

# Persistent Early Knee Osteoarthritis Symptoms From 6 to 12 Months After Anterior Cruciate Ligament Reconstruction

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**Context:** Early identification of knee osteoarthritis (OA) symptoms after anterior cruciate ligament reconstruction (ACLR) could enable timely interventions to improve long-term outcomes. However, little is known about the change in early OA symptoms from 6 to 12 months post-ACLR.

**Objective:** To evaluate the change over time in meeting classification criteria for early knee OA symptoms from 6 to 12 months after ACLR.

**Design:** Prospective cohort study.

**Setting:** Research laboratory.

**Patients or Other Participants:** Eighty-two participants aged 13 to 35 years who underwent unilateral primary ACLR. On average, participants' first and second visits were 6.2 and 12.1 months post-ACLR.

**Main Outcome Measure(s):** Early OA symptoms were classified using generic (Luyten Original) and patient population-specific (Luyten Patient Acceptable Symptom State [PASS]) thresholds on Knee injury and Osteoarthritis Outcome Score (KOOS) subscales. Changes in meeting early OA criteria were compared between

an initial and follow-up visit at an average of 6 and 12 months post-ACLR, respectively.

**Results:** Twenty-two percent of participants exhibited persistent early OA symptoms across both visits using both the Luyten Original and PASS criteria. From initial to follow-up visit, 18% to 27% had resolution of early OA symptoms, while 4% to 9% developed incident symptoms. In total, 48% to 51% had no early OA symptoms at either visit. No differences were found for change in early OA status between adults and adolescents.

**Conclusions:** Nearly one-quarter of participants exhibited persistent early knee OA symptoms based on KOOS thresholds from 6 to 12 months post-ACLR. Determining if this symptom persistence predicts worse long-term outcomes could inform the need for timely interventions after ACLR. Future researchers should examine if resolving persistent symptoms in this critical window improves later outcomes. Tracking early OA symptoms over time may identify high-risk patients who could benefit from early treatment.

**Key Words:** posttraumatic, PTOA, KOOS, knee injury, OA illness

## Key Points

- Nearly one-quarter of participants experienced persistent early knee OA symptoms from 6 to 12 months after ACL reconstruction.
- Early knee OA symptoms resolved in 18% to 27% of participants, while only 4% to 9% developed new symptoms during this period.
- Persistent symptoms at 6 and 12 months post-ACLR may indicate early OA rather than just normal postsurgical recovery.

Anterior cruciate ligament (ACL) injury and subsequent reconstruction (ACLR) substantially increase the risk of developing posttraumatic knee osteoarthritis (OA).<sup>1</sup> Osteoarthritis presents both as a structural disease and a symptomatic illness.<sup>2,3</sup> Although imaging modalities can detect early

structural changes of OA disease, monitoring patient-reported symptoms provides crucial insight into OA illness.<sup>4</sup> While early OA symptoms often precede radiographic evidence, they typically align with changes detectable through early magnetic resonance imaging (MRI) structural alterations,

highlighting a critical intervention window before substantial structural and symptomatic progression.<sup>5–8</sup> Assessing these symptoms is vital, not only because they serve as early indicators of OA but also due to their significant effect on patients' quality of life and functional status, as seen by the association between quadriceps strength and early OA symptoms.<sup>9</sup> The onset of early OA illness or symptoms may represent a critical window in which progression to irreversible joint damage could still be prevented or delayed with appropriate intervention.<sup>3,8,10,11</sup> However, little is known about the typical development and course of early OA symptoms from 6 to 12 months after ACLR.<sup>12</sup> Improved understanding of the change in early OA symptoms could better guide post-ACLR clinical care, especially regarding the timing of interventions.<sup>3,8,10</sup>

Classification criteria are urgently needed to standardize definitions and identify patients experiencing early OA symptoms after knee injury who may benefit from preventative interventions.<sup>8,10</sup> Unlike diagnostic criteria, classification criteria prioritize specificity over sensitivity to capture homogeneous high-risk cohorts for research.<sup>13</sup> Recent efforts have proposed an early OA classification criteria that identifies early OA symptoms based on a combination of scores on the Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire.<sup>8,10,14,15</sup> These early OA symptoms criteria were recently applied to patients after ACLR, finding 24% to 42% met thresholds for early OA symptoms at 6 months postsurgery.<sup>15</sup> While this highlights a concerning prevalence of early OA symptoms at 6 months after ACLR, symptoms at this period are commonly considered normal postsurgical pain that is assumed to eventually subside. However, in the pain literature, chronic postsurgical pain has been defined as pain that developed after a surgical procedure with a duration of at least 2 months.<sup>16,17</sup> Therefore, while the transition between normal postsurgical pain and signs of early OA symptoms is complex, in this study, we consider the 6-month post-ACLR mark as a critical point for evaluating the transition from postsurgical responses to early signs of OA. However, it is unclear how a patient's early OA symptom status will change over time after ACLR. Understanding changes in early OA symptoms over time is not just crucial for clinical decision-making but could also help determine long-term patient outcomes.<sup>8,10</sup> Detecting persistent, clinically meaningful early OA symptoms after ACLR is crucial, as it may enable targeted treatments in a vital window to halt or slow down joint damage progression, thereby significantly improving long-term outcomes.<sup>3,8,10,11</sup> This emphasizes the importance of early OA symptom evaluation post-ACLR, as detection of early OA symptoms presents a critical opportunity to alleviate clinically relevant symptoms as well as the potential for preventing structural OA progression.

Patient-reported symptoms offer a cost-effective and accessible means of monitoring early OA progression, allowing clinicians to capture real-time, subjective experiences of patients.<sup>11</sup> This approach contrasts with the complexities of measuring other clinical outcomes that may be related to early OA such as strength, gait, or physical activity, which often require specialized equipment and may not immediately reflect the patient's personal experience of OA.<sup>18</sup> Therefore, the purpose of this study was to evaluate the change over time in meeting proposed classification criteria for early knee OA symptoms in participants from 6 to 12 months after ACLR.<sup>14</sup> We focused on participants who had an initial assessment 5 to 7 months post-ACLR and then determined the within-participants change in meeting early OA symptom classification criteria between

the initial visit and a follow-up visit at an average of 12 months post-ACLR.<sup>14</sup> Based on previous cross-sectional findings, we hypothesized that at least 25% of participants would meet early OA classification criteria persistently at both the initial and follow-up visits.<sup>15</sup> Evaluating the change in early OA symptoms will provide crucial information to guide post-ACLR clinical care and determine which patients may benefit most from early interventions.

## METHODS

### Study Design

We used a cohort study design to determine a within-participants change in meeting the early OA symptom classification criteria over time. We included participants who had (1) an initial visit between 5 and 7 months post-ACLR (mean  $\pm$  SD = 6.2  $\pm$  0.7 months), (2) at least 2 months between their initial and follow-up visit (6.2  $\pm$  4.1 months between visits), and (3) their follow-up visit within 24 months post-ACLR (mean  $\pm$  SD = 12.1  $\pm$  4.3 months). All these visits were research visits and were not necessarily linked to a patient's clinical visit. If a participant had more than 1 follow-up visit, we used the latest follow-up post-ACLR as their included visit.

### Participants

Participants were included if they were between 13 and 35 years and underwent a primary, unilateral ACLR. We limited the age range to 35 because it is recommended for post-ACLR OA prevention clinical trials.<sup>19</sup> We recruited participants from a single university sports medicine department. Participants were excluded if they underwent a multiligament reconstruction during their ACLR surgery or had a neurological, cardiovascular, or other medical condition that prohibited participation in our ongoing longitudinal study that included biomechanics and strength testing. Participants were not excluded if they sustained a concomitant meniscal injury or underwent a meniscal procedure at the time of ACLR. Participants were excluded if they had a previous lower extremity surgery. If a participant was 18 years or older at enrollment, he or she provided written informed consent. If a participant was less than 18 years at enrollment, he or she provided written assent, and a legal guardian provided written consent. The local institutional review board approved all experimental procedures before participant enrollment.

### Knee Injury and Osteoarthritis Outcome Score

The KOOS questionnaire is validated in various patient populations with or at-risk for knee OA.<sup>20</sup> Four of the KOOS subscales are used in the early OA symptoms classification criteria: Symptoms, Pain, Activities of Daily Living (ADL), and Quality of Life (QOL). Each subscale has multiple 5-point Likert scale questions that range from 0 = *best* to 4 = *worst*. After completing the KOOS, the subscales were converted to a score from 0 to 100, with 100 indicating no self-reported dysfunction.

### Self-Reported Early Knee OA Symptoms Classification Criteria

Since no consensus exists on how to classify early knee OA symptoms, we used 2 previously published sets of criteria

**Table 1. Knee Injury and Osteoarthritis Outcome Score (KOOS) Subscale Thresholds for the Early Knee Osteoarthritis (OA) Classification Criteria**

KOOS Subscale	KOOS Subscale Threshold	
	Luyten <sup>a</sup>	
	Original	PASS <sup>b</sup>
Quality of Life	85.0%	62.5%
Pain	85.0%	88.9%
Symptoms	85.0%	57.1%
Activities of Daily Living	85.0%	100.0%

Abbreviation: PASS, Patient Acceptable Symptom State.

<sup>a</sup> Luyten early OA symptom classification criteria: below the threshold on 2 of the 4 KOOS subscales.

<sup>b</sup> Developed in individuals 1 to 5 years after a primary anterior cruciate ligament reconstruction.

that differ only in the thresholds in KOOS scores that are considered symptomatic (Table 1).<sup>14,21</sup>

**Luyten Original Early OA Criteria.** We operationally defined early OA symptoms using the KOOS based on the symptoms portion of the Luyten early OA classification criteria (Luyten Original).<sup>14</sup> The Luyten Original criteria defined early OA symptoms as a participant scoring less than or equal to 85% on at least 2 of the 4 KOOS subscales.<sup>14</sup> These early OA symptom classification criteria have been applied to participants post-ACLR.<sup>9,21</sup>

**Luyten Patient Acceptable Symptom State Early OA Criteria.** While the Luyten Original criteria are a key step toward defining early knee OA illness, the previous authors highlight the proposed classification strategy is a starting point that needs additional refinement.<sup>14</sup> One area for refinement may be to update the KOOS subscale thresholds to make the classification criteria more specific to population groups at risk for knee OA. In a previous report, the Luyten criteria were refined for participants post-ACLR by adjusting the KOOS subscale thresholds to established patient acceptable symptoms state (PASS) scores for participants post-ACLR (Symptoms  $\leq$  57.1%, Pain  $\leq$  88.9%, QOL  $\leq$  62.5, and ADL  $\leq$  100.0%).<sup>21,22</sup> With the Luyten PASS criteria, early OA symptoms are defined if a participant scores below the threshold on at least 2 of the 4 KOOS subscales. Therefore, the Luyten PASS allows us to use the KOOS criteria logic from the Luyten Original early OA classification criteria coupled with the patient population-specific KOOS subscale thresholds so that they reflect meaningful symptoms post-ACLR.<sup>21</sup>

## Statistical Analysis

We determined the change in early knee OA symptoms across 2 visits at an average of 6 and 12 months post-ACLR. We created a composite variable to define change over time in early OA symptoms based on their status at both visits: (1) *no early OA symptoms* = not meeting the early OA symptom classification criteria at either visit, (2) *resolution of early OA symptoms* = early OA symptoms at the initial visit but not at the follow-up visit, (3) *incident development of early OA symptoms* = no early OA symptoms at the initial visit but meeting criteria at the follow-up visit, and (4) *persistent early OA symptoms* = meeting early OA symptom classification criteria at both visits. We determined the frequency of participants that met all criteria for within-participants change in early OA status for both the Luyten Original and Luyten

**Table 2. Participant Demographics and Knee Injury and Osteoarthritis Outcome Score (KOOS) Scores at the Initial and Follow-Up Visit Within the First 2 Years Post-Anterior Cruciate Ligament Reconstruction (ACLR)**

Demographic	Visit	Total
No. female (% female)	V1	56 (68%)
Age, y	V1	19.4 $\pm$ 4.9
Height, cm	V1	172.6 $\pm$ 9.5
Mass, kg	V1	72.5 $\pm$ 13.8
Graft type, No. (%)	V1	PT: 20 (24%) Ham: 54 (66%) Quad: 2 (2.5%) Allo: 4 (5%) Unknown: 2 (2.5%)
Months since ACLR	V1	6.2 $\pm$ 0.7
	V2	12.1 $\pm$ 4.3
Months between visits		6.2 $\pm$ 4.1
KOOS Activities of Daily Living	V1	96.9 $\pm$ 5.5
	V2	98.6 $\pm$ 2.6
KOOS Pain	V1	91.0 $\pm$ 8.8
	V2	92.2 $\pm$ 6.1
KOOS Quality of Life	V1	58.8 $\pm$ 20.9
	V2	76.2 $\pm$ 18.4
KOOS Symptoms	V1	83.1 $\pm$ 13.0
	V2	86.4 $\pm$ 12.3
Prevalence of early OA symptoms, No. (%)	V1	33 (40%)
	V2	25 (30%)

Abbreviations: Allo, allograft; Ham, hamstrings graft; OA, osteoarthritis; PT, patellar tendon graft; Quad, quadriceps tendon graft; V1, initial visit; V2, follow-up visit.

PASS criteria across 6 and 12 months post-ACLR. Since our inclusion criteria include participants across a wide age range, a sensitivity analysis was conducted, dividing the cohort into adolescents (aged 13 to 18 years) and adults (aged 18 to 35 years), to compare the prevalence of early OA symptoms between these age groups. A  $\chi^2$  test was conducted to examine the association between these criteria for within-participants change in early OA symptom status and age group. To identify which subscales were drivers of meeting the early OA symptom threshold, the Supplemental Figure (available online at <https://dx.doi.org/10.4085/1062-6050-0470.23.S1>) was created comparing the percentage of participants below each KOOS subscale threshold, for those with and without early OA symptoms at both visits. Additionally, we used a  $\chi^2$  test or analysis of variance to compare baseline demographics between the 4 groups of within-participants change in early OA symptom status based on the Luyten Original classification criteria (see Supplemental Table).

## RESULTS

### Demographics

The demographics of the 82 participants are found in Table 2. Most participants were female (68%) at an average age of 19.4 years with an average height of 172.6 cm and an average weight of 72.5 kg. Participants were on average 6.2 months post-ACLR at their first visit and 12.1 months post-ACLR at their follow-up visit. Table 2 highlights the group means in the KOOS subscales at the initial and follow-up visit. Additionally, 40% and 30% of the participants met the classification criteria for early OA symptoms at the first and follow-up visits, respectively (Table 2).



**Table 3. Longitudinal Change in Participants Meeting Classification Criteria for Early Knee Osteoarthritis (OA) Symptoms Across the First 2 Years Post–Anterior Cruciate Ligament Reconstruction (ACLR) Using the Luyten Original and Luyten PASS Criteria**

Classification Criteria	No Early OA at First Visit, No. (%)		Early OA at First Visit, No. (%)	
	No Early OA Sx at Both Visits	Incident Early OA Sx <sup>a</sup>	Resolved Early OA Sx <sup>b</sup>	Persistent Early OA Sx <sup>c</sup>
Luyten Original				
All (n = 82)	42 (51%)	7 (9%)	15 (18%)	18 (22%)
Adolescent (n = 43)	26 (60%)	8 (19%)	2 (5%)	7 (16%)
Adult (n = 39)	16 (41%)	7 (18%)	5 (13%)	11 (28%)
Luyten PASS				
All (n = 82)	39 (48%)	3 (4%)	22 (27%)	18 (22%)
Adolescent (n = 43)	26 (60%)	9 (21%)	1 (2%)	7 (16%)
Adult (n = 39)	13 (33%)	13 (33%)	2 (5%)	11 (28%)

Abbreviations: PASS, Patient Acceptable Symptom State; Sx, symptoms.

<sup>a</sup> Incident Early OA Sx = not meeting early OA symptom classification criteria at the first visit but met early OA symptom classification criteria at follow-up.

<sup>b</sup> Resolved Early OA Sx = met early OA symptom classification criteria at the first visit but not at follow-up.

<sup>c</sup> Persistent Early OA Sx = met early OA symptom classification criteria at both visits.

### Within-Participants Change Over Time in Early OA Criteria

Table 3 highlights the criteria for within-participants change in meeting classification criteria for early OA symptoms from 6 to 12 months post-ACLR when using the Luyten Original and PASS classification criteria. When using the Luyten Original criteria, 22% of participants met the classification criteria for early OA symptoms at both visits (ie, persistent early knee OA symptoms; Table 3). Fifty-one percent of participants did not meet the classification criteria for early OA symptoms at either visit (ie, no early OA symptoms). Eighteen percent of participants met the classification criteria for early OA symptoms at the initial visit but not the follow-up visit (ie, resolution of early OA symptoms). Lastly, only 9% of participants did not meet the classification criteria for early OA symptoms at the initial visit but did meet the criteria at the follow-up visit (ie, incident early OA symptoms).

When using the Luyten PASS criteria, 22% of participants experienced persistent early OA symptoms across both visits (Table 3). Forty-eight percent of participants reported no early OA symptoms at either visit. Twenty-seven percent of participants experienced resolution of early OA symptoms from the initial to follow-up visit. Lastly, only 4% of participants experienced incident early OA symptoms from the initial to follow-up visit.

Table 3 also highlights the frequency of the within-participants change in early OA symptom status criteria separately for adolescents and adults. No statistically significant association was found between within-participants early OA symptom status change and age group for the Luyten Original ( $\chi^2 = 4.44$ ,  $P = .22$ ) and PASS ( $\chi^2 = 6.10$ ,  $P = .11$ ) classification criteria. Despite the lack of significance, having persistent early OA symptoms was 6% more common, and having no early OA symptoms at either visit was 27% less common in adults than adolescents for the Luyten PASS classification criteria.

The Supplemental Figure shows the percentage of participants below the KOOS threshold for each subscale used in the Luyten Original early OA symptoms definition. At each visit, the KOOS QOL and KOOS Symptoms subscales typically had the greatest percentage of people that scored below the 85% threshold in those with (QOL = 96%–100%;

Symptoms = 100%) or without (QOL = 46%–76%; Symptoms = 6%–7%) early OA symptoms (see Supplemental Figure). The Supplemental Table provides the baseline demographics and statistical comparisons between the 4 within-participants changes in early OA symptom status groups based on the Luyten Original classification criteria. No statistically significant differences were found in any of the demographics between groups.

### DISCUSSION

The key finding of this study was that approximately one-quarter of participants exhibited persistent symptoms that met current early OA symptom classification criteria at both 6 and 12 months after ACLR. When applying both the Luyten Original and PASS criteria, 22% of participants presented with early OA symptoms at both the initial and follow-up visits. The consistency between criteria indicates that a substantial proportion of patients report OA symptoms that persist past 1-year post-ACLR. Given that these criteria identify symptoms considered clinically meaningful, the subset of ACLR patients with persistent symptoms may require closer monitoring and consideration as ideal candidates for secondary OA prevention interventions.<sup>23,24</sup> Alternatively, the proportion who did not meet early OA criteria at either time point suggests that symptoms resolve for many patients by 6 months and remain absent at 12 months after ACLR. Taken together, within-participants change in these early OA symptom classification criteria can identify people with persistent early OA symptoms who may be a high-risk patient group that needs additional interventions to inform care after ACLR. Our findings offer valuable insights for the continuing education of athletic trainers, emphasizing the need for focused training on early OA detection and management after ACLR. Our study's findings are crucial in raising awareness among athletic trainers about the potential for early OA symptoms in patients post-ACLR. The significant proportion of patients with persistent symptoms at 6 and 12 months post-ACLR suggests a need to reinterpret these symptoms. Symptoms persisting at 6 months should not be dismissed as normal postsurgical recovery but rather considered potential indicators of early OA. This shift in perspective can guide athletic trainers in early intervention strategies to prevent the progression of OA symptoms.

In this study, we used 2 sets of early OA classification criteria—the original criteria proposed by Luyten et al and modified criteria using a patient population–specific PASS-based criteria—that differed in their KOOS symptom thresholds.<sup>14,21,22</sup> Despite different thresholds, the criteria showed good agreement in identifying patients with persistent and no early symptoms at 6 and 12 months post-ACLR. Approximately 22% of participants met both sets of criteria for early OA symptoms persistently, while 48% to 51% did not meet either set of criteria at both visits. This suggests the criteria similarly identify patients with persistent early OA symptoms. Incident early OA symptoms were rare from 6 to 12 months with both sets of criteria (4% to 9%). The main difference was in the resolved early OA symptoms group (18% versus 27%), indicating the PASS-based criteria may better capture patients that will experience early OA symptom resolution from 6 to 12 months post-ACLR. Overall, the consistent detection of persistent early OA symptoms supports the utility of these criteria. Using patient population–specific thresholds like PASS may optimize sensitivity; however, broader validation is required. Further researchers should continue to refine and validate early OA criteria for optimal application after joint injury. Specifically, future studies are needed to identify if early OA symptoms classification criteria could be used to identify the patients at highest risk for structural OA progression. Additionally, most participants in our study were asymptomatic at both time points, suggesting a subgroup with potentially favorable outcomes. The participants in this asymptomatic group could be instrumental in future research, as examining their characteristics may uncover modifiable factors. These factors could serve as critical targets in developing interventions for those with symptomatic ACLR outcomes, thereby enhancing postsurgical care strategies.

Our finding that 22% of participants exhibited persistent early OA symptoms aligns with previous literature in which poor outcomes at 6 and 12 months after ACLR were defined based on self-reported dichotomous questions regarding the patient's perception of treatment failure or acceptable symptoms.<sup>12,25</sup> For example, authors of studies have reported that 11% to 13% of patients consider their ACLR a failure, and 33% to 36% experience unacceptable symptoms at 1 to 2 years post-surgery.<sup>25</sup> Despite differences between the prior study and our study in defining unacceptable symptoms, the comparable proportions across studies suggests our use of early OA classification criteria effectively identifies patients with clinically meaningful persistent early OA symptoms during ACLR recovery when they are likely cleared for full activity. However, further research is needed to determine if those with persistent early OA symptoms are at greater risk for progression to radiographic knee OA. Regardless, the substantial number of patients with sustained issues points to a need for developing effective strategies to resolve early OA symptoms and improve outcomes when patients do not recover as expected after ACLR. Researchers have identified several factors linked to symptomatic and radiographic progression in OA, such as gait biomechanics or strength.<sup>26,27</sup> However, these measures often do not directly reflect the patient's subjective experience and symptom severity. Our focus on early OA symptom assessment addresses this gap, providing a more patient-centered approach that complements these biomechanical and functional evaluations, thereby offering a more holistic understanding of OA progression post-ACLR. Evaluating predictors of persistent early OA symptoms could yield targets for optimizing post-ACLR management.

In this study, we found a very low incidence of early OA symptoms developing between 6 and 12 months after ACLR, irrespective of classification criteria used. These findings suggest that early OA is more likely characterized by persistent symptoms throughout the recovery period after ACLR. This persistence in early OA symptoms, not fully resolving within the initial year postinjury and postsurgery, raises the possibility that individuals with such early OA symptoms are at a higher risk of future radiographic knee OA. While, in this study, we provide insights at 6 and 12 months post-ACLR, we acknowledge the limitation in not capturing the full spectrum of longitudinal changes, particularly earlier symptom fluctuations. The relatively close time points and proximity to the ACLR event may not sufficiently reveal the gradual development or resolution of symptoms, especially those occurring before 6 months. This highlights a potential area for future researchers to explore earlier and more varied time points for a comprehensive understanding of symptom trajectories post-ACLR. While our study does not include any assessments of radiographic knee OA, authors of prior studies have demonstrated the presence of symptoms often preceding radiographic evidence or have shown that early symptoms after ACLR are associated with early MRI structural alterations, which highlights a critical intervention window before substantial structural and symptomatic progression.<sup>5–7</sup> Given the rarity of incident early OA symptoms within 1 year of surgery, preventing early OA symptom onset may not be the most appropriate outcome for clinical trials targeting the early post-ACLR window. However, criteria identifying persistent early OA symptoms post-ACLR could be leveraged to select patients for inclusion in trials focused on early OA symptom resolution in a patient group that has demonstrated symptoms at both 6 and 12 months post-ACLR. Additionally, our sensitivity analysis revealed no statistically significant association between age groups and the prevalence of early OA symptoms. This suggests that change in early OA symptom status in our cohort is not significantly influenced by age. It highlights the potential of other factors, beyond age, contributing to the development of early OA symptoms after ACLR. Future researchers should continue to clarify optimal applications of early OA classification criteria in trials and care pathways aimed at maximizing benefit during this early postinjury period.

In this study, we highlight the within-participants change in early OA symptoms over time in participants post-ACLR, but some limitations must be discussed. First, we relied solely on patient-reported outcome measures to define early OA symptoms and did not include imaging to assess structural disease progression. However, authors of prior research found just 4% of ACLR patients demonstrate radiographic knee OA between 1 to 2 years postoperatively, suggesting minimal disease progression in our sample.<sup>28</sup> Despite this, the same authors also highlighted that one-third of patients have MRI-defined early OA at 1 year post-ACLR.<sup>28</sup> Therefore, authors of future studies should determine how more sensitive measures of joint health alterations are related to early symptom changes. Second, our cohort was recruited from a single center, which may limit generalizability of findings to other settings and geographic regions. Third, we did not assess intraindividual changes in activity levels or rehabilitation progress between visits, which could provide context about symptom change. Fourth, our sample was predominantly young, and findings may differ in older patients. Additionally, while we captured 2 time points, more frequent follow-ups are needed to fully characterize the early

OA symptom trajectory after ACLR. This limitation means that, in this study, we may not have fully captured fluctuating symptoms over time, and as such, we cannot definitively conclude that symptoms resolved in certain subgroups represent a long-term resolution or sustained incidence. Also, the younger age of our participants may have resulted in including participants at different levels of skeletal maturity. While we did not directly assess skeletal maturity in this study, it is unclear how skeletal maturity may influence the presence and progression of early OA symptoms. Future research is needed to explore the relationship between skeletal maturity and early OA symptoms post-ACLR. Finally, most of the participants included in this analysis received a hamstrings graft during their ACLR, and it is currently unclear how our results would change if a larger prevalence of patellar tendon or quadriceps tendon grafts existed. Despite these limitations, in this study, we provide initial evidence that 22% of participants will experience persistent early OA symptoms at 6 to 12 months after ACLR. Authors of future multicenter studies with expanded demographic representation, rehabilitation data, and long-term patient-reported and imaging outcomes would build on these preliminary findings.

In this study, we provide new evidence that approximately one-quarter of young patients exhibit persistence of early OA symptoms from 6 to 12 months after ACLR, based on proposed classification criteria. Participants in the subgroup meeting criteria for early OA symptoms at multiple time points may warrant future study to determine if they are at a higher risk for progression and poor outcomes. Both generic and population-specific classification criteria consistently identified patients with persistent early OA symptoms, supporting their utility as screening tools to select high-risk cohorts needing preventative interventions after ACL injury. Given the rarity of incident early OA symptoms in this timeline, targeting patients with existing persistent symptoms in the first 5 to 7 months after ACLR may better guide clinical care and optimize outcomes. Moving forward, continued validation of early OA criteria in diverse populations is critical, along with researchers clarifying whether early classification predicts symptomatic progression and radiographic OA development. Overall, standardized criteria for classifying early OA symptoms hold tremendous potential to improve posttraumatic joint injury management if rigorously validated.

## FINANCIAL DISCLOSURES

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## REFERENCES

- Luc B, Gribble PA, Pietrosimone BG. Osteoarthritis prevalence following anterior cruciate ligament reconstruction: a systematic review and numbers-needed-to-treat analysis. *J Athl Train*. 2014;49(6):806–819. doi:10.4085/1062-6050-49.3.35
- Lane NE, Brandt K, Hawker G, et al. OARSI-FDA initiative: defining the disease state of osteoarthritis. *Osteoarthritis Cartilage*. 2011;19(5):478–482. doi:10.1016/j.joca.2010.09.013
- Whittaker JL, Runhaar J, Bierma-Zeinstra S, Roos EM. A lifespan approach to osteoarthritis prevention. *Osteoarthritis Cartilage*. 2021;29(12):1638–1653. doi:10.1016/j.joca.2021.06.015
- Frobell RB, Le Graverand MP, Buck R, et al. The acutely ACL injured knee assessed by MRI: changes in joint fluid, bone marrow lesions, and cartilage during the first year. *Osteoarthritis Cartilage*. 2009;17(2):161–167. doi:10.1016/j.joca.2008.06.020
- Case R, Thomas E, Clarke E, Peat G. Prodromal symptoms in knee osteoarthritis: a nested case-control study using data from the Osteoarthritis Initiative. *Osteoarthritis Cartilage*. 2015;23(7):1083–1089. doi:10.1016/j.joca.2014.12.026
- Pietrosimone B, Nissman D, Padua DA, et al. Associations between cartilage proteoglycan density and patient outcomes 12 months following anterior cruciate ligament reconstruction. *Knee*. 2018;25(1):118–129. doi:10.1016/j.knee.2017.10.005
- O’Connell D, Golightly Y, Lisee C, Pietrosimone B. Interlimb differences in T1ρ MRI relaxation times linked with symptomatic knee osteoarthritis following anterior cruciate ligament reconstruction. *Knee*. 2023;41:353–359. doi:10.1016/j.knee.2023.02.006
- Mahmoudian A, Lohmander LS, Mobasheri A, Englund M, Luyten FP. Early-stage symptomatic osteoarthritis of the knee—time for action. *Nat Rev Rheumatol*. 2021;17(10):621–632. doi:10.1038/s41584-021-00673-4
- Arhos EK, Thoma LM, Grindem H, Logerstedt D, Risberg MA, Snyder-Mackler L. Association of quadriceps strength symmetry and surgical status with clinical osteoarthritis 5 years after anterior cruciate ligament rupture. *Arthritis Care Res (Hoboken)*. 2022;74(3):386–391. doi:10.1002/acr.24479
- Hawker GA, Lohmander LS. What an earlier recognition of osteoarthritis can do for OA prevention. *Osteoarthritis Cartilage*. 2021;29(12):1632–1634. doi:10.1016/j.joca.2021.08.007
- Emery CA, Whittaker JL, Mahmoudian A, et al. Establishing outcome measures in early knee osteoarthritis. *Nat Rev Rheumatol*. 2019;15(7):438–448. doi:10.1038/s41584-019-0237-3
- Driban JB, Harkey MS, Liu S-H, Salzler M, McAlindon TE. Osteoarthritis and aging: young adults with osteoarthritis. *Curr Epidemiol Rep*. 2020;7:9–15. doi:10.1007/s40471-020-00224-7
- Aggarwal R, Ringold S, Khanna D, et al. Distinctions between diagnostic and classification criteria? *Arthritis Care Res (Hoboken)*. 2015;67(7):891–897. doi:10.1002/acr.22583
- Luyten FP, Bierma-Zeinstra S, Dell’Accio F, et al. Toward classification criteria for early osteoarthritis of the knee. *Semin Arthritis Rheum*. 2018;47(4):457–463. doi:10.1016/j.semarthrit.2017.08.006
- Harkey MS, Baez S, Lewis J, et al. Prevalence of early knee osteoarthritis illness among various patient-reported classification criteria after anterior cruciate ligament reconstruction. *Arthritis Care Res (Hoboken)*. 2022;74(3):377–385. doi:10.1002/acr.24809. Published correction appears in *Arthritis Care Res (Hoboken)*. 2023;75(11):2399–2402.
- Bruce J, Quinlan J. Chronic post surgical pain. *Rev Pain*. 2011;5(3):23–29. doi:10.1177/204946371100500306
- Jones I, Bari F. Chronic pain after surgery. *Surgery (Oxford)*. 2017;35(2):93–96. doi:10.1016/j.mpsur.2013.12.003
- Osteoarthritis Action Alliance, Secondary Prevention Task Group; Driban JB, Vincent HK, Trojjan TH, et al. Evidence review for preventing osteoarthritis after an anterior cruciate ligament injury: an Osteoarthritis Action Alliance consensus statement. *J Athl Train*. 2023;58(3):198–219. doi:10.4085/1062-6050-0504.22
- Watt FE, Corp N, Kingsbury SR, et al; Arthritis Research UK Osteoarthritis and Crystal Disease Clinical Study Group Expert Working Group. Towards prevention of post-traumatic osteoarthritis: report from an international expert working group on considerations for the design and conduct of interventional studies following acute knee injury. *Osteoarthritis Cartilage*. 2019;27(1):23–33.
- Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes*. 2003;1(1):64. doi:10.1186/1477-7525-1-64



21. Harkey MS, Baez S, Lewis J, et al. Prevalence of early knee osteoarthritis illness among various patient-reported classification criteria after anterior cruciate ligament reconstruction. *Arthritis Care Res (Hoboken)*. 2022;74(3):377–385. doi:10.1002/acr.24809
22. Muller B, Yabroudi MA, Lynch A, et al. Defining thresholds for the patient acceptable symptom state for the IKDC Subjective Knee Form and KOOS for patients who underwent ACL reconstruction. *Am J Sports Med*. 2016;44(11):2820–2826. doi:10.1177/0363546516652888
23. Driban JB, Vincent HK, Trojian TH, et al. Preventing osteoarthritis after an anterior cruciate ligament injury: an Osteoarthritis Action Alliance consensus statement. *J Athl Train*. 2023;58(3):193–197. doi:10.4085/1062-6050-0255.22
24. Whittaker JL, Culvenor AG, Juhl CB, et al. OPTIKNEE 2022: consensus recommendations to optimise knee health after traumatic knee injury to prevent osteoarthritis. *Br J Sports Med*. 2022;56(24):1393–1405. doi:10.1136/bjsports-2022-106299
25. Ingelsrud LH, Granan LP, Terwee CB, Engebretsen L, Roos EM. Proportion of patients reporting acceptable symptoms or treatment failure and their associated KOOS values at 6 to 24 months after anterior cruciate ligament reconstruction: a study from the Norwegian Knee Ligament Registry. *Am J Sports Med*. 2015;43(8):1902–1907. doi:10.1177/0363546515584041
26. Øiestad BE, Juhl CB, Culvenor AG, Berg B, Thorlund JB. Knee extensor muscle weakness is a risk factor for the development of knee osteoarthritis: an updated systematic review and meta-analysis including 46 819 men and women. *Br J Sports Med*. 2022;56(6):349–355. doi:10.1136/bjsports-2021-104861
27. Andriacchi TP, Favre J. The nature of in vivo mechanical signals that influence cartilage health and progression to knee osteoarthritis. *Curr Rheumatol Rep*. 2014;16(11):463. doi:10.1007/s11926-014-0463-2
28. Culvenor AG, Collins NJ, Guermazi A, et al. Early knee osteoarthritis is evident one year following anterior cruciate ligament reconstruction: a magnetic resonance imaging evaluation. *Arthritis Rheumatol*. 2015;67(4):946–955. doi:10.1002/art.39005

## SUPPLEMENTAL MATERIAL

**Supplemental Table.** Participant Demographics Between the Longitudinal Early Osteoarthritis (OA) Symptoms Status Groups. **Supplemental Figure.** Percentage of participants below the Knee injury and Osteoarthritis Outcome Score (KOOS) subscale threshold. For participants with (dark gray bars) and without (light gray bars) early osteoarthritis (OA) symptoms using the Luyten Original classification criteria, the figure highlights the percentage of participants below the KOOS subscale threshold for each subscale used in the early OA symptom definition. The KOOS Quality of Life (QOL) and KOOS Symptoms (Sx) subscales appear to be the primary drivers of a participant meeting the early OA symptom definition. Abbreviation: ADL, activities of daily living.

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