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Is the long head of the biceps related to anterior shoulder pain? A histopathological study

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ABSTRACT

Objectives. Pathologies of the long head of the biceps have been viewed as a source of anterior shoulder pain and disability. Thus, we performed a histopathological and immunohistochemical examination of the biceps tendon with regard to the neuronal structure, the number of mechano-receptors and immunohistochemical types, to investigate the relationship of these factors with pain. *Materials and Methods*. This is a single-center prospective comparative study, on 11 patients divided into Group A (n=5) and Group B (n=6). Patients who underwent arthroplasty due to Neer type-4 proximal humeral fractures were selected as the control group (Group A). Group B consisted of patients with chronic anterior shoulder pain who underwent subpectoral biceps tenodesis during arthroscopic rotator cuff repair. The long head of biceps tenodesis was performed in all patients. *Results*. Hyalinization in the tendon was observed in 2 patients of group B. Chondroid degeneration was found in one patient with hyalinization. Inflammation, calcification, or matrix formation were not detected in any patients. Normal nerve fibers were observed around the tendon in 9 patients with S-100 immunohistochemical staining. In 1 patient, weak staining was observed in the nerve sheath with EMA immunohistochemical stain. No tactile body was detected. *Conclusions*. We did not observe any histo-pathological findings that could be considered the cause of pain in the two groups. Biomolecular and biomechanical studies, in addition to microscopic studies, are needed to explain why the biceps is a potential source of pain.

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Introduction

The long head of the biceps tendon (LHB) is in a unique anatomical position in the bicipital groove. Tendon stabilizes the anterosuperior rotator cuff by attaching it to the glenoid labrum [1,2]. The biomechanical studies show that LHB stabilizes the glenohumeral joint and decreases the humeral head's anterior, superior, and/or inferior translation [3-5].

LHB pathologies have been regarded as a source of anterior shoulder pain and disability because repeated movements and excessive overuse may cause thickening of the synovial sheath, thus squeezing the tendon in the bicipital groove [6,7]. However, only some patients with anterior shoulder pain have biceps tendon pathology arthroscopically [8,9]. Whatever the cause, it is known that biceps tenotomy or tenodesis can successfully reduce pain [10-12], but the mechanism of this positive effect of tenotomy or tenodesis is still unknown [13,14].

The effect of mechanoreceptors should also be kept in mind when explaining the relationship between biceps and pain. Mechanoreceptors aim to increase joint positional awareness, but this may cause pain with inflammation of the glenohumeral joint capsule. The number and type of mechanoreceptors included in the biceps long head are unclear. How much the proprioception of the shoulder joint is affected after biceps long head tenotomy/tenodesis is also an unexplained issue [15-17].

Our study performed a histopathological and immunohistochemical examination of the biceps tendon that we sacrificed in shoulder arthroplasty and multi-part proximal humerus fracture surgeries. We aim to compare the samples of the biceps long head of patients with biceps tendinopathy and those without shoulder pathology. We aimed to determine possible neuronal structure differences, the number of mechanoreceptors and types with the immunohistochemical examination, to verify relationship of these factors to pain.

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Materials and Methods

This single-center prospective comparative study was conducted between 2018 and 2021. All participants were informed about the study and signed and returned informed consent forms. The ethical board approved the study with the number 147-34. All reported research involving "Human beings" was conducted by the principles set forth in the Helsinki Declaration 2008.

Eleven patients included in the study were divided into two groups: Group A (n=5) and Group B (n=6). Patients who underwent arthroplasty due to Neer type-4 proximal humeral fractures were selected as the control group, which was noted as Group A. The average patient age was 68 years (57-79 years). Patients with chronic shoulder pain, rheumatologic disease, or shoulder joint surgery for any reason before trauma were not included in group A patients. Operations were performed by the same surgeon experienced in this field. During the shoulder arthroplasty surgery, long head of biceps tenodesis was performed in all patients as a standard procedure. Proximal parts of the long head of the biceps were placed in sample containers for histopathological and immunohistochemical examination.

Group B consisted of patients who underwent subpectoral biceps tenodesis during arthroscopic rotator cuff repair. All patients had chronic anterior shoulder pain before presentation. The average patient age was 53 years (48-62 years). Subpectoral biceps tenodesis was performed by the same surgeon. The diagnosis of biceps tendinopathy was made by a physical examination in addition to clinical and imaging evaluation with MRI. The patients had sensitivity with palpation on the bicipital groove, and the Speed and Yergason tests were positive. Patients with rheumatological diseases, a history of surgery related to the shoulder joint, patients who received corticosteroid injection around the bicipital groove or into the joint, as well as patients who refused to participate were excluded from the study.

Samples taken from both groups were examined under a light microscope by the same pathologist. Samples were prepared after formalin fixation for at least 24 hours by taking slices from both ends and middle. Hematoxylin-eosin (H&E) staining was applied after samples were prepared in 8-micron sections. Inflammation, degeneration, calcification, matrix, and hyalinization formation were investigated in tendon fragments.

5-micron sections were taken from the pieces and deparaffinized for S-100 and EMA staining in the immunohistochemical study. Antigen retrieval procedures were performed, and S-100 and EMA antibodies were applied. A fully automated immunohistochemical staining machine performed immunohistochemical staining steps. It investigated whether the tendon fragments contain neuronal proliferation and mechanoreceptors.

Results

Hyalinization in the tendon was observed in 2 patients belonging to group B. Chondroid degeneration was found in one patient with hyalinization (Figure 1).

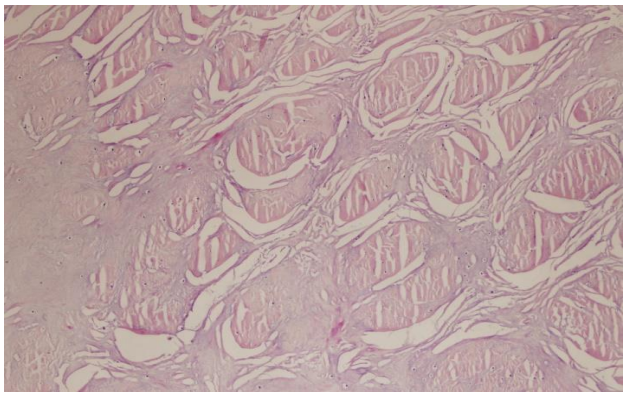

Figure 1. Hyalinization and chondroid degeneration at 10x staining with Hematoxylin-eosin (H&E)

Inflammation, calcification, or matrix formation were not detected in any patients. Normal nerve fibers were observed around the tendon in 9 patients with S-100 immunohistochemical staining. In 1 patient, weak staining was observed in the nerve sheath with EMA immuno-histochemical stain (Figure 2). No tactile body was detected.

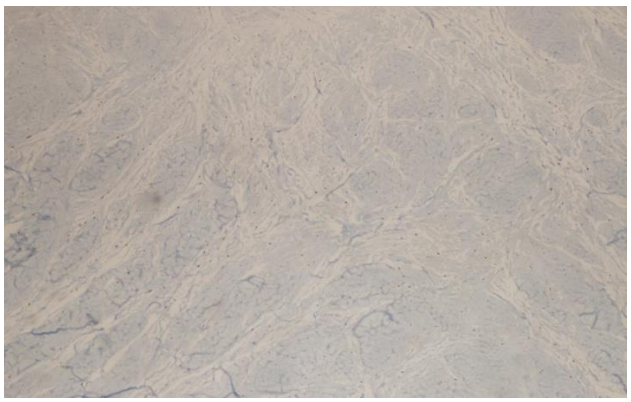

Figure 2. Normal tendon tissue at 10x staining with S-100 immunohistochemical staining (no positive staining observed)

Discussion

We compared the biceps tendon samples of patients with chronic shoulder pain and the samples of acute trauma patients with no shoulder pathology (histopathological and immunohistochemical). The most important finding of our study is that there are no histopathological and immunohistochemical differences in the examinations of Group A, which we determined as the control group, and Group B, which is the study group. Another important finding in our study is that neither mechanoreceptor formation was found with hematoxylin-eosin, S-100 staining, and EMA staining in the proximal biceps samples in both groups.

The long head of the biceps is considered a pain source for the shoulder. However, there is insufficient evidence to

explain the isolated pathology or its contribution to pain in complex pathologies [18-20]. Many immunohistochemical and histological studies are conducted to reveal the structural changes in the tendon and their effect on pain development [21-23]. The long course of the biceps tendon and intra-articular and extra-articular parts make it difficult to determine the exact cause of the pain.

Studies are conducted to investigate the structural changes in biceps tendinopathies to explain the cause of pain. These studies aim to determine whether the cause is acute inflammation or chronic degeneration. It was reported that the pathological processes were not acute inflammation but chronic degeneration in the examination of biceps samples taken from patients with biceps long head tendinopathy both in the intra-articular and extra-articular part of the biceps [24-26]. No signs of acute inflammation were found in the histopathological examinations performed in our study. Disorganized collagen, tenocyte enlargement, increased roundness of tenocyte nuclei, or myxoid degenerative changes are associated with pain and show chronic degeneration. Histopathological changes related to chronic degeneration were not observed in Group A and B. We did not notice any histopathological findings that could be considered the cause of pain in both groups. In this respect, our study differs from studies claiming that the cause of pain is chronic degeneration.

The possible causes for these microscopic findings may be interpreted in two ways. First, tenodesis operations may have been performed before degenerative changes occurred. Our patients in group B were relatively younger. Biceps tenodesis may have been performed before the process that led to microscopic structural changes in the samples. Secondly, there is no consensus about the absolute indications of biceps long head tenodesis. The fact that rotator cuff injury or other structures with which the biceps long head is in contact during the long anatomical course may also cause pain on their own. In support of our study, Singaraju et al. stated that they could not find a significant correlation between the histopathological changes of the long head of biceps and shoulder pain [6]. The fact that tendon degeneration findings have also been shown in cadavers without shoulder problems and in acute trauma cases other than chronic cases may suggest that the cause of the pain is too complex to be explained by only histological results [23]. Tosounidis et al. examined the long head of biceps tendon samples of patients who underwent arthroplasty after acute trauma and cadaveric long head of biceps tendon samples. They reported results in favor of neuronal differentiation with histopathological changes [23]. They concluded that the biceps could be a source of pain, and arthroplasty for biceps tenotomy/ tenodesis should routinely be performed at proximal humerus fractures treatment.

Contrary to Tosounidis et al. [23], we did not find any neuronal differentiation in both groups after S-100 and Ema staining. We think that Tosounidis et al. chose acute trauma patients without biceps-related pain as the study group and said, according to the histopathological results, that the biceps may be the cause of pain due to their misinterpretation of the results. Histopathological changes found in their trauma patients without a known anterior shoulder pain can be misinterpreted as pain and histopathology not being correlated. The conclusion that can be drawn from this study is that anterior shoulder pain, which is thought to be caused by the biceps, can occur when more than one cause is found either simultaneously or separately.

We have two limitations regarding our study. The entire biceps long head tendon of the patients could not be examined. We examined only the biceps tendon's proximal 3-4 cm portion, approximately 2 cm proximal to the musculotendinous junction. However, examining the entire biceps is practically impossible except for cadaver studies. Another limitation of our study is the number of cases. Perhaps a new study with a control group that can be formed with as many cadavers as possible and a larger number of study groups with anterior shoulder pain will build more information on what we have learned in this article. The strongest part of our study is the painting variety of the sections. Along with routinely applied hematoxylin-eosin staining, S-100 and EMA stains were used in our study.

The absence of significant histopathological differences between the two groups suggests that we should change our perspective to explain the mechanisms that cause pain. Different biomolecular, biomechanical, and anatomical studies will reveal the reason exactly and examine microscopic structural changes. Biomolecular and biomechanical studies are needed to evaluate the biceps tendon and its associated anatomical structures (rotator cuff, coracohumeral ligament, glenoid superior labrum, capsule, etc.), if possible, throughout its anatomical course.

Guanche et al. detected Golgi tendon organ, Pacinian corpuscular, and Ruffini terminations in the superior, middle, and inferior glenohumeral ligaments. They detected only free nerve terminations in the biceps tendon and labrum [27]. They concluded that neural elements correlate with the specific functions of some glenohumeral ligaments. Perhaps that the disruption of this mixed relationship of these neuronal elements and glenohumeral ligaments can be considered the cause of pain. This is also an issue that needs to be studied further.

Unlike the studies of Guanche et al., free nerve endings and mechanoreceptors were not found in either group in our study. This may be because Guanche et al. took samples from the mid-biceps tendon [27]. According to another result of our study, the long head of the biceps does not

contain mechanoreceptors. It can be interpreted that tenodesis surgeries do not affect shoulder proprioception based on this result. However, we think that clinical studies should support this inference.

Conclusions

As a result, we suggest that the causes of pain in the biceps are not related to the histological structure and changes in the biceps. Biomolecular and biomechanics studies are required besides microscopic structural studies to explain why the biceps are a potential source of pain. According to our other result in our study, no mechanoreceptor was found in our examinations of the long head of biceps samples. According to this result, we think that biceps tenotomy or tenodesis will not impair shoulder proprioception. However, this idea needs to be supported by other clinical studies.

Authors' contribution

All authors contributed to the study's conception and design. ATP, BK, and YI performed material preparation and data collection. AK, AY, and AK performed analysis. BK wrote the first draft of the manuscript and all authors commented on previous versions of the manuscript.

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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