OBESITY IMPAIRS ENTHESIS HEALING AFTER ROTATOR CUFF REPAIR IN A RAT MODEL

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Background & Methods

Background:

- **Being overweight/obese is associated with poor outcomes and increased risk of failure after rotator cuff surgery [1].**
- **However, this association is based only on observational evidence that does not identify whether obesity is only an associated factor or has a central role in the pathogenesis of impaired tendon healing [2].**

Hypothesis:

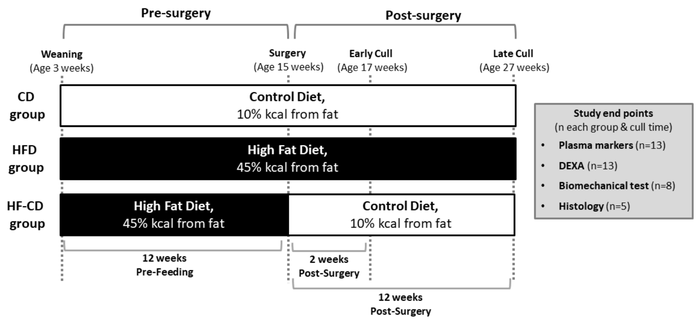
- **We hypothesized that diet-induced obesity would result in inferior enthesis healing in a rat model of rotator cuff repair**

Aim:

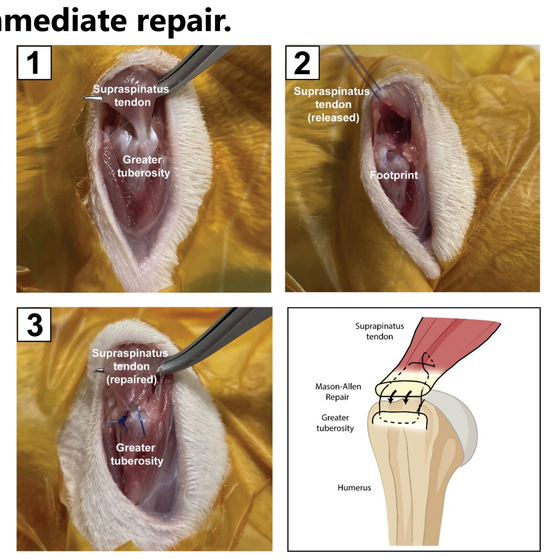
- **To understand the effect of obesity on enthesis healing after rotator cuff repair in a rat model**
- **To determine if restoring normal weight and metabolic function with dietary intervention improves enthesis healing**

Methods:

- **Seventy-eight Sprague Dawley male rats were taken from weaning and randomly allocated into three age- and weight-matched groups.**
- **Each group was fed ad libitum either: [1] control diet (CD; 10% kcal fat), [2] HFD (45% kcal fat), or [3] HFD until surgery, then CD thereafter (HF-CD).**



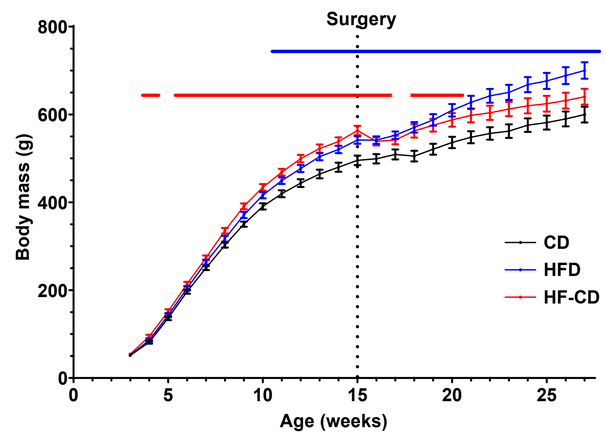
- **After 12 weeks the left supraspinatus tendon was detached, followed by immediate repair.**



- **Supraspinatus tendons were used for mechanical testing (n=8 per group) and histological assessment (n=5 per group).**
- **Metabolic end points were assessed with dual energy X-ray absorptiometry (DEXA) and plasma analyses (insulin, leptin, adiponectin, IL-1β, IL-6, TNFα, LDL, HDL, TC.**
- **Statistical comparisons were performed using a two-way ANOVA with post-hoc Tukey's test and a Pearson r test was used for correlation analyses (* p< 0.05).**

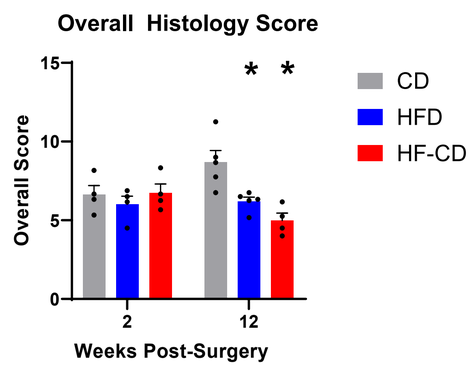
Results

Obesity was established in the HFD and HF-CD groups prior to surgery, and subsequently reversed in the HF-CD group after surgery.



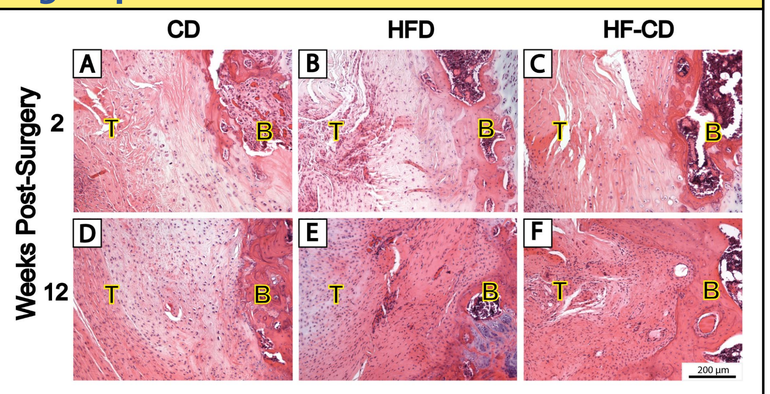
- **Mean body mass of each group over the study period. CD, HFD and HF-CD groups are indicated with black, blue and red lines, respectively.**
- **Consistently significant differences were noted from weeks 10 and 6 of age in the HFD and HF-CD groups, respectively, then the HF-CD group became consistently normalized to the CD group at 21 weeks of age.**
- **At weeks 27 of age, body fat percentage and plasma leptin concentrations were significantly (p<0.01) higher in the HFD group compared to the CD group**

Histologically, the appearance of the repaired entheses was poorer in both the HFD and HF-CD compared to the CD group at 12 weeks



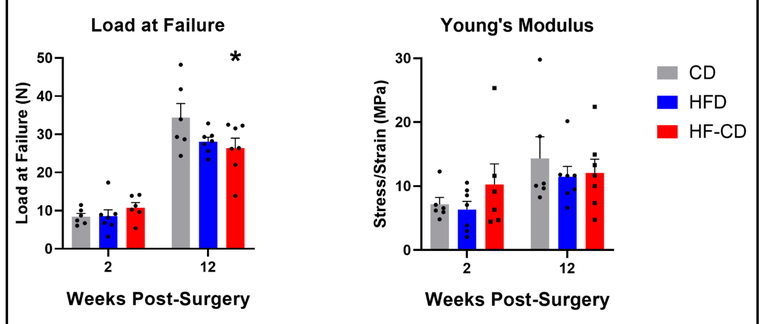
Histological Scoring Criteria for Enthesis Healing [3]

Score	Collagen fiber density	Collagen fiber orientation	Bone-tendon interface	Vascularity	Inflammation
0	None	None	0-24% interdigitation	Abundant vascularity	Abundant inflammatory cells
1	Low	Disorganized fibers	25-49% interdigitation	Moderate vascularity	Moderate inflammatory cells
2	Medium	Moderate alignment	50-75% interdigitation	Minimal vascularity	Minimal inflammatory cells
3	High	Highly aligned	>75% interdigitation	No vascular network	No inflammatory cells



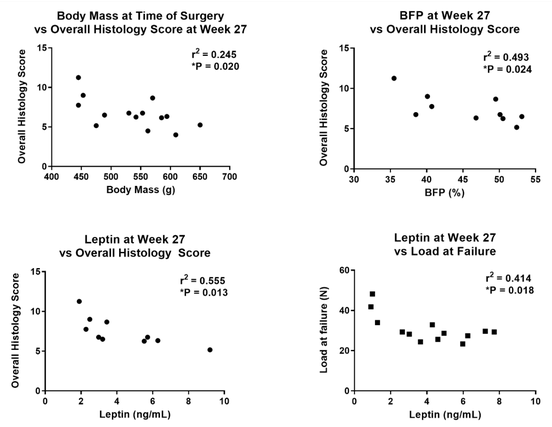
- **Representative images of healing entheses stained with Haematoxylin and Eosin at 2 [A,B,C] and 12 [D,E,F] weeks post-surgery. Bone (B), tendon (T).**
- **At the early time point, the overall quality of healing was similar across the groups, except higher vascularity in the HFD group**
- **At the late time point, the CD [D] group showed a maturing enthesis junction, However in the HFD [E] and HF-CD [F] groups, there remained poor inter-digitation and abundant inflammation and vascularization.**

Effect of HFD on the biomechanical properties of the healing enthesis



- **The repaired entheses in HF-CD group had significantly lower load-at-failure 12 weeks post-surgery compared to the CD group**
- **While the HFD group was low, but not significantly different (P=0.0960).**
- **There were no differences in the biomechanical between groups at the 2-week post-surgery time point.**

Body mass, plasma leptin and body fat % were negatively correlated with histology scores, and load-at-failure post-surgery.



- **The correlation between body mass and body fat % (BFP) with overall histology score at Week 27 of age.**
- **Plasma leptin at Week 27 was negatively correlated with overall histology scores and load at failure of the enthesis**

Conclusions

- **Obesity impaired enthesis healing in this rat rotator cuff repair model, with inferior biomechanical and histological outcomes.**
- **Restoring normal weight with dietary change after surgery did not improve healing outcomes.**
- **This pre-clinical rodent model demonstrates that obesity has a clear role in impairing the healing response after rotator cuff surgery.**
- **Obesity is a potentially modifiable factor that impairs rotator cuff healing and increases the risk of failure after surgery**
- **Exploring interventions that improve the metabolic state of obese patients, and counselling patients appropriately about their modest expectations post-repair should be considered.**

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2. Anandacoomarasamy et al. 2008. PMID: 17848940
3. Street et. al. J Orthop Surg Res. 2015. PMID: 26482900

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