THE EFFECTS OF WEIGHT-BEARING EXERCISE AND ESTROGEN ON VERTEBRAL BONE STRUCTURE IN RATS

+*Tanck, E; **Tromp AM; *Janssen, L; *Van der Sman IM; **Bravenboer N, **Lips, P
*Orthopaedic Research Lab, UMCN, Nijmegen, The Netherlands
e.tanck@orthop.umcn.nl

Introduction

Osteoporosis is a very common disorder in the elderly, especially in postmenopausal women. It is characterized by low bone mass and a deteriorated bone structure with increased fracture risk as a result; particularly in the hip and vertebra. Mechanical loading and estrogen play important roles in bone homeostasis. However, the combined effects of estrogen and mechanical loading on bone in vivo remain unclear. In a previous experiment with female rats, it was demonstrated that a short episode of running (15 minutes) with an additional load in a backpack had a positive effect on total bone mass [2]. As the rate of bone remodeling is higher in trabecular bone than in cortical bone, the major increase in bone mass is expected to be found in the main trabecular regions like the vertebral bodies.

We studied the effects of estrogen and mechanical loading on bone structure in vivo. The hypothesis was that bone physical activity and estrogen administration increase the trabecular bone volume fraction and trabecular thickness in normal and osteoporotic vertebrae. To investigate this hypothesis vertebral bone from normal and ovariectomized rats that underwent exercise and/or estrogen administration were used.

Materials and Methods

Sixty, 12 weeks old, female Wistar rats were weight-matched and assigned to one of 6 groups in a 2*3 factorial design. The groups consisted of three sedentary groups: sham (SED), ovariectomized (SED+OVX), or ovariectomized with estrogen replacement (SED+OVX+E2) and three exercise groups: EX, EX+OVX or EX+OVX+E2.

Exercise started 5 weeks after surgery. The training consisted of running with a backpack during 15 minutes/day, 5 days/week, for 19 weeks. The load in the backpack was gradually increased to 18-21% of body weight. This protocol was approved by the VU University Committee on Animal Experiments.

After the experiment, rats were sacrificed and L5 vertebrae were dissected and analyzed using micro-CT at a resolution of 14 microns (SkyScan 1072). The 3-dimensional trabecular structure of each vertebral body, without endplates, was analyzed for bone volume fraction (BV/TV), trabecular thickness (Tb.Th.), number of trabeculae (Tb.N), and Structure Model Index (SMI) (Fig. 1).

Two-way ANOVA was used to evaluate the effect of exercise and estrogen status. Furthermore, interactions between the factors 'exercise' and 'estrogen status' were tested.

Results

The results showed an effect of exercise on the structural bone parameters. On average, exercise caused a significant increase in bone volume fraction of 18% (p<0.01, Fig. 2); trabecular thickness and trabecular number increased significantly from 92 μm to 97 μm and from 2.2/mm to 2.5/mm, respectively, whereas structure model index decreased from a rod-like structure towards a more plate-like structure, i.e. from 2.0 to 1.8 (p<0.05).

Ovariectomy showed significant decreases in bone volume fraction and trabecular number (p<0.001) but an increase in trabecular thickness (p<0.05), whereas structure model index was not affected. The results of estrogen administration were not statistically different from the sham groups, i.e. SED and EX. Interactions between exercise and estrogen status were found for trabecular thickness and structure model index (p<0.05).

![Fig. 1 Left: example of a cross-section of a rat vertebra with the region of interest marked by the black line. Right: example of a 3D reconstruction of the trabecular region of the vertebral body.](image)

Discussion

The results of this study confirmed our hypothesis that exercise increases the trabecular bone volume fraction and trabecular thickness. Furthermore, it was shown that the effects of estrogen deficiency on trabecular bone structure could be prevented by estrogen administration as was also found by Lane et al. [1].

Significant interactions between exercise and estrogen status were shown for Tb.Th. and SMI. This means that the effect of exercise on trabecular thickness and SMI depended on estrogen status. For example, the Tb.Th. in ovariectomized rats (SED+OVX) did not increase due to exercise, whereas it did increase in the SED and SED+OVX+E2 groups. As anticipated, ovariectomy (OVX) caused a decrease in bone volume fraction. However, the trabecular thickness increased due to OVX.

Together with the result of the decreased trabecular number, this suggests that the increased thickness compensated for the trabecular loss; the load on the remaining trabeculae increased so that bone formation was stimulated.

In conclusion, the results of this study showed that both exercise and estrogen administration positively influenced the trabecular bone structure in rat vertebrae.

References


Affiliated institutions for co-authors

** Research Institute for Endocrinology, Reproduction and Metabolism, VUMC Amsterdam, The Netherlands

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