ORIGINAL RESEARCH ARTICLE





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Abstract

Background Patellofemoral pain (PFP) is among the most common injuries in runners. While multiple risk factors for patellofemoral pain have been investigated, the interactions of variables contributing to this condition have not been explored. This study aimed to classify runners with patellofemoral pain using a combination of factors including biomechanical, anthropometric, and demographic factors through a Classification and Regression Tree analysis.

Results Thirty-eight runners with PFP and 38 healthy controls (CON) were selected with mean (standard deviation) age 33 (16) years old and body mass index 22.3 (2.6) kg/m². Each ran at self-selected speed, but no between-group difference was identified (PFP = 2.54 (0.2) m/s x CON = 2.55 (0.1) m/s, P = .660). Runners with patellofemoral pain had different patterns of interactions involving braking ground reaction force impulse, contact time, vertical average loading rate, and age. The classification and regression tree model classified 84.2% of runners with patellofemoral pain, and 78.9% of healthy controls. The prevalence ratios ranged from 0.06 (95% confidence interval: 0.02-0.23) to 9.86 (95% confidence interval: 1.16-83.34). The strongest model identified runners with patellofemoral pain as having higher braking ground reaction force impulse, lower contact times, higher vertical average loading rate, and older age. The receiver operating characteristic curve demonstrated high accuracy at 0.83 (95% confidence interval: 0.74-0.93; standard error: 0.04; P < .001).

Conclusions The classification and regression tree model identified an influence of multiple factors associated with patellofemoral pain in runners. Future studies may clarify whether addressing modifiable biomechanical factors may address this form of injury.

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Key Points

- This study highlights interactions between multiple biomechanical factors associated with patellofemoral pain.
- Interactions between braking ground reaction force impulse, contact time, vertical average loading rate, and age
 correctly identified runners with patellofemoral pain and controls.
- Step rate, sex, and body mass index were not predictors of patellofemoral pain in runners when a classification and regression tree analysis was used

Keywords Etiology, Biomechanics, Running injuries, Statistical approach

Background

Running is a popular activity that has clear cardiovascular and other health benefits [1]. However, participation in running has an annual rate of injury estimated at 19.4% to 79.3% [2], particularly in novice runners [3, 4]. The most common location of injury is the knee, and a strong risk factor for sustaining a knee injury is history of a previous injury in the past year [2, 5].

Patellofemoral Pain (PFP) is one of the most common types of knee injury in runners. It is defined as pain around or behind the patella during functional activities such as running, squatting, climbing and descending steps [6–8]. While conservative treatment can be effective, Collins and colleagues [9] found nearly half of patients had incomplete recovery at one year and Lankhorst and colleagues [10] identified over half of all patients may have incomplete recovery in 5–8 years.

Given that PFP is both common and challenging to treat, it is important to identify factors that may be related to PFP in runners [11-13]. Running biomechanical studies have added value in determining key kinetic and kinematic variables for a running-related injury (RRI) including PFP. Ground reaction force (GRF) variables associated with the impact phase of running, such as vertical loading rates have been associated with RRIs in general [14, 15] and specific to PFP [15]. However, other studies have found the opposite [16-18], suggesting the value of further study of these variables. In the anteroposterior direction, reduced braking ground reaction force impulse (BGRFI) has been noted in runners with PFP [19]. Additionally, greater contact time has been found in these runners [19]. Also, while step rate has not been associated with PFP [20], increases in step rate of 7.5-10% has been shown to reduce symptoms in those with PFP [21-23].

Other factors may also contribute to PFP. For example, while one study found no association of sex and PFP [13], two separate investigations have reported that females have approximately 2 times the incidence of PFP compared to their male counterparts [24, 25]. While higher body mass index (BMI) and age have not been found

to be related to PFP [12, 26], further study is needed to determine whether they might interact with other factors to increase the risk of PFP.

Prior studies have explored risk factors for PFP; however, the association of different biomechanical, anthropometric, and demographic factors has not been consistent. These studies have been limited to addressing the bivariate associations between risk factors and PFP. The assumption of non-linearity must be considered in sports injuries [27]. It may be helpful to search for the interactions between risk factors to guide understanding of this condition [27, 28]. Regression models and Classification and Regression Trees (CART) are statistical approaches that can be used to explore risk factors for PFP. Regression models determine the average effect of an independent variable on an outcome while CART identifies subgroups of a population with common aspects that influence an outcome [29].

Complex problems, such as PFP, must be analyzed through the detection of interactions and not through the addition of factors. The main advantage of the CART analysis is that the assumption of linearity is not assumed and interactions between risk factors are identified by the development of clinical prediction rules. As a result, CART analysis may be better than regression models to identify profiles of runners that share common characteristics that are associated with PFP. Besides the identification of subgroups, CART produces a visual multilevel tree that is easy to interpret even when more than three variables are included in the model [29].

Previous studies using the CART approach have been able to identify runners with Achilles tendinopathy [30] and soccer players who sustained a re-injury of the anterior cruciate ligament [31]. The objective of this study was to identify different patterns of interaction among biomechanical, anthropometric, and demographic factors associated with PFP in runners using a CART analysis. We hypothesized that interactions involving various aspects of the GRFs and spatiotemporal variables, along with sex, age, body mass index, would correctly identify runners with and without PFP.

Methods

Study Design

This cross-sectional study followed the recommendations of STROBE (Strengthening the Reporting of Observational Studies in Epidemiology). Patients of the Spaulding National Running Center (SNRC) who were being treated for the primary condition of PFP were identified from clinic records and included as the injured cohort. A matched cohort of healthy runners were identified from a separate study.

Setting

The SNRC was founded in 2012 and it is an ambulatory outpatient clinic that specializes in the diagnosis, treatment, and prevention of RRIs including PFP. A standard biomechanical evaluation is performed to guide physical therapy exercises and gait retraining, as needed. Participants were self-referred or referred from their sports physicians, orthopedic surgeons, and family physicians. Data were collected from September 2012 to July 2022 using standard procedures of collecting relevant history and gait assessment. Clinical charts were reviewed from August 2022 to October 2022.

Participants

The injured group included runners with PFP who ran with a rearfoot strike pattern and were older than 18 years of age. Chart review of key aspects of history and examination findings were used to confirm the PFP diagnosis using the following criteria: pain around or behind the patella during running and at least one other task that engages the patellofemoral joint, including squatting, climbing, and descending steps, kneeling, or extending the knee with resistance [6]. Runners were excluded who presented with concomitant primary diagnoses, with underlying neurological/neuromuscular disorders, history of surgery in the lower extremity within six months of evaluation, or history of knee surgery at any time. Runners could have unilateral or bilateral symptoms, and the knee with highest pain intensity was used for analysis.

Healthy runners were identified from a study on the effects of footwear and foot strike pattern on running biomechanics. Participants were selected who were rearfoot strike runners with no RRIs 6 months prior the evaluation [30], no neurological/neuromuscular disorders, no history of surgery in the lower limbs in the 6 months prior to the evaluation, and no history of PFP. An equal number of healthy controls to injured runners were selected. Running speed is a potential confounding factor for biomechanical variables, so healthy participants were matched to the PFP group according to speed. The control runners came from a normative database of

healthy runners. As speed has a significant impact on ground reaction forces, subjects were matched for speed. Also, participants had to run at least 10 miles/week to be included.

As the data were collected on injured runners to guide clinical treatment, the Institutional Review Board approved this protocol with waiver of informed consent (Protocol 2017P000481). Written informed consent was obtained from each healthy participant prior to participation in a study designed to develop a normative database of healthy runners (2012P002373).

Data Collection

All participants (PFP and healthy control group (CON)) completed the same gait analysis on an instrumented treadmill embedded with two force plates (AMTI, Watertown, MA, USA; sampling rate = 1500 Hz). Sagittal plane high-speed video (125 fps) was used to determine foot strike pattern. Runners were classified as rearfoot strikers if they landed on the heel first [32]. A short warmup (slow run of 2 to 3 min) was provided followed by instructions for each runner to increase speed to reach a self-selected running speed, described as a comfortable training pace for an easy training run [15, 33]. After reaching the self-selected speed, 10 consecutive foot strikes were collected for analysis. Runners with PFP ran in their own shoes. The healthy runners were part of a larger study that required lab-issued shoes to accurately measure foot kinematics. However, they were provided a type of shoe that matched their habitual footwear.

Variables

The dependent variable was the presence of PFP. The independent variables included age, sex (male x female), BMI, vertical average loading rate (VALR), vertical instantaneous loading rate (VILR), braking ground reaction force impulse, contact time, and step rate.

Biomechanical Data Processing

Ground reaction force data were filtered at a cut-off frequency of 50 Hz using a low pass, fourth-order Butterworth filter. A custom program written in MATLAB (MathWorks, Natick, Massachusetts USA) was used to process data as reported previously [15, 32, 33]. The point of interest (POI) was defined as the first point above 75% of a subject's body weight (BW) with a vertical GRF slope less than 15 BW/s. The VALR (BW/s) region was defined as the largest region between 20 and 80% of the force at the POI with a continuous slope above 15 BW/s. The VILR (BW/s) was defined as the peak vertical load rate between any two successive points from 20 to 100% of the force at the POI. BGRFI (BW*s) was determined as the time integral of the anteroposterior GRF over stance [34]. Contact time (s) was considered as the time during which a vertical force greater than 10 N was applied to the force plate. Cadence was calculated in steps per minute.

Sample Size/Bias

No a priori sample size calculation was performed as the sample was one of convenience. Measures to avoid potential sources of bias are described below: (I) rigorous criteria were chosen to classify patients in the patellofemoral pain group [6] and control group; (II) variables were chosen to be those that were related with PFP [13, 15–19, 24–26] or changes in symptoms in PFP runners [21–23]; (III) the matching process was done before gathering biomechanical variables to eliminate selection bias.

Statistical Analysis

IBM SPSS (Statistical Package for Social Sciences, v.25) and Open-Epi were used to perform the statistical analysis. Normality was assessed using Shapiro–Wilk test and histograms. Parametric data were described as mean and standard deviation (SD) and non-parametric data as median and interquartile range (IQR). Categorical data were described as frequencies and percentages. A correlation matrix was performed within biomechanical variables to detect collinearity. In the case of collinearity (r > 0.71), only the most important variable was kept in the model. This was done to prevent splits that could overlap each other. A significance level of P < 0.05 was used.

The interactions between independent variables were assessed using a CART analysis. The predictors and their respective cut-off values that best classify the participants regarding the presence and absence of PFP were selected through CART. The predictors were selected based on the strength of association with the dependent variable (presence of PFP). The CART model begins with the total sample (node 0), and it is divided into 2 groups (sub-nodes) according to the best predictor and specific cut-off values. This process is applied recursively until the subgroups reach a minimum size or no improvement can be done (terminal node) [29, 35]. In the end, a tree representing the non-linear relationship among predictors that best classify the participants with and without patellofemoral pain is obtained. The criteria to produce the partitions were a minimum of 14 participants in each node to make a division and a minimum of 7 participants to generate a node [36]. Gini index of 0.0001 was used to maximize the node's homogeneity and a tenfold crossvalidation to avoid overfitting. Finally, a receiver operating characteristic (ROC) curve was created to verify the accuracy of the model and prevalence ratios (PR) with 95% confidence intervals (CI) were calculated for each terminal node to investigate the strength of associations.

Results

Data were collected from September 2012 to July 2022. Review of clinical charts from August 2022 to October 2022 identified 38 runners with PFP who met the inclusion criteria (Fig. 1). Therefore, 38 healthy controls were matched according to self-selected running speed. No between-group difference was found for this aspect (PFP=2.54 (0.2) m/s x CON=2.55 (0.1) m/s, P=0.660). Patients reported months experiencing symptoms of PFP, with a range from 0.5 months to 163 months reported. Descriptive data for group characteristics are presented in Table 1.

The correlation matrix identified interactions between VALR and VILR (r=0.99/ P<0.001). To avoid multicollinearity, VILR was removed from the CART analysis. Figure 2 illustrates the final model of the 4-level decision tree, including 8 nodes and 5 terminal subgroups. Terminal nodes 1, 4, and 8 classified runners with PFP while nodes 5 and 7 classified healthy runners. The CART analyses showed that the variables of BGRFI, contact time, VALR, and age identified runners with PFP. The CART model correctly classified 32 (84.2%) runners with PFP, and 30 (78.9%) of the healthy runners. Correct classification was achieved in most runners (81.6%), and the area under the ROC curve (accuracy) was 0.83 (95% CI 0.74–0.93; SE, 0.04; P<0.001).

Node 1 (low BGRFI), node 4 (high BGRFI and low contact time), and node 8 (high BGRFI, low contact time, high VALR and older age) accurately classified participants with PFP. Node 5 (high BGRFI, low contact time, low VALR) and node 7 (high BGRFI, low contact time, high VALR, and young age) accurately classified participants without PFP. Specific cut-off values are presented in Fig. 2. Statistically significant differences in the proportion of runners with and without PFP were found in nodes 1, 4, 5, and 8 (P < 0.05) (Table 2).

Discussion

The purpose of this study is to characterize differences in runners with PFP compared to uninjured runners using CART analysis. We hypothesized runners with PFP would exhibit different patterns of interactions among predictor variables compared to healthy controls. As expected, interactions among BGRFI, contact time, VALR, and age were captured through CART analysis. The interactions of different variables and combination of factors associated with PFP illustrates the challenges in isolating single risk factors for this condition.

BGRFI was the first variable to enter the CART model. The observed lower BGRFI in runners with PFP is consistent with a prior systematic review on biomechanical risk factors for RRIs that showed moderate evidence for a reduced BGRFI in runners with PFP [19]. It could be hypothesized that a reduced BGRFI could be related to a reduced knee extensor moment. Theoretically, this node may indicate a subgroup of participants that adopt a quadriceps avoidance running pattern. In one prior study, lower peak resultant patellofemoral joint reaction forces (PFJRFs) during running were found in females with PFP. The reductions in PFJRFs were seen in parallel with a reduction in knee extensor moment and were explained as a compensatory measure [37]. Therefore, rather than identify a risk, this node may reflect those runners who are trying to compensate for their symptoms.

We also noted that runners with PFP may have *higher* BGRFI through an interaction with greater contact time. Moderate evidence for higher contact time was reported in runners with PFP [19]. Previous studies have shown that a reduced step rate was related to higher BGRFI and greater contact time [38]. Theoretically, this node



Fig. 1 Study flowchart. FSP = foot strike pattern; NRFS = non-rearfoot strike pattern; PFP = patellofemoral pain

Table 1 Personal and biomechanical data for those with and without PFP (n = 76)

Variables	Total (N = 76)	PFP (N = 38)	CON (N = 38)
Sex. %			
Male Female	42 (55.3) 34 (44.7)	24 (63.2) 14 (36.8)	18 (47.4) 20 (52.6)
Age, y	33 (16)	34 (15)	31 (19)
Weight, kg	65.6 (15.7)	65.1 (14)	67.5 (17.5)
Height, cm	172.1 (18.4)	173.2 (8.4)	169.6 (21.4)
BMI, kg/m ²	22.3 (2.6)	22.3 (2.3)	22.2 (2.3)
VALR, BW/s	60.3 (25.5)	67.8 (21.3)	55.7 (23.1)
VILR, BW/s	69.4 (30.9)	77.2 (22.9)	65.8 (25.8)
BGRFI, BW*s	0.014 (0.002)	0.014 (0.002)	0.015 (0.002)
Contact Time, s	0.26 (0.02)	0.27 (0.02)	0.26 (0.02)
Step rate, steps/min	165.2 (9.6)	167.0 (8.9)	165.6 (10.4)

^a BGRFI = braking ground reaction force impulse; BMI = body mass index; CON = controls; PFP = patellofemoral pain; VALR = vertical average loading rate; VILR = vertical instantaneous loading rate

^b Continuous variables = mean (SD) or median (IQR)

^c Categorical variables = n (%)

may indicate a subgroup of participants with an overstride posture. This pattern may lead to greater knee flexion excursion during stance and increase negative knee work. An association between components of an overstride posture with peak knee flexion, quadriceps peak force, knee extensor moment, peak patellofemoral force and negative knee work was reported previously [38, 39]. The association between an overstride posture and PFP should be studied prospectively.

Runners who had increased BGRFI, and reduced contact time had an observed interaction in the CART model when accounting for elevated VALR and older age. Higher load rates were found in runners with PFP when compared with healthy controls [15]. It is intuitive that higher load rates may result in greater demands to the PF joint. Older runners present less contact time, leg stiffness, and knee excursion [40]. Theoretically, this pattern together with age-tissue changes such as reduction of skeletal muscle mass and muscle strength could potentially compromise the ability of the PF joint to dissipate energy. Previously, runners with PFP presented higher vertical stiffness [15] and reductions in relative skeletal muscle starting in the third decade were reported [41].

It was interesting to note that sex was not a significant factor in PFP given that it has been reported and is commonly stated that females are twice as likely to have PFP than their male counterparts. This may have been a function of the sex distribution of this study, whereby 24 of the PFP group were males and only 14 were female [24, 25]. This was a cross-sectional study with a convenience sample of runners with PFP. This sample reflects only the patients who sought care in the clinic. Our study may lack the power to detect differences regarding sex and that a prospective study may promote a different view regarding this aspect.

To our knowledge, this study is the first to assess the interactions between ground reaction forces, spatiotemporal, anthropometric, and demographic data through CART to characterize factors associated with PFP in runners. The model may have clinical implications when considering what biomechanical factors to include when evaluating the biomechanics of a runner with PFP. Results from nodes 1 and 8 may indicate that appropriate rehabilitation may be needed to improve the capacity of the knee joint to take further load during running. Results from node 4 may indicate that changes in running biomechanics may be required to impose less demand on the knee joint during this activity. Clinicians should focus on the identification of which interactions may represent a cause and which ones may represent a consequence. The goal is to recognize the pattern presented in the runner with PFP and choose the more suitable approach to help with their symptoms.

There are limitations to this study. The results must be interpreted with caution due to the very wide confidence intervals presented in the terminal nodes. Causal relationships cannot be inferred due to the design of the analysis. Also, a larger sample could provide different insight regarding the profiles of runners with PFP. The runners analyzed were limited to rearfoot strike runners, therefore it is unclear whether similar results would be obtained in non-rearfoot strike runners. Some evidence suggest that hip kinematics may be associated with PFP [19]. Unfortunately, kinematic data were not available for the PFP participants. Prior work has suggested training factors are strongly associated with RRIs [5], however, these were not available in all runners. While the analysis did consider BMI, other aspects of body composition were not measured. Higher body fat and lower skeletal muscle mass have been observed in women with PFP and these factors are associated with pressure hyperalgesia [42, 43]. PFP is influenced by a variety of biopsychosocial factors such as catastrophizing and pain-related fear [44]; the present study considered primarily the biomechanical factors. Future studies should include some of these aspects along with the variables presented in our paper.



Fig. 2 Classification and regression tree model for Patellofemoral Pain. BGRFI braking ground reaction force impulse; CI = confidence interval; CON = controls; PFP = presence of patellofemoral pain; PR = prevalence ratio; VALR = vertical average loading rate. Bold represents the largest proportion of subjects classified as PFP or CON at the terminal node

Conclusions

In conclusion, BGRFI, contact time, VALR, and age were the factors which best identified runners with current PFP. The model with these aspects correctly identified 84.2% of runners with PFP, and 78.9% of runners without PFP. The total correct classification was 81.6%. The area under the ROC curve was 0.83 indicating that our results were not due to chance. The profile that best classified participants with PFP was BGRFI higher than 0.012 BW*s, contact time lower than 0.29 s, VALR higher than 66.9 BW/s, and being older than 27.5 years of age. Interesting, step rate, sex, and BMI did not enter in the CART model. More research is needed to determine if these are causative or compensatory factors. Our results may serve as a basis for future prospective studies with the goal of identifying risk and protective profiles for PFP in runners. **Table 2** Prevalence Ratios and 95% Confidence Intervals for the profiles identified through the model (n = 76)

PR (95% CI)
4.95 (1.45–16.93)*
4.16 (1.04–16.60)*
9.86 (1.16–83.34)*
0.06 (0.02–0.23)*
0.29 (0.05–1.57)

* P < .05, proportion of participants with and without PFP

Abbreviations

Abbievia	1013		
BGRFI	Braking ground reaction force impulse		
BMI	Body mass index		
BW	Body weight		
CART	Classification and regression tree		
CI	Confidence interval		
CON	Control group		
FSP	Foot strike pattern		
GRF	Ground reaction force		
IQR	Interquartile range		
NRFS	Non-rearfoot strike pattern		
PFJRF	Patellofemoral joint reaction force		
PFP	Patellofemoral pain		
POI	Point of interest		
PR	Prevalence ratio		
ROC	Receiver operating characteristic		
RRI	Running-related injury		
SD	Standard deviation		
SPSS	Statistical package for social sciences		
STROBE	Strengthening the reporting of observational studies		
	Vertical average leading rate		
VALK	vertical average loading rate		
VILK	Vertical instantaneous loading rate		

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Author contributions

JRSJ participated in the conceptualization, methodology, and formal analysis. LWG participated with the resources, and data curation. CDJ participated with the resources, and data curation. JPCM participated in the conceptualization,

and supervision. TVL participated in the conceptualization and supervision. ISD participated in the conceptualization, resources, data curation and supervision. AST participated in the conceptualization, methodology, resources, data curation, and supervision. All authors contributed to the manuscript writing. All authors have read and approved the final version of the manuscript and agree with the order of presentation of the authors.

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Availability of Data and Materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics Approval and Consent to Participate

A waiver of informed consent was obtained from the Institutional Review Board at Mass General Brigham for data collected on PFP patients. For the study involving healthy runners, all study procedures were approved by the Institutional Review Board, and written informed consent was obtained from participants prior to innating study procedures.

Consent for Publication

Healthy participants completed a written informed consent for publication.

Competing interests

José Roberto de Souza Júnior, Logan Walter Gaudette, Caleb D. Johnson, João Paulo Chieregato Matheus, Thiago Vilela Lemos, Irene S. Davis, and Adam S. Tenforde declare that they have no conflict of interest.

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