Journal of Clinical Densitometry: Assessment & Management of Musculoskeletal Health, vol. ■, no. ■, 1–12, 2016

1094-6950/■:1–12/$36.00
http://dx.doi.org/10.1016/j.jocd.2016.07.002

Original Article

Bone Traits Seem to Develop Also During the Third Decade in Life—Normative Cross-Sectional Data on 1083 Men Aged 18–28 Years

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Abstract

By identifying individuals with low peak bone mass (PBM) at young age, early targeted interventions to reduce future fracture risk could be possible. Peripheral quantitative computed tomography (pQCT) is in many ways superior to the gold standard dual-energy X-ray absorptiometry (DXA), as cortical and trabecular compartments as well as the volumetric density and bone structure can be examined separately. Because each of these traits contributes independently to bone strength, it is probable that pQCT provides an even better fracture risk estimation than DXA. Currently, the clinical applications of pQCT are limited partly because comprehensive normative pQCT data, especially in young men, are not readily available. We therefore set up a study in young men with the following objectives: (1) to identify peak ages in pQCT bone traits with special reference to PBM and peak bone strength; and (2) to provide normative pQCT data. We measured volumetric bone mineral density and structural parameters at *ultradistal* (trabecular bone) and *diaphyseal radius* and *tibia* (cortical bone) by pQCT scans (Stratec XCT2000®; Stratec Medizintechnik GmbH, Pforzheim, Germany) in a population-based age-stratified sample of 1083 men aged 18–28 yr residing in greater Malmö, Sweden. Group differences in 1-yr classes were evaluated by analysis of variance. We found similar bone traits in age groups at *ultradistal* sites whereas most bone traits at *diaphyseal* sites were higher with higher ages, however with different increment patterns depending on the specific trait. In Swedish young adult men, we found that different bone traits continued to change after age 18, but at different rates, indicating that peak areal bone mineral density (as measured by DXA) and peak bone strength may be reached at different ages.

Key Words: Bone mass; bone size; males; normative; pQCT.

Introduction

Peak bone mass (PBM) has often been defined as the highest amount of bony tissue an individual reaches during life and is usually determined by the surrogate estimate areal bone mineral density (aBMD) from dual-energy X-ray absorptiometry (DXA). PBM is said to occur as early as ages 17 and 18 in the hip *(1,2)*, but the age differs between skeletal locations and gender *(2)*. Reports also indicate that aBMD "tracks" from childhood to adolescence *(3)*, from adolescence to young adulthood *(4)*, and during 10 adult years in ages 25–44 yr *(5)* and 45–84 yr *(6)* which further supports the clinical importance of PBM.

The bone mass of an old individual at a certain time point is the result of PBM minus age-related bone loss *(7)*. PBM is thus an important determinant for the risk of develop-

Received 01/26/16; Revised 05/3/16; Accepted 07/26/16.
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ing osteoporosis *(8)*, and it has been suggested that it would take 28 yr of increased bone loss (+1 standard deviation [SD]) in postmenopausal women to offset an increase in PBM by +1 SD *(9)*.

The gold standard for determining bone mass (and PBM) is aBMD as estimated by DXA, and substantial normative DXA data are available *(10–12)*. However, the fact that DXA is a two-dimensional technique results in shortcomings as aBMD is derived by dividing the amount of bone mineral by the scanned area. That is, aBMD (g/cm^2) is not a true density based on volume (g/cm^3) but only a composite estimate of both amount of bone mineral and bone area. This is of importance because each of these traits independently and positively contributes to bone strength *(13)*. For example, in the case of stable bone mineral content (BMC) and increased bone size, aBMD would decrease even though bone strength probably increases *(14)*. Bone strength may thus increase not only by an increase in the amount of bone mineral but also by a larger bone size. This underlines the importance of assessing structural bone traits individually. In the hip, for example, the cross-sectional bone area alone seems to explain as much as 83% of the variance in bone strength *(15)*, and the difference in aBMD between young men and women is the result of differences in bone size, not in volumetric bone mineral density (vBMD). Peripheral quantitative computed tomography (pQCT), which is a three-dimensional technique, can address this concern by providing data on both vBMD (mg/cm^3) and structural traits. Another advantage of pQCT is that trabecular and cortical bone compartments may be evaluated separately *(16)*, and with pQCT it is therefore possible to estimate if PBM coincides with peak bone strength. It should be clearly stated that the measurement of vBMD alone does not fully appreciate all facets of PBM, especially since vBMD from pQCT relies on nonperfect estimate of true bone volume. A disadvantage of pQCT from the clinical perspective is that comprehensive normative data, especially in young men, are not readily available. We therefore set up a study in young men with the following objectives: (1) to identify trait by age trends and the age when peak, the highest value of a specific pQCT trait, is reached; and (2) to provide normative pQCT data.

Materials and Methods

Subjects

Up to 4503 males aged 18–28 yr residing in the greater city of Malmö (population 318,107; year 2014), Sweden, were randomly selected from the official population registry by a 1-yr age-stratified sampling procedure. Of the responding 2223 men, 1340 (60%) agreed to participate. Prespecified exclusion criteria were inability to understand the Swedish language or severe movement impairments rendering pQCT scans impossible to perform. Furthermore, some invited subjects who answered their invitation late were not measured due to sufficient amount of subjects in respective age group or due to age exceeding 28 yr at the time of consenting participation. After the above-mentioned exclusions and withdrawals, 1083 young men were assessed by pQCT between August 2006 and May 2012 (Fig. 1). By this, we had 86–117 men in each 1-yr age group. Ninety-eight percent (n = 1074) were of Caucasian ethnicity. Four experienced scan technicians conducted all measurements. The study was approved by the regional ethical review board (2005:75/205) and was conducted in accordance with the Declaration of Helsinki. Written consent was obtained from all participants prior to study start.

PQCT

Scans using the model XCT 2000s (software versions 5.5 and 6.0; Stratec Medizintechnik GmbH, Pforzheim, Germany) were conducted examining the nondominant forearm (*radius*) and the lower leg (*tibia*) of the same side. We chose to include measurements of the radius, to represent a bone exposed to lower load, and the tibia, which is a bone exposed to higher load. We further chose to evaluate distal sites to capture predominantly trabecular bone and mid-diaphyseal sites to capture predominantly cortical bone. The ultradistal vBMD of the cortical compartment was excluded as this site is known to be difficult to accurately estimate by pQCT *(17,18)*. Extremity lengths were measured using standardized methods and equipment provided by the manufacturer. Scout views (coronary slices) enabled scans at regions of interest and scans were performed at *ultradistal* (*4%* [both *tibia* and *radius*]) and *diaphyseal* (*38%* [*tibia* only] and *66%* [both *tibia* and *radius*]) sites relative to baseline (*0%*). Cortical and trabecular traits acquired from the scans included vBMD (mg/cm^3), pQCT BMC (mg/mm), cross-sectional area (CSA, mm^2), cortical thickness (Ct.Th, mm), periosteal circumference (PC, mm), endosteal circumference (EC, mm), polar cross-sectional moment of inertia (CSMI, mm^4) of the total bone area, and polar strength strain index (mm^3).

The scanner was calibrated daily using a standard phantom and monthly using a cone phantom, both provided by the manufacturer.

Anthropometry

Height and weight were measured using standard equipment. Body mass index (BMI) was calculated as weight in kilograms divided by height in centimeters squared.

Statistical Analysis

We used IBM SPSS Statistics for Windows (version 22.0; IBM Corp., Armonk, NY) for statistical analyses. Descriptive data are reported as means with SDs within brackets and outcomes as means with 95% confidence interval within brackets. Analysis of variance (ANOVA) was used to determine any differences between 1-yr age groups and statistical significance was considered for p values < 0.05. We utilized ANOVA to test overall differences in trait values between 1-yr age classes but did not proceed with *post hoc* tests between specific years as such analyses would be data