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Ultrasound-detected effusion-synovitis is associated with greater limb loading rate asymmetry during walking post-ACL reconstruction: A pilot study

Matthew S Harkey^{a,*}, Corey D Grozier^a, Jessica Tolzman^a, Arjun Parmar^a, Molly Fagan^b, Katherine Collins^c, Christopher Kuenze^d, Ryan Fajardo^e

^aMichigan State University, 308W. Circle Drive 112, East Lansing 48824, MI, United States

^bGrand Valley State University, United States

^cUniversity of North Carolina at Chapel Hill, United States

^dUniversity of Virginia, United States

^eLansing Radiology Associates, United States

Abstract

Objective: Chronic inflammation and altered walking biomechanics are common after ACL reconstruction (ACLR) and contribute to the development of osteoarthritis. Clinically accessible techniques are needed to monitor inflammation (ultrasound-assessed effusion-synovitis) and walking biomechanics (force-measuring insoles), and they must improve the translation of these assessments and determine whether inflammation and walking biomechanics are related in patients after ACLR. This study aimed to determine the association between ultrasound-detected knee effusion-synovitis and limb loading asymmetries during walking in patients 1–5 years post-ACLR.

Design: 15 participants (9 women; age: 26 ± 6 yrs; mass: 71 ± 15 kg; height: 173 ± 9 cm; months post-ACLR: 29 ± 13) were included in this cross-sectional study. Knee effusion-synovitis was assessed using a standardized protocol and graded using a validated scoring atlas (0 = absent, 1 = mild, 2 = moderate, 3 = severe) in the ACLR limb. Force-measuring insoles were used to capture the vertical ground reaction force (vGRF) during a one-minute treadmill walking trial. Limb symmetry indices (LSIs) were used to quantify limb loading asymmetry for the peak vGRF and the instantaneous loading rate (vGRF-LR). Spearman correlations determined whether effusion-synovitis grade was associated with peak vGRF and vGRF-LR LSI.

Results: Effusion-synovitis was present in the ACLR limb of 13/15 (87 %) participants (Grade 0: $n = 2$; Grade 1: $n = 8$; Grade 2: $n = 4$, Grade 3: $n = 1$). Effusion-synovitis grade was not

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*Corresponding author: harkeym1@msu.edu (H. MS).

Declaration of competing interest

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significantly associated with peak vGRF LSI (mean±sd: 98.0 ± 5.6 ; $\rho = 0.38$, $p = 0.162$), but was significantly associated with vGRF-LR LSI (98.2 ± 11.4 ; $\rho = 0.55$, $p = 0.035$).

Conclusion: Most participants 1–5 years post-ACLR have ultrasound-detected effusion-synovitis. Participants with more severe effusion-synovitis load their ACLR limb more rapidly. This study highlights the utility of clinically accessible techniques in assessing inflammation and walking biomechanics in ACLR patients.

Keywords

Biomechanics; Gait; Knee; Inflammation; Early osteoarthritis

Introduction

Knee injuries are common and account for over 625,000 emergency department visits annually in the United States [1] Anterior cruciate ligament (ACL) injury is the most common of these injuries, and approximately 75 % are treated with ACL reconstruction (ACLR) [2] Unfortunately, a third of those who undergo ACLR will develop radiographic signs of osteoarthritis (OA) within 10 years post-surgery [3] There is growing consensus that OA management needs to shift from the current reactive approach of treating patients with established OA to a more proactive strategy that targets preventive treatments to those at most risk of developing OA [4,5] Patients with ACLR represent an ideal population to study for OA prevention as they have a clearly defined inciting event that increases their OA risk [5] Identifying modifiable risk factors in patients post-ACLR is necessary to direct preventive strategies to those most likely to benefit.

ACL rupture initiates a sequence of events involving persistent inflammation and altered walking biomechanics [6,7], which significantly contributes to the onset and progression of post-traumatic OA [8, 9] Extensive evidence indicates ACL injury triggers an initial inflammatory response associated with poor patient-reported outcomes at 2-year follow-up [10,11] Subsequent ACLR then reinitiates this inflammatory response leading to elevated inflammatory biomarkers (i.e., IL-1 β , IL-6, IFN γ) persisting ≥ 5 year post-operatively [12,13] Moreover, the presence of effusion-synovitis, an imaging marker of inflammation, is frequently detected on magnetic resonance imaging (MRI) at 3 and 6 months post-ACLR, and this finding relates to degenerative joint changes by 2 years after surgery [14,15] Concurrently, altered walking biomechanics, including vertical ground reaction force peak magnitude (vGRF) and loading rate (vGRF-LR), are pervasive post-ACLR and by modifying knee joint loads are considered instrumental in development of OA [6,16] Beyond their individual significance, there seems to be an intricate interplay between walking biomechanics and inflammation that could be pivotal in determining an individual's susceptibility to developing OA [8,9] Specifically, using real-time gait biofeedback in participants post-ACLR to change their vGRF during walking will alter the levels of pro-inflammatory biomarkers and enzymes that break down cartilage [17], thus escalating the risk of chronic inflammation and joint damage [18,19] However, the exact nature of the interaction between biomechanics and chronic inflammation following ACLR remains unclear.

While chronic inflammation and altered gait biomechanics are implicated in post-ACLR OA risk, limitations of traditional measurement techniques often restrict their use in research settings.^{20,21} Conventional techniques for quantifying inflammation (e.g., synovial fluid biomarkers [10,22], MRI [23]) and walking biomechanics (e.g., forceplates [21], 3D motion capture [24]) require expensive equipment, expertise, and extensive analysis time. Recently, however, novel techniques have been developed to offer more clinically accessible alternatives to monitor effusion-synovitis (i.e., diagnostic ultrasound [25]) and walking biomechanics (i.e., force-measuring insoles [26]). Specifically, validated ultrasound scoring systems now allow for standardized assessment and grading of effusion-synovitis [25,27]. Additionally, force-measuring insoles have recently been used in patients post-ACLR to quantify biomechanics during walking and more dynamic tasks (e.g., drop-landing) without the need for traditional motion capture equipment [26,28,29]. Ultrasound, however, has never been used to determine the prevalence of effusion-synovitis in patients post-ACLR, nor have ultrasound and force-sensing insoles been used together to determine whether effusion-synovitis relates to altered walking biomechanics after ACLR. Establishing an association between inflammation and biomechanics will provide evidence to guide future studies to determine whether interventions aimed at one will affect the other.

Therefore, this study was to determine the association between knee effusion-synovitis and limb loading asymmetry during treadmill walking in people 1 to 5 years after ACLR. We focused on participants 1 to 5 years following ACLR to ensure that the presence of effusion-synovitis was chronic and not an acute response to the injury and surgery [10]. Given that chronic joint inflammation and changes in walking biomechanics often persist for extended periods after ACLR [6,7], and both factors are recognized as modifiable contributors to OA risk [8,9], this study seeks to clarify whether relative overloading or underloading of the ACLR limb correlates with the severity of effusion-synovitis. Based on prior studies that have demonstrated a link between ACLR limb underloading and other OA-related structural alterations, we hypothesize that greater ACLR limb underloading (i.e., lesser vGRF and vGRF-LR LSI) will be associated with more severe grades of effusion-synovitis.

Methods

Study design

We used a cross-sectional laboratory study to determine how effusion-synovitis asymmetry is associated with limb loading asymmetry during treadmill walking. Within the same laboratory during the same visit, we conducted an ultrasound assessment of the ACLR limb and a bilateral treadmill walking biomechanics assessment.

Participants

We recruited individuals who were 1–5 years post ACLR and had received clearance for full physical activity from their orthopedic surgeon. To identify potential participants for this study, we utilized our laboratory's existing research database, reaching out to individuals who had previously engaged in our studies. These patients were initially recruited through recommendations from their orthopedic surgeons, as part of our laboratory's ongoing research efforts. We chose 1–5 years post-ACLR to focus on chronic effusion-synovitis

rather than acute effusion-synovitis in response to the initial injury and surgery. As these patients were recruited from prior clinical research studies in collaboration with participating orthopedic surgeons, we had access to the patient's operative notes. To be eligible for the study, participants had to be between 18 and 35 years old with a body mass index (BMI) of less than 40 kg/m². Exclusion criteria included a history of previous knee surgery, articular cartilage damage exceeding grade 3A based on the International Cartilage Repair Society Criteria, and meniscectomy involving removal of more than one-third of either meniscus. The articular cartilage damage was graded by the operating orthopedic surgeon during the surgery. Prior to study participation, written informed consent was obtained from all participants, and the experimental procedures received approval from the local Institutional Review Board. In this study, we investigated a cohort of 15 individuals post-ACLR. The sample size was determined based on the availability of participants who met our specific inclusion criteria. This selection is a convenience sample, reflecting the feasibility of recruitment within the constraints of our research setting. Recognizing the constraints of a small sample size, this study is intended as an exploratory analysis, primarily to generate hypotheses for future research.

Ultrasound image acquisition

Ultrasound-based knee effusion-synovitis was assessed bilaterally using a longitudinal suprapatellar scan with the participant lying supine and the knee supported on a bolster in 20–30° flexion (Fig. 1A) [25]. Ultrasound images were obtained using a GE LOGIQ P9 R3 ultrasound system and L3–12-RS wideband linear array transducer (GE Healthcare, Chicago, IL). Following a previously published standardized imaging protocol [25], we acquired bilateral longitudinal images of the suprapatellar recess aligned with the quadriceps tendon proximal insertion on the patella (Fig. 1B). We did not instruct the participants to limit their physical activity on the day prior to or day of the ultrasound scan.

Ultrasound image grading effusion-synovitis

An initial single reader scored knee effusion presence using a previously published semi-quantitative grading atlas [25]. The effusion-synovitis grades were all reviewed and approved by a board-certified musculoskeletal radiologist (RF). Effusion was identified as an abnormally hypoechoic (dark) area deep to the quadriceps tendon between the prefemoral and suprapatellar fat pads (Fig. 1c). Effusion was graded as: 0 = none: no joint capsule distension; 1 = mild: joint capsule distension parallel to bone or small hypoechoic/anechoic region beneath capsule; 2 = moderate: joint capsule distension or elevation parallel to joint; 3 = severe: convex or bulging joint capsule distension [25]. This semi-quantitative, ordinal effusion-synovitis grading scale was used in our statistical analysis to determine the association between effusion-synovitis grade and limb loading asymmetry. The initial reader and the musculoskeletal radiologist were both blinded to the participant's limb loading asymmetry results when the images were graded.

Walking biomechanics assessment force-measuring insoles

Lower limb loading was assessed using force-measuring insoles (loadsol®, Novel Electronics) in the participant's personal shoes (Fig. 2). Shoe type was not controlled between participants. The loadsol is a single capacitive force sensor along the length of the

insole that allows for the collection and storage of vGRF outcomes via Bluetooth without the need for traditional forceplates or cables [30] The following procedures have been used with these insoles to produce reliable and valid measurements of walking biomechanics [31] The loadsol-s mobile application on an iPad (Apple Inc., Cupertino, CA) was used to calibrate and collect the walking biomechanics data. After the proper size insole was fitted in the participant's shoe, each participant's comfortable over-ground walking speed was determined using infrared timing gates (TF100; TracTronix; Belton, MO) by averaging their walking speed across five walking trials over a 6-meter walk-way [32] Following manufacturer recommendation, we then calibrated the insoles through a series of three cycles of unloading and loading the insoles with the participant's full body weight during a single-limb stance [30] We then tested the calibration with single limb stance trials on both limbs and confirmed that the insoles measured $\pm 5\%$ of the participant's body weight [30] The participants were then positioned on a treadmill (Commercial 2450; NordicTrack; Logan, UT) for the walking biomechanics assessment. We increased the treadmill walking speed to the participant's previously determined comfortable overground walking speed. For data analysis, we recorded one 60 s test trial to collect continuous vGRF data with the force-measuring insole collecting at 100 Hz.

Quantifying altered lower extremity loading during walking

The loadsol data was exported and processed using the Loadsol Analysis Program, an open-source MATLAB program freely available at github.com/GranataLab/LAP [33] We did not filter the vGRF data based on prior recommendations [30] Initial contact and terminal stance were defined as the first frame in which the vertical ground reaction force value rose above or fell below 50 Newtons for 20 consecutive frames [30] The Loadsol Analysis Program then automatically identified the vGRF curve for each step during the 60 s test trial and automatically calculated and normalized the peak vGRF and vGRF-LR across each step for both limbs. Peak vGRF was determined in the first 50 % of stance phase during each step and normalized to body mass [24] vGRF-LR was quantified as the peak of the first derivative of the force-time curve during the first 50 % of stance phase during each step and normalized to body mass [24] We then calculated a between-limb loading limb symmetry index (LSI) using the following equation: $(\text{ACLR limb vGRF} / \text{Contralateral limb vGRF}) * 100$. Between-limb loading LSIs greater than 100 indicate that there is greater loading in the ACLR limb relative to the contralateral limb.

Statistical analysis

Means and standard deviations and frequencies were used to assess common participant characteristics (i.e., age, BMI, months since ACLR, graft type, sex). To demonstrate the prevalence of effusion-synovitis grade in the ACLR limb, we highlight the prevalence of participants presenting with any effusion-synovitis (i.e., total of Grades 1, 2, and 3), as well as the prevalence of each individual grade. Since effusion-synovitis is scored on an ordinal scale, we used a Spearman rank order correlation to determine if effusion-synovitis grade was associated with peak vGRF and vGRF-LR. Post-hoc associations between effusion-synovitis grade and age, body mass index, and time since surgery were assessed to better understand if these factors should be included as covariates in future studies. Jamovi

(version 1.6) was used for all statistical analysis and data visualization. An alpha level of $p < 0.05$ was considered statistically significant.

Results

Of 15 participants enrolled in this study, 9 were women (60 %), the average age was 25.8 ± 5.7 years old, and the average BMI was 23.5 ± 3.2 kg/m². Participants were on average 29 ± 12 months post-ACLR and the graft types were hamstring ($n = 8$), patellar tendon ($n = 6$), and quadriceps tendon ($n = 1$). In the ACLR limb, effusion-synovitis was present in 13 of 15 (87 %, 95 % CI = 70 % - 100 %) participants. Specifically, 2 (13 %) were Grade 0, 8 (53 %) were Grade 1, 4 (27 %) were Grade 2, and 1 (7 %) was Grade 3. The mean $\pm$ standard deviation of peak vGRF was 1.08 ± 0.01 body weight in the ACLR limb, 1.11 ± 0.01 BW in the contralateral limb, with an LSI of 98.0 ± 5.6 %. The mean $\pm$ standard deviation of vGRF-LR was 15.3 ± 4.1 BW/s in the ACLR limb, 16.0 ± 4.8 BW/s in the contralateral limb, with an LSI of 98.2 ± 11.4 %.

Fig. 1 includes the scatterplot figures that depict the relationship between effusion-synovitis grade, peak vGRF, and vGRF-LR. Effusion-synovitis grade in the ACLR limb was not significantly associated with peak vGRF LSI ($\rho = 0.38$, 95 % CI = $-0.18 - 0.75$, $p = 0.162$, Fig. 3a). There was, however, a significant, positive association between effusion-synovitis grade in the ACLR limb and vGRF-LR LSI ($\rho = 0.55$, 95 % CI = $0.03 - 0.83$, $p = 0.035$, Fig. 3b), as participants with poorer effusion-synovitis grades were loading their ACLR limb faster than their contralateral limb. There were no significant associations between ACLR limb effusion-synovitis grade and age ($\rho = 0.04$, $p = 0.900$), body mass index ($\rho = -0.13$, $p = 0.640$), or time since surgery ($\rho = 0.11$, $p = 0.687$).

Discussion

Effusion-synovitis is highly prevalent in individuals 1 to 5 years post-ACLR, highlighting the persistent nature of inflammation in this population. Among the participants, 13 out of 15 exhibited effusion-synovitis in their ACLR limb. This study introduces an innovative ultrasound-based method to grade effusion-synovitis participants after ACLR, building upon prior research that developed OA ultrasound grading scales for diverse structural pathologies [25,27] Furthermore, we employed novel force-measuring insoles to assess walking biomechanics, enhancing the study's innovation by integrating clinically accessible imaging and biomechanics assessments. Our findings reveal that greater effusion-synovitis in the ACLR limb is associated with greater ACLR limb vGRF-LR relative to the contralateral limb during treadmill walking. As with previous evidence [7,10,13,20,34], our results indicate a prolonged inflammatory response post-ACLR and to the interplay of chronic inflammation and altered biomechanics. Additionally, based on our post-hoc analysis, there is no association between time since surgery and effusion-synovitis grade, which indicates that this prolonged inflammation may be relatively constant from 1 to 5 years post-ACLR. Our study's novel approach, using clinically accessible tools like diagnostic ultrasound and force-measuring insoles, bridges research and clinical practice. This integration offers practical ways to monitor effusion-synovitis and biomechanics in clinical settings.

The current study builds upon prior research regarding ongoing joint inflammation in patients after ACL injury [7,10,13,20,35] Specifically, a recent study found that patients with a dysregulated inflammatory response (i.e., amplified pro-inflammatory biomarker response) after ACL injury had significantly greater effusion-synovitis than patients with a more normal inflammatory response to injury, as well as effusion-synovitis associated with biochemical biomarkers indicative of cartilage breakdown [7] This underscores the clinical importance and potential impact of initial and persistent effusion-synovitis on the long-term health of the joint. Additionally, our findings of highly prevalent effusion-synovitis substantiate and expand upon prior reports of persistent effusion-synovitis observed on MRI for years following ACLR [15,34,36] Despite these individuals being 1–5 years post ACLR, it is concerning that 87 % of the participants in this study presented with effusion-synovitis in their ACLR knee. Of the 13 participants presenting with effusion-synovitis, however, only 8 had mild effusion-synovitis. Additionally, our innovative use of ultrasound to quantify effusion-synovitis in participants after ACLR demonstrates an accessible approach for monitoring this key inflammatory marker, offering a translatable imaging approach comparable to traditional MRI techniques. We hope that this pilot study encourages future, larger studies aimed at using ultrasound as a clinically accessible tool to monitor effusion-synovitis longitudinally following ACLR.

We also demonstrated that worse effusion-synovitis grade in the ACLR limb is associated with greater asymmetry in vGRF-LR during treadmill walking. Specifically, we found that participants with moderate and severe levels of ultrasound-detected effusion-synovitis in their ACLR limb also had greater ACLR limb loading rates relative to the other limb during treadmill walking. This cross-sectional association builds on prior work that suggests a possible link between inflammation and biomechanical alterations [7,19,37,38] A recent study provided a theoretical framework on the time-dependent relationships between effusion-synovitis, altered joint biomechanics, pain, and the progression to post-traumatic OA [7] The study is based on prior work demonstrating that altered biomechanics are related to both biochemical markers of inflammation and cartilage degradation [21,39,40], as well as longitudinal declines in MRI cartilage compositional changes [41–43] Similarly, interventions that reduce mechanical loading at the joint also result in reduced effusion-synovitis [38] While the observed vGRF-LR were relatively small in some participants, differences in as little as 5 % between limbs have been suggested to be clinically meaningful in walking gait after ACLR [24] Even subtle increases in the rate of knee joint loading can provoke inflammatory responses linked to OA progression [16,44,45] For example, just a 5 % increase in vGRF during a 20-minute treadmill walking session resulted in amplified levels of inflammatory biomarkers compared to symmetrical walking [46] In addition to its inflammatory effects, elevated effusion-synovitis also leads to joint distention which can disrupt proprioception and neuro-muscular function and lead to altered gait biomechanics [47,48] This could potentially lead to a self-reinforcing loop where inflammation influences biomechanics and vice versa, highlighting the need for further investigation to determine causality.

Despite the significance of this paper highlighting the prevalence of effusion-synovitis and its association with altered walking biomechanics, there are limitations. This study is preliminary in nature due to its relatively small sample size. Our findings should

be considered as a basis for hypothesis generation rather than conclusive evidence, underscoring the need for larger, more statistically powered future studies. Additionally, our results are derived from a specific cohort of patients at 1 to 5 years post-ACLR, which limits the generalizability of the findings. Future studies involving a more diverse population early after ACLR are necessary to validate and broaden the understanding of the association between ultrasound-detected synovitis and joint biomechanics post-ACLR. Given the cross-sectional design of this study, it does not capture the temporal progression of effusion-synovitis or its long-term impact on biomechanics post-ACLR. Longitudinal studies are essential to elucidate these aspects and to establish a clearer causal relationship. There are also limitations to the ultrasound technique used here as the suprapatellar ultrasound assessment produces only a single image captured at the suprapatellar joint recess and cannot provide a full joint assessment of effusion-synovitis. This technique is, however, commonly used in various OA grading scales to assess effusion-synovitis and previous reports have shown an association between this grading system and MRI-assessed whole knee effusion-synovitis [25,27,49]

In conclusion, this study provides preliminary evidence that ultrasound can detect effusion-synovitis that is highly prevalent even years after ACLR surgery. Additionally, those with more effusion-synovitis in their ACLR knee tended to exhibit more asymmetry in lower extremity loading rate during treadmill walking. Our findings highlight the potential of ultrasound and instrumented footwear as clinically accessible tools to monitor inflammation and biomechanics in patients following ACLR. Overall, this study underscores the prevalence of ongoing inflammation and its relation to biomechanical alterations years after ACLR.

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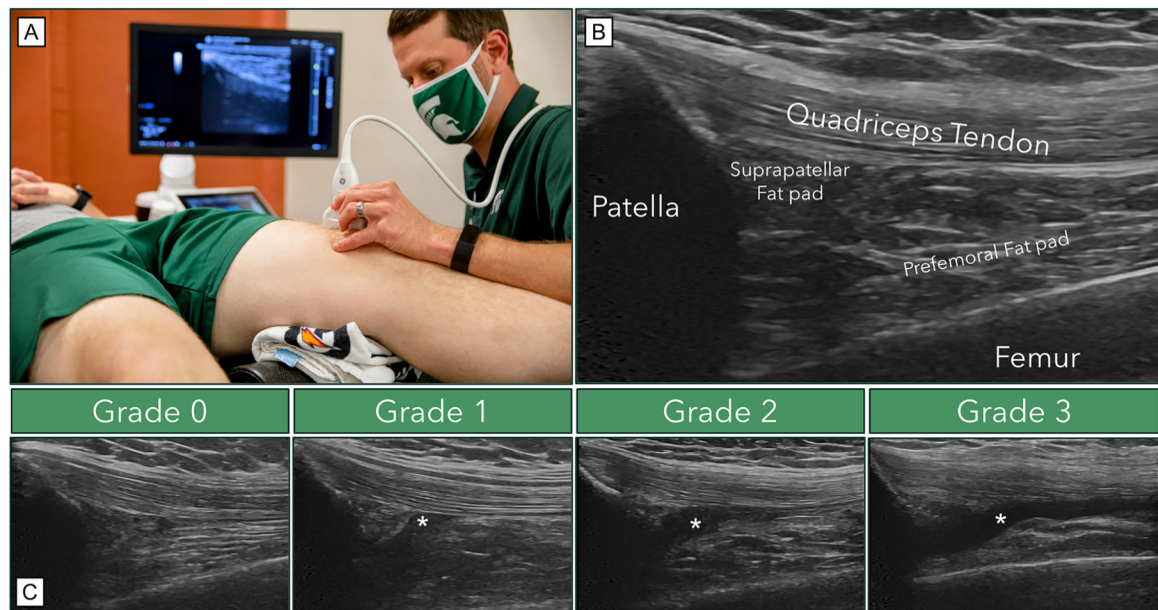


Fig. 1.

Knee Ultrasound Assessment to Quantify Effusion-Synovitis. A) Ultrasound-based knee effusion-synovitis was assessed bilaterally using a longitudinal suprapatellar scan with the participant lying supine and the knee supported on a bolster in 20–30° flexion. We acquired bilateral longitudinal images of the suprapatellar recess aligned with the quadriceps tendon proximal insertion on the patella B) This image highlights an ultrasound image acquired using this longitudinal suprapatellar scan with the common observable anatomical landmarks labelled in a knee without effusion-synovitis. C) Effusion was identified as an abnormally hypoechoic (dark) area deep to the quadriceps tendon between the prefemoral and suprapatellar fatpads using a previously published semi-quantitative grading atlas. Effusion (* in the images) was graded as: 0 = none: no joint capsule distension; 1 = mild: joint capsule distension parallel to bone or small hypoechoic/anechoic region beneath capsule; 2 = moderate: joint capsule distension or elevation parallel to joint; 3 = severe: convex or bulging joint capsule distension.

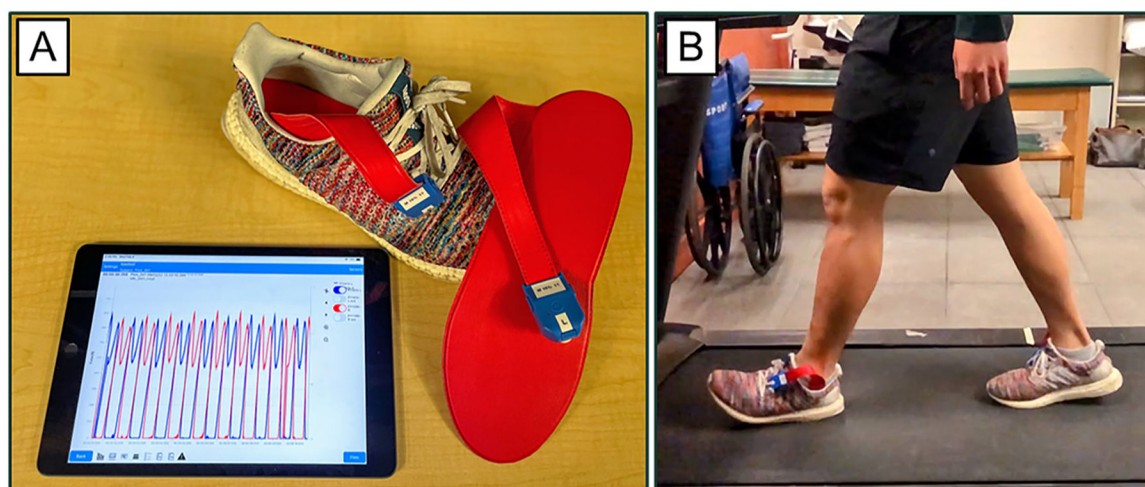
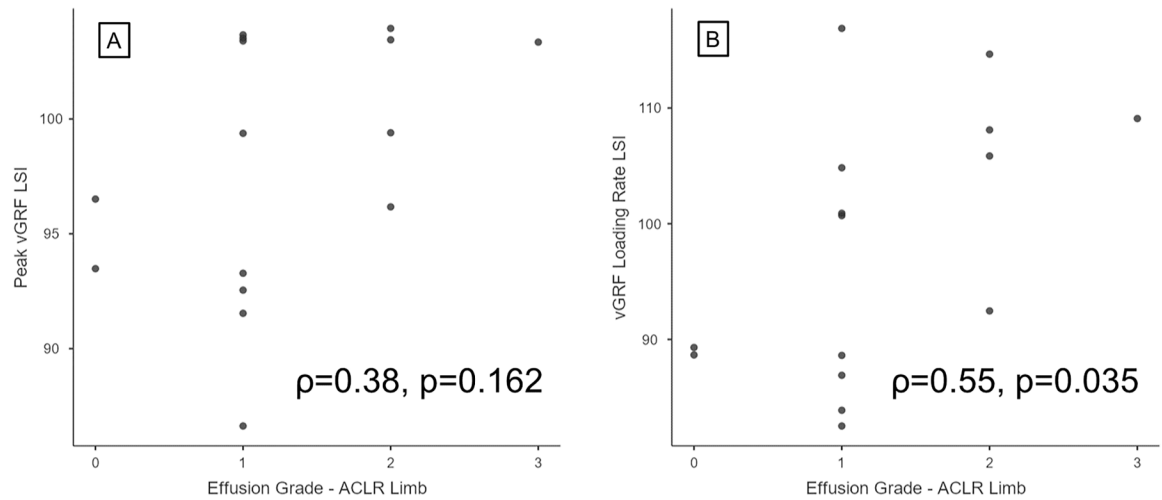


Fig. 2. Walking Biomechanics Collection with Force-Measuring Insoles. A) This image demonstrates the loadsol force-measuring insole, how the insole fits within a participant's shoe, as well as an image of the vertical ground reaction force collected via Bluetooth on a tablet. B) This image depicts a participant fitted with the loadsol force-measuring insoles while completing the treadmill walking assessment.

**Fig. 3.**

Association Between Effusion-Synovitis and Lower Limb Loading Asymmetry. Fig. 3a depicts the lack of association between peak vertical ground reaction force (vGRF) limb symmetry index (LSI) and grade of ultrasound-detected effusion-synovitis in the anterior cruciate ligament reconstructed (ACLR) limb. Fig. 3b highlights the statistically significant association between more asymmetrical vGRF loading rate LSI and worse effusion-synovitis grade in the ACLR limb.