



## Factors associated with degeneration of rotator cuff tendon : a histological study in patients with rotator cuff tear

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Factors associated with tendon degeneration have not been fully investigated. The purpose of this study was to identify factors associated with tendon degeneration in patients with rotator cuff tear. A total of 93 patients with a full-thickness rotator cuff tear (fRCT) were included in the study. A full-thickness supraspinatus tendon sample was harvested from the middle portion between the lateral edge and the musculotendinous junction, and assessed histologically. Association between the degree of tendon degeneration and factors in demographic, clinical, radiologic, and arthroscopic categories were investigated. The mean of the total degeneration score was significantly lower in patients with symptom duration of 6 months or less than longer than 6 months ( $13.1 \pm 2.6$  vs  $14.4 \pm 2.3$ ,  $p = 0.010$ ). This study showed that tendon degeneration significantly progressed 6 months after the onset of symptoms, and suggested early intervention to avoid further deterioration of tendon degeneration.

**Keywords :** Rotator cuff tear ; Rotator cuff repair ; Tendon degeneration ; healing ; retear

### INTRODUCTION

Rotator cuff disease is one of the most frequently causes of shoulder pain and dysfunction (20). It

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represents a spectrum of tendon lesions from tendinopathy, partial-thickness tear, full-thickness tear and eventually to cuff tear arthropathy (21). Surgical management of rotator cuff tear has evolved over the past decades, from open or minimally open repairs to all-arthroscopic techniques, and mostly has shown good functional results and patient satisfaction (1,9,10). However, retear or healing failure remains significant problems (8).

In general, rotator cuff repair was accomplished by tendon-to-bone healing. Despite improvements in mechanical strategy through efforts toward a more secure fixation (5), rotator cuff repair has been reported to fail structurally from 20% to 94% of cases (8-10). Tendon degeneration has been known as the primary cause of rotator cuff disease (11,14) as well as a cause affecting the healing process after rotator cuff repair (4). However, the current repair

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methods cannot convert the degenerated tendon to the normal tendon (2). It is believed to be one of the most crucial reasons why the latest advanced fixation technique still fails (1,3). Various biological strategies to overcome fundamental limitations of current rotator cuff repair, to reduce the retear rate, and to improve long-term shoulder function through improving the degeneration of tendon itself or tendon-to-bone interface have been investigated (3). For this, we believe that establishment of a solid tool for objective assessment of tendon degeneration would be the first step. Currently, one of the objective methods evaluating tendon degeneration is to use a histological grading systems (13-17). Studies using histological evaluations have consistently demonstrated that tendon degeneration is significantly greater in patients with a full-thickness rotator cuff tear (fRCT) than in patients without it. Histological evaluation could only be performed with surgically harvested tendon samples. Thus, surgeons would not have enough time to be properly prepared for managing patients with severe tendon degeneration who may need a biological strategy in addition to advanced biomechanical fixation. If factors associated with tendon degeneration could be identified prior to surgery, it would be helpful to plan appropriate pre-, intra-, and postoperative treatment strategy.

The purpose of this study was to investigate factors associated with tendon degeneration in patients with a fRCT. Our hypothesis was that there was an identifiable factor associated with tendon degeneration of rotator cuff.

## METHODS

Our institutional review board approved this retrospective study, and all participants provided informed consents. The inclusion criteria included a fRCT with available tissue samples of rotator cuff tendon that were harvested at the time of surgery. The exclusion criteria included a partial-thickness rotator cuff tear, an isolated subscapularis tear, infection around shoulder, previous subacromial injection within past 3 months, and calcific tendinitis.

Tendon samples were harvested en bloc in the middle portion of the tendon (between the lateral edge and the musculotendinous junction) from patients undergoing arthroscopic rotator cuff repair using a biopsy punch with a diameter of 3mm, and were placed in 20mL of sterile 10% formalin. Once fixed, the samples were dehydrated, embedded in paraffin, and cut at section of 4  $\mu$ m in thickness. The sections were stained with hematoxylin and eosin (H&E), and examined under a light microscope. Three sections were made per each tendon, and one section was randomly selected and examined. The whole area of each slide was observed, and the most severely degenerated area that would show the worst score was selected. The sections were evaluated with a modified semi-quantitative grading scale for tendon degeneration ; (13,16) fiber structure (0 = linear, no interruption, 3 = short with early truncation) ; fiber arrangement (0 = well ordered and regular, 3 = no pattern identified) ; appearance of nuclei (0 = flat, 3 = rounded) ; regional variations in cellularity (0 = uniform ; 3 = high regional variation) ; vascularity (0 = absent, 3 = high) ; stainability (0 = vivid, 3 = pale) ; and hyalinization (0 = absent, 3 = high). The total degeneration score could vary between 0 (closest to normal tendon) and 21 (most severely degenerated). The examinations were performed twice. The first examination was performed by two orthopedic surgeons, and the second one – a week after the first – was performed by one of the two previous examiners. The inter- and intra-observer reliability was confirmed, and the measures of the second examination were used in the study.

Factors potentially associated with tendon degeneration were grouped as demographic, clinical, radiological, and arthroscopic categories. The demographic factors included age, gender, symptom duration, symptom aggravation, and dominance. The clinical factors included pain, range of motion (ROM), strength of the supraspinatus, and commonly used functional scores. VAS was used to evaluate pain at rest, at motion and at night. Patients were asked to use a 10 cm scale marked from “no pain” to “unbearable pain.” The average pain scores were also calculated and compared. Active and passive forward flexion and abduction of the bilateral

shoulders were measured with a goniometer, and the difference between the two shoulders was calculated. Strength of the supraspinatus was measured with a hand-held electronic scale (CHS, CAS, Yangju, Korea) and the difference between bilateral shoulders was calculated. The functional scorings included the American Shoulder and Elbow Surgeons (ASES) system, the Constant system, the University of California at Los Angeles (UCLA) system, the Disabilities of the Arm, Shoulder and Hand (DASH) system, the Simple Shoulder Test (SST), and the Shoulder Pain and Disability Index (SPADI). The radiologic factors included the measurement of fatty infiltration and muscle atrophy of the supraspinatus. MRI was performed with a 3.0-T scanner (Achieva 3.0-T, Philips Medical Systems, Eindhoven, Netherlands) with a dedicated shoulder coil. The arm was placed in a neutral position at the side of the body, and kept a consistent position throughout the study. All assessments were performed on T1 oblique sagittal images where the coracoid process and the scapular spine meet the scapular body. Fatty infiltration was measured with the Goutallier grade modified by Fuchs, and muscle atrophy was evaluated with a modified tangent sign and occupation ratio (7,24). MRI was assessed by two orthopedic surgeons under supervision of a musculoskeletal radiologist. The arthroscopic factors included rotator cuff tear size, rotator cuff retraction, and gross tendon quality. The anteromedial size and mediolateral retraction of tear were measured during the operation under direct arthroscopic visualization after minimal debridement of degenerated tendon edge according

to Cofield and Boileau.<sup>(1,6)</sup> The gross tendon quality was assessed using the three gross tendon grades based on gross appearance at time of surgery with respect to three criteria ;16 (1) Fraying over half the tendon thickness, (2) delamination, and (3) thinning of less than half the thickness of the normal rotator cuff, which is less than 6 mm. The gross tendon quality was graded as 'A' if none of these criteria were met, as 'B' if fraying or delamination was identified, and as 'C' if both fraying and delamination or thinning with or without the other two criteria were identified.

To assess the intra-observer and inter-observer reliability, Cohen's kappa statistic was used for each variable in the modified semi-quantitative grading scale for tendon degeneration, and the inter-class correlation coefficient (ICC) was used for the total degeneration score. To determine the association between demographic clinical, radiological, and arthroscopic factors and total degeneration score of rotator cuff tendon, Mann-Whitney test for 2 groups, Kruskal-Wallis test for multiple groups, and Spearman test for continuous variables were used. All analyses were performed by using SPSS version 13.0 (SPSS Inc, Chicago, IL, USA). P values of less than 0.05 were considered statistically significant.

## RESULTS

From July 2009 and October 2011, a total of 276 consecutive patients underwent arthroscopic surgery for rotator cuff disease at our institution. Among them, 183 were excluded ; 94 without tissue samples, 66 with partial-thickness rotator cuff tears,

Table 1. — Inter- and intra-observer reliability of the histological assessment

Variables	Inter-observer		Intra-observer	
	Kappa	p	Kappa	p
Fiber structure	0.239	0.039	0.617	< 0.001
Fiber arrangement	0.184	0.018	0.608	< 0.001
Rounding of the nuclei	0.300	0.004	0.244	0.007
Variations in cellularity	0.268	0.003	0.369	< 0.001
Increased vascularity	0.148	0.045	0.329	< 0.001
Decreased stainability	0.378	< .001	0.313	< 0.001
Hyalinization	0.174	0.057	0.288	< 0.001
Total degeneration score	ICC (95% CI)	p	ICC (95% CI)	p
	0.594 (0.256- 0.779)*	0.002	0.897 (0.692-0.875) *	< 0.001

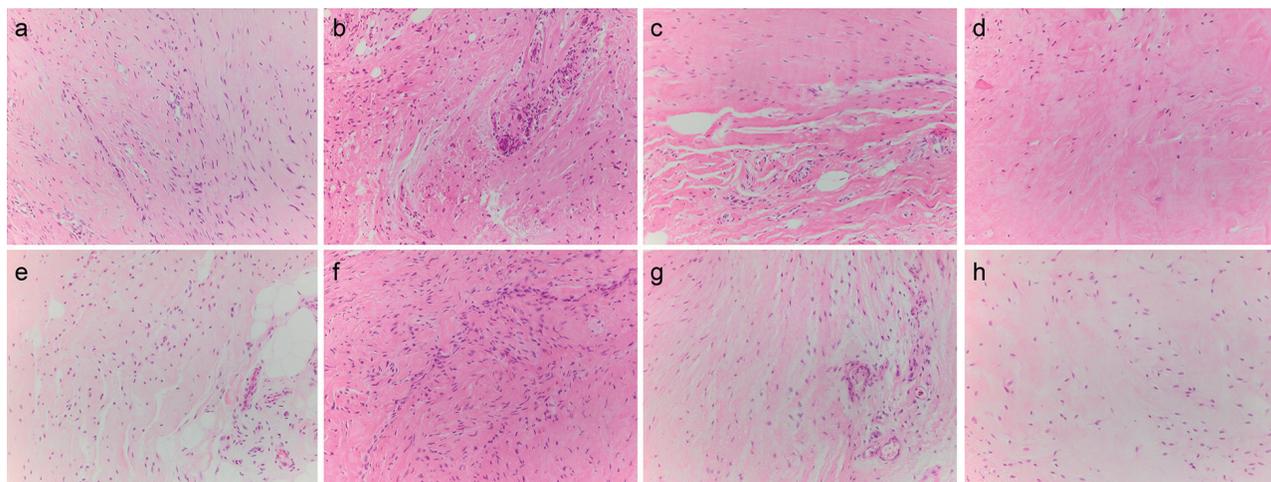
1 with isolated subscapularis tear, 7 with infection, 10 with bursitis, and 5 with calcific tendinitis. Finally, 93 patients (the fRCT group) were included in this study. The mean age of patients was  $61.7 \pm 8.5$  and around one third was male. Patients had a long history of shoulder pain, with an average of  $25.3 \pm 52.0$  months, and the symptoms were recently aggravated since about 4.5 months ago.

The histological assessment with the modified semi-quantitative grading scale showed high inter- and intra-observer reliability (Table 1). The interclass correlation coefficient (ICC) of the inter-observer and intra-observer reliability for the total tendon degeneration score was 0.594 ( $p = 0.002$ ) and 0.897 ( $p < 0.001$ ), respectively.

Most of tendon samples presented typical findings of severe tendon degeneration; loss of organized fiber structure and parallel arrangement,

fewer and rounded nuclei, increased cellularity and vascularity, reduced and paler H&E stainability, as well as some evidence of hyalinization (Fig. 1) (13,15). Then mean of total degeneration score was  $13.81 \pm 2.54$ . These results were consistent with previous studies (Table 2) (13,14,17). Among 7 variable of the grading scale, the mean scores of fiber structure, fiber arrangement, rounding of the nuclei and variations in cellularity were above 2.0, and those of increased vascularity, decreased stainability, and hyalinization were around.

Of variables in the demographic, clinical, radiological and arthroscopic categories, symptom duration was the sole variable that was significantly associated with the total degeneration score (correlation coefficient = 0.213,  $p = 0.041$ ), and all the other variables were not significantly associated with the total degeneration score (Table 3).



**Figure 1.** — Histological findings of the supraspinatus tendons from patients with a full-thickness rotator cuff tear

a. From a 60-year-old female with symptom duration of 3 months (original magnification :  $\times 200$ ). Fiber structure, 2 ; fiber arrangement, 2 ; rounding of the nuclei, 2 ; regional variations in cellularity, 3 ; increased vascularity, 3 ; decreased collagen stainability, 1 ; hyalinization, 0 ; total degeneration score, 12. b. From a 60-year-old female with VAS for average pain of 0.2 (original magnification :  $\times 200$ ). Fiber structure, 3 ; fiber arrangement, 3 ; rounding of the nuclei, 3 ; regional variations in cellularity, 3 ; increased vascularity, 3 ; decreased collagen stainability, 1 ; hyalinization, 0 ; total degeneration score, 16. c. From a 64-year-old female with Goutallier grade 1 (original magnification :  $\times 200$ ). Fiber structure, 3 ; fiber arrangement, 2 ; rounding of the nuclei, 3 ; regional variations in cellularity, 3 ; increased vascularity, 3 ; decreased collagen stainability, 2 ; hyalinization, 0 ; total degeneration score, 16. d. From a 39-year-old male with a small tear (original magnification :  $\times 200$ ). Fiber structure, 3 ; fiber arrangement, 3 ; rounding of the nuclei, 3 ; regional variations in cellularity, 1 ; increased vascularity, 0 ; decreased collagen stainability, 1 ; hyalinization, 3 ; total degeneration score, 14. e. From a 54-year-old male with symptom duration of 36 months (original magnification :  $\times 200$ ). Fiber structure, 3 ; fiber arrangement, 3 ; rounding of the nuclei, 3 ; regional variations in cellularity, 2 ; increased vascularity, 3 ; decreased collagen stainability, 2 ; hyalinization, 0 ; total degeneration score, 16. f. From a 61-year-old female with VAS for average pain of 8.7 (original magnification :  $\times 200$ ). Fiber structure, 2 ; fiber arrangement, 3 ; rounding of the nuclei, 3 ; regional variations in cellularity, 3 ; increased vascularity, 2 ; decreased collagen stainability, 0 ; hyalinization, 0 ; total degeneration score, 13. g. From a 65-year-old female with Goutallier grade 3 (original magnification :  $\times 200$ ). Fiber structure, 3 ; fiber arrangement, 2 ; rounding of the nuclei, 3 ; regional variations in cellularity, 3 ; increased vascularity, 3 ; decreased collagen stainability, 1 ; hyalinization, 0 ; total degeneration score, 15. h. From a 61-year-old female with a massive tear (original magnification :  $\times 200$ ). Fiber structure, 3 ; fiber arrangement, 3 ; rounding of the nuclei, 3 ; regional variations in cellularity, 3 ; increased vascularity, 0 ; decreased collagen stainability, 2 ; hyalinization, 1 ; total degeneration score, 15.

Table 2. — Histological assessment of the supraspinatus tendon degeneration in patients with a full-thickness rotator cuff tendon

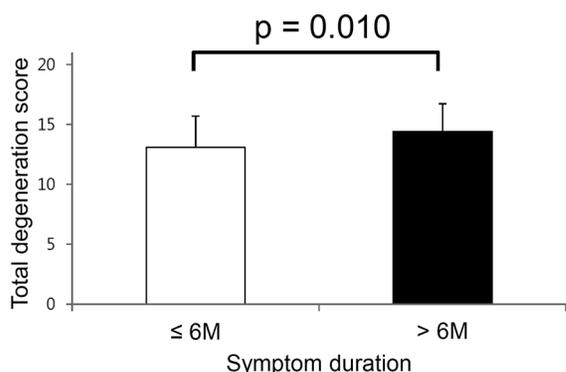
Variables	Score				Mean
	0	1	2	3	
Fiber structure	0	5	13	75	2.75±0.545
Fiber arrangement	1	12	17	63	2.53±0.760
Rounding of the nuclei	0	5	17	71	2.71±0.563
Variations in cellularity	1	22	23	47	2.25±0.855
Increased vascularity	36	19	14	24	1.28±1.228
Decreased stainability	25	39	18	11	1.16±0.959
Hyalinization	44	13	16	20	1.13±1.227
Total degeneration score					13.81±2.54

fRCT: full-thickness rotator cuff tear

Table 3. — Association of the demographic, clinical, radiological, and arthroscopic factors in patients with a full-thickness rotator cuff tear with the total degeneration score of the supraspinatus tendon

Category	Factor	Value	Correlation coefficient	p
<b>Demographic</b>	Mean Age (years)	61.73 ± 8.506	-0.170	0.104
	Gender (m:f)	31:62	n.a.	0.342
	Symptom duration (months)	25.28 ± 51.954	0.213	0.041
	Symptom aggravation (months)	4.5 ± 7.34	0.158	0.184
	Dominance (%)	72 (77.4%)	n.a.	0.220
<b>Clinical</b>	VAS pain at rest	4.07 ± 2.47	-0.157	0.134
	VAS pain at motion	6.06 ± 2.45	-0.055	0.598
	VAS pain at night	5.72 ± 2.73	-0.036	0.732
	VAS at average	5.27 ± 2.01	-0.086	0.415
	Difference of active forward flexion (degree)*	38.49 ± 44.25	0.021	0.844
	Difference of active abduction (degree)*	40.00 ± 50.36	-0.036	0.734
	Difference of passive forward flexion (degree)*	25.10 ± 33.17	-0.021	0.843
	Difference of passive abduction (degree)*	28.60 ± 37.17	-0.071	0.501
	Difference of supraspinatus strength (lbs)*	4.29 ± 3.8	-0.048	0.649
	ASES	43.95 ± 18.55	-0.047	0.681
	Constant	44.45 ± 17.94	-0.004	0.972
	UCLA	14.72 ± 5.17	-0.007	0.950
	DASH	50.65 ± 20.69	0.102	0.373
	SST	4.23 ± 2.89	-0.115	0.318
SPADI	54.55 ± 20.97	0.030	0.795	
<b>Radiologic</b>	Fatty infiltration grade (0:1:2:3:4)	3:29:37:17:7	n.a.	0.896
	Modified tangent sign (1:2:3)	61:25:7	n.a.	0.655
	Occupation ratio grade (A:B:C)	33:47:13	n.a.	0.654
<b>Arthroscopic</b>	Anteroposterior size (mm)	28.52 ± 17.87	0.011	0.914
	Mediolateral size (mm)	17.59 ± 9.93	-0.023	0.825
	Cofield stage (S:M:L:MSV)	10:49:21:13	n.a.	0.251
	Boileau stage (I:II:III:IV)	40:26:11:16	n.a.	0.608
	Gross tendon grade (A:B:C)	25:58:10	n.a.	0.150

n.a. : not available



**Figure 2.** — The mean total degeneration scores of patients with a full-thickness rotator cuff tear with respect to symptom duration of 6 months.

And the mean of the total degeneration score in patients with symptom duration of 6 months or less was significantly lower with that in patients with symptom duration longer than 6 months,  $13.1 \pm 2.6$  and  $14.4 \pm 2.3$ , respectively ( $p = 0.010$ ) (Fig. 2).

## DISCUSSION

The results of the study showed, among potential factors in the demographic, clinical, radiological and arthroscopic categories, that the duration of symptoms was associated with the degree of tendon degeneration, and that the mean total degeneration score in patients with symptom duration of 6 months or less was significantly lower with that in patients with longer than 6 months. These results indicate that once fRCT is diagnosed, better results can be achieved with early rotator cuff repair, possibly within 6 months of symptom onset, by avoiding further deterioration of tendon degeneration.

There have been some reports that studied factors associated with tendon degeneration. Hashimoto et al reported that degenerative changes of tendon were not varied with age and the size and type of tears, while degenerative changes such as chondroid metaplasia and calcification were found in patients with the longer duration of symptoms (11). Chillemi et al also reported direct correlation between tendon hyperplasia and duration of symptoms (4). Warner et al described that the gross tendon quality was associated with the duration of symptoms, and any delay in the proper diagnosis has a consequence of poor prognosis (24). These results are consistent with

our results, suggesting that early intervention after onset of symptom would result in more favourable outcomes.

The patient's age has been regarded as an important factor in the outcome of rotator cuff repair, and generally it is known that aging has a negative effect on the outcome (12). Although aging can cause functional and structural changes in the tendon, and about one third of general population is known to show signs of tendon degeneration, there is little evidence of association between age and tendon degeneration (11,22). The results of this study are consistent with previous studies. Therefore, potential inferior outcomes after rotator cuff repair in elderly patients might be based on factors such as tendency to have a larger tear, decreased bone quality and comorbidities (23).

The results of this study showed that the degree of tendon degeneration was not associated with the size of tear. We assumed that it was because fRCT was already at the end stage of rotator cuff disease regardless of the tear size. A recent study confirmed that lesser degree of tendon degeneration existed in earlier stage of rotator cuff disease (14).

However, these results are contrary to previous histological studies. Mathews et al showed that degenerative changes became more pronounced as the tear size increased to large and massive tear (19). Tilley et al also reported that degeneration progressed as tear size increased (22). We assumed that the diversity of results would rise from differences in the histological evaluation system, and the harvesting location of tissue samples (19,22).

We believed that tendon degeneration was not only associated with the progress of rotator cuff disease, but also related with healing of rotator cuff tear after repair. Matthews et al reported greater reparative responses in terms of increased fibroblast cellularity, cell proliferation and a thickened synovial membrane in intact rotator repair than in (18). Chillemi et al reported that neoangiogenesis, hypertrophy/hyperplasia, and disarray were associated with healing, while chondral metaplasia was negatively associated. They suggested that histological evaluation should be employed routinely to assess the tissue quality to predict future clinical evolution at the time of repair (4). The

modified semi-quantitative grading scale used in this study failed to show any difference in the degree of tendon degeneration in patients with a fRCT, but it is worth continuing efforts to assess tendon degeneration, predict outcomes, and prepare evolution.

There are limitations to this study. First, the modified the semi-quantitative grading scale would not adequately reflect degenerative changes of rotator cuff tendon. Second, there were no evaluation of myxoid, lipid, or calcific degeneration in this system.

### CONCLUSION

This study showed that tendon degeneration significantly progressed 6 months after the onset of symptoms, and suggested early intervention to avoid further deterioration of tendon degeneration.

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