INTRODUCTION:

Rotator cuff tears (RCT) are the most common tendon injury seen in orthopedic patients. Although small tears are amenable to arthroscopic repair, massive RCT repairs can result in re-tears and poor clinical outcomes. Muscle atrophy and fatty infiltration in rotator cuff muscles are major complications of chronic massive RCT and are thought to be among the factors responsible for the failure of attempted massive RCT repair. The pathophysiology of rotator cuff muscle atrophy and fat infiltration remains largely unknown, and no small animal model has been demonstrated to reproduce the histologic and molecular changes seen in massive RCT. In this study, we have successfully generated a massive RCT injury in rat by complete transection of supraspinatus (SS) and infraspinatus (IS) tendons. Significant and consistent muscle atrophy and fat infiltration were observed in rotator cuff muscles after massive RCT in our novel model. Furthermore, we have investigated the role of denervation in muscle atrophy and fat infiltration after RCT in this model.

METHODS:

Surgical Procedure: Adult female Sprague Dawley rats at 200-250g underwent complete transection of the tendons of SS and IS on one shoulder (TT group). In some animals, supraspinatus nerve was also transected after tendon transection on the same shoulder (TT+DN group). Sham surgery was performed on the opposite shoulder to serve as internal control. All procedures were approved by our Institutional Animal Care and Use Committee. In TT group, animals were sacrificed 1, 2, 6 and 12 weeks after surgery. In TT+DN, animals were sacrificed 6 weeks after surgery. SS and IS were then harvested and weighted immediately and flash frozen for histology analysis. Muscle weight was used as a marker for atrophy.

Histology: Muscle samples were sectioned using a cryostat. Oil Red O staining was performed to evaluate the muscle fat infiltration. Collagenous connective tissue was stained with picrosirius red. The areas of specific tissues (Fat or collagen content) on each section was measured using Image J (NIH) and calculated as the percentages of collagenous collective tissue (or fat) area over the cross section area of the muscle section. Reviewers were blinded to treatment group.

High Resolution MRI: In 4 animals in the TT group, shoulder joints with complete scapula and proximal half of humerus were harvested after animals sacrificed 6 weeks after surgery for MRI scanning using a 7T high resolution MRI scanner.

Statistical Analysis: One-way ANOVA was used for data analysis. Significance was defined as a p value of less than 0.05.

RESULTS SECTION:

Significant muscle weight loss compared to control was observed in both SS and IS at 1 week to 12 weeks. The average wet weight of the SS and IS decreased 24.8% and 23.5% as early as 1 week after surgery. SS slowly regained its muscle weight with a 13.2% weight loss at 12 weeks after surgery. IS has a persistent weight loss during this 12 weeks period with 36.2% weight loss at 12 weeks after surgery. No significant difference was found between SS and IS at any time point during this period (N=6, P>0.05). (Figure 1)

Dramatically increased collagenous connective tissue was found in both SS and IS in both TT and TT+DN group as early as 6 weeks after surgery. Significant fat infiltration was observed only in the IS 6 weeks after surgery in both TT and TT+DN groups (Figure 2). High resolution MRI confirmed the presence of intramuscular fat infiltration in IS (Figure 3).

DISCUSSION:

Rat models have been primarily used to study tendon healing and augmentation of tendon repair, but analysis of muscle atrophy and fatty infiltration has been limited by the fact that most of the previous studies have evaluated isolated supraspinatus injuries and the natural resilience of rats to heal smaller injuries. Kim et al. has reported muscle fat infiltration in a chronic RCT rat model 8-16 weeks after combined tendinotomy and neurotomy [1]. In our current study, we found that by creating a large rotator cuff tear, we could demonstrate changes that were consistent with the pathophysiology, including muscle atrophy, fibrosis and fat infiltration as early as 6 weeks after surgery. Though the supraspinatus regained weight at 6 weeks after surgery, consistent muscle atrophy and significant fat infiltration were observed in the infraspinatus. This suggests that the infraspinatus muscle in a rat model may be a better subject in future muscle studies to evaluate muscle atrophy and fatty infiltration changes compared to supraspinatus. In addition, we found that denervation of the rotator cuff with transection of the suprascapular nerve increased the amount of muscle atrophy, suggesting a possible role of suprascapular nerve injury in the setting of massive rotator cuff tears. We believe this novel model will serve as a powerful tool in future studies in muscle atrophy and degeneration after RCT.

REFERENCES:


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