

Effects of high-impact training and detraining on femoral neck structure in premenopausal women:

A Hip Structural Analysis (HSA) of an 18-month randomized controlled intervention with a 5-year follow-up

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Liikunnan avulla voidaan edistää luuston terveyttä läpi koko elämän. Yksi murtumariskiin vaikuttavista tekijöistä on luun kokonaislujuus, johon luukudoksen määrän lisäksi vaikuttavat myös sen rakenteelliset ominaisuudet. Tämän tutkimuksen tarkoituksena oli selvittää 18 kk kestäneen, iskutyypistä kuormitusta sisältäneen, harjoitteluintervention vaikutuksia premenopausaalisten naisten reisiluun kaulan rakenteeseen. Harjoitteluvaikutusten pysyvyyttä arvioitiin viiden vuoden seurannan avulla.

Alkuperäiseen satunnaistettuun ja kontrolloituun harjoitteluinterventiotutkimukseen (18 kk) osallistui 98 tervettä 35 - 45-vuotiasta naista. Harjoittelua toteutettiin ohjatusti kolmesti viikossa siten, että jokainen harjoitustunti sisälsi iskutyypistä (high-impact) kuormitusta 20 minuutin ajan. Kontrolliryhmä sai ohjeet säilyttää entisen aktiivisuustasonsa. Retrospektiivisesti reisiluun kaulan DXA luumittausaineisto oli saatavilla 22 harjoitus- ja 22 kontrolliryhmäläiseltä alkutilanteessa, 18 kk intervention ja viiden vuoden seurannan jälkeen. Reisiluun kaulan kapeimmasta kohdasta arvioitiin rakenneanalyysin (HSA) avulla luun taivutuslujuus (Z , mm^3), luun poikkipinta-ala (CSA, mm^2) sekä luun läpimitta (W , mm). Koehenkilöiden fyysistä suorituskykyä arvioitiin vertikaalihyppy- ja kävelytestillä.

Reisiluun kaulan taivutuslujuus Z oli 18 kk intervention jälkeen keskimäärin 3.2 % ($p=0.047$) ja viiden vuoden seurannan jälkeen 2.2 % ($p=0.237$) suurempi harjoitusryhmällä kontrolliryhmään verrattuna (paino, pituus ja ikä huomioon otuna). CSA erot harjoitusryhmäläisten eduksi olivat vastaavasti 2.8 % ($p=0.043$) ja 2.6 % ($p=0.090$) sekä W ero 1.0 % ($p=0.231$) ja 0.1 % ($p=0.877$). Vertikaalihypyn lentoajassa ryhmien välinen ero harjoitusryhmän eduksi 18 kk:n jälkeen oli 4.2 % ($p=0.002$) ja 5 vuoden seurannassa 5.1 % ($p=0.003$). Arvioidussa maksimaalisessa hapenottokyvyssä ($\text{VO}_{2\text{max}}$) ryhmien väliset erot olivat vastaavasti 5.6 % ($p=0.002$) ja 4.6 % ($p=0.005$).

Iskutyypistä kuormitusta sisältävä harjoittelu lisäsi reisiluun kaulan lujuutta parantamalla luun rakenteellisia ominaisuuksia premenopausaalisilla naisilla. Seurannassa 3.5 vuotta intervention päättymisen jälkeen tilastollisesti merkitseviä eroja ryhmien välillä ei havaittu, mutta trendi harjoitusryhmäläisten eduksi oli silti nähtävissä. Harjoitteluvaikutuksia fyysisessä suorituskyvyssä oli mahdollista ylläpitää kohtuullisella fyysisellä vapaa-ajan aktiivisuudella yli kolmen vuoden ajan.

Asiasanat: luun lujuus, luun rakenne, harjoittelu

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Exercise seems to be very promising in order to promote bone health during lifespan. The purpose of this study was to evaluate training effects and their maintenance of an 18-month high-impact exercise intervention with the 5-year follow-up on femoral neck structure in premenopausal women.

An 18-month randomized controlled high-impact trial with the 5-year follow-up was carried out. Participants (N=98) of the original intervention were healthy and sedentary women, aged 35-45 years. The progressive 18-month high-impact loading exercise regimen included supervised one hour training session three times per week, while the control group was informed to maintain their normal level of activity. Retrospectively, the femoral neck dual energy X-ray absorptiometry (DXA) data was available from 22 trainees and 22 controls at baseline, 18-month and 5-year follow-up point. A Hip Structural Analysis (HSA) was used to estimate the section modulus (Z , mm³, an index of a bending resistance), cross-sectional area (CSA, mm²) and subperiosteal width (W , mm) at the narrowest section of the femoral neck. Besides the HSA, the neuromuscular performance was assessed.

The body weight, height and age adjusted between-group differences were observed after the 18-month intervention in favour of trainees in Z (3.2 %, $p=0.047$) and CSA (2.8 %, $p=0.043$), but not in W (1.0 %, $p=0.231$). At the 5-year follow-up point the exercise benefits in Z (2.2 %, $p=0.237$), CSA (2.6 %, $p=0.090$) and W (0.1 %, $p=0.877$) were lost. In neuromuscular performance, percentual between-group differences were observed in favour of trainees both after the intervention and at 5-year follow-up in vertical jump flight time (4.2 %, $p=0.002$ and 5.1 %, $p=0.003$) and in VO_{2max} (5.6 %, $p=0.002$ and 4.6 %, $p=0.005$), respectively.

High-impact exercise increased the femoral neck strength by improving structural properties of bone in the femoral neck in premenopausal women. At the 5-year follow-up, the exercise-induced benefits were lost. However, the exercise benefits on neuromuscular performance were maintained for over 3 years with common physical activities only.

Keywords: bone strength, bone structure, exercise

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Effects of high-impact training and detraining on femoral neck structure in premenopausal women: **A Hip Structural Analysis (HSA) of an 18-month randomized controlled intervention with a 5-year follow-up**

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1. ABSTRACT

Introduction: Exercise seems to be very promising in order to promote bone health during lifespan. The purpose of this study was to evaluate training effects and their maintenance of an 18-month high-impact exercise intervention with the 5-year follow-up on femoral neck structure in premenopausal women.

Materials and methods: A randomized controlled 18-month high-impact trial with the 5-year follow-up was carried out. Participants (N=98) of the original intervention were healthy and sedentary women, aged 35-45 years. Retrospectively, the femoral neck dual energy X-ray absorptiometry (DXA) data was available from 22 trainees and 22 controls at baseline, 18-month and 5-year follow-up point. A Hip Structural Analysis (HSA) was used to estimate the section modulus (Z , mm^3 , an index of a bending resistance), cross-sectional area (CSA, mm^2) and subperiosteal width (W , mm) at the narrowest section of the femoral neck. Besides the HSA, the neuromuscular performance was assessed.

Results: The body weight, height and age adjusted between-group differences were observed after the 18-month intervention in favour of trainees in Z (3.2 %, $p=0.047$) and CSA (2.8 %, $p=0.043$), but not in W (1.0 %, $p=0.231$). At the 5-year follow-up point the exercise benefits in Z (2.2 %, $p=0.237$), CSA (2.6 %, $p=0.090$) and W (0.1 %, $p=0.877$) were lost. In neuromuscular performance, percentual between-group differences were observed in favour of trainees both after the intervention and at 5-year follow-up in vertical jump flight time (4.2 %, $p=0.002$ and 5.1 %, $p=0.003$) and in $\text{VO}_{2\text{max}}$ (5.6 %, $p=0.002$ and 4.6 %, $p=0.005$), respectively.

Conclusion: High-impact exercise increased the femoral neck strength by improving structural properties of bone in the femoral neck in premenopausal women. At the 5-year follow-up, the exercise-induced benefit was lost. The exercise benefits on neuromuscular performance were maintained for over 3 years with common physical activities only.

2 INTRODUCTION

Preventing osteoporotic fractures is a great challenge to health-care organizations worldwide. The incidence and costs of hip fractures are already high and they are predicted to arise in the future. ^(1,2) Many factors such as age, fracture history, balance, falling mechanics, neuromuscular function and bone strength are associated with the risk of fractures due to falls. ⁽³⁻⁵⁾ Bone health related factors such as genetics, bone cell mechanisms, hormonal factors, exercise and nutrition are all under an investigation. Mechanical loading is one of the important external factors that determine bone strength and structure. ⁽⁶⁻⁸⁾ Thus, exercise seems to be very potential option in order to improve bone quality and strength.

There is evidence that regular training can increase areal bone mineral density (aBMD, g/cm²) in premenopausal women. ⁽⁹⁻¹¹⁾ According to the randomised controlled exercise studies, areal bone mineral density (aBMD) gain has been 1-3 % at the loaded regions of the skeleton. ⁽¹²⁻¹⁷⁾ Majority of the previous exercise studies have focused on measuring bone mineral content (BMC, g) or aBMD as an outcome of an exercise intervention. Because the bone mineral mass is only a factor of bone strength, the exercise response to bone structure should be examined. ⁽¹⁸⁻²²⁾ Bone structure may also be more sensitive to loading and provide more specific information about exercise-induced benefits on bone. Recently, a hip structural analysis (HSA) has been developed for evaluating bone structure from dual energy X-ray absorptiometry (DXA) scans. ⁽²³⁾

Therefore, the purpose of this study was to evaluate training effects of an 18-month high-impact exercise intervention and maintenance of the exercise-induced benefits with a 5-year follow-up on femoral neck structure in premenopausal women using the HSA method. According to our knowledge, intervention studies with similar study design have not been reported previously.

3 MATERIALS AND METHODS

3.1 Design and participants

In the present study, a hip structural analysis (HSA) was performed from the DXA measurements for the baseline, 18-month and the 5-year follow-ups. Originally, participants (N=98) for the randomized controlled trial were first recruited with a newspaper advertisement. After the telephone interview, 140 of the 242 volunteer responders were excluded based on the exclusion criteria. Of the remained 102 women, 4 were also excluded after a medical examination. The specific exclusion criteria and trial profile was described previously.⁽¹⁶⁾

In the original study design, 84 healthy, sedentary, normally menstruating premenopausal women aged 35-45 years completed the initial randomized controlled 18-month exercise intervention.⁽¹⁶⁾ At the 18-month and 5-year follow-up measurements (3.5 years after the end of the intervention), 22 of the 39 original trainees and 22 of the 45 original controls were available for HSA. The design of the 5-year follow-up has been described in detail previously.⁽²⁴⁾

Baseline characteristics of the participants are shown in Table 1. At baseline, there were no statistically significant differences between the groups. We have previously reported that there were no intergroup differences in any of the background characteristics such as diet or other living habits, medication, injuries, diseases and general physical activity at the baseline or during the follow-up.⁽²⁴⁾ Also the types of physical activity during the follow-up were similar in both groups consisting mostly walking, cycling or other non-impact aerobic and low-resistance activities.

The 18-month progressive high-impact exercise program included supervised one hour training session three times per week. Each workout session consisted of 15 min warm-up, 20 min high-impact training (jumping and step-aerobics), 15 min non-impact and stretching exercises and 10 min of cooling down.⁽¹⁶⁾ The control group was informed to maintain their normal level of activity.

3.2 Bone structure and neuromuscular performance

Bone measurements were done from the right femoral neck using the dual energy X-ray absorptiometry (DXA) device (XR-26; Norland Corporation, Wisconsin, USA). The femoral neck scans were analysed with hip structural analysis (HSA) software developed by Beck et al. ⁽²³⁾ using principles introduced originally by Martin and Burr. ⁽²⁵⁾ The structural bone strength analysis was carried out using the method of least area of the femoral neck from DXA scan images of 22 trainees and 22 controls available.

A section modulus (Z , mm^3 , an index of a bending resistance), cross-sectional area (CSA, mm^2) and subperiosteal width (W , mm) were calculated from the narrowest section of the femoral neck and sections (lateral and medial) beside it. The mean of these three sections was used in calculations. In vivo precision at the UKK institute bone research laboratory, explained as coefficient of variables, is 4.5 % for Z , 2.7 % for CSA and 2.5 % for W . ⁽²⁶⁾ Neuromuscular performance was assessed by measuring lower leg explosive power with vertical jump on contact platform and cardiorespiratory fitness with a 2 km walking test. ⁽¹⁶⁾

3.3 Statistical analysis

Means and SD are given as descriptive statistics. The analysis of covariance (ANCOVA) was used to estimate the between-group differences at 18 months and 5 years. The differences between the groups for bone and neuromuscular variables were adjusted by baseline values (age, weight and height). The level of statistical significance was set at 5%. Statistical analyses were done with SPSS (version 11.5; SPSS, Chicago, IL, USA).

4 RESULTS

The anthropometric characteristics showed no major changes in either group during the study. Average weight gain in both groups was 0.6 kg at 18-month measurements. At the 5-year follow-up body weight had been increased 0.4 kg in the training group and 0.2 in controls. There were no differences between the groups in calcium intake during the 18-month intervention.

Baseline femoral neck Z, CSA and W values (means and SD) and their mean differences (95 % CI's) between the groups at the 18-month and 5-year follow-up points are given in Table 2. The percentage bone variable changes are shown in Figure 1. Training effects were seen in Z and CSA, but not in W after the 18-month intervention. At 5-year follow-up point the exercise benefits on femoral neck were lost. The adjusted between-group difference at the femoral neck Z was 3.2 % ($p=0.047$), at 18-month, and 2.2 % ($p=0.237$) at the 5-year follow-up, CSA (2.8 %, $p=0.043$ and 2.6 %, $p=0.090$, respectively) and W (1.0 %, $p=0.231$ and 0.1 %, $p=0.877$) in favour of trainees.

Baseline values for neuromuscular performance (means and SD) and between-group differences (95 % CI's) at the 18-month and 5-years follow-ups are given in Table 2. A significant ($p<0.05$) group differences in favour of trainees were observed at the 18-month and 5-year follow-up point. The percentage changes on neuromuscular performance are shown in Figure 2. The percentage differences between the groups were in vertical jump flight time 4.2 % ($p=0.002$), after the 18-month intervention, and 5.1 % ($p=0.003$) at the 5-year follow-up. In $\text{VO}_{2\text{max}}$, the percentage differences between the groups were 5.6 % ($p=0.002$) and 4.6 % ($p=0.005$), respectively.

5 DISCUSSION

In the present study, 18-month high-impact exercise increased the femoral neck strength by improving structural properties (CSA and Z) of bone in premenopausal women. However, these exercise-induced bone benefits were mainly lost at the 5-year follow-up. On neuromuscular performance the training effects were also seen 3.5 years after the end of the intervention

The results of this study show that the cross-sectional area and section modulus increased relevantly more than outer diameter of the femoral neck. It may be due to a corticalization process of the trabecular bone under the endocortical surface, which can lead thickening of the cortical bone without any external expansion. Similar observations on femoral neck were previously found in triplejumpers. ⁽²⁷⁾ In other studies, skeletal loading has increased the outer diameter of the long bones more significantly. ^(18, 20) It has been suggested that the enlargement of the bone outer diameter during aging could be a compensatory mechanism against the bone mineral loss. ⁽²⁸⁾ Further, the expansion of the femoral neck does not necessarily lead to stronger bone structure, because in the same time of aging occurs thinning of the cortical bone (endosteal resorption). The cortical wall thickness appears to be a major determinant of a bone structural strength.

Percentage changes in bone properties in this study were greater in CSA and Z than that we have reported previously in aBMD. ⁽¹⁶⁾ It seems that femoral neck structure has a capacity to adapt mechanical loading in adulthood despite more constant aBMD. Similar findings were recently observed in young women by Petit et al. ⁽²⁹⁾ The results of this study support the previous findings that exercise-induced bone benefits can be understood and measured more appropriately, when information about structural and material properties of bone are combined. The aBMD as an outcome variable of an exercise intervention can be misleading, because it ignores possible exercise-induced structural adaptation to bone. This should be noted when the outcome variables of the intervention studies are chosen or interpreted. Reduced aBMD may be observed because of expanded femoral neck while total BMC can remain same. The enlargement

of the femoral neck can be a consequence of the normal aging process or be caused by external loading.

Major limitation of this study was a quite small number of participants (44) available for the HSA. Originally 84 of the 98 participants completed the 18-month intervention. With bigger sample size, the quite wide 95 % CI 's would have been narrower and the between-group difference in CSA and Z could have been statistically significant also at 5-year follow-up point.

Another limitation of the study is interpreting the 3-dimensional femoral neck structure using the 2-dimensional DXA scan. Despite the HSA software is developed for dealing with the problem, the program cannot calculate other projections than the anterior image only. In this method, femoral neck structure is seen as a hollow symmetric cylinder which is not the case. Also changes in scanning position (the amount of the femoral rotation) can misrepresent the real dimensions of the femoral neck. In addition, possible training effects on bone structure may not occur in the imaged plane or in the narrowest section of the femoral neck that the HSA is interpreting. DXA scanner is clearly not an ideal instrument to measure bone structure. In the future, more appropriate imaging techniques, for example, magnetic resonance imaging (MRI) may provide better information of structural properties of the femoral neck. ^(30, 31) Meanwhile, HSA method can offer useful information for interpreting widely used DXA scan images of the femoral neck despite the known limitations. ⁽³²⁾

The maintenance of an exercise-induced bone benefits are not yet well understood and results are conflicting. Total immobilization may have harmful effects on bone and also detraining can decrease bone strength. ⁽³³⁻³⁶⁾ However, there is some evidence that previous training history can indicate at least some positive bone benefits in later life ⁽³⁷⁻⁴⁰⁾, although some athlete studies indicate that positive training effects on bone are gradually lost after cessation of an active career. ^(41, 42) According to the retrospective studies, exercise-induced benefits on bone seems to be maintained for many years and even several decades at least in early adulthood. ^(37, 43, 44) In the present study according to the HSA, the statistically significant between-group differences on bone structure had almost been lost in 3.5 years after the intervention. On the other hand, we have previously reported that the exercise-induced benefit on femoral neck aBMD was

maintained at least for over 3 years. ⁽²⁴⁾ Although the between-group differences on bone variables were not statistically significant after the 5-year follow-up in this study, a positive trend of maintenance at least some of the high-impact training effects on bone structure in favour of the trainees can be seen. A major future question is what is the needed minimum level of physical activity for maintaining exercise-induced bone benefits?

Although the required physical activity level and also the exact type of exercise that would be optimal for promoting bone strength are unclear, it seems that high-impact type of loading such as jumping or loading which includes high acceleration forces and unusual directions like in squash and soccer, may be the most beneficial for increasing bone strength. ^(26, 45-48) In the present study the training regimen included jumping and step-aerobic exercises which in a pilot study were tested to conduct peak forces from 2 to 5 times of body weight. ⁽¹⁶⁾ Some authors suggest that quite a short period of loading can be enough for remodelling and strengthening the bone if the mechanical stimulus exceeds the normal level of loading. ⁽⁴⁹⁻⁵¹⁾ Most likely, this was the case also in sedentary women who participated in this intervention study.

Surprisingly the training effects on neuromuscular performance (vertical jump and predicted VO_{2max}) in favour of the trainees were observed not only after the intervention but also after 5 years. Although most of the women had described their physical activity levels (frequency, intensity and duration) moderate only and the types of exercise also were quite similar (mostly non-impact) during the follow-up, these moderate activities might have been enough to remain the between-group differences. More specific information about the activity levels during the follow-up would have been needed, and therefore, the possibility of bias also exists. However, some of the exercise-induced benefits on neuromuscular performance can be maintained with the moderate level of physical activity only. ^(52, 53)

In conclusion, results of this study indicate that high-impact type of exercise can increase the femoral neck strength in premenopausal women by improving cross-sectional area and bending strength of bone. Although the differences between the groups were not statistically significant at 5-year follow-up, a positive trend in favour of the trainees was observed also in the maintenance at least some of the exercise-

induced bone benefits on femoral neck. Even though, the training effects on bone structure are biologically quite small in adulthood, exercise may have some clinical usefulness offering an inexpensive and safe option to prevent or decrease age-related bone loss and promote bone health.

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APPENDIX

Table and figure legends

Table 1: Baseline characteristics of participants

Table 2: Age, weight and height adjusted intergroup differences in bone and neuromuscular performance variables at the 18-month and 5-year follow-ups.

Figure 1: Percentage Z, CSA and W change at the femoral neck during 18-month exercise period and after the 5-year follow-up. *Dark circles* represent the training group (n=22) and *lighter boxes* the control group (n=22). *Bars* indicate the 95% confidence intervals

Figure 2: Percentage change on neuromuscular performance during 18-month exercise period and after the 5-year follow-up. *Dark circles* represent the training group (n=22) and *lighter boxes* the control group (n=22). *Bars* indicate the 95% confidence intervals

Table 1

	Training group (n=22)	Control group (n=22)
	Mean (SD)	Mean (SD)
Age (years)	39 (2)	38 (2)
Weight (kg)	61, 6 (8)	61,0 (7)
Height (cm)	164 (1)	165 (1)
Body-mass index (kg/m ²)	23,0 (3)	22,5 (2)
Calcium intake (mg/day)	1102 (330)	1102 (300)

Table 2

	Baseline	Intergroup difference at the 18-month follow-up		Intergroup difference at the 5-year follow-up				
		Mean (SD)	Difference	95% CI	P-value	Difference	95% CI	P-value
Bone variables								
An index of bending resistance (Z, mm ³)	Trainees	1386 (161)						
	Controls	1373 (240)	46.528	0.556 - 92.499	0.047	30.421	- 20.801 - 81.644	0.237
Cross sectional area (CSA, mm ²)	Trainees	285 (33)						
	Controls	281 (38)	7.866	0.246 - 15.486	0.043	7.404	- 1.207 - 16.014	0.090
Subperiosteal width (W, mm)	Trainees	30.9 (1.7)						
	Controls	30.8 (1.3)	0.314	- 0.208 - 0.836	0.231	0.036	- 0.429 - 0.500	0.877
Neuromuscular performance								
Vertical jump flight time (ms)	Trainees	447 (39)						
	Controls	449 (36)	20.0	8.0 - 32.0	0.002	23.0	8.0 - 37.0	0.003
VO ₂ max (ml /kgmin)	Trainees	36.5 (3.5)						
	Controls	37.9 (2.8)	2.095	0.839 - 3.351	0.002	1.722	0.554 - 2.890	0.005

Figure 1

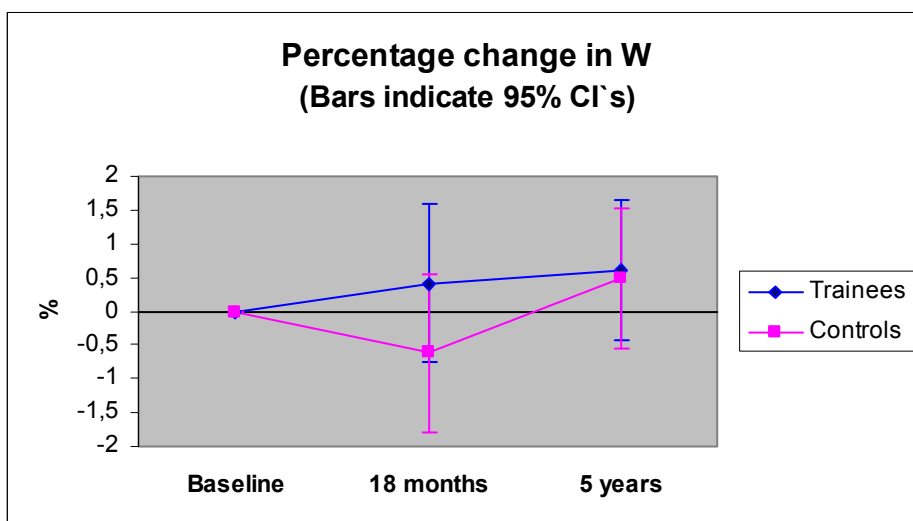
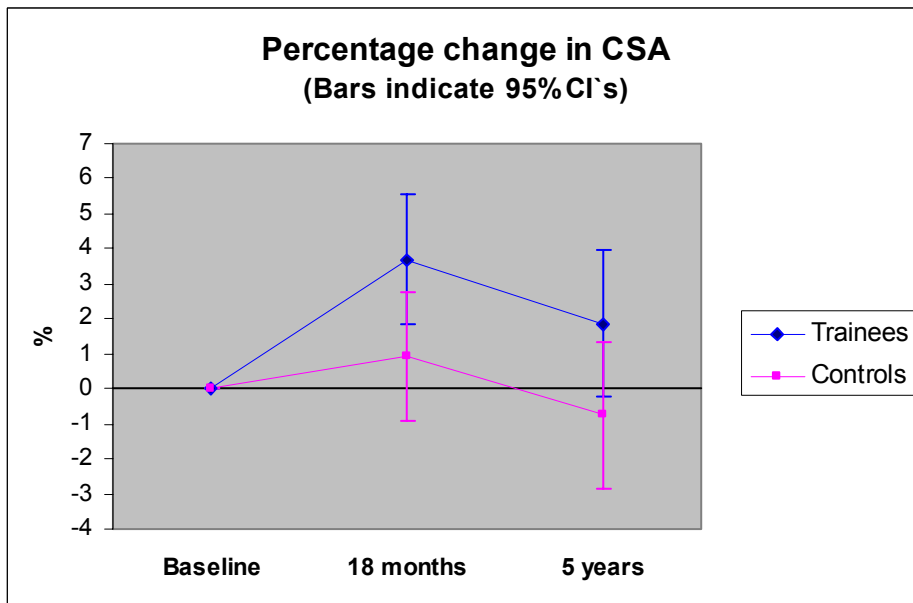
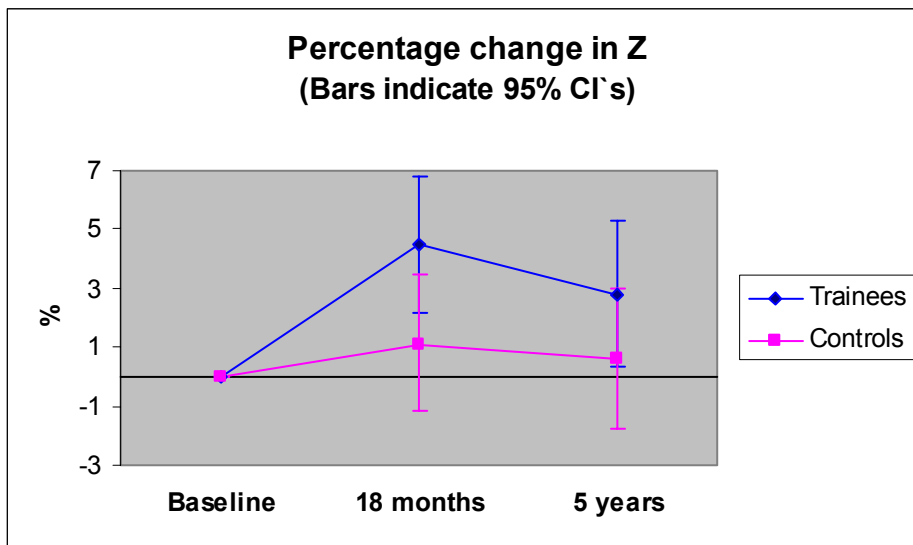


Figure 2

