Table 2
Multivariate Linear Regression Between Gait Biomechanics Outcomes and Measures of Synovial MVD and Edemic MVD ($n = 98$)

Outcomes:	Edemic MVD (vessels/mm²)[1]	MVD (vessels/mm²)[1]	Edemic MVD adjusted for MVD (vessels/mm²)[2]
1st Peak Knee Adduction Moment (Nm)[3]	**0.539 (0.237 to 0.841)**	0.361 (-0.165 to 0.887)	**0.437 (0.170 to 0.703)**
Knee Adduction Moment Impulse (Nm•s)	**0.735 (0.343 to 1.128)**	**0.704 (0.017 to 1.392)**	**0.551 (0.192 to 0.910)**
Peak Knee Flexion Moment (Nm)	-0.349 (-0.701 to 0.003)	-0.357 (-0.952 to 0.238)	-0.247 (-0.560 to 0.066)
Peak Knee Extension Moment (Nm)	0.299 (-0.004 to 0.602)	0.236 (-0.279 to 0.750)	0.232 (-0.036 to 0.499)
Peak Internal Rotation Moment (Nm)	**1.082 (0.141 to 2.023)**	0.361 (-1.251 to 1.974)	**0.978 (0.155 to 1.801)**
Peak External Rotation Moment (Nm)	-0.228 (-6.496 to 6.040)	-4.805 (-15.22 to 5.607)	1.199 (-4.308 to 6.707)

MVD = microvessel density; EMVD = edemic microvessel density; mm= millimeter; Nm = newton-meter; s = second
[1]Adjusting for sex, age, BMI, and gait speed
[2]Adjusting for sex, age, BMI, gait speed, and MVD
[3]Two patient had no discernable 1st Peak Knee Adduction Moment, therefore $n = 96$ for the 1st Peak Knee Adduction Moment models

Table 3
Multivariate Linear Regression Between Knee Adduction Moment Impulse and Synovial Fluid Endoglin and PlGF Concentration ($n = 80$)[1]

Outcome:	Endoglin (pg/ml)	PlGF (pg/ml)
Predictor	β estimate (95%CI)	β estimate (95%CI)
Intercept	196.4 (-302.9 to 695.7)	-35.35 (-260.8 to 190.1)
Sex		
Female	Reference	Reference
Male	30.12 (-40.15 to 100.4)	0.976 (-30.65 to 32.60)
Age (years)	-1.002 (-5.239 to 3.234)	**2.186 (0.270 to 4.103)**
BMI (kg/m²)	5.916 (-0.704 to 12.54)	-1.503 (-4.474 to 1.467)
Gait Speed (m/s)	-70.49 (-245.1 to 104.2)	18.52 (-59.65 to 96.70)
Knee Adduction Moment impulse (Nm•s)	**2.486 (0.185 to 4.786)**	**1.493 (0.460 to 2.526)**

pg = picogram, ml = millilitre, CI = confidence interval, BMI = body mass index, kg = kilogram, m = meter, s = second, Nm = newton=meter, PlGF = placental growth factor
[1]PlGF concentration could not be measured in one patient's synovial fluid, therefore $n = 79$ for PlGF

Table 1. Variables contributing to prediction of worsening knee pain over 2 years (Frequency % across 100 test iterations from an ensemble prediction model[a])

***The top ten variables selected during 100 iterations* (n= frequency %)**

- CES-D[b] (100): depressive symptoms
- Gait speed (90) : walking speed in meters/second
- BMI[b] (82) : Body Mass Index
- Phase Coordination Index (72) : a measure of the bilateral coordination of gait
- Stride Time coefficient of variation (61) : quantifies magnitude of stride-to-stride variability in stride time
- Gait Asymmetry (51) : a measure of temporal left-right asymmetry of swing time
- Phase Difference (51) : % of the absolute difference from 180 degrees; a higher value indicates increased asymmetry
- Walking pain at 144 months, for designated knee (47)
- Stride Time (47): Mean duration of the gait cycle (i.e. a stride)
- Step Length (40) : Distance walked divided by # steps taken

Notes a.Algorithms included: Bayesian adaptive regression trees (BART), extreme gradient boosting, generalized linear models with convex penalties (that consisted least absolute shrinkage and selection operator [LASSO], ridge regression, and elastic net), logistic regression, random forest, and support vector machine.
b. BMI: Body Mass Index; CES-D: Center for Epidemiologic Studies Depression Scale; KL: Kellgren and Lawrence Grading System.
c. Gait parameters extracted include those describing spatiotemporal features (e.g., step length, velocity, cadence, stride time, double stance time, swing time), gait symmetry (e.g., step acceleration symmetry, phase coordination index, swing time symmetry), and gait variability (e.g., step regularity, entropy).

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MACHINE LEARNING FOR ASSOCIATION OF WEARABLE-SENSOR DERIVED GAIT MEASURES WITH WORSENING KNEE PAIN OVER 2-YEARS: THE MULTICENTER OSTEOARTHRITIS STUDY

K.L. Bacon [1], D.T. Felson [1], S.R. Jafarzadeh [1], V.B. Kolachalama [1], J.M. Hausdorff [2], E. Gazit [3], N.A. Segal [4], C.E. Lewis [5], M.C. Nevitt [6], D. Kumar [1]. [1] *Boston Univ. Sch. of Med., Boston, MA;* [2] *Tel Aviv Univ., Tel Aviv, Israel;* [3] *Tel Aviv Sourasky Med. Ctr., Tel Aviv, Israel;* [4] *Univ. of Kansas Med. Ctr., Kansas City, KS;* [5] *Univ. of Alabama at Birmingham, Birmingham, AL;* [6] *Univ. of California, San Francisco, CA*

Purpose: Altered gait is related to structural worsening of knee osteoarthritis (OA). However, it is not known if altered gait is associated with increased risk of pain worsening over time. We applied machine learning approaches to gait data collected in a large epidemiological cohort to identify markers of gait alterations in people with worsening knee pain over 2 years.

Methods: The MultiCenter Osteoarthritis (MOST) study includes participants age 45-90 with, or at risk for, knee OA. Participants were categorized by presence/absence of worsening knee pain over 2-years, defined as an MCID increase in WOMAC pain (2+ points on a 0-20 point scale). Gait was assessed at the 144 month visit using inertial sensors (OPAL, APDM, Portland, OR) worn on the trunk and both ankles during a 20-meter walk test in which participants walked at a self-selected pace. We used an ensemble machine learning technique ("super learning") that uses multiple algorithms (Table 1 footnote) to improve outcome classification. All gait variables (for both legs, Table 1 footnote), presence of pain during walking and K-L grade of each knee, age, BMI, depressive symptoms (CES-D), and sex were entered as possible predictors in the ML process. Data were randomly split into 70% training and 30% test sets; the data split and model training and testing were repeated 100 times, with values saved for each run. We used a variable importance measure (VIM) statistic to identify the top 10 variables that most frequently contributed to the prediction of worsening knee pain during the ML process. A Generalized Estimating Equation (GEE) model accounting for correlated outcomes (2 knees/person) was used to evaluate the association of "important" variables with worsening knee pain over 2 years. We evaluated model variables for collinearity by reviewing correlations, tolerance values, and variable inflation factors. All continuous variables included in the model were standardized. Potential confounders age, BMI, sex, baseline walking pain and K-L status were included in the model even if they were not selected in the ML process.

Results: Our sample included 4464 knees for 2232 participants (mean age=63.6 SD=10.5 years; 57% female). 19.5% of knees had worsening pain over 2 years. The top contributing variables from the ensemble machine learning process (AUC=0.69) are shown in Table 1. In a GEE regression model using predictors chosen by the ensemble ML process (Table 2), longer step length was associated with increased likelihood of worsening pain over 2 years.

Conclusions: Our results suggest higher step length was associated with worsening knee pain over 2 years in individuals with or at risk of knee OA. Walking with longer step length is associated with greater knee joint loading and shortening step length has been recommended as a gait intervention to reduce knee joint loading in people with knee OA. Our findings, using gait data from a large cohort and using machine learning to agnostically identify important gait variables, provide further support for this recommendation.

Table 2. GEE regression model: association of worsening knee pain over 24 months with predictors chosen by ensemble ML methods. Adjusted odds ratio (95% confidence intervals) are presented.

Parameters[c]	All knees, Total=4375, Cases=851
Phase Coordination Index (PCI)[a]	1.06(0.93-1.21)
Gait Asymmetry[a]	1.11(0.99-1.26)
Stride Time[a]	0.99(0.81-1.20)
Step Length[a]	**1.34(1.05-1.72)**
Stride Time coefficient of variation[a]	0.99(0.91-1.07)
Walking pain, ipsilateral limb (baseline)	**0.32(0.21-0.48)**
Walking pain, contralateral limb (baseline)	1.32(0.97-1.80)
Gait Speed[a]	0.76(0.54-1.06)
K-L[b] Grade >1, ipsilateral limb (baseline)	**1.36(1.08-1.71)**
K-L[b] Grade >1, contralateral limb (baseline)	**1.28(1.02-1.60)**
CES-D[a]	**1.23(1.13-1.35)**
BMI[a]	**1.16(1.06-1.28)**
Age[a]	0.98(0.87-1.09)
Male Sex	**0.72(0.58-0.90)**
Race	**1.31(1.03-1.67)**

Notes
a. Continuous variables are standardized: PCI, Gait Asymmetry, Stride Mean Time, Average Step Length, Stride Time CV, age, BMI, CES_D, Gait Speed
b. K-L: Kellgren and Lawrence Grading System
c. Phase Difference variable was dropped from the GEE model due to collinearity concerns.

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ASSOCIATION OF CHANGES IN GAIT BIOMECHANICS AFTER HIGH TIBIAL OSTEOTOMY WITH SUBSEQUENT TOTAL KNEE REPLACEMENT

C.A. Primeau [1,2,3,4], T.B. Birmingham [1,2,4,3], K.M. Leitch [4,3], D.M. Bryant [1,2,3], K.R. Willits [5,2,3], R.B. Litchfield [5,2,3], P.J. Fowler [3], R. Giffin [5,2,3,4]. [1] *Sch. of Physical Therapy - Western Univ., London, ON, Canada;* [2] *Bone and Joint Inst. - Western Univ., London, ON, Canada;* [3] *Fowler Kennedy Sport Med. Clinic, London, ON, Canada;* [4] *Wolf*