

BMJ Open Single versus double hamstring tendon graft in anterior cruciate ligament reconstruction in the paediatric patient: a single-blind randomised controlled trial study protocol

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ABSTRACT

Introduction There is currently no clear indication in the literature regarding a single or double hamstring tendon (single bundle) autograft for anterior cruciate ligament (ACL) reconstruction in the paediatric patient. The primary aim of this single blind randomised controlled trial is to determine whether a single or double hamstring tendon graft ACLR leads to superior clinical outcomes postsurgery in paediatric patients with ACL injury.

Methods and analysis Single site, prospective, single blind, randomised controlled trial with two parallel treatment arms. 100 patients aged 10–18 years who present with an isolated ACL tear±meniscal injury, verified on MRI, will be randomly allocated to one of the two surgical groups. The primary outcomes will be side-to-side difference in anterior tibial translation and graft failure incidence 12 months postsurgery. Primary and secondary outcomes will also be assessed at 2-year and 5-year postsurgery.

Ethics and dissemination Results will be presented in peer-reviewed journals and at international conferences and disseminated to participants and healthcare professionals via newsletters and hospital presentations. This study is approved by the Children's Health Queensland Hospital and Health Service Human Research Ethics committee.

Trial registration number ACTRN12620001170910p; Australian New Zealand Clinical Trials Registry.

BACKGROUND

The diagnosis of anterior cruciate ligament (ACL) injury and reconstruction (ACLR) in skeletally immature patients is climbing at a rate significantly higher than adults.¹ The increased incidence has been attributed to several factors including a rise in competitive sport participation, decreased incidental activity, increased clinical awareness of a potential for ACL tear in this population, more comprehensive diagnosis and evaluation with MRI and a shift in clinical practice

STRENGTH AND LIMITATION OF THIS STUDY

- ⇒ This is the first study to compare these two anterior cruciate ligament reconstruction techniques in a randomised control trial in the paediatric patient assessing multiple outcome parameters.
- ⇒ Comprehensive evaluation of knee joint laxity, growth disturbance, lower limb function, muscle and graft morphology, patient-reported outcome measures and cost-utility in the paediatric patient.
- ⇒ One limitation is that follow-up at present is set for 5 years postoperatively—longer (up to 10 years) has been suggested in the literature.
- ⇒ A second limitation is that we are comparing surgical techniques and using only one type of autograft; it could be beneficial, given the acceptance of alternative graft choices in adults, to compare different graft choices in the paediatric population—however not the scope of this study.
- ⇒ A third limitation is the difference in tibial graft fixation between the two surgical techniques, which is necessary because the single hamstring tendon technique will result in a shorter graft compared with the double hamstring tendon technique

to provide early intervention.^{2–5} Most ACL injuries are non-contact with the mechanism and/or consequence of injury a combination of tibiofemoral joint external rotation and valgus.⁶ Historically, conservative management of ACL tears was the preferred clinical method in skeletally immature patients with bracing and modification of activities until skeletal maturity when ACLR could be safely performed.^{3,7} The weight of available evidence now supports reconstruction over conservative management with minimal complications^{8–12} and there is a growing body of evidence indicating that delayed ACL reconstruction increases the

risk of secondary articular injuries including irreparable meniscal tears meniscal tears and chondral injuries in paediatric patients.^{13 14} Nonetheless, evidence regarding the ideal surgical technique for the skeletally immature patient is still lacking. Indeed, ACLR techniques that aim to reproduce the native ACL morphology with emphasis on graft placement within the native femoral footprint is well supported in the adult literature;¹⁵ however, the risk in the skeletally immature patient is the potential for growth disturbance.^{2 9 16}

Restoration of native anatomical laxity is a fundamental principle in ACLR. Indeed, suboptimal postoperative laxity may alter knee loading and have long-term consequences for the patient (ie, development of osteoarthritis). In studies of adults, positive rotational laxity results have been reported for double-bundle techniques, which use two smaller grafts to replicate the morphology of the native ACL.¹⁷⁻¹⁹ Nonetheless, a combined physeal-sparing, double-bundle method has led to less promising mid-term results in skeletally immature patients.²⁰ Regarding graft selection, there are a number of options including allografts, quadriceps tendon autografts, hamstrings tendon autografts, patellar tendon autografts and iliotibial band autografts. Nonetheless, there remains a lack of evidence surrounding the optimal graft selection when considering functional outcomes, failure rates and patient satisfaction for paediatric ACLR.²¹

At our institution, single bundle hamstring autografts are preferred for the skeletally immature patient using a single (semitendinosus tendon) or double (semitendinosus plus gracilis tendon) hamstring tendon graft. We acknowledge that hamstring tendon harvest is not without limitation or comparison (ie, quadriceps tendon, iliotibial band, various soft tissue allografts). In studies of adults, harvest of the semitendinosus and gracilis tendons has led to postoperative donor muscle atrophy as well as proximal retraction of the musculotendinous junction.²²⁻²⁴ This retraction is believed to occur until the regenerated tendon reaches an attachment site,²⁵ which may take longer than 2 years,²³ or it may not occur at all.^{22 26} These changes in donor muscle-tendon properties and impaired capacity to transmit force to the skeleton after medial hamstring harvest might be expected to contribute to the knee muscle weakness that has been reported in flexion^{23 27-30} and internal tibial rotation^{31 32} at up to 2 years after surgery. In a study of muscle and tendon morphology of 20 adult patients who underwent ACLR with hamstring autograft, Konrath *et al*³³ found only 35% of patients showed regeneration of both the semitendinosus and gracilis tendons. Furthermore, combined hamstring muscle volumes on the surgical side were reduced by 12%, although 7% larger volume was observed in the surgical limb for the biceps femoris muscle. The difference in volume, peak cross-sectional area (CSA) and length of the semitendinosus and gracilis correlated significantly with the deficit in knee flexion strength. To the authors' knowledge, no previous research has assessed muscle morphology in donor site muscles

or compared functional outcomes between single and double hamstring tendon graft methods following ACLR in paediatric patients.

Aims and hypotheses

There is currently no clear indication in the literature regarding a single or double hamstring tendon (single bundle) autograft for ACLR in the paediatric patient. The primary aim of this single blind randomised controlled trial is to determine whether a single tendon, single bundle ACLR or a double tendon, single bundle ACLR leads to superior clinical outcomes postsurgery in paediatric patients with ACL injury. Primary outcome measures will include graft failure and side to side difference in graft laxity.³⁴ Secondary outcome measures will investigate growth disturbance rates, passive and dynamic knee joint function (range, strength), lower limb function (power, agility, stability), muscle and ligament morphology and patient-reported outcomes. The primary timepoint will be 1-year postsurgery and secondary timepoints will be 2-year and 5-year postsurgery. We hypothesise that compared with double hamstring tendon graft ACLR, patients who receive a single hamstring tendon graft ACLR will have reduced rerupture rates and smaller side-to-side laxity deficits.

METHODS AND ANALYSES

Study design and setting

We will conduct a single-site, prospective, single blind, randomised controlled trial with two parallel treatment arms. The study will be conducted in the Queensland Children's Hospital (QCH), the only paediatric focused quaternary hospital covering a population of 5 million people. We will offer recruitment to patients enrolled in the Australian Paediatric ACL Injury Registry at the QCH site. Inclusion will start in July 2021 and is expected to finalise in July 2023, which will allow for read-out of the primary endpoint in July 2024. The proposed flow of patients thought the trial is displayed in [figure 1](#).

Recruitment strategy

All consecutive patients between the age of 10 and 18 who present to the orthopaedic outpatient's clinic at the QCH with an isolated ACL±meniscal injury will be provided with a recruitment package during their outpatient appointment. A follow-up phone call will be made to ensure that potential participants received the study information.

Inclusion and exclusion criteria

Potential participants will be excluded if they have:

1. Concomitant posterior cruciate ligament injury.
2. Collateral ligament instabilities of grade I or greater (2–5 mm).
3. Bilateral ACL deficiency.
4. Combined knee surgery with high tibial osteotomy or medial patellofemoral ligament.

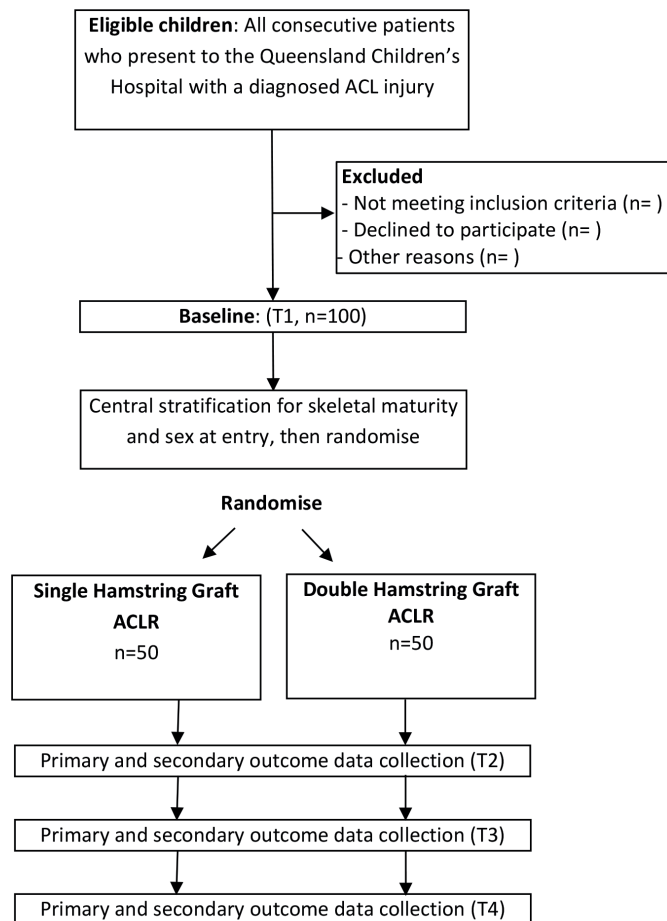


Figure 1 Experimental design flowchart according to the Consolidated Standards Of Reporting Trials (CONSORT) statement guidelines. ACL, anterior cruciate ligament; ACLR, ACL reconstruction.

5. Evidence of early knee osteoarthritis on MRI.
6. Previous knee surgery on the affected side.
7. Chronic musculoskeletal conditions.
8. BMI > 35.
9. Surgeon recommendation for an extraphyseal technique for ACLR.

Study procedure

Potential participants will first be screened against the inclusion criteria in the orthopaedic outpatient clinic at the QCH. Following baseline testing (T1 MRI), eligible participants will be randomised into one of the two surgical groups. The surgeons performing the surgeries will be well versed in both ACLR techniques and will be advised of the patient's randomised surgical technique just prior to the surgery and will proceed accordingly.

Patient and public involvement

Patients were not involved

- ▶ In the development of the research question.
- ▶ In the decision of the outcome measures.
- ▶ In the study design.
- ▶ In the recruitment to and conduct of the study.
- ▶ In how the results will be disseminated.

- ▶ In patient burden assessment.

Surgical techniques

Two senior surgeons will perform all the randomised ACLR surgeries as detailed below. Both have been allowed a surgical learning curve of 20 cases (minimum) before the start of the trial. So that there is no variability among equipment used, Smith & Nephew (S&N) will be used for the two techniques: single hamstring graft technique will use UltraButton+round ExtendoButton; double hamstring graft technique will use Endobutton+Biosure Regenesorb screw.^{35 36} Patients who exhibit a pivot-shift of grade 2 or greater following ACLR will be considered for an additional lateral-tenodesis.³⁷

Tendon harvest and graft preparation

The semitendinosus hamstring tendon alone will be harvested for the single graft technique and the semitendinosus +gracilis hamstring tendons will be harvested for the double graft technique. A tendon stripper will be used to release the tendons from their proximal attachment via a standard push technique to an appropriate length.

Graft preparation for the single hamstring technique will involve tripling the single semitendinosus tendon over two S&N UltraButton loops (with a round ExtendoButton being attached to the tibial UltraButton). Graft preparation for the double hamstring technique will involve doubling the semitendinosus+gracilis tendons over one S&N Endobutton loop. For both methods, the ends of the tendon complex are sutured via a whip-stitch technique using a #1 Ethibond suture on a J-needle. The prepared tendon complex will be set aside and soaked in a Vancomycin laden Raytec sponge and placed into the soft tissue tunnel where the hamstring tendons were harvested.

Once prepared, the graft is measured for both length (to ensure that the graft will adequately span the knee joint and sufficiently pass through both tunnels) and diameter (to determine the required femoral and tibial tunnel diameters for reaming).

Knee arthroscopy

The knee arthroscopy is performed using standard lateral and medial portal sites. All compartments of the knee are identified and examined for any additional pathology (chondral injuries, meniscal tears, etc), the notch is identified, and femoral and tibial attachments are identified. The pathological ACL is identified, and its stump or scarred remnant is debrided sufficiently. As much of the tibial stump/footprint is left to allow for optimal tibial tunnel placement and to aid in revascularisation of the graft,^{38 39} however, enough is debrided away, so that it does not interfere with passing of the graft or cause impingement. The lateral wall of the notch is cleared with either a shaver or via radiofrequency ablation and prepped with a curette. The fat pad is debrided to allow for adequate visualisation. If any meniscal pathology is identified, it is addressed prior to the ACLR.

Tunnel drilling

The femoral tunnel is drilled first. Once the notch has been cleared, the optimal position is determined—this is usually 30° lateral from the roof of the notch (11 o'clock in the right knee, 1 o'clock in the left knee) at the point 5 mm anterior to the posterior cortex of the notch.³⁶ The patient's knee is positioned into full flexion (normally 120°) to allow for adequate placement of the guide pin at the desired position. The pin is drilled through the femur and pushed through the soft tissues and skin of the anterolateral thigh. The desired position is achieved using an Acuflex offset drill guide and is reviewed on scope. In skeletally mature patients, the pin should be directed approximately 30° anteriorly and 30° laterally, with respect to the femoral long axis, however, in the younger patient with open physes the pin is directed as vertical as possible to ensure that the physis and subsequent growth is disrupted as little as possible.⁴⁰ With the knee still in full flexion, the femoral tunnel is drilled first with a 4.5 mm drill through the lateral femoral cortex, this tunnel is measured to determine tunnel length, then the preliminary tunnel is reamed to desired diameter as determined by graft measurement.

The tibial tunnel is positioned using an S&N ACUFEXTM drill guide. The tip of the guide is passed through the anteromedial portal and positioned to create a tunnel that enters the joint through the posteromedial portion of the ACL footprint.^{13 41} In the skeletally immature patient, the length and angle of the tunnel may be more variable as the surgeon will target the drill tunnel perpendicular to the growth plate to minimise the likelihood of growth disturbance. A 2.4 mm drill-tipped guide wire is used to establish the line of the tibial tunnel using the jig. Using the positioned guidewire, this tunnel is reamed to desired diameter as determined by graft measurement earlier. The tunnel is again measured.

Both femoral and tibial tunnels are smoothed cleared of any debris using a shaver to allow for smooth graft passage in the subsequent steps. The graft is marked at either end using a sterile marking pen factoring in tunnel lengths and desired graft length spanning the knee joint. A nylon suture is threaded into the slot of a passing pin. The loop end of the suture is held externally, the passing pin is drawn into the joint and out through the femur, drawing the free ends of the suture out through the lateral thigh.^{35 36}

Single tendon, single bundle, graft passing and fixation

The nylon suture is pulled through the tibial tunnel, so that the loop end is exiting out of the tibial tunnel. The graft is orientated and the Ethibond sutures are placed through the nylon loop. The Ethibond sutures are passed through the tibial and femoral tunnels and out of the skin of the anterolateral thigh. The arthroscope is placed into the knee joint and the Ultrabutton loop and graft are pulled into the femoral tunnel under vision to the line drawn on the graft from previous measurements. The Ultrabutton is toggled and flipped on the femoral

side. The graft is held taut and the Femoral UltraLoop is reduced pulling the graft into the femoral tunnel to its desired length (~20 mm). The knee is then brought out to 30–40° flexion, and the tibial UltraLoop is reduced to pull the graft into the tibial tunnel. Final tensioning of the graft is done with knee extended to 0° flexion the ExtendoButton is secured down to the tibia.³⁵

Double tendon, single bundle, graft passing and fixation

As above, however, in this case, an Endobutton loop is used as opposed to the Ultrabutton loop. The graft is held taut with the Ethibond suture tails on the tibial side of the graft and, the knee is cycled through flexion/extension a number of times and the knee is then brought out to 20–30° flexion, the assistant is asked to secure the foot as well as place anterior directed force the distal femur. A wire is inserted behind the graft in the tibial tunnel and a Biosure Regenesorb screw is fully advanced and secured to fix the graft into the tibial tunnel.³⁶

Postoperative care and rehabilitation

The knee is placed in a Richard splint in full extension. In-patient (oral analgesia with option for intramuscular opioid injection) and discharge medication (oral analgesia only) doses as per individual patient requirements. The patient is seen by the physiotherapist day 1 postoperatively for assessment and treatment as per the Children's Health Queensland ACL Post-operative Rehabilitation Guidelines (online supplemental file 1).

In cases where meniscal repair was concomitantly performed weight-bearing and range of motion (ROM) restrictions are surgeon dependent based on extent and location of repair, but the majority will be non-weight bearing and have ROM restricted for 6 weeks postoperatively. These patients will all be discharged in an ROM brace with increasing ROM allowed over the 6-week period as per surgeon advice. Following 6 weeks, the brace is removed and patients can complete ROM and full weight bearing.

All patients will undergo rehabilitation as per the Children's Health Queensland ACL Reconstruction Rehabilitation Guidelines for Physiotherapists will be advised to completely abstain from full return to sports for at least 12 months and prior to return, they will be required to meet phase 5 criteria of the Rehabilitation Protocol (online supplemental file 1).

Standard medical imaging protocol

All patients enrolled into the randomised controlled trial obtain the following standardised imaging in accordance with current clinical practices at the QCH.

Preoperative medical imaging:

- ▶ Plain X-rays of the affected knee, in both coronal and sagittal projections
- ▶ Bilateral anterior–posterior lower limb weight-bearing X-rays to assess leg length and coronal plane alignment (ie, mechanical axis deviation, lateral distal femoral angle, medial proximal tibial angle).

- ▶ Wrist or elbow anterior–posterior and lateral X-rays for assessment of patient’s bone age.
- ▶ MRI to assess chondral status, menisci status, ACL or graft morphology, growth plate status.
- Day 1 postoperative medical imaging:
 - ▶ Plain X-rays of the affected knee, in both coronal and sagittal projections
 - 1, 2 and 5-year postoperative medical imaging:
 - ▶ Plain X-rays of the affected knee, in both coronal and sagittal projections
 - ▶ Bilateral anterior–posterior lower limb weight-bearing X-rays to assess leg length and coronal plane alignment (ie, mechanical axis deviation, lateral distal femoral angle, medial proximal tibial angle).
 - ▶ MRI to assess chondral status, menisci status, ACL or graft morphology, growth plate disturbance, position of tunnels and hardware.

Study outcome measures

Primary outcomes

1. Passive anterior–posterior knee laxity: side-to-side difference in anterior tibial translation will be measured by a GNRB device attached to the patient’s leg, measuring tibiofemoral displacement by performing an automated Lachman test and obtaining a force–displacement curve.^{42 43} Three measurements will be made on each knee, and the final value will be recorded as per the GNRB guidelines. Anterior–posterior tibiofemoral laxity will be categorised as a ‘low’ side-to-side difference (<3mm), a ‘moderate’ side-to-side difference (3 to 5mm) or a ‘severe’ side-to-side difference (>5mm or ruptured). The manual Lachman test and the pivot-shift test will also be graded according to International Knee Documentation Committee guidelines.⁴⁴
2. Graft failure incidence: the incidence of graft failures will be quantified at T2, T3 and T4. Failure in this study will be defined by a side-to-side difference in anterior–posterior knee laxity >6mm or a pivot shift ≥grade 2.
3. Muscle-tendon morphology and quality: in addition to the standardised imaging protocol for ACL patients at the QCH, additional medical imaging protocols will be performed at T1, T2, T3 and T4 to assess musculotendon volume, CSA and length of quadriceps and donor muscles in accordance with.^{33 33}
4. Graft morphology: a paediatric-trained radiologist consultant will be reviewing and reporting on the T2, T3 and T4 MRI scans. The three-dimensional graft structures will be segmented in Mimics Research 20.0 (Materialise, Belgium) from each participant’s MRI scan. Graft structure and morphology will be assessed for CSA and integrity, both within the tunnels and spanning the knee joint.⁴⁶
5. Patient-reported outcome measures: patient-reported outcome measures will be collected at T1, T2, T3 and T4 and will include the Pedi-IKDC (paediatric international knee document committee),⁴⁷ HSS Pedi-FABS (hospital for special surgery paediatric functional activity brief scale)⁴⁸ and Paediatric KOOS (knee injury and osteoarthritis outcome score).⁴⁹
6. Physical/functional outcome measures will be collected at T2, T3 and T4 and will include: (1) Y-balance test, (2) forward step-down test, (3) double jump for distance, (4) vertical jump for height, (5) single hop for distance, (6) cross-over hop for distance.
7. Postoperative pain: the patient/family will be required to complete pain diaries and record medication usage for the first 2 weeks after the surgery.

Secondary outcomes

1. Growth disturbance incidence and type: in accordance with the previous assessments of growth disturbances, following ACLR, measurements will be recorded at T2, T3 and T4, and limb length will be assessed. A limb length discrepancy or angular malformation will be classified as a difference of 1 cm and/or 3° between the operated and non-operated limbs, respectively.^{9 45}
2. Knee joint ROM: the flexion or extension deficit will be calculated at T1, T2, T3 and T4 by subtracting the respective degrees of the operative knee from those of the contralateral knee.
3. Isokinetic strength evaluation: an isokinetic dynamometer (Humac NORM, Massachusetts) will be used to evaluate knee flexion/extension concentric strength as well as internal/external tibial rotation concentric strength on both the surgical and contralateral lower limbs. For knee flexion strength measurements, participants will be seated with their pelvis, chest and thigh

stabilised using Velcro straps, their hip flexion angle set at 90 degrees and their ankle flail and held in place above the medial malleoli to the Humac NORM shank with a Velcro strap. At T1, flexion/extension isokinetic concentric strength tests will be performed at an angular velocity of 60 deg/s through the patient’s available knee flexion ROM and isometrically at standardised angles within the patient available knee flexion ROM. At T2, T3 and T4, repeat T1 knee flexion/extension assessment at 60 and 180°/s and additionally perform knee internal/external rotation isokinetic concentric strength tests at 60 and 180°/s, across an ROM between each participant’s maximum comfortable internal/external rotation limits. Testing will be performed on both the non-operative and operative limbs, with the order of limb tested randomised to negate any fatigue effects. In addition to individual peak strength measurements, agonist/antagonist strength ratios will be calculated using the peak strengths for flexion/extension and internal/external tibial rotation.

4. Muscle-tendon morphology and quality: in addition to the standardised imaging protocol for ACL patients at the QCH, additional medical imaging protocols will be performed at T1, T2, T3 and T4 to assess musculotendon volume, CSA and length of quadriceps and donor muscles in accordance with.^{33 33}
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7. Physical/functional outcome measures will be collected at T2, T3 and T4 and will include: (1) Y-balance test, (2) forward step-down test, (3) double jump for distance, (4) vertical jump for height, (5) single hop for distance, (6) cross-over hop for distance.
8. Postoperative pain: the patient/family will be required to complete pain diaries and record medication usage for the first 2 weeks after the surgery.

Sample size determination

Our sample size calculations are based on a three-level outcome variable comparing anterior-posterior tibiofemoral laxity in the reconstructed and unaffected knee (‘low’ side-to-side difference (<3mm), ‘moderate’ side-to-side difference (3 to 5mm) or ‘severe’ side-to-side difference (>5mm or ruptured) as differences of this magnitude were considered to be clinically important.^{44 50} Pilot data

from our hospitals' perspective ACL injury registry classified 74% as low, 7% as moderate and 19% as severe or rupture, and we assume that these percentages will hold in our single hamstring tendon graft ACLR group. We expect that in the experimental arm, the equivalent probabilities will be 93%, 2% and 5%. This is equivalent to specifying a proportional OR of 0.07. With $\alpha=0.05$ and power=80%, we are required to record outcome data on 43 participants in each group to detect a between-group difference of this size or greater. To increase the power of the study and allow the maximal tolerated level of dropout at T2, 100 patients will be randomised.

Randomisation

Participants will be randomly allocated by the Griffith University randomisation service to the single hamstring tendon graft ACLR group or the double hamstring tendon graft ACLR intervention group. Participants will be stratified according to skeletal maturity and sex to minimise confounding bias and a randomly varied block size will be used to ensure participants are more evenly allocated throughout the entire trial. The Griffith University randomisation service will conceal group allocation from the study investigators until the participant has been enrolled and baseline data have been collected.

Blinding

To minimise ascertainment-bias, this trial is single-blinded, where patients are blinded to surgical technique. External entry points for surgery are equivalent for both surgical techniques and, therefore, patients will not be able to guess group allocation. Due to the nature of the intervention, the treating surgeons cannot be blinded to group allocation. Furthermore, it is not feasible to blind the postoperative management team as surgical notes will be reviewed prior to follow-up appointments.

Data management

The percentage of eligible participants successfully recruited, and numbers of eligible who choose not to participate will be recorded along with their age and sex. Participant retention will be recorded throughout the trial period. Paper documents and files will be deidentified, labelled with a participant identification code and stored in a locked filing cabinet. Consent forms and demographic information will be kept separately, also in a locked filing cabinet. The list of patient identification codes and all other electronic data will be stored securely through a Research Electronic Data Capture database (<https://www.project-redcap.org/software/>) on a secured network accessible only to the registered members of study team.

Statistical analysis plan

Standard principles for RCTs will be followed, and primary analyses will be conducted using between-group comparisons on all participants on an intention-to-treat basis. There is a small risk that the surgeon may deem a harvested hamstring tendon inadequate for a single

tendon graft (see safety consideration below) and, therefore, need to break randomisation. To account for this potential, a secondary, per-protocol analysis will be used to assess the effect of treatment received and models will be adjusted for potentially confounding variables if necessary. The primary timepoint will be after 1 year, and the primary comparison will be the quantitative anterior-posterior laxity results between the two surgical techniques. Effect of surgical technique will be assessed using ordinal logistic regression with technique (single/double) included as the main effect. To determine between-group differences at 2 and 5 years postsurgery, we will employ mixed effects ordinal logistic regression models with patient included as a random effect, and time (1, 2 and 5 years) and surgical technique included as main effects and a time-by-technique interaction included as fixed effects. For continuous outcomes, comparison will be by linear regression models. Where continuous data do not meet linearity assumptions, as assessed by inspection of boxplots and the Shapiro-Wilk test, it will be assessed using non-parametric methods such as median regression. For dichotomous outcomes, comparison will be by logistic regression models. For count outcomes, comparison will be by Poisson regression models. Significance will be accepted at $p<0.05$. Sensitivity analyses to assess the effect of missing data will be undertaken on an outcome-by-outcome basis using MAR (multiple imputation) or NMAR (using pattern-mixture models) according to the pattern of the missing data.

Cost-utility analysis

Utility values will be obtained from the EQ-50 (with a 1-week recall) at baseline (T1), and 1-year, 2-year and 5-year postsurgery and will be transformed into Quality of life-adjusted years with means and variances. The health economic evaluation will be determined using the incremental cost-utility ratio. Resource utilisation will be determined from hospital finance reports related to the initial stay in hospital and using a patient (or parent) administered case report form that documents information on patient and caregiver demographics, educational and employment information, used of health resources (ie, visits to general practitioners, physiotherapists, emergency department, patient expenses related to medication and out-of-pocket transportation costs to receive additional medical care, patient or caregiver days off work) using a health resource utilisation questionnaire. Furthermore, the following health service utilisation data will be collected:

- ▶ Details of hospital admissions, outpatient episodes and emergency department presentations including episode, clinical, demographic and costing information (such as diagnosis, procedures, length of stay, cost of encounter, etc) for the duration of the study and 12 months prior to consenting—from routinely collected hospital and emergency department administrative data.

- ▶ Medicare Benefits Schedule claim details, costs and service provider information and Pharmaceutical Benefits Scheme item description, costs and prescribing details—from Services Australia.

Safety, adverse events and complications

Surgical treatment and clinical follow-up will be conducted in accordance with current clinical practices for the participating surgeons at the QCH. Intraoperatively, if a harvested hamstring tendon is deemed to be inadequate (ie, <6 mm in diameter and/or of poor quality) the decision may need to be made to convert from the single to the double hamstring graft technique. Presence of meniscus injuries, defined by the necessity to repair or partially resect tissue due to meniscus instability, will be determined during ACLR. Any adverse events occurring during preoperative and follow-up testing sessions will be recorded on an Excel spreadsheet. Minor adverse events are classified as muscle soreness, muscular fatigue or mild injuries that do not require medical attention. Major adverse events are conditions that require medical attention, such as a fracture, equipment failure or infection and would likely result in the child discontinuing the testing session. All adverse events, regardless of their severity, will be documented and reported to a senior study advisor and if serious, escalated to the ethics committee with information reported to the child's treating physician as necessary. Risk assessments, including strategies to minimise adverse events, will be completed prior to participation in the testing session. For all onsite testing, participants will be directly supervised by an investigator who is trained to deliver first aid and CPR. Postoperative complications (ie, thrombosis, infection, rupture) will be recorded. A data monitoring committee will convene every 6 months to monitor patient safety and treatment efficacy during the surgical stage of the trial. The DSMB membership comprising a Chair, Medical Monitor and Secretary, will be independent to the trial and will not participate as investigators of the trial or have any financial, scientific or other conflict of interest with the trial.

Ethics and dissemination

Full ethical approval for this study has been obtained by the Children's Health Queensland Human Research Ethics committee (HREC/21/QCHQ/73043, Protocol V.2.1 29072021). The study will be conducted in agreement with the Helsinki declaration. Written and informed parent/guardian consent will be obtained prior to study enrolment by the study investigator. Verbal assent will be obtained from children under the age of 12 years and written assent will be obtained from children who are 12 years and older. This trial is registered with the Australian New Zealand Clinical Trials Registry and the study protocol is reported according to the Standard Protocol Items: Recommendations for Intervention Trials statement⁵¹ (see Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist online supplemental file 2). Changes to the study protocol will

be communicated to the ethics committee and updated on the trial registry. The primary study results will be submitted for publication to an international, peer-reviewed journal and disseminated to participants and healthcare professionals via newsletters and conference presentations.

DISCUSSION

This study protocol describes a prospective randomised controlled trial design to determine whether a single or double hamstring tendon graft ACLR leads to superior clinical outcomes at 1, 2 and 5-year postsurgery in skeletally immature patients with ACL injury. The International Olympic Committee (IOC) has advocated for further research with regards to efficacy of graft choice and different surgical reconstruction techniques.¹³ We aim to add to the current knowledge putting to test these two reconstruction techniques with long-term clinical follow-up and imaging. To our knowledge, this will be the first RCT study to investigate two different randomised ACLR techniques in the skeletally immature patient with standardised rehabilitation protocols, clinical follow-up and postoperative imaging to track the patient's progress and assess graft and intra-articular integrity.

The surgical procedures have been selected based on commonly used reconstruction techniques using hamstring autograft for the skeletally immature patient. The difficulty is that within the literature or among surgeons that there is no true consensus for which has better long-term results with regard to both graft longevity and patient recovery postoperatively.⁴⁰ The literature supports other graft choices in adults such as quadriceps tendon or patella tendon;^{52 53} however, the paediatric literature remains scarce. At present, hamstring autograft is the most common technique used to reconstruct the ACL in the skeletally immature patient. As with all injuries, options exist for both operative and non-operative treatment of ACL injuries in the paediatric population; however, the literature supports early reconstruction to avoid the potential consequences of arthritis and consequent chondral and meniscal pathology.¹³

Primary outcome measures will include graft failure and graft laxity. Secondary outcome measures will investigate growth disturbance rates, passive and dynamic knee joint function (range, strength), lower limb function (power, agility, stability), muscle and ligament morphology and patient-reported outcomes at 1, 2 and 5-year postsurgery. Children with open or closed physes and children of differing sex are likely to respond differently to the intervention. For this reason, we will stratify randomisation enable equal distributions across intervention groups. Children with meniscal tears at baseline may be managed differently, and, for this reason, results may also be stratified on this basis.

A limitation of this study is that our follow-up at present is set for 5 years postoperatively—the IOC has suggested that follow-up goes as long as 10 years so that long-term

knee-health and quality of life can be captured.¹³ A second limitation is that we are comparing surgical techniques and using only one type of autograft; it could be beneficial, given the acceptance of alternative graft choices in adults, to compare different graft choices in the paediatric population.

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