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Geographic and other determinants of BMD change in European men and women at the hip and spine. A population-based study from the Network in Europe for Male Osteoporosis (NEMO)

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Abstract

Introduction: While the determinants of BMD change have been studied in women, there have been few longitudinal studies in men. As part of the Network in Europe for Male Osteoporosis (NEMO) study, data were analysed from 1337 men and 1722 women aged 50–86y (mean=67 years) from 13 centres across Europe to assess determinants of BMD change and between-gender contrasts.
Methods: BMD was measured at the femoral neck, trochanter and/or L2–L4 spine on 2 occasions 0.8–8 years apart (mean=3.5 years) using DXA densitometers manufactured by Hologic ($n=6$), Lunar ($n=5$) and Norland ($n=2$). Each was cross-calibrated using the European Spine Phantom and annual rates of BMD change (g/cm^2/year) were calculated from the standardised paired BMD values. The EPOS risk factor questionnaire was administered at baseline.
Results: In multivariate linear regression models, there were large between centre differences in the mean rates of BMD change in all 3 sites for both genders ($P<0.0001$) with the standard deviation of the between centre heterogeneity in the adjusted means being 0.005 g/cm^2/year at the femoral neck. The overall adjusted mean annual rates of BMD change in g/cm^2/year (95% CI) pooled across centres by random effects meta-analysis in men were: femoral neck −0.005 (−0.009, −0.001); trochanter −0.003 (−0.006, −0.001); and spine 0.000 (−0.004, 0.004). In women the respective estimates were: −0.007 (−0.009, −0.005); −0.004 (−0.006, −0.003); and −0.005 (−0.008, −0.001). The I^2 statistic for heterogeneity was between 81% and 94%, indicating strong evidence of between centre heterogeneity. Higher baseline BMD value was associated with subsequent greater decline in BMD ($P<0.001$). Preserved BMD was associated with higher baseline body weight in all 3 sites in men ($P<0.012$) but not in women. Weight gain preserved BMD ($P<0.039$) in all 3 sites for both genders, except the male spine. Increasing age was associated with faster BMD decline at the trochanter in both genders ($P<0.026$) and with a slower rate of decline at the female spine ($P=0.002$). Effects of lifestyle, physical activity, medications, and reproductive factors were not consistent across sites or between genders.

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Conclusion: These results show major geographic variations in rates of BMD change in men and women over 50 years of age across diverse European populations and demonstrate that body weight and weight gain are key determinants of BMD change in men.

Keywords: Ageing; Bone loss; BMD change; Bone mineral density; Osteoporosis

Introduction

Bone mineral density (BMD) is an important determinant of risk of fracture in both men and women [1,2]. But while reduced BMD levels in postmenopausal women are substantially attributable to faster BMD decline after menopause in association with reduced oestrogen levels[3], little is known about the patterns of BMD change in men and their determinants. Much of the published evidence of associations with BMD levels has come from cross-sectional studies. A diversity of anthropometric, physical activity, lifestyle, dietary, and other hormonal factors (besides oestrogen) have been associated with BMD levels in many cross-sectional studies in women [4–8] and in fewer studies including men [9,10]. Factors that have been associated with low BMD in women have included: lower body weight [11], reducing levels of physical activity [12], and a range of lifestyle and dietary variables, including smoking, alcohol consumption [13,14] and low fruits and vegetables intake [15,16]. There is also evidence of large geographical variation in BMD levels across diverse populations in Europe [11]; but it is unknown whether such geographic variations exist for rates of within person BMD change.

Findings from cross-sectional studies are limited in the information they can provide about determinants of within-person BMD changes, since the former are confounded by cohort effects. Indeed, a number of longitudinal studies on BMD change have failed to replicate findings from cross-sectional studies [17,18] or have even found effects contradicting cross-sectional results from the same studies [19,20]. As part of the Network in Europe for Male Osteoporosis Study (NEMO), we analysed data from men and women aged 50 to 86 years in the European Prospective Osteoporosis Study (EPOS) who had two hip BMD scans. Our purpose was to assess key determinants of BMD change and to quantify the magnitude of between-centre differences in rates of change, with particular emphasis on identifying the reasons why some men lose BMD from middle age on.

Subjects and methods

Participants

The subjects were participants from 13 centres that undertook repeat BMD measurements in the European Prospective Osteoporosis Study (EPOS), a multi-centre study conducted in 31 centres in 19 countries across Europe. Details of the EPOS study have been reported in previous publications [21–23]. Briefly, each centre recruited a random sample of up to 300 men and 300 women from population registers stratified into six 5-year age bands: 50–54, 55–59, 60–64, 65–69, 70–74 and 75+. Those who took part answered the interviewer-administered EPOS risk factor questionnaire and had lateral spine radiographs performed at baseline. Twenty-two of the EPOS centres undertook hip and/or spine BMD measurements from 10 to 100% of their recruited participants at baseline and, among these, repeat BMD measurements done an average of 3.6 years apart (range = 0.8 to 6.3 years) were available at the hip for 809 men and 1167 women, and at the spine for 610 men and 899 women.

Additionally, BMD data from participants recruited into a bone fragility study following the EPOS protocol and embedded within the European Prospective Investigation of Cancer in Norfolk, UK (EPIC-Norfolk) [24] were included in this evaluation. The bone fragility study in EPIC-Norfolk consisted of 528 men and 555 women aged 67–79 years at baseline who had two hip BMD measurements done at an average of 2.9 years apart (range = 1.9 to 8.0 years). The EPOS risk factor questionnaire was administered to the EPIC-Norfolk study participants at baseline.

BMD measurement

The densitometers in each of the 13 centres were pencil beam dual-energy X-ray absorptiometry (DXA) machines made by Lunar, Hologic or Norland. They were cross-calibrated using the European Spine Phantom (ESP) [25]. The ESP is a semi-anthropomorphic phantom with three "vertebrae" of known densities of 0.5, 1.0 and 1.5 g/cm^2 [25]. At least 5 measurements of the phantom were made on each machine at baseline and a two-parameter empirically fitted linear or exponential calibration curve used to convert measured density values into standardised values, as described by Pearson [26]. The same cross-calibration equations were used to convert BMD measurements on the second occasion to standardised values and then BMD changes were calculated as the difference between the second and baseline measurement divided by the time interval between them i.e. in g/cm^2/year units.

The first stage of quality assessment (QA) of the repeat DXA scans was done at the individual centres where the second scan was compared to the baseline scan to ensure congruence of analysis regions. Technically unacceptable scans were excluded from the calculation of BMD changes. Only BMD measured at the femoral neck, trochanter and L2–L4 spine regions of interest were available for this evaluation since other sub-regions such as the total hip and the intertrochanter were not available for the Lunar and Norland densitometer brands. Detailed descriptions of the densitometry procedures as they applied to the subjects are presented elsewhere [11,27].

This paper is based on analyses of paired BMD data from 13 centres with a total of 1337 men and 1722 women having hip BMD and a total of 610 men and 899 women having spine BMD.

Second stage QA

The scans for the German centres were submitted to CCG for formal QA [28]. The QA for the other centres followed the same procedures as outlined to them by CCG. The Norland scans were submitted to a QA analyst in Aberdeen and the Lunar scans were all submitted to QA by NJC, as previously described [29]. The remaining Hologic scans were similarly quality-assured in Cambridge. Data from scans of manufacturer's daily QC phantom were used to assess whether densitometers had drifted between scans by regressing the phantom BMD values on time in years since baseline in each centre. This was supplemented by examining the machine printouts of QC charts or by estimating drift from repeat measurements of ESP when the electronic daily QC data were unavailable. When significant densitometer drift was detected, the BMD values for each participant on the second occasion were corrected by recalculating them as: observed BMD − (drift per year * time between scans).