# THE EFFECT OF CORTICOSTEROID INDUCED OSTEOPOROSIS ON TENDON INSERTION SITES IN A RABBIT MODEL

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**Relevance to Musculoskeletal Conditions:** Peri-articular osteoporosis is common following joint immobilization after injury or surgery as well as in older patients.

**Introduction:**
The effects of osteoporosis on ligament and tendon insertion sites are poorly understood. For instance, most patients with rotator cuff tears are older and have some degree of underlying osteoporosis. Also, measurable regional osteoporosis has been demonstrated following joint immobilization. In this study we used systemic corticosteroids to induce osteoporosis in rabbits and then evaluated the histological and biomechanical characteristics of the insertion of the infraspinatus tendon to the proximal humerus.

**Methods:**
Twenty-one adult New Zealand White Rabbits were divided into two groups. In Group 1 there were 9 rabbits that were treated with Prednisone 0.150mg/kg subcutaneously daily for 14 weeks to induce osteoporosis. Group 2 was comprised of 12 untreated control rabbits. All of the animals were sacrificed at 14 weeks, and the bilateral humerii were harvested with the infraspinatus muscle attached and frozen at –80° C until testing. Bone mineral density (BMD) of the proximal humerus was measured by dual-energy x-ray absorptiometry (DEXA). One paired shoulder specimen from each group (total 4 shoulders) was processed for histology with hematoxilyn and eosin, Goldner's trichrome, and Von Kossa stains. The humerii of the remaining specimens were potted in epoxy using special molds to improve gripping of the specimen. The specimens were tested in tension at a strain rate of 100%/sec until failure using a MTS® materials testing machine. We measured failure load and failure mode, and calculated stiffness.

**Results:**
DEXA scan: The BMD of the proximal humerus was significantly lower in the osteoporotic group compared to the normal group (0.344gms/cm$^2$ vs. 0.422gms/cm$^2$, $p<0.001$).

Biomechanics: Three failure modes occurred – failure at the grip (due slippage or failure), failure at the insertion, and failure due to fracture (at the humeral neck or by greater tuberosity avulsion). There was no significant correlation between BMD and failure load or failure stiffness (average failure load for the osteoporotic group was 250.8 ± 59N (n=16) vs. 278 ± 75N (n=22) for the normal group). The median stiffness of the tendon-bone unit of the osteoporotic group compared to the normal group was 539.9 ± 302.0N/strain vs. 333.4 ± 281.9N/strain, p=0.18. For those that failed at the insertion, the mean failure load was 188.1 ± 37.5N (n=6) for the osteoporotic group vs. 240.7 ± 75.6N (n=12), for the normal group, p=0.13. The median stiffness was 231.7 ± 138.2N/strain (n=6) for the osteoporotic group vs. 305.9 ± 203.0N/strain (n=12) for the normal group, p=0.48. For those that failed by fracture, the mean failure load was 283.9 ± 31.1N (n=8) for the osteoporotic group vs. 311.4 ± 57.8N (n=4) for the normal group, p=0.30. The mean stiffness was 746.4 ± 209.6N/strain (n=8) for the osteoporotic group vs. 626.6 ± 522.6N/strain (n=4) for the normal group, p=0.57.

There was a tendency for the osteoporotic specimens to fail by fracture (osteoporosis 8/16 vs. normal 4/22, p=0.075). Of note, avulsion fractures of the greater tuberosity were seen only in the osteoporotic group (4/8). The average BMD in those that failed as fracture was 0.369 ± 0.057 gms/cm$^2$ (n=14) compared to 0.399 ± 0.063 gms/cm$^2$ (n=26) for those that failed at the insertion. These differences were not statistically significant.

Histology: There was no significant difference between the two groups in the overall micro-architecture of the insertion site. A direct insertion with four transition zones (tendon, unmineralized fibrocartilage, mineralized fibrocartilage, and bone) from tendon to bone was noted. There were no apparent differences in trabecular architecture, tendon matrix organization, or tendon cellularity.

**Discussion:**
There was a tendency for a difference in failure mode between the two groups: more osteoporotic specimens tended to fail by fracture as opposed to normal specimens which tended to fail at the insertion. Although not statistically significant, the average BMD tended to be lower in those that failed as fracture compared to those that failed at the insertion.

It is well established that local corticosteroid administration weakens tendons and ligaments[1]. The effects of *systemic* corticosteroids on soft tissues are less clearly established. In a previous study, short-term steroid administration around tendon and ligament resulted in more failures to occur by bone avulsion than by failure in the tendon substance during tensile loading[2]. We found a similar tendency toward a change in failure site in animals that had received systemic corticosteroids. It is well established that steroid administration may result in osteoporosis. It is hypothesized that tissue with a shorter turnover time (bone) weakens faster than tissue with a longer turnover time (tendon, ligament) when corticosteroids are administered. This differential collagen turnover may lead to a more profound decrease in strength of bone compared with tendon, resulting in failure at the bone instead of tendon.

Although not statistically significant, we found a consistent elevation in stiffness of the tendon-bone construct in the steroid-treated animals, which runs contrary to the general finding that steroids weaken fibrous tissues. A previous study also reported that short-term steroid administration around tendon and ligament resulted in increased strength and stiffness during tensile loading[2]. Although it is well established that corticosteroids inhibit fibroblast proliferation and collagen synthesis[3], it has also been demonstrated that the steroid-induced reduction in collagen turnover can increase the proportion of insoluble collagen, which may increase stiffness[4]. Such a mechanism may explain increased stiffness following short-term steroid administration. Longer-term steroid administration eventually results in weakening of the tissue due to continued inhibition of collagen synthesis[5].

It is also possible that different effects are found with systemic steroid administration since the local steroid concentration in the tendon is probably much lower than that following direct administration of steroid in or around a tendon. Furthermore, we (and most other authors) have examined the effect of steroid on normal tendon; further study is needed to understand the effect of steroid on diseased tendon. Further studies are ongoing to characterize the structural and biochemical alterations in tendon in animals receiving systemic steroid.

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