Obesity Increases Precision Errors in Dual X-ray Absorptiometry Measurements.

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Abstract

The precision errors of dual energy x-ray absorptiometry (DXA) measurements are important for monitoring osteoporosis. This study investigated the effect of body mass index (BMI) on precision errors for lumbar spine, femoral neck, total hip and total body bone mineral density using the GE Lunar Prodigy. 102 women with BMI's ranging from 18.5-45.9kg/m^2 were recruited. Participants had duplicate DXA scans of the lumbar spine, left hip and total body with repositioning between scans. Participants were divided into three groups based on their BMI and the percentage coefficient of variation (%CV) calculated for each group. The %CVs for the normal (<25 kg/m^2) (n=48), overweight (25-30 kg/m^2) (n=26) and obese (>30 kg/m^2) (n=28) BMI groups respectively were: lumbar spine BMD: 0.99%, 1.30% and 1.68%; femoral neck BMD: 1.32%, 1.37% and 2.00%; total hip BMD: 0.85%, 0.88% and 1.06%; total body BMD: 0.66%, 0.73% and 0.91%. Statistically significant differences in precision error between the normal and obese groups were found for lumbar spine (P = 0.0006), femoral neck (P = 0.005) and total body BMD (P = 0.025). These results suggest that serial measurements in obese subjects should be treated with caution since the least significant change may be larger than anticipated.

Keywords: Dual energy x-ray absorptiometry; Precision; Obesity; Bone mineral density

Introduction

Dual energy x-ray absorptiometry (DXA) is the gold standard for the clinical measurement of bone mineral density (BMD) for the diagnosis of osteoporosis and the prediction of fracture risk [1]. The precision errors of DXA measurements are important for characterising the ability to detect longitudinal changes [2] as a result of therapeutic intervention or disease progression. Precision errors are partly dependent on quality assurance systems to detect scanner changes and on operators' training and experience [2]. The evaluation of precision errors involves repeated measurements, with the International Society of Clinical Densitometry (ISCD) recommending either duplicate scans of 30 subjects or triplicate scans of 15 subjects[3] [4]. Precision errors may vary between individuals due to differences in bone status and biological variations, such as tissue inhomogeneity, and it is therefore important to measure a representative set of subjects [5].

Obesity is becoming increasingly prevalent in the western world with levels in men and women rising from 13% to 22% and 16% to 24% respectively between 1993 and 2009 in England [6]. It is estimated that by 2012 obesity levels in England will rise to 31.2% and 31.0% in men and women respectively [7]. While obesity is usually thought to be protective against osteoporosis due to the positive correlation between weight and BMD [8], recent studies have reported increased lower limb and vertebral fracture rates with increasing body mass index (BMI) suggesting that the increased BMD is not as protective against fracture as previously thought [9,10]. This means that it is likely that more overweight patients will require DXA scans in the future.

Previous studies of DXA precision errors have investigated subjects representing the typical postmenopausal and elderly clinical populations. However, the number of overweight and obese participants in these previous studies has been limited. To date no well-powered study has been purposely designed to investigate DXA precision errors. We hypothesise that

precision errors will be larger in an obese population than a normal BMI population as a result of increased tissue thickness that results in reduced signal to noise ratio and increased inhomogeneity in soft tissue composition. Increased soft tissue inhomogeneity is likely to occur from a greater and/or more variable amount of visceral fat surrounding the organs in overweight and obese patients.

This study investigated the effect of increasing BMI and percentage body fat on DXA precision errors at the lumbar spine, proximal femur, and total body using the GE Lunar Prodigy.

Materials and Methodology

Participants

The study consisted of 102 female volunteers aged between 18 and 75 years recruited from the general population via poster advertisements. The participants were allocated to one of three BMI groups <25 kg/m^2; 25-29.9kg/m^2 and ≥30kg/m^2 representing normal, overweight and obese respectively based upon the WHO criteria for body mass index classification [11]. Subjects were analyzed according to BMI groups determined from the measured height and weight at their DXA scan visit. The aim of the study was to recruit 30 subjects in each BMI group, yielding a sufficiently robust study to determine differences between the groups with 27 degrees of freedom (df) in each group. The exclusion criteria included, aged under 18 or over 75 years, male and the presence of internal prosthetic implants. The study was approved by the Devon and Torbay Research Ethics Committee and all subjects gave written informed consent.

Methods

All participants had their height measured to the nearest 0.01m using a stadiometer (Holtain, Crymych, Dyfed, UK) and body weight measured to the nearest 0.1 kg in minimal clothing

using beam balance scales (Avery, Birmingham, UK) respectively prior to their scan. BMI was calculated as weight (kg)/height (m^2).

DXA scans were performed using the GE Lunar Prodigy (GE Healthcare, Bedford, UK). All subjects had repeat postero-anterior (PA) scans of the lumbar spine, left proximal femur and total body with repositioning between scans, involving the participant getting off and back onto the table between each set of the above mentioned three scans. The scan modes used (standard or thick) were selected automatically by the scanner software. Scans were analysed using the GE Lunar Encore 2005 software version 9.30.044.

Statistical Analysis

For statistical analysis women were grouped by BMI. The three BMI groups were <25 kg/m^2; 25-29.9 kg/m^2 and ≥30 kg/m^2 representing normal, overweight and obese respectively based upon the WHO criteria for BMI classification [12]. It proved more difficult than expected to recruit overweight and obese subjects and the final study population consisted of 48 women in the normal BMI group, 26 in the overweight group and 28 in the obese group. In a secondary analysis the women were also classified based on their DXA derived total body fat expressed as a percentage of total body weight. Four body fat groups were examined representing <30%, 30-39.9%, 40-44.9% and ≥45% fat respectively [11].

Descriptive statistics (means and standard deviations) were calculated for anthropometric variables and bone mineral density at lumbar spine (L1-L4) (LS), femoral neck (NOF), total hip (TH) and total body (TB) for participants by BMI group using SPSS version 15.0.

Precision errors of DXA derived variables were expressed as the percentage coefficient of variation (%CV) and calculated by expressing the root mean square standard deviation as a percentage of mean BMD [5]. The 95% confidence intervals were calculated using the Chi-

Squared distribution [5]. Differences between precision errors were tested for statistical significance using the F-test.

The %CV was calculated for LS, NOF, TH and TB BMD for women grouped by both BMI and % body fat as described above. The least significant change (LSC) was calculated by multiplying the precision error by 2.77 [13]. Finally, the influence of scan mode on precision error was examined by computing the %CV for LS BMD for subjects scanned in thick mode compared with a group of participants matched for body fatness scanned in standard mode in the two highest % body fat groups (≥40%). Significant differences in precision errors were reported using a significance level of $p \leq 0.05$.

Results

The participant characteristics for each BMI group are shown in Table 1. No statistically significant differences were found between the groups for age, height, or BMD, while statistically significant differences were found between the groups for weight and % body fat as would be expected based on the criteria for inclusion within the groups.

The precision errors with the women categorised by BMI group are shown in Table 2, which lists the %CVs and 95% confidence intervals from the lowest to the highest BMI group for lumbar spine, femoral neck, the total hip and total body BMD. A trend for increasing precision errors with increasing BMI is seen, with the differences between the normal BMI and obese groups reaching statistical significance for the lumbar spine, femoral neck and total body sites. Table 3 shows the same data when the women were divided based on their percentage body fat measured by their total body DXA scans. The results demonstrate a trend for precision errors to increase with increasing %fat mass, with many differences between groups reaching statistical significance.

When the precision errors for the women with > 40% body fat scanned in “thick” and “standard” modes at the lumbar spine were compared there was a small reduction in %CV using the “thick” scan mode compared to the “standard” scan mode (1.35% (n=13) vs. 1.68% (n=29)) that was not statistically significant (P = 0.21).

Discussion

These results demonstrate a trend for precision errors to increase within increasing BMI and % body fatness with an effect that was most marked for the lumbar spine and femoral neck regions of interest (ROIs). With the increasing incidence of obesity in the population [7,14] and recent evidence that there is a greater fracture incidence in obese patients [15,16] and lower than expected BMD in a sub-population of obese women [17], the larger precision errors in obese populations demonstrated in this study will be increasingly significant for clinical studies.

The BMI groups were well matched, with no significant differences for mean age, height, lumbar spine BMD, femoral neck BMD and total hip BMD, demonstrating that the differences in precision errors expressed as the %CV were not explained by different mean BMD between the groups. The precision errors reported in the present study were comparable with previous studies in clinical populations [1,18-21] demonstrating that the scanning practices at the unit undertaking the DXA scans were appropriate and that the volunteer population recruited for this study produced precision errors broadly comparable to previous studies in clinical populations. Since the women in this study were recruited from volunteer subjects, based on their BMI the mean age of the subjects was younger and their mean BMD higher than that expected in a typical clinical population selected on the basis of clinical risk factors.

The results demonstrate a trend for precision errors to increase with increasing BMI and % body fat that was particularly noticeable in the lumbar spine (Table 2, Table 3). It is likely that the main reasons for the effect on precision errors in the spine are the greater body thickness at the spine and the greater inhomogeneity of soft tissue in the abdomen. The algorithms used by DXA systems to calculate BMD assume that the soft tissue overlying the spine has the same composition as in the soft tissue reference area either side of the spine [22,23]. However, soft tissue in the abdominal cavity is not held in a fixed position and therefore has the ability to differ from scan to scan. With increasing body fatness, the amount of visceral adipose tissue also increases, thus increasing the potential for greater BMD differences due to tissue inhomogeneity between scans.

The precision errors for the two hip ROIs yielded quite different results, with a greater effect of BMI and % body fat on %CV at the femoral neck compared with the total hip site. Rajamanohara et al also reported a study that found a larger effect of BMI and patients' body weight on precision errors at the femoral neck than the total hip ROI [24]. In obese patients the femoral neck ROI is frequently overlain by a fat panniculus that may alter its position when the subject is rescanned generating the potential for greater errors due to inhomogenieties in soft tissue composition [25]. In contrast, the DXA intertrochanteric ROI is less likely to be covered by the fat panniculus resulting in a smaller effect on the precision of total hip BMD measurements. The poor precision for the femoral neck ROI in the highest body fat group may also be associated with the challenges of accurate positioning of patients for the hip scan in the most obese subjects, for example achieving consistent rotation of the femoral neck [24]. To investigate if there were any underlying clinical reasons for poor precision at the femoral neck ROI in the highest body fat group, the clinical histories of the volunteers were examined for any indication of osteoarthritis (OA) of the hips, which may have been greater in this group leading to potential difficulties in positioning. However, there were no significant differences in reported OA between any of the groups, suggesting this was not a contributing factor.

The increased precision errors at the spine reported in the higher percentage body fat groups are considered to be associated with increased tissue thickness and fat inhomogeneity. Svendsen et al and Formica et al have reported random accuracy errors of BMD measures due to fat inhomogeneity [22,23]. The increasing precision errors with increasing % body fat within this study fit well with this effect.

There are some limitations to this study. This study was conducted using a GE Lunar Prodigy and these results should not be generalised to other manufacturers DXA scanners or to other GE Lunar bone densitometers. The participants were drawn from a volunteer population, which does not reflect the typical clinical population. A volunteer population was more appropriate for this study since the DXA scanner used was based in a research centre where clinical studies are not performed. It was felt inappropriate to approach a clinical population from a local service, since the volunteers would be undergoing duplicate scans as part of the study and there would be no benefit to the women undertaking the study had they already had a recent DXA scan from the local scanning service. The subjects in this study underwent duplicate scans on the same day, which has been reported as yielding lower precision errors than when duplicate scans are performed on different days [25]. However, scanning on different days was not feasible for this study in terms of potential attrition from the study based on the large geographical area from which participants were drawn. This is mitigated to an extent by ensuring that all participants were asked to get up from the table between scans so that repositioning was performed. Finally, the fat panniculis was not retracted as recommended as recommended by Binlkey et al [

When the impact of obesity on the least significant change was examined, the LSC at the lumbar spine was markedly increased at higher levels of obesity, suggesting that in an obese population a greater scanning interval is required to be sure that changes in BMD are real and not just resulting from measurement errors. This means that based on an annual

percentage change in BMD in the lumbar spine of between 0.45 and 3.2% [26, CHINGFORD], in a population with over 45% body fat, the scanning intervals to be certain of a real change range from 1.6 to 10.9 years depending on the lower or higher estimate of the rate of change in bone expected. The results of this study reinforce the increased precision error at the lumbar spine with increasing BMI reported by Nelson et al. However, the femoral neck results of this study demonstrate an increase in precision error in overweight / over-fat and obese participants which is at odds with that reported by Nelson et al. This may be as a result of the different DXA scanners used in the two studies, population differences with differing fat distributions or resulting from the exploration of the effect of percentage body fat in this study in addition to BMI, which yielded more significant increases in precision error [Nelson]. Long-term precision has been reported to be 50% greater than short-term precision [21], therefore with this in mind, the LSC and thus scanning intervals are likely to be even greater than reported above. In practice, patients in the obese range are also more likely to exhibit large weight changes between scans, which further confound repeat measurements. This demonstrates that service delivery needs to be adapted to the individual patient depending on their menopausal status, their treatment and their BMI status. The total hip is least affected by increases in body fatness and BMI and is equally as predictive of fracture risk as the femoral neck ROI [Cummings], so this would be the most appropriate site for diagnosis and monitoring of treatment. Clinical services may also wish to consider different follow-up periods for patients in the different BMI bandings if they are keen to have monitoring information from the lumbar spine results.

In conclusion, increased BMI and % body fatness have a clinically significant effect on precision errors, with higher precision errors in those in higher BMI and body fatness groups. This was most marked for the lumbar spine and femoral neck ROIs. The impact of increased BMI and % body fatness resulted in a higher least significant change, leading to an increased interval between scans being required in obese populations.

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Table 1: Descriptive statistics (Mean (SD)) of women by BMI group

BMI Group	<25 kg/m^2 (n = 48)	25-29.9 kg/m^2 (n = 26)	≥30 kg/m^2 (n = 28)	P value*
Age (y)	45 (13)	49 (14)	49 (13)	ns
Stature (m)	1.65 (0.06)	1.64 (0.07)	1.66 (0.08)	ns
Body mass (kg)	61.1 (5.9)	72.4 (7.6)	95.1(16.3)	P < 0.01
Fat (%)	30.6 (7.6)	39.4 (3.5)	46.8 (3.6)	P < 0.01
Lumbar spine BMD (g/cm^2)	1.202 (0.150)	1.199 (0.123)	1.254 (0.127)	ns
Total hip BMD (g/cm^2)	1.012 (0.145)	1.036 (0.120)	1.075 (0.145)	ns
Femoral neck BMD (g/cm^2)	0.998 (0.144)	0.996 (0.116)	1.015 (0.155)	ns

*ns: not significant P > 0.05; P < 0.01: all inter-group comparisons significant

Table 2: Precision errors (CV%) (95% confidence interval) by BMI group

BMI group	<25 kg/m^2 (n = 48)	25-29.9 kg/m^2 (n = 26)	≥30 kg/m^2 (n = 28)
Lumbar Spine BMD	0.99 (0.82-1.23)%	1.30 (1.03-1.79)%	1.68 (1.33-2.27)%*†
Femoral Neck BMD	1.32 (1.10-1.64)%	1.37 (1.08-1.88)%	2.00 (1.59-2.71)%*†
Total Hip BMD	0.85 (0.71-1.06)%	0.88 (0.69-1.20)%	1.06 (0.84-1.43)%
Total Body BMD	0.66 (0.55-0.83)%	0.73 (0.57-0.99)%	0.91 (0.73-1.24)%*

* p=<0.05 when compared to < 25kg/m^2 group
† p=<0.05 when compared to 25-30kg/m^2 group

Table 3: Precision errors (CV%) (95% confidence interval) by % fat group

% fat group	<30% (n = 20)	30-39.9% (n = 40)	40-44.9% (n = 22)	≥45% (n = 20)
Lumbar Spine BMD	0.80 (0.61-1.16)	1.18 (0.97-1.51)*	1.40 (1.08-1.98)* †	1.77 (1.35-2.55)*
Femoral Neck BMD	1.05 (0.80-1.51)	1.44 (1.18-1.84)	1.14 (0.88-1.62)	2.36 (1.80-3.40)* †◊
Total Hip BMD	0.80 (0.62-1.16)	0.89 (0.73-1.14)	0.69 (0.54-0.98)	1.22 (0.93-1.76)* †◊
Total body BMD	0.64 (0.49-0.92)	0.67 (0.55-0.86)	0.70 (0.54-0.99)	1.02 (0.78-1.48)* †◊

* p=<0.05 when compared to <30% fat group
† p=<0.05 when compared to 30-39.9% fat group
◊ p=<0.05 when compared to 40-44.9% fat group