Title

Leisure time physical activity in adulthood is positively associated with bone mineral density 22 years later. The Tromsø Study.

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Abstract

Although the positive association between physical activity and bone mineral density (BMD) is well established, few epidemiological studies have investigated the long-term associations between physical activity during adulthood and BMD later in life. The aim of this prospective, population-based study was to examine the association between leisure time physical activity in adulthood and areal BMD (aBMD) later in life. We examined 1,766 women and 1,451 men aged 20-54 years at baseline who were followed up 22 years later, as part of a population-based study in Norway. Leisure time physical activity was assessed by questionnaire at baseline and follow-up. aBMD was measured at the hip and forearm at follow-up, using X-ray absorptiometry. The association between aBMD and physical activity was analyzed using general linear models. We observed a positive linear trend in aBMD across physical activity levels in both women and men, after adjustments for baseline age, height, weight, and smoking status ($P < 0.05$). The relationship between aBMD and leisure time physical activity was consistent over different sites of the hip (total hip, femoral neck and trochanter area) and forearm (distal and ultradistal area). In a subsample of 2436 men and women under 70 years of age, those who where sedentary at both baseline and follow-up (6%) had lower aBMD than those who were moderately active or active at both baseline and follow-up (71%) ($P \leq 0.01$). This study suggests that leisure time physical activity in adulthood is associated with higher aBMD and reduced risk of osteoporosis later in life.

Key words

Bone mineral density

Epidemiology

Exercise

Follow-up study

Osteoporosis

Physical activity

Abbreviations

aBMD: areal bone mineral density

CI: confidence interval

DXA: dual-energy X-ray absorptiometry

MET: metabolic equivalent

OR: odds ratio

QCT: quantitative computed tomography

SD: standard deviation

SXA: single X-ray absorptiometry

Introduction

Osteoporotic fractures constitute a substantial cause of disability, morbidity, and mortality in older people in many regions of the world [1, 2]. The high prevalence of osteoporosis in the elderly necessitates preventive strategies with minimal side effects that are feasible for most people [3]. One relevant strategy is physical activity, which could contribute to an increase in peak bone mass and postpone the age-related increase in bone fragility [3, 4].

Data from numerous cross-sectional and short-term prospective studies support a positive association between areal bone mineral density (aBMD) and physical activity at all ages [4-6]. However, benefits of physical activity on aBMD are more pronounced and consistent during growth than in adulthood [4-6], whereas risk of fracture is substantially higher in old age [7]. Therefore, any long-term influence of lifetime physical activity on aBMD at ages when osteoporotic fractures are more frequent would be of interest.

The benefits of physical activity during growth seem to be sustained into young adulthood [8-11]. Understanding of the association between adulthood physical activity and aBMD during old age comes from retrospective studies [12-24]. These studies show that former elite athletes have higher aBMD than sedentary persons, at least one or two decades after retirement [12, 13, 16-18, 21, 24]. However, studies of the association between more moderate physical activity in the past and aBMD in elderly have reported inconsistent results [14, 15, 19, 20, 22, 23], possibly due to recall bias, small sample sizes, and crude measures of physical activity. To the best of our knowledge, there are no prospective, population-based studies of the effects of adulthood physical activity on aBMD measured in middle and old age.

Therefore, the aim of this prospective, population-based study was to examine whether leisure time physical activity in a cohort of adult women and men is associated with aBMD and risk of osteoporosis later in life.

Materials and methods

Study design and population

The Tromsø Study is a population-based health study in Tromsø, Norway [25], consisting of six repeated surveys and examinations. In the present study, we included participants from the second Tromsø Study in 1979–1980 (baseline), who also underwent aBMD measurements in the fifth Tromsø Study in 2001–2002 (follow-up). The study was approved by the Norwegian Data Inspectorate and recommended by the Regional Committee of Research Ethics, and each participant signed a written informed consent.

The baseline source population comprised total birth cohorts of men aged 20-54 years and women aged 20-49 years. All men born between 1925 and 1959 and all women born between 1930 and 1959 who were living in the municipality of Tromsø, totally 21,440 persons, were invited to participate in the study. Of those invited, 53.5% (11,481 persons) were men, and 59.2% (12,694 persons) were younger than 35 years. In total, 16,546 persons (77%) attended and answered the question on leisure time physical activity at baseline.

In 2001-2002, 4,443 persons from the baseline cohort were invited to participate in the follow-up survey, which included aBMD measurements of the hip and forearm and a questionnaire, in addition to an examination of several other variables. Altogether 3,217 persons (1,766 women and 1,451 men) participated in the aBMD measurements. This represents 72% of the attendees to the baseline survey who also were eligible for measurement of aBMD at the hip at follow-up.

Assessment of leisure time physical activity

In 1979–1980, the participants responded to a self-administered questionnaire concerning several health related topics (the Norwegian version of the questionnaire is available online at http://www.tromsostudy.com). The participants were asked the following question about leisure time physical activity: *"State your bodily movement and physical exertion in leisure time. If your activity varies much, for example between summer and winter, then give an average. The question refers only to the last twelve months"*. This question comprised four response options:

1) Reading, watching TV, or other sedentary activity.
2) Walking, cycling, or other forms of exercise at least four hours a week.
3) Participation in recreational sports, heavy gardening etc. at least four hours a week (including walking or cycling to place of work, Sunday walking, etc).
4) Participation in hard training or sports competitions regularly several times a week.

The physical activity question was repeated at follow-up in 2001-2002; however, only in subjects younger than 70 years of age, owing to the study design.

Leisure time physical activity assessed according to this question has been validated against various measures [26-29]. In a cohort study of Caucasians, there was a positive association between physical activity level and MET [29]. In other validation studies, physical activity measured using this question correlated with the IPAQ-L (an international questionnaire about physical activity) [26] and aerobic capacity [27, 28].

Measurement of aBMD

The outcome measures were areal BMD (aBMD, expressed as g/cm^2) at the hip (total hip, trochanter, and femoral neck area) and forearm (distal and ultradistal area). Dual-energy X-ray absorptiometry (DXA) (GE Lunar Prodigy, LUNAR Corporation, Madison, WI, USA) was used to measure aBMD of the total hip, femoral neck, and trochanter area. We excluded technically incorrect scans, scans with metal in the region of interest and scans of hips with severe deformities. In men, 199 and 124 scans of the right and left hip, respectively, were excluded. In women, 183 and 210 scans were excluded [30]. Scans of the left hip were primarily used for analyses. However, when the left hip measurement was ineligible, the right hip scan was used. Two different single X-ray absorptiometric (SXA) devices (DTX-100, Osteometer MediTech, Inc., Hawthorne, CA, USA) were used to measure aBMD of the distal and ultradistal forearm, as described elsewhere [31]. The non-dominant arm was measured except when it was considered ineligible.

Specially trained technicians performed all scans according to the protocol provided by the manufacturer and reviewed and reanalyzed the scans if necessary. Throughout the study, all densitometers underwent daily phantom measurements to secure stability [31]. In a recent validation study, the short-term in vivo precision error for the Lunar Prodigy was 1.7% and 1.2% for the femoral neck and total hip measurements, respectively [32]. The mean in vitro precision error for the SXA devices was 0.9% when using the European Forearm Phantom [31].

Measurement of covariates

As previously reported [33], the baseline questionnaire also included questions about educational level, smoking habits, and prevalent cardiovascular diseases. At the physical examination, height and weight were measured to the nearest centimeter and half-kilogram, respectively, with subjects wearing light clothing and no shoes. Women were interviewed about their use of oral contraceptives and menopausal status. At follow-up in 2001-2002, the subjects were interviewed about their use of osteoporosis medicine, and women were asked about their use of oral contraceptives, estrogen, and menopausal status.

Statistical analyses

The participants were divided into three groups based on the four answer options from the questionnaire. Because category 4 ("*Hard training or sports competitions*") included only 41 men and 6 women, category 4 was combined with category 3 ("*Recreational sports, heavy gardening*") into a new category (denoted "Active"), and the main analyses were performed with three categories, denoted sedentary, moderately active, and active, respectively. Changes in physical activity level from baseline in 1979-1980 to follow-up in 2001-2002 were categorized into four levels: 1. Sedentary at both surveys, 2. Change from sedentary to moderately active or active, 3. Change from moderately active or active to sedentary, 4. Moderately active or active at both surveys.

The association between aBMD at follow-up as dependent variable and baseline physical activity as independent variable (modeled as a continuous variable) was analyzed using multivariable linear regression models. aBMD differences between groups of physical activity level were analyzed using analysis of covariance, followed by simple contrasts using sedentary (sedentary unchanged when analyzing physical activity changes) as reference category.

Baseline age, smoking status, height, weight, and sex (except when analyzes were stratified by sex) were included in the model as possible confounders. Adjusting for height, weight, and smoking status at follow-up gave similar results. Therefore, only results adjusted for baseline covariates are presented in this study. An interaction term, the cross product between physical activity and age, was added to the model to examine possible effect modifications by age. Model assumptions were verified by residual analyses.

Binary logistic regression models were used to assess the association between baseline physical activity and osteoporosis at follow-up. Prevalence of osteoporosis was calculated based on the peak total hip aBMD. Osteoporosis was defined by a gender-specific T-score (aBMD value) of 2.5 SD or more below the mean total hip aBMD value [7]. For the 354 women in the age group 20-35 years, the mean total hip aBMD was 1.003 g/cm2 (SD 0.11). For men (n = 242), the corresponding value was 1.063 g/cm2 (SD 0.12). These values were used as reference values.

Two-sided *P* values < 0.05 were considered statistically significant. All analyses were performed using SPSS (Statistical Package for Social Sciences, Chicago, IL, USA), version 16.

Results

In this study, 3,217 subjects with a mean age of 41.5 years (SD 6.6), range 20-54 years (20-49 years in women), at baseline were followed up 22 years later. Among the women, 19% were sedentary, 67% were moderately active, and 15% were active at baseline. In men, 19% were sedentary, 51% were moderately active, and 31% were active. Smoking and height differed between baseline physical activity groups, in men also age and body mass index, and in women educational level (Table 1). Use of osteoporosis medicine, oral contraceptives, or estrogen at follow-up did not differ between baseline physical activity groups ($P \geq 0.16$); therefore, we did not include these variables in the analyses.

In both sexes, we found a significant positive linear relationship between aBMD and physical activity levels, after adjustments for baseline age, smoking status, height, and weight (Table 2). The increasing linear trend in mean aBMD across the physical activity levels was consistent at the hip (total hip, femoral neck and trochanter area) and forearm (distal and ultradistal area) (all $P_{\text{trend}} < 0.05$) (Table 2). Unadjusted means of aBMD are not presented, as they were similar. No significant interaction between age and physical activity level was found in either women or men ($P > 0.2$).

At all sites, there were significant differences in aBMD between the groups ($P \leq 0.05$) (Table 2). The active women had 0.011 to 0.030 g/cm^2 (2.7 to 4.6%) higher aBMD than the sedentary women at both the hip and forearm sites ($P < 0.05$); the corresponding difference in men was 0.010 to 0.027 g/cm^2 (1.9 to 3.0%). The moderately active subjects had significantly higher aBMD than the sedentary at the ultradistal forearm (women and men) and distal forearm (men) ($P < 0.05$), and non-significantly higher aBMD at the hip ($P > 0.05$).

Due to paucity of cases of osteoporosis in men and women, the analyses assessing the relationship between physical activity and osteoporosis were not stratified by sex. The prevalence of osteoporosis decreased with increasing level of physical activity (sedentary 8.4% (n=50), moderately active 5.8% (n=110), and active 4.2% (n=30)). We found an inverse linear trend in odds of osteoporosis across physical activity levels (OR 0.7, 95% CI: 0.56, 0.93, *P* trend = 0.013), after adjustments for baseline age, smoking status, height, weight, and sex.

In a subsample of 2436 men and women under the age of 70 years in 2001-2002, we examined changes in physical activity from 1979-1980 to 2001-2002 in relation to aBMD (Figure 1). We found that 71% were either moderately active or active at both baseline and follow-up, while 6% were sedentary at both surveys. Those who where sedentary at both surveys, had lower aBMD than those who were moderately active or active at one or both surveys ($P \leq 0.01$).

Discussion

In this prospective, population-based study, leisure time physical activity was positively associated with aBMD measured 22 years later, when the subjects were 42 to 76 years old. The results uniformly showed a positive linear trend in aBMD across physical activity levels; this dose-response relationship was consistent at both the hip and forearm in both sexes, after adjustments for baseline age, height, weight, and smoking status. Likewise, we found a reduced risk of osteoporosis with higher levels of leisure time physical activity.

Based on data from a subsample of the participants (those aged < 70 years in 2001), we found that 71% were moderately active or active both at baseline and at follow-up, and that being physically active at either baseline and follow-up or both was associated with a higher aBMD than being sedentary at both surveys. These results indicate that any activity is better than being sedentary, and that not only past, but also recent activity may influence bone. However, the subgroup excluded all persons older than 70 years.

Our study extends the existing knowledge about long-term benefits of physical activity into middle age and old age by using a prospective design. Retrospective studies, which are susceptible to recall bias, have reported inconsistent results. Some studies of elderly men and women show an association between past physical activity and BMD at the hip and forearm at older age [15, 22]. Moreover, former elite athletes seem to maintain higher BMD 10 years after retirement compared to controls [12, 24], and even up to 40 years after retirement [21]; however, former athletes may have had higher levels of adulthood physical activity than non-athletes. Other studies of BMD in elderly individuals did not demonstrate any association with past physical activity in adulthood [14, 23, 34], although physical activity in adolescence predicted BMD at older age [14, 23]. In our study, we showed that even moderate physical activity was associated with higher aBMD.

Previous studies have demonstrated that the risk of hip fracture increases 2.6-2.9 times for one SD decrease in aBMD at the femoral neck [35-37], and that the risk of hip fracture decreases 1.9 times with 0.1 g/cm^2 increase in hip aBMD [38]. The differences in aBMD between physical activity levels in this study were relatively small, but consistent across all measured sites, which could indicate an association between physical activity and fracture risk.

Physical activity may also reduce fracture risk through other mechanisms than BMD, by affecting structural properties of the bone positively [39, 40]. Although aBMD measured with DXA is a common surrogate of bone strength, it is possible to measure other aspects of bone strength such as bone geometry and volumetric BMD, using three-dimensional imaging techniques. For example, Daly and Bass [39] reported that lifetime and mid-adulthood physical activity was associated with 6-15% higher mid-femur total and cortical areas as measured by quantitative computed tomography (QCT), while there was no observed association between aBMD and lifetime physical activity. In our study, three-dimensional imaging techniques were not available, but as suggested by Daly and Bass, because of the two-dimensional nature of aBMD measures, DXA may actually underestimate the effect of physical activity on bone strength.

Observational study designs are prone to selection bias, which may also have affected our study. The participation rate in the baseline survey was high (78%), but persons with poor health may not have attended. However, relatively few individuals aged 20-54 years have serious chronic diseases [41]. The subjects who were lost to follow-up for some reason (dropped out, moved, dead, excluded due to study design etc.) tended to be younger, taller, had higher education and a higher percentage of smokers. Although any non-attendance should be a matter of concern, we believe that it is unlikely that the association between physical activity and aBMD differed substantially between the participants in our study and eligible persons who did not attend.

Self-report of physical activity may result in misclassification; however, in most situations, misclassification leads to weaker relationships. The question regarding leisure time physical activity used in the Tromsø Study was introduced by Saltin and Grimby [42] 40 years ago and has ever since been widely used in population studies. The question is validated against various measures [26-29].

The physical activity question in our study covers partly duration (more or less than 4 hours per week) and a crude measure of intensity, but not type or frequency of the activity. Therefore, we have used the answer as an estimate of the total volume of activity only. Generally, total volume is regarded sufficient to show a dose-response relationship, although too inaccurate to find the exact level of physical activity to prevent disease [43]. With this in mind, we noticed that physical activity in this study, defined as activity more than four hours per week with moderate or high intensity, is in accordance with the Nordic Health Authorities' recommendations, which is 30 minutes physical activity with moderate intensity most days of the week [44].

Because aBMD was not measured at baseline, we were unable to control for baseline differences in aBMD between the groups. Lack of information about baseline BMD limits conclusions about causal relationship. Still, it is interesting to see that a rather rough measure of physical activity is significantly associated to aBMD 22 years later.

Adjustments for important risk factors (age, smoking status, height, weight, and sex) minimize the potential for confounding. Replacing weight and height with BMI as possible confounders gave similar results; therefore, we chose a model with weight and height, as these are direct measures, with height directly related to bone size. However, because of the observational study design, residual confounding or unmeasured confounders may have influenced our findings. Unfortunately, we did not have adequate information about nutritional intake.

An important strength of this study was the large population-based cohort and the prospective assessment of physical activity. Thus, we were able to detect a dose-response relationship, which may have implications for public health advice about physical activity [43].

In conclusion, our results showed that leisure time physical activity in adulthood was positively associated with aBMD later in life, at ages when individuals are more prone to fragility fractures. The results imply a reduced risk of osteoporosis among individuals who are physically active in adulthood.

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Figure legend

Fig. 1: Areal bone mineral density at the hip (a) and forearm (b) in relation to changes in physical activity level from baseline to follow-up. Results are adjusted for baseline age, smoking status, sex, height, and weight. *Significant higher areal bone mineral density than those who were sedentary at both baseline and follow-up ($P<0.05$).

Table 1. Baseline characteristics according to level of physical activity

Characteristics	Physical activity level			$P_{Equality}$
	Sedentary	Moderately active	Active	
Women (n = 1,766)	***n* = 326**	***n* = 1179**	***n* = 261**	
Age (years)	39.6 (5.6)	40.3 (5.6)	40.0 (5.3)	0.17
Height (cm)	162.3 (6.1)	163.0 (6.1)	164.1 (6.0)	0.002
Weight (kg)	61.3 (9.7)	62.0 (8.7)	62.0 (7.8)	0.42
Body mass index (kg/m^2)	23.3 (3.6)	23.3 (3.1)	23.0 (2.5)	0.33
Education (years)	9.2 (2.9)[b]	9.6 (2.9)[b]	9.8 (3.0)[b]	0.049
Smoking daily *n* (%)	152 (46.6)	423 (35.9)	91 (34.9)	0.001
Cardiovascular diseases[a] *n* (%)	5 (1.5)	14 (1.2)	4 (1.5)	0.83
Postmenopausal *n* (%)	30 (9.2)	102 (8.7)	25 (9.6)	0.87
Use of oral contraceptive *n* (%)	15 (4.6)	37 (3.1)	8 (3.1)	0.41
Men (n = 1,451)	***n* = 270**	***n* = 733**	***n* = 448**	
Age (years)	42.8 (7.0)	43.7 (6.5)	43.0 (6.7)	0.057
Height (cm)	175.7 (6.5)	175.8 (6.6)	176.6 (6.3)	0.059
Weight (kg)	78.5 (10.9)	77.2 (9.2)	77.0 (8.5)	0.088
Body mass index (kg/m^2)	25.4 (2.9)	25.0 (2.6)	24.7 (2.3)	0.001
Education (years)	9.7 (3.0)[c]	9.8 (3.3)[c]	10.1 (3.5)[c]	0.22
Smoking daily *n* (%)	155 (56.6)	343 (46.0)	172 (37.7)	<0.001
Cardiovascular diseases[a] *n* (%)	9 (3.3)	16 (2.2)[d]	7 (1.6)	0.3

Values are means (SD) or n (percentages).

[a]Previous myocardial infection, angina pectoris, or stroke

[b]Sedentary: n = 291, Moderate: n = 1049, Active: n = 231

[c]Sedentary: n = 244, Moderate: n = 651, Active: n = 393

[d]Moderate: n = 732

Table 2. Adjusted[a] means of areal bone mineral density at the hip and forearm in relation to level of physical activity at baseline

	Mean aBMD (95% CI) (g/cm^2)[a]			*P*	
	Physical activity level			Equality	Trend
	Sedentary	Moderately active	Active		
Women	*n = 326*	*n = 1179*	*n = 261*		
Total hip	0.905 (0.892, 0.919)	0.918 (0.911, 0.925)	0.935 (0.920, 0.949)[b]	0.016	0.004
Trochanter	0.758 (0.746, 0.771)	0.771 (0.764, 0.777)	0.786 (0.772, 0.800)[b]	0.014	0.004
Femoral neck	0.849 (0.836, 0.861)	0.855 (0.848, 0.861)	0.875 (0.861, 0.888)[b]	0.011	0.006
Distal forearm	0.406 (0.399, 0.412)	0.412 (0.409, 0.416)	0.417 (0.410, 0.424)[b]	0.043	0.013
Ultradistal forearm	0.307 (0.301, 0.314)	0.315 (0.312, 0.319)[b]	0.321 (0.314, 0.328)[b]	0.017	0.005
Men	*n = 270*	*n = 733*	*n = 448*		
Total hip	1.007 (0.991, 1.022)	1.017 (1.008, 1.026)	1.029 (1.018, 1.041)[b]	0.059	0.017
Trochanter	0.893 (0.878, 0.908)	0.909 (0.900, 0.918)	0.920 (0.909, 0.931)[b]	0.018	0.005
Femoral neck	0.922 (0.908, 0.937)	0.929 (0.921, 0.938)	0.944 (0.933, 0.955)[b]	0.040	0.014
Distal forearm	0.527 (0.519, 0.534)	0.537 (0.532, 0.541)[b]	0.537 (0.532, 0.543)[b]	0.037	0.043
Ultradistal forearm	0.430 (0.422, 0.437)	0.440 (0.435, 0.445)[b]	0.441 (0.435, 0.447)[b]	0.045	0.035

[a]Adjusted for baseline age, smoking status, height, and weight.

[b]Significantly different from the Sedentary group, $P < 0.05$.