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Does sensorimotor function predict graft rupture, contra-lateral injury or failure to return to sports after ACL reconstruction? A protocol for the STOP Graft Rupture study

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ABSTRACT

Introduction People with anterior cruciate ligament (ACL) reconstruction (ACLR) are at high risk of sustaining a graft rupture and/or contra-lateral ACL injury. The main factors that may predispose individuals for subsequent ACL injuries are, however, not established. To reduce the risk of reinjuries, it is of particular interest to identify modifiable risk-factors, for instance, those related to sensorimotor control which are responsive to training. The aim of the current study protocol is to present the design of our prospective cohort study STOP Graft Rupture investigating sensorimotor function as predictors for graft rupture, contra-lateral ACL injury and/or failure to return to sport (RTS) within 3 years following ACLR.

Methods and analysis We aim to recruit 200 individuals (15–35 years, ~50% women) with ACLR from Norrland University Hospital, Umeå and Lund University Hospital, Lund, Sweden. Participants will be assessed with a comprehensive test battery for sensorimotor muscle function, including hop performance, muscle strength, muscle activation, hip and ankle range of motion and postural orientation as well as patient-reported function 1 year after ACLR (baseline). For a subgroup of individuals (Umeå cohort), 3D kinematics and joint position sense will also be evaluated. At follow-up (≥3 years post-ACLR), the participants will be asked to answer questions related to new ACL injuries to either knee and about RTS. Separate logistic regression models, adjusting for possible confounders, will be used to evaluate the influence of the different sensorimotor predictors on the prospective outcomes (graft rupture, contra-lateral ACL injury, RTS).

Ethics and dissemination This study was approved by the Swedish Ethical Review Board (Dnr 2016/319 and Dnr 2019-04037). The results will be published in international peer-reviewed scientific journals and presented at clinical and scientific congresses.

Trial registration number NCT04162613.

Strengths and limitations of this study

► There is a lack of studies as the present one that identify modifiable risk factors for secondary anterior cruciate ligament (ACL) injuries.
► The use of not only patient-reported outcomes but also a comprehensive test battery of sensorimotor function to identify risk factors that may be modifiable by training, will shed new light on optimisation of rehabilitation protocols to substantially reduce further injuries after ACL injury.
► The prospective design and the inclusion of participants both in Northern and Southern Sweden will facilitate broad and longitudinal investigation of risk factors for secondary knee injuries after ACL injury.
► The prospective design of this study may constitute a risk of drop-out at follow-up which potentially may have implications for data analysis and, subsequently, interpretation of findings.
► While we will adjust for possible demographic confounders, it will not be possible to adjust for extrinsic confounders, for example, playing surface, which may have implications for the analysis and interpretation of the result.

thorough rehabilitation, it takes approximately 2 years for these patients to regain preinjury function.[6] Many persons still suffer from persistent functional limitations several years after injury[1–4] and may never return to their preinjury activity level.[6] In Sweden, around 50% of the ACL injuries are treated with surgical reconstruction of the ACL.[7] However, the risk of rerupture of the ACL after reconstruction is high, and is suggested to be greatest within 2 years following ACL reconstruction (ACLR).[8] The overall reinjury rate is estimated to be around 7% in Sweden[9] but in a systematic review on international studies it was reported to be as high as 23% in younger individuals involved in sport on an elite level.[10] A second ACL injury to either

BACKGROUND

Anterior cruciate ligament (ACL) injury is a devastating injury with major consequences for the individual including functional limitations, poor quality of life and an increased risk of early-onset knee osteoarthritis.[1–5] Despite

knee may have devastating consequences for this group of patients. This may present as a further decline in function[11] and quality of life[12 13] as well as further increasing the risk of future radiographic knee osteoarthritis[14 15] compared with individuals with a unilateral injury. Yet, the factors that may predispose some individuals for recurrent knee injuries are not well established.

Return to sport (RTS) too early after ACLR has been reported as a major reason for the observed high reinjury rate.[16] This may be due to that the individuals may return to their previous activity before gaining adequate functional capacity and physical readiness to RTS, rather than the specific timing of RTS.[17–19] Several sensorimotor factors, such as poor proprioception, kinematic asymmetry and deteriorated muscular activation pattern, have been theorised to contribute to secondary ACL injury.[18] Moreover, previous studies have reported reduced lower extremity strength,[20] altered trunk and knee biomechanics[20] as well as restricted hip rotation[20] and ankle range of motion (ROM)[21] to be linked to sustaining a primary lower extremity injury. Despite this, a recent systematic review (of ours) shows that research on the contributing risk factors for secondary ACL injuries have mainly focused on demographic factors such as age, sex, family history and body mass index, while studies including functional sensorimotor measures as risk factors for reinjury are limited.[22] Studies on the association between factors that are modifiable by training, and the risk of secondary injuries are thus highly warranted. In this prospective cohort study, we aim to identify risk factors for subsequent ACL injuries that are modifiable by training, in order to optimise training and rehabilitation after ACLR to minimise the risk of reinjury and secure a safer RTS. Specifically, we want to determine if poor sensorimotor function at baseline (1 year post-ACLR) can predict graft rupture within 3 years following ACLR. Secondary aims are to study the association between sensorimotor function at baseline and (i) the risk of contra-lateral ACL injury and (ii) failure to RTS within the same time period.

METHODS AND ANALYSIS
Study design
A prospective cohort study, adhering to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines (www.strobe-statement.org).

Participants
Two hundred participants (50% women) who have had ACLR will be consecutively recruited from the Clinics of Orthopedics, Norrlands University Hospital and Clinics of Sports Medicine, Umeå, Sweden (n~100) and from an ongoing study (SHIELD (NCT03473873)) including patients recruited from the Department of Orthopedics, Skåne University Hospital, Sweden (n~100). Inclusion criteria: (i) approximately 1 year after surgical reconstruction of the ACL, with or without associated injuries to other structures of the knee, (ii) 15–35 years

old. Exclusion criteria: (i) previous ACL injury to either knee; (ii) less than 8 months or more than 16 months after ACLR; (iii) diseases or disorders over-riding the knee condition (eg, neurological disease); (iv) not understanding the language of interests (any Scandinavian language or English). All participants will provide a written informed consent.

Procedure
The participants will be assessed with a comprehensive test battery for sensorimotor function (hop tests, muscle strength, muscle activation, ROM, postural orientation, proprioception as joint position sense (JPS) test) and patient-reported outcomes at 1-year post surgery (baseline) as described in table 1 (full description of all collected data is given). The same researcher (AC) will be carrying out data collection in Umeå and in Lund and will give standardised verbal instructions. ROM, proprioception and strength tests will be performed without shoes whereas the postural orientation tasks and hop tests will be performed with training shoes. Both the injured and the non-injured legs will be assessed for sensorimotor function for all tests except for muscle activation pattern for which only the injured leg will be assessed. Irrespective of which knee is the injured knee, the right leg will be tested first (except for isokinetic knee strength for which the non-injured leg will be tested first). A warm up of 5 min of stationary cycling, 10 squats, 10 jumps on both legs and 5 jumps on the right and left legs, respectively[3] precedes the tests.

Predictors
The Limb Symmetry Index ((LSI) calculated as dividing the result for the injured leg by that of the non-injured leg and multiplying by 100) for the single-leg hop for distance (SLHD), will be the main predictor. Absolute hop distance, ROM measures, muscle strength, muscle activation, proprioception, postural orientation and patient-reported outcomes will be the secondary predictors. Collection of patient-reported outcomes and assessment of sensorimotor muscle function will be carried out in the order described later.

Patient-reported outcomes
Data for the following valid questionnaires will be collected and managed using an electronic data capture tool (REDCap) prior to the functional testing[23]; for patient-reported knee specific function, the Knee injury and Osteoarthritis Outcome Score (all subscales),[24] the Anterior Cruciate Ligament—Quality of Life questionnaire[25] and Global Knee Function[26] will be used. For assessment of preinjury and current activity level the Tegner Activity Scale[27] will be used and for assessing psychological readiness to RTS the ACL RTS after injury[28] will be used. The Perceived Stress Scale[29] will be used to evaluate the participants' self-perceived stress.

Hip and ankle ROM
Passive hip ROM will be measured with a digital inclinometer (Commander Echo, JTECH Medical, Salt Lake City,

Table 1 Demographics, patient-reported outcomes and sensorimotor factors to be collected at baseline (1-year post-ACLR)

Demographics	Patient-reported questionnaires	Sensorimotor function
Sex	Tegner activity scale (preinjury and current)	Hop performance (SLHD (cm, LSI), SH (n, LSI)
Age (years)	Knee injury and Osteoarthritis Outcome Score (all subscales)	Knee, hip and trunk isometric peak muscle torque (Nm/kg)
Height (cm)	ACL quality of life	Knee isokinetic peak torque (Nm/kg)
Body mass (kg)	Global knee function: numeric rating scale, 1 (worst) to 10 (best)	Hip and ankle ROM (degrees)
Primary sport	RTS (yes/no, level)	Postural orientation errors during the SLMS, FL, SD and SLHD (visual movement quality scoring)
Years in primary sport	Perceived Stress Scale—10	*Kinematics and kinetics during the SLMS, FL, SD and SLHD (three-dimensional motion analysis)
Injured knee (left/right)	ACL-RSI	*Proprioception (JPS (degrees))
Date of injury		Muscle activation pattern of the hip, trunk and knee during the SLHD (mV)
Date of reconstruction		
Graft type		
Injury situation (game/practice/other)		
Contact/non-contact injury		
Associated injuries (eg, collateral ligament, meniscal injury) to the index knee (from medical records)		
Current pain (numeric rating scale, 0 (none) to 10 (worst))		
Family history of ACL injury		

*Assessed only in Umeå.
ACL, anterior cruciate ligament; ACLR, ACL reconstruction; FL, forward lunge; JPS, joint position sense; ROM, range of motion; RSI, Return to Sport after Injury; RTS, return to sport; SD, stair descending; SH, side hop; SLHD, single leg hop for distance; SLMS, single leg mini squat.

Utah, USA). Internal and external hip rotation will be measured with the patient in a seated position with 90° of flexion in the hip and knee joints. Maximal passive medial and lateral rotation ROM, respectively, will be recorded when the assessor visually observes a lateral pelvic tilt. The mean of two tests will be used in the analysis.[30] Ankle dorsi-flexion ROM will be assessed in a standing position according to a previously described method.[31] The ankle dorsiflexion ROM will be assessed with a standard plastic goniometer. The mean of three subsequent measurements will be used for statistical analysis.

Proprioceptive ability
Participants recruited in Umeå will be assessed for proprioceptive ability using a weight-bearing JPS test developed at Umeå University.[32] Prior to the assessment, reflective markers will be placed on anatomical landmarks and the knee angle will be calculated with a three-dimensional movement analysis system (Oqus cameras, Qualisys AB, Gothenburg, Sweden). Three practice trials will be performed before testing, and five trials on each leg will then be performed. The mean knee joint angle error resulting from the five trials will be used in the analysis.

Good reliability has been reported for this measurement (intraclass correlation coefficient $(ICC)_{3.1}=0.72$).[32]

Isometric muscle strength
Isometric peak force (N) of the knee, hip and trunk will be measured with a hand held dynamometer (Power Track II Commander Echo, JTECH Medical, Salt Lake City, Utah, USA). The leverage (m) will be measured from the joint axis of rotation to the point of application of the force transducer for each test. The peak value of three trials will then be calculated to Newton metre (Nm), by dividing the peak force value with the corresponding leverage. For analysis, all values will be normalised to body weight (Nm/kg). Good inter-reliability and intrareliability has been reported for these measurements (ICCs 0.86–0.91, SEM% 9.5–14.4).[33]

Postural orientation
Visual assessment
The test battery consists of five functional tasks; single-limb mini squat (SLMS), stair descending (SD), forward lunge (FL), SLHD and side hop (SH).[34] The participants will perform the SLMS and SD five times. The FL and SLHD will be performed three times and maximum hops

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in 30s for the SH. The tasks will be video-recorded from a frontal view for later assessment of the patient's postural orientation. The videos can be viewed several times and/or in slow motion if needed. Between two and six segment-specific postural orientation errors (POEs) will be observed and scored for each task. The total knee joint POE across all tasks and the total POE score will be used in the analysis. One to two test trials will be allowed for each task. High inter-rater reliability has been reported for this test battery in patients with ACL injury.[34 35]

Three-dimensional motion analysis

The participants from Umeå will be assessed for three-dimensional kinematics with a three-dimensional motion analysis system with eight infrared cameras (Oqus, Qualisys AB) during all postural orientation tasks (SLMS, FL, SD, SLHD, SH). Forty-four reflective markers will be attached to anatomical landmarks on the shoulders, torso and lower extremities. One assessor (AC) will perform all landmark palpations and marker attachments to ensure standardisation. Spatial and temporal kinematic and kinetic variables for the knee, hip, pelvis and trunk will be calculated.

Isokinetic muscle strength

Maximal isokinetic concentric muscle strength tests during knee extension and flexion will be measured at 60°/s with a dynamometer (Biodex Medical Systems, Shirley, New York). Five test repetitions will be performed and recorded. Normalised peak torque (Nm/kg) for knee extension and flexion will be used in the analysis.[36]

Hop tests

Two commonly used and reliable hop tests, the SLHD and the SH will be performed as described by Gustavsson et al.[37] The SLHD will be performed three times and the distance in centimetres from the toe at the push-off to the heel at the landing position will be measured. The SH is performed once on each leg and the maximum number of jumps in 30s will be recorded. Absolute values for the injured leg and the LSI for both hop tests will be calculated and used in the analysis.

Muscle activation pattern

Muscle activation timing and preactivation amplitudes will be collected using surface electromyography (EMG) electrodes with a wireless EMG system (Desktop DTS, Noraxon U.S.A., Scottdale, Arizona, USA), with a sampling frequency of 1500Hz and a lowpass filter of 500Hz. Data will be collected for the following muscles during the landing of the SLHD (injured side only); gluteus maximus, gluteus medius, semitendinosus, biceps femoris, vastus medialis, medial gastrocnemius and iliocostalis (bilaterally). All electrodes will be placed according to the SENIAM (surface EMG for non-invasive assessment of muscles) guidelines[38] and all values will be normalised to each participants maximum voluntary contraction (MVC). MVC for all muscles will be synchronously collected with the peak torque data described earlier and calculated from the maximum value of three repetitions.

Outcomes

At follow-up at 2 years (3 years post-ACLR), the participants will be contacted by email/phone and asked to answer questions regarding any new ACL injuries and RTS details.

Primary outcome

Rupture of the reconstructed ACL within 2 years from inclusion (self-reported, dichotomous reply (yes/no)).

Secondary outcomes

1. ACL injury to the contra-lateral knee within 2 years from inclusion (self-reported, dichotomous reply (yes/no)).
2. Failure to return-to-sport after ACLR. The participants will be asked to answer a questionnaire regarding if they plan to return/have returned to the same activity or different activity or activity level as well as time point of return.

Statistical analysis

Separate logistic regression models, adjusting for possible confounders (eg, sex, age), will be used to evaluate the influence of the different sensorimotor predictors, respectively, on the prospective outcomes (graft rupture, contra-lateral ACL injury and RTS). With the LSI for the single-leg hop test as main predictor and graft rupture as main outcome, power calculations show that with a graft rupture rate of 7%, an estimated OR of 0.95 for the SLHD, power=80% and alpha=5%, at least 174 individuals are needed. Based on this calculation, we will include 200 individuals allowing for an approximate drop-out of 10%.

Patient and public involvement

This study incorporates previously validated objective and subjective outcomes for this particular group of patients. Patients were not invited to comment on the study design, develop patient-relevant outcomes or interpret the results.

Ethics and dissemination

This study is approved by the Swedish Ethical Review Board (Dnr 2016/319 and Dnr 2019-04037). The results will be published in international peer-reviewed scientific journals. In addition, the results will be presented in appropriated clinical and scientific congresses.

Time line

The recruitment of participants started in March 2018 and is expected to continue until March 2022.

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