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The effect of altered loading following rotator cuff tears in a rat model on the regional mechanical properties of the long head of the biceps tendon

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Abstract

Biceps tendon pathology is a common clinical problem often seen in conjunction with rotator cuff tears. A previous study found detrimental changes to biceps tendons in the presence of rotator cuff tears in a rat model. Therefore, the objective of this study was to utilize this model along with models of altered loading, to investigate the effect of altered loading on the initiation of these detrimental changes. We created supraspinatus and infraspinatus rotator cuff tears in the rat and followed these tears with either increased or decreased loading. Mechanical properties were determined along the length of the biceps tendon four and eight weeks following injury. At the insertion site, stiffness increased with decreased loading while detrimental changes were seen with increased loading 4 weeks following detachments. Increased loading resulted in decreased mechanical properties along the entire tendon length at both timepoints. Decreased loading resulted in both increased and decreased tendon properties at different regions of the tendon at four weeks, but by eight weeks, there were no differences between decreased loading and detachment alone. We could not conclude where changes begin in the tendon with altered loading, but did demonstrate that regional differences exist. These results support that there is an effect of altered loading, as decreased loading resulted in variable changes at 4 weeks that were no different from detachment alone by 8 weeks, and increased loading resulted in detrimental properties along the entire length at both 4 and 8 weeks.

Keywords

biceps; rotator cuff; tendon mechanics; animal model; altered loading

1. Introduction

Damage to the long head of the biceps tendon is a common clinical condition that has often been identified as a source of shoulder pain. Although proximal long-head biceps tendon ruptures account for 96% of all biceps tendon ruptures (Harwood and Smith, 2004), they rarely occur as isolated injuries and are often found in conjunction with pathologic

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CONFLICT OF INTEREST

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conditions of the rotator cuff. Specifically, biceps tendon damage has been found in conjunction with rotator cuff tears, and this damage is thought to increase with increasing tear size (Chen et al., 2005; Murthi et al., 2000). Considering that tears of the rotator cuff are thought to occur in up to 50% of the population (Gomoll et al., 2004), damage to the long head of the biceps tendon is a prevalent clinical problem.

Although the function of the biceps tendon at the elbow is well-characterized, its function, even in a normal shoulder, is not. The general consensus is that it is a weak shoulder flexor that may also play a role as a humeral head depressor and glenohumeral stabilizer (Kumar et al., 1989; Warner and McMahon, 1995). However, the possible role of the biceps tendon as a humeral head depressor at the shoulder is controversial, as several EMG studies have shown no biceps muscle activity during various shoulder motions (Yamaguchi et al., 1997; Levy et al., 2001). Although this role as a humeral head depressor is controversial, it is this proposed role that is thought to be a significant contributor to changes seen in the tendon in the presence of a cuff tear, where one or more of the more significant superior stabilizers (supraspinatus and/or infraspinatus) would not be present. Clinical studies support this theory, as several have found that tear size correlates with advanced biceps tendon lesions (Chen et al., 2005; Murthi et al., 2000). Specifically, Chen et al found that the greatest incidence of biceps tendon lesions occurred in the presence of a tear involving both the supraspinatus and infraspinatus. However, not all studies have found pathology present (Carpenter et al., 2005; Yamaguchi et al., 1997) and there is still some debate over the role of the biceps tendon at the shoulder following a rotator cuff tear.

What remains unknown is the mechanism responsible for these pathologic changes and while clinical and cadaveric studies can tell us if pathology exists, they are unable to address the underlying causes or monitor the pathological process with time. In clinical studies, it is possible to biopsy a small portion of the biceps tendon during a rotator cuff repair surgery. However, the entire tendon cannot be removed, and therefore, regional differences cannot be examined. There is also difficulty in isolating a patient population with the same tear type and size, history, as well as surgeries performed at the same time post-tear. While one can harvest the entire tendon for analysis from a cadaveric shoulder with a rotator cuff tear, little information exists on how long the tear has been present. In addition, cadaveric studies do not allow investigation of the in vivo time course of pathological changes. A previous study in our lab used the established rotator cuff rat model to investigate the effect of these tears on the long-head of the biceps tendon. In this study, we found that the presence of rotator cuff tears led to a biceps tendon with increased area and eventually decreased modulus (Peltz et al., 2009). We also found that two tendon tears resulted in more pathologic changes than a one tendon (supraspinatus) tear, and that a combination of the supraspinatus and infraspinatus was worse than a supraspinatus and subscapularis combination.

Therefore, the objective of this study was to use this established rat model to investigate the effect of altered loading on the biceps tendon following rotator cuff tears in order to begin to elucidate the mechanism by which these pathologies occur. Our hypotheses were that: 1) changes will begin near the insertion site and progress along the tendon length with time, 2) increased loading will result in further detrimental changes, and 3) decreased loading will result in improved tendon properties to those in the presence of a rotator cuff tear alone.

2. Methods

2.1 Injury model

Fifty-nine Sprague-Dawley rats (Charles River, 400–450g) were used in this study approved by the University of Pennsylvania Institutional Animal Care and Use Committee. Rats were divided into 3 groups sacrificed at 4 and 8 weeks after surgical tendon detachments:

supraspinatus+infraspinatus tendon detachment only (n=10 at 4 wks, n=10 at 8 wks), supraspinatus+infraspinatus tendon detachment followed by decreased loading (n=10 at 4 wks, n=10 at 8 wks), and supraspinatus+infraspinatus tendon detachment followed by increased loading (n=10 at 4 wks, n=9 at 8 wks). In all groups, a unilateral surgery was performed to sharply detach the rotator cuff tendons from their bony insertion, as previously described (Perry et al., 2009). Briefly, with the arm in external rotation, a 2 cm skin incision was made followed by blunt dissection down to the rotator cuff musculature. The rotator cuff was exposed, and the tendons were visualized at their insertion on the humerus. The supraspinatus was first separated from the other rotator cuff tendons before sharp detachment at its insertion on the greater tuberosity. The infraspinatus tendon was then detached in the same manner. Any remaining fibrocartilage at the insertion was left intact, and detached tendons were allowed to freely retract without attempt at repair, creating a gap ~4 mm from their insertion sites. The overlying muscle and skin were closed. Animals in the supraspinatus and infraspinatus detachment only group (SI Only) were then allowed unrestricted cage activity. Animals in the post-detachment decreased loading group (SI +DEC) were immediately immobilized post-operatively using Vetrap (Sarver, Peltz). In order to achieve increased loading on the long head of the biceps tendon following rotator cuff detachments, animals in the post-detachment increased loading group (SI+INC) had an additional surgical detachment of the short-head of the biceps tendon immediately following rotator cuff detachments. Additionally, these same animals were prescribed a moderate treadmill running protocol (10 m/min) beginning 3 days after surgery. This protocol began initially at 10 minutes on the first day and increased over a 2 week period to 1 hour/day and continued at this time until the end of the study at 4 or 8 weeks.

2.2 Mechanical testing

After sacrifice, the scapula and the long-head of the biceps tendon were removed. The associated muscle was removed, and the tendons were fine dissected under a microscope. Five Verhoeff stain lines were then placed along the length of each tendon denoting the insertion site (0–1.5mm), the portion of the tendon in the intra-articular space (1.5–3.5mm), and the portion in the bicipital groove (3.5–8.5mm). A fifth stain line was placed at 11.5mm to identify grip placement, and these stain lines were used to determine the distribution of strain along the length of the tendon. These positions were determined using histology to identify the length of the insertion site and gross dissections to determine the portion in the bicipital groove (Peltz et al., 2009). Although the insertion of the biceps tendon anatomically is at the elbow, for the purposes of this study, the biceps origin at the glenoid is defined as the biceps inserting on the glenoid and is referred to as the “insertion site”. Tendon geometry was measured in each tendon portion using a laser based system (Favata, 2006).

For biomechanical testing, the scapula was embedded in a holding fixture using polymethylmethacrylate (PMMA). The holding fixture was inserted into a specially designed testing fixture. The proximal end of the tendon was then held at the fifth stain line (11.5mm) in a screw clamp lined with fine grit sandpaper. The specimen was then immersed in a 39°C PBS bath, preloaded to 0.1N, preconditioned for 10 cycles from 0.1N to 0.5N at a rate of 1%/sec, and held for 300sec. Immediately following, a stress relaxation experiment was performed by elongating the specimen to a strain of 4% at a rate of 5%/sec (0.575 mm/sec) followed by a 600sec relaxation period. Specimens were then returned to the initial preload displacement and held for 60 seconds, and ramp to failure was then applied at a rate of 0.3%/sec. Using the applied stain lines, local tissue strain in each region of the tendon was measured optically with a custom program (MATLAB). Elastic properties, such as stiffness and modulus, were calculated using linear regression from the visually determined linear region of the load-displacement and stress-strain curves, respectively.

2.3 Statistical analysis

Significance was assessed between groups at each time point using one-way ANOVAs with Bonferroni post-hoc comparisons. To correct for the number of comparisons, significance was set at $p < 0.017$ ($0.05/3$) and trends at $p < 0.033$ ($0.1/3$).

3. Results

3.1 Four week results

At the insertion site, area increased with increased loading 4 weeks following a supraspinatus+infraspinatus tear (Figure 1). Also, with increased loading, modulus (Figure 2) and stiffness (Figure 3) decreased at the insertion site. With decreased loading, there was an increase in stiffness at the insertion site (Figure 3). In the intra-articular space, modulus and stiffness were decreased with increased loading (Figures 2 and 3, respectively). Decreased loading resulted in increased area and decreased modulus in the intra-articular space. Finally, in the bicipital groove, modulus and stiffness decreased with increased loading. With decreased loading, area increased in the bicipital groove.

3.2 Eight week results

No differences in area were seen between groups 8 weeks post detachment. However, eight weeks following a supraspinatus+infraspinatus tear, modulus (Figure 4) and stiffness (Figure 5) were decreased at all locations (insertion site, intra-articular space and bicipital groove) with increased loading. No differences between decreased loading and detachment only were found at any tendon location at 8 weeks.

4. Discussion

Our first hypothesis was that tendon changes with alterations in loading would begin at the insertion site and progress along the tendon length with time. Unfortunately, the results of this study do not allow us to conclude where tendon changes begin. After 4 weeks of altered loading, detrimental changes were seen with increased loading, and increased stiffness was seen with decreased loading at the insertion site. Detrimental changes were also seen with increased loading along the entire tendon length. Also, the results regarding decreased loading differed at other locations, while increased stiffness was seen at the insertion site. Increased area and decreased modulus were found in the intra-articular space and increased area in the bicipital groove. After 8 weeks of altered loading, the results were more consistent, with decreased properties along the entire tendon length with increased loading and no differences between decreased loading and detachment alone at any location. Additionally, the majority of tendon failures during mechanical testing occurred at the tendon-grip interface, therefore failure properties could not be reported.

While the location at which changes first occur was not determined, it was shown that regional differences do exist. While the changes were more uniform after 8 weeks, earlier changes varied by tendon location. In our study, if only the insertion site at 4 weeks had been evaluated, the results regarding decreased loading would have been inconclusive, as only increased stiffness was found; on the other hand, if only the intra-articular space had been examined at that time point, it would have been concluded it was harmful, as decreased modulus and increased area were found. It is also possible that differences may be missed if the entire tendon is analyzed, as the modulus has been found to vary along the length, making an “average modulus” a parameter that may have very high variations. This may help to explain some of the conflicting results of other studies investigating the effect of rotator cuff tears on pathology of the long head of the biceps tendon. For example, one study found no differences in area or material properties in biceps tendons from cadaveric

shoulders with and without rotator cuff tears (Carpenter et al., 2005). However, in that study, only stamped central portions of the tendons were tested. Conversely, another recent study looked separately at the intra- and extra-articular portions of tenotomized biceps tendons from shoulders with rotator cuff tears (Joseph et al., 2009). In this study, the intra-articular portion of the tendon had a significantly higher proteoglycan content, decreased organization and increased expression of collagen III and MMP-1 and 3 compared to the extra-articular portion. While these results were not mechanical in nature, it has been shown that differences in composition and organization can affect mechanical behavior and may influence some of the results seen here.

Results regarding the effect of increased loading support our second hypothesis that increased loading would result in further detrimental changes compared to detachment alone. At both 4 and 8 weeks, significantly decreased modulus and stiffness were found at the insertion site, in the intra-articular space and in the bicipital groove. Increased area was also shown at the insertion site at 4 weeks. In a previous study (Peltz et al., 2009), we found increased area 4 weeks following a supraspinatus+infraspinatus tear but did not find decreased modulus until 8 weeks following detachment. Changes in stiffness were not observed in that study. From these results, insight into the role that increased loading may play as a mechanism for biceps damage in the presence of a rotator cuff tear can be obtained. Future studies will continue to elucidate this role by examining histological, organizational and compositional changes at these and other timepoints.

Our third hypothesis was that decreased loading would result in improved mechanical properties compared to supraspinatus+infraspinatus detachment alone. After 4 weeks of altered loading, conflicting results were found in different portions of the tendon. At the insertion site, stiffness was increased with decreased loading compared to detachment alone. In the intra-articular space, detrimental changes were seen with increased area and decreased modulus. Finally, area increased in the bicipital groove, which is most likely a negative change. However, at 8 weeks, there were no differences between the decreased loading and detachment alone groups. This may be due to initial detrimental changes in tendon properties that are now attempting to return to normal with increased immobilization time. Although investigating the effect of immobilization on tendon to bone healing, other studies in our lab have shown that it can take up to 16 weeks of immobilization for increased mechanical properties to result (Gimbel et al., 2007; Thomopoulos et al., 2003). While a longer timepoint was not included in this study, future studies will investigate compositional and organizational changes in these tendons, which we found to precede changes in mechanical parameters in our tendon to bone healing studies (Gimbel et al., 2007; Thomopoulos et al., 2003).

The rotator cuff tendon tears in this study were made acutely, which may be considered a limitation of this model. However, biceps tendon pathology occurs over time without surgical injury to the tendon itself. Additionally, detachment of the short-head of the biceps tendon is not common clinically and therefore this method of increased loading would not likely occur in patients. However, short-head detachment was used in this study specifically as part of our model to increase the load on the biceps tendon and therefore we feel it is appropriate for this study. The actual amount of load that was added to or taken away from the tendon in our altered loading scenarios was not determined, although we are confident from preliminary studies that the loads on the tendon are truly decreasing and increasing. Lastly, the majority of biceps tendons in this study failed at the grip interface, and therefore failure properties could not be evaluated. Future directions of this work include immunohistochemical staining in order to determine compositional changes that may be occurring in these tendons at these and earlier time points. Additionally, we will be

evaluating the regional collagen organization and histological characteristics (cellularity, cell shape) of these tendons.

In summary, it was shown that increasing the load on the biceps tendon following a rotator cuff tear causes detrimental changes in mechanical properties along the entire tendon length. This begins to implicate altered loading as a possible mechanism for biceps tendon damage in the presence of a rotator cuff tear. Our results regarding the effect of decreased loading were less clear, but promising; there were changes at 4 weeks, but by 8 weeks, there were no differences from detachment alone. Lastly, although it cannot be concluded at which location changes begin, it was shown that regional differences do exist and are important in biceps tendon studies.

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Figure 1.

Area changes with altered loading 4 weeks following rotator cuff detachments. (*sig from SI only, #trend from SI only)

Figure 2.

Modulus is decreased at all locations with increased loading and in the intra-articular space with decreased loading 4 weeks following detachments. (*sig from SI only, †sig from SI +DEC, ‡trend from SI+DEC)

Figure 3.

Four weeks following detachments, stiffness is decreased with increased loading at all locations and increased with decreased loading at the insertion site. (*sig from SI only, †trend from SI only, #sig from SI+DEC)

Figure 4.

Eight weeks following detachments, modulus is decreased with increased loading at all tendon locations. (*sig from SI only, #trend from SI only, †sig from SI+DEC)

Figure 5.

Stiffness is decreased at all tendon locations with increased loading compared to both detachment only and decreased loading 8 weeks following detachments. (*sig from SI only, #trend from SI only, †sig from SI+DEC, ‡trend from SI+DEC)