CLINICAL TRIAL

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Bone Adaptation in Adult Women Is Related to Loading Dose: A 12-Month Randomized Controlled Trial

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ABSTRACT

Although strong evidence exists that certain activities can increase bone density and structure in people, it is unclear what specific mechanical factors govern the response. This is important because understanding the effect of mechanical signals on bone could contribute to more effective osteoporosis prevention methods and efficient clinical trial design. The degree to which strain rate and magnitude govern bone adaptation in humans has never been prospectively tested. Here, we studied the effects of a voluntary upper extremity compressive loading task in healthy adult women during a 12-month prospective period. A total of 102 women age 21 to 40 years participated in one of two experiments: (i) low ($n = 21$) and high ($n = 24$) strain magnitude; or (ii) low ($n = 21$) and high ($n = 20$) strain rate. Control ($n = 16$) no intervention. Strains were assigned using subject-specific finite element models. Load cycles were recorded digitally. The primary outcome was change in ultradistal radius integral bone mineral content (iBMC), assessed with QCT. Interim time points and secondary outcomes were assessed with high resolution pQCT (HRpQCT) at the distal radius. Sixty-six participants completed the intervention, and interim data were analyzed for 77 participants. Likely related to improved compliance and higher received loading dose, both the low-strain rate and high-strain rate groups had significant 12-month increases to ultradistal iBMC (change in control: $-1.3 \pm 2.7\%$, low strain rate: $2.7 \pm 2.1\%$, high strain rate: $3.4 \pm 2.2\%$), total iBMC, and other measures. "Loading dose" was positively related to 12-month change in ultradistal iBMC, and interim changes to total BMD, cortical thickness, and inner trabecular BMD. Participants who gained the most bone completed, on average, 128 loading bouts of (mean strain) 575 $\mu\varepsilon$ at 1878 $\mu\varepsilon$/s. We conclude that signals related to strain magnitude, rate, and number of loading bouts contribute to bone adaptation in healthy adult women, but only explain a small amount of variance in bone changes. © 2020 The Authors. *Journal of Bone and Mineral Research* published by American Society for Bone and Mineral Research.

KEY WORDS: BIOMECHANICS; BONE MODELING AND REMODELING; BONE QCT/μCT; CLINICAL TRIALS; EXERCISE

Introduction

Exercise-based interventions have long been considered a viable option for preserving and enhancing bone strength[1] because bone adapts to best resist its habitual mechanical loading environment. Individuals who play sports and load with highly variable, off-axis loads (eg, soccer, squash) have been observed to have better bone mechanical properties than those who do not.[2,3] Clinical trials have shown that high impact activities such as jumping and hopping can improve bone density in growing children[4] and young adults[5] and maintain bone density in older adults.[6] However, although the evidence is strong that certain activities can increase bone density and structure in some individuals, it is not clear what specific mechanical factors govern the response. Furthermore, these factors interact with individual physiology to create a variable response, which is not well understood.

Animal in vivo loading models demonstrate that mechanical signals related to strain rate[7–9] and magnitude[10,11] regulate bone adaptation. There is no consensus on which specific

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