

# Effects of Multiple-Group Muscle Weakness on the Retro-patellar Cartilage in Rabbits

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## INTRODUCTION

Osteoarthritis (OA) is one of the most prevalent chronic musculoskeletal disorders in North America. The etiology of OA is thought to be multifactorial. Studies have mainly focused on the changes occurring following intra-articular derangement such as ligament transection. Little is known on how changes in periarticular structures, such as skeletal muscles, may affect the fully intact joint. Muscle weakness is an acknowledged associate of joint degeneration and OA. There is evidence that muscle weakness might be an independent contributor to the initiation and development of OA [1]. Recently, degeneration of the retro-patellar cartilage was evident after induced quadriceps muscle weakness [2]. The muscle weakness induced in that study was restricted to a single muscle group, the knee extensors. Although such muscle weakness can occur due to muscle or peripheral nerve injury, it likely does not represent a large population. On the contrary, general muscle weakness, affecting all limb muscles occurs to a great extent in many sub-populations, for example the elderly. Therefore, the purpose of this study was to investigate micro-structural changes in the rabbit knee cartilage following a period of systematic knee extensor and ankle plantar flexor muscle weakness. We hypothesized that multiple group muscle weakness is associated with degenerative changes in the knee cartilage, thereby, providing evidence that muscle weakness might be an independent risk factor for joint degeneration leading to OA.

## METHODS

Ten skeletally mature, 11-month-old, female New Zealand white rabbits were divided randomly into sham control (n=5) and experimental (n=5) groups. The experimental group received 3.5 units/kg botulinum type-A toxin (BTX-A) (*Botox, Allergan Inc, Canada*) injections into the quadriceps muscles and 1.75 units/kg into the plantar flexor muscles. The sham control animals received injections of 0.9% sodium chloride solution using an identical

procedure and an equal injection volume. After four weeks, quadriceps weakness, quadriceps and plantar flexor muscles atrophy and degenerative changes in the retro-patellar cartilage were measured.

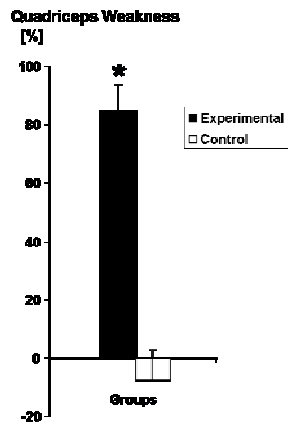
**Knee extensor weakness** was quantified as the maximum isometric knee extensor torque at three different knee angles (80°, 100° and 120°). Immediately after sacrifice, **quadriceps atrophy** was determined by measuring the difference in the wet mass between corresponding hind limbs. Cartilage was stained with India-Ink and **gross morphology** was graded [3]. The **degenerative changes** in the retro-patellar cartilage were assessed by histological analysis using the Mankin grading system [4]. Statistical analyses were done using non-parametric tests ( $\alpha=0.05$ ).

## RESULTS

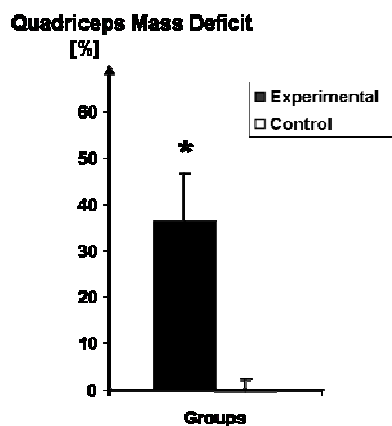
**Isometric knee extensor torque** averaged across all knee angles tested were significantly smaller ( $p<0.01$ ) in the experimental (85%±9) compared to the control group (-7%±10) (Figure 1).

**Atrophy** was significantly greater in the experimental rabbits compared to the control group rabbits (Figure 2,  $p<0.01$ ). The relative difference in the quadriceps total mass between the corresponding hind limbs of the experimental rabbits was 36%±10, whereas it was -0.15%±2 in the control group rabbits. The relative difference in total mass of the plantar flexors was 34%±6 in the experimental and -0.35%±9 in the control group rabbits (Figure 3,  $p<0.01$ ).

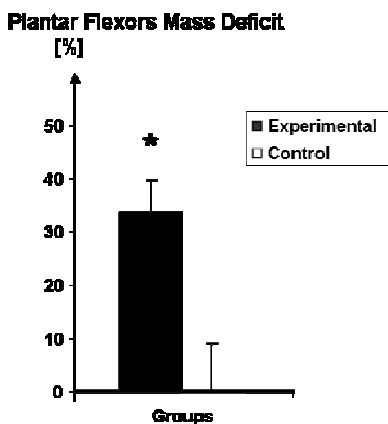
**Gross Morphology** grades of the retro-patellar cartilage were statistically the same between the corresponding hind limbs within each group as well as between the two study groups. This was also true for the degenerative changes graded by the **Mankin scores** (Figure 4,  $p>0.05$ ). The tibiofemoral cartilage gross morphology and histology are being analyzed.



**Figure 1:** Quadriceps percent weakness of the experimental and the sham control rabbits, averaged across all knee angles tested. Group means and SD are shown. (\* $p < 0.01$ )



**Figure 2:** Quadriceps percent mass deficit of the experimental and the sham control rabbits. Group means and SD are shown. (\* $p < 0.01$ )

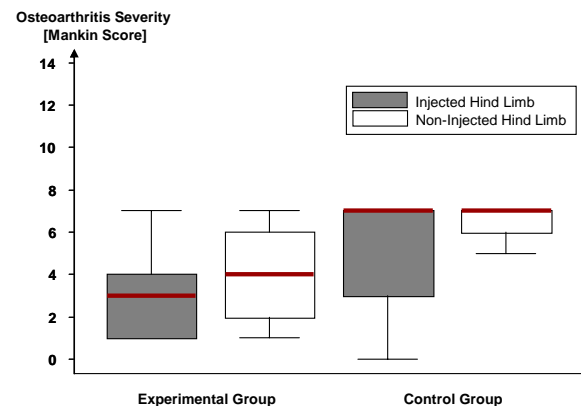


**Figure 3:** Plantar flexors percent mass deficit of the experimental and the sham control rabbits. Group means and SD are shown. (\* $p < 0.01$ )

## DISCUSSION

The results of decreased isometric torque and increased muscle mass deficit confirmed the development of muscle weakness following Botox injections. Cartilage gross morphology and

histology grades of the retro-patellar cartilage were the same for the two study groups, which is in contrast to previous findings of isolated quadriceps weakness [2]. There are many possibilities to explain the differences between the model of isolated muscle weakness and full hind limb weakness. Most likely, but unproven, is the idea that hind limb use differed substantially between the two models. For isolated quadriceps weakness, it is known that rabbits were weight bearing during the experimental protocol, although with reduced vertical ground reaction forces[5]. Unfortunately, such data are not available for the full hind limb weakness model. Another possible explanation is that animals in this study received a higher volume of Botox. BTX-A is a diffusible substance [6] and could have entered the knee joint. Botox has been shown to have a chondroprotective effect [7], thus possibly explaining the current results.



**Figure 4:** Box plots of the Mankin scores from the injected and the non-injected hind limbs of the study groups.

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