1. Introduction

Knee osteoarthritis (KOA) is a worldwide disease leading to knee function loss and disorders. However, traditional assessment by X-ray cannot assess patients’ knee functions and disorders dynamically, making it impossible to achieve a direct functional assessment of KOA. To solve this problem, here it is shown that 3D knee gait parameters could be used to diagnose KOA and guide its therapeutic strategy through direct functional assessment. We employ a total of 1201 participants, and successfully build and validate diagnostic and predictive models for KOA diagnosis and therapeutic strategy using an artificial intelligence (AI)-based method, logistic regression, a kind of interpretable machine learning. Four diagnostic models are successfully established including angular (AM), translational (TM), composite (CM), and ATCM (a parallel conjoint model of AM, TM, and CM) model with a Youden index of 0.7312, 0.6689, 0.8214, and 0.7492, respectively. The same AI-based method is also used to develop medical decision classification (MDC) for predicting whether a KOA patient needs operative intervention or not. MDC has a Youden index, sensitivity, and specificity of 0.8886, 92.11%, and 96.75%, respectively. These findings contribute to new knowledge of knee kinematics and KOA diagnosis and represent a new approach to accurate KOA diagnosis and assessment.

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Knee osteoarthritis (KOA) is a worldwide disease leading to knee function loss and disorders. However, traditional assessment by X-ray cannot assess patients’ knee functions and disorders dynamically, making it impossible to achieve a direct functional assessment of KOA. To solve this problem, here it is shown that 3D knee gait parameters could be used to diagnose KOA and guide its therapeutic strategy through direct functional assessment. We employ a total of 1201 participants, and successfully build and validate diagnostic and predictive models for KOA diagnosis and therapeutic strategy using an artificial intelligence (AI)-based method, logistic regression, a kind of interpretable machine learning. Four diagnostic models are successfully established including angular (AM), translational (TM), composite (CM), and ATCM (a parallel conjoint model of AM, TM, and CM) model with a Youden index of 0.7312, 0.6689, 0.8214, and 0.7492, respectively. The same AI-based method is also used to develop medical decision classification (MDC) for predicting whether a KOA patient needs operative intervention or not. MDC has a Youden index, sensitivity, and specificity of 0.8886, 92.11%, and 96.75%, respectively. These findings contribute to new knowledge of knee kinematics and KOA diagnosis and represent a new approach to accurate KOA diagnosis and assessment.

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dynamic function and relieve knee pain.\textsuperscript{[7]} As a result, a current imaging-based diagnosis method could not directly assess the knee function of patients with KOA and may mislead or delay the therapy of KOA. So far there has been no report on the use of a dynamic method for diagnosing and assessing KOA clinically.

As a method of dynamic observation, gait analysis of the knee has been used to investigate the gait features of KOA for many years. Elbaz et al. found that single limb support from gait analysis could be related to the functional severity of KOA.\textsuperscript{[8]} Marcum et al. found that gait speed could be correlated with the arthritis aspect of KOA.\textsuperscript{[9]} In addition, previous studies found that KOA knees reduced both knee flexion angle and ranges of motion during the gait.\textsuperscript{[10]} Mezghani et al. analyzed the relationship between a small amount of angular kinematic data and KL score (imaging assessment) and found that it is possible that knee kinematics might be applied in the diagnosis of KOA.\textsuperscript{[11]} These reports show that there might be strong correlations between alterations of gait variables and KOA. However, knee kinematics, especially six degrees of freedoms (6DOFs) has not yet been used and validated to diagnose KOA or to guide the therapy of KOA in a dynamic way clinically, probably because of the lengthy time needed for using old generation gait analyzers, the large amount of data required from the patients, and the difficulty in dealing with complicated gait characteristics. Recently, with the development of 3D gait analysis, it is possible to gather numerous parameters for the AI to screen and select the most effective gait characteristics to diagnose and assess KOA. Most importantly, as a functional assessment, 3D gait analysis may help clinicians pay attention to the knee function of patients with KOA.

Multiple studies show that artificial intelligence (AI) is accurate as a statistical tool in assisting clinicians with the diagnosis or assessment of diseases such as lung cancer.\textsuperscript{[12]} However, there have been no studies on the use of AI-based strategies for the diagnosis of orthopedic diseases such as KOA. Machine learning, one of the popular AI areas of interest, can easily and quickly discover obvious or deep correlations among variables and guide disease diagnosis using AI techniques including logistic regression analysis (LR), Fisher linear discriminated analysis, artificial neural network (ANN), decision tree, and others.\textsuperscript{[12,13]} Among all machine learning techniques, LR is an effective and interpretable method in disease assessment. It should be noted that LR is a type of probabilistic, statistical, interpretable classification machine learning technique. LR was usually used to predict the probability of the target event based on one or more variables.

A gait cycle is made of a stance phase and a swing phase. There are seven key events in a gait cycle during gait.\textsuperscript{[14]} Four key events are in the stance phase and termed initial contact (IC), heel rise (HR), opposite toe-off (OT), and opposite initial contact (OI). The other three key events are in the swing phase including feet adjacent (FA), tibia vertical (TV), and toe-off (TO). The seven key events describe the characteristics of the whole gait cycle, and therefore can be set to study gait characteristics of patients. In this study, a novel infrared-navigational portable 3D gait analysis system was used to collect gait data (6DOFs) with an average time of 10 min/person. Hence, in this study, we assume 3D gait analysis could be used to diagnose KOA and assess its therapeutic strategy.

With the convenience of the gait system, we collected gait data from a large population of subjects, employed machine learning (LR) to analyze those data, and finally established novel methods for KOA diagnosis (Figure 1). To establish the methods for KOA diagnosis, we set up LR models of 3D kinematic gait parameters (6DOFs) for the diagnosis of KOA, identified the best cut-off point by using receiver operating characteristic curve (ROC) analysis to improve models, and finally, built diagnostic models with the parallel conjoined diagnosis method. ROC analysis was first used to assess the effectiveness of receiving radar and was developed for assessing the accuracy of diagnostic tests.\textsuperscript{[15]} The advantage of ROC analysis is its ability to figure out sensitivity, specificity, Youden index, and best cut-off points. Hence, we used ROC analysis to determine the best cut-off point of each model.

A great number of therapeutic methods have been discovered and taken to treat KOA, including conservative therapy (e.g., taking anodyne, sodium hyaluronate injection, exercise training, and physical therapy) or operative therapy (e.g., high tibial osteotomy and total knee arthroplasty). Many experts have reached an agreement on the usage of these methods by gathering clinical experience and referring to clinical studies.\textsuperscript{[16]} For patients with severe and mild KOA, operative and conservative therapies are chosen, respectively. However, it is difficult and exhausting for clinicians to decide whether to take operative or conservative strategies for KOA patients. AI may help clinicians by providing a suggestive prediction of therapy for them.

So, except for diagnosis, to further explore whether 3D gait parameters could be used to guide the therapy of KOA or not, we try to set up a new protocol to enroll 3D gait parameters to establish a medical decision classification (MDC) model for KOA therapy comprehensively. We used LR to analyze the 3D knee gait characteristics, along with Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and function sections, walking speeds, KL scores, and genders. The WOMAC is a measurable questionnaire most widely used to assess the symptoms by clinicians and researchers.\textsuperscript{[17]} It is well-validated and reliable to assess the symptoms (especially knee pain and function) of KOA.\textsuperscript{[18]} KL score was widely used and accepted by clinicians and researchers to describe the classification level of KOA knees structure based on X-ray imaging.\textsuperscript{[6]} In addition, the severity of KOA is also correlated with the patients’ walking speed and demographic characteristics such as obesity, age, and gender.\textsuperscript{[28]}

Hence, WOMAC pain and function sections, KL score, walking speed, and gender, along with the 3D knee gait characteristics, are collectively used to establish the objective comprehensive measurable system for the decision on the choice of conservative or operative therapy for KOA. With all these variables in mind, we took LR to analyze them and finally built the AI-based novel methods for the clinical decision (Figure 1) and proved 3D gait parameters could be used to guide the therapy of KOA. ROC analysis was also used to improve the methods. To validate AI-based methods for both diagnostics and therapeutic prediction of KOA, new subjects were recruited to test the diagnostic and predictive performance by Kappa test.\textsuperscript{[19]}
The objective of this study was to explore whether 3D knee kinematic parameters could be used in KOA diagnosis and its therapeutic strategy guidance. A total of 1201 participants were enrolled in this study, including 744 healthy subjects and 457 KOA subjects. All the participants’ demographic, clinical information, and 3D knee kinematic data were gotten. To validate our hypothesis, LR and ROC analysis was employed to set up diagnostic and predictive dynamic models and test their performance by Kappa test.

2.2. Subjects

The process of this study (Figure 1) started with the training to establish the KOA diagnosis and medical decision classification model, followed by testing the effectiveness of the models from newly recruited subjects. The training stage included subject recruitment, data collecting, establishing logistic models, and evaluating and improving models with ROC analysis. The model testing stage included new subject recruitment, data collecting, and evaluating models with the Kappa test. KOA diagnosis models were improved by a parallel conjoint diagnosis method (ATCM) before all models were tested. To demonstrate the application of the models, ATCM was used to diagnose a suspected patient. If the patient was diagnosed with KOA, then the MDC model was used to identify whether the patient needed conservative or operative therapy.

The research was carried out in Guangzhou General Hospital of Guangzhou Military Command and was permitted by the Institutional Review Board of the hospital. KOA patients were diagnosed by ACR criteria and assessed by WOMAC and KL score.[6,20] The KL score has five grades: grade 0, no x-ray changes of OA; grade I, possible osteophytic liping and doubtful joint space narrowing; grade II, possible joint space narrowing and definite osteophytes; grade III, moderate definite narrowing of joint space, multiple osteophytes, and some sclerosis and possible deformity of bone ends; grade IV, severe sclerosis and definite deformity of bone ends, large osteophytes, and marked narrowing of joint space. KL score was commonly used in the assessment of radiographic severity of KOA in clinics. 528 normal subjects (28.3 ± 7.4 years old, 21.1 ± 2.8 kg m⁻², 2.5 ± 0.5 km h⁻¹) and 306 medial KOA patients (63.2 ± 10.1 years old, 24.7 ± 3.6 kg m⁻², 1.7 ± 0.5 km h⁻¹, WOAMC 37.9 ± 12.5, 31 patients with KL grade I, 132 patients with KL grade II, 96 patients with KL grade III, 47 patients with KL grade IV) were enrolled to set up models. The clinical outcomes of all the patients would be recorded and divided into conservative (154 patients, accepting conservative therapy, e.g., taking anodyne, sodium hyaluronate injection) and operative (152 patients, accepting operative therapy, e.g., total knee arthroplasty) groups based on international clinical consensus[160] by two orthopedic doctors. All subjects were recruited via hospital advertisement in this study from January 2013 to March 2017. Informed consent of all subjects were gotten. The controls were eligible if they fitted in the inclusion criteria, including: a) age over 20; b) no history of major injury or diseases in ankle/hip; c) free from KOA according to a physical examination; d) body mass index below 30. The inclusion criteria of patients included: a) age over 20; b) no history of major injury or diseases in ankle/hip; c) free from KOA according to a physical examination; d) body mass index below 30.
40 years; b) body mass index below 30; c) KOA confirmed radiographically; d) gonyalgia for a minimum of three months; e) medial KOA in terms of atlas criteria\(^{(21)}\); f) movement without a cane or other devices.

The exclusion criteria of groups contained: a) history of major injury or diseases in ankle/hip/foot; b) Sodium hyaluronate or corticosteroid injection within 6 months; c) rheumatoid or neuropathic arthritis; d) any neurological or muscular diseases; e) any training, devices or therapy (e.g., kneepad) used to improve KOA symptoms; f) walk with a cane or other devices; g) heart disease; h) lateral KOA in term of atlas criteria\(^{(21)}\); i) age over 90 years; j) body mass index over 30; k) fail to complete the process of the experiment. To the patients who were recruited, the most symptomatic knees were selected as the experimental sides. Participants were excluded if they had any missing information on any variables.

216 normal subjects (26.5 ± 4.6 years old, 21.0 ± 2.8 kg m\(^{-2}\), 2.6 ± 0.3 km h\(^{-1}\)) and 151 patients (62.0 ± 10.0 years old, 24.7 ± 3.6 kg m\(^{-2}\), 1.7 ± 0.6 km h\(^{-1}\), WOMAC38.2 ± 14.4, 16 patients with KL grade I, 63 patients with KL grade II, 49 patients with KL grade III, 23 patients with KL grade IV) were recruited as a new testing group to test the actual effectiveness of models. The inclusion and exclusion were the same as before.

2.3. Gait Analysis

The subjects were evaluated by a 3D gait system\(^{(22)}\) (Opti_Knee\(^{®}\), Innomotion Inc., Shanghai, China). The gait system consisted of a workstation with a navigation stereo infrared tracking device and a high-speed optical camera, a handset digital probe, a couple of markers, and a bidirectional treadmill. The navigation stereo infrared tracking device has an accuracy of 0.3 mm root mean square (RMS)\(^{(23)}\). The gait system was reported with a repeatability of less than 1.3° in rotation and 0.9 mm in translation\(^{(24)}\). The sampling rate of the gait system is 60 Hz. The experiment process (Figure 2) includes the following steps: 1) a couple of markers were tied to the middle of thigh and calf; 2) the handset digital probe was used to identify seven bone markers of the subjects to establish personalized 3D coordinate systems of the femur and tibia with the subjects at an erect posture (tibia relative to femur), and the seven bone markers included medial malleolus (MM), lateral malleolus (LM), medial

![Figure 2](http://www.advancedsciencenews.com/)

Figure 2. a) The process of collecting gait data and definition of the coordinate systems of the femur and tibia. The gait system consists of a computer workstation and a treadmill. b) Before data collection, two markers were fastened to the thigh and shin. d) Then, seven bony landmarks (greater trochanter, lateral epicondyle, medial epicondyle, lateral plateau, medial plateau, medial malleolus, and lateral malleolus) were used to establish individualized 3D coordinate systems of the femur and tibia with subjects at a neutral standing position. c,e) The gait system collected knee kinematic data while the subjects were walking on the treadmill barefoot for 15 s. The six degrees of freedom (6DOF) in gait are shown in (e). The participant displayed in the figure consented for his photo being published.
epicondyle (ME), lateral epicondyle (LE), greater trochanter (GT), lateral plateau (LP), and medial plateau (MP); 3) knee kinematic data was collected by the gait system when the subjects were walking on the treadmill barefoot (before data collection, every subject was well guided as to how to walk on the treadmill barefoot); 4) after the subjects were well trained, the data was collected with the subjects at a self-selected velocity for 15 s (about 15–20 gait cycles).

The knee kinematic data of 6DOFs were collected, including addition/abduction (degree), flexion/extension (degree), anteroposterior translation (mm), internal/external femoral rotation (degree), medial/lateral translation (mm), and proximal/distal translation (mm) of the knees (Figure 2). Statistical analysis was used to set up models based on total ROM and magnitude of 6DOFs at seven key events (Figure 3 and 4), including IC, about 0% of gait, OT, about 12% of gait, HR, about 32% of gait, OI, about 52% of gait, TO, about 62% of gait, FA, about 76% of gait, and TV, about 85% of gait.[14]

2.4. Statistical Analysis

Binary logistic regression, one kind of supervised machine learning,[25] was used to train three models for KOA diagnosis based on 6DOF parameters by IBM SPSS Statistics 19.0 (IBM Corp., New York, USA) including angular model (AM) based on angular parameters of 6DOFs, translational model (TM) based on translational parameters of 6DOFs, and composite model (CM) based on all the 6DOFs. To have a higher sensitivity in KOA diagnosis, parallel conjoint diagnosis was applied to set the fourth model, ATCM, with a combination of the three models (AM, TM, CM).

ROC curve analysis (Figure 4a–d) was used to compare the effectiveness of the four models during the training stage under the significant level of 0.05 by MedCalc 15.0 (MedCalc Software bvba, Seoul, Republic of Korea). The maximum Youden index, sensitivity, specificity, and the best cutoff point of models were obtained from the ROC curve analysis. Kappa test was used to evaluate the actual effectiveness of models and select the best model in the KOA diagnosis in detecting the new unknown subjects by IBM SPSS Statistics 19.0. Binary Logistic Regression was also employed to build the MDC model for KOA patients. The variables included WOMAC pain and function sections, KL score, walking speed, gender (Figure 5), and gait parameters (Figure 6). ROC analysis and Kappa test were used to evaluate MDC (Figure 4e–h). The model builder was blinded by the participants’ information and clinical outcomes.

3. Results

3.1. Gait Analysis and Variables Establishment

Figure 2 shows the process of collecting gait data and define the coordinate systems of the tibia and femur. Figure 3 demonstrates the alterations of 6DOFs of seven key events (IC, OT, HR, OI, TO, FA, and TV) and the range of motion of 6DOFs for both the normal and KOA subjects in training and testing groups used for establishing diagnostic models. It suggests that the 6DOFs at the seven key events and their range of motion (ROM) are significantly different between the normal and KOA subjects. To establish the medical decision classification model, Figure 6 demonstrates the alterations of 6DOFs of seven key events (IC, OT, HR, OI, TO, FA, and TV), and the range of motion of 6DOFs. Figure 5 shows demographic characteristics, walking speed, WOMAC pain and function sections, and KL score in training and testing groups. These results imply that all the variables are significantly different between the conservative and operative subjects. Therefore, we used them as parameters to generate logistic models (Table 1 and 2).

3.2. KOA Diagnostic Model Development using Training Subjects

By using these parameters of the KOA patients (306) recruited for training and diagnosed by X-ray imaging, along with the normal people (528) as control, we carried out the binary logistic training to establish the diagnostic methods based on the DOFs in the gait analysis. By a binary LR method (Table 1), we successfully identified three models, including AM, TM, and CM, with a Youden index of 0.7312, 0.6689, and 0.8214, respectively, by ROC analysis (Figure 4a,b). AM, TM, and CM use the angular DOFs, translational DOF, and a combination of both to diagnose KOA, respectively. It should be noted that the Youden index reflects the accuracy of detecting the disease in the training subjects and a higher Youden index indicates a better accuracy. Thus CM is more accurate in detecting KOA than AM and TM. To have a higher sensitivity of KOA diagnosis, a parallel diagnosis method was used to combine the three models (AM, TM, and CM) as a parallel diagnosis model, termed ATCM, with a Youden index of 0.7492 and a sensitivity of 92.16% (Figure 4a,b). Figure 4a–d clearly shows that ATCM presents the highest sensitivity of KOA diagnosis.

3.3. The Regression Equation of models and the Establishment of Parallel Diagnosis Model of KOA

Binary LR using the gait data from the training subjects (Table 1) showed that AM contained abduction/adduction angle (at OT and FA), flexion/extension angle (at IC, OT, and OI), and ROM of flexion/extension angle. TM contained anterior/posterior translation (at IC, HR, OI, and FA), ROM of anterior/posterior translation, medial/lateral translation at TV, and ROM of medial/lateral translation, and distal/proximal translation (at HR, OI, and TV). CM contained abduction/adduction angle (at OT, TO, and FA), internal/external rotation angle (at OI and TO), flexion/extension angle at (IC, OT, TO, FA, and TV), ROM of flexion/extension angle, distal/proximal translation (at OT, TO, and TV), and anterior/posterior translation (at HR and OI), medial/lateral translation at FA, and ROM of medial/lateral translation. It seems that CM has a higher Youden index (0.8214) than AM and TM because CM uses both angular and translational variables (Figure 4a–d).

By using binary LR (Table 1), we could obtain the following regression equation[26] of AM: Logit $(P)_A = 9.507 - 0.069X_1 + 0.170X_2 + 0.204X_3 - 0.134X_4 - 0.181X_5 - 0.186X_6$, where $P$-value is the probability for a patient to be diagnosed with KOA. According to the ROC curve (Figure 5a–b), the best cut-off point of the $P$-value is 0.3692 for AM. When the
P-value is over and below this cutoff point, the subject is a KOA patient and normal person, respectively. Similarly, the regression equation of TM and CM was determined as follows (Table 1).

For TM: Logit \( (P)_{T} = 3.524 - 0.135X_{f} + 0.139X_{g} + 0.332X_{9} - 0.104X_{10} - 0.145X_{11} - 0.292X_{12} + 0.236X_{13} + 0.138X_{14} + 0.049X_{15} - 0.152X_{16} \).
For CM: \[ \text{Logit} (P) = 10.863 - 0.203X_1 + 0.266X_{17} + 0.163X_2 + 0.217X_{16} - 0.143X_{19} + 0.166X_{30} - 0.149X_4 - 0.149X_{21} - 0.082X_{22} + 0.138X_{23} - 0.122X_6 - 0.201X_{24} - 135X_{25} - 0.219X_8 + 0.186X_9 + 0.136X_{26} - 0.052X_{27} - 0.095X_{29}. \]

Also, the best cutoff point of TM and CM is determined to be 0.3687 and 0.4130 (Figure 5a,b). The equation of ATCM was AM/STM/CM. Namely, the ATCM identifies a subject to be a patient when any one of the three models (AM, TM, and CM) diagnoses the subject to be a patient. As a consequence, the KOA diagnosis of ATCM depends on the combination of AM, TM, and CM, and thus ATCM doesn’t have a numeric best cut-off point.

### 3.4. Testing the Effectiveness of the Four KOA Diagnostic Models Using Testing Subjects

We proceeded to test whether the four diagnostic models (AM, TM, CM, ATCM) are effective in diagnosing KOA. To achieve this goal, we first recruited 151 KOA patients (confirmed by X-ray imaging) and 216 normal people. Then we used the diagnostic models established above to diagnose KOA from the testing subjects by comparing the P-value and the cutoff point of each model. By using the Kappa test, a Kappa value was determined (Figure 4c) for each method. The Kappa value reflects the accuracy of each model; a higher Kappa value indicates that this model is more accurate in KOA diagnosis. The Kappa test (Figure 4c) demonstrates that ATCM has the highest accuracy (Kappa value, 0.871) in KOA diagnosis among the four diagnostic models. We also found that 94.4% of normal people were correctly diagnosed to be normal whereas 94.0% of KOA patients were correctly diagnosed with KOA by ATCM (Figure 4d). Figure 4d collectively confirmed that the ATCM has the best accuracy among all of the four models.

### 3.5. Establishing MDC Model of KOA

By using LR and the data (Figure 4 and 6) including gait characteristics, demographic characteristics, walking speed, WOMAC pain, and function sections and KL score from 154 conservative patients and 152 operative patients, MDC was successfully built and improved by ROC analysis with its Youden index, sensitivity, and specificity of 0.8886, 92.11%, 96.75%, respectively. According to Table 2, MDC contains 7 parameters including KL score, WOMAC pain, gender, abduction/adduction angle (at TO and TV), internal/external rotation at TO, ROM of flexion/extension angle. According to the ROC curve (Figure 4e,f), the best cutoff point of the P-value is 0.3853. The regression equation of the model for different KOA levels is described as follows.

When the X-ray based KOA level is I, namely, KL(X) = 1, Logit (P)_A can be expressed as Logit (P)_A = 0.273 + 1.267X_2 - 0.442X_4 + 0.367X_5 + 0.115X_6 - 0.071X_7 (for male patients) or Logit (P)_A = 0.273 + 1.267X_2 - 1.735 - 0.442X_4 + 0.367X_5 + 0.115X_6 - 0.071X_7 (for female patients).
When \( KL(X_1) = 2 \), Logit \( (P)_A \) can be expressed as 

\[
\text{Logit} (P) = 0.273 + 1.267X_2 - 0.442X_4 + 0.367X_5 + 0.115X_6 - 0.071X_7 - 3.733 \quad \text{(for male patients)} \\
\text{Logit} (P) = 0.273 + 1.267X_2 - 1.735 - 0.442X_4 + 0.367X_5 + 0.115X_6 - 0.071X_7 - 3.733 \quad \text{(for female patients)}
\]

When \( KL(X_1) = 3 \), Logit \( (P)_A \) can be expressed as 

\[
\text{Logit} (P) = 0.273 + 1.267X_2 - 0.442X_4 + 0.367X_5 + 0.115X_6 - 0.071X_7 - 4.428 \quad \text{(for male patients)} \\
\text{Logit} (P) = 0.273 + 1.267X_2 - 1.735 - 0.442X_4 + 0.367X_5 + 0.115X_6 - 0.071X_7 - 4.428 \quad \text{(for female patients)}
\]

When \( KL(X_1) = 4 \), Logit \( (P)_A \) can be expressed as 

\[
\text{Logit} (P) = 0.273 + 1.267X_2 - 0.442X_4 + 0.367X_5 + 0.115X_6 - 0.071X_7 - 0.818 \quad \text{(for male patients)} \\
\text{Logit} (P) = 0.273 + 1.267X_2 - 1.735 - 0.442X_4 + 0.367X_5 + 0.115X_6 - 0.071X_7 - 0.818 \quad \text{(for female patients)}
\]

### 3.6. Testing the Effectiveness of the MDC Model

151 KOA subjects for testing were recruited and used to test the effectiveness of MDC. By using the Kappa test, the Kappa value of MDC was carried out to be 0.934 with an accuracy of 96.1% and 97.3% for the conservative and operative groups, respectively (Figure 4g–h). These results suggest that our MDC model is effective for doctors to make medical decisions on conservative or operative treatment for KOA patients after the diagnosis.
4. Discussion

KOA diagnosis usually depended on static imaging methods, particularly radiography. As of now, gait analysis, a dynamic method, hasn’t been applied to the KOA diagnosis and its therapeutic strategy assessment. Our AI-based analysis of 3D kinematic parameters of the knee collected on a portable gait system filled this gap and proved and validated the ability of gait
Table 1. Descriptions of kinematic parameters (collected from the training subjects using gait analysis) used for generating diagnostic models.

| Variable (a) | Variable code | Constant [β] | Standard deviation | P-value |
|--------------|---------------|--------------|--------------------|---------|
| Angular Model (AM) | | | | |
| Abd/Add angle at OT | X$_1$ | -0.069 | 0.030 | 0.021 |
| Abd/Add angle at FA | X$_2$ | 0.170 | 0.026 | <0.001 |
| Fle/Ext angle at IC | X$_3$ | 0.204 | 0.028 | <0.001 |
| Fle/Ext angle at OT | X$_4$ | -0.134 | 0.030 | <0.001 |
| Fle/Ext angle at OI | X$_5$ | -0.181 | 0.024 | <0.001 |
| ROM of Fle/Ext angle | X$_6$ | -0.186 | 0.016 | <0.001 |
| Constant (b) | | 9.507 | 0.853 | <0.001 |
| Translational Model (TM) | | | | |
| Ant/Pos translation at IC | X$_7$ | -0.135 | 0.032 | <0.001 |
| Ant/Pos translation at HR | X$_8$ | 0.139 | 0.050 | 0.006 |
| Ant/Pos translation at OI | X$_9$ | 0.332 | 0.047 | <0.001 |
| Ant/Pos translation at FA | X$_{10}$ | -0.104 | 0.026 | <0.001 |
| ROM of Ant/Pos translation | X$_{11}$ | -0.145 | 0.032 | <0.001 |
| Dis/Pro translation at HR | X$_{12}$ | -0.292 | 0.059 | <0.001 |
| Dis/Pro translation at OI | X$_{13}$ | 0.236 | 0.060 | <0.001 |
| Dis/Pro translation at TV | X$_{14}$ | 0.138 | 0.020 | <0.001 |
| Med/Lat translation at TV | X$_{15}$ | 0.049 | 0.018 | 0.007 |
| ROM of Med/Lat translation | X$_{16}$ | -0.152 | 0.040 | <0.001 |
| Constant | | 3.524 | 0.442 | <0.001 |
| Composite Model (CM) | | | | |
| Abd/Add angle at OT | X$_{17}$ | 0.206 | 0.067 | 0.002 |
| Abd/Add angle at TO | X$_{18}$ | 0.163 | 0.038 | 0.000 |
| Int/Ext Rotation at OI | X$_{19}$ | 0.217 | 0.059 | 0.000 |
| Int/Ext Rotation at TO | X$_{20}$ | -0.143 | 0.057 | 0.013 |
| Fle/Ext angle at IC | X$_{21}$ | 0.166 | 0.037 | 0.000 |
| Fle/Ext angle at OT | X$_{22}$ | -0.149 | 0.043 | 0.000 |
| Fle/Ext angle at OI | X$_{23}$ | -0.149 | 0.034 | 0.000 |
| Fle/Ext angle at FA | X$_{24}$ | -0.108 | 0.045 | 0.009 |
| Fle/Ext angle at TV | X$_{25}$ | 0.138 | 0.043 | 0.001 |
| ROM of Fle/Ext angle | X$_{26}$ | -0.122 | 0.031 | 0.000 |
| Ant/Pos translation at HR | X$_{27}$ | -0.201 | 0.044 | 0.000 |
| Ant/Pos translation at OI | X$_{28}$ | -0.219 | 0.044 | 0.000 |
| Dis/Pro translation at OT | X$_{29}$ | 0.186 | 0.050 | 0.000 |
| Dis/Pro translation at TO | X$_{30}$ | 0.136 | 0.035 | 0.000 |
| Med/Lat translation at FA | X$_{31}$ | -0.052 | 0.022 | 0.018 |
| ROM of Med/Lat translation | X$_{32}$ | -0.095 | 0.046 | 0.041 |
| Constant | | 10.863 | 1.203 | 0.000 |

(a) The data of the gait was based on the tibia relative to the femur. Abd/Add: Abduction/Adduction; Int/Ext: Internal/External; Fle/Ext: Flexion/Extension; Ant/Pos: Anterior/Posterior; Dis/Pro: Distal/Proximal; Med/Lat: Medical/Lateral; IC: Initial contact; OT: Opposite toe off; HR: Heel rise; OI: Opposite initial contact; TO: Toe off; FA: Feet adjacent; TV: Tibia vertical; ROM: Range of motion.

Table 2. Descriptions of kinematic parameters (collected from the training subjects using gait analysis) used for generating predictive models for treatment decision by LR ($P = e^{\beta x_1 + \beta x_2 + \ldots + \beta x_n + \beta_0}$).

| Variable (a) | Variable code | Constant [β] | Standard deviation | P-value |
|--------------|---------------|--------------|--------------------|---------|
| MDC model | | | | |
| KL = 1 | X$_1$ | 0 | 0 | 0.000 |
| KL = 2 | X$_2$ | -3.733 | 1.913 | 0.051 |
| KL = 3 | X$_3$ | -4.428 | 1.287 | 0.001 |
| KL = 4 | X$_4$ | -0.818 | 1.291 | 0.526 |
| WOMAC Pain | X$_5$ | 1.267 | 0.224 | 0.000 |
| Gender = female | | -1.735 | 0.797 | 0.029 |
| Abd/Add angle at TO | X$_6$ | -0.442 | 0.136 | 0.001 |
| Abd/Add angle at TV | X$_7$ | 0.367 | 0.100 | 0.000 |
| Int/Ext Rotation at TO | X$_8$ | 0.115 | 0.057 | 0.044 |
| ROM of Fle/Ext angle | X$_9$ | -0.071 | 0.027 | 0.010 |
| Constant (b) | | 0.273 | 1.779 | 0.878 |

(a) The data of the gait was based on the tibia relative to the femur. Abd/Add: Abduction/Adduction; Int/Ext: Internal/External; IC: Initial contact; OT: Opposite toe off; HR: Heel rise; OI: Opposite initial contact; TO: Toe off; FA: Feet adjacent; TV: Tibia vertical; ROM: Range of motion.

The data (6DOFs) in diagnosing KOA and guiding its therapy. The guideline for selecting kinematic parameters in this study was similar to the diagnostic criteria of cardiac diseases in an electrocardiogram (ECG). Clinicians usually diagnose cardiac diseases by looking for characteristics of different leads in ECG (usually 12-lead). Examples of these characteristics include waveforms and magnitudes of curves at key time points. Inspired by ECG, our AI-based method is to study the characteristics of 6DOFs of the knee at seven key events to set up LR models (just like a 6-lead ECG). Hence, we designed an AI-based method to discover the patterns of the characteristics of KOA from 3D gait data so as to set up diagnostic models for KOA. Furthermore, we also established an objective MDC to indicate whether the patients should be treated by conservative or operative therapy. To have interpretable statistical analysis, we employed LR, a kind of interpretable machine learning, to analyze the data and formed diagnostic predictive models.

Our KOA diagnosis training was performed using a total of 28 kinematic parameters from the 6DOFs in the gait analysis (Table 1). The training study confirmed that CM is more accurate than AM and TM alone. This is because to include both angular and translational parameters in a model will more effectively reflect the full characteristics of the knee in gait that are correlated with KOA than to include either angular or translational parameters alone. In CM, abduction/adduction and internal/external rotation, flexion/extension angle, distal/lateral translation, as well as medial/lateral and anterior/posterior translation were included. According to previous studies,[27] KOA knees were correlated with many parameters such as reduced knee
flexion angle and narrowed space of joint (leading to narrowed motion). It is consistent with the alterations of 6DOFs in Figure 3. Based on the results in Figure 4a–d and Table 1, the parameters included in CM are effective and could be functional parameters that could be used to better diagnose KOA and are probably related to alterations in the structures of KOA knees.

Due to the severe damage of KOA to the knees, it is meaningful and necessary to sensitively diagnose KOA to prevent further damage. A parallel conjoint method was usually used to improve the sensitivity in disease diagnosis by combining different kinds of diagnostic methods. In our study, we successfully combined AM, TM, and CM into an ATCM model and the resultant ATCM was found to have the highest sensitivity (92.16%) in the KOA diagnosis among the four models (AM, TM, CM, and ATCM). Besides, ATCM has a Youden Index of 0.7492 and a specificity of 82.77%, suggesting that ATCM is accurate and specific enough in diagnosing KOA diagnosis. Namely, our training study confirms that ATCM is a useful diagnostic model (ATCM) in KOA diagnosis. As a method of parallel conjoint diagnosis, ATCM would diagnose a subject to have KOA when one of the models (AM, TM, or CM) diagnosed this subject to have KOA. Consequently, ATCM is the most sensitive method in KOA diagnosis.

In our testing study, we test the effectiveness of the four models (AM, TM, CM, and ATCM) in diagnosing KOA in the recruited subjects. By using the Kappa test to compare the consistency in diagnosing KOA between our diagnostic methods and the diagnostic method of using ACR criteria,\textsuperscript{[14,29]} we found that ACTM had the highest accuracy in detecting both normal and KOA knees (Figure 4c–d). It should be noted that the Kappa value reflects the accuracy of KOA diagnosis methods in the testing subjects and a higher Kappa value indicates a better accuracy with an acceptable Kappa value over 0.4 and an excellent Kappa value over 0.8.\textsuperscript{[19,29]} The results of the consistency test showed that the Kappa value increased from 0.751 to 0.871 in the order of AM (0.751), TM (0.806), CM (0.840), and ATCM (0.871). The Kappa value was acceptable and meaningful for all the models since it was greater than 0.4 for all of these models. The Kappa value of ATCM (≥0.80) showed an excellent agreement between our diagnostic method (ATCM) and the method of using ACR criteria.\textsuperscript{[4]} Our results showed that ATCM achieved the best diagnostic effectiveness in detecting unknown subjects among all of the four models. Our study also confirmed that the 3D knee kinematic parameters could be a novel approach to direct functional assessment for developing a dynamic diagnosis of KOA.

Our MDC training was performed using a total of 7 kinematic parameters including gait parameters (Table 2). We successfully built MDC with an excellent Youden index, sensitivity, and specificity of 0.8886, 92.11%, and 96.75%, respectively. In a medical situation, MDC could precisely identify whether a KOA patient needs operative treatments or not, helping the doctors make a proper decision. In the model of MDC, four 3D gait parameters were enrolled, including abduction/adduction at TO, TV, internal/external rotation at TO, and ROM of flexion/extension. In testing MDC, the consistency between the results of MDC and the clinical outcome is excellent with a Kappa value of 0.934 (Figure 4g,h). Specifically, 96.1% of conservative patients and 97.3% of operative patients were correctly determined by our MDC. These results verify that MDC can be reliable and gait parameters enrolled in MDC could be used to assess the therapeutic strategy of KOA.

Our method for KOA diagnosis and medical decision prediction is noninvasive, time-saving, dynamic knee-functional-based, and does not require much space. Our method was based on the knee function assessment of KOA. This met the urgent requirement of knee function assessment on patients with KOA in clinics. It takes about 10 min/person to collect gait data. It then soon seconds to judge whether this person has KOA. Namely, only about 10 min is needed for a doctor to diagnose KOA in a dynamic way. Only a small space with a volume measuring $2 \times 3 \times 2.5$ m$^3$ is needed to accommodate the gait system and a subject for using our method to diagnose KOA. Hence, it is possible to use our method to diagnose KOA patients in a short time and within a small space, similar to an ECG. With the convenience of using a gait system, our AI-based method could be widely used in the medical community to screen for KOA. For those patients confirmed with KOA, our MDC method can predict whether they need operative treatment or not. Hence, the AI-based gait analysis system of this study could not only diagnose KOA, but also help doctors to make proper therapeutic decisions. Traditionally, doctors pay more attention to the pain and the “static” deformity of the knees. With our AI-based method, the doctors will be able to focus on the dynamic functions of the knees due to the use of the dynamic gait system. Consequently, the patients’ athletic ability can be restored on time and more effectively. There are some limitations of the study needed to be addressed. First, although we achieved excellent KOA diagnosis in AI models, the logistic models may not be efficient to cover all the valid information, so we would next design a new AI method to achieve a higher detection rate. Second, we recruited young healthy adults as controls. This may be not most suitable for KOA diagnosis. However, old adults are facing knee joint degeneration which may also bring bias for the study. Next, we will recruit aged healthy adults as controls. Finally, this is a single-center study, the AI models may not be suitable for other regions. So, we will consider a multi-center study to build the AI models in the future.

5. Conclusion

In summary, we employed an AI-based (LR) strategy to set up four models (AM, TM, CM, and ATCM) in the KOA diagnosis in a rapid and dynamic manner. Both angular and translational parameters from the gait analysis were used as inputs in LR. By ROC analysis, a cut-off value for the probability of a subject being diagnosed as a KOA patient is determined and a P-value calculated from LR is used to compare with the cut-off value. Then the output in our AI-based strategy is whether a subject is a KOA patient or not. ATCM, a parallel diagnostic combination of the three models (AM, TM, and CM), had a better performance in the KOA diagnosis than the other three models alone. Furthermore, we successfully established a clinical MDC model for KOA patients by a similar AI-based method. The MDC model can precisely identify whether KOA patients need conservative or operative therapy after diagnosis. In essence, 3D knee kinematic parameters (6DOFs) could be used to diagnose KOA and guide
its therapeutic strategy by using machine learning to discover deep correlations between gait data and KOA.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords

artificial intelligence, diagnosis, gait, knee osteoarthritis, medical decision classification

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