

In healthy elderly postmenopausal women variations in BMD and BMC at various skeletal sites are associated with differences in weight and lean body mass rather than by variations in habitual physical activity, strength or VO₂max

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Abstract

The objective of this study was an integrated cross-sectional investigation for answering the question whether differences in bone mineral density in elderly postmenopausal women are associated with differences in habitual physical activity and unspecific exercise levels. Two hundred and ninety nine elderly women (69 ± 3 years), without diseases or medication affecting bone metabolism were investigated. The influence of weight, body composition and physical activity on BMD was measured at multiple sites using different techniques (DXA, QCT, and QUS). Physical activity and exercise level were assessed by questionnaire, maximum strength of the legs and aerobic capacity. Variations in physical activity or habitual exercise had no effect on bone. The only significant univariate relation between strength/VO₂max and BMD/BMC that remained after adjusting for confounding variables was between arm BMD (DXA) and hand-grip strength. The most important variable for explaining BMD was weight and for cortical BMC of the femur (QCT) lean body mass. Weight and lean body mass emerge as predominant predictors of BMD in normal elderly women, whereas the isolated effect of habitual physical activity, unspecific exercise participation, and muscle strength on bone parameters is negligible. Thus, an increase in the amount of habitual physical activity will probably have no beneficial impact on bone.

Keywords: Anthropometric Parameters, Bone Mass, Muscle Strength, Physical Activity, VO₂max

As has been shown by several meta-analyses, physical activity benefits the musculoskeletal system and may reduce fracture risk due to an increase of bone density^{1,2}. The exact mechanisms of the impact of exercise as well as of daily physical activity are rather complex. Not surprisingly, so far there is neither agreement on a specific type of exercise program nor on the level of required habitual physical activity to prevent bone loss with aging.

Methodically there are three main approaches (Figure 1) to investigate the effects of exercise and physical activity on bone: the first is the direct path by correlating or predicting bone parameters such as bone mineral density (BMD) or bone mineral density changes with or from variables characterizing the exercise or physical activity. However, a particular limitation of this approach is the adequate identification and quantification of the components of an exercise program that directly impact on bone. For example, many studies in the field only focused on frequency (how often) and duration (how long) but not on intensity which is the more important parameter when assessing bone adaptation^{3,4}. Also all these physical activity parameters can only be assessed using subjective scores via questionnaires. This may be the reason that some studies reported positive effects of physical activity and unspecific exercise on bone, suggesting that an increase in the amount of habitual physical activity would be adequate

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Exercise discipline	Example	Intensity factor
No exercises		0
Exercises with no or low ground-, and joint reaction forces	cycling, swimming	0
Exercises or games with low ground-, and joint reaction forces	bowling, walking	1
Exercises or games with moderate ground-, and joint reaction forces	dancing, low impact aerobic, calisthenics	2
Exercises or games with ground reaction forces >1000 μ E	running, high impact aerobic, tennis, squash	3
Exercises with high joint reaction forces	high intensity strength training at machines	3

Table 1. Grading of exercise intensity factor.

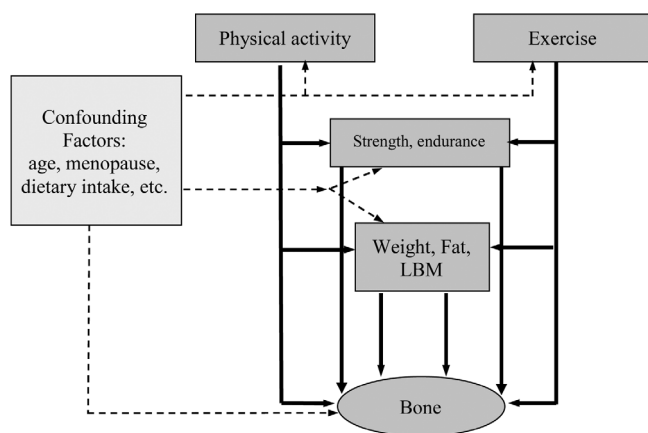


Figure 1. Relationship between variables affecting bone.

for augmenting or maintaining bone mass, whereas other studies reported the contrary and recommended more specific exercise programs.

In the second approach, parameters such as muscle strength or VO_2 max, which characterize the physiologic result of the activity/exercise are associated with bone parameters (Figure 1). Typically, these parameters can better be quantified than those derived from questionnaires. However, this approach is also not straightforward. Many cross-sectional studies have reported a positive correlation between muscle strength that plays a dominant role in the mechanostat theory⁵ and bone mass or density⁶⁻⁹. But as pointed out by several authors these correlations were either rather low¹⁰ or often vanished after adjusting for factors such as age, body weight, or lean or fat body mass^{3,8,10,11}. Just as controversial are results from studies investigating the relationship between VO_2 max and BMD: some were significant^{12,13}, others were not^{3,9,10}. Again, despite being more quantitative and more objective than questionnaires, the types of variables and the methods for their assessment may be partly responsible for the ambiguous study outcomes. For example, there are a large variety of tests in which muscle strength is determined: concentric versus eccentric, static

versus dynamic, or strength versus power. Another complicating factor is the compliance of subjects to perform tests with maximum effort.

The third approach shown in Figure 1 is independent of strength measurements and compliance. Here the relations between bone parameters and anthropometric variables affected by exercise and habitual activity, such as muscle mass, lean body mass (LBM), or muscle cross-sectional area, are investigated. There is plenty of evidence that in addition to age, weight is a strong predictor of bone mineral density^{3,8,9,14}. In contrast, there is less information on the effect of body composition, i.e., lean body and fat mass. Cross-sectional studies assessing the relative relevance of body fat versus lean body mass in premenopausal women found higher correlations between LBM and BMD^{15,16}. In contrast in postmenopausal women correlations were higher for body fat^{9,15,17}. One difficulty in using this third approach is the fact that in addition to the predominantly local effects caused by exercise and physical activity these anthropometric variables were potentially even stronger influenced by systemic effects such as Estradiol aromatase activity¹⁴.

Finally, in almost all exercise and physical activity studies, bone mineral density was determined with the projectional DXA technique, which does not fully capture changes of bone size. Also cortical and trabecular bone cannot be separated. Therefore, exercise-related effects on bone may have been missed. The technique of quantitative computed tomography (QCT) may be the better choice but has rarely been used in exercise studies^{18,19}.

The overall aim of this study was guided by the question whether in elderly people current or reasonably increased levels of habitual activity and exercise are sufficient to maintain bone mineral density or whether specific exercise programs are required. The objective of this study was an integrated cross-sectional investigation of effects of habitual physical activity and unspecific exercise on bone in normal postmenopausal women 65 years and older. An in-depth analysis using all three approaches discussed above was performed in order to capture the various effects on bone. The data presented here are baseline data from the SEFIP (Senior Fitness and Prevention) study carried out in Erlangen, Germany. Therefore, exercise in this study does not refer to a specific

	Mean \pm SD	Minimum	Maximum
Anthropometric parameters			
Age [y]	69.0 \pm 2.9	65	80
Body height [cm]	161.2 \pm 5.6	141.5	178.5
Body weight [kg]	68.8 \pm 9.8	46.4	108.4
Body Mass Index [kg \cdot m ⁻²]	26.5 \pm 3.9	18.8	40.0
Body fat [%]	36.9 \pm 5.4	5.91	21.2
Fat mass [kg]	26.5 \pm 6.8	11.6	54.1
Lean mass [kg]	43.9 \pm 4.7	32.1	60.9
Gynecological risk factors			
Age at menarche [y]	13.9 \pm 1.4	9.5	18
Age at menopause [y]	49.4 \pm 5.7	29	61
Estrogen exposition [y]	35.5 \pm 5.6	16	47
Number of pregnancies [n]	1.9 \pm 1.1	0	7
Dietary parameters			
Energy intake [kJ \cdot d ⁻¹]	6628 \pm 1756	2131	12748
Calcium intake [μ g \cdot d ⁻¹]	921 \pm 474	206	3573
Magnesium intake [μ g \cdot d ⁻¹]	310 \pm 142	86	1057
Vitamin D intake [μ g \cdot d ⁻¹]	2.9 \pm 5.3	0.09	34.6
Further risk factors			
Ever smoked [%]	21.4	---	---
Use of glucocorticoids >3 months during life [%]	3	---	---
Use of contraceptive >1 year during life [%]	45.2	---	---

Table 2. Mean \pm SD, minimum, and maximum values of anthropometric and dietary parameters, and of several other osteoporosis risk factors measured in this study.

program designed and carried out to prevent bone loss but to the entity of various exercise activities carried out by the subjects prior the start of the SEFIP study.

Material and methods

The SEFIP Study is a controlled exercise trial in elderly women approved by the Ethics Committee of the University of Erlangen (Ethik Antrag 3354), and the Bundesamt für Strahlenschutz (Z5-22462/2-2005-026). All study participants gave written informed consent. The trial is fully registered and design details, in addition to those presented below, can be obtained from www.clinicaltrials.gov.

Subjects

Two hundred ninety and nine postmenopausal community dwelling women (69 \pm 3 years of age) were recruited from population registers of Erlangen and vicinity using local advertisements and individual letters. Exclusion criteria were current or recent (within 2 years before study start) use of medication (i.e., bisphosphonates, HRT, PTH, SERMs, calcitonin, fluorides, active Vitamin D metabolites or gluco-

corticoides) or diseases affecting bone metabolism. Further exclusion criteria were inflammatory diseases and history of cardiovascular disease, as well as low physical capacity (<75 Watt with bicycle ergometry).

Anthropometric data

Body height was measured on a stadiometer and weight was measured with minimal clothing on a calibrated digital scale. The body mass index (BMI) was calculated as usual from weight and height in kg/m². Total body lean and fat mass were determined from a body composition analysis of a total body DXA scan.

Variables describing exercise and physical activity

The various tests and procedures to obtain measures of physical activity are very similar to those used in the Erlangen Fitness Osteoporosis Prevention Study (EFOPS). A detailed description of all the procedures is beyond the scope of this contribution; therefore, here we include a succinct summary and refer the reader more interested in finer details to recent publications of the EFOPS study^{20,21}.

Isometric muscle strength

Maximum isometric muscle strength of the trunk extensors and trunk flexors were measured using a Schnell M-3 isometric tester (Schnell, Peutenhausen, Germany). The maximum isometric muscle strength of the leg extensors was measured with a static leg press using a force plate (MTD Systems, Neuburg v. Wald, Germany), on which the subjects were instructed to push in a lying position with the knees and the hip bent at 90°.

We employed the isometric test protocol from Tusker²² that is recommended for research. After a detailed oral instruction, two initial attempts with low intensity were performed to prepare the subjects. Then without further warm-up, two maximum efforts lasting 5 seconds each with a 40-second rest period in between were carried out. The higher value of the two maximum efforts was used for data analysis. Subjects were not particularly motivated for the test nor were results immediately provided to them. Grip strength of the dominant hand was measured with a Jamar dynamometer (Jamar, Bolingbrook, IL) according to the protocol suggested by Mathiowetz et al.²³.

Dynamic muscle power

The maximum muscle power was determined for the leg extensors in the same way as described above. The subjects were instructed to push as fast and as strong as possible on the force plate. Power was then determined as the highest value of the derivative of the smoothed force-time curve.

Treadmill ergometry

Aerobic fitness was measured as peak oxygen uptake obtained during a stepwise treadmill test (Uno Fitness LTX 5 Pro, Bonn, Germany) up to a voluntary maximum. Starting with an velocity of 5 km/h at 0°; the slope was increased every 1.5 minutes by 2°. The maximal oxygen consumption (VO₂max) was recorded "breath by breath" using a spirometric system from Viasys (Oxycon mobile, Viasys, Conshohocken, PA, USA).

Questionnaires of physical and overall activity

For the assessment of the average daily activity levels, detailed questionnaires were used which included work, household and immediate pre-study exercise levels. One activity and two exercise indices were calculated from the questionnaires in the same way as reported earlier¹⁰.

The habitual physical activity was rated on a subjective rate between 1 and 7. It summarized household, hobby, and gardening activities as well as occupational activities.

The exercise index EI [min/week] characterizes weekly exercise frequency and duration:

$$EI = \sum_i t_i,$$

where t_i is the duration of an exercise session i is in minutes and i runs over all weekly exercise sessions.

The osteogenic exercise index OI [min/week] additionally considers the osteogenically relevant intensity of a specific exercise discipline:

$$OI = \sum_j a_j EI_j,$$

where EI_j is the exercise index for an exercise discipline j , for example the total minutes of cycling per week. a_j is the intensity factor for exercise discipline j . We termed it osteogenic impact factor and assigned values between 0 and 3¹⁰.

With respect to the physical activity and exercise section of the questionnaire, participants were specifically informed about the character of the questions. The physical activity sections of the completed questionnaires were validated by the assistants together with the study subjects to avoid mistakes. In the questionnaire, subjects were specifically asked about type, intensity, and duration of their exercise history. The reproducibility of the questionnaires had been tested in an earlier study²⁴ and was higher than 95%. In order to determine the influence of habitual physical activity on bone, we separated our cohort into different groups. The following three schemes (S1-S3) were used: S1: three groups were distinguished with either a low, medium or high self-rated physical activity index; S2: based on their exercise index two groups were distinguished representing exercising and non-exercising women; and S3: based on their exercise intensity factor (Table 1) two groups were distinguished representing a smaller or larger than 0.

Bone densitometry

Bone densitometry was performed by DXA, QCT, and quantitative ultrasound (QUS). DXA (QDR 4500A Hologic, Bedford, MA) was determined at the lumbar spine (L1-L4), the proximal femur and for total body. BMD of the arms were derived from the regional analysis of the total body scan. Volumetric bone mineral density was measured by QCT (Siemens Somatom Sensation 64, Erlangen, Germany) at the lumbar spine (L1-L3)²⁵ and at the proximal femur²⁶. For the total and trabecular compartment we determined BMD, but for the cortical compartment we used bone mineral content (BMC), which is less affected by partial volume artifacts caused by the limited resolution of the CT scanner in order to assess cortical structures. Speed of sound (SOS), broadband ultrasound attenuation (BUA), and the combined quality of ultrasound index (QUI) were measured by ultrasound at the calcaneus using the Sahara device (Hologic, Bedford, MA).

Dietary intake

The individual dietary intake was assessed by a 4-day protocol of the food consumed. The participants were supplied with household scales for accurate weighing. Each participant was instructed individually and in detail and was additionally provided with a printed document. For the analysis of the protocols Prodi 4,5/03 Expert software (Wissenschaftlicher Verlag, Freiburg, Germany) was used.

	Mean \pm SD	Minimum	Maximum
Present activity	4.3 \pm 1.2	1	7
Exercise index (EI) [min \cdot week ⁻¹]	86 \pm 177	0	960
Osteogenic exercise index (OI) [min \cdot week ⁻¹]	87 \pm 212	0	1380
Grip strength [kg]	27.4 \pm 3.9	14	42
Trunk flexion strength [Nm]	38.4 \pm 10.6	12	87
Trunk extension strength [Nm]	111 \pm 25	24	221
Leg extension strength [N]	699 \pm 159	208	1412
Leg extension power [N/ms]	4.4 \pm 2.4	1.0	14.5
Rel. VO ₂ max [ml \cdot min ⁻¹ \cdot kg ⁻¹]	23.4 \pm 4.0	14.2	34.1

Table 3. Mean \pm SD, minimum, and maximum values of parameters used to describe physical activity, exercise, muscle strength, and endurance.

	Mean \pm SD	Minimum	Maximum
Lumbar Spine			
QCT: Trabecular BMD LS [mg \cdot cm ⁻³]	86.7 \pm 22.8	19.1	167.9
QCT: Cortical BMD LS [mg \cdot cm ⁻³]	259 \pm 43.6	130	425
DXA: BMD L1-L4 [mg \cdot cm ⁻²]	925 \pm 145.6	545	1405
Proximal Femur			
QCT: Neck total BMD [mg \cdot cm ⁻³]	296.3 \pm 51.34	158.1	437.3
QCT: Neck Trabecular BMD [mg \cdot cm ⁻³]	133.6 \pm 46.3	31.1	308.7
QCT: Neck Cortical BMC [mg]	4123 \pm 982	1089	7593
QCT: Hip total BMD [mg \cdot cm ⁻³]	263.5 \pm 45.6	120.6	384.9
QCT: Hip Trabecular BMD [mg \cdot cm ⁻³]	108.8 \pm 35.8	18.6	218.9
QCT: Hip Cortical BMC [mg]	13364 \pm 2250	6664	20677
DXA: BMD Neck [mg \cdot cm ⁻²]	709 \pm 90.3	488	1083
DXA: BMD HIP [mg \cdot cm ⁻²]	836 \pm 110	481	1195
DXA: BMD Trochanter [mg \cdot cm ⁻²]	644 \pm 90.3	321.2	978.6
DXA: BMD Arms [mg \cdot cm ⁻²]	678 \pm 77	502	1493
Calcaneus			
US: BUA [dB \cdot MHz ⁻¹]	85.5 \pm 15.6	46.8	137.7
US: SOS [m \cdot s ⁻¹]	1533 \pm 28.66	1476	1627
US: QUI	85.5 \pm 16.46	46.8	137.7

Table 4. Mean \pm SD, minimum, and maximum values of parameters of bone densitometry.

Statistical analysis

Baseline measurements are reported as mean values (MV) and standard deviations (SD). Normality of distributions and homogeneity of variance were investigated using the Kolmogorov-Smirnov and Levine's F-tests. Depending on type of data, differences between two groups were assessed with unpaired t-tests or Mann-Whitney U-tests. Differences between more than two groups were assessed with one-way analysis of variance or with the non-parametric Kruskal-Wallis-test.

First, Pearson or Spearman correlation coefficients were used to investigate univariate correlation between independent variables and dependent bone parameters. Second, stepwise multiple regressions were used to select an optimum regression model. The percentage of variance attributable to each independent variable was calculated as the square of the coefficients (r^2) obtained from the multiple regression models. In order to limit the numbers of independent variables we included only those parameters in the stepwise regressions that had shown significant correlations in the univariate analyses.

R	Age	Height	Weight	Lean mass	Fat mass	Handgrip strength	Trunk extension	Trunk flexion
Lumbar Spine								
L1-L4 (DXA)	-	.247	.436	.440	.367	.169	.224	-
Proximal Femur								
total Hip (QCT)	.304	.428	.428	.345	.419	.151	.318	-
total Hip (DXA)	.291	.559	.559	.513	.503	.223	.386	-
Neck (QCT)	.304	.350	.350	.286	.341	-	.260	-
Neck (DXA)	.295	.203	.559	.503	.441	.204	.327	-
Trochanter (QCT)	.321	-	.480	.375	.475	.139	.370	-
Trochanter (DXA)	.278	.207	.553	.491	.509	.204	.404	-
Intertroch (QCT)	.291	-	.363	.315	.341	.182	.252	-

Table 5. Significant ($p < 0.05$) univariate correlations between variables of Table 2 and Table 3 with total BMD of the central skeleton.

R	Age	Weight	Fat mass	Lean mass	Handgrip strength	Trunk extension	Trunk flexion
Lumbar Spine							
L1-L3 BMD tra.	.316	.183	.234	.270	.241	.197	-
L1-L3 BMC cor.	.181	.164	-	.180	-	-	-
Proximal Femur							
total hip BMD tra.	.306	.467	.439	.395	.156	.325	-
total hip BMC cor.	.193	.527	.376	.629	.347	.401	.323
Neck BMD tra.	.325	.425	.401	.359	.163	.271	-
Neck BMC cor.	-	.208	.238	.374	.140	.265	.282
Trochanter BMD tra.	.243	.458	.433	.383	.142	.343	-
Trochanter BMC cor.	.194	.563	.415	.644	.317	.425	.255
Intertroch BMD tra.	.298	.421	.382	.380	.157	.290	-
Intertroch BMC cor.	.123	.313	.210	.398	.295	.229	.182

Table 6. Significant ($p < 0.05$) univariate correlations between variables of Table 2 and Table 3 with trabecular BMD and cortical BMC of the central skeleton as measured by QCT.

Although age was significantly correlated with the bone parameters, we could not include it in the multiple regressions because it was not normally distributed. Therefore, for the evaluation the influence of age, in a third step we calculated partial correlations using age as controlling variable.

A 5% probability level was considered significant (*). SPSS 14.0 (SPSS Inc., Chicago IL) was used for all statistical analyses.

Results

Tables 2 and 3 list $MV \pm SD$ and minimum and maximum values of all parameters used in the analysis. For group separation scheme S1, there were no significant inter-group differ-

ences either for strength, VO_2max , or any of the bone parameters determined in this study. S2 and S3 showed borderline significant differences between the two groups for weight ($p=0.04$), fat mass ($p=0.07$), and VO_2max ($p=0.06$). For S2, but not for S3, QUI and SOS showed significant differences ($p=0.008$ and $p=0.005$, respectively) with higher values for the "exercisers". Based on these results in the following, we pooled all subjects and did not further separate groups.

All variables listed in Table 2 and Table 3 were univariately correlated with those listed in Table 4. Significant correlations are shown in Tables 5 and 6, separately for central and the peripheral skeleton as explained in more detail below. All other variables described in Tables 2 and 3, in par-

Dependent Variable	Independent variable	Total r ²	Corrected r ²	p
Peripheral Skeleton central				
Total BMD				
Lumbar spine (DXA)	Lean mass	.194	.188	.000
total Hip (DXA)	Weight	.312	.307	.000
total Hip (QCT)	Weight	.183	.177	.000
Neck (DXA)	Weight	.264	.259	.000
Neck (QCT)	Weight	.264	.259	.000
Trochanter (DXA)	Weight	.306	.301	.000
Trochanter (QCT)	Weight	.231	.225	.000
Intertrochanter (QCT)	Weight	.132	.125	.000
Trabecular BMD				
Lumbar spine (QCT)	Lean mass + handgrip strength	.073 .099	.066 .086	.001 .050
Total hip (QCT)	Weight	.218	.212	.000
Neck (QCT)	Weight	.180	.174	.000
Trochanter (QCT)	Weight	.210	.204	
Intertrochanter (QCT)	Weight	.178	.172	.000
Cortical BMC				
Lumbar spine (QCT)	Lean mass	.032	.025	.035
Total hip (QCT)	Lean mass	.415	.411	.000
Neck (QCT)	Lean mass + trunk flexion	.140 .174	.134 .162	.000 .020
Trochanter (QCT)	Lean mass + height	.395 .425	.391 .417	.000 .009
Intertrochanter (QCT)	Lean mass + handgrip strength	.158 .187	.152 .175	.000 .030
Peripheral skeleton				
Arm (DXA)	Lean mass + handgrip strength	.237 .271	.231 .260	.000 .013
Calcaneus (US-BUA)	Fat mass	.061	.054	.004

Table 7. Results of the stepwise regression analyses.

ticular muscle power measured for leg extension or VO₂max, did not significantly correlate with variables of bone densitometry.

Central skeleton

Total BMD

Significant univariate correlations for total BMD are shown in Table 5. After the stepwise regressions (Table 7) for the spine, lean mass and for the hip, weight remained the only significant variables in the models explaining 18% to 30% of the variability of total BMD as measured by DXA or QCT. All strength parameters that at least weakly correlated univariately with total BMD were removed in the stepwise regressions.

Trabecular BMD and cortical BMC

Univariate correlations are shown in Table 6. It should be noted here that, all measurements were done with QCT because with DXA trabecular and cortical bone cannot be distinguished. At the spine, trabecular BMD was correlated with all anthropometric and strength variables except for trunk flexion force. In contrast, cortical BMC was only correlated with age, weight and lean mass. Similarly at the hip, trabecular BMD again correlated significantly with all anthropometric and strength variables except for trunk flexion force. However, here in all volumes of interest cortical BMC correlated with all variables shown in the table.

At the spine, the multiple regression analysis (Table 7) determined lean mass to be the most important predictor but included handgrip strength as a further predictor for tra-

R	Age	Height	Weight	Lean mass	Fat mass	Handgrip strength	Trunk extension	Trunk flexion
Arm								
BMD (DXA total body scan)	.365	.317	.418	.311	.487	.333	.370	.171
Calcaneus								
QUI	.292	-	-	-	.160	.160	-	-
BUA	-.247	-	.233	.162	.247	.147	.159	-
SOS	-.303	-	-	-	-	.156	-	-

Table 8. Significant ($p < 0.05$) univariate correlations between variables of Table 2 and Table 3 with total BMD of the dominant arm and QUI of the calcaneus using age as the controlling variable.

becular BMD. At the hip for trabecular BMD, only weight remained significant after the multiple regressions whereas for cortical BMC, lean mass was the most important predictor. Trunk flexion strength was a further predictor for cortical BMC of the neck, height for cortical BMC of the trochanter, and handgrip strength for cortical BMC of the intertrochanter. R^2 -values for trabecular BMD were between 0.09 and 0.21, and somewhat weaker than for total BMD. At the hip, the highest r^2 -values were found for cortical BMC of the total hip and the trochanter. Here lean mass explained 41% and 39%, respectively, of the BMC variation.

After adjusting for lean mass the partial correlation between hip cortical BMC and handgrip strength ($r=0.195$) and trunk flexion force ($r=0.194$) remained, as well as the correlation between trochanter cortical BMC and handgrip strength ($r=0.138$) and the correlations between trunk flexion force and cortical BMC of the neck ($r=0.198$, $p=0.002$). However, only the correlation between hip cortical BMC and handgrip strength remained after additionally adjusting for age ($r=0.19$; $p=0.030$). After adjusting for lean body mass and age none of the univariate correlations could be maintained.

Peripheral skeleton

In the periphery, BMD of the dominant arm determined from a total body scan was positively correlated with handgrip strength, trunk flexion force, and trunk extension force as well as with age, height, weight and lean and fat mass (Table 8). At the calcaneus investigated by QUS, SOS, BUA and the combined QUI index were positively correlated with maximal handgrip strength and age. In addition, QUI and BUA were positively correlated with maximal trunk extension force. After the stepwise regression analyses for the arm lean mass and handgrip strength and for the calcaneus, fat mass remained in the models, only.

Effect of age

Age in our population ranged from 65 to 80 with a mean of 69 and a standard deviation of 2.9 years (Table 2). Despite this

narrow distribution, most of the densitometric variables correlated significantly with age. As described in the section on statistical analysis age could not be included in the stepwise regression models. Thus as a last step, partial correlations for all relations shown in Table 7 were carried out using age as a controlling variable. Apart from DXA of the forearm the effect of age was negligible: compared to the univariate correlations for total BMD of the spine, and all cortical BMC measurements the partial correlations with lean mass did not change r significantly after correcting for age. For the trabecular measurements of the hip, the correlation coefficient with weight decreased on average significantly by 2% after correction for age. For the DXA measurement in the arm, the age correction decreased the correlation with lean mass from $r=0.31$ in the univariate correlation to $r=0.23$ in the adjusted correlation.

In those cases in which two independent variables remained significant in the stepwise regression models (trabecular BMD of the spine, cortical BMC of the neck and of the intertrochanter and DXA of the arm) a strength variable was the second most important predictor. Here we also carried out partial correlations using these strength variables. In contrast to the anthropometric variables that were hardly affected by age, the correlation coefficients of all strength variables became insignificant after age adjustment, again with the exception for DXA of the arm where grip strength remained significant ($r=0.19$, $p=0.03$).

Discussion

In this study, we determined the impact of habitual physical activity, non-athletic exercise, muscle strength and body composition on bone in a large cohort of elderly Caucasian women. As a central result, we found that variations of total and trabecular BMD of the hip were almost exclusively predicted by weight, whereas variations of BMD at the spine and of cortical BMC at the hip were almost exclusively predicted by lean mass. Overall, the contribution of strength and endurance parameters in explaining densitometric variations at the spine, femur, arm and calcaneus was negligible, which implies that in this age group typical variations in

habitual physical activity and exercise have no impact on bone mineral density. With respect to trabecular bone the results generated here confirm our previous study in which we analyzed baseline data of the EFOPS study¹⁰ as well as a number of other recent studies^{3,10,11,27}. To our knowledge, studies with cortical measurements derived from QCT have not been published yet.

As described in the introduction, in this study we investigated the impact of exercise and physical activity along three pathways (Figure 1). With respect to the first several physical activity questionnaires such as the Stanford 7 day Physical Activity Recall Questionnaire²⁸ exist but the adequate method to assess osteogenic activity or exercise is still under discussion. Thus, not surprisingly, in different studies various criteria are used for the determination of physical activity.

As we did not presuppose a linear correlation between physical activity and BMD, we first differentiated our cohort into three groups according to a self-rated physical activity index recorded on the questionnaires. We found no group differences with respect to strength, VO_2max , or any of the bone parameters. Similar results have been reported by several studies, which concluded that the influence of physical activity on BMD was non-significant after adjusting for confounding variables^{3,9,29-31}. Other authors, however, showed an independent influence of physical activity on BMD^{27,32-34}.

In order to better differentiate the amount, intensity, and impact of exercise we used schemes S2 to categorize subjects into an exercise or a sedentary group and S3 to categorize them according to osteogenic exercise. Again, when comparing bone parameters, no significant differences between groups were found with the exception of QUS at the calcaneus. In contrast to our results, some authors reported significant effects of current³⁵⁻³⁷ or previous^{32,37,38} exercise on BMD, even after adjusting for relevant confounding factors. One possible explanation may be the fact that less than 24% of our population participated in any sportive exercise. Furthermore, the average osteogenic impact factor of the exercises carried out in our cohort was rather low. Most of the subjects in this study preferred sports with no (swimming, cycling) or little (walking) osteogenic impact.

In a second analysis step, we directly investigated the effect of primary target parameters of exercise such as muscle strength and endurance on bone density. We used four parameters describing muscle strength and measured a large variety of bone parameters at the lumbar spine, proximal femur, arm, and the calcaneus with a variety of techniques. We also included a measurement of muscle power to account for high strain rates, which may have a higher effect on BMD than conventional forces applied in isometric or dynamic modes.

In the univariate correlations, handgrip strength, trunk extension and partly trunk flexion correlated with most bone density variables; but after the stepwise regression analysis, a significant strength contribution only remained in three models: handgrip strength for trabecular BMD of the lumbar spine and the arm and trunk flexion for cortical BMC of the neck. Even in these models, the strength contribution

was very weak compared to the contribution of lean mass in explaining the variance of BMD or BMC. After the partial correlations that also included age, the only remaining significant strength variable was handgrip strength for explaining BMD of the arm.

These results are in accordance with other investigations in which significant univariate relationships were drastically reduced after adjusting for confounding variables^{3,11,39,40} such as body weight. Nevertheless, despite these reductions after adjustment most authors still found significant relationships between strength and/or VO_2max with bone parameters in postmenopausal women^{7,8,18,39,41,42}. Yet, a closer inspection of these studies show adjusted regression or correlation coefficients that are almost always negligible ($r^2 < 10\%$). Thus, in particular at weight-bearing sites i.e., the spine and the hip, the impact of muscle strength on BMD must not only be adjusted for age but also for weight.

It is obvious that our results cannot be interpreted in a sense that muscle strength does not have an effect on BMD but in normal elderly women, who do not participate in specific exercise programs but who are neither extremely inactive, variations of trabecular or total BMD and cortical BMC are not explained by the variation of activity levels typical for this population. Thus, we speculate that a moderate increase in daily physical activity or unspecific exercise may not significantly benefit bone in women of this age range. Obviously, a cross-sectional study has limitations in proofing this hypothesis, and it also remains unclear what increase would be needed in order to show an effect. On the other hand several exercise studies such as the EFOPS study showed that with dedicated high-impact and/or high intensity training bone mineral density can be maintained or even slightly increased in postmenopausal women^{1,2}.

Our study has several strengths: (1) Compared to similar studies our study population was large; (2) All women were recruited from the same region and were of Caucasian background, reducing the impact of environmental, ethnical and gender differences; and (3) Subjects with medication or diseases affecting bone metabolism were not included. In contrast to most other studies, we used three indices¹⁰ defined in validated questionnaires to account for amount, intensity, and impact of various exercise types and daily activities. In order to incorporate strain impact we ranked exercise types according to their osteogenic impact similar to other recent cross-sectional studies in athletes comparing the effect of different sport disciplines on BMD⁴³⁻⁴⁵. In order to locally evaluate the muscle impact on bone, we measured several strength parameters, including a measurement of muscle power of the leg extensors. A large variety of densitometric variables were determined at four different skeletal sites, including the proximal femur and the lumbar spine. As a novelty, we included QCT of the hip that allowed differentiating cortical and trabecular parameters.

Our results for cortical and trabecular bone are very interesting. So far, weight has been reported to be the most significant predictor of BMD^{14,46,47}. We confirmed this for trabecu-

lar and total BMD of the hip. However, for cortical BMC of the hip as well as for total, and trabecular BMD of the spine lean body mass was more important explaining as much as 40% of the variation of cortical BMC at the hip. A low but still significant contribution of LBM was also found for the cortical lumbar spine. LBM, weight, and fat mass are highly correlated. In our cohort we found a correlation between weight and lean mass of $r=0.833$ and between weight and fat mass of $r=0.929$. Differential effects of lean and fat mass on bone compartments have been reported in the literature¹⁴. Furthermore, the impact of lean body mass vs. fat mass on bone differs among pre- and postmenopausal females^{15,17}.

The discussion above is complicated by the fact that we measured BMC for cortical and BMD for trabecular and total bone because for cortical bone QCT accuracy errors for BMC should be smaller than for BMD measurements. BMD per definition is already adjusted by size and thus at least partially also by weight, whereas BMC obviously depends on size. However, in the univariate correlations height was only significant for total BMD but not for cortical BMC (Tables 4 and 5) and dropped out altogether in the stepwise regression model. On the other hand, for trabecular BMC of the hip also LBM and not weight remained in the model (data not shown here). Thus based on our results, it is speculative to discuss different effects of LBM and weight on different bone compartments. The simultaneous inclusion of weight and lean body mass may cause subtle effects that should be investigated further. Our results also highlight potential methodological difficulties when analyzing the bone muscle relationships using cortical BMC and lean body or muscle mass from pQCT measurements without considering BMD and weight.

Interestingly, in most univariate correlations with bone parameters, age was significant despite the fact that the age range was narrowly peaked around 69 years in our study. However, as proofed in the adjusted correlations, age did not, or almost did not, weaken the correlations of weight and lean mass with BMD and BMC.

We conclude that in normal elderly women typical variations of habitual physical activity, non-athletic exercise, and muscle strength on trabecular bone density and cortical bone mass are almost insignificant after corrections for confounding parameters. Body weight proved to be the most important factor for trabecular and total BMD at the hip. Lean body mass correlated most highly with BMD in the spine and cortical BMC at the hip. In our cohort, an increase of habitual activity and unspecific exercise is not very promising but a dedicated exercise regimen increasing gravitational forces, as well as muscle strain, should be used in order to achieve a significant effect on bone. Increasing weight by increased muscle mass may be one option to be pursued.

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