Association of Graft Maturity on MRI With Return to Sports at 9 Months After Primary Single-Bundle ACL Reconstruction With Autologous Hamstring Graft

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Background: The relationship between graft maturity on magnetic resonance imaging (MRI) and return to sports (RTS) after anterior cruciate ligament (ACL) reconstruction is unclear.

Purpose: To compare signal-to-noise quotient (SNQ) values and ACL graft T2* (gradient echo) values between patients who did RTS and those who did not RTS (NRTS) after ACL reconstruction and to evaluate the predictive value of T2* mapping for RTS after ACL reconstruction.

Study Design: Case-control study; Level of evidence, 3.

Methods: At a minimum of 9 months after arthroscopic single-bundle ACL reconstruction with autologous hamstring tendon graft, 82 patients underwent RTS assessment as well as MRI evaluation. The patients were classified into RTS (n = 53) and NRTS (n = 29) groups based on the results of the assessment. The SNQ values in the proximal, middle, and distal regions of the graft and the T2* values of the graft were measured on MRI. The correlation between T2* values and RTS was assessed using Spearman correlation analysis. Receiver operating characteristic curves were constructed to compare the diagnostic performance, and the optimal T2* cutoff value for detecting RTS was determined based on the maximum Youden index.

Results: At 9 months after ACL reconstruction, the proximal, middle, and mean SNQ values in the RTS group were significantly lower than those in the NRTS group (proximal: 17.15 ± 4.85 vs 19.55 ± 5.05, $P = .038$; middle: 13.45 ± 5.15 vs. 17.75 ± 5.75, $P = .001$; mean: 12.37 ± 2.74 vs 15.07 ± 3.32, $P < .001$). The T2* values were lower in the RTS group (14.92 ± 2.28 vs 17.69 ± 2.48; $P < .001$) and were correlated with RTS ($r = -0.41$; $P = .02$). The area under the curve of T2* was 0.79 (95% CI, 0.75-0.83), and the optimal cutoff value for T2* was 16.65, with a sensitivity and specificity for predicting failure to RTS of 67.9% and 88.2%, respectively.

Conclusion: Study findings indicated that the SNQs (mean, proximal, and middle) and the T2* values of the graft in the RTS group were significantly lower than those in NRTS group. A T2* value of 16.65 was calculated to predict patients who failed RTS tests with a sensitivity of 67.9% and specificity of 88.2%.

Keywords: anterior cruciate ligament reconstruction; return to sports; graft; signal-to-noise quotient; T2*

Arthroscopic anterior cruciate ligament (ACL) reconstruction is one of the most common treatments for those patients with high demands of pivoting. The ultimate goal of ACL reconstruction is to restore the biomechanical function of the knee joint and help patients return to sports (RTS).[22] An accurate and comprehensive assessment of graft and knee function after ACL reconstruction is necessary for guiding patients to RTS at the most appropriate time to avoid possible secondary injuries.[27] However, the current criteria for RTS after ACL reconstruction are still debated, and most RTS criteria lack a valid assessment of graft maturity.[5,20] It has been reported that grafts after ACL reconstruction undergo a period of remodeling and vascularization before reaching a mature state and

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exerting a biomechanical function.[14,28] The signal-to-noise quotient (SNQ) of the graft under magnetic resonance imaging (MRI) is currently widely used to assess graft maturity after ACL reconstruction.[15,18] Nevertheless, the application of multichannel coils and parallel imaging methods has led to variation of SNQs between different equipment, impeding its use in clinical practice.[8] Li et al[16] found that MRI-based ACL graft maturity did not predict clinical and functional outcomes during the first year after ACL reconstruction. Quantitative MRI, on the other hand, can overcome the above shortcomings and maintain a high degree of consistency across different clinical centers.[6] The measurement of T2* relaxation time, a tissue property reflecting collagen organization, hydration, and the local magnetic environment, has been reported to show progressive and continued graft maturation after ACL reconstruction.[9] However, the relationship between graft maturity and RTS after ACL reconstruction and whether T2* values can be used as biomarkers to predict RTS remain unclear.

The purposes of this study were to (1) compare the differences in SNQ and T2* relaxation times in the proximal, middle, and distal regions of the graft in patients who passed and failed an RTS assessment at 9 months after ACL reconstruction; (2) determine the relationship between the T2* values and RTS criteria; and (3) determine the diagnostic value and optimal T2* cutoff value for predicting patients who did not RTS. We hypothesized that the SNQ and T2* values would be different in patients who passed the RTS tests and those who failed and that T2* values would be useful for predicting which patients are not suitable for RTS.

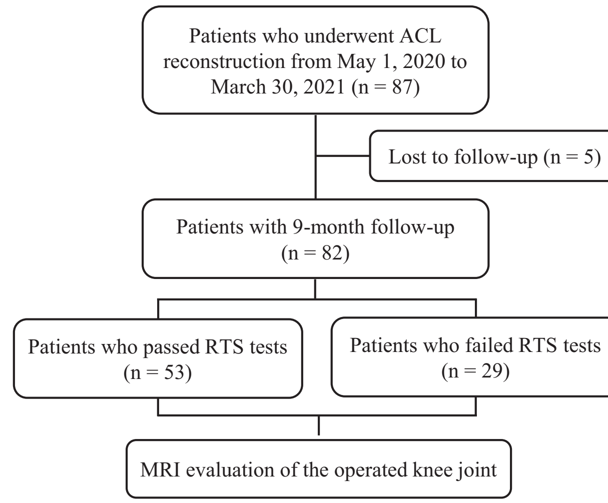

Figure 1. Flowchart of the study enrollment process. ACL, anterior cruciate ligament; MRI, magnetic resonance imaging; RTS, return to sports.

METHODS

Study Design

This study was approved by the ethics committee of our institution, and all included patients provided written informed consent. Patients who were diagnosed with primary ACL rupture at a single institution and who underwent arthroscopic autologous hamstring tendon single-bundle ACL reconstruction between May 1, 2020, and March 30, 2021, were eligible for inclusion. The study inclusion and exclusion criteria were as follows: (1) age >18 years old, (2) diagnosis of ACL rupture under arthroscopy, (3) anatomic single-bundle reconstruction of the ACL with hamstring tendon, and (4) willingness to complete 1 year of regular follow-up. The exclusion criteria were as follows: (1) other severe knee injuries (ie, collateral ligament, posterior cruciate ligament), (2) ACL reconstruction with other graft types (bone-patellar tendon-bone, artificial ligament, etc) and surgical techniques, (3) history of severe lower extremity trauma that may affect knee motion (posterior cruciate ligament injury, collateral ligament injuries, etc), and (4) unwillingness to participate in the trial or to complete the follow-up.

A total of 87 patients were initially included in the study. Five patients were lost to follow-up, leaving 82 patients included in the RTS assessment. Of these patients, 53 passed all RTS criteria, for an overall RTS rate of 64.6% at 9 months after ACL reconstruction. Thus, 53 patients were included in the RTS group and 29 patients were included in the no-RTS (NRTS) group (Figure 1).

Surgery Technique and Postoperative Management

In this study, the ACL injury was first determined under arthroscopy and the combined meniscal injury was treated with meniscal suture technique. Then, the semitendinosus and gracilis tendons were harvested and braided into 6 strands. Using the anteromedial approach, the tibial and

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Ethical approval for this study was obtained from Changhai Hospital (ref No. CHEC2020098).

TABLE 1
MRI Parameters Used in This Study[a]

Parameter	PD TSE	T2* Mapping
Coil	Quad knee coil	Knee phased-array coil
Plane	Sagittal-oblique	Sagittal-oblique
Fat suppression	Yes	No
No. of slices	26	224
FOV, mm	100	80
Slice thickness/gap, mm	3.5/4	3.5/3.7
Flip angle, deg	150	—[b]
Matrix (phase × frequency)	320 × 272	256 × 256
TR, ms	2600	800
TE, ms	26	2

[a]FOV, field of view; MRI, magnetic resonance imaging; PD TSE, proton-density turbo spin-echo; TE, echo time; TR, repetition time.
[b]Not applicable.

femoral tunnels were drilled at the ACL tibial and femoral footprints, respectively. The remnant tissue of both sides was preserved. The femoral and tibial ends of the graft were fixed with Endobutton (Smith+Nephew) and Intrafix (Smith+Nephew) screws, respectively. Finally, range of motion of the knee joint, graft tension, and graft impingement were checked under arthroscopy. ACL reconstruction in all patients was performed by the same senior surgeon, who had 20 years of experience (W.X.).

All the patients were treated with the standard postoperative rehabilitation protocol as reported by Badawy et al.[1] During the first 2 weeks postoperatively, patients were asked to perform exercises including straight-leg raises, ankle pumps, passive/active knee flexion and extension, and hip adduction to control the inflammatory response (swelling, pain, etc); restore the partial range of motion of the knee joint (full extension to 90° of flexion); restore the patellar range of motion; and strengthen the quadriceps femoris. From 3 to 5 weeks postoperatively, rehabilitation measures such as moving upstairs and downstairs and standing on 1 leg were used to restore the normal range of motion and normal gait of the knee joint. Patients were allowed to engage in running and jumping at 3 months postoperatively and noncontact sports at 6 months postoperatively. RTS and graft maturity assessments were performed at 9 months postoperatively.

RTS Criteria and Outcome Assessment

According to the Panther Consensus Group,[21] RTS criteria should include the postoperative time, a subjective score, an objective assessment of knee function, and a psychological readiness assessment. On this basis, we referred to related research and determined a number of RTS criteria.[12,25] Patients who met all of the following criteria were considered to have passed the RTS test:

1. Postoperative time of ≥9 months;
2. Limb symmetry index of >90% on 3 hop tests (single, triple, and triple crossover);
3. International Knee Documentation Committee (IKDC) 2000[13] subjective score of >90;
4. ACL Return to Sport After Injury scale (ACL-RSI)[30] score of >56.

All patients were asked to complete the subjective IKDC 2000 and ACL-RSI questionnaires at the 9-month postoperative outpatient follow-up; scores from both questionnaires were converted to a 100-point system. In addition, all patients were assessed with the Lachman test and pivot-shift test by senior professional physicians, all of whom had >5 years of experience (T.Z. and Y.X.). The Lachman test was graded as normal (no side-to-side difference), grade 1 (mild; 3-5 mm more translation of the tibia on the femur), grade 2 (moderate; 6-10 mm more translation of the tibia on the femur), or grade 3 (severe; >10 mm more translation of the tibia on the femur), while pivot shift was graded as normal (absent), grade 1 (slight), grade 2 (definite subluxation), or grade 3 (subluxation and momentary locking). The hop tests were performed as described by Noyes et al.[24] The patients were fully informed of the relevant rules and requirements when conducting the hop test. They decided whether to participate in this test according to their knee joint function recovery. If the patient gave up or did not take the test because of poor knee recovery, the test result was considered unqualified (limb symmetry index, ≤90%).

Measurement of Graft Maturity

All patients underwent a 3.0-T MRI (Siemens) of the operative knee at the 9-month follow-up. The MRI system parameters are listed in Table 1. After downloading the MRI data of the operative knee in DICOM (Digital Imaging and Communications in Medicine) format, we imported them into U-REVIEWER software (United Imaging) to calculate the SNQ at different regions of the graft. Regions of interest (ROIs) with diameters of 6 to 9 mm were selected at the proximal, middle, and distal portions of the grafts in oblique fat-suppressed sequences of the sagittal plane. The

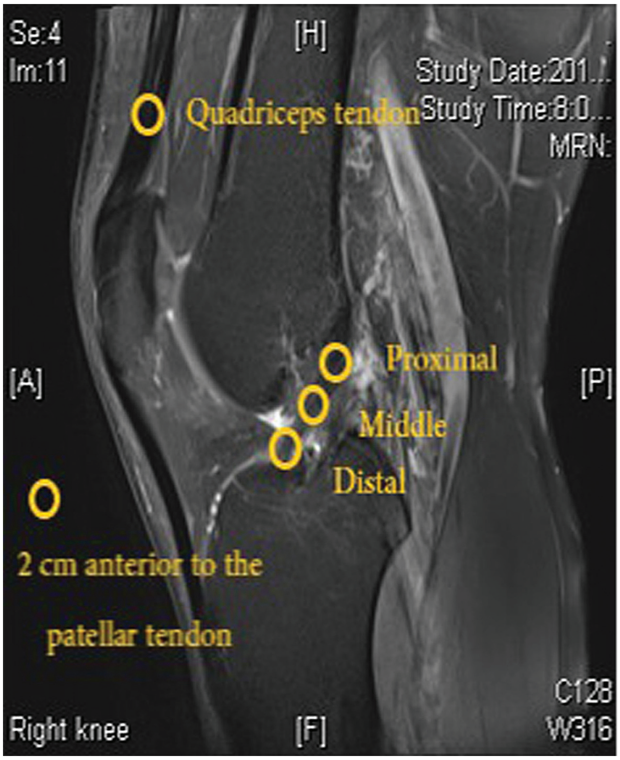

Figure 2. Placement of the regions of interest (ROIs; shown as circles) used to calculate the signal-to-noise quotient, measured on sagittal view magnetic resonance imaging. Three ROIs were placed on the graft (proximal, middle, and distal), 1 ROI was 2 cm proximal to the patella, and 1 ROI was on an empty area 2 cm anterior to the patellar tendon.

quadriceps tendon was selected as the reference area, and a background area was selected 2 to 3 cm anterior to the patella (Figure 2). The SNQ calculation formula for each part was as follows: *SNQ* (*ROIs*) = (*mean signal intensity of study area* – *mean signal intensity of reference area*)/*standard deviation of the signal intensity of the background area*. The formula for calculating the mean SNQ of the graft according to Liu et al[18] was as follows: [*SNQ* (*proximal*) + *SNQ* (*distal*) + *SNQ* (*middle*)]/3. T2* maps were directly calculated on a pixel-by-pixel basis by using a monoexponential fitting algorithm available on the scanner. The equation is expressed as follows: *SI*(*TE*) = *S0**exp(–*TE*/*T2**), where *SI*(*TE*) is the signal intensity at each echo time and *S0* is the equilibrium magnetization. To evaluate maturation of the intra-articular portion of the graft, T2* maps were manually segmented to assess graft tissue. Intra-articular graft ROIs were segmented from a single sagittal slice. The T2* and graft SNQ values of all patients were independently measured by 2 radiologists with >10 years of clinical experience (X.Z. and H.W.), and 1 of them repeated the measurement after 2 weeks to determine the reliability of this indicator (X.Z.).

TABLE 2
Comparison of Patient and Physical Examination Characteristics by Study Group[a]

	RTS Group (n = 53)	NRTS Group (n = 29)	*P*
Age, y	27.65 ± 6.04	28.25 ± 6.45	.676
Mass, kg	175.55 ± 3.31	174.73 ± 4.32	.337
Body height, cm	74.27 ± 8.65	75.53 ± 8.91	.538
Body mass index, kg/m^2	23.81 ± 1.91	24.09 ± 2.75	.512
Time from surgery, mo	9.50 ± 0.37	9.43 ± 0.52	.471
Sex, male/female	42/11	22/7	.723
Laterality, right/left	33/20	18/11	.986
Graft diameter, mm	8.60 ± 0.52	8.61 ± 0.54	.603
Meniscal pathology			.839
None	25	15	
Partial meniscectomy	10	6	
Meniscal repair	18	8	
Lachman test			.351
Normal	35	15	
Grade 1	11	9	
Grade 2	7	4	
Grade 3	0	1	
Pivot-shift test			.087
Normal	50	23	
Grade 1	3	5	
Grade 2	0	1	
Grade 3	0	0	

[a]Data are reported as mean ± SD or No. of patients. NRTS, no return to sports; RTS, return to sports.

Statistical Analysis

Statistical analyses were performed using SPSS software (Version 24; IBM). Continuous variables (including age, mass, body mass index, time from surgery, T2* values, and SNQ) were reported as means with standard deviations and were compared between groups using the independent-samples *t* test, whereas the chi-square test or Fisher exact test was used to compare categorical variables between groups. The intraclass correlation coefficient (ICC) with 95% CI were calculated to determine the intraobserver and interobserver reliability. Based on ICC values, the test-retest reliability was interpreted as *excellent* (>0.90), *good* (0.75-0.90), *moderate* (0.50-0.74), or *poor* (<0.50). Spearman correlation coefficients were calculated to assess the relationship between T2* values and RTS. A receiver operating characteristic (ROC) curve analysis was completed to determine the optimal cutoff value for detecting RTS with the use of T2*. The Youden index[10] was utilized to determine the ideal cutoff point with the highest sensitivity and specificity. The threshold for statistical significance was set at $P < .05$. A post hoc power analysis for the outcome of the SNQ value was calculated with G*Power (Version 3.1.9.2; Heinrich Heine Universität) and revealed that a sample of this size (53 cases in the experimental group and 29 cases in the control group) would be able to detect a clinically meaningful difference with 95% power.

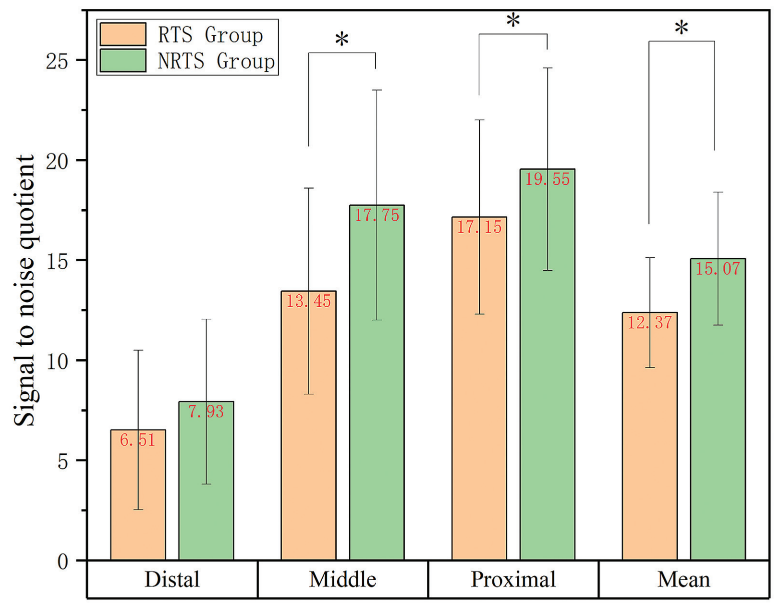

Figure 3. Comparison of the signal-to-noise quotient values of different regions of the graft between the return to sports (RTS) and no return to sports (NRTS) groups. *Significant difference between groups (P < .05).

RESULTS

The demographic data and postoperative assessment of the patients according to study group are shown in Table 1. The 2 groups did not differ significantly in age, height, body mass index, time from surgery, sex, operative side, graft diameter, concomitant meniscal injuries, Lachman test, or pivot-shift test (Table 2). No obvious ligament retear was observed for any patient on MRI, but effusion was found in some patients.

The ICCs for graft SNQ were 0.89 (95% CI, 0.85-0.91) for interobserver reliability and 0.78 (95% CI, 0.72-0.83) for intraobserver reliability, indicating good agreement for both. At 9 months after ACL reconstruction, the proximal, middle, and mean SNQ values of the graft in the RTS group were significantly lower than those in the NRTS group (proximal: 17.15 ± 4.85 vs 19.55 ± 5.05, P = .038; middle: 13.45 ± 5.15 vs 17.75 ± 5.75, P = .001; mean: 12.37 ± 2.74 vs 15.07 ± 3.32, P < .001). However, there was no significant difference in the SNQ values of the distal site of the graft between the 2 groups (6.51 ± 3.98 vs 7.93 ± 4.12; P = .131). The comparison of SNQ of different sites of grafts between the RTS group and NRTS group is shown in Figure 3.

The ICCs for T2* values were 0.93 (95% CI, 0.89-0.97) for interobserver reliability and 0.91 (95% CI, 0.87-0.95) for intraobserver reliability, indicating excellent agreement in both cases. The T2* values for intra-articular ACL graft tissues at 9 months postoperatively were significantly higher in the NRTS group compared with the RTS group (17.69 ± 2.48 vs 14.92 ± 2.28; P < .001). A correlation analysis was conducted for T2* value with RTS. Spearman correlation coefficient of T2* value with RTS was −0.41 (P = .02). The ROC analysis of T2* for predicting failure to RTS resulted in an area under the curve of 0.79 (95% CI, 0.75-0.83). The ROC curve analysis revealed that a cutoff of 16.65 for T2* yielded a sensitivity of 67.9% and specificity of 88.2% for predicting failure to RTS (Figure 4).

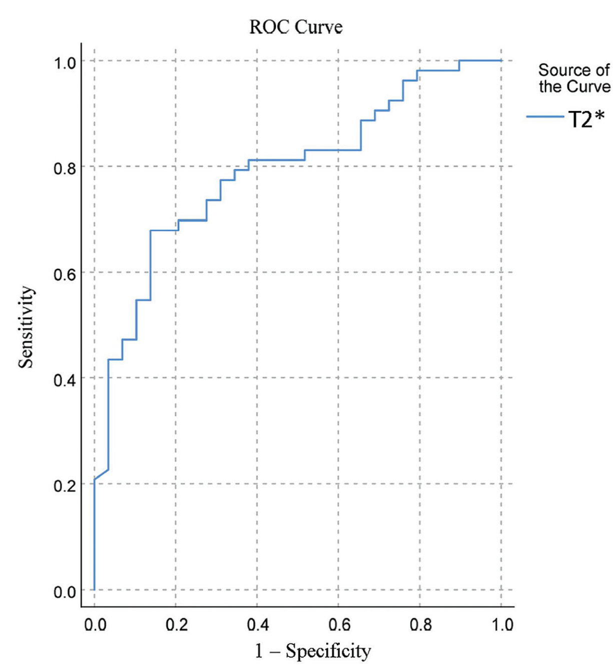

Figure 4. The receiver operating characteristic (ROC) curve of the T2* value for predicting failure to return to sports.

DISCUSSION

In this study, it was found that only 64.6% of patients passed the RTS tests at 9 months after primary ACL reconstruction with autologous hamstring single-bundle graft. Compared with patients who did not pass the RTS test (NRTS group), patients in the RTS group had lower SNQs at the proximal and middle sites of the graft (proximal: 17.15 ± 4.85 vs 19.55 ± 5.05, $P = .038$; middle: 13.45 ± 5.15 vs 17.75 ± 5.75, $P = .001$). In addition, compared with the NRTS group, patients in the RTS group showed smaller T2* values on quantitative MRI (17.69 ± 2.48 vs 14.92 ± 2.28; $P < .001$), which was found to be significantly associated with RTS ($r = -0.41$; $P = .02$). Finally, we found that if a T2* value <16.65 was set as an RTS criterion, the sensitivity and specificity of predicting patients who did not RTS were 67.9% and 88.2%, respectively. However, these results will need to be confirmed in another population.

After ACL reconstruction with autograft, biological studies on graft changes have confirmed that the graft must go through a series of ligamentization processes in the human body, which can be visualized on MRI images.[28] The SNQ is the most commonly used measurement of graft maturity. Based on second-look arthroscopy, Kim et al[15] found that well-synovialized grafts showed significantly lower SNQs than poorly synovialized grafts. This study found that SNQ values of the proximal and middle regions of the graft in the RTS group were significantly lower than those in the NRTS group at 9 months after ACL reconstruction, suggesting that the graft maturity in the RTS group was better than that of the NRTS group. Some studies have found a correlation between the SNQ values of an ACL graft and the IKDC 2000 scores after ACL reconstruction ($r = -0.454$; $P = .003$).[4,17] In fact, the relationship between graft SNQ values and functional outcome is controversial because conventional MRI sequences are susceptible to MRI scanning techniques including multichannel coils and parallel imaging, which can influence both the statistical and the spatial distribution of noise.[2,8]

To overcome the above shortcomings, we used T2* mapping in this study to evaluate the relationship between graft maturity and RTS after ACL reconstruction. The T2* mapping sequence is one of the most widely used MRI quantitative detection sequences. The T2* value measured by T2* mapping is related to the tissue structure of the ROI, and it is less sensitive to image acquisition parameters. Therefore, T2* mapping is suitable for imaging highly organized collagen structures such as tendons and ligaments.[3] Chu and Williams[6] found that the mean ACL graft T2* increased 25% to 30% during the first 6 months ($P < .013$) and decreased 19% between 1 and 2 years after ACL reconstruction. Naghibi et al[23] found a correlation between T2* and mechanical properties (stiffness and rupture force) of human knee ligaments. In this study, we found that the T2* value of the NRTS group was significantly larger than that of the RTS group (17.69 ± 2.48 vs 14.92 ± 2.28; $P < .001$) and a moderate correlation ($r = -0.41$; $P = .02$) was found between T2* and RTS. The results of this study indicate that T2* is an effective indicator of graft maturity after ACL reconstruction and that the T2* value is related to RTS.

This study evaluated the value of T2* in predicting failure to RTS and found that the area under the curve was 0.79 (95% CI, 0.75-0.83). Based on the Youden index,[10] the optimal cutoff value of T2* was 16.65, with a sensitivity and specificity of 67.9% and 88.2%, respectively, in identifying patients who were not suitable for RTS. Although T2* alone has low sensitivity for predicting RTS, the results of this study indicate that the graft T2* value can be used with other indicators for predicating RTS after ACL reconstruction.

RTS after ACL reconstruction is a common matter of concern to clinicians and rehabilitation therapists. Current RTS assessments generally include the postoperative time, patient-reported subjective knee scores, objective knee function tests, and psychological readiness.[29] However, these assessment criteria may not be comprehensive enough, and their role in preventing secondary injury is debated.[11,31] Losciale et al[19] found that the incidence of secondary injury in patients who passed RTS tests after ACL reconstruction was still as high as 14.4%, and there was no significant reduction in those patients compared with patients who failed the tests. Therefore, improving the current RTS criteria and adding new meaningful metrics are necessary to increase their value and efficacy.[7] The results of this study indicate that graft T2* value, an MRI-based graft maturity indicator, can predict the likelihood of NRTS after ACL reconstruction. Although the sensitivity and specificity of T2* in predicting patients who do not RTS alone are not satisfactory, they may be used in combination with other indicators for better accuracy.

Limitations

This study has the following limitations. First, the MRI-based graft SNQs are affected by MRI parameter settings (eg, repetition time, echo time), MRI scanner, and coils, which lead to SNQ values measured on different equipment being incomparable.[27] Therefore, SNQs in this study were only used to qualitatively compare the difference in graft maturity between the RTS and NRTS groups. T2*, a quantitative MRI mapping, was used in this study to objectively assess ACL graft healing. In addition, the measurement of grafts in this study were susceptible to the "magic angle" phenomenon, a special type of artifact that occurs in sequences with short echo times.[26] In this study, the patient was repositioned to change the angle of orientation of the structure to the static magnetic field when the magic angle phenomenon was found. More in-depth studies are needed to further address these shortcomings and explore the application of graft T2* value in RTS assessment. Finally, the follow-up time of this study was only 9 months, thus studies with longer follow-ups should be performed in the future to enhance the methodological strength. Due to the limitations of the experimental conditions, this study only investigated the predictive value of T2* for RTS, and the value of metrics in other sequences such as ultra-short echo time T2* and 3-dimensional constructive interference in steady state remains unclear.

CONCLUSION

The study findings indicated that 9 months after ACL reconstruction, the mean, proximal, and middle graft SNQs and T2* values in the RTS group were significantly lower than those of the NRTS group. There was a correlation between T2* values and RTS after ACL reconstruction. A T2* value of 16.65 was calculated to predict patients who failed RTS tests with a sensitivity of 67.9% and specificity of 88.2%.

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