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Knee flexion strength deficits correlate with distal extent of tendon regeneration after hamstring harvest. Preliminary data from an Ultrasound based classification

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Background: As more evidence comes to light that hamstring harvesting may not be as benign a procedure as previously thought, considerable interest is being generated towards corelating the knee flexural strength deficits with the degree of tendon regeneration. The current study aimed to corelate knee flexion strength deficits with ultrasonographically quantified degree of hamstring regeneration after tendon harvest.
Study design: 31 patients of ACL reconstruction with hamstring grafts were divided into 2 groups (6 months and 1-year post op) according to time of follow up. Ultrasonography of both the knees to assess Semitendinosus tendon dimensions was done. Regeneration was classified as non-significant, mild (Zone 1, till 4 cm above the lateral joint line), moderate (Zone 2 ,at the level of the lateral joint line) and significant (Zone 3, 1.5 cm below the lateral joint line) as the regenerate happens from proximal to distal. Regenerate dimensions were compared with US measurements from the opposite knee. Bilateral isokinetic strength tests of the knees were done to evaluate flexion strength, and strength deficits were compared with degree of tendon regeneration.
Results: 14 (45%) of cases had no regeneration at both time periods. 7 patients (41%) in the 6-month post-op group showed some form of regeneration, and 10 patients (71%) in the 1-year post-op group showed regeneration. 29/31 patients had some flexion strength deficit. Strength deficit correlated with the level and degree of tendon regeneration, with non-significant regeneration cases showing higher strength deficit (mean - 28.51%), and cases with significant regeneration showing least amount of strength deficit (mean - 3.66%).
Conclusion: Flexion strength deficits after hamstring harvest are significant and corelate with degree of tendon regeneration, which improves over time. US is adequate to quantify degree of tendon regeneration, which in turn can help prognosticate return of flexion strength.

1. Introduction

Regeneration of the hamstring tendons after harvesting has been discussed for the last 35 years or more. The increasing popularity of these as a graft for ACL reconstruction coincided with studies documenting significant regeneration of these tendons[1,2]; this was reiterated by subsequent authors who thought that these tendons could even be reused.[3] Contrary opinions started surfacing as early as 2005, with reports of limited regeneration and strength deficits after harvest[4,5]; some authors even started advocating the use of a single hamstring or partial graft harvesting to minimize the residual functional deficits.[6]

The process and degree of tendon regeneration is still unclear; some authors have noted a proximal to distal regeneration of varying extent, while others have labelled it a "*lizard tail*" effect.[7,8]

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Nevertheless, the degree of regeneration is not specifically quantified, nor is this regeneration correlated specifically with flexural muscle strength deficits. Flexion strength deficits have been varyingly documented as a concern; Simonian et al.[9] did not find significant compromise in strength and function after harvest, despite a more proximal re-insertion of the regenerating tendon. However other studies[10–14] have documented various degrees of flexion strength deficit in association with hamstring tendon harvest.

The modalities used for evaluating regeneration vary, ranging from ultrasonography to CT scans and MRI.[4,9–20] These studies have been done at various stages after hamstring harvesting, with varying objectives in mind. MRI is an expensive test, despite the fact that it can define regeneration most accurately; CT is not a test done routinely for soft tissue evaluation and involves radiological exposure. On the other hand, ultrasonography (US) as a testing modality can be widely used, as it is cheap and is easily mastered by radiologists giving accurate and reproducible results. Although this modality is user dependent, experienced musculoskeletal radiologists have used US in previous studies with reproducible demonstration of regenerating tissue.[3,8,19]

One of the major drawbacks of the published literature seems to be a lack of classification of tendon regeneration according to longitudinal regeneration, and a correlation of this with flexural strength deficit. We specifically designed the current study to quantify the extent of longitudinal regeneration; US was used to evaluate hamstring regeneration at different levels in relation to the knee joint line. This was then correlated with knee flexion strength, which was calculated as a percentage of strength in the contralateral limb.

2. Materials

After institutional ethical clearance and informed patient consent, two groups of patients were identified and included in this study. Cases of ACL reconstruction done by a single surgeon (SA) over a one-year period, using 4 strand hamstring graft harvested by standard technique, were randomly allocated into 2 groups. Group 1 consisted of cases evaluated six months post-operative and group 2 had cases evaluated at one-year post-operative. All the cases had a similar postoperative rehabilitation protocol.

US images were acquired in axial and coronal planes from the muscle belly to the insertion site at the pes anserenus, with the patient in prone position and both knees fully extended. Three zones for evaluation were identified; zone 1- at 4 cm above lateral joint line, zone 2 - at the level of the lateral joint line and zone 3—1.5 cm below the lateral joint line just above tendon insertion. Scanning was done using a Toshiba APLIO 500 ultrasound machine with a linear high frequency [~10—14 Mhz frequency range] by one of 2 trained radiologists (RR, PMVS). The regenerating tissue was classified as non-significant if no tendon was visualized anywhere along its course (Fig. 1), mild regeneration if the tendon was visualized 4 cm above the lateral joint line (Zone1, Fig. 2), moderate regeneration if the tendon was visualized at the level of the lateral joint line (Zone 2,Fig. 3), and significant if the tendon was visualized 1.5 cm or more below the lateral joint line (Zone 3, Fig. 4)). The width and dimensions of the tendon on the un-injured knee was measured for comparison with the regenerate.

Isokinetic strength testing of both the knees was done using a System Pro™ Biodex Dynamometer. Before testing, the patients were asked to perform a 10-min warm up. Both the knees were tested separately at 3 speeds; 60°/second, 180°/second and 300°/second using 10 repetitions each. Once finished, a result was obtained from the machine that showed the flexion strength deficit of the involved knee compared to the uninvolved knee.

The results were tabulated, and comparison was made between the flexion strength documented and the degree of regeneration of the hamstring tendons.

Normality of data was ascertained by the Shapiro-Wilk test. For statistical analysis of the flexion strength deficit, we divided the patients into two groups; those with no or mild regeneration (zone 1) and those with moderate (zone 2) or significant regeneration (zone 3). Owing to the non-parametric nature of the outcome data, the Mann-Whitney *U* test was used to determine statistically significant differences between these two groups. All analysis was done by Stata Version MP14.0.

3. Observations and results

31 patients were included in this study; there were 4 females and 27 males. Hamstring harvest had been done from 21 right knees and 10 left knees. On the basis of time of post-operative evaluation, group 1 had 17 cases, and group 2 had 14 cases. US imaging showed that 14/31 (45%) had no significant regeneration; of the remaining 17, 5 (16%) showed mild regeneration (limited to Zone 1), 2 (7%) showed moderate regeneration (limited to Zone 2) while 10 (32%) showed significant regeneration (till Zone 3, below the knee joint line). Classified according to time of follow up, 10 of 17 (59%) had no significant regeneration at 6 months, while only 4 of 14 (29%) showed no significant regeneration at 1 year (Table 1). Mild regeneration limited to Zone 1 was seen in 4 (23%) cases at 6 months and in 1 (7%) case at 1 year. At 6 months follow up no moderate regeneration was documented while 2 cases (14%) showed moderate regeneration at 1 year follow up. 3 cases (18%) showed significant regeneration at 6 months post op, while 7 (50%) showed significant regeneration at 1 year. All the patients showed proximal retraction of the muscle belly on the operated side.

Isokinetic strength testing was done for all the patients (Table 2). In group 1 (evaluated 6 months post op), 10 (59%) of the 17 cases with no significant regeneration showed a high flexion deficit of 23.43%. 4 (23%) patients with mild regeneration showed a flexion deficit of 14.63% and 3 (18%) patients with significant regeneration showed a flexion deficit of 11.66%. In group 2 (evaluated 1-year post op), 4/14 (29%) patients had no significant regeneration and showed a very high flexion deficit of 41.21%; 1 (7%) patient who had mild regeneration showed a flexion deficit of 12.9%, 2 (14%) cases having moderate regeneration showed flexion deficit of 7.6% and 7 (50%) patients with significant regeneration showed a very low flexion deficit of 1.23%.

On comparing to the US documented regeneration, it was seen that the 14 patients with non-significant regeneration had a high mean deficit of 28.51%. 5 patients with mild regeneration had a mean deficit of 14.28%, 2 patients with moderate regeneration had a mean deficit of 7.6% and 10 patients who had significant regeneration had mean flexion strength deficit of only 3.66%.

Comparison of patients with no or mild regeneration versus those with moderate or significant regeneration was done. We noted that patients with no or mild regeneration had approximately four-fold higher flexion strength deficit as compared to those with moderate or significant regeneration, and this difference was statistically significant ($P = 0.002$).

4. Discussion

Despite advances in our understanding, and the significant surge in utilization of hamstrings as grafts in many situations, many things about hamstring tendon regeneration are still debated. From a thought process that said that there is no problem after hamstring harvest in the late 20th century[1,2] we now know that almost half the tendons don't regenerate fully, or do so only to a limited extent. Bedi et al.[8] evaluated 18 knees using US, and found *"some tissue"* at

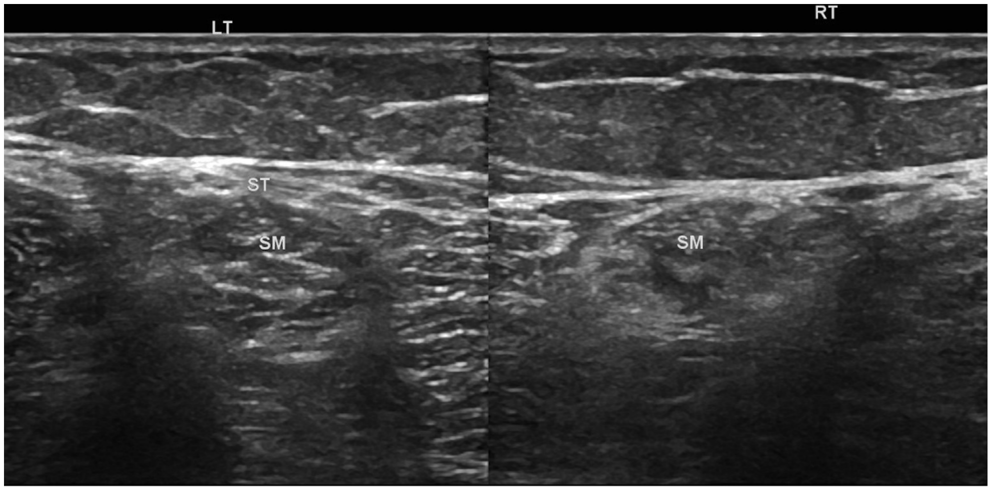

Fig. 1. Shows ultrasonographic image of both knees (right operated). There is no evidence of regeneration in the operated limb.

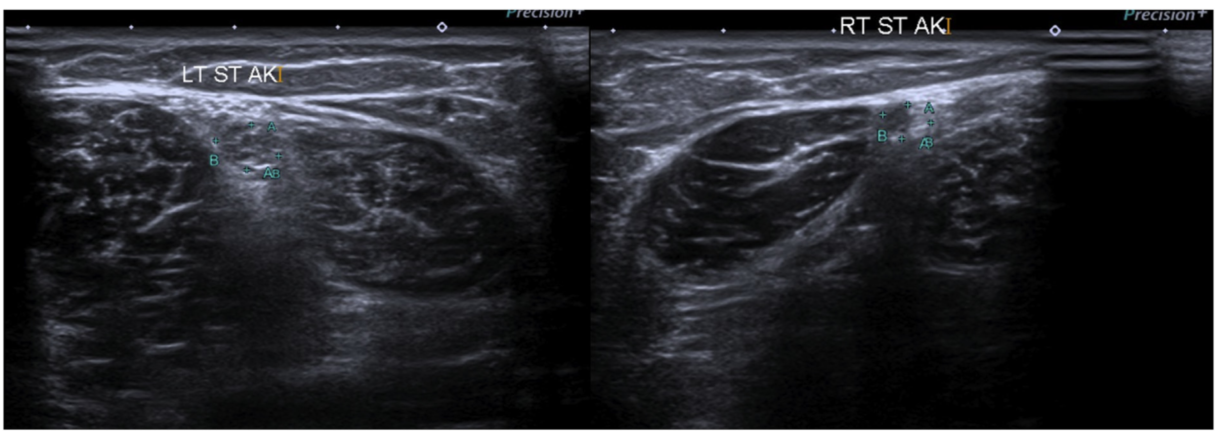

Fig. 2. Shows ultrasonographic image of both knees (left operated). Regenerated tendon can be seen in zone 1 (4 cm above the lateral joint line) of the operated knee.

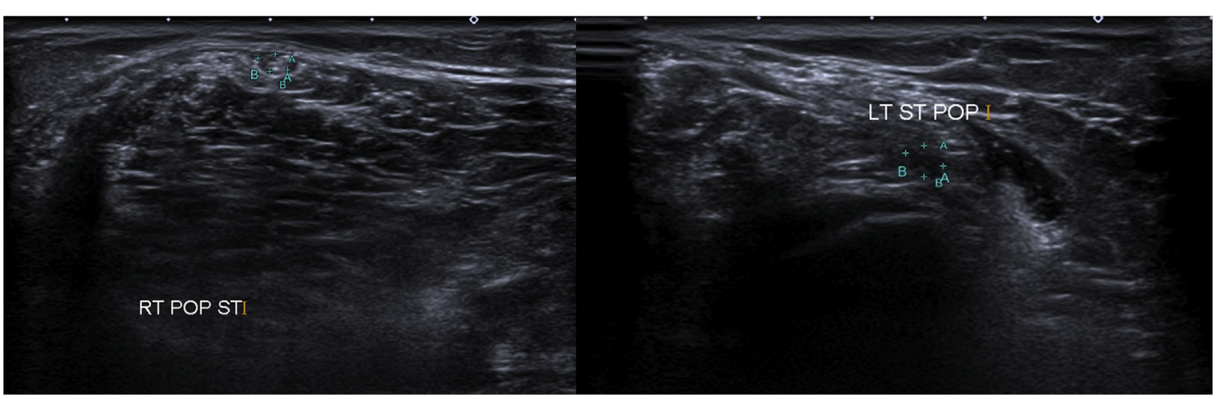

Fig. 3. Shows ultrasonographic image of both knees (right operated). Regenerated tendon can be seen in zone 2 (at the level of the lateral joint line) of the operated knee.

the harvest site in only 9 cases, 5 of whom had disorganized tissue seen in the "*harvest gap*". They concluded that whatever tissue forms is disorganized, and noted on dynamic US that this did not have physiological function similar to the original hamstring muscle. In our study also, we found that 45% of the cases did not show any regenerate in the harvested area, which is a significant number. However, Suijkerbuijk et al.,[21] in a systematic review of 18 publications done in 2014, noted regeneration rates in excess of 70%; but they also stated that they could not conclude whether the absence of regeneration disadvantages hamstring function. Subsequently in 2016 Konarth and colleagues[11] evaluated 20 cases by MRI and strength testing; they documented a 35% regeneration rate and showed a significant correlation of strength deficits with difference in volume measured and lengths of these tendons.

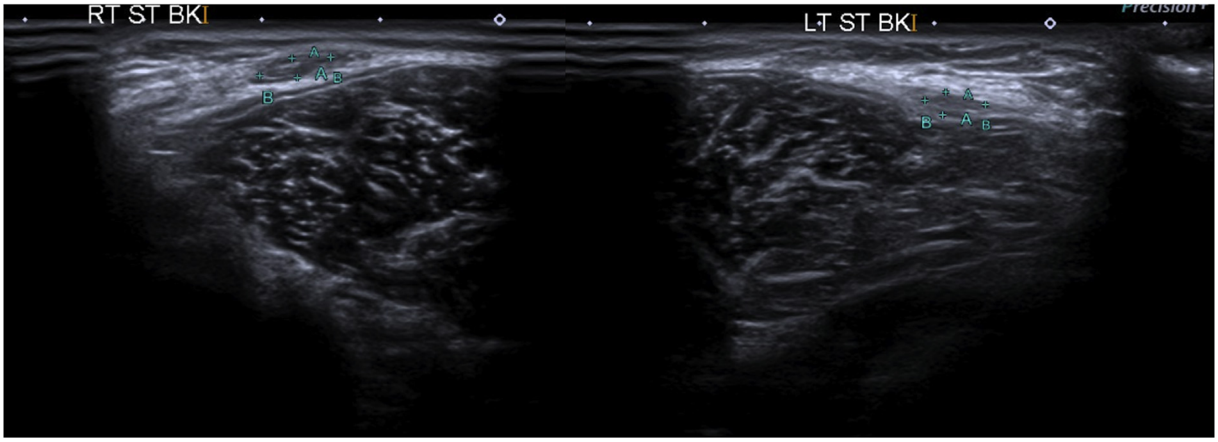

Fig. 4. Shows ultrasonographic image of both knees (right operated). Regenerated tendon can be seen in zone 3 (1.5 cm below the lateral joint line) of the operated knee.

Table 1
Ultrasonographic measurement of regenerated tendons.

Ultrasonographic Measurement of Tendon				
Type of regeneration; No of cases	Group 1,2 (Time post op)	Cross section area regenerated (mean mm^2)	Normal side (mean mm^2)	%age of normal cross section
Mild: 5 (16%)	6 months 4	11.45 mm^2 (10.1–14.35 mm^2)	13.92 mm^2 (12.42–15.64 mm^2)	82.25%
	1 year 1	27.28 mm^2	13.64 mm^2	200%
Moderate regeneration: 2 (7.6%)	6 months (0)	NA	NA	NA
	1 year 2	7.02 mm^2 (5.58–8.47 mm^2)	9.78 mm^2 (6.2–10.32 mm^2)	71.77%
Significant Regeneration: 10 (32%)	6 months 3	12.15 mm^2 (1.4–21.6 mm^2)	12.05 mm^2 (2.0–15.68 mm^2)	100.82%
	1 year 7	8.69 mm^2 (0.24–20.16 mm^2)	8.24 mm^2 (5.28–14.08 mm^2)	105%

Table 2
Flexion strength deficit in comparison to degree of regeneration.

Flexion Deficit - Group 1 (6 months post-op)		
Regeneration	Number of Patients	Mean Flexion Strength Deficit
No Regeneration	10 (59.%)	23.43%
Mild Regeneration	4 (23%)	14.63%
Moderate Regeneration	0	
Significant Regeneration	3 (18%)	11.66%
Flexion Deficit - Group 2 (1-year post-op)		
Regeneration	**Number of Patients**	**Mean Flexion Strength Deficit**
No Regeneration	4 (29%)	41.21%
Mild Regeneration	1 (7%)	12.9%
Moderate Regeneration	2 (14%)	7.6%
Significant Regeneration	7 (50%)	1.23%

However, no quantification of the degree of longitudinal regeneration was done, and nor has this been correlated previously with strength deficits. Nevertheless, this regeneration process improves over time, as was noticed by us in the cases evaluated at 1 year follow up, who had higher rates and better regeneration. As was noted in our study, strength deficits correlate well with degree of regeneration, but they may not correlate with time of follow up; in non-regenerated tendons, we noted larger average strength deficits at 1 year follow up as compared to 6 months, which could indicate that despite sufficient attempts at muscle rehabilitation, it is the degree of regeneration and not the follow up that determines the residual functional deficit. Konarth and colleagues[11] have followed up cases for 2 years or more, and have noted that regeneration deficits after harvest persist, which alters the muscle tendon properties leading to knee flexor weaknesses.

Documentation of the process of regeneration from proximal to distal[22] and the fact that the tendon growth is *"similar to a lizard tail"*,[7] makes it a rational assumption that progression of regeneration along the path of the original tendon could be a reflection of regaining functionality. Changes in actual hamstring muscle function have been variably documented, which could also reflect on the degree of regeneration. Takeda et al.[23] evaluated hamstring muscle belly function and noted no difference in T2 relaxation times on MRI in both operated and non-operated knees, concluding that the hamstrings are able to maintain their contractile ability after harvest. On the other hand, Ristanis et al.[24] showed significant electromechanical delays in 12 patients compared with controls 2 years after use of hamstrings for ACL reconstruction, and advocated further research to clarify the confusion. This goes on to substantiate the belief that further research is needed to prognosticate residual functional deficits, and quantification of longitudinal regeneration maybe one such option. Our preliminary work is a step in this direction.

The process of tendon regeneration progresses and improves over time; Rispoli et al.[25] studied the chronological progression of regeneration using 1.5T MRI and correlated it to anatomical

Table 3
Significance of flexion strength deficits in cases with no/mild regeneration versus moderate/significant regeneration.

	No regeneration & mild regeneration (n = 19)	Moderate & significant regeneration (n = 12)	P Value
No. of cases	24.8 ± 13.6	4.3 ± 19.6	0.002

landmarks like the superior pole of patella, knee joint line and the tibial attachment site of the hamstrings. They noted the earliest evidence of regeneration at 4 weeks, with further progression happening till 1 year, with an "*apparent normalization*" of tendons 1–2 cm above their attachment by 32 months. The long-term effects after tendon harvesting were evaluated by Snow et al.[26] at 9–11 years follow up; they noted variability of tendon regeneration, persistent hamstring muscle atrophy and evidence of fatty infiltration. Contrary to this, Ahlen et al.[27] found that the majority of their 19 patients regained an almost normal point of reinsertion of the tendons at 6 year follow up, with a cross sectional area similar to the non-operated side. Strength deficits, however persisted in their cases.

Despite the contradictory data available in the published literatures, some things are clear in 2020. There is a variable rate of regeneration of the tendons, and the Semitendinosus may regenerate differently from the Gracilis, leading some authors to advocate harvest of one tendon alone, or partial harvesting of the Semitendinosus.[6,28] Nevertheless, whether regeneration happens or not is not the significant issue after ACL reconstruction; what is relevant is functional recovery for these young adults, many of whom are sportspersons. There is no doubt that functional deficits of varying degree do occur and prognosticating residual deficits and potential return to full activity or sport is the key point. For that purpose, a simple classification of longitudinal regeneration, using a simple and cheap tool like US, maybe a step in the right direction. Our preliminary study has shown that this is possible.

The effectiveness of US to evaluate hamstring regeneration has been shown by other authors too (Table 3). Although it not as good as MRI, US is nevertheless an effective option when cost and ease of availability are taken into consideration. A point of note is that the actual tissue quality of the regenerate (tendon tissue or not) is not possible by either MRI or US, and requires a biopsy; nevertheless the thickness of the regenerating tissue can be documented and correlated with strength deficits. A limitation of our study is that we have not done a longitudinal assessment over time on the same patients; this would a better predictor of regeneration and could reveal the extent and rate of distal migration of the regenerate, which we have shown correlates with strength deficits. A larger cohort of patients followed for a period of 12–18 months would further validate these preliminary findings.

5. Conclusions and take home points

This preliminary study has shown the effectiveness of US in documenting and classifying the longitudinal extent of tendon regeneration after hamstring harvesting. We offer this preliminary classification according to distal extent of documented regeneration, which has been shown to correlate with residual muscle deficits, as a tool to prognosticate functional deficits, and clarify decision making about return to sports/full function in active individuals.

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