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Generalised joint hypermobility leads to increased odds of sustaining a second ACL injury within 12 months of return to sport after ACL reconstruction

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ABSTRACT

Objectives To determine the 12-month risk of a second anterior cruciate ligament (ACL) injury in a population of patients with and without generalised joint hypermobility (GJH) who return to sports (RTS) at competition level after ACL reconstruction (ACL-R).

Methods Data were extracted from a rehabilitation-specific registry for 16–50-year-old patients treated with ACL-R between 2014 and 2019. Demographics, outcome data and the incidence of a second ACL injury within 12 months of RTS, defined as a new ipsilateral or contralateral ACL, were compared between patients with and without GJH. Univariable logistic regression and Cox proportional hazards regression were performed to determine the influence of GJH and time of RTS on the odds of a second ACL injury, and ACL-R survival without a second ACL injury after RTS.

Results A total of 153 patients, 50 (22.2%) with GJH and 175 (77.8%) without GJH, were included. Within 12 months of RTS, 7 (14.0%) patients with GJH and 5 (2.9%) without GJH had a second ACL injury (p=0.012). The odds of sustaining a second ipsilateral or contralateral ACL injury were 5.53 (95% CI 1.67 to 18.29) higher in patients with GJH compared with patients without GJH (p=0.014). The lifetime HR of a second ACL injury after RTS was 4.24 (95% CI 2.05 to 8.80; p=0.0001) in patients with GJH. No between-group differences were observed in patient-reported outcome measures.

Conclusion Patients with GJH undergoing ACL-R have over five times greater odds of sustaining a second ACL injury after RTS. The importance of joint laxity assessment should be emphasised in patients who aim to return to high-intensity sports following ACL-R.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Generalised joint hypermobility (GJH) increases the risk for anterior cruciate ligament (ACL) injury and is associated with inferior patient outcomes following ACL reconstruction (ACL-R).
⇒ Delayed return to sport (RTS) up to 9 months following ACL-R is an effective measure to decrease the risk of ACL reinjury in the general population.

WHAT THIS STUDY ADDS

⇒ This prospective observational registry study reports that a greater proportion of patients with GJH participating in competition-level sports activity sustains a second ipsilateral or contralateral ACL injury within 12 months of RTS compared with those without GJH.
⇒ Patients with GJH have a 5.53-fold greater risk of a second ACL injury compared with patients without GJH in the first 12 months following RTS after ACL-R. There were no differences in patient-reported outcome measures between the GJH and non-GJH groups.
⇒ To our best knowledge, this is the first and largest prospective registry-based study with the aim to investigate the incidence of a second ACL injury after ACL-R in patients with GJH.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study confirms that GJH is a risk factor for a second ACL injury after primary ACL reconstruction. Therefore, the importance of GJH assessment using the Beighton score should be emphasised in all patients with ACL-R.
⇒ The results of this study suggest that approximately one out of seven patients with GJH sustains a second ACL injury within 12 months of RTS. The considerable increase in reinjury risk calls for further investigation of the impact of modifiable surgery—and rehabilitation-specific factors, such as graft choice, rehabilitation criteria and the timing of RTS, in patients with GJH and ACL-R.

INTRODUCTION

A large proportion of patients who return to high-intensity sports activity after anterior cruciate ligament (ACL) reconstruction (ACL-R) are at risk of a second ACL injury. The second ACL injury rate in the young and active population may reach up to 23%, considering both reinjury of the ipsilateral knee and new injury to the contralateral knee.[1] Typically, patients go on to sustain a second ACL injury during the early period following return to sport (RTS), where the risk of reinjury is greater in athletes attempting RTS within 9 months of ACL-R.[1 2]

Generalised joint hypermobility (GJH) is a clinical phenotype characterised by hyperextensibility of the synovial joints.[3] In 2017, efforts were made to establish a clear definition of GJH in the form of a consensus statement.[4] In general, GJH is confirmed based on examination of several synovial joints. It is recommended that screening is conducted using the Beighton score[5] (based on 9 point tests), which requires ≥5 positive tests for adults and ≥6 positive tests for prepubertal children and adolescents to verify GJH.[3] The point tests used for GJH screening with the Beighton score include the assessment of knee hyperextension, where >10° is considered positive. Importantly, preoperative knee hyperextension ≥5° is reported to be present in one-third of patients with revision ACL-R,[6] and contralateral knee hyperextension >10° is predictive of increased rotatory knee instability after ACL-R.[7] Additionally contralateral knee hyperextension >5° is reported to be an independent risk factor for ACL graft failure in patients with hamstring tendon autograft ACL-R.[8]

GJL was previously reported to magnify the risk of sustaining primary ACL[9] and other knee injuries.[10] In addition to a higher ACL injury risk in the GJH population, inferior postoperative outcomes were reported in patients with GJH who undergo ACL reconstruction (ACL-R) compared with those without GJH.[11–13] Additionally, one-third of patients with GJH based on the Beighton criteria sustained either a contralateral ACL tear, an ipsilateral ACL graft tear or excessive ACL graft laxity at a mean 6-year follow-up after ACL-R.[13] Despite existing evidence with regards to risk factors associated with sustaining a second knee injury after ACL-R (age, high activity level, patient sex, graft choice in case of reruptures, returning to knee-strenuous sports activity before 9 months after surgery),[1 2 14 15] there is a shortage of studies with the aim to determine the influence of GJH on the incidence of a second ipsilateral or contralateral ACL injury subsequent to primary ACL-R.

The primary aim of this study was to compare the incidence of a second ipsilateral or contralateral ACL injury within 12 months of RTS at competition level following primary ACL-R, in patients with and without GJH. Secondary aims were to investigate the 12-month and cumulative lifetime risk of a second ACL injury in patients with GJH and to compare patient-reported outcomes preoperatively and at RTS between the GJH and non-GJH groups. It was hypothesised that patients with GJH would show a higher rate of second ipsilateral and/or contralateral ACL injury within 12 months of RTS, and that GJH would be associated with a greater lifetime risk of second ACL injury.

MATERIALS AND METHODS

Equity, diversity and inclusion statement

The current study aims to determine the impact of GJH on second ACL injury risk based on data from a Swedish rehabilitation-specific registry and is inclusive of all registered participants irrespective of sex, ethnicity, culture and socioeconomic background. The Project ACL investigator network and current author team consist of students, physicians and physical therapists with a broad range of research experience. While our analysis accounted for sex differences between the GJH and non-GJH groups, it did not specifically address between-group differences in ethnicity, culture, socioeconomic status and may, therefore, be limited in terms of generalisability.

Study sample and eligibility criteria

Prospectively collected data were queried from a Swedish rehabilitation-specific registry named Project ACL. Patients between 16 and 50 years old, registered in Project ACL between 1 January 2014 and 31 December 2019 treated with a primary ACL-R, were deemed eligible for inclusion. Patients with missing GJH data, failure to RTS, less than 1 year of follow-up from RTS and Tegner activity level <6 or missing data prior to surgery or at the time of RTS were excluded from further analysis. Patients undergoing primary ACL-R were stratified into two groups based on whether they fulfilled criteria for GJH according to the Beighton score (≥5 points). The Beighton score was recorded at the time of the initial clinical encounter for each patient. Extracted data for eligible patients consisted of demographics, surgical variables, patient-reported outcome measures (PROs) and the incidence of a second ACL injury within 12 months of RTS after ACL-R, registered as a dichotomous variable. A second ACL injury was defined as a second ipsilateral or primary contralateral ACL injury. RTS was defined as return to ≥6 Tegner activity level (cut-off for participation in knee-strenuous competitive sports activity),[16 17] and five positive tests on the Beighton scale were considered to fulfil criteria for GJH.

Project ACL

Project ACL is a Swedish rehabilitation-specific registry established in 2014, which focuses on the regular assessment of patients following operatively and non-operatively treated ACL injuries. When possible, patients participating in the registry are assessed preoperatively, and at 10 weeks, 4, 8, 12, 18, 24 months, and beyond with standardised PROs, including but not limited to the ACL-Return to Sports after Injury scale (ACL-RSI), Knee injury and Osteoarthritis Outcome Score (KOOS), Knee Self-efficacy Scale (K-SES) and Tegner Activity Scale. Muscle function tests measuring unilateral knee extension and flexion strength as well as unilateral hop tests are performed at the specified follow-up intervals. Additionally, Project ACL collects information pertinent to patient demographics, surgical variables and the incidence of second ACL injuries following the index event. Previous studies include detailed descriptions of Project ACL.[18 19]

Outcomes

The primary outcome of this study was the rate of a second ACL injury within 12 months of RTS following ACL-R in patients with and without GJH. Second, ACL injury was defined as the incidence of a second ipsilateral or primary contralateral ACL injury following the index ACL-R within the 12-month follow-up period. In order to determine the timing of second ACL injuries, the incidence of each event was reported according to 4-month intervals for both ipsilateral and contralateral reinjuries (none within 12 months, and 0–4, 4–8, 8–12 months from RTS). A second ACL injury was confirmed with clinical examination and eventually with MRI.

Secondary outcomes included the incidence and lifetime risk of a second ipsilateral or contralateral ACL injury since the inception of Project ACL in patients with 12-month or longer follow-up after RTS. Additionally, PROs evaluated preoperatively and at the time of RTS were compared between GJH and non-GJH groups. The PROs assessed included the ACL-RSI, KOOS, K-SES and a modified version of the Tegner Activity Scale.[17] The validated 12-item short version of the ACL-RSI measures emotions, confidence and risk-appraisal of patients with ACL injury to RTS. Adequate outcomes supporting RTS are defined as lower levels of negative emotions, lower levels of risk appraisal and increased levels of confidence in performance.[20] Grading of the individual items is performed on a scale of 0 to 10, where 10 indicates the greatest measure of emotions and confidence and lowest measure of risk appraisal towards RTS. The KOOS is a PRO developed to measure subjective knee function in patients with knee-related conditions following operative and non-operative interventions.[21] The KOOS consists of five subscales to report subjective knee function: symptoms, pain, activities of daily living (ADL), sports/recreation and quality of life. Items are rated on a 5-point Likert scale, and values for each KOOS subscale range from 0 to 100, where 0 represents the worst possible state and 100 represents the best possible knee function. The KOOS$_4$ is a composite score derived from all KOOS subscales, excluding ADL due to lack of responsiveness.[22] The K-SES[23] assesses the perceived knee-related self-efficacy of the patient through the ability to perform physical tasks (such as swimming, bicycling, jumping) and consists of 18 items with two subscales, evaluating present (14 items) and future (4 items) knee self-efficacy. Items are graded from 0 to 10, where 10 represents the greatest belief in being able to perform a physical task. A mean value is derived from the sum of individual items divided by the total number of K-SES items. The modified Tegner Activity Scale[16 17] is a rating system of physical activity level, reporting the current ability of the patient to participate in sports activity. Scores range from 1 to 10, where 1 corresponds to no participation in physical activity and 10 indicates participation in elite-level competitive pivoting sports.

Statistical analysis

Statistical analyses were performed using SAS/STAT (V.9.4, SAS Institute, Cary, North Carolina). Data analysis and presentation were consistent with the CHecklist for statistical Assessment of Medical Papers (CHAMP) statement.[24] Demographic, surgical and follow-up data were reported using descriptive statistics including frequency (n) and proportion (%) for categorical variables, median and range for ordinal variables and mean±SD or mean with a 95% CI for continuous variables. Pairwise comparisons of variables were performed between the GJH and non-GJH groups. The Fisher exact test was used for pairwise comparison of dichotomous variables (lowest one-sided p value multiplied by 2). The χ^2 exact test was used for non-ordered categorical variables and the Fisher's non-parametric permutation test was used for continuous variables. The CIs for mean differences between groups were based on the Fisher non-parametric permutation test. The CI for dichotomous variables corresponds to the unconditional exact confidence limits. When exact limits could not be computed, the asymptotic Wald confidence limits with continuity correction were calculated instead. Univariable logistic regression was performed to determine the influence of GJH and timing of RTS on the odds of a second ACL injury after RTS. P values, ORs and area under the receiver operating characteristics (ROC) curve were based on original values and not on stratified groups.

Cox regression models were applied to calculate the proportional HR of primary ACL-R survival without a second ACL injury after RTS since the inception of Project ACL (2014–2019). Patients without an outcome of interest were censored at the last date of follow-up. Significantly different variables between the two groups determined with logistic regression analysis were treated as potential confounders for Cox regression and were used for model adjustment. Since logistic regression analysis did not identify additional confounding variables, further adjustment of the Cox regression model, stratified based on GJH and non-GJH groups, was not warranted. The Supremum test for proportional hazards assumption was performed to verify that the assumption for proportionality was not incorrect. The result of the Cox regression analysis was reported as an unadjusted HR with 95% CIs. All statistical tests were two sided. Alpha was set at 0.05.

RESULTS

A total of 225 patients were eligible for inclusion, of which 50 (22.2%) patients fulfilled criteria for GJH (table 1). The remaining 175 (77.8%) patients were included in the non-GJH group (figure 1). The mean age of patients with GJH was 22.3 years, while the mean age for non-GJH patients was 25.0 years at the time of index ACL-R (p=0.031). Time from injury to surgery was 4.90 (95% CI 3.46 t0 6.33) months for GJH patients and 8.86 (95% CI 5.28 to 12.44) months for non-GJH patients (p=0.17). There was a significant difference in time from surgery to RTS between the GJH and non-GJH groups (9.2 vs 11.5 months; p=0.031). The median Beighton score for patients in the GJH group was 6 (range=5–9). The majority of patients in both the GJH and non-GJH groups underwent ACL-R with hamstring tendon autograft (68.0% and 79.4%, respectively;p=0.25).

Table 1 Comparison of baseline demographic variables and the incidence of a second ACL injury between GJH and non-GJH patients

Variable	GJH (n=50)	Non-GJH (n=175)	P value
Age at reconstruction, mean±SD (years)	22.3±6.4	25.0±8.1	**0.031**
Male, n (%)	19 (38.0%)	86 (49.1%)	0.22
Height, mean±SD (cm)	174.6±9.3	175.1±9.5	0.79
Weight, mean±SD (kg)	71.4±11.0	72.6±12.5	0.55
BMI, mean±SD (kg/m^2)	23.3±2.1	23.6±2.8	0.56
Right knee, n (%)	30 (60.0%)	96 (54.9%)	0.63
Smoking n (%)	1 (2.0%)	1 (0.6%)	0.79
Beighton score, median (range)	6 (5-9)	2 (1-4)	
Time from injury to surgery, mean (95% CI) (months)	4.90 (3.42 to 6.33)	8.86 (5.28 to 12.44) n=174	0.17
Graft type, n (%)			0.25
Hamstring tendon autograft	34 (68.0%)	139 (79.4%)	
Patellar tendon autograft	16 (32.0%)	32 (18.3%)	
Quadriceps tendon autograft	0	1 (0.6%)	
Allograft	0	2 (1.1%)	
Other	0	1 (0.6%)	
Time until RTS (Tegner activity level≥6), mean (95% CI) (months)	9.2 (7.7 to 10.7)	11.5 (10.4 to 12.7)	0.031
Second ACL injury within 12 months of RTS, n (%)	7 (14.0%)	5 (2.9%)	0.012
Ipsilateral second ACL injury			
None within 12 months of RTS	46 (92.0%)	171 (97.7%)	
0–4 months from RTS	1 (2.0%)	3 (1.7%)	
4–8 months from RTS	2 (4.0%)	0	
8–12 months from RTS	1 (2.0%)	1 (0.6%)	
Contralateral second ACL injury			
None within 12 months of RTS	47 (94.0%)	174 (99.4%)	
0–4 months from RTS	0	0	
4–8 months from RTS	2 (4.0%)	1 (0.6%)	
8–12 months from RTS	1 (2.0%)	0	
Time from RTS to second ACL injury in patients with a 12-month or longer follow-up, mean (95% CI) (months)	21.0 (11.3 to 30.6)	18.0 (9.3 to 26.6)	0.63
Cumulative incidence of a second ACL injury in patients with a 12-month or longer follow-up, n (%)	15 (38.2%)	14 (10.1%)	<0.001
Ipsilateral second ACL injury	8 (16.0%)	7 (4.0%)	
Contralateral second ACL injury	7 (14.0%)	7 (4.0%)	

ACL, anterior cruciate ligament; BMI, body mass index; GJH, generalised joint hypermobility; N, number; RTS, return to sport.

Incidence of a second ACL injury

Incidence of a second ACL injury within 12 months of RTS occurred in seven (14.0%) patients with GJH and five (2.9%) patients without GJH (p=0.012). Of the second ACL injuries sustained within 12 months of RTS, four (57%) were of the ipsilateral knee and three (43%) of the contralateral knee in the GJH group, while four was of the ipsilateral knee and one of the

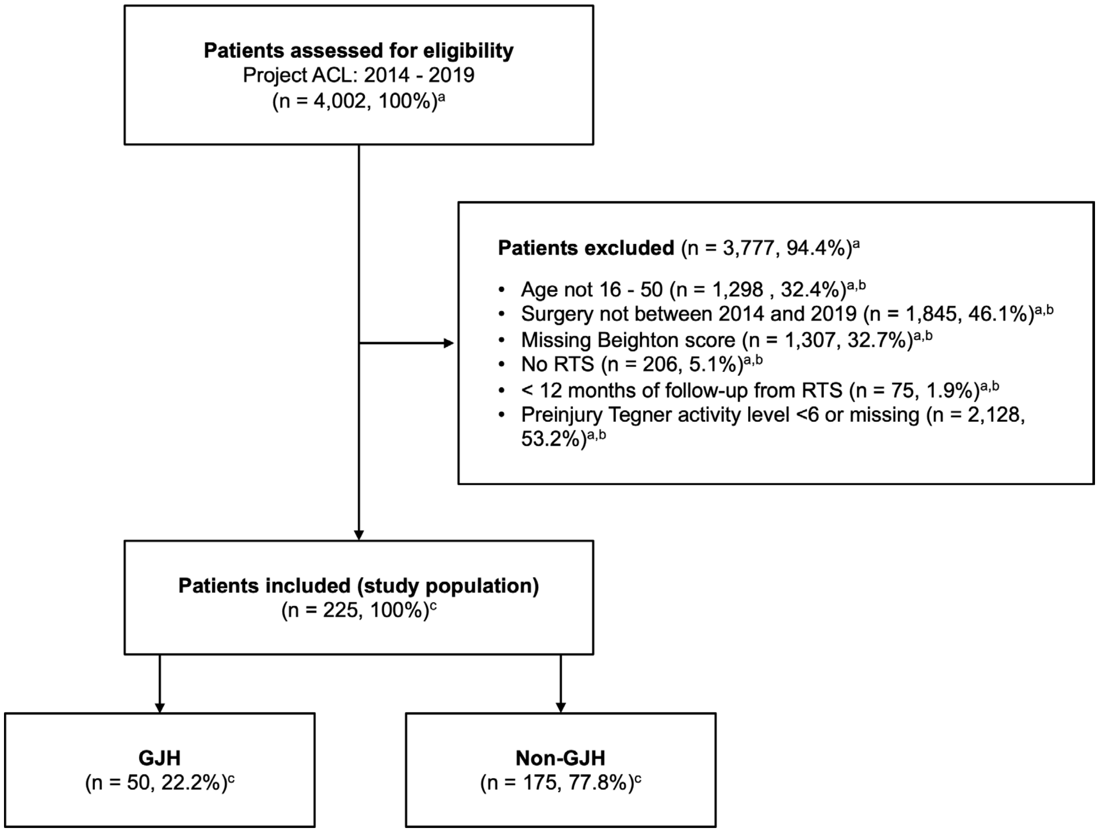

Figure 1 Flowchart displaying the implementation of inclusion and exclusion criteria. Values are presented as count (n) and proportion (%). [a]Percentage of patients assessed for eligibility; [b]Patients may fulfil multiple exclusion criteria; [c]Percentage of patients included in the final study population. ACL, anterior cruciate ligament; GJH, generalised joint hypermobility; Non-GJH, non-GJH; RTS, return to sport.

contralateral knee in the non-GJH group. The mean time from RTS until a second ACL injury in the GJH and non-GJH groups with at least a 12-month or longer follow-up from RTS was 21.0 (95% CI 11.3 to 30.6) months and 18.0 (95% CI 9.3 to 26.6) months, respectively (p=0.63; table 1).

Logistic regression analysis of second ACL injury incidence regardless of laterality, stratified based on GJH and non-GJH groups identified that GJH leads to a 5.53-fold (95% CI 1.67 to 18.29; p=0.005) odds of sustaining a second ACL injury within 12 months of RTS after ACL-R (table 2). Independently, there was a 4.21-fold (95% CI 1.01 to 17.56; p=0.049) odds of sustaining an ipsilateral second ACL injury and a 12.85-fold (95% CI 1.30 to 126.84; p=0.029) odds of sustaining a contralateral second ACL injury (tables 3 and 4). Cox regression analysis of patients with 12 months or longer follow-up after RTS

Table 2 Univariable logistic regression analysis performed to assess the influence of GJH and time until return to Tegner activity level ≥6 on sustaining an ipsilateral or contralateral second ACL injury within 12 months of RTS after ACL-R

Variable	Value	n (%) of event	OR (95% CI) of second ACL injury within 12 months of RTS	P value	Area under ROC curve (95% CI)
GJH	Non-GJH	5 (2.9%)			
	GJH	7 (14.0%)	5.53 (1.67 to 18.29)	**0.005**	0.69 (0.54 to 0.84)
Time until RTS (Tegner activity level ≥6) (months)			0.96 (0.87 to 1.06)	0.43	0.57 (0.43 to 0.71)

ACL, anterior cruciate ligament; ACL-R, ACL reconstruction; GJH, generalised joint hypermobility; RTS, return to sport.

Table 3 Univariable logistic regression analysis performed to assess the influence of GJH and time until return to Tegner activity level ≥6 on sustaining a second ipsilateral ACL injury within 12 months of RTS after ACL-R

Variable	Value	n (%) of event	OR (95% CI) of second ACL injury within 12 months of RTS	P value	Area under ROC curve (95% CI)
GJH	Non-GJH	4 (2.4%)			
	GJH	4 (9.3%)	4.21 (1.01 to 17.56)	0.049	0.65 (0.47 to 0.84)
Time until RTS (Tegner activity level ≥6) (months)			0.95 (0.84 to 1.08)	0.43	0.59 (0.40 to 0.78)

ACL, anterior cruciate ligament; ACL-R, ACL-reconstruction; GJH, generalised joint hypermobility; RTS, return to sport.

Table 4 Univariable logistic regression analysis performed to assess the influence of GJH and time until return to Tegner activity level ≥6 on sustaining a second contralateral ACL injury within 12 months of RTS after ACL-R

Variable	Value	n (%) of event	OR (95% CI) of second ACL injury within 12 months of RTS	P value	Area under ROC curve (95% CI)
GJH	Non-GJH	1 (0.6%)			
	GJH	3 (7.1%)	12.85 (1.30 to 126.84)	0.029	0.78 (0.53 to 1.00)
Time until RTS (Tegner activity level ≥6) (months)			0.97 (0.82 to 1.14)	0.71	0.56 (0.37 to 0.74)

ACL, anterior cruciate ligament; ACL-R, ACL reconstruction; GJH, generalised joint hypermobility; RTS, return to sport.

found that the lifetime HR of second ACL injury with RTS was 4.24 (95% CI 2.05 to 8.80; p<0.001; figure 2; table 5).

Patient-reported outcomes

The median preinjury Tegner activity level was 9 (range=6–10) for GJH and 8 (range=6–10) for patients without GJH. There was a significant difference in Tegner activity level between patients with and without GJH prior to injury (p=0.015) but not at the time of RTS (p=0.098). Return to preinjury Tegner activity level was achieved by 38 (76.0%) patients with GJH and 118 (67.4%) patients without GJH (p=0.32; table 6).

No significant difference was observed in any of the KOOS subscales or $KOOS_4$, preoperatively or at RTS, based on the available data (table 6). The mean ACL-RSI at RTS was 63.3 (95% CI 56.0 to 70.7; n=33) and 65.4 (95% CI 62.1 to 68.8; n=128) for the GJH and non-GJH groups, respectively (p=0.58). The median $K\text{-}SES_{18}$ present at RTS was 8.4 (range=0.4–10; n=49) for patients with GJH and 8.6 (range=1.3–10; n=169) for patients without GJH (p=0.13). The median $K\text{-}SES_{18}$ future at RTS was 8.0 (range=1.3–10; n=49) and 8.0 (range=3.3–10; n=169) in the GJH and non-GJH groups, respectively (p=0.39).

DISCUSSION

The main finding of this registry study was that the incidence of a second ACL injury within 12 months of RTS after primary ACL-R is greater in patients with GJH compared with patients without GJH (figure 3). The findings of logistic regression and Cox proportional hazards regression models further underscore the susceptibility of patients with GJH to ACL reinjury after ACL-R. These results are consistent with our hypothesis

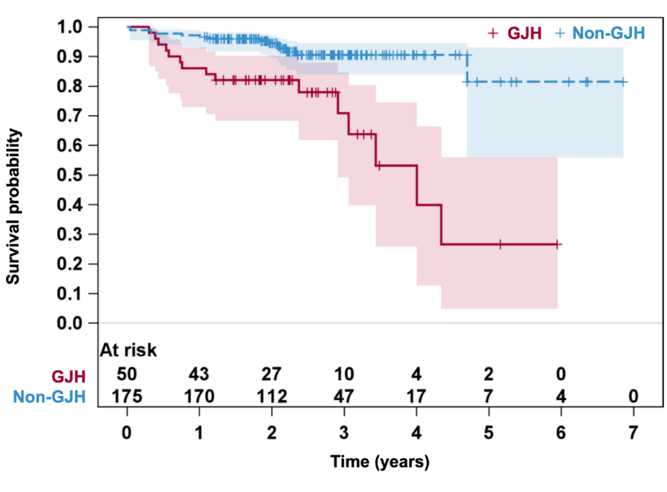

Figure 2 Survival analysis of GJH and non-GJH groups without a second ACL injury following RTS after ACL-R. ACL, anterior cruciate ligament; ACL-R, ACL-reconstruction; GJH, generalised joint hypermobility; Non-GJH, non-GJH; RTS, return to sport.

and with previous studies investigating the influence of GJH on ACL reinjury in surgically treated patients.[13 25 26] Additionally, our results highlight that GJH is independently associated with increased second ACL injury risk, in terms of both ipsilateral ACL reinjury and injury to the contralateral ACL.

The present study did not identify any differences in PROs between patients with GJH and without GJH preoperatively or at the time of RTS. The study cohort consisted of patients functioning at high physical activity levels prior to injury, with the majority of patients in both groups attempting return to preinjury activity level after ACL-R (table 6). There was a consistent improvement in self-reported knee function following ACL-R in both patient groups. However, it is important to mention that while PRO collection and assessment of risk appraisal were recorded at RTS for both patient groups, the timing of RTS differs (p=0.031) between patients with GJH and patients without GJH (9.2 months vs 11.5 months, respectively). A potential explanation to the between-group difference in time to RTS is that patients in the GJH group were on average slightly younger athletes with higher activity levels (supported by the median preinjury Tegner activity level of 9 among patients with GJH compared with 8 in patients without GJH) and aimed for an earlier return to elite-level sports participation.[27–29] However, all patients included in the study returned to sports activity at a competitive level, and the Tegner activity level may only reflect differences in the types of sporting activities performed between patient groups. While the timing of RTS was not identified as a confounder for the assessment of ACL reinjury risk in patients with and without GJH, it should nonetheless be considered as a potential contributor to second ACL injury, especially when RTS is attempted by high-level athletes within 9 months of ACL-R.[2] In the current cohort, shorter time between surgery and RTS in the GJH group compared with the non-GJH group may have had an impact on the high ACL reinjury rate in patients with GJH. Consequently, our findings suggest that patients with GJH may benefit from counselling to optimise RTS timing and thereby reduce second ACL injury risk.

It is hypothesised that GJH caused by alterations in collagen fibres important to the structure of connective tissue may exacerbate the forces exerted on intra-articular knee ligaments during the tibiofemoral rotatory and valgus moments typically associated with ACL injury.[9 10 30] Image-based analysis demonstrates a weak association between quantitative pivot shift and increased

Table 5 HR for a second ACL injury after RTS in GJH and non-GJH patients undergoing ACL-R

Parameter	χ^2	$Pr>\chi^2$	Hazard ratio	95% HR CI	
GJH	15.0908	0.0001	4.24	2.05	8.80

ACL, anterior cruciate ligament; ACL-R, ACL-reconstruction; GJH, generalised joint hypermobility; $Pr>\chi^2$, p-value for Chi-square test; RTS, return to sport.

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Table 6 Comparison of Tegner activity level and patient reported outcome measures between GJH and non-GJH patients at the time of surgery and RTS

Variable	GJH (n=50)	Non-GJH (n=175)	P value
Preinjury Tegner activity level, median (range)	9 (6–10)	8 (6–10)	
Preinjury Tegner activity level, n (%)			0.015
6	3 (6.0%)	13 (7.4%)	
7	3 (6.0%)	29 (16.6%)	
8	11 (22.0%)	49 (28.0%)	
9	18 (36.0%)	56 (32.0%)	
10	15 (30.0%)	28 (16.0%)	
Tegner activity level at RTS, n (%)			0.098
6	9 (18.0%)	55 (31.4%)	
7	16 (32.0%)	45 (25.7%)	
8	6 (12.0%)	32 (18.3%)	
9	14 (28.0%)	29 (16.6%)	
10	5 (10.0%)	14 (8.0%)	
Returned to preinjury Tegner activity level, n (%)	38 (76.0%)	118 (67.4%)	0.32
Preoperative KOOS, mean (95% CI);			
KOOS symptoms	68.3 (57.5 to 79.1) n=9	66.4 (60.7 to 72.0) n=44	0.79
KOOS pain	80.6 (72.0 to 89.1) n=9	72.5 (67.2 to 77.8) n=44	0.18
KOOS ADL	88.7 (81.2 to 96.1) n=9	85.2 (80.2 to 90.3) n=44	0.59
KOOS sports/recreation	30.0 (10.6 to 49.4) n=9	40.0 (32.8 to 47.3) n=44	0.26
KOOS QOL	34.1 (13.9 to 54.3) n=9	37.5 (32.9 to 42.1) n=44	0.61
$KOOS_4$	53.3 (42.8 to 63.7) n=9	54.1 (49.3 to 58.9) n=44	0.88
Postoperative KOOS at RTS, mean (95% CI)			
KOOS Symptoms	78.4 (73.5.4 to 83.3) n=48	77.5 (75.2 to 79.7) n=169	0.72
KOOS Pain	86.7 (82.9 to 90.4) n=48	87.2 (85.5 to 88.9) n=169	0.77
KOOS Daily living	97.8 (95.4 to 100.1) n=19	95.8 (93.9 to 97.7) n=60	0.28
KOOS Sports and recreation	69.5 (61.8 to 77.2) n=48	69.9 (66.7 to 73.0) n=169	0.92
KOOS Quality of life	56.1 (49.9 to 62.3) n=48	61.1 (58.4 to 63.8) n=169	0.099
$KOOS_4$	72.7 (67.8 to 77.6) n=48	73.9 (71.8 to 76.0) n=169	0.60
ACL-RSI at RTS, mean (95% CI)	63.3 (56.0 to 70.7) n=33	65.4 (62.1 to 68.8) n=128	0.58
K-SES_{18} present at RTS, median (range)	8.4 (0.4–10) n=49	8.6 (1.3–10) n=169	0.13
K-SES_{18} future at RTS, median (range)	8.0 (1.3–10) n=49	8.0 (3.3–10) n=169	0.39

ACL-RSI, anterior cruciate ligament return to sports index; ADL, activities of daily living; GJH, generalised joint hypermobility; KOOS, Knee injury and Osteoarthritis Outcome Score; K-SES, Knee Self-efficacy Scale; QOL, quality of life; RTS, return to sport.

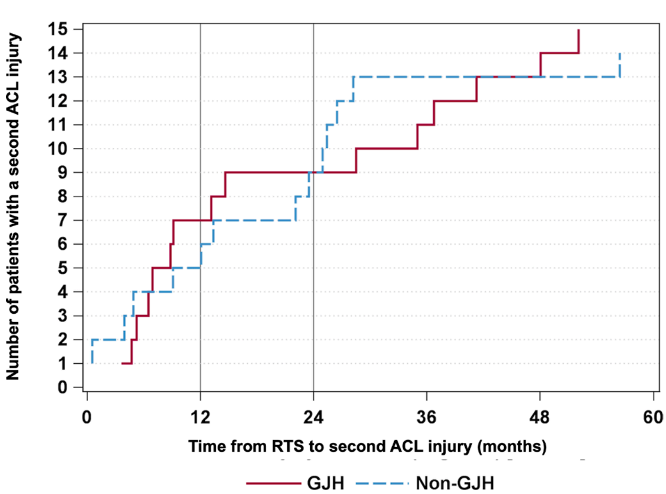

Figure 3 Incidence of a second ACL injury in the GJH and non-GJH groups following RTS after ACL-R, including all patients with a 12 month or longer follow-up. ACL, anterior cruciate ligament; ACL-R, ACL-reconstruction; GJH, generalised joint hypermobility; Non-GJH, non-GJH, non-GJH; RTS, return to sport.

rotatory knee laxity in patients with GJH.[31] As demonstrated in the current study and previous literature,[11 13 25 26] GJH magnifies the risk of a second ACL injury and should be factored into the aggregated risk assessment of patients who aim to return to high-intensity sports following primary ACL-R. In contrast, previous studies did not report statistically significant differences in the incidence of contralateral ACL injury after primary ACL-R in patients with GJH.[11 13] In the present study, GJH magnified the odds of contralateral second ACL injury, which may indicate the need for further studies with larger patient populations to clarify contralateral ACL injury incidence after ACL-R in relation to GJH.

Patients with GJH may consequently benefit from individualised ACL-R, involving careful consideration of multiple factors to combat the incidence of graft failure and reinjury. The majority of ACL-Rs in patients with and without GJH were performed with hamstring tendon autograft (68.0% and 79.4%, respectively). While the current study does not demonstrate differences in graft choice and PROs between the two patient groups, a higher ACL reinjury rate in patients with GJH suggests that more robust graft options may be advantageous for this population. Moreover, recent reports highlight that the addition of lateral extra-articular tenodesis (LET) improves anteroposterior and rotatory knee laxity and results in a lower ACL-R failure rate.[25 32] In light of the existing evidence regarding the influence of graft choice on persistent postoperative rotatory laxity and PROs in patients with ACL-R, future research will be required to determine the effect of graft choice and augmentation with LET on ACL reinjury risk.[12 25 33 34] Finally, the relatively early timing of RTS (9 months on average) and high rate of second ACL injury observed in the GJH population warrants further consideration of delaying RTS. Delayed RTS reduces ACL reinjury risk by up to 51% per month until 9 months after surgery in the general ACL-injured population, which may also be beneficial to patients with ACL injury and GJH.[2 35] In the future, it may be advantageous to consider specific rehabilitation criteria for patients with GJH and ACL-R before clearance for RTS.

Strengths and Limitations

The key strength of the study design is the prospective assessment of second ACL injury risk in patients with GJH and without GJH within a 12-month time period of RTS after ACL-R. The assessment of 12-month ACL reinjury risk is further complemented by the evaluation of survival without reinjury, allowing for long-term assessment of the effect of GJH on second ACL injury risk. While injury-free survival should be interpreted with caution due to limited data availability since the nascence of the registry, the data presented herein strongly suggest that patients with GJH are more susceptible to a second ipsilateral and contralateral ACL injury after primary ACL-R compared with patients without GJH.

The most important limitations of the study are the size of the GJH population, the scarcity of information with regards to surgical variables and concomitant intra-articular injuries and incomplete PRO data. The limited size of the study cohort is a consequence of the application of strict inclusion criteria and the relatively short lifetime of Project ACL. It is important to acknowledge that a large number of otherwise eligible patients (n=1307) were excluded due to missing Beighton scores, as the variable was introduced only recently. The Beighton score is recorded by a single investigator, and incorrect measurements cannot, therefore, be ruled out, despite substantial to near perfect inter-rater and intra-rater reliability reported in the literature.[36] Additionally, measurement of GJH with the Beighton score may be affected by limited joint motion due to injury or surgery. While it was not feasible to record the Beighton score for patients included in the current study, it is important to consider that the recorded scores may underrate the prevalence of patients with GJH. Since a priori sample size calculation was not performed, some of our analyses may be statistically underpowered, which increases the risk of a type 2 error. Additionally, the large number of between-group comparisons may also increase the risk of type 1 error. However, the risk of a second ACL injury as a function of GJH was significantly different, and, therefore, unaffected by the low power, resulting from the small group sizes.

The risk of reinjury after ACL-R is multifactorial, and no statistically significant differences were identified between the study populations in terms of several known risk factors (gender, graft type, risk appraisal). However, not all known risk factors of ACL reinjury were considered in the current study, which may confound the reported results. Moreover, KOOS data were unavailable in a large proportion of both GJH and non-GJH groups (table 6), which warrants cautious interpretation of outcomes related to subjective knee function. In contrast, the availability of injury-related risk appraisal data permits more definitive conclusions to be drawn regarding the confidence, emotions and risk appraisal of the study population to attempt RTS. Future studies of ACL reinjury risk in patients with GJH should focus on increasing sample size, collecting long-term outcome data and investigation of the influence of surgical variables on postoperative outcomes. Importantly, the relationship between knee hyperextension and GJH warrants further studies to disambiguate the role of GJH as a risk factor for ACL reinjury independent of knee hyperextension.[8 13 26]

CONCLUSION

Patients with GJH undergoing ACL-R have more than five times greater odds of sustaining a second ACL injury after RTS. Consequently, GJH should be considered a risk factor for ipsilateral or contralateral ACL reinjury. The importance of joint laxity assessment should be emphasised in the aggregated risk appraisal of patients who aim to return to high-intensity sports following ACL-R.

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