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Forecasting neuromuscular recovery after anterior cruciate ligament injury: Athlete recovery profiles with generalized additive modeling

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Abstract

A retrospective analysis of longitudinally collected athlete monitoring data was conducted to generate a model of neuromuscular recovery after anterior cruciate ligament (ACL) injury and reconstruction (ACLR). Neuromuscular testing data including countermovement jump (CMJ) force-time asymmetries and knee extensor strength (maximum voluntary contraction$_{ext}$) asymmetries (between-limb asymmetry index—AI) were obtained from athletes with ACLR using semitendinosus (ST) autograft (*n* = 29; AI measurements: *n* = 494), bone patellar tendon bone autograft (*n* = 5; AI measurements: *n* = 88) and noninjured controls (*n* = 178; AI measurements: *n* = 3188). Explosive strength measured as the rate of torque development was also calculated. CMJ force-time asymmetries were measured over discrete movement phases (eccentric deceleration phase, concentric phase). Separate additive mixed effects models (additive mixed effects model [AMM]) were fit for each AI with a main effect for the surgical technique and a smooth term for the time since surgery (days). The models explained between 43% and 91% of the deviance in neuromuscular recovery after ACLR. The mean time course was generated from the AMM. Comparative neuromuscular recovery profiles of an athlete with an accelerated progression and an athlete with a delayed progression after a serious multiligament injury were generated. Clinical Significance: This paper provides a new perspective on the utility of longitudinal athlete monitoring including routine testing to develop models of neuromuscular recovery after ACLR that can be used to characterize individual progression throughout rehabilitation.

KEYWORDS

athlete monitoring, generalized additive mixed models, knee injury, mixed effects, multilevel modeling, return to play, sport injury

1 | INTRODUCTION

Longitudinal athlete monitoring has become increasingly commonplace in sport performance settings.[1] This includes routine neuromuscular testing after anterior cruciate ligament (ACL) injury and ACL reconstruction surgery (ACLR) to track progress throughout rehabilitation and inform return to sport (return to play) decision making.[2,3] Longitudinally collected neuromuscular testing data can provide sport practitioners and clinicians with novel data-informed models of individual progression throughout rehabilitation after sport injury.[4] This is important as neuromuscular testing is recommended after ACLR to determine return to sport readiness.[5] Yet, the sensitivity of typical performance-based clinical testing batteries (e.g., single leg hop for distance or time) for detecting ACL reinjury risk is questionable,[6–8] and a high fraction of athletes who suffer ACL injury do not return to their preinjury performance level.[9] Further, as sport performance teams often utilize an interdisciplinary and multidisciplinary team approach to support athletes throughout the return to health and performance transitions after ACL injury,[10,11] models of functional recovery based on multifaceted neuromuscular testing can help performance teams target their rehabilitation approach alongside forecasting individual athlete recovery throughout rehabilitation. To this end, forecasting neuromuscular recovery throughout rehabilitation may help sport performance teams manage the individual variability that exists in post-ACLR rehabilitation timelines and potentially improve return to sport decision making.[3] For instance, the individual recovery trajectory can be compared against the average time course generated from statistical modeling to identify athletes who are tracking behind expectations to allow more time for rehabilitation before returning to sport.

Broad, multifaceted neuromuscular testing programs are recommended for athletes with ACLR. Notably, maximal muscle strength testing is important for athletes with ACLR and restoring between-limb symmetry in quadriceps muscle strength is associated with positive return to sport outcomes.[7] In addition to maximal strength testing, assessments of maximal muscle power and reactive strength (plyometric) capacity,[11,12] along with explosive strength measured as the rate of force development (RFD) using isometric dynamometry are separate, trainable, and often deficient neuromuscular capacities after ACL injury.[13] Further, in addition to the ACL injury itself, the surgical technique (e.g., semitendinosus—ST autograft vs. bone patellar tendon bone—BPTB autograft) may cause graft-specific neuromuscular impairments including diminished explosive strength capacity (i.e., RFD) that need to be accounted for throughout rehabilitation.[13] For example, the ST autograft has been shown to cause joint-angle specific impairments in knee flexion RFD that are correlated with semitendinosus muscle cross-sectional area,[14] the BPTB autograft leads to reductions in knee extensor strength[15] and elevated countermovement jump (CMJ) asymmetry measured as the between-limb asymmetry index (AI) has been shown to exist after BPTB autograft compared to ST autograft.[16,17] Taken together, these results suggest the importance of including maximal muscle strength testing alongside an assessment of explosive muscle strength capacity in athletes with ACL injury specific to the surgical comorbidities to individualize rehabilitation and training.

Further, performance-based single leg hop tests for time or distance appear to provide limited predictive validity with respect to return to sport outcomes for athletes with ACL injury.[7] Consequently, kinetic and kinematic analysis of jumping, landing and change of direction maneuvers including the use of dual force plate systems to evaluate between-limb force-time asymmetries and lower limb mechanical muscle function have become commonplace in ACL rehabilitation research, and certain measures like vertical drop jump reactive strength have been shown to predict the risk of ACL reinjury in an athlete population.[18] This type of biomechanical analysis may also help practitioners identify trainable neuromuscular deficits after ACLR.[17,19–24] Here, the between-limb AI assessed in a bilateral CMJ over discrete movement phases has been proposed to monitor neuromuscular function longitudinally after ACLR.[16,17,22,23,25] Several CMJ force-time (kinetic) variables have been measured in the eccentric deceleration (braking) and the concentric (propulsive) phases and these have been used to differentiate between an ACLR and noninjured status,[22] the comorbidities arising from the autograft technique[16] and time from surgery[17] in an athlete population. However, test reliability is a crucial consideration for effective athlete monitoring[26] and while some measures such as the CMJ eccentric RFD show relatively high variation (coefficient of variation >15%) the kinetic impulse obtained by time integration of the vertical ground reaction force is a stable outcome measure[27] that has been used frequently in the context of return to sport testing after ACLR.[3,16,17,22]

Muscle strength, muscle power and explosive strength assessments have become a regular part of post-ACLR rehabilitation with athlete populations, and the *monitoring* approach has increased the size of preinjury and postinjury datasets.[2,3] However, to maximize the utility of longitudinal athlete monitoring data, statistical models used in sport science and the study of sport injury should address the correlation that occurs consequent to the repeated measurements on the same athletes over time, the potential for nonlinear time dependencies, non-normal data distributions, and the frequent occurrence of participant drop-out and/or unbalanced datasets that occur readily in a real-world training environment in which limited experimental control can be exercised.[28,29] The generalized additive model technique has been used in other scientific disciplines to model correlated and complex data inherent in biological systems,[30] and this may be useful for sport science and sport medicine practitioners to account for these challenges in the post-ACLR rehabilitation time period.

Routine neuromuscular monitoring that includes measures of between-limb AI has become commonplace to track individual progress throughout rehabilitation after ACLR.[2,3,5,11] Individual recovery may unfold differently depending on the combined injuries, the type of surgery and the neuromuscular capacity that is measured. Statistical modeling of the time-course change in the between-limb AI using GAMM may characterize individual progress during rehabilitation and forecast post-ACLR neuromuscular recovery. To elucidate these notions, we conducted a retrospective analysis of longitudinally collected neuromuscular testing data from athletes with ACLR who underwent ST autograft and BPTB autograft using additive mixed effects modeling (GAMM). We hypothesized that neuromuscular function quantified as the between-limb AI obtained for knee extensor maximal strength and explosive strength (RFD) alongside CMJ kinetic impulse asymmetry in the eccentric deceleration phase (reversal of the downward acceleration of the body centre of mass [BCM]) and concentric phase (vertical propulsion) would display a time dependent decrease throughout rehabilitation after ACLR. Further, as an illustrative example of the application of this modeling technique, we present the neuromuscular recovery of an athlete with ACLR who progressed faster than the average time-course compared to a second athlete with a severe multiligament knee injury who displayed a slower recovery. We also present a comparison of the between-limb AI data for ACLR athletes stratified by the surgical technique and time since surgery. Finally, we provide between-limb AI data from a cohort of noninjured control athletes and preinjury data from the ACLR athletes as benchmarks of comparison to contextualize the post-ACLR recovery profiles generated by the model.

2 | METHODS

2.1 | Study design

A database containing 10 years of longitudinally collected neuromuscular testing data from 214 athletes training in a sport performance centre was accessed alongside athlete injury data. The research team that included qualified sport medicine practitioners used medical records to confirm athletes with ACL injury ($n = 34$; ST: $n = 29$; BPTB: $n = 5$) and noninjured control athletes ($n = 178$). Preinjury data existed for 18 participants in the ACLR group, but these data were excluded from the statistical modeling and are reported only for comparison purposes. Data from the noninjured control group were also not included in the statistical modeling and are presented only for comparison purposes. Data on ACLR athletes were collected between 2 and 24 months postsurgery (mean ± *SD* = 10 ± 4 months). There were 13 left knee ACL injuries and 21 right knee ACL injuries. Surgical records were not accessible for all athletes in the present study. However, in addition to isolated ACL tears, the participant pool included athletes who sustained a range of combined injuries with their primary ACL rupture, including three athletes with full knee dislocations, but we are unable to provide a detailed account of injuries such as concurrent meniscal tears and chondral lesions across all participants. Additionally, for athletes who sustained bilateral ACL injury, data from the timepoint of the first ACLR to the timepoint of the second ACLR were included in the statistical model but data obtained after the second ACLR were removed. Six athletes who sustained bilateral ACL injuries including two athletes with simultaneous left and right ACL rupture (i.e., bilateral ACL rupture in the same injury event) had no data between the first ACL injury and the second ACL injury.

Athletes with a history of sport injuries other than ACLR such as leg fractures, other non-ACL knee injuries (e.g., isolated meniscal tears), ankle injuries, soft tissue injuries (e.g., muscle tears), hip injuries and lumbar spine injuries were excluded from the analysis. The Conjoint Research Ethics Board at the University of Calgary approved the experimental protocols, and participants gave written informed consent before involvement in the testing protocols.

2.2 | Neuromuscular testing

2.2.1 | Dual force plate vertical jump kinetic analysis

Maximal CMJ testing performed on a dual force plate system was conducted regularly throughout the testing period as a part of routine athlete monitoring after a standardized warm up procedure before training. The protocol included a 5-jump CMJ test with 3 s of still standing between jumps using a self-determined depth. All jump tests were performed with the hands placed firmly on the hips and were supervised by a certified exercise professional.

A detailed explanation of the vertical jump testing protocol and kinetic analysis procedures have been described elsewhere.[22,23] Briefly, the vertical ground reaction force (Fz) from the right and left legs were measured simultaneously using a dual force plate system (Accupower Force Platform, AMTI) at a sampling frequency of 1500 Hz and recorded on a personal computer (MyoResearch Version 3.8; Noraxon). Data were exported and analyzed using a custom-built computer program (Matlab R 2018b, Mathworks). The velocity of the BCM was obtained by time integration of the instantaneous acceleration signal ([Fz/body mass] × $-9.81\ m/s^2$) calculated from the total Fz, summed from the right and left limbs.

A between-limb vertical jump force-time AI was calculated over discrete jump phases by time integration of Fz over the eccentric deceleration phase (reflecting the capacity to reverse the downward acceleration of the BCM) and concentric phase (vertical propulsion of the BCM), respectively.[22] The right and left total impulse were compared using the 5-jump mean AI using the following formula:

$$\mathrm{AI}(\%) = \left[\left(\frac{\text{Right Impulse} - \text{Left Impulse}}{\text{Maximum of Left } vs. \text{ Right Impulse}}\right) \times 100\right]$$

2.2.2 | Knee extensor muscle strength testing

Maximum voluntary contraction (MVCs) of isometric knee extension were conducted using a customized Cybex dynamometer instrumented with a third-party load cell (LC703-500; Omega) and force was sampled at 1500 Hz (MyoResearch Version 3.8; Noraxon).[3,14] For the knee extension trials, participants were positioned in a seated position with the knee joint angle set at 70° of knee flexion. The tester then instructed the participant to perform 3 × 3 s MVCs of isometric knee extension separated by a 20 s rest period as “fast and as hard as possible.” Visual feedback and strong verbal encouragement were provided throughout the testing protocol.

The moment arm (distance from the axis of rotation to the point of force application) of the shank was obtained to calculate knee extensor torque. The isometric torque-time curves were smoothed (Matlab "smooth" function using 33 ms centered moving average window). A 200 ms average around the peak value was calculated to obtain the maximum torque. The derivative of the signal was then calculated to identify the peak rate of torque development (RTD). A 100 ms average around this timepoint was calculated to obtain maximum RTD. The maximum knee extensor peak torque value and the 3-repetition RD mean value were compared using the following formula:

$$\mathrm{AI}(\%) = \left[\left(\frac{\text{Right Torque} - \text{Left Torque}}{\text{Maximum of Left vs. Right Torque}}\right) \times 100\right]$$

2.3 | Statistical analysis

First, all between-limb AIs were corrected for the ACL group so that a positive value reflected non-injured limb dominance and a negative value injured limb dominance (i.e., the AI was multiplied by −1 for athletes with right knee ACL injury). Next, neuromuscular testing data including the CMJ eccentric deceleration phase, the CMJ concentric phase, the knee extensor MVC strength and the knee extensor RTD were cleaned and inspected for statistical outliers. The data from a single noninjured athlete with a consistent record of between-limb asymmetry in the CMJ eccentric deceleration phase of more than 20% were subsequently removed from the noninjured group.

A descriptive analysis was conducted to compare ACL injured group stratified by the time from surgery and the surgical technique alongside a comparison to the preinjury measurements when it existed. A comparison to the noninjured controls was also done. The ACLR athletes were then selected to generate the GAMMs (i.e., the noninjured controls and the preinjury data were excluded from the GAMM). Models were first built with multiple predictor variables. However, to achieve an optimal fit, separate GAMMs (GAMM 1) were fit for each of the between-limb AI measures for the ACL injured participants with main effects for the surgical technique, a smooth term for the time since surgery measured in days, and random intercepts for athlete. A second version of the GAMM (GAMM 2) was also fit allowing for different temporal recovery profiles between the ST and the BPTB autograft techniques. The distribution and structure of model residuals were checked along with a model diagnostic check, and the fit of the two GAMMs were compared using the Akaike Information Criteria (AIC), where a lower AIC indicates a better model fit. Finally, a time course of neuromuscular recovery was generated for an athlete with ACLR who showed an accelerated progression compared to the average profile alongside comparison to a delayed progression of an athlete who sustained a severe multiligament injury. All statistical analyses were conducted in R Studio Version 1.3.1093 l (R Version 4.03). The "mgcv" package was used to generate the GAMMs, run model diagnostics and check model fit. The "itsadaug" package was used to generate the model plots and the individual neuromuscular recovery profiles ($\alpha = 0.05$).

TABLE 1 Breakdown of measurement count and sample size by sport and graft type

		ACLR	
	Control Count (*n*)	BPTB	STG
Total number of athletes (athletes with pre-ACLR data)	196 (18)	5	29
CMJ concentric phase tests	195	5	28
CMJ eccentric deceleration phase tests	195	5	28
Knee extension MVC strength tests	67	3	21
Knee extension RTD tests	67	3	21
Alpine skiing	70	–	11
Freestyle skiing	33	–	6
Snowboarding	5	–	–
Skier cross	22	–	4
Ski jumping	10	–	1
Hockey	–	1	–
Luge	23	–	1
Football	4	1	1
Soccer	1	2	–
Wrestling	35	2	1
Other	–	–	2
Mean measurements/athlete	18	18	17
Standard deviation of measurements/athlete	27	27	19

Abbreviations: ACLR, anterior cruciate ligament reconstruction; BPTB, bone patellar tendon bone autograft; CMJ, countermovement jump; MVC, maximum voluntary contraction; RTD, rate of torque development; ST, semitendinosus autograft.

3 | RESULTS

The sample size and count of AI measures for the BPTB, ST and control groups are shown in Table 1 (total measurements ACLR: $n = 582$; total measurements noninjured control: $n = 3188$; total measurements pre-ACLR: $n = 374$), and an aggregated comparison of four AI variables across two tests (CMJ eccentric deceleration phase, CMJ concentric phase, knee extension MVC strength and knee extension RTD) for the ACLR group stratified by the time since surgery is given in Figure 1. A comparison to the noninjured controls and the preinjury testing is also provided. Across the four AI metrics, the absolute value of the aggregated mean ± standard deviation AI

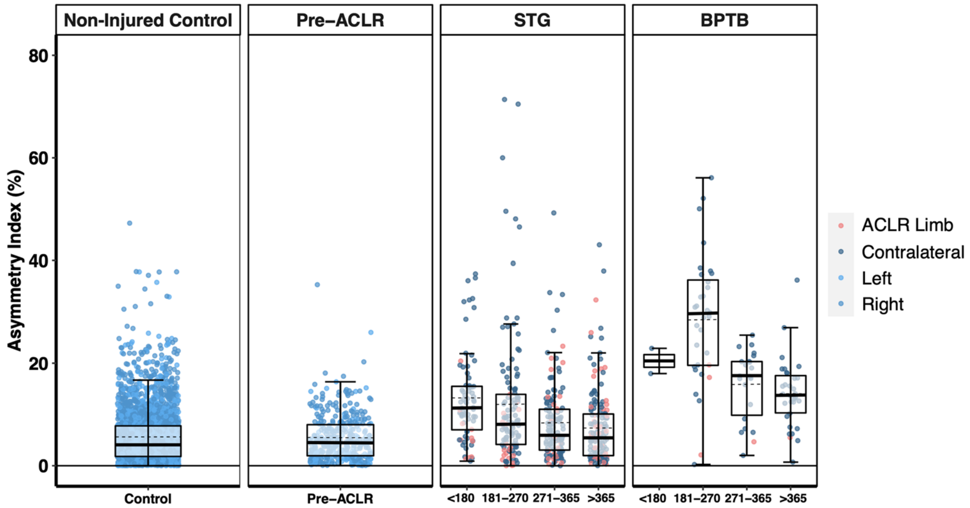

FIGURE 1 A comparison of the aggregated asymmetry index (AI) scores across countermovement jump and knee extension strength (expressed as the absolute value) stratified by time since surgery. Black dashed line shows the group mean. The colour of the point estimate represents the dominant limb. ACLR, anterior cruciate ligament reconstructed; BPTB, bone patellar tendon bone autograft; ST, semitendinosus autograft [Color figure can be viewed at wileyonlinelibrary.com]

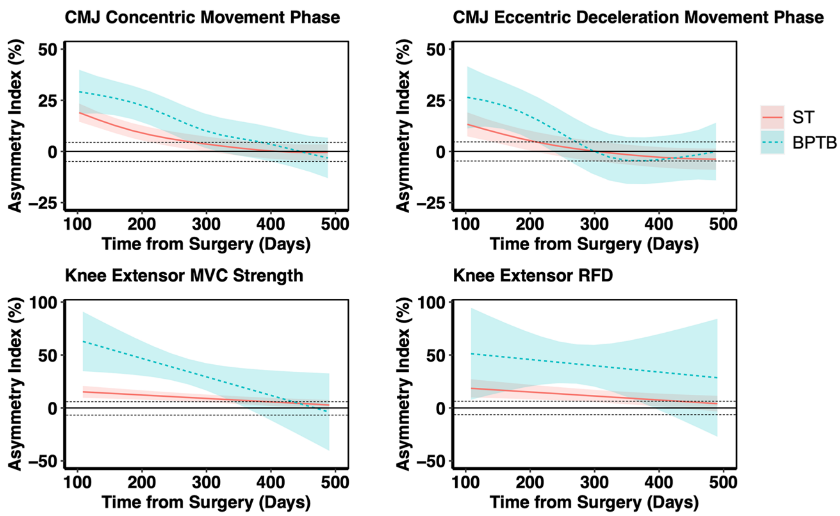

FIGURE 2 Time course change in the between-limb asymmetry index (AI) for the participants with anterior cruciate ligament (ACL) reconstruction. Black dashed horizontal lines show mean AI for noninjured controls (±5%). BPTB, bone patellar tendon bone autograft; CMJ, countermovement jump; ST, semitendinosus autograft [Color figure can be viewed at wileyonlinelibrary.com]

decreased from 13 ± 9% at <180 days postsurgery timepoint to 8 ± 7% at the >365 days timepoint for the ACL group. The mean AI for the noninjured control group was 5 ± 5%.

The GAMM models for each of the between-limb AI outcome measures is presented in Figure 2 along with the model parameters in Table 2. Model fit for the CMJ concentric phase AI was best with GAMM 2 ($\chi^2 = 20.1$, $df = 2$, $p < 0.001$). There were no effects found for the surgical technique ($p = 0.53$). The concentric phase AI decreased over time ($p < 0.001$), and the deviance explained by the model was 91%. Model fit for the CMJ eccentric deceleration phase AI was also best with GAMM 2 ($\chi^2 = 12.7$, $df = 2$, $p < 0.001$). There was no difference in the eccentric deceleration phase AI between surgical technique ($p = 0.71$). The eccentric deceleration phase AI decreased over time ($p < 0.001$), and the deviance explained by the model was 79%.

Model fit for the knee extensor MVC strength AI was best with GAMM 2 ($\chi^2 = 5.0$, $df = 2$, $p < 0.01$) and knee extensor strength AI was higher in the BPTB group ($p < 0.05$). Knee extensor MVC strength AI decreased over time for the ST autograft group ($p < 0.001$) and the BPTB group ($p < 0.05$). The deviance explained by the model was 43%. Finally, GAMM 2 provided only a marginal improvement in model fit compared to GAMM 1 for knee extensor RFD ($\chi^2 = 3.9$, $df = 2$, $p < 0.05$). The recovery in knee extension RFD asymmetry was slower for BPTB ($p < 0.05$), and an effect of time since surgery on RFD AI was only present for the ST autograft condition ($p < 0.01$). The deviance explained in the knee extensor RFD AI by GAMM 2 was 47%.

The GAMM for the CMJ concentric phase AI (deviance explained = 91%) and the CMJ eccentric deceleration phase (deviance explained = 79%) were subsequently used to develop individualized

TABLE 2 Comparison of fit between two additive mixed effects models using the Akaike Information Criteria (AIC)

Movement	Asymmetry index metric	Model	AIC	R^2	Deviance explained
Countermovement jump	Eccentric deceleration phase	Model 1	1387.0	0.71	75%
		Model 2	1354.1*	0.75	79%
	Concentric phase	Model 1	1207.3	0.87	89%
		Model 2	1161.1*	0.89	91%
Knee extension	Maximum torque (MVC)	Model 1	589.0	0.34	42%
		Model 2	588.3*	0.35	43%
	Rate of torque development (RTD)	Model 1	647.0*	0.36	46%
		Model 2	648.5	0.36	47%

Note: Model 2 allows for the time course change of the asymmetry index to differ by surgical technique. Lower AIC indicates better model fit. The model formulas used to fit Models 1 and 2 were done in R via the bam function in the mgcv package.

The model formulas used to fit Models 1 and 2 were done in R via the *bam* function in the mgcv package.

Model 1: bam(Asymmetry_Index ~ Surgical_Technique + s(Time) + s(Athlete, bs = "re"), method = "REML")

Model 2: bam(Asymmetry_Index ~ Surgical_Technique + s(Time, by = Surgical_Technique) + s(Athlete, bs = 're'), method = 'REML')

*$p < 0.05$

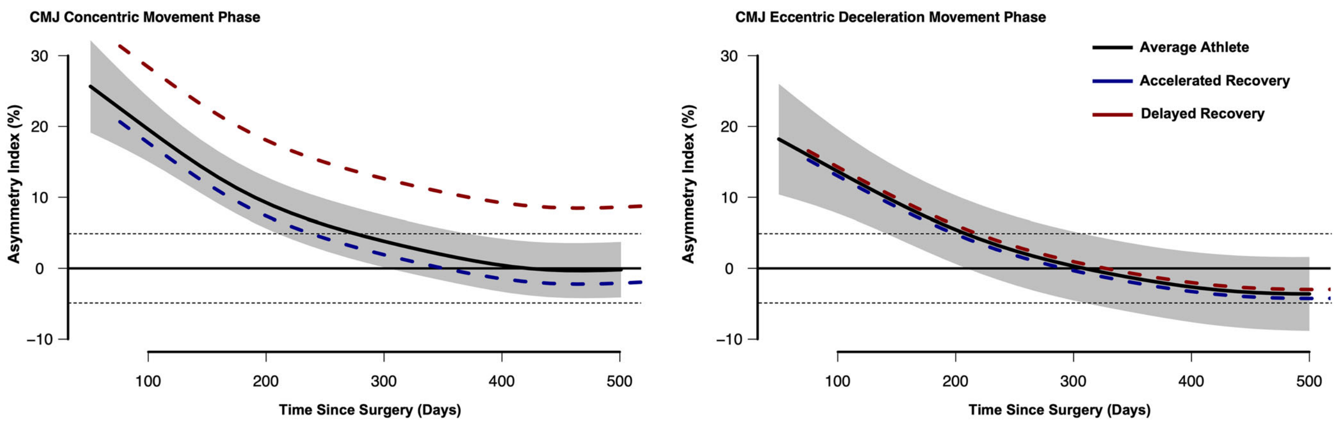

FIGURE 3 Two functional recovery plots for the countermovement jump (CMJ) concentric phase AI and the eccentric deceleration phase AI obtained from the additive mixed effects model (AMM) showing an accelerated recovery after anterior cruciate ligament reconstruction (ACLR) (blue dashed line) and a delayed recovery resulting from a severe multiligament knee injury (red dashed line). Black dashed horizontal lines show mean asymmetry index for noninjured controls (±5%) [Color figure can be viewed at wileyonlinelibrary.com]

neuromuscular recovery profiles for two athletes with ACLR compared to the average recovery profile including an athlete with an accelerated progression and a second athlete with a delayed progression consequent to a severe multiligament knee injury (Figure 3). Only the concentric phase AI profile differed compared to the group average. No differences were found for the recovery profile of the eccentric deceleration phase.

4 | DISCUSSION

The aim of this retrospective analysis was to present how longitudinal athlete monitoring and nonlinear statistical methods (i.e., generalized additive modelling, and in the present study AMM) can be combined to model individual progress throughout rehabilitation after ACL injury. The capacity to forecast individual neuromuscular recovery after ACLR is particularly useful for clinicians and practitioners as the postinjury recovery may unfold differently over time depending on the type of surgery and the combined injuries associated with the primary ACL tear. Specifically, we showed that neuromuscular function measured as the between-limb AI across a range of muscle strength, muscle power and explosive strength (RFD) measures were time dependent and explained a high fraction of the variance (42%–91%) in the neuromuscular recovery of athletes with ACLR. Further, the AMM method was capable of distinguishing athlete recovery on an individual basis, including an athlete who displayed an accelerated progression compared to the group average and an athlete with a delayed progression consequent to a multi-ligament injury (*c.f.* Figure 3). The notion that neuromuscular recovery differs between measures was evidenced by the relative similarity in the recovery profiles of the two athletes for the eccentric deceleration phase of the CMJ but divergent recovery profiles for the concentric phase of the CMJ. The eccentric deceleration phase of the CMJ involves braking (negative muscle power) or the capacity to reverse the downward acceleration of the BCM. This high RFD phase ends at the minimum downward displacement of the BCM whereas the concentric phase reflects the generation of positive muscle power and vertical propulsion from this position. The capacity to generate high vertical RFD throughout the eccentric deceleration phase of the CMJ is key indicator of vertical jump performance and is strongly associated with the capacity to perform coupled eccentric-concentric (stretch shorten cycle—SSC) movements measured as the reactive strength index (RSI).[31,32] In the context of ACL injury, diminished RSI has been shown to predict future ACL reinjury in an athlete population, highlighting the importance of assessing SSC capacity in athletes with ACLR.[12] Additionally, analysis of vertical jumps obtained from patients with BPTB autograft showed diminished vertical ground reaction force in the eccentric deceleration phase of the bilateral CMJ for both the injured and noninjured limb in those with a low subjective knee score rating compared to those with a high rating.[25] As eccentric versus concentric strength capacities have different physiological determinants, quantifying recovery of each neuromuscular capacity separately may provide practitioners with an opportunity to prescribe resistance training loading parameters in a more targeted and individualized manner.

This paper introduced the use of the GAMM statistical technique (i.e., nonlinear, mixed effects, multilevel modeling) to profile individual neuromuscular recovery after ACLR surgery and address the correlation that exists in longitudinal athlete monitoring data arising from the repeated measurements over time. This type of statistical modeling has been used in other scientific disciplines to account for complex data structures,[30,33] and mixed effects, multilevel statistical modeling has been recommended for use in sport science.[29] As the occurrence of sport injuries is also complex, statistical models like GAMMs may be of interest to sport medicine practitioners and clinicians to support decision making after ACL injury.[28] Here, a frequent question of interest is: "how is the individual athlete recovering after surgery and is the trajectory according to expectations?" In fact, the questions surrounding the temporality of recovery after injury/illness are broadly important in medicine.[34] Applications of sport injury return to sport forecasting might include managing the individual variation that is present in post-injury rehabilitation progression, providing data-informed recovery timeline estimates for management personnel, coaches, or the athlete themself, and ultimately to help a multidisciplinary team identify athletes who may require more time for physical reconditioning before returning to sport. As opposed to indiscriminate time-based criteria, modeling recovery after ACLR using longitudinal neuromuscular testing allows the post-injury recovery trajectory to be estimated on an individualized basis.

Enhancing return to sport testing with longitudinal athlete monitoring including expansive neuromuscular testing and the GAMM method may address certain limitations that exist between current functional testing practices and the lack of predictive validity with respect to return to sport outcomes after ACLR.[8] Post-ACLR neuromuscular testing is often limited to performance-based testing like single leg hops for distance and/or time, which may fail to identify neuromuscular deficits that are associated with poorer outcomes after return to sport and return to competition.[7] Further, the incorporation of kinetic analysis of the vertical jump,[16,21–24] alongside knee extensor/flexor strength assessments[7,35] including an evaluation of explosive strength (rapid muscle force generation) measured as RFD[13,35] can help identify trainable neuromuscular deficits and develop targeted rehabilitation strategies. Importantly, these assessment methods have become increasingly common in sport performance settings and permit a higher frequency of neuromuscular testing over the course of the post-ACLR time period, providing greater opportunity for data-informed decision making.[2,3]

A strength of the GAMM approach is the flexibility in applying the smoothing splines for the predictor variables, which may be important after ACL injury where the trajectory of the time course recovery may differ on a group level (e.g., trained vs. untrained, adolescent vs. adult, BPTB autograft vs. ST autograft) and an individual basis (e.g., adherence to rehabilitation, psychological readiness). In the present study, we fit separate GAMMs for each neuromuscular capacity, permitting an analysis of recovery in a targeted manner. Further, we modeled each between-limb AI separately using a smoothing spline technique that permitted the time-dependent recovery trajectory to vary between the BPTB and ST autograft surgical techniques. Not only was the model fit superior with this approach but also, it accounted for the effects of the ACLR surgical technique itself on postinjury recovery.

Factors such as the surgical technique or choice of graft often fall outside of the control of the rehabilitation team and may vary between athletes with ACLR. The decision to choose one graft over another, for example, is multifactorial. While the BPTB autograft may be superior to the ST autograft in terms of graft failure rate and ACL reinjury outcomes,[18,36] in certain sport settings, a surgical technique may be preferred to mitigate the risk of surgically-related comorbidities after return to sport. The ST autograft technique, for instance, has been reported as the most used graft type in elite Canadian alpine skiers to minimize the risk of anterior knee pain after return to skiing.[37]

Attending to the potential covariates that may impact individual recovery after ACL injury like the surgical technique is essential,[14,16,18,36] and this is a strength of generalized additive modeling and the AMM approach used here. For example, the bilateral CMJ loading strategy measured as the between-limb asymmetry in kinetic impulse has been shown to differ between graft type (i.e., BPTB vs. ST).[16] Here, participants undergoing BPTB autograft displayed higher CMJ between-limb AI compared to those with ST autograft. Interestingly, while both the BTPB and ST autograft groups showed higher asymmetry in the CMJ concentric phase, only the BPTB group had higher asymmetry in the eccentric deceleration phase compared to noninjured controls.[16] Further, a study including elite alpine skiers with and without ACLR found elevated between-limb asymmetry only for the CMJ concentric phase whereas high between-subject variation in the directionality of the limb asymmetry was found for the eccentric deceleration phase.[22] The data presented in our study were consistent with the literature as neuromuscular recovery was impacted by the graft type[16,22] and was specific to the parameter in question.[17] Notably, higher CMJ and knee extensor strength asymmetry and a slower post-ACLR progression were observed across all four measures for the BPTB group compared to the ST group, and more than 300 days from surgery were required for the between-limb asymmetry to diminish to the mean value of the non-injured control group (i.e., asymmetry <5%). Increased time was required for recovery of the CMJ concentric phase and knee extensor explosive strength (RD) (*c.f.* Figures 1 and 2). The finding of elevated asymmetry and slower time course of recovery for the concentric phase of the vertical jump and knee extensor explosive strength have been found elsewhere as well.[13,17,22,35] The two individual neuromuscular recovery profiles presented in Figure 3 including that of an accelerated recovery and a delayed recovery, provide further support and an illustrative example of how practitioners can apply AMM to forecast individual progression throughout rehabilitation after ACLR and the notion that neuromuscular recovery depends on the measure in question. Further, the case example presented here shows a similar recovery rate for the two athletes, suggesting the possibility that the time course may depend (exclusively) on the initial asymmetry test values for athletes with ST autograft.

Taken together there are at least four possible advantages for clinicians and practitioners to build a data set of expansive neuromuscular testing using an athlete monitoring approach and additive mixed effects modeling to forecast recovery after ACLR instead of relying on return to sport testing at a discrete timepoint or worse, solely on time-from-surgery: (1) similar to a weather forecast, the post-ACLR recovery forecast allows the practitioner to *predict* the time course of neuromuscular recovery to provide a robust rehabilitation plan and a data-informed estimate of when an athlete will be sufficiently prepared for a return to sport; (2) this approach allows the early identification of a lagging neuromuscular capacity so that targeted training or rehabilitation can be administered before return to sport; (3) modeling post-ACLR progression can help practitioners identify an athlete who is tracking behind expectations either due to ineffective rehabilitation or other factors like injury severity so that adjustments can be made to the rehabilitation plan including potentially delaying return to sport to permit more recovery time; and (4) this modeling technique allows practitioners to account for the variation, complexity and intra-subject correlation that is inherent in the post-ACLR rehabilitation process.

However, our study does have several limitations that were primarily driven by the relatively small and heterogeneous sample, along with substantial between-subject variation in terms of the frequency of measurements across time. First, the majority of ACLR athletes in the present study were from winter slope sports including alpine skiing, skier cross and freestyle skiing. Consequently, given the existence of a dominant surgical technique in this population,[37] 84% of the participants underwent ST autografts at the time of their ACLR. The fact we were unable to include more participants with BPTB autografts is a limitation of our study. We also did not include a time-dependent smooth term for the random effects (i.e., the athlete) nor were we able to include a model with multiple neuromuscular predictor variables, which may have served to increase the individualization of the neuromuscular recovery profiles. This limitation stemmed from the small sample size. Future studies using the GAMM approach and larger sample sizes should consider this to develop even more tailored predictions of neuromuscular recovery after ACLR. These improvements may help to increase the generalizability of the GAMM. This study was also limited by the retrospective analysis and the lack of experimental control over the testing frequency between athletes, between surgical technique and sport. While the neuromuscular testing protocols were conducted in a standardized manner with stringent control including supervision by a certified exercise practitioner, there was substantial variation in the frequency of measurements across the study period. Finally, we were unable to obtain detailed surgical reports for all participants and consequently we could not account for additional confounders in our model that may exert an effect on neuromuscular recovery like the pattern of combined injury. These are inherent limitations of retrospective analyses of longitudinal athlete monitoring programs in a sport performance environment. Practitioners can mitigate these challenges by ensuring tests are conducted regularly and that appropriate statistical methods are used.[26,29] It should also be noted that a broad battery of neuromuscular testing is recommended after ACLR,[2,3,5,11,12] and there are numerous metrics that can be derived from CMJ kinetic analysis assessments for lower limb mechanical muscle function.[17,24,38]

The decision to focus our analysis on the CMJ kinetic impulse was based on its relatively good reliability, but future research should consider exploring the value of other accepted vertical jump metrics, for example, the eccentric deceleration RFD.[24] For instance, Hart et al.[24] observed no difference in eccentric deceleration impulse asymmetry when comparing previously injured elite soccer players with noninjured players but a substantial effect size for eccentric deceleration RFD asymmetry, highlighting the importance of the signal to noise ratio. Further, as SSC function may be impaired after ACL injury and predict future ACL reinjury,[12] and SSC impairment in an ACLR population may include reduced countermovement depth and eccentric demand that can impair concentric phase performance,[39] future research should consider CMJ strategy measures as a component of a comprehensive post-injury neuromuscular test battery. Further, due to the well-established effects of ACL injury on contralateral limb strength, future research should also compare the potential differences between forecasting models that use measures of between-limb asymmetry in conjunction with limb-specific strength. This was initially attempted in the present analysis, but the model fits were poor. Finally, the limitations of this study highlight the need for greater interdisciplinary practice for managing sport injuries and rehabilitation, especially between sport medicine clinicians and sport performance practitioners to relate clinical measures like concurrent injuries with ACL rupture or graft choice to neuromuscular testing outcomes.[3,10,11]

In conclusion, profiling the neuromuscular recovery of individual athletes after ACLR using a data-informed approach and expansive testing is novel perspective on longitudinally collected athlete monitoring data that can potentially add value for clinicians and practitioners to forecast recovery and progress throughout rehabilitation. As the time course of neuromuscular recovery may be nonlinear and highly individual with dependency on factors such as the surgical technique itself, additive mixed effects modeling (AMM) can help sport science and sport medicine practitioners accurately forecast post-ACLR recovery on an athlete-by-athlete basis. In this paper, we showed that additive mixed effects modeling accounted for a high fraction of the variance in neuromuscular recovery after ACLR measured as the between-limb AI in CMJ force and knee extensor strength, and that the AMM approach could be used to map the individual recovery profiles. Future studies with greater experimental control over the testing frequency along with larger sample sizes and greater sample size balance for the various surgical techniques should be considered to further investigate the value of additive mixed effects modeling for forecasting individual neuromuscular recovery after ACLR.

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AUTHOR CONTRIBUTIONS

Matthew J. Jordan: Prepared manuscript and conducted the statistical analysis. **Nathaniel Morris, Jeremiah Barnert, Drew Lawson, Isabel Aldrich Witt**: collected data, assisted with data analysis, revised manuscript. **Walter Herzog**: approved final draft and guided overall research direction. All authors have read and approved this manuscript.

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REFERENCES

1. Foster C, Rodriguez-Marroyo JA, De Koning JJ. Monitoring training loads: the past, the present, and the future. *Int J Sports Physiol Perform*. 2017;12(2):2-8.
2. Taberner M, van Dyk N, Richter C, et al. Physical preparation and return to performance of an elite female football player following anterior cruciate ligament reconstruction: a journey to the FIFA Women's World Cup. *BMJ Open*. 2020;6(1):e000843.
3. Jordan MJ, Morris N, Lane M, et al. Monitoring the return to sport transition after ACL injury: an alpine ski racing case study. *Front Sport Act Living*. 2020;2(12):1-16.
4. Bittencourt NFN, Meeuwisse WH, Mendonça LD, Nettel-Aguirre A, Ocarino JM, Fonseca ST. Complex systems approach for sports injuries: moving from risk factor identification to injury pattern recognition—narrative review and new concept. *Br J Sports Med*. 2016;50(21):1309-1314. Available from doi:10.1136/bjsports-2015-095850
5. Hewett TE, Stasi SLDi, Myer GD. Current concepts for injury prevention in athletes after anterior cruciate ligament reconstruction. *Am J Sports Med*. 2013;41(1):216-224.
6. Capin JJ, Snyder-Mackler L, Risberg MA, Grindem H. Keep calm and carry on testing: a substantive reanalysis and critique of "what is the evidence for and validity of return-to-sport testing after anterior cruciate ligament reconstruction surgery? A systematic review and meta-analysis." *Br J Sports Med*. 2019;53:1444-1446.
7. Grindem H, Snyder-Mackler L, Moksnes H, Engebretsen L, Risberg MA. Simple decision rules can reduce reinjury risk by 84% after ACL reconstruction: the Delaware-Oslo ACL cohort study. *Br J Sports Med*. 2016;50(13):804-808. Available from doi:10.1136/bjsports-2016-096031
8. Webster KE, Hewett TE. What is the evidence for and validity of return-to-sport testing after anterior cruciate ligament reconstruction surgery? A systematic review and meta-analysis. *Sports Med*. 2019;49(6):917-929 Available from doi:10.1007/s40279-019-01093-x
9. Ardern CL, Taylor NF, Feller JA, Webster KE. Fifty-five per cent return to competitive sport following anterior cruciate ligament reconstruction surgery: an updated systematic review and meta-analysis including aspects of physical functioning and contextual factors. *Br J Sports Med*. 2014;48(21):1543-1552. Available from http://www.ncbi.nlm.nih.gov/pubmed/25157180
10. Buckthorpe M, Frizziero A, Roi GS. Update on functional recovery process for the injured athlete: return to sport continuum redefined. *Br J Sports Med*. 2019;53(5):265-267.
11. Buckthorpe M. Optimising the late-stage rehabilitation and return-to-sport training and testing process after ACL reconstruction. *Sport. Med*. 2019;49(7):1043-1058. Available from doi:10.1007/s40279-019-01102-z
12. King E, Richter C, Daniels KAJ, et al. Can biomechanical testing after anterior cruciate ligament reconstruction identify athletes at risk for subsequent ACL Injury to the contralateral uninjured limb? *Am J Sports Med*. 2021;49(3):609-619. http://www.ncbi.nlm.nih.gov/pubmed/33560866
13. Turpeinen JT, Freitas TT, Rubio-Arias JÁ, Jordan MJ, Aagaard P. Contractile rate of force development after anterior cruciate ligament reconstruction—a comprehensive review and meta-analysis. *Scand J Med Sci Sport*. 2020;30(May):1572-1585.
14. Morris N, Jordan MJ, Sumar S, et al. Joint angle specific impairments in rate of force development, strength and muscle morphology after hamstring autograft. *Transl Sport Med*. 2020;4:1-11.
15. Hiemstra LA, Webber S, MacDonald PB, Kriellaars DJ. Knee strength deficits after hamstring tendon and patellar tendon anterior cruciate ligament reconstruction. *Med Sci Sport Exerc*. 2000;32(8):1472-1479. Available from http://www.ncbi.nlm.nih.gov/pubmed/10949014
16. Miles JJ, King E, Falvey ÉC, Daniels KAJJ. Patellar and hamstring autografts are associated with different jump task loading asymmetries after ACL reconstruction. *Scand J Med Sci Sports*. 2019;29(8):1212-1222.
17. Read PJ, Michael Auliffe S, Wilson MG, Graham-Smith P. Lower limb kinetic asymmetries in professional soccer players with and without anterior cruciate ligament reconstruction: nine months is not enough time to restore "functional" symmetry or return to performance. *Am J Sports Med*. 2020;48(6):1365-1373.
18. King E, Richter C, Jackson M, et al. Factors influencing return to play and second anterior cruciate ligament injury rates in level 1 athletes after primary anterior cruciate ligament reconstruction: 2-year follow-up on 1432 reconstructions at a single center. *Am J Sports Med*. 2020;48(4):812-824. Available from doi:10.1177/0363546519900170

19. Paterno MV, Ford KR, Myer GD, Heyl R, Hewett TE. Limb asymmetries in landing and jumping 2 years following anterior cruciate ligament reconstruction. *Clin J Sport Medcine*. 2007;17(4):258-262. Available from http://graphics.tx.ovid.com.ezproxy.lib.ucalgary.ca/ovftpdfs/FPDDNCOBCBKGLH00/fs046/ovft/live/gv023/00042752/00042752-200707000-00005.pdf
20. King E, Richter C, Franklyn-Miller A, Wadey R, Moran R, Strike S. Back to normal symmetry? biomechanical variables remain more asymmetrical than normal during jump and change-of-direction testing 9 months after anterior cruciate ligament reconstruction. *Am J Sports Med*. 2019;47(5):1175-1185.
21. King E, Richter C, Franklyn-Miller A, et al. Biomechanical but not timed performance asymmetries persist between limbs 9 months after ACL reconstruction during planned and unplanned change of direction. *J Biomech*. 2018;81:93-103.
22. Jordan M, Aagaard P, Herzog W. Lower limb asymmetry in mechanical muscle function: a comparison between ski racers with and without ACL reconstruction. Scand. *J Med Sci Sports*. 2015;25(3):e301-e309. Available from doi:10.1111/sms.12314
23. Holsgaard-Larsen A, Jensen C, Mortensen NHM, Aagaard P. Concurrent assessments of lower limb loading patterns, mechanical muscle strength and functional performance in ACL-patients—a cross-sectional study. *Knee*. 2014;10(1):66-73. Available from http://www.ncbi.nlm.nih.gov/pubmed/23835518
24. Hart LM, Cohen DD, Patterson SD, Springham M, Reynolds J, Read P. Previous injury is associated with heightened countermovement jump force-time asymmetries in professional soccer players even after return to play. *Transl Sport Med*. 2019;2(5):256-262.
25. Baumgart C, Hoppe MW, Freiwald J. Phase-specific ground reaction force analyses of bilateral and unilateral jumps in patients with ACL reconstruction. *Orthop J Sport Med*. 2017;5(6):1-9.
26. Bailey C. Longitudinal monitoring of athletes: statistical issues and best practices. *J Sci Sport Exerc*. 2019;1(3):217-227. Available from doi:10.1007/s42978-019-00042-4
27. Nibali ML, Tombleson T, Brady PH, Wagner P. Influence of familiarization and competitive level on the reliability of countermovement vertical jump kinetic and kinematic variables. *J Strength Cond Res*. 2015;29(10):2827-2835. Available from doi:10.1123/ijspp.2018-0935
28. Fonseca ST, Souza TR, Verhagen E, et al. Sports injury forecasting and complexity: a synergetic approach. *Sport Med*. 2020;50(10):1757-1770. Available from doi:10.1007/s40279-020-01326-4
29. Windt J, Ardern CL, Gabbett TJ, et al. Getting the most out of intensive longitudinal data: a methodological review of workload-injury studies. *BMJ Open*. 2018;8(10):e022626.
30. Pedersen EJ, Miller DL, Simpson GL, Ross N. Hierarchical generalized additive models in ecology: an introduction with mgcv. *Peer J*. 2019;2019(5):1-42.
31. Barker LA, Harry JR, Mercer JA. Relationships between countermovement jump, ground reaction forces and jump height, reactive strength index and jump time. *J Strength Cond Res*. 2018;32(1):248-254.
32. McMahon JJ, Jones PA, Suchomel TJ, Lake J, Comfort P. Influence of the reactive strength index modified on force– and power–time curves. *Int J Sports Physiol Perform*. 2018;13(2):220-227.
33. Guisan A, Edwards TC, Hastie T. Generalized linear and generalized additive models in studies of species distributions: setting the scene. *Ecol Modell*. 2002;157(2-3):89-100.
34. Reddy MC, Dourish P, Pratt W. Temporality in medical work: time also matters. *Comput Support Coop Work*. 2006;15(1):29-53.
35. Jordan M, Aagaard P, Herzog W. Rapid hamstrings/quadriceps strength in ACL-reconstructed elite alpine ski racers. *Med Sci Sports Exerc*. 2015;47(1):109-119.
36. Mohtadi N, Chan D, Barber R, Paolucci EO. Reruptures, reinjuries, and revisions at a minimum 2-year follow-up: a randomized clinical trial comparing 3 graft types for ACL Reconstruction. *Clin J Sport Med*. 2016;26(2):96-107.
37. Jordan MJ, Doyle-Baker P, Heard M, Aagaard P, Herzog W. A retrospective analysis of concurrent pathology in the ACL reconstructed knees of elite alpine ski racers. *Orthop J Sport Med*. 2017;5(7):1-7.
38. Jordan M, Aagaard P, Herzog W. A comparison of lower limb stiffness and mechanical muscle function in ACL-reconstructed, elite, and adolescent alpine ski racers/ski cross athletes. *J Sport Heal Sci*. 2018;7(4):416-424. Available from doi:10.1016/j.jshs.2018.09.006
39. Bobbert MF, Casius LJR. Is the effect of a countermovement on jump height due to active state development? *Med Sci Sport Exerc*. 2005;37(3):440-446. Available from http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage%26an=00005768-200503000-00015

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