

Contents lists available at [ScienceDirect](#)

Asia-Pacific Journal of Sports Medicine, Arthroscopy, Rehabilitation and Technology

journal homepage: www.ap-smart.com

Original Article

Regression modelling combining MRI measurements and patient anthropometry for patient screening and prediction of graft diameter in hamstring autograft arthroscopic ACL reconstruction



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ARTICLE INFO

Article history:

Received 27 November 2016

Received in revised form

5 February 2017

Accepted 9 February 2017

Available online 27 February 2017

ABSTRACT

Background: Previous studies have associated anthropometric data and pre-operative hamstring tendon measurements to intraoperative graft diameter for hamstring autograft ACL reconstruction, although an integrated model has yet to be described. The aim of this study was to present such a predictive model for quadrupled semitendinosus (4-ST) and doubled semitendinosus-gracilis (4-STG) graft constructs combining anthropometry (height and weight) and preoperative measurements of tendon as predictors. **Methods:** ACL reconstructions using 4-STG and 4-ST were retrospectively reviewed. The outlines of the semitendinosus and gracilis tendons were identified manually in the axial slice of a preoperative T2 weighted MRI using a region-of-interest tool. Regression analysis using intraoperative graft diameter as the dependent variable was performed with tendon cross-sectional area (XSA), gender and height as predictors.

Results: 108 ACL reconstructions in 107 patients were examined, 75 of which were performed using the 4-STG construct, and 33 which employed the 4-ST construct. The mean graft diameter in the 4-ST group (8.6 ± 0.8 mm) was significantly ($p < 0.001$) greater than the 4-STG group (7.9 ± 0.7 mm). Female gender and 4-STG graft construct were associated with increased risk of graft diameter < 8 mm. Predictive models of graft diameter were accurate to ± 1 mm for both construct types.

Conclusions: An integrated method for assessing patient risk of producing a diminutive graft diameter and planning augmentation in select cases has been presented. The present findings describe a validated predictive model that builds on previous univariable analyses. Further investigation of larger samples, including factors associated with graft preparation, is required to improve model accuracy for routine clinical application.

Level of evidence: IV, Retrospective Cohort Study

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1. Introduction

Patient outcomes following anterior cruciate ligament reconstruction (ACLR) are driven by non-modifiable factors (age and gender), as well as surgeon-controlled factors. Of particular interest is graft selection and preparation in relation to the final diameter of the implanted graft, with some studies suggesting that a graft diameter exceeding 8mm is associated with reduced risk of re-rupture.^{1,2} Although hamstring autografts hold advantages over

bone-patella tendon grafts with respect to extensor mechanism preservation³ and reduced patellofemoral pain,^{3,4} a key limitation of standard graft preparation (quadrupled 4-strand semitendinosus/gracilis) techniques is an inability to control graft diameter. For this reason, techniques that enable consistent achievement of desired graft diameter warrant further investigation.

The conventional, four-stranded semitendinosus/gracilis (4-STG) technique for hamstring autograft preparation is limited by the need to remove both the semitendinosus and gracilis tendons to create grafts of sufficient dimensions. Harvesting both tendons has a negative effect on knee function, such as reduced knee flexion strength^{5,6} and it remains unclear whether two tendons are required to consistently achieve adequate graft diameter.⁷ An

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accurate model to predict graft diameter preoperatively could be useful to determine whether a single hamstring tendon is adequate, or if augmentation with a second tendon is required, increasing intraoperative efficiency and reducing the incidence of unnecessary tendon harvesting.^{8,9} Such a model could also ensure that the surgical plan produces a graft diameter in line with the surgeon's preferences on a case-by-case basis.

Patient anthropometry (e.g. height and weight)^{10,11} and magnetic resonance imaging (MRI) measurements of tendon size (e.g. tendon cross-sectional area)^{9,12} are significantly ($P < 0.05$) positively correlated with the graft diameter measured intraoperatively. It has been concluded, perhaps prematurely, that this correlation is equivalent to the prediction of graft diameter.¹³ While related, correlation and prediction are not interchangeable and more investigation is required to develop a valid, clinically applicable prediction tool in this context. In addition, previous studies relied on univariate analysis to examine the contribution of each predictor to graft diameter, without considering the confounding or interaction effects of anthropometry and tendon properties with respect to graft diameter. In addition, previous efforts have considered a single technique of hamstring autograft preparation (4-STG) and have not compared different constructs with respect to graft diameter. Early clinical experience suggests that an alternative graft preparation technique, such as a four-stranded semitendinosus (4-ST) using the Graftlink construct (Arthrex®, Naples, Florida) may achieve larger and more predictable graft diameters through a more consistent graft shape. To-date, the literature lacks any comparison between preparation techniques. Therefore, this study aimed to present a predictive model of intraoperative graft diameter in the quadrupled semitendinosus (4-ST) and doubled semitendinosus-gracilis (4-STG) constructs using anthropometry and MRI measurements as predictors.

2. Materials & methods

The records of patients undergoing ACLR between April 2009 and June 2015 were retrieved from a clinical research database (Socrates v3.5, Ortholink, Aus). These patients underwent primary ACL reconstructions performed in one of two private hospitals by one of three fellowship-trained surgeons, each of whom employed similar graft preparation and measurement techniques. Only patients who received hamstring (semitendinosus with/without gracilis) autografts using either the 4-STG, or 4-ST technique and who had complete anthropometry, MRI and intraoperative graft diameter data were included. Ethics approval for this data collection was granted by the North Sydney local health district (reference number: AU/1/9AAB014), and patient informed consent collected as part of routine clinical follow-up. A total of 108 knees in 107 patients were retrieved who satisfied the above criteria.

2.1. Graft preparation (4-STG)

Semitendinosus and gracilis grafts were harvested by the three surgeons using a similar technique. An oblique linear incision 3 cm in length, 4cm below the joint line was made. The dissection was carried down to the sartorius fascia. Two surgeons incised the sartorius fascia slightly superior to the pes tibial insertion. The tendons were identified and an open stripper was applied to the semitendinosus followed by the gracilis. Surgeon 1 preserved the vinculae and included them in the stripper whereas Surgeon 2 cut the vinculae. Surgeon 3 detached the entire pes tibial insertion then harvested the semitendinosus followed by the gracilis. Any muscle and fatty tissue remnants attached to the tendon were removed by the stripper. With the tendons fixed in tension and held at the ends, the ST and GT were whipstitched with a no 2 ethibond (©Ethicon

US, LLC. 2010–2015.DSL312-9000) suture at both ends. Starting from one side of each end, five throws were taken on each side of the tendon, totalling 10 throws at each end of both tendons. The ends of the ethibond suture were cut to at least 10 cm in length. One end of the ST was passed into the button loop and the length of each arm was adjusted till they were equal. The GT was passed through the loop in the same way to lie just above the ST in a collinear fashion and both ends equalised.

2.2. Graft preparation (4-ST)

The ST was harvested in the same fashion as described above. Muscle and fatty tissue remnants attached to the tendon were removed and the tendon cut to 280 mm. The 4-ST construct was prepared as previously described¹⁴ with some modifications. The graft preparation board posts were loaded with clamps for both the Tightrope (Arthrex, USA) adjustable suspensory fixation at the femoral end, and the Tightrope adjustable suspensory loop of the tibia at the other end with an Attachable Button System (Arthrex, USA). The semitendinosus was passed through the loop of the side without the button such that two arms of equal length were formed and held together with an allis forceps. A No. 2 FiberLoop (Arthrex, USA) was then used to whipstitch both ends with a minimum of five throws. The distance between the two ends of the holders on the graft board were then adjusted to obtain a quadrupled graft length of 70 mm. The needle at the end of the fibre loop was removed and the free ends were passed through the loop with the button and one end passed between the two arms of the graft to dock between the ends at the tibial end. The ends were wound around the holder and the quadrupled graft encircled at 20mm from the femoral and tibial end with 1-0 fibre wire.

2.3. Graft diameter

The dependent variable was final graft diameter (mm) sized for both preparation techniques with a sizing tray graduated in 0.5 mm increments. The final diameter was defined as the smallest diameter through which the graft passed from end to end.

2.4. Pre-operative MRI

Patients underwent a pre-operative MRI as part of the standard clinical workup, which was not controlled specifically for this analysis and patients attended the most convenient radiology practice to undergo scanning. The knee was imaged in full extension with the patient supine and a knee coil applied. Each imaging study was retrieved from the respective practice PACS using Inteleviewer (v4, Intelrad, Liverpool, UK) and the axial sequence (Table 1) selected for analysis. Scans were viewed from proximal to distal, and the widest trans-epicondylar slice was identified visually and confirmed with measurement using the linear distance tool. The selected slice was then magnified (4X) and the tendinous portion outlined manually using the region-of-interest tool which automatically calculated the

Table 1
Imaging details for pre-operative MR measurements.

Scanner	Signa HDc (GE Medical Systems) Avanto (Siemens) Intera/Achieva (Phillips Medical Systems)
Magnet strength (Tesla)	1.5–3
Plane	Axial
Sequences	Proton density (with/without fat saturation) T2 fat-saturated
TR (ms)	1700–5200
TE (ms)	15–66.6

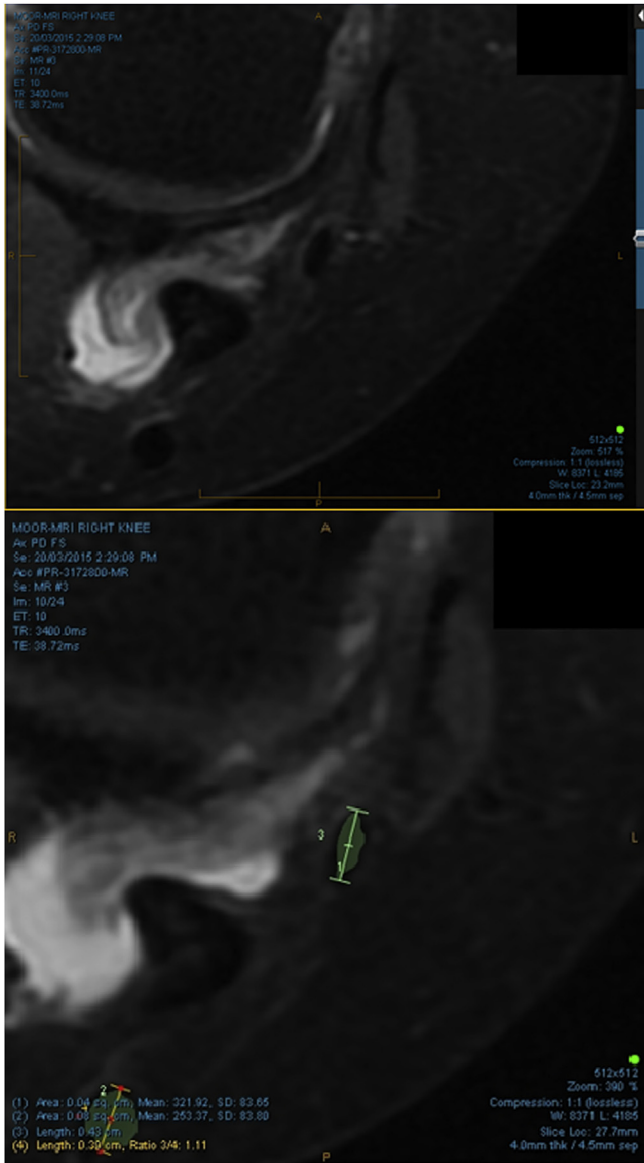


Fig. 1. Measurements performed on the digital MR images using IntelViewer system, before (top) and after (bottom) the region-of-Interest and diameter measurement tools were applied manually to the tendon regions of the image.

cross-sectional-area (cm²) (Fig. 1). The diameter of the tendon was also measured using the linear distance tool (Fig. 1). These procedures were repeated at the same magnification for the slices immediately superior and inferior to the selected slice. Measurements were primarily performed by an orthopaedic fellow. To measure intra-observer reliability, a subset of scans (n = 20) were measured twice, one week apart by the primary observer. A secondary observer also performed measurements on these scans to determine inter-observer reliability (see Table 4).

2.5. Statistical analysis

The median cross sectional areas (XSA) and diameters of the ST and GT measured on the three MR slices was calculated for each patient used as the variables for subsequent analyses. Intra- and inter-observer reliability of the MRI measurements of tendon size were assessed with the standard deviation of differences between measurements (typical error) and intraclass correlations.^{15,16} Continuous variables (patient height, ST XSA and diameter, GT XSA and graft diameter) were assessed for normality with Ryan-Joiner normality tests and summarised by mean and standard deviation. Comparisons were made between graft preparation techniques (4STG vs 4ST) using Student t-tests, while categorical variables (gender and side) were compared using Fisher's exact tests. Pearson's product moment correlations were performed between each continuous predictor (height, ST XSA, sum ST/GT XSA) and graft diameter. A series of ordinal logistic regression models were established using all data, as well as sub-group models of those receiving 4STG grafts and 4ST grafts, with graft diameter categorised into an ordinal response variable (>8 mm, 8 mm, <8 mm). Proportion of concordance between group membership and model-predicted probabilities was used to assess model goodness of fit. In addition, partial least squares regression models were constructed with graft diameter (continuous variable) measured intraoperatively as the response variable. Partial least squares regression (PLSR) using the nonlinear iterative algorithm (NIPALS) is a technique that reduces the number of predictors into uncorrelated variables (components) to model the response (graft diameter) in a multiple linear regression approach.¹⁷ Models for cohort and subgroups (4-STG and 4-ST) included interactions for the predictor terms (Table 2), with the number of components (maximum = 10) selected based on the model with the lowest prediction sum of squares and highest predicted R². Models were validated using leave-one-out cross validation, with each observation omitted from the sample one at a time and the model recalculated with a predicted value (cross-validated fit. A prediction interval of the cross-validated

Table 2
Regression model (logistic and PLSR) predictors for cohort and subgroup analyses.

	Cohort	4STG	4ST
N	108	75	33
Categorical Predictors	Gender Graft preparation Operating Surgeon	Gender Operating Surgeon	Gender Operating Surgeon
Continuous Predictors	Height Median ST XSA Median ST Diameter Median GT XSA Median GT diameter	Height Median ST XSA Median ST Diameter Median GT XSA Median GT diameter	Height Median ST XSA Median ST Diameter
Interaction Terms	Height * Gender Height * Graft Median ST XSA * Gender Median ST XSA * Graft Median ST Diameter * Gender Median ST Diameter * Graft	Gender *	Height * Gender Height * Graft Median ST XSA * Gender Median ST XSA * Graft Median ST Diameter * Gender Median ST Diameter * Graft

Table 3
Comparisons of patient demographics and graft diameter between the 4-STG and 4-ST groups.

	4-STG (X ± SD)	4-ST (X ± SD)	P value
N	75	33	
Age (yrs)	30.7 ± 13.9	28.6 ± 9.5	0.34
Height	172.9 ± 9.6	173.7 ± 8.2	0.66
Sex (male)	58.7%	60.6%	0.85
Side (left)	52.0%	60.6%	0.40
Graft diameter (mm)*	7.9 ± 0.7	8.6 ± 0.8	<0.001

residual for a single future patient was calculated to represent the accuracy of the model in predicting future graft diameters. All statistical analyses were performed in Minitab (v17, Minitab Inc, USA) and alpha set a-priori at 0.05 for all tests.

3. Results

A total of 108 knees in 107 patients were retrieved who satisfied the patient inclusion and exclusion criteria.

3.1. Graft preparation comparison

No significant differences were detected between groups for gender distribution, age, height or side of surgery. Median graft diameter measured intraoperatively was significantly larger in the 4-ST group compared to the 4-STG group (Table 3).

3.2. MRI measurement reliability

MRI measurements for XSA and diameter of both tendons exhibited high intra-observer reliability (Table 4), with high reliability also observed for inter-observer measurements of tendon diameter and moderate agreement for XSA (Table 4).

3.3. Univariable correlations

The sum of ST and gracilis tendons XSA demonstrated statistically significant correlations with graft diameter in both 4-STG ($r = 0.48$) and 4-ST ($r = 0.71$) constructs. A similar relationship was observed between height and graft diameter for 4-STG ($r = 0.45$) and 4-ST ($r = 0.67$) (Fig. 2).

3.4. Ordinal logistic regression

For the entire cohort, female gender and the 4-STG preparation technique were associated with increased odds of receiving grafts <8 mm, while every 1 mm² increase in ST XSA reduced the log odds of receiving a graft <8 mm by 0.39 (87.2% concordance) (Table 5). In the 4-STG subgroup, the model identified female gender with increased odds of grafts <8 mm, while a similar reduction in log odds was apparent for ST XSA (83.7% concordance) (Table 5). In the 4-ST subgroup, the model revealed a 1cm increase in height and a 1 mm² increase in ST XSA reduced the log odds of receiving a graft <8mm by 0.46 and 0.97 respectively (97.6% concordance) (Table 5).

Table 4
Intra and inter-observer reliability of XSA and diameter from MR measurements.

	Intra Typical Error (ICC _{2,1})	Inter Typical Error (ICC _{1,1})
XSA (mm ²)		
GT	1.5 (0.93)	2.5 (0.73)
ST	1.4 (0.95)	3.8 (0.59)
Diameter (mm)		
GT	0.7 (0.95)	0.5 (0.96)
ST	0.4 (0.93)	0.7 (0.73)

3.5. Partial least squares regression and graft diameter prediction

The regression model for all data identified median ST XSA and height as key predictors of graft diameter (Table 6). An interaction between height and graft type was also identified (Fig. 3 – top), which confirmed that graft diameter increased with height, while the 4-ST graft achieved larger diameters regardless of height. The 95% prediction error for the overall model for a single future patient was 0.9 mm (Table 6). That is, predicted graft diameters of 8.92 mm or above would have a 2.5% chance of being <8 mm in theatre. In the sub-group analyses, tendon size and height were identified as key predictors, with similar prediction errors for both 4-STGT and 4-ST subgroups (Table 6). The interaction between ST XSA and gender was also identified in the 4-ST cohort, with higher female graft diameters derived from ST XSA >11mm² compared to males (Fig. 3 - bottom).

4. Discussion

The ability to predict graft diameter prior to surgery can improve surgical efficiency for ligament reconstruction, particularly if a minimum graft diameter is sought. Previous correlational studies have suggested that anthropometry and MRI tendon measurements in isolation are viable tools for predicting intraoperative graft diameter.^{8,9,12,18–20} Our study confirmed the respective correlations between patient anthropometry and tendon size and intraoperative graft diameter, however, the predictive ability of these reported correlations remains yet to be validated and it is logical that an accurate model would incorporate and control for multiple factors. Thus our study aimed to integrate and build on previous work by producing a multivariable, validated predictive model. It should be kept in mind that screening of every patient undergoing ACLR is not possible in most busy clinical practices and may be unnecessary in the majority of cases. Instead, a focused screening process is proposed for patients that may be at-risk of receiving grafts below a threshold associated with increased risk of re-rupture or unsatisfactory outcomes. The results identify females receiving 4-STG constructs at-risk of receiving grafts <8 mm and should be screened with MRI-based measurements of tendon size. Further, patients with a predicted graft diameter of <8.9 mm should be considered for augmentation, either with additional tendon harvest, allograft or other means. It should also be noted that using 8 mm as a cut-off for acceptable graft diameter remains a topic of ongoing debate.^{1,13,21} However, a refined model able to predict graft diameter to sufficient for routine clinical application enables the surgical plan to produce any graft diameter to the surgeon's preference on a case by case basis.

The correlation between graft diameter and MRI measurements was stronger in the 4-ST group, as opposed to the 4-STG group. Whilst it may be expected that the correlation should be stronger in the 4-STG group as the graft is only doubled, as opposed to quadrupled in the 4-ST group (and thus less theoretically prone to tendon diameter variations), the contrary was found. This may be because the gracilis graft has a more flattened shape, which may be less predictable or reliably measurable. It was also found that females generally produced higher graft diameters when median ST XSA >11 mm², although this may be a product of sample size, as only 9 female patients had ST XSA >11 mm². Nevertheless, these findings could be explored further and confirmed via future research with larger sample sizes.

Partial least squares regression (PLSR) was selected as the chosen regression method for a number of reasons. Firstly, PLSR is able to analyse variables which are highly correlated, and ameliorates the issue faced by conventional multiple linear regression, where regression coefficients are difficult to interpret in the case of collinear data.²² Rather than considering the raw predictors to form the

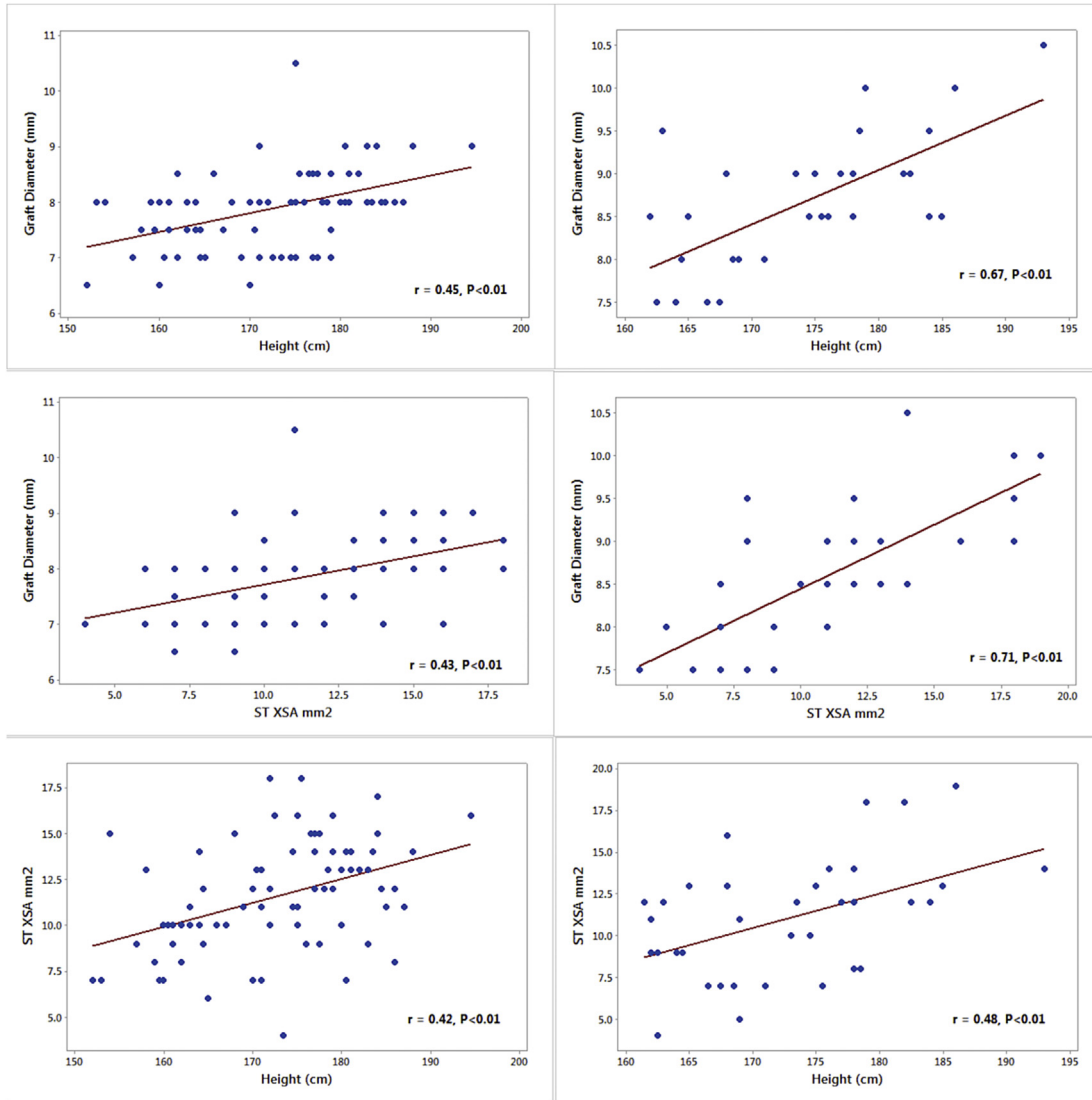


Fig. 2. Scatterplots between height and graft diameter for 4-STG (a) and 4-ST (b), ST XSA versus graft diameter in 4-STG grafts (c) and 4-ST grafts (d) and the interaction scatterplot between ST XSA and height in 4-STG grafts (e) and 4-ST grafts (f).

Table 5
Logistic regression results summary.

	Predictors	β (SE)	OR (95%CI)	P-Value	Goodness of fit Concordance (%) Pearson (P-value)
All	Female	2.2 (0.48)	8.6 (3.4–21.9)	<0.001	85.6 0.48
	4-STG	2.9 (0.59)	18.5 (5.8–59.3)	<0.001	
	Median ST XSA	-0.39 (0.08)	0.67 (0.57–0.79)	<0.001	
4-STG	Female	2.3 (0.53)	10.2 (3.6–28.6)	<0.001	84.2 <0.001
	Median ST XSA	-0.25 (0.10)	0.79 (0.65–0.97)	0.022	
	Median GT XSA	-0.27 (0.13)	0.76 (0.59–0.98)	0.032	
4-ST	Height	-0.46 (0.19)	0.63 (0.44–0.91)	0.013	96.9 1.0
	Median ST XSA	-0.97 (0.37)	0.38 (0.18–0.79)	0.009	

regression equation, PLS combines the predictors into uncorrelated principle components to produce a more accurate representation of the contribution of the predictors to the output variable.²³ The PLS then uses leave-one-out cross validation in order to determine the appropriate number of components to maximise predictive ability. Secondly, PLS has been historically reported as being suitable for limited numbers of observations, which reduces the chance of a study being underpowered. A post-hoc power analysis revealed that

our model was adequately powered (1- β error probability of 1.00). Therefore, we believe that partial least squares is an appropriate statistical approach to modelling intraoperative graft diameter in this setting, given the correlated nature of the candidate predictors as demonstrated in Figs. 2 and 3. However, as the raw predictor variables are amalgamated into components, the model itself does not produce a simple regression formula as would be encountered with ordinary linear regression. Therefore, once the model is further

Table 6
Partial least squares regression results summary.

	Components selected	Key Predictors (standardized β)	Adjusted R^2 (predictors) %	Predicted R^2 (graft diameter) %	Model error 95% lower prediction interval (mm) Single patient
All	5	Median ST XSA (0.41) Height (0.22) Height * Graft (4STGT) (-0.17)	93.8	50.5	0.92
4-STG	2	Median ST XSA (0.16) Median GT XSA (0.15)	70.5	34.4	0.89
4-ST	3	Median ST Diameter (0.10) Height (0.52) Median ST XSA (0.38) Median ST XSA * Gender (Female) (0.16)	82.9	45.8	0.97

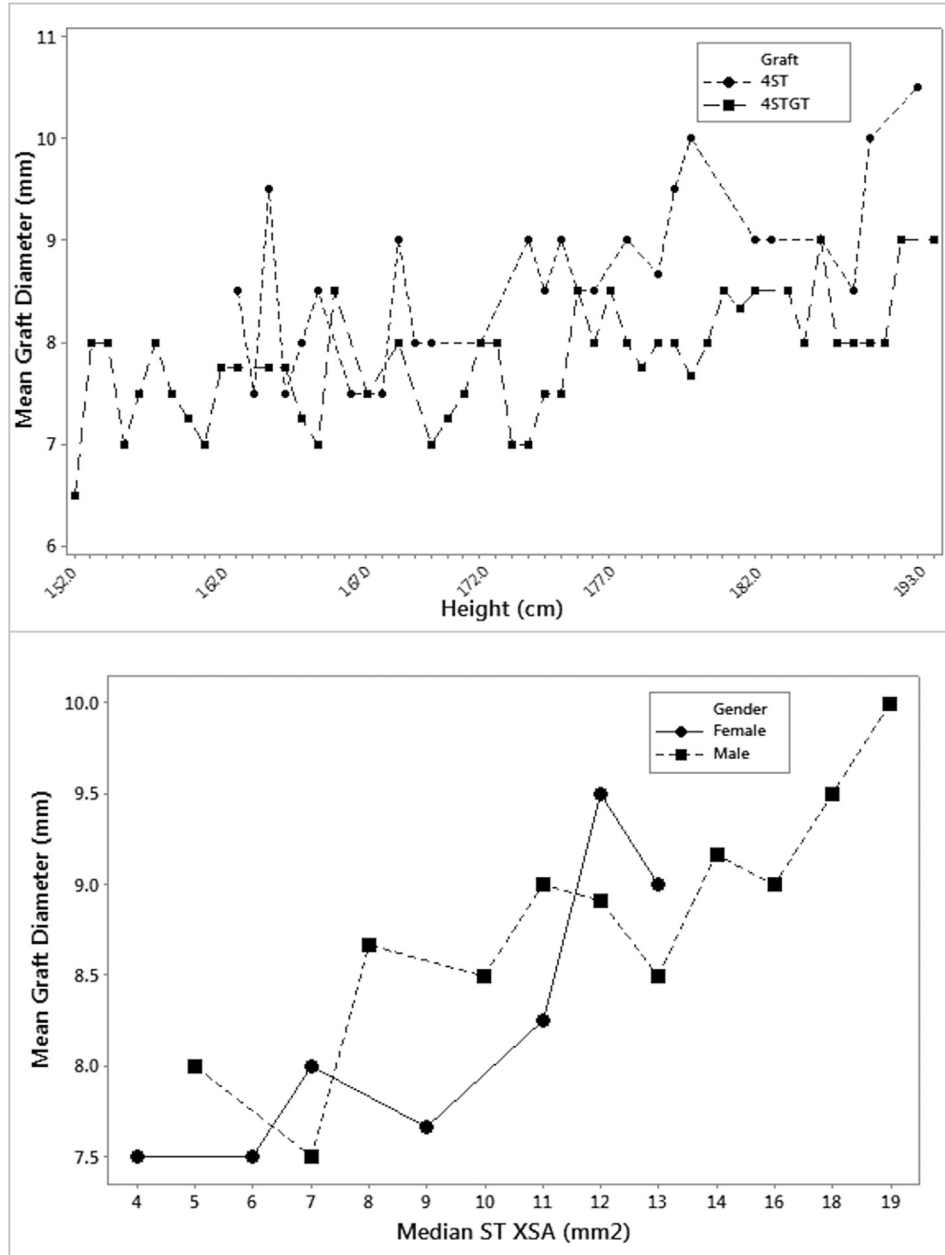


Fig. 3. Significant interaction terms appearing in the regression models for all patients (top) and the 4-ST subgroup (bottom).

refined for clinical application, it could be directly translated onto a working program which could operate in a “black box” manner to predict graft diameter in the clinical setting.

While the present study demonstrates a validated prediction model for graft diameter, the results should be interpreted in light of the limitations of the study. Firstly, the intraoperative measurement

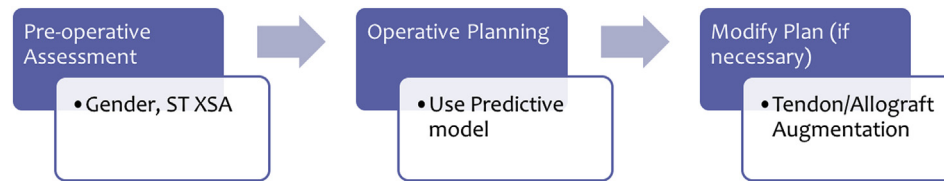


Fig. 4. Proposed clinical pathway to assess patient graft diameter pre-operatively prior to their ACLR.

of graft diameter had a precision of ± 0.5 mm, which exceeded the prediction interval of model. While future studies should attempt to replicate these findings with a more accurate method of graft diameter measurement intraoperatively, the use of the sizing tray remains standard practice in ACLR, and thereby the present analysis mimics the clinical scenario. Secondly, the proposed model did not include other intraoperative and graft-related variables which may have affected its diameter, such as surgeon-applied tension,²⁴ graft compressibility or variations in diameter or geometry along its length. It is possible that these variables differ between preparation techniques, as indicated by the differences detected in the present study. While others are encouraged to explore a more comprehensive model, unless intraoperative factors are standardised within a particular technique, or graft material properties can be predicted, it will be difficult to refine a model adequately for routine use. Lastly, the MR images analysed were not captured in a protocol specific to this study and may have introduced between-patient variability in tendon measurements, with a subsequent impact on model accuracy. However, the sequences are widely used and reflect standard practice for diagnosis of ACL rupture and improve the generalisability of the present results. In addition, the lack of control over the image sequence reflects the clinical scenario where patients will present with images taken from various sites and strengthens the clinical applicability of the findings.

Recently published papers have noted individual variations in patients' native ACL anatomy, such as in terms of the tibial insertion site, which may influence graft size.^{25,26} Therefore patient-specific ACL reconstruction using individualised graft characteristics to reproduce native patient anatomy may pave the way to better functional and structural outcomes.

This study presents an initial iteration of a clinical tool which could stratify patient specific risk of producing diminutive graft diameters based on their anthropometry and MRI tendon measurements and also allow for customisation of graft size according to these characteristics. Females undergoing 4-STG ACLR are at increased risk of producing grafts smaller than 8mm, and therefore may be more prone to graft failure.¹ These at-risk patients should undergo MRI measurements in order to produce a predicted graft diameter. Patients with a predicted graft diameter of less than 8.9 mm are at risk of producing an actual graft of less than 8 mm. In this subset of patients, surgeons who wish to have a graft of at least 8 mm should consider graft augmentation methods, or alternative graft constructs (see Fig 4). However, the diameter may be underestimated by the same amount and an 8.9 mm prediction may provide a graft up to 9.9 mm, which may be inappropriate for smaller patients and increase the risk of impingement at full extension. Once the model is refined with future study, it could be used by surgeons to plan the tendons and surgical steps required to produce the graft diameter they deem appropriate for their patient.

5. Conclusion

Patient anthropometry (height or gender) and MRI cross-sectional measurements were combined in a predictive model of graft diameter relevant to two graft constructs for hamstring

autograft ACL reconstruction. For surgeons wishing to predict the risk of inadequate graft diameter, this paper describes and proposes a novel method of stratifying and assessing patient risk of producing diminutive graft diameter. With further refinement, the proposed model could be used by surgeons to tailor graft diameter to their own preferences in certain patients that may be at risk of a diminutive graft.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

Acknowledgements

The authors wish to acknowledge the funding support of the Sydney Orthopaedic Research Institute to perform this work and to Myles Coolican for access to his patient data.

List of Abbreviations

ACLR	Anterior cruciate ligament reconstruction
4-STG	four-stranded semitendinosus/gracilis (graft construct)
4-ST	four-stranded semitendinosus (graft construct)
MRI	Magnetic resonance imaging
XSA	cross-sectional area
PLSR	Partial least squares regression
NIPALS	non-linear iterative algorithm

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