Four Distinct 5-Year Trajectories of Knee Function Emerge in Patients Who Followed the Delaware-Oslo ACL Cohort Treatment Algorithm

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Background: Impairments and dysfunction vary considerably after anterior cruciate ligament (ACL) injury, and distinct subgroups may exist.

Purpose: (1) To identify subgroups of patients with ACL injury who share common trajectories of patient-reported knee function from initial presentation to 5 years after a treatment algorithm where they chose either ACL reconstruction (ACLR) plus rehabilitation or rehabilitation alone. (2) To assess associations with trajectory affiliation.

Study Design: Cohort study; Level of evidence, 3.

Methods: We included 276 patients with a acute first-time complete unilateral ACL injury. All patients underwent a 5-week neuromuscular and strength training program before a shared decision-making process about treatment. Within their latest attended follow-up, 62% of patients had undergone early ACLR (<6 months after the 5-week program), 11% delayed ACLR (>6 months after the 5-week program), and 27% progressive rehabilitation alone. Patients completed the International Knee Documentation Committee Subjective Knee Form (IKDC-SKF) at inclusion, after the 5-week program, and at 6 months, 1 year, 2 years, and 5 years after ACLR or completion of the 5-week program (patients treated with rehabilitation alone). We used group-based trajectory modeling to identify trajectories of IKDC-SKF and multinomial logistic regression to assess associations with trajectory affiliation.

Results: Four distinct trajectories of IKDC-SKF were identified: Low (n = 22; 8.0% of the cohort), Moderate (n = 142; 51.4%), High (n = 105; 38.0%), and High Before Declining (n = 7; 2.5%). The High trajectory had higher scores at inclusion than the Moderate trajectory, but both improved considerably within 1 year and had thereafter stable high scores. The High Before Declining trajectory also started relatively high and improved considerably within 1 year but experienced a large deterioration between 2 and 5 years. The Low trajectory started low and had minimal improvement. New knee injuries were important characteristics of the High Before Declining trajectory, concomitant meniscal injuries were significantly associated with following the Low (vs Moderate) trajectory, and early/preoperative quadriceps strength and hop symmetry (measured at inclusion) were significantly associated with following the High (vs Moderate) trajectory.

Conclusion: We identified 4 distinct 5-year trajectories of patient-reported knee function, indicating 4 subgroups of patients with ACL injury. Importantly, 88% of the patients who followed our treatment algorithm followed the Moderate and High trajectories characterized by good improvement and high scores. Due to eligibility criteria and procedures in our cohort, we can only generalize our model to athletes without major concomitant injuries who follow a similar treatment algorithm. Concomitant meniscal injuries and new knee injuries were important factors in the unfavorable Low and High Before Declining trajectories. These associations were exploratory but support the trajectories' validity. Our findings can contribute to patient education about prognosis and underpin the importance of continued secondary injury prevention.

Keywords: knee; prognosis; rehabilitation; anterior cruciate ligament injury

Short- and long-term impairments and dysfunction after anterior cruciate ligament (ACL) injury vary considerably, and patients progress at different paces,[1,13,27,36,37] indicating diversity in response to ACL injury and treatment. Researchers, however, too often report outcomes averaged over all patients.

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In other areas of musculoskeletal research, sophisticated statistical methods such as group-based trajectory modeling[30,31] have been used to identify homogeneous subgroups or phenotypes that share common trajectories of knee function.[3,5,18] Identifying such subgroups among patients with ACL injury may improve our understanding of longitudinal differences in responses to injury or surgery and could develop our knowledge about prognosis. This information could help clinicians to better educate patients about expected outcomes and time to recovery. Further, associations with trajectory affiliation may help to identify at-risk patients and targets of intervention.

Our prospective cohort study, the Delaware-Oslo ACL Cohort, has assessed patient-reported knee function using the International Knee Documentation Committee Subjective Knee Form (IKDC-SKF)[2,19,20,39] at 6 timepoints from initial presentation to 5 years, a very good base for exploring different trajectories of knee function. We included patients early after injury, before a 5-week rehabilitation program and shared decision-making process about treatment. Following our treatment algorithm, we have previously reported equivalent 2-year and 5-year clinical, functional, physical activity, and radiographic outcomes after progressive rehabilitation alone, early ACL reconstruction (ACLR), and delayed ACLR[13,33,34] and assessed prognostic factors for short-term outcomes.[15,26,27,37]

We, therefore, aimed to identify subgroups of patients with ACL injury who share common trajectories of patient-reported knee function from initial presentation to 5 years after a treatment algorithm where they chose either ACLR plus rehabilitation or rehabilitation alone. Further, we aimed to assess clinical associations with trajectory affiliation.

METHODS

Participants

We included 276 patients with a first-time complete unilateral ACL injury from the Delaware-Oslo ACL cohort study, a prospective cohort study including 300 patients from the University of Delaware, Newark, Delaware, USA, and the Norwegian Sports Medicine Clinic, Oslo, Norway, between 2006 and 2012. The diagnosis was verified with magnetic resonance imaging (MRI) and $\geq$3 mm of increased anterior knee joint laxity (manual maximal test using a KT-1000 arthrometer; MED Metric). Concomitant injuries were diagnosed with MRI. The patients were between 13 and 56 years of age (mean age, 26.5 years; 20 patients aged $\geq$45 years), participated in pivoting sports (level I sports such as soccer, team handball, basketball, floorball, American football, and lacrosse or level II sports such as alpine skiing, racket sports, and martial arts)[17] $\geq$2 times per week preinjury, and had resolved acute impairments (no/minimal pain or effusion during or after plyometric activities) before inclusion (within 3 months after ACL injury in Oslo and within 7 months in Delaware). We excluded patients with current or previous ipsilateral or contralateral knee injuries, concomitant grade III ligament injury, full-thickness articular cartilage damage, or fracture.

We obtained informed consent or assent with parental consent and approvals from the Regional Committee for Medical and Health Research Ethics of Norway and the University of Delaware Institutional Review Board before inclusion.

Treatment Algorithm

After inclusion and resolution of acute impairments (mean 59 days after injury), all patients underwent a 5-week rehabilitation program with progressive neuromuscular and strength training exercises as previously described by Eitzen et al.[9] All patients were educated about treatment alternatives before they underwent functional testing, and they made their treatment choice in consultation with their physical therapists and orthopaedic surgeons. Among 270 patients with a confirmed treatment status (6 patients lost before 2-year follow-up without a confirmed surgery), 167 patients (62%) had undergone early ACLR (<6 months after the 5-week rehabilitation program), 30 patients (11%) delayed ACLR (>6 months after the 5-week rehabilitation program), and 73 patients (27%) were treated with progressive rehabilitation alone at the latest attended follow-up. We previously reported that patients who chose progressive rehabilitation alone were older than those who underwent early or delayed ACLR (mean 31.9 years vs 24.7 and 24.4, respectively), were less likely to participate in level I sports (46% vs 77% and 83%) and hence more likely to participate in level II sports preinjury, and had fewer concomitant medial meniscal injuries (11% vs 27% and 27%, respectively).[34] The main patient-reported reason for choosing rehabilitation alone was the achievement of good knee function after

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rehabilitation, whereas intention to return to level I sports was the main reason for choosing early ACLR.[13] Delayed ACLR was indicated if patients experienced dynamic knee instability[40] or if they changed their minds.

Several experienced sports orthopaedic surgeons performed the ACLRs using bone–patellar tendon–bone autografts (21.5%), hamstring autografts (51.5%), or allografts (27%). At the time of ACLR, 69 of 167 (41%) in the early and 12 of 30 (40%) in the delayed ACLR groups also had meniscal surgery (26% had excisions, 56% had repairs, and 18% had trephination/rasping). Postoperative rehabilitation consisted of 3 phases: (1) acute postoperative phase, (2) rehabilitation phase, and (3) return to sport phase, as previously described.[11,13,14] Postoperative rehabilitation was tailored according to the surgeons' recommended restrictions and the patients' symptoms. Patients who did not undergo ACLR typically continued progressive rehabilitation for 3 to 4 months, with the same goals and phases as the patients who underwent ACLR.

Assessments, Outcomes, and Timepoints of Follow-ups

We explored trajectories of patient-reported knee function using the IKDC-SKF (see the Appendix, available in the online version of this article), a patient-reported questionnaire for symptoms, function, and sports activity, which is scored from 0 (worst) to 100 (best).[19] The IKDC-SKF is reliable and valid at various timepoints after ACL injury and is frequently used as a stand-alone outcome measure.[2,6,19-21,39]

Patients completed the IKDC-SKF at inclusion, after the 5-week rehabilitation program (mean 6 weeks after inclusion), and at follow-ups 6 months, 1 year, 2 years, and 5 years after either ACLR (patients treated surgically) or completion of the 5-week rehabilitation program (patients treated with rehabilitation alone). If delayed ACLR was performed before the 2-year follow-up, patients' timelines were reset and they were scheduled for new 6-month and 1-year follow-ups as surgically treated. To allow for more equal comparisons of individual trajectories, we included only the postoperative 6-month and 1-year follow-ups for the delayed ACLR group to avoid postoperative periods at different timepoints and differences in number of follow-ups across treatment groups.

Associations With IKDC-SKF Trajectory Affiliation

We explored associations between trajectory affiliation and the following factors: patient characteristics at inclusion (age, sex, body mass index [BMI], preinjury activity level), injury severity (concomitant meniscal or cartilage injuries), new ipsilateral and contralateral knee injuries, knee function and symptoms at inclusion (giving way episodes, KT-1000 arthrometer measurements, quadriceps muscle strength limb symmetry index [LSI], single hop for distance), treatment status at last attended follow-up (rehabilitation alone, early ACLR, or delayed ACLR), and graft choice.

At inclusion, patients reported preinjury activity level (level I or II) and giving way episodes since injury. BMI was calculated from height and weight measures. Anterior knee joint laxity (manual maximal test using a KT-1000 arthrometer) was reported as side-to-side difference at inclusion. Concomitant injuries were diagnosed with MRI. Graft choice was reported by the surgeon. Due to differences in available test equipment, we assessed quadriceps strength with maximal isometric contraction testing in Delaware and concentric isokinetic testing in Oslo.[25] We chose the single hop for distance[32] among a cluster of single-leg hop tests due to its superior measurement properties and previous association with outcomes.[4,15,26] One practice trial was performed before we recorded 2 trials, from which the mean score was calculated. We considered trials valid if patients performed stable landings (without touching the floor or walls with the other foot or hands or performing additional hops but with no further restrictions for arm movements). For strength and hop tests, we tested the uninjured leg first and expressed the results as the LSI (ipsilateral limb performance as a percentage of the contralateral). We also reported total distance in centimeters for the single hop for distance. New knee injuries were patient-reported and verified with clinical examination plus MRI and/or during surgery if indicated.

Statistical Methods

The previous publications from our cohort, showing equivalent 2-year and 5-year clinical, functional, physical activity, and radiographic outcomes after progressive rehabilitation alone, early ACLR, and delayed ACLR after our treatment algorithm,[13,33,34] form the basis for combining the treatment groups in one analysis.

For our first aim, we used group-based trajectory modeling (GBTM) to identify subgroups of patients who followed distinct trajectories of IKDC-SKF from initial presentation to 5 years.[29,30] We used the *traj* software plugin for Stata.[23] We used the censored normal model because our outcome was measured on a continuous scale with a prespecified range.[23] The timepoints of the model were fixed intervals corresponding with the follow-up timepoints. GBTM imputes missing values based on available data points.[29]

We used a 2-stage model selection process (more details in the Appendix, available online).[29] In the first stage, we found the optimal number of trajectories. The procedures changed the number of trajectories and repeated the analyses until we found the trajectory number with the highest (least negative) Bayesian information criterion (BIC) value; a higher BIC value indicates better model fit because it balances improvements in model likelihood with the number of parameters estimated.[29] In the second stage, we found the optimal trajectory shapes by changing the order of the polynomial for each trajectory (zero-order, linear, quadratic, or cubic). Finally, we chose the optimal model with the highest BIC value, while we also evaluated trajectory sizes (optimally, >5% of the cohort should belong to the smallest trajectory).[29]

Thereafter, we calculated posterior group-membership probabilities and odds of correct classification to assess model adequacy. The posterior group-membership probability is the probability that an individual with a specific profile belongs to each possible trajectory: The sum of probabilities for

TABLE 1
Descriptive Characteristics at Inclusion[a]

	Missing Values, n (%)	Whole Cohort (n = 276)
Inclusion site Delaware/Oslo, n	0	134/142
Age, y	0	26.5 ± 9.8
Female sex	0	128 (46)
Body mass index	0	24.6 ± 4.0
Preinjury sports participation	0	
Level I		191 (69)
Level II		85 (31)
Concomitant injuries[b]		
Meniscus	0	91 (33)
Cartilage	0	22 (8)
≥1 giving way episode between injury and inclusion	2 (1)	92 (34)
KT-1000 arthrometer measurement, mm (involved knee minus contralateral knee)	19 (7)	5.2 ± 2.5
Quadriceps strength LSI, %	0	90 ± 11
Single hop for distance	12 (4)	
Index limb, cm		117 ± 32
LSI, %		89 ± 13

[a]Values are expressed as n (%) or mean ± SD. LSI, limb symmetry index.
[b]Number of patients diagnosed with the injury using magnetic resonance image at inclusion.

each patient is 1, and all patients are assigned to the trajectory with the highest posterior group-membership probability. The mean posterior probability for each trajectory should be ≥0.7 (scale from 0 to 1, where 1 indicates the smallest probability that the individuals could belong to a different trajectory than the one to which they were assigned).[29] The odds of correct classification for each trajectory should be >5, and estimated group probabilities and percentages actually assigned should correspond well.[29]

We performed 2 sensitivity analyses to assess the robustness of the chosen model: (1) excluding patients with only 1 datapoint for IKDC-SKF (n = 5) and (2) using months since inclusion as the time variable and including all follow-up timepoints (both as nonsurgically and surgically treated) for the patients who underwent delayed ACLR. This model contained the most valid timeline but introduced challenges with different number of follow-ups between different treatment groups. It was also challenging to compare individual trajectories using this model because it allowed postoperative periods at different timepoints.

For our second aim, we used multinomial logistic regression to assess associations with trajectory affiliation. Due to sample size, we chose univariable analyses. We chose the reference trajectory of the analysis post GBTM analysis based on clinical relevance and power. To increase statistical power, we merged the different types of new ipsilateral and contralateral injuries.

RESULTS

Subjects

At the 6 timepoints (chronological order), 96%, 89%, 86%, 82%, 77%, and 80% filled out the IKDC-SKF. Data from all 276 patients were included, and their characteristics are described in Table 1.[34]

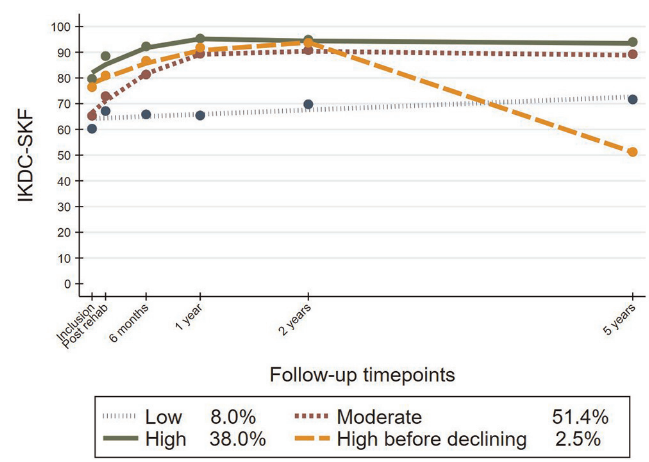

Figure 1. Trajectories of International Knee Documentation Committee Subjective Knee Form (IKDC-SKF) from inclusion to 5 years. The red, blue, green, and orange colors represent the Low, Moderate, High, and High Before Declining trajectories, respectively. The points represent the mean IKDC-SKF scores at each timepoint. The solid lines represent the predicted trajectories. The percentage assigned to each trajectory is indicated.

Trajectories of IKDC-SKF

The model selection process is described in the Appendix (available online). We identified 4 distinct trajectories of IKDC-SKF from inclusion to 5 years: Low (n = 22; 8.0%), Moderate (n = 142; 51.4%), High (n = 105; 38.0%), and High Before Declining (n = 7; 2.5%) (Figure 1). We found that 9 of 10 of the patients belonged to the 2 largest trajectories—Moderate and High. The patients with High trajectory had higher scores at inclusion than those with

TABLE 2
Model-Fit Parameters of the Selected Model

Trajectory	Mean Average Posterior Probability	Odds of Correct Classification	Percentage Assigned	Estimated Group Probability
Low	0.95	222.0	8.0	8.9
Moderate	0.87	6.4	51.4	50.2
High	0.86	9.8	38.0	37.5
High Before Declining	0.98	2064.1	2.5	3.4

Moderate trajectory (mean 80 ± 9 vs 65 ± 10, respectively), but both improved considerably up to 1 year (mean 96 ± 5 and 89 ± 8) and had stable high scores over time. The patients with High Before Declining trajectory also started out with relatively high scores (mean 77 ± 12) and improved considerably up to 1 year (mean 92 ± 8) but experienced a large deterioration between 2 and 5 years (mean 49 ± 10 at 5 years). The patients with Low trajectory had low scores at inclusion (mean 60 ± 12) and minimal improvement over time.

The model-fit parameters indicated good model fit for all 4 trajectories (Table 2): average posterior group-membership probabilities above the recommended threshold of 0.7 (0.86-0.98), odds of correct classification above the recommended threshold of 5.0 (6.4-2064.1), and good correspondence between estimated group probabilities and percentages actually assigned.[29]

Sensitivity Analyses

The first sensitivity analysis looked almost identical to the original model and led to minor changes in model-fit parameters. The second sensitivity analysis led to moderate changes: the polynomials of the optimal model were slightly different, the BIC values were slightly lower, the trajectory sizes changed moderately, and the model-fit parameters changed substantially but were still within the recommended thresholds (Appendix, available online).

Trajectory Profiles

Profiles for the patients belonging to the 4 trajectories are described in Table 3. Compared with the Moderate and High trajectories, the patients who belonged to the Low trajectory had a high rate of graft ruptures and concomitant meniscal and cartilage injuries. The High Before Declining trajectory consisted predominantly of males (n = 6/7) who were active in level I sports preinjury (n = 6/7) and experienced one or more new ipsilateral or contralateral knee injuries (n = 6/7 patients, all between 2 and 5 years) and/or underwent delayed ACLR ≤7 months before the 5-year follow-up (n = 2/7).

Associations With IKDC-SKF Trajectory Affiliation

We used the Moderate trajectory as reference in the analysis due to high n (statistical power) and because the comparison between the Low and Moderate trajectories was especially clinically interesting—both had low IKDC-SKF scores at inclusion but only the Moderate trajectory progressed. Too few patients belonged to the High Before Declining trajectory to assess statistical associations, but all patients with this trajectory either had sustained a new ipsilateral or contralateral knee injury or underwent delayed ACLR ≤7 months before final follow-up.

Concomitant meniscal injuries were significantly associated with belonging to the Low versus the Moderate trajectory (Table 4). The factors significantly associated with belonging to the High versus the Moderate trajectory were undergoing rehabilitation alone instead of early ACLR, having better quadriceps strength LSI and single hop for distance (LSI and distance), and experiencing no giving way episodes between injury and inclusion. Hence, early/preoperative quadriceps strength and hop symmetry were clear predictors of a High trajectory; for every 1% increase in quadriceps strength LSI and single hop for distance LSI, there were 5% and 2% higher odds of affiliation to the High trajectory, respectively.

DISCUSSION

We identified 4 distinct 5-year trajectories of patient-reported knee function after a treatment algorithm where all patients first went through a 5-week neuromuscular and strength training program before they chose either ACLR plus rehabilitation or rehabilitation alone; the trajectories were Low (8.0%), Moderate (51.4%), High (38.0%), and High Before Declining (2.5%), indicating 4 subgroups of patients with ACL injury. Indeed, the trajectory with the largest number of patients (Moderate) followed typical clinical expectations: start low, end high. A slightly smaller but also considerable number of patients had relatively high scores at baseline and also progressed over time (High). 1 of 10 patients, however, either started low and stayed low (Low) or started high and experienced a large deterioration between the 2-year and 5-year follow-up (High Before Declining). Importantly, 9 of 10 of the patients who followed our treatment algorithm belonged to the favorable Moderate and High trajectories, including 68 of the 73 patients who were treated with rehabilitation alone at their latest attended follow-up. Early/preoperative quadriceps strength and hop symmetry (measured at inclusion) were clear predictors of a High trajectory. Further, we found that concomitant meniscal injuries and new ipsilateral and contralateral knee injuries were the main characteristics of the patients who belonged to the

TABLE 3
Trajectory Profiles[a]

Factor	Low Trajectory (n = 22)	Moderate Trajectory (n = 142)	High Trajectory (n = 105)	High Before Declining Trajectory (n = 7)
Factors measured at inclusion				
Age, y (n = 276)	27.4 ± 10.7	27.4 ± 9.8	25.1 ± 9.4	24.3 ± 9.8
Female sex (n = 276)	12 (55)	70 (49)	45 (43)	1 (14)
Body mass index (n = 276)	24.3 ± 4.3	25.0 ± 4.2	24.3 ± 3.7	22.3 ± 1.7
Preinjury sports participation (n = 276)				
Level I	17 (77)	94 (66)	74 (70)	6 (86)
Level II	5 (23)	48 (34)	31 (30)	1 (14)
Concomitant injuries[b] (n = 276)				
Meniscus	14 (64)	49 (35)	27 (26)	1 (14)
Cartilage	3 (14)	10 (7)	9 (9)	0 (0)
≥1 giving way episode between injury and inclusion (n = 274)	6 (27)	58 (41)	25 (24)	3 (43)
KT-1000 arthrometer measurement, mm (involved knee minus contralateral knee) (n = 257)	5.3 ± 2.8	5.3 ± 2.5	5.1 ± 2.4	5.6 ± 3.4
Quadriceps strength LSI, % (n = 276)	92 ± 11	87 ± 10	93 ± 12	86 ± 5
Single hop for distance (n = 264)				
Index limb, cm	114 ± 32	112 ± 32	123 ± 33	144 ± 30
LSI, %	88 ± 18	88 ± 12	92 ± 12	90 ± 8
Factors measured within the 5-year follow-up				
Treatment status at last attended follow-up (n = 270)				
Early ACLR	16 (73)	93 (67)	55 (53)	3 (43)
Delayed ACLR	3 (14)	13 (9)	12 (12)	2 (29)
Rehabilitation alone	3 (14)	32 (23)	36 (35)	2 (29)
Graft used for ACLR (n = 194/197 ACLR patients)				
Allograft	5 (26)	26 (25)	20 (31)	1 (25)
Patellar tendon	6 (32)	24 (23)	12 (18)	0 (0)
Hamstrings tendon	8 (42)	56 (53)	33 (51)	3 (75)
New ipsilateral knee injuries (n = 228)				
Graft rupture	5 (25)	12 (10)	6 (7)	1 (14)
PCL/MCL/LCL injury	2 (11)	1 (1)	1 (1)	0 (0)
Meniscal injury	0 (0)	10 (9)	4 (5)	5 (71)
Cartilage injury	1 (5)	2 (2)	0 (0)	0 (0)
New contralateral knee injuries (n = 228)				
ACL injury	1 (5)	6 (5)	7 (8)	2 (29)
PCL/MCL/LCL injury	0 (0)	0 (0)	0 (0)	0 (0)
Meniscal injury	0 (0)	1 (1)	3 (4)	1 (14)
Cartilage injury	0 (0)	0 (0)	1 (1)	0 (0)

[a]Values are expressed as n (%) or mean ± SD. ACL, anterior cruciate ligament; ACLR, anterior cruciate ligament reconstruction; LCL, lateral collateral ligament; LSI, limb symmetry index; MCL, medial collateral ligament.
[b]Number of patients diagnosed using magnetic resonance image at inclusion.

unfavorable Low and High Before Declining trajectories. Interestingly, age and preinjury activity level were not associated with trajectory affiliation. In opposition to a common belief, undergoing ACLR instead of rehabilitation alone was not associated with affiliation to the favorable trajectories.

The trajectories identified in this study are visual tools that are informative of expected outcomes and time to recovery for patients who undergo a similar treatment algorithm. These trajectories have a potential for use in patient education about prognosis. Additionally, the clinical associations with each trajectory support the trajectories' validity: They appear as clinically meaningful, and several associations correspond with previous prognostic studies, as described below.

Our trajectory profiles and associations with trajectory affiliation may help clinicians to identify at-risk patients and targets of intervention. Concomitant meniscal injuries were associated with 3-fold higher odds of belonging to the Low versus the Moderate trajectory, which means increased odds of starting low and staying low instead of progressing to a good level of knee function. Optimizing other aspects of follow-up and rehabilitation[12,38] may therefore be crucial for patients with concomitant meniscal injuries. That concomitant meniscal injuries were an important negative prognostic factor in patients with ACL injury is also consistent with previous research[7,35] and may be attributed to more symptoms and delayed progression in rehabilitation due to postoperative restrictions. New ipsilateral and contralateral knee injuries with quite late timing (between 2 and 5 years) were frequent

TABLE 4
Associations With IKDC-SKF Trajectory Affiliation[a]

	Low Trajectory (vs Moderate)		High Trajectory (vs Moderate)	
	Odds Ratio (95% CI)	*P* Value	Odds Ratio (95% CI)	*P* Value
Factors measured at inclusion				
Age	1.00 (0.96-1.05)	.998	0.98 (0.95-1.00)	.073
Male sex (female ref.)	0.81 (0.33-2.00)	.647	1.30 (0.78-2.15)	.316
Body mass index	0.96 (0.85-1.08)	.457	0.96 (0.90-1.02)	.192
Preinjury sports participation (level I ref.)	0.58 (0.20-1.66)	.306	0.82 (0.48-1.41)	.476
Concomitant injuries (none ref.)				
Meniscus	3.32 (1.30-8.46)	**.012**	0.66 (0.38-1.15)	.140
Cartilage	2.08 (0.53-8.26)	.296	1.24 (0.48-3.16)	.656
≥1 giving way episodes between injury and inclusion (none ref.)	0.53 (0.20-1.44)	.212	0.44 (0.25-0.77)	**.004**
KT-1000 arthrometer measurement	0.99 (0.81-1.21)	.929	0.97 (0.87-1.08)	.567
Quadriceps strength LSI	1.04 (1.00-1.09)	.051	1.05 (1.03-1.08)	**<.001**
Single hop for distance				
Index limb	1.00 (0.99-1.02)	.858	1.01 (1.00-1.02)	**.015**
LSI	1.00 (0.96-1.03)	.891	1.02 (1.00-1.05)	**.031**
Factors measured within the 5-year follow-up				
Treatment status at last attended follow-up[b]				
Early ACLR vs rehabilitation alone	1.84 (0.50-6.71)	.359	0.53 (0.29-0.94)	**.030**
Delayed ACLR vs rehabilitation alone	2.46 (0.44-13.82)	.306	0.82 (0.33,2.05)	.673
Graft used for ACLR[c]				
Patellar tendon vs allograft	1.30 (0.35-4.82)	.694	0.65 (0.26-1.61)	.351
Hamstrings tendon vs allograft	0.74 (0.22-2.49)	.630	0.77 (0.37-1.58)	.471
New ipsilateral knee injury (none ref.)	2.44 (0.87-6.85)	.091	0.47 (0.20-1.12)	.088
New contralateral knee injury (none ref.)	0.85 (0.10-7.32)	.882	1.59 (0.55-4.56)	.391

[a]Bold *P* values indicate statistical significance ($P < .05$). Odds ratios >1 favor affiliation to the Low or High trajectory instead of the Moderate trajectory, whereas odds ratios <1 favor affiliation to the Moderate trajectory. ACLR, anterior cruciate ligament reconstruction; CI, confidence interval; IKDC-SKF, International Knee Documentation Committee Subjective Knee Form; LSI, limb symmetry index.

[b]The odds ratios express the likelihood of following the Low and High trajectory instead of the Moderate trajectory, if patients underwent early or delayed ACLR compared with rehabilitation alone.

[c]The odds ratios express the likelihood of following the Low and High trajectory instead of the Moderate trajectory, if patients received a patellar tendon or hamstrings tendon autograft compared with an allograft.

in the High Before Declining trajectory (6/7 patients) and had deteriorating consequences. This finding underscores the importance of long-term follow-up with aims of normalizing knee function, applying strict return-to-play criteria, and providing secondary prevention of new injuries[12,16,24]—and continuing these measures over time. The factors associated with belonging to the High versus the Moderate trajectory were mainly related to better early knee function and underscore the importance of high-quality early rehabilitation as suggested by current clinical guidelines.[12] For every 1% increase in early/preoperative quadriceps strength LSI and single hop for distance LSI, we found 5% and 2% higher odds of affiliation to the High trajectory, respectively. Again, this underscored the value of preoperative rehabilitation beyond impairment resolution. This finding adds to the body of evidence of associations between early functional performance and short- and long-term patient-reported outcomes.[8,10,22]

We used a data-driven statistical method, and the differences between the trajectories appeared clinically meaningful: The patients with Low trajectory had mean IKDC-SKF scores well below the previously established patient acceptable symptom state (PASS) at 75.9 points[28] at all timepoints, whereas the patients with Moderate and High trajectories had scores well above the PASS at all follow-ups ≥6 months. The improvement from inclusion to 1 year of the patients with Moderate and High trajectories exceeded the minimally clinically important change for the IKDC-SKF at 11.5 points[20] (mean 15 and 24 points, respectively). There was a clinically meaningful difference in mean IKDC-SKF score (larger than the minimally clinically important change) between the High and the Moderate trajectories early on (from inclusion to 6 months), but not from 1 to 5 years, which is potentially important for patients with high knee demands who aim to return to sports or a physically demanding job as soon as possible.

To our knowledge, this study is the first to explore different trajectories after ACL injury or in a comparable patient group (young active patients with acute knee injuries). Berg et al[3] found trajectories similar to the Low, Moderate, and High trajectories for middle-aged patients with degenerative meniscal tears and no/minimal concomitant knee osteoarthritis.

Limitations

The identified trajectories resulted from a data-driven statistical method that provides an estimation. Although the model-fit parameters show low likelihood of poor model fit and 2 sensitivity analyses were performed without substantially changing the model, our results should be validated or repeated in other data sets. Including only the IKDC-SKF as the outcome is a possible weakness, although it has good measurement properties.[2,6,19-21,39]

Because we assessed associations with trajectory affiliation using univariate analyses, the factors identified may not be causal: They are exploratory, and spurious associations may exist. For example, we should interpret the association between choosing rehabilitation alone and affiliation to the High trajectory carefully because patients with poor knee function were likely to undergo delayed ACLR. Some potential important factors were not measured in our study: for example, patients' expectations.

Due to eligibility criteria and procedures in our cohort, we can generalize our model only to athletes without major concomitant injuries who follow a similar treatment algorithm. The many different surgeons and treatment options pose a possible weakness but may also strengthen the generalizability of the study.

The definition of early ACLR as that performed <6 months after the 5-week rehabilitation program was a practical decision as to when we collected information about their treatment status. Because 6 months may be a long time in this context, this definition is a possible weakness.

CONCLUSION

We identified 4 distinct 5-year trajectories of patient-reported knee function after a treatment algorithm where all patients first went through a 5-week rehabilitation program before they chose either ACLR plus rehabilitation or rehabilitation alone; these trajectories were Low (8.0%), Moderate (51.4%), High (38.0%), and High Before Declining (2.5%), indicating 4 subgroups of patients with ACL injury. Importantly, 9 of 10 of the patients who followed our treatment algorithm belonged to the favorable Moderate and High trajectories characterized by good progression and IKDC-SKF scores above the PASS threshold. Concomitant meniscal injuries and new knee injuries were important factors in the unfavorable Low and High Before Declining trajectories, whereas factors associated with belonging to the High trajectory were mainly related to having better knee function early after injury. These associations were exploratory but support the trajectories' validity. Our findings contribute to patient and clinician education about prognosis and underpin the importance of continued secondary prevention of new knee injuries and high-quality early rehabilitation.

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