Title:
Diet-Induced Weight Loss in Preclinical Models Negatively Affects Bone Remodeling Activities and Reduces Bone Mass

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Conflict(s) of Interest:
The authors declare there is no conflict of interest. Animal work was approved by the MaineHealth Institute for Research IACUC committee (Protocol #2209).

Introduction:
Although weight loss is beneficial for some aspects of surgery, weight loss due to anorexia significantly reduces bone quality. Similarly, weight loss in obese preclinical models may negatively affect bone remodeling capacity and may affect procedures requiring osseointegration, such as arthroplasty. We hypothesized that caloric restriction disrupts bone quality and remodeling in obese mice.

Methods:
To induce obesity, C57BL6 mice (8 wks old) received a 60% high fat diet for 12 wks. Mice continued to receive a HFD (HFD) or acclimated to a control 10% low fat diet for 2 wks before receiving 30% caloric restriction for 8 wks (HFD-CR). A final group received a low fat diet for the experiment duration (LFD). Body composition and weight were recorded at baseline and at the end of each diet. At euthanasia (30 wks), bone morphology was assessed with micro-computed tomography. Progenitor cells were cultured in osteoclast differentiation media. Osteoclast number was quantified (ImageJ) and serum P1NP and CTx were measured.

Results:
Compared to LFD, HFD and HFD-CR mice gained body weight and fat mass during high fat feeding. After restriction, body weight and fat mass were reduced in HFD-CR compared to HFD and LFD mice. Weight loss following a high fat diet reduced cortical measurements compared to HFD and LFD mice. Compared to HFD, HFD-CR mice had reduced trabecular thickness. Male mice, following restriction, generated fewer osteoclasts compared to HFD. Caloric restriction reduced serum CTx levels in females. Serum P1NP was lower in HFD-CR mice compared to controls in both sexes.

Discussion:
Caloric restriction in obese preclinical models reduced bone mass and remodeling. Bone remodeling was negatively affected by caloric restriction, reflected by decreased osteoclastogenesis and bone formation. Future studies should investigate the impact of weight loss-mediated reductions in bone remodeling and osseointegration success in total joint arthroplasty.

Images/Tables/Charts:

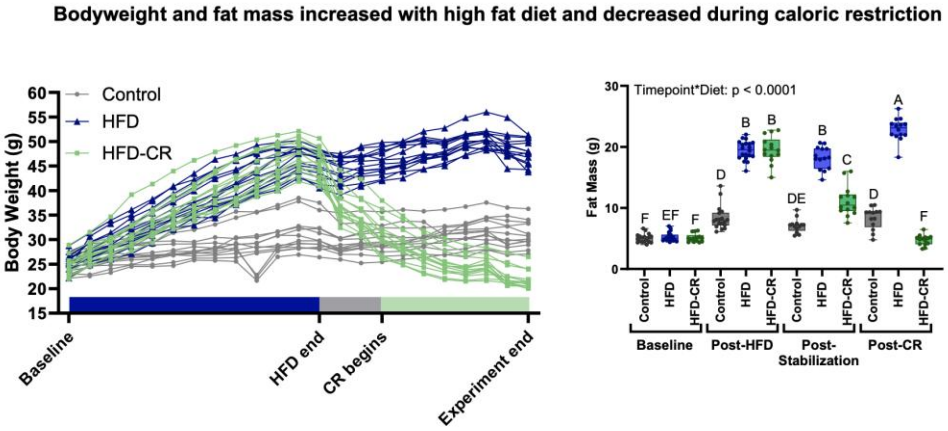

Figure 1: Comparison of body weight and fat mass between the LFD (control), HFD, and HFD-CR groups.

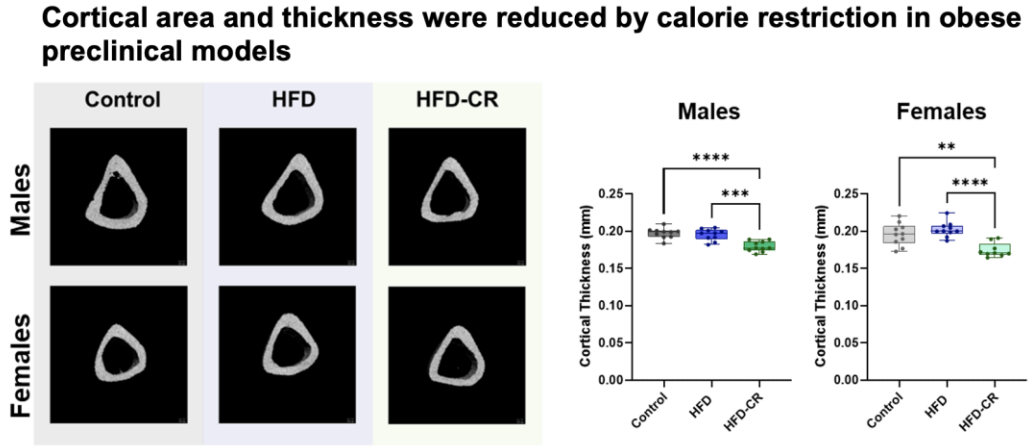

Figure 2: Comparison of cortical bone area and thickness between the LFD (control), HFD, and HFD-CR groups. Micro-computed tomography displayed on left.

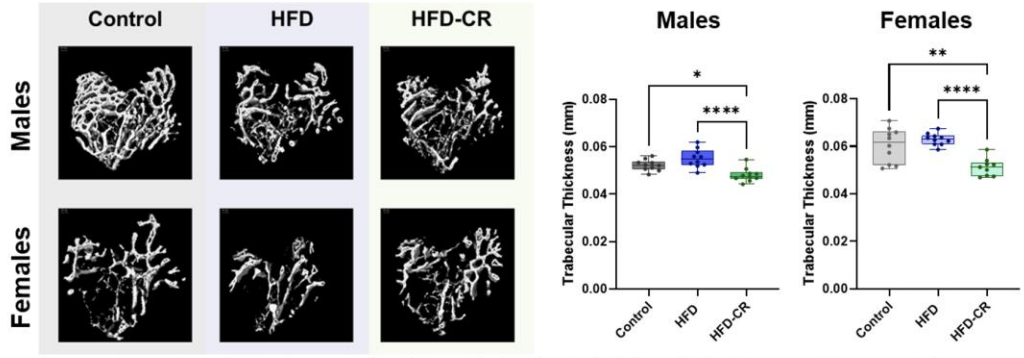

Figure 3: Comparison of trabecular morphology between the LFD (control), HFD, and HFD-CR groups. Micro-computed tomography displayed on left.

Calorie-restricted males generated fewer osteoclast progenitors compared to obese mice

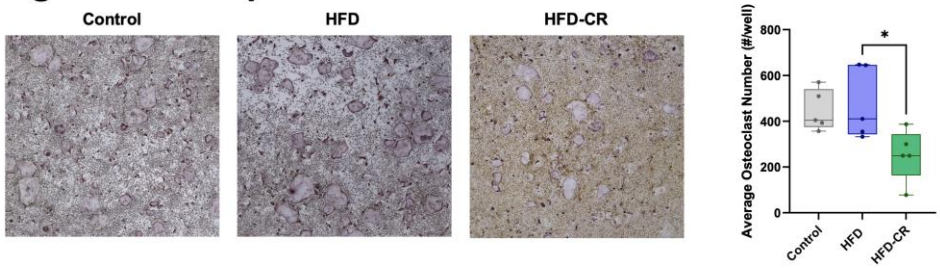

Figure 4: Hematopoietic progenitor cells were cultured in osteoclast differentiation media. Osteoclast size and number were quantified in ImageJ.

Systemic bone formation, but not resorption, was reduced with calorie restriction

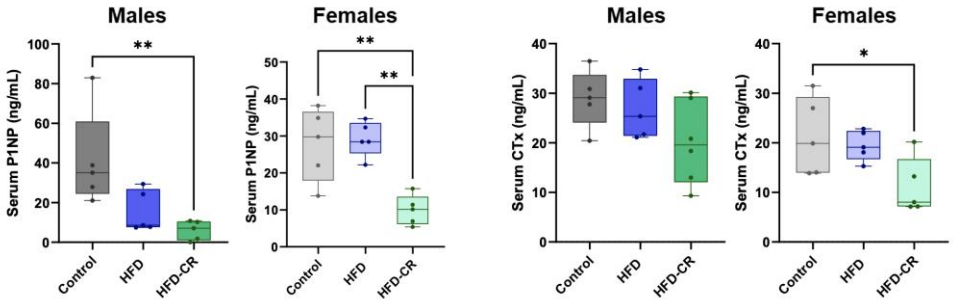

Figure 5: Serum P1NP and CTx were measured to evaluate systemic bone formation and resorption, respectively.