Bone 89 (2016) 1–6

Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Full Length Article

Exercise frequency and bone mineral density development in exercising postmenopausal osteopenic women. Is there a critical dose of exercise for affecting bone? Results of the Erlangen Fitness and Osteoporosis Prevention Study

Wolfgang Kemmler [a,*], wolfgang.kemmler@imp.uni-erlangen.de,, Simon von Stengel [a], Matthias Kohl [b]

[a] Institute of Medical Physics, University of Erlangen, Germany
[b] Faculty of Medical and Life Sciences, University of Furtwangen, Germany

ARTICLE INFO

Article history:
Received 24 October 2015
Revised 13 April 2016
Accepted 19 April 2016
Available online 21 April 2016

Keywords:
Exercise frequency
Minimum effective dose
Bone mineral density
Participation rate
Postmenopausal women

ABSTRACT

Due to older people's low sports participation rates, exercise frequency may be the most critical component for designing exercise protocols that address bone. The aims of the present article were to determine the independent effect of exercise frequency (ExFreq) and its corresponding changes on bone mineral density (BMD) and to identify the minimum effective dose that just relevantly affects bone.

Based on the 16-year follow-up of the intense, consistently supervised Erlangen Fitness and Osteoporosis Prevention-Study, ExFreq was retrospectively determined in the exercise-group of 55 initially early-postmenopausal females with osteopenia. Linear mixed-effect regression analysis was conducted to determine the independent effect of ExFreq on BMD changes at lumbar spine and total hip. Minimum effective dose of ExFreq based on BMD changes less than the 90% quantile of the sedentary control-group ($n = 43$). Cut-offs were determined after 4, 8, 12 and 16 years using bootstrap with 5000 replications.

After 16 years, average ExFreq ranged between 1.02 and 2.96 sessions/week (2.28 ± 0.40 sessions/week). ExFreq has an independent effect on LS-BMD ($p < .001$) and hip-BMD ($p = .005$) changes. Bootstrap analysis detected a minimum effective dose at about 2 sessions/week/16 years (cut-off LS-BMD: 2.11, 95% CI: 2.06–2.12; total hip-BMD: 2.22, 95% CI: 2.00–2.78 sessions/week/16 years).

In summary, the minimum effective dose of exercise frequency that relevantly addresses BMD is quite high, at least compared with the low sport participation rate of older adults. This result might not be generalizable across all exercise types, protocols and cohorts, but it does indicate at least that even when applying high impact/high intensity programs, exercise frequency and its maintenance play a key role in bone adaptation.

1. Introduction

Exercise maintains bone, but do people maintain exercise [1]? Indeed, considering the rather low sports participation rate of elderly subjects along with the reduction of exercise at older age [2,3], the dose/responses interaction of exercise (frequency) and bone mineral density is highly relevant in this area of non-pharmacologic intervention. Although several exercise studies (e.g. [4–8]) focus on this issue, no current study consistently adjusts for parameters that may affect exercise (e.g. mood swings/depressive symptoms), bone (e.g. weight loss, strength) or both aspects (e.g. diseases, medication). Further, no study addressed the effect of changes of exercise frequency (ExFreq) during the exercise program. However, the latter issue can only be evaluated by long-term trials with regular evaluations of the dose/response effect of exercise frequency on BMD during the intervention. So we used data from the Erlangen Fitness and Osteoporosis Prevention Study (EFOPS), a non-randomized controlled study involving 16 years of consistently supervised high intensity exercise by osteopenic, initially early postmenopausal women [9,10]. The purpose of the present study was (a) to determine the proper dose/response effect of ExFreq[1] on BMD, and (b) to identify the minimum effective dose that relevantly affects bone.

Our primary hypothesis was that (a) there was an independent significant effect of exercise frequency on bone in the representative, realistic and applicable range of 1–3 sessions/week and (b) based on our previous studies [7,8], we hypothesize that there is a cut-off of ExFreq

---

* Corresponding author at: Institute of Medical Physics, University of Erlangen, Henkestrasse 91, 91052 Erlangen, Germany.
E-mail addresses: simon.von.stengel@imp.uni-erlangen.de (S. von Stengel), Matthias.Kohl@hs-furtwangen.de (M. Kohl).

[1] Exercise frequency.

http://dx.doi.org/10.1016/j.bone.2016.04.019
8756-3282/

at around two sessions/week below which exercise loses its "effectivity".

2. Material and methods

The Erlangen Fitness and Osteoporosis Prevention Study (EFOPS) is a controlled exercise trial focusing primarily on clinical fractures and Bone Mineral Density in early-postmenopausal, osteopenic women. The study was conducted by the Institute of Medical Physics, University of Erlangen (FAU), Germany, from 1998 to 2014. The study complied with the Helsinki Declaration "Ethical Principles for Medical Research Involving Human Subjects" and was approved by the ethics committee of the University of Erlangen (Ethikantrag 905, 4209, 4914 B) and the Bundesamt für Strahlenschutz (S9108-202/97/1). After detailed information, all study participants gave written informed consent. The study was registered under www.clinicaltrials.gov. (NCT01177761).

2.1. Participants

Recruitment procedures, eligibility criteria and participant flow during the phases of the study have been given in detail in earlier publications [9,10], thus only a brief description will be reported here. In summary, 137 early postmenopausal (1–8 years post-), osteopenic [11] women were eligible after applying the exclusion criteria (a) present low-trauma fractures, (b) secondary osteoporosis, (c) use of medication (including HRT) or diseases affecting bone metabolism, and (d) inflammable diseases or cardiovascular events (e.g. myocardial infarction, stroke) were included. Women were free to join the non-training control (CG: n = 51) or the exercise group (EG: n = 86) which conducted an intense multipurpose exercise program aimed particularly at bone. In this article however, we primarily focus on the participants in the exercise group (with control group data being used to determine the cut off value for "exercise effectiveness") (Table 1).

2.2. Study intervention

A detailed overview of the exercise protocol of the EFOPS and corresponding adaptions over the 16 study years has been described elsewhere [9,10,12], thus only a brief summary with special focus on bone-specificity will be provided.

Generally, the EFOPS exercise protocol was based on a high intensity strategy that applied several types of exercise in order to address the complex risk factor constellation of (early) menopause. Four exercise sessions structured as two (years 4 and 5: three) consistently supervised group sessions and two (years 4 and 5: one) home training sessions/week were regularly applied for 49–50 weeks/year for 16 years. Group sessions (65 min) consisted of (a) 20 min of aerobic dance exercises, structured as intervals with high intensity (up to 85% HRmax), high impact (ground reaction forces (GRF): 2–3× body weight) aerobic excises intermitted by short periods (1–2 min) of low–moderate intensity (70% HRmax). (b) 4 × 15 multilateral jumping exercises (GRF: 3–4.5× body weight) with varying movement velocity and 30 s of rest between the jumping exercises. (c) A periodized resistance exercise training with one session/week on machines (TechnoGym, Italy) and one session/week using free weights (PowerBlock, USA), elastic bands (TheraBand, Germany) and isometric exercises addressing 10–14 muscle groups/session. Periodized high intensity exercise periods of 12 weeks (1–4 sets, 4–12 reps, 70–90% 1 RM, 2–3 min rest) regularly alternated with periods of 4–6 weeks of lower intensity but higher volume (2–3 sets, 20–25 reps, 50–55% 1 RM, 1–2 min rest). Besides exercise intensity, movement velocity was consistently manipulated with periods of explosive (concentric phase only), moderate or slow (up to 4–2–4 s) movement velocity. Of importance, the number of high impact elements was decreased slightly after year 8, and movements with a more challenging character for static and dynamic balance and general coordination were increasingly introduced. In order to accommodate the growing orthopedic vulnerability of our cohort, the complexity and impact of the jumping exercises were reduced (Peak-GRF ≤ 3–3.5× body weight) after year 12 while the resistance exercise protocol remained unchanged.

Table 1

Baseline characteristic of study participants. Data of the control group (CG) were not included in the linear mixed-effect regression model but used to determine the cut off value for "exercise effectiveness".

Variable	EG (n = 55)	CG (n = 43)
Age [years]	55.1 ± 3.4	55.5 ± 3.2
BMI [kg/m^2]	25.4 ± 3.2	25.0 ± 3.9
Age at menopause [years]	50.6 ± 2.8	50.6 ± 3.0
Physical activity[a]	4.3 ± 1.1	4.2 ± 1.3
Grip strength [kg][b]	26.4 ± 4.2	25.9 ± 3.6
Energy intake [kJ/day][c]	7916 ± 1408	7551 ± 11,743
Calcium intake [mg/day][c]	1048 ± 363	992 ± 291
Vit.-D intake [μg/day]	5.3 ± 4.5	5.3 ± 4.6
Smokers [% per group]	7%	11%
BMD at LS [mg/cm^2]	0.878 ± 0.090	0.883 ± 0.096
BMD at total hip [mg/cm^2]	0.851 ± 0.083	0.841 ± 0.085

[a] Self-rated physical activity score (1: very low to 7: very high) [27].

[b] Jamar Dynamometer, testing according to Mathiowetz [28].

[c] 5-day dietary protocol.

The home training session (20–25 min) was introduced 5 months after study start and consisted of a 5–10 min warm-up sequence with running/running variations in place and rope skipping, isometric and dynamic resistance exercises (10–15 min) and stretching and flexibility exercises (5 min), all carefully practiced in the joint sessions beforehand. Every 3 to 6 months, exercises were replaced by more challenging exercises to generate a progression and to maintain compliance.

All participants (EG and CG) were supplied with calcium and Vitamin D, based on dietary records kept by the study participants. Correspondingly, supplements were provided to ensure an intake of at least 1000 mg/day calcium (first 10 years: 1500 mg/day) and 500 IU/day Vitamin D.

2.3. Measurements

All assessments were performed in a blinded fashion. Staff were not informed or allowed to ask about the group membership. BMD scans were conducted consistently and analyzed at baseline and follow-up by the same two researchers.

2.3.1. Anthropometry

Height (Holtain, Crymych Dyfed., Great Britain) and body weight were measured using calibrated devices (Tanita BF-305, Tokyo, Japan). Bone Mineral Density (BMD) was measured by dual energy X-ray absorptiometry (DXA; QDR 4500a; Hologic, Bedford, Ma) at the lumbar spine (L1–L4) and the proximal femur (total hip-ROI), using standard protocols provided by the manufacturer. In four cases, scans were not taken during the lumbar spine (LS) analysis due to distinct degenerative changes that prevented a proper comparison with baseline data.

2.3.2. Questionnaires

Baseline questionnaires were used to assess general characteristics (e.g. age, family status, education), diseases and medication with special regard to parameters affecting bone metabolism, lifestyle including physical activity and exercise levels, quality of life and pain parameters and osteoporotic risk factors including falls.

Follow-up questionnaires and structured interviews were conducted to detect possible changes in confounding parameters that may affect our primary outcome (e.g. changes of medication, diseases, quality of life including mood swings/depressive symptoms and pain parameters, lifestyle, physical activity, nutritional intake including calcium and Vitamin D intake).