Confusion matrix and the AUROC values for the 10-fold classification result of the random forest algorithm

	KL 0	KL 1	KL 2	KL 3	KL 4	AUC*
KL 0	64	0	4	2	4	0.974
KL1	0	75	0	0	0	0.992
KL 2	8	7	42	7	4	0.845
KL 3	2	3	13	50	11	0.894
KL 4	7	1	7	19	43	0.905

*AUC, area under the curve of receiver operating characteristic curve.

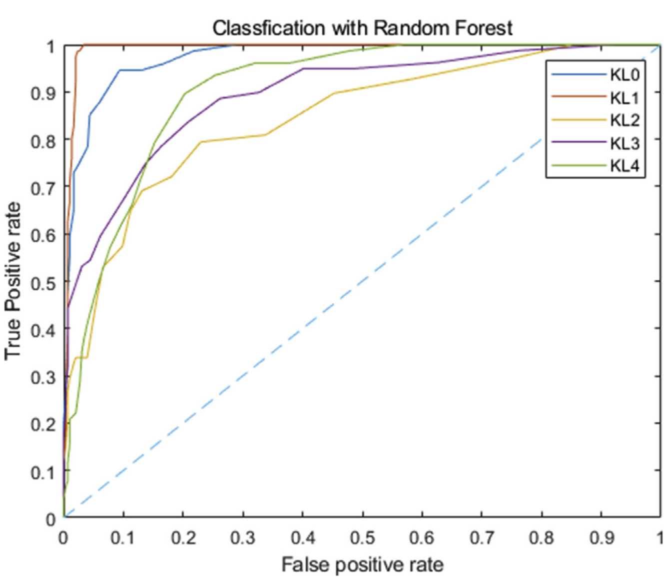

Fig. 2. ROC curves for the KOA classification results using the random forest algorithm and identified key features.

that the range of peak knee flexion angle differed significantly for severe OA patients and that the peak knee flexion angle during stance phase significantly differed progressively. They also reported that the minimum hip flexion moment during late stance differed significantly for all OA and that the hip flexion angle range significantly differed progressively. The peak and minimum ankle flexion moments were also reported to differ significantly for patients with severe OA[18].

The features listed in Table II have different abilities to discriminate the severity of disease. Some differed significantly for all severities, while others differed only in the controls, mild OA, or severe OA. The stride length differed significantly progressively, while maximum value during the late swing phase of hip extension moment differed significantly for KL grades 3 and 4. In comparison, area under the curve of hip abduction moment differed significantly between the most severe groups, KL grades 3 and 4, whereas all features extracted from the hip extention moment differed significantly between the control group.

Features like the peak and minimum values of gait data are reported to be limited to load or motion at an instance during the gait cycle and cannot contain information on the duration[9]. Features with duration information, such as the KAM impulse, are better discriminators than features without duration information, such as the peak KAM[9,17]. Most of the features extracted in this study, such as the variance, RMS, and area under the curve, contain duration information. The variance and RMS are well-known, widely used parameters that contain overall information on the signal. Area under the curve is an integral of the signal and is also a representative parameter. The classification model based on the identified features performed better than any reported models, supporting our hypothesis.

The input features for the classification model contains kinetic and kinematic data of functional status of the knee. Also, the model and features are non-invasive and objective measurement. Along with X-ray assessment of the disease, which contains static and structural information about the knee, the result from the model could provide an extra functional information to clinician to diagnose KOA patients.

There are limitations to our study. Our methodology considered only OA severity based on a radiographic assessment. Indexes such as WOMAC incorporate information on the patient's pain, stiffness, and physical function of the joint[22]. It would be meaningful to investigate the relationship between the gait data and WOMAC. In addition, few studies have compared the classification performance examined in our study. Before clinical application, our methodology needs to be validated by other studies. Further, this study was validated internally. In order to validate the model for overfitting, it needs an external validation.

For a future work for this study, our algorithm can be applied to data collected from wearable sensors. Many studies have reported that kinetic and kinematic gait data can be obtained from wearable inertial measurement unit sensors and force sensors[23–25]. Applying our algorithm with wearable sensors will allow frequent and long-term monitoring of changes in gait features and could help to guide treatment plans for KOA patients.

In conclusion, we identified 20 features that can be used as biomarkers for discriminating the severity of KOA. The features were validated using both traditional statistics and by building a classification model using a machine-learning algorithm. The classification model along with biomechanical features can be used as an extra tool for objective and repeatable KOA diagnosis, representing joint function from the early to the final stage of the disease.

Author contributions

1) Conception and design: Han HS, Lee MC, Kim HC. Acquisition of data: Ro DH Song MK. Analysis and interpretation of data: Kwon SB, Ro DH.
2) Drafting the manuscript: Kwon SB, Ro DH. Critical revisions for important intellectual content: All authors
3) Final approval of the version to be submitted: All authors

Competing interests

The authors declare no conflicts of interest.

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