

# Biomechanical Threshold Values for Identifying Clinically Significant Knee-Related Symptoms 6 Months After Anterior Cruciate Ligament Reconstruction

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**Context:** Slower habitual walking speed and aberrant gait biomechanics are linked to clinically significant knee-related symptoms and articular cartilage composition changes linked to posttraumatic osteoarthritis after anterior cruciate ligament reconstruction (ACLR).

**Objectives:** To (1) determine whether specific gait biomechanical variables can accurately identify individuals with clinically significant knee-related symptoms post-ACLR and (2) determine the corresponding threshold values, sensitivity, specificity, and odds ratios for each biomechanical variable.

**Design:** Cross-sectional study.

**Setting:** Laboratory.

**Patients or Other Participants:** A total of 71 individuals (38 female, 33 male; age =  $21 \pm 4$  years, height =  $1.76 \pm 0.11$  m, mass =  $75.38 \pm 13.79$  kg, time after primary unilateral ACLR =  $6.2 \pm 0.4$  months).

**Main Outcome Measure(s):** Three-dimensional motion capture of 5 overground walking trials was used to calculate discrete gait biomechanical variables of interest during stance phase (first and second peak vertical ground reaction force [vGRF], midstance minimum vGRF, peak internal knee-abduction and -extension moments, and peak knee-flexion angle), along with habitual walking speed. Previously established Knee Injury and Osteoarthritis Outcome Score cutoff scores were used to define

patients with (ie, symptomatic;  $n = 51$ ) and those without (ie, asymptomatic;  $n = 20$ ) clinically significant knee-related symptoms. Separate receiver operating characteristic curves and respective areas under the curve (AUCs) were used to evaluate the capability of each biomechanical variable of interest to identify individuals with clinically significant knee-related symptoms.

**Results:** Habitual walking speed (AUC = 0.66), vGRF at midstance (AUC = 0.69), and second peak vGRF (AUC = 0.76) demonstrated low to moderate accuracy for identifying individuals with clinically significant knee-related symptoms. Individuals who exhibited habitual walking speeds  $\leq 1.27$  m/s, midstance minimum vGRF  $\geq 0.82$  body weights, and second peak vGRF  $\leq 1.11$  body weights demonstrated 3.13, 6.36, and 9.57 times higher odds of experiencing clinically significant knee-related symptoms, respectively.

**Conclusions:** Critical thresholds for gait variables may be used to identify individuals with increased odds of clinically significant knee-related symptoms and potential targets for future interventions.

**Key Words:** vertical ground reaction force (vGRF), Knee Injury and Osteoarthritis Outcome Score (KOOS), gait, post-traumatic osteoarthritis (PTOA)

## Key Points

- Individuals with slower habitual walking speeds 6 months after anterior cruciate ligament reconstruction demonstrated greater odds of experiencing knee symptoms.
- Less dynamic, more sustained (ie, flatter) vertical ground reaction forces (greater midstance and lower second peak) were linked to greater odds of knee symptoms 6 months after anterior cruciate ligament reconstruction.

Approximately 40% of individuals with anterior cruciate ligament (ACL) injury report clinically significant knee-related symptoms at 2 and 6 years after ACL reconstruction (ACLR) that persist for the first decade post-

ACLR.<sup>1,2</sup> Clinically significant knee symptoms are associated with radiographic posttraumatic osteoarthritis (PTOA),<sup>3</sup> cartilage composition changes consistent with future PTOA development,<sup>4</sup> and multiple gait-specific changes<sup>5,6</sup> that are linked

to PTOA-related outcomes post-ACLR.<sup>7-13</sup> However, an initial study is needed to build upon previous literature and determine the magnitudes of biomechanical variables capable of identifying individuals with clinically significant knee-related symptoms post-ACLR. Evaluation of the capacity and properties of critical thresholds for gait variables (ie, sensitivity, specificity, and odds ratios) may be further used to develop and inform future clinical screening methods and inclusion criteria for clinical trial design that aim to mitigate clinically significant knee-related symptoms post-ACLR.

A slower habitual walking speed is associated with a greater incidence of idiopathic knee OA,<sup>14,15</sup> and individuals with ACLR who walk slower demonstrate greater serum concentrations of biomarkers related to cartilage breakdown,<sup>16</sup> worse femoral cartilage composition,<sup>11</sup> and clinically significant knee-related symptoms.<sup>5</sup> In addition, differences in vertical ground reaction forces (vGRFs), knee kinematics, and knee kinetics during gait have been observed in individuals with ACLR compared with uninjured controls.<sup>6</sup> In the first 6 to 12 months post-ACLR, individuals exhibit more sustained vGRF loading patterns (eg, lower first and second peak vGRF, and greater vGRF at midstance) and smaller peak knee-extension moment (KEM) and peak knee-flexion angle (KFA) compared with uninjured controls.<sup>6</sup> Lower first peak vGRF, peak KFA, and peak knee-abduction moment (KAM) are similarly associated with deleterious changes in joint-tissue metabolism and decreased cartilage health.<sup>7,8,10,17,18</sup> In addition, lower first peak vGRF, greater vGRF at midstance, and smaller KAM are associated with worse magnetic resonance imaging outcomes of tibiofemoral cartilage composition in individuals with ACLR.<sup>8,9,12</sup> Finally, in the first 6 to 12 months post-ACLR, sustained loading gait patterns are linked to worse knee-related symptoms.<sup>5,19</sup> Although multiple gait-related variables demonstrate changes post-ACLR, and some are linked to early PTOA development and clinically significant knee-related symptoms, determining which variables demonstrate increased odds of clinically significant knee-related symptoms is important for advancing early clinical detection and proper prescription of rehabilitation programs, such as gait retraining, to mitigate poor patient-reported outcomes post-ACLR.

Therefore, the primary purpose of our study was to determine whether select biomechanical gait variables (habitual walking speed; first and second peak vGRFs; midstance minimum vGRF; and peak KAM, KEM, and KFA during the first 50% of stance) can be used to identify individuals with clinically significant knee-related symptoms 6 months post-ACLR. The secondary purpose was to determine the properties and characteristics (ie, odds ratios, sensitivity, specificity, and optimal threshold values) of the gait variables that can be used to identify individuals with clinically significant knee-related symptoms. Previously established Knee Injury and Osteoarthritis Outcome Score (KOOS) cutoff scores were used to define individuals with (ie, symptomatic) and without (ie, asymptomatic) clinically significant knee-related symptoms.<sup>20</sup> We hypothesized that identifiable cutoff values for each gait variable capable of identifying those with clinically significant knee-related symptoms 6 months post-ACLR would be present. The results of our study are intended to be hypothesis-generating and serve as the initial step for informing the future development of clinical screening tools to identify

those with greater odds of experiencing clinically significant knee-related symptoms.

## METHODS

### Study Design

Data from 3 separate cohort studies were combined for this cross-sectional analysis of gait biomechanics and knee-symptom status at 6 months post-ACLR. All participants underwent ACLR surgery with 1 (J.T.S.) of 3 participating surgeons through the Department of Orthopaedics of the School of Medicine at the University of North Carolina at Chapel Hill and received either bone-patellar tendon-bone autograft or quadriceps tendon autograft. All data were collected in the same laboratory using the same equipment and biomechanics protocols (A.N.B., C.M.L., and E.S.B.).<sup>5,12,19,21,22</sup> Gait data were processed specifically for our study by an investigator (A.N.B.) blinded to symptomatic group assignment. Gait measurements were collected after the completion of patient-reported outcomes surveys. All participants provided written informed consent, and all study protocols were compliant with Human Subjects Research Ethics and Guidelines and approved by the Institutional Review Board at the University of North Carolina at Chapel Hill.

### Participants

A total of 71 individuals (n = 51 symptomatic and n = 20 asymptomatic) were included in our final analysis (Table 1). We included participants who were between the ages of 18 and 35 years and  $6.2 \pm 0.4$  months (range, 5.7–7.2 months) post-primary unilateral ACLR at the time of data collection. Individuals with concomitant meniscal injury were included if no more than one-third of their meniscus was removed at the time of ACLR surgery.<sup>5-7</sup> Individuals were excluded if they reported any of the following: ACLR revision surgery, contralateral ACLR or injury, multiligament reconstruction at the time of ACLR, history of any other lower extremity orthopaedic surgery, physician-diagnosed knee osteoarthritis, neuromuscular disorders, balance disorders, or history of orthopaedic injury in either limb within 6 months before testing.<sup>19,22</sup>

### Procedures and Measurements

Gait biomechanical and KOOS data were collected during a single-session laboratory visit.

**Knee Injury and Osteoarthritis Outcome Scores.** We used KOOS data to evaluate patient-reported outcomes and clinically significant knee-related symptoms. The 5 KOOS subscales were collected to assess pain (KOOS Pain), other symptoms (KOOS Symptoms), function in activities of daily living (KOOS ADL), function in sport and recreation (KOOS Sports), and knee-related quality of life (KOOS QOL).<sup>23</sup> All subscales have demonstrated acceptable reliability (intraclass correlation coefficient, 0.75–0.96) and validity in individuals with ACLR.<sup>24</sup> To minimize error, participants directly input KOOS responses into electronic forms; questionnaires were scored on a scale from 0 to 100, with higher scores indicating better patient-reported outcomes.

After data collection, participants were retrospectively dichotomized into 2 groups using previously published KOOS criteria: those with clinically significant knee-related

**Table 1. Participant Characteristics and Outcome Measures**

	Entire Cohort (N = 71)	Symptomatic (n = 51)	Asymptomatic (n = 20)	P Value	Cohen's <i>d</i> Effect Size
	No. (%)				
Sex				NC	NC
Female	38 (54)	23 (45)	15 (75)		
Male	33 (46)	28 (55)	5 (25)		
Meniscal repair	41 (58)	31 (61)	10 (50)	NC	NC
Autograft				NC	NC
Patellar tendon	70 (99)	51 (100)	19 (95)		
Quadriceps tendon	1 (1)	0 (0)	1 (5)		
	Mean ± SD (range)				
Age, y	21.3 ± 3.6	21.6 ± 3.5 (18.0–32.7)	20.4 ± 3.7 (18.2–30.0)	.06 <sup>a</sup>	–0.33
Height, m	1.8 ± 0.1	1.8 ± 0.1 (1.5–2.0)	1.8 ± 0.1 (1.6–1.9)	.61 <sup>b</sup>	0.13
Mass, kg	75.4 ± 13.8	75.7 ± 14.1 (49.5–104.7)	74.6 ± 13.3 (53.2–108.4)	.78 <sup>b</sup>	0.07
Time since ACLR, mo	6.2 ± 0.4	6.2 ± 0.4 (5.7–7.2)	6.2 ± 0.3 (5.7–6.7)	.85 <sup>b</sup>	–0.12
KOOS					
Symptoms	78.51 ± 13.62	74.01 ± 12.91 (21.0–96.4)	90.60 ± 6.23 (78.6–100.0)	<.001 <sup>a,c</sup>	1.50
Pain	82.66 ± 10.45	79.83 ± 10.75 (33.0–100.0)	90.43 ± 3.16 (75.0–97.0)	<.001 <sup>a,c</sup>	1.02
ADL	95.16 ± 8.54	93.84 ± 9.61 (38.0–100.0)	98.78 ± 1.72 (94.1–100.0)	<.001 <sup>a,c</sup>	0.59
Sports	66.86 ± 16.48	62.35 ± 16.20 (0.00–95.00)	79.21 ± 9.61 (50.0–90.0)	<.001 <sup>a,c</sup>	1.06
QOL	52.14 ± 13.89	49.53 ± 13.09 (25.00–81.00)	59.28 ± 13.86 (25.00–81.20)	.04 <sup>b,c</sup>	0.59

Abbreviations: ADL, function in activities of daily living; KOOS, Knee Injury and Osteoarthritis Outcome Score; NC, not conducted; QOL, knee-related quality of life; Sports, function in activities of sport and recreation.

<sup>a</sup> Wilcoxon rank sum test.

<sup>b</sup> Independent *t* test.

<sup>c</sup> Statistically significant difference between symptomatic and asymptomatic groups ( $P < .05$ ).

symptoms (symptomatic) and those without clinically significant knee-related symptoms (asymptomatic).<sup>20</sup> Participants who reported KOOS QOL  $\leq 87.5$  and met  $\geq 2$  of the following criteria of the other 4 subscales were categorized as *symptomatic*: KOOS Symptoms  $\leq 85.7$ , KOOS Pain  $\leq 86.1$ , KOOS ADL  $\leq 86.8$ , and KOOS Sports  $\leq 85.0$ .<sup>20</sup>

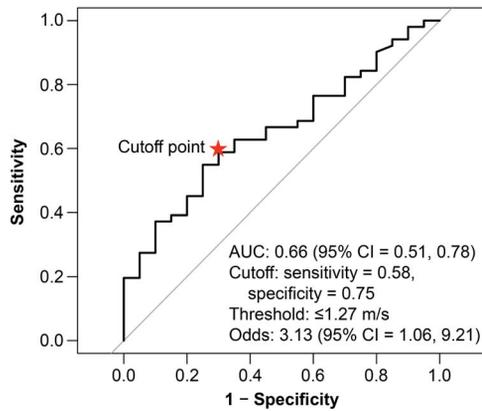
**Gait Biomechanics Procedures.** Twenty-six retroreflective markers were placed on palpable bony landmarks on the upper and lower extremities, and a rigid cluster of 3 markers was placed on the sacrum, as described previously.<sup>5,9,19,22</sup> A static trial was collected and used to create the segment-linkage model and calculate participant weight via force-plate measurements. After the static trial, 4 medial lower extremity markers were removed (2 knee and 2 ankle). Next, participants completed 5 successful overground barefoot walking trials across a 6-m walkway with 3 staggered and embedded force plates (model FP406010; Bertec Corp). Participants were instructed to walk at their habitual speed, look straight ahead, and maintain a constant speed through 2 sets of timing gates (Dashr 2 Gate System; Dashr Systems).<sup>5,9,19</sup> Five practice trials were allowed to familiarize participants with the gait task. The timing gates were used to calculate the average walking speed from the practice trials. To ensure a consistent gait speed was maintained for each gait trial, we used the timing gates to determine real-time gait speed and confirm that each gait trial was within  $\pm 5\%$  of the average speed calculated from participants' practice trials. A gait trial was considered successful if the ACLR limb maintained full contact with a single force plate throughout the entirety of stance phase, the participant maintained a forward gaze, gait was not visibly altered or abnormal, and the participant walked within  $\pm 5\%$  of the average walking speed measured during the practice trials.<sup>5,9,19,22</sup>

Kinematic data were collected at a sampling frequency of 120 Hz using a 10-camera, 3-dimensional motion-capture

system (Vicon, Nexus; Vicon Motion Systems), and kinetic data were collected at a frequency of 1200 Hz using the force plates.

**Gait Biomechanics Processing.** Biomechanical data were imported into Visual 3D (v2021.09.01; C-Motion) for processing each of the 5 trials after data collection. Kinematic and kinetic data were low-pass filtered at 10 Hz with a fourth-order recursive Butterworth filter.<sup>6,9,22,25,26</sup> Using custom Visual 3D and MATLAB codes (MATLAB version R2022a; Mathworks, Inc), we calculated the following discrete biomechanical variables during stance phase: first and second peak vGRF; *midstance minimum vGRF*, defined as the lowest discrete vGRF value between 33% to 66% of stance phase; peak internal KEM; peak internal KAM; and peak KFA. Peak KEM, KAM, and KFA were calculated from the first 50% of stance phase.

All biomechanical outcomes were analyzed on a local coordinate system.<sup>26</sup> Knee kinematic values were calculated as the angle of the shank relative to the thigh using Euler angles, and positive sagittal-plane values were defined as *flexion*. Hip-joint centers were calculated via the Bell and Brand hip joint CODA coordinate system; knee- and ankle-joint centers were calculated as the radius of half the distance between the medial and lateral epicondyles and malleoli, respectively.<sup>27</sup> Internal joint moments were calculated via traditional inverse dynamics in Visual 3D. Body weight (BW) was calculated from the force-plate measurements during the static trial and used to normalize vGRF data to BW; KAM and KEM were normalized to the product of BW \* height (in meters).<sup>5,11,19,21</sup> The stance phase of gait was considered to be the interval between initial contact (vGRF  $\geq 20$  N) and toe-off (vGRF  $\leq 20$  N). Stance phase was non-time-normalized to avoid the dampening of discrete peak values. The real-time walking speeds that were calculated for



**Figure 1. Receiver operating characteristic (ROC) curve for habitual walking speed identifying clinically important knee-related symptoms in individuals 6 months after anterior cruciate ligament reconstruction. A gait speed cutoff value of 1.27 m/s was found to optimize sensitivity (0.58) and specificity (0.75), as indicated by the star, for identifying individuals with clinically important knee-related symptoms. Overall, the ROC curve demonstrated low accuracy (area under the curve [AUC] = 0.66; 95% CI = 0.51, 0.78). Abbreviation: Odds, odds ratio.**

each gait trial using the timing gates were only used to ensure that a consistent gait speed was maintained for each data-collection trial (ie,  $\pm 5\%$  of average walking speed during practice trials) and not the speeds used in statistical analyses. Habitual walking speed values used in statistical analyses were calculated using the trajectories of the sacral-plate markers as the participant travelled over the force plates (0.91 m) during each gait trial.<sup>5,9,19,22</sup> The average habitual walking speed calculated from the sacral-marker trajectories from each of the 5 trials was defined as the *habitual walking speed* used for statistical analyses.

## Statistical Analyses

All statistical analyses were performed using SPSS (version 28.0; IBM Corp). Means and standard deviations were calculated for all continuous variables (eg, kinetics, kinematics, habitual walking speed, and KOOS scores); frequencies and percentages were calculated for demographic dichotomous variables. Normality of continuous data was evaluated via the Shapiro-Wilk test before analyses. Height, mass, months post-ACLR, and KOOS QOL were normally distributed, whereas age, KOOS Symptoms, KOOS Pain, KOOS Sports, and KOOS ADL were not normally distributed. The appropriate parametric (independent *t* test) or nonparametric (Wilcoxon

rank sum test) statistical test was subsequently used to evaluate mean differences of continuous variables between the symptomatic and asymptomatic groups (Table 1). Cohen's *d* effect sizes were calculated via pooled standard deviation to estimate between-group effects. We interpreted effect sizes of 0.20 as *small*, 0.50 as *medium*, and 0.80 as *large*. To address our primary aim, we constructed separate receiver operating characteristic (ROC) curves (sensitivity versus 1 – specificity) to determine the individual capacity of the continuous variables of interest (habitual walking speed; first and second peak vGRF; midstance minimum vGRF; and peak KFA, KEM, and KAM) to identify symptom status. The area under the curve (AUC) and corresponding 95% confidence intervals were used to determine the accuracy of each continuous variable for identifying symptomatic individuals. The strength of the AUC was described as follows: *perfect* (AUC = 1.0), *highly accurate* ( $0.9 < \text{AUC} < 1.0$ ), *moderately accurate* ( $0.7 < \text{AUC} \leq 0.9$ ), *less accurate* ( $0.5 < \text{AUC} \leq 0.7$ ), or *noninformative test* (AUC < 0.5).<sup>28</sup> A *significant AUC* was defined as having a 95% CI that did not span 0.5.<sup>28</sup> Cutoff scores of the continuous variables were values that optimized sensitivity and specificity for accurately identifying patients with clinically significant knee-related symptoms. Optimal values were defined as the values positioned closest to the upper left corner of the ROC curve that maximized the sensitivity and specificity values closest to 1. Secondly, logistic regression was used to generate odds ratios and corresponding 95% CIs for experiencing clinically significant knee-related symptoms based on ROC curve cutoff values.

## RESULTS

### ROC Predictive Capacity and Odds Ratios

**Habitual Walking Speed.** Habitual walking speed (all participants =  $1.24 \pm 0.12$  m/s, symptomatic group =  $1.23 \pm 0.02$  m/s, asymptomatic group =  $1.30 \pm 0.02$  m/s) demonstrated significant low accuracy (AUC = 0.66; 95% CI = 0.51, 0.78) for identifying symptomatic individuals. A cutoff walking speed of 1.27 m/s maximized sensitivity (0.55) and specificity (0.75; Figure 1). Individuals who walked at a speed  $\leq 1.27$  m/s demonstrated a 3.13 (95% CI = 1.06, 9.21) times greater odds of exhibiting symptoms compared with participants who walked at a speed  $> 1.27$  m/s (Tables 2 and 3).

**First Peak vGRF.** First peak vGRF (all participants =  $1.05 \pm 0.06$  BW, symptomatic group =  $1.06 \pm 0.01$  BW, and asymptomatic group =  $1.07 \pm 0.02$  BW) demonstrated low accuracy (AUC = 0.62; 95% CI = 0.48, 0.76) for identifying

**Table 2. Group Characteristics and Areas Under the Curve (AUCs) for Gait Variables Identifying Symptomatic Individuals 6 Months After Anterior Cruciate Ligament Reconstruction**

	Entire Group (N = 71)	Symptomatic (n = 51)	Asymptomatic (n = 20)	AUC (95% CI)
First peak vGRF, BW	$1.05 \pm 0.06$	$1.05 \pm 0.06$	$1.07 \pm 0.07$	0.62 (0.48, 0.76)
Midstance minimum vGRF, BW	$0.80 \pm 0.06$	$0.81 \pm 0.06$	$0.78 \pm 0.05$	0.69 (0.55, 0.83) <sup>a</sup>
Second peak vGRF, BW	$1.09 \pm 0.06$	$1.08 \pm 0.06$	$1.12 \pm 0.04$	0.76 (0.63, 0.88) <sup>a</sup>
Walking speed, m/s	$1.24 \pm 0.12$	$1.23 \pm 0.02$	$1.30 \pm 0.02$	0.66 (0.51, 0.78) <sup>a</sup>
Peak KFA, °	$8.92 \pm 5.63$	$9.13 \pm 5.57$	$8.39 \pm 5.90$	0.47 (0.32, 0.61)
Peak KAM, N-m/kg	$-0.019 \pm 0.008$	$-0.023 \pm 0.009$	$-0.011 \pm 0.007$	0.60 (0.45, 0.72)
Peak KEM, N-m/kg	$-0.023 \pm 0.013$	$-0.018 \pm 0.013$	$-0.024 \pm 0.013$	0.58 (0.43, 0.73)

Abbreviations: BW, body weight; KAM, internal knee-abduction moment; KEM, internal knee-extension moment; KFA, knee-flexion angle; ROC, receiver operating characteristic; vGRF, vertical ground reaction force.

<sup>a</sup> Statistically significant ROC AUC (95% CI does not span 0.5).

**Table 3. Contingency Table for Gait Variables and Clinically Significant Knee-Related Symptoms**

	Symptom Status		Total
	Symptomatic	Asymptomatic	
Walking speed, <sup>a</sup> m/s			
≤1.27	32	7	39
>1.27	19	13	32
Total	51	20	71
Midstance minimum vGRF, <sup>b</sup> BW			
<0.82	24	17	41
≥0.82	27	3	30
Total	51	20	71
Second peak vGRF, <sup>c</sup> BW			
≤1.11	41	6	47
>1.11	10	14	24
Total	51	20	71

Abbreviations: BW, body weight; OR, odds ratio; vGRF, vertical ground reaction force.

<sup>a</sup> Cutoff value = 1.27 m/s (OR = 3.13; 95% CI = 1.06, 9.21).

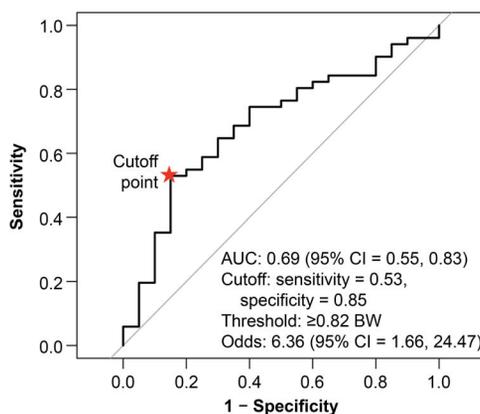
<sup>b</sup> Cutoff value = 0.82 BW (OR = 6.36; 95% CI = 1.66, 24.47).

<sup>c</sup> Cutoff value = 1.11 BW (OR = 9.57; 95% CI = 2.94, 31.34).

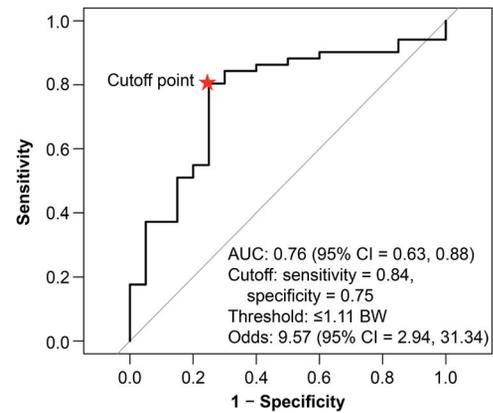
symptomatic individuals; however, the AUC was not statistically significant because the 95% CI spanned 0.5.

**Midstance Minimum vGRF.** Midstance minimum vGRF (all participants =  $0.81 \pm 0.05$  BW, symptomatic group =  $0.81 \pm 0.01$  BW, and asymptomatic group =  $0.78 \pm 0.01$  BW) demonstrated low accuracy (AUC = 0.69; 95% CI = 0.55, 0.83) for identifying symptomatic individuals. A midstance minimum cutoff value of 0.82 BW optimized sensitivity (0.53) and specificity (0.85; Figure 2). Individuals who exhibited a midstance minimum vGRF  $\geq 0.82$  BW demonstrated a 6.36 (95% CI = 1.66, 24.47) times greater odds of exhibiting symptoms compared with those who demonstrated a midstance minimum vGRF  $< 0.82$  BW (Tables 2 and 3).

**Second Peak vGRF.** Second peak vGRF (all participants =  $1.09 \pm 0.06$  BW, symptomatic group =  $1.08 \pm 0.01$  BW, and



**Figure 2. Receiver operating characteristic (ROC) curve for midstance minimum vertical ground reaction force (vGRF) identifying clinically important knee-related symptoms in individuals 6 months after anterior cruciate ligament reconstruction. A vGRF midstance minimum cutoff value of 0.82 body weights (BW) was found to optimize sensitivity (0.53) and specificity (0.85), as indicated by the star, for identifying individuals with clinically important knee-related symptoms. Overall, the ROC curve demonstrated low accuracy (area under the curve [AUC] = 0.69; 95% CI = 0.55, 0.83). Abbreviation: Odds, odds ratio.**



**Figure 3. Receiver operating characteristic (ROC) curve for second peak vertical ground reaction force (vGRF) identifying clinically significant knee-related symptoms in individuals 6 months after anterior cruciate ligament reconstruction. A second peak vGRF cutoff value of 1.11 body weights (BW) was found to optimize sensitivity (0.84) and specificity (0.75), as indicated by the star, for identifying individuals with clinically significant knee-related symptoms. Overall, the ROC curve demonstrated moderate accuracy (area under the curve [AUC] = 0.76; 95% CI = 0.63, 0.88). Abbreviation: Odds, odds ratio.**

asymptomatic group =  $1.12 \pm 0.01$  BW) exhibited moderate accuracy (AUC = 0.76; 95% CI = 0.63, 0.88) for identifying symptomatic individuals. A cutoff value of 1.11 BW for second peak vGRF optimized sensitivity (0.84) and specificity (0.75; Figure 3). Individuals who exhibited a second peak vGRF  $\leq 1.11$  BW demonstrated a 9.57 (95% CI = 2.94, 31.34) times greater odds of exhibiting symptoms compared with those who presented with a second peak vGRF  $> 1.11$  BW (Tables 2 and 3).

**Peak KEM.** Peak KEM demonstrated low accuracy (AUC = 0.58; 95% CI = 0.43, 0.73) for identifying symptomatic individuals, with an AUC that was not statistically significant.

**Peak KAM.** Peak KAM also demonstrated low accuracy (AUC = 0.60; 95% CI = 0.45, 0.72) for identifying symptomatic individuals; however, the AUC was not significant.

**Peak KFA.** Peak KFA was not informative (AUC = 0.47; 95% CI = 0.32, 0.61) in identifying symptomatic individuals.

## DISCUSSION

At 6 months post-ACLR, habitual walking speed, midstance minimum vGRF, and second peak vGRF demonstrated the capacity to identify individuals with clinically significant knee-related symptoms with low to moderate accuracy. Conversely, peak KEM, KAM, and KFA did not demonstrate the same capacity to accurately identify symptomatic individuals. Specifically, individuals post-ACLR with slower habitual walking speeds, greater midstance minimum vGRF, and smaller second peak vGRF were found to have greater odds of experiencing clinically significant knee-related symptoms compared with those who walked faster, had smaller midstance minimum vGRF, and had greater second peak vGRF. Our findings support and add to previous work indicating that slower habitual gait speeds, greater midstance minimum vGRF, and smaller second peak vGRF are linked to clinically significant knee symptoms post-ACLR by determining critical thresholds and

corresponding threshold properties (ie, sensitivity, specificity, and odds ratios) for walking speed, midstance minimum vGRF, and second peak vGRF to accurately identify symptomatic individuals.<sup>5,19</sup> The critical thresholds and corresponding properties reported in our study may be important for the following: (1) guiding the development of clinical screening procedures that identify individuals at high risk for experiencing significant knee-related symptoms post-ACLR and (2) establishing therapeutic targets for precision gait retraining interventions aimed at modifying gait biomechanics linked to persistent knee-related symptoms post-ACLR.

Slower habitual walking speed has been linked to a greater incidence of radiographic and symptomatic OA,<sup>14</sup> along with serum biomarker concentrations indicative of cartilage breakdown after ACLR.<sup>11,16</sup> Previous researchers have found that individuals with ACLR walk slower than healthy controls,<sup>6,22</sup> and symptomatic individuals with ACLR walk slower than their asymptomatic counterparts.<sup>5</sup> The cutoff value of >1.27 m/s that we determined for identifying asymptomatic individuals with ACLR is similar to the habitual walking speed demonstrated by uninjured controls, 1.30 m/s,<sup>6,22</sup> and is a similar speed reported for asymptomatic individuals in other ACLR cohorts.<sup>29</sup> Similarly, previous research reports that symptomatic individuals 6 to 12 months post-ACLR walk at an average speed of 1.24 m/s, which is slower than our 1.27 m/s threshold and further supports our findings.<sup>5,29</sup> Furthermore, slower habitual walking speeds are associated with joint tissue-related changes post-ACLR including worse articular cartilage composition in the medial femoral condyle<sup>11</sup> and greater serum concentrations of biomarkers related to type II collagen breakdown.<sup>16</sup> Although our study was not designed to determine causal associations between habitual walking speed and clinically significant knee-related symptoms, it is possible that slower habitual walking speeds may influence changes in cartilage health and thus patient-reported knee symptoms. Articular cartilage is viscoelastic and therefore deforms under compressive stress in a time-dependent manner.<sup>30</sup> Slower walking speeds may exert compressive forces to joint tissues over longer durations as stance time increases, and previous research has demonstrated that slower habitual walking speed is associated with greater femoral cartilage deformation assessed via ultrasonography.<sup>31</sup> Future mechanistic studies are needed to accurately estimate causal effects and confirm the hypothesis that slower habitual walking speeds lead to changes in joint-tissue health and worse patient-reported outcomes. Regardless of the cause of the association, our study adds to robust previous evidence and highlights potential clinical value of monitoring habitual walking speed as an indicator of clinically significant knee-related symptoms.<sup>11,14-16</sup>

Research evaluating limb-level loading, patient-reported knee symptoms, and biomarkers indicative of deleterious cartilage composition changes consistent with future PTOA development post-ACLR have largely focused on investigating gait events early in stance phase when the limb attenuates forces after contacting the ground.<sup>13,17</sup> Previous investigators have documented that peak vGRF, peak KEM, and peak KAM are lower in the first half of stance within the first 6 to 12 months post-ACLR compared with uninjured controls.<sup>6,22</sup> Recently, research has also reported that, at 6 months post-ACLR, individuals with ACLR demonstrate greater vGRF at midstance and smaller second peak vGRF compared with uninjured controls.<sup>6,22</sup> Research

has shown that symptomatic individuals <12 months post-ACLR demonstrate greater vGRF during midstance and smaller second peak vGRF compared with asymptomatic individuals.<sup>5</sup> To be consistent with previous evidence that demonstrated differences in midstance between 32% and 53% of stance, we extracted the discrete minimum vGRF value from between 33% to 66% stance phase and found the midstance minimum occurred between 48% to 49% of stance phase for the symptomatic and asymptomatic groups in our study.<sup>5</sup> Greater midstance minimum vGRF is most strongly associated with worse cartilage composition in the first 12 months post-ACLR compared with other discrete points during the vGRF waveform (eg, first and second peak vGRF).<sup>9</sup> Our study adds to these previous findings by demonstrating that midstance minimum vGRF and second peak vGRF are more strongly associated with clinically relevant knee symptoms than first peak vGRF at 6 months post-ACLR. Furthermore, peak KEM, KAM, and KFA did not demonstrate capabilities for identifying symptomatic individuals in this study. We chose to evaluate KEM and KAM during the first 50% of stance phase because this variable is commonly evaluated in the literature, yet it is possible that other KEM- and KAM-related metrics that incorporate data from other parts of stance may still be informative.<sup>7,17</sup> Thus, although peak KEM, KAM, and KFA are variables that differ between individuals post-ACLR and uninjured controls, vGRF at midstance and second peak vGRF may be relevant in identifying those with clinically significant knee-related symptoms.<sup>6,21</sup> Therefore, gait biomechanical evaluations can be employed as clinical functional tests to better serve patients by identifying those with greater odds of clinically relevant knee symptoms. Threshold values for gait biomechanical assessments may also be used to further guide clinical frameworks and as potential benchmarks for success in rehabilitation programs.

Although we demonstrated specific gait variables that identify individuals with clinically significant knee-related symptoms 6 months post-ACLR, our study had some limitations that can be used to inform future research. Given the observational and cross-sectional design of our study, the findings cannot explicitly establish causal relations between gait variables and clinically significant knee-related symptoms. Similarly, the analyses cannot predict future knee-symptom status or corroborate clinically significant knee-related symptoms with radiographic PTOA. We also only evaluated outcomes at 6 months post-ACLR, and previous research has found that aberrant gait patterns at 6 months are associated with worse longitudinal outcomes.<sup>19</sup> Therefore, future studies should conduct longitudinal analyses to determine if outcomes earlier than 6 months post-ACLR can predict persistent clinically relevant knee symptoms >12 months post-surgery. In addition, we evaluated linear associations between gait variables and clinically significant knee-related symptoms, and these associations may be nonlinear; however, evaluating linear associations in this cohort is likely acceptable, as most individuals did not demonstrate excessive vGRF values or walking speeds > 1.30 m/s. Some bias may be introduced when using continuous KOOS scores to dichotomize individuals as symptomatic or asymptomatic. To overcome some of the potential bias of external validity, future studies may be done to analyze which gait variables are associated with symptomatic status in independent samples or when using other methods to define symptomatic and asymptomatic individuals.

When interpreting our findings, the homogeneous surgical nature of our cohort (ie, 70 participants received a bone-patellar tendon-bone autograft, 1 participant received a quadriceps tendon autograft, and all reconstruction surgeries were performed by 1 of 3 participating orthopaedic surgeons at our university) should be considered, and future research may seek to implement similar analyses to determine whether these findings apply to individuals who received other grafts or underwent reconstruction surgery at a different orthopaedic clinic. Lastly, our analyses were conducted during barefoot overground walking.

## CONCLUSIONS

We found that slower habitual walking speed, greater midstance minimum vGRF, and smaller second peak vGRF are gait biomechanical variables that are capable of accurately identifying patients with clinically significant knee-related symptoms 6 months post-ACLR. We also identified specific threshold values for each gait variable that demonstrated increased odds of experiencing clinically significant knee-related symptoms at a critical timepoint of the ACLR recovery process. The identified gait variables and corresponding thresholds may be used to inform future work to improve the identification of individuals with greater odds of exhibiting clinically significant knee-related symptoms. These data may be considered when developing future clinical screening methods, inclusion criteria for clinical trials, and benchmarks for early intervention and rehabilitation success post-ACLR.

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