

Contents lists available at ScienceDirect

Bone Reports

journal homepage: www.elsevier.com/locate/bonr



Aging, lifestyle factors, hormones and bone health in Singaporean men



Victor Hng Hang Goh *, William George Hart

Curtin Medical School, Faculty of Health Sciences, Bldg 400, Curtin University, Kent Street, Bentley, WA 6102, Australia

ARTICLE INFO

Article history: Received 18 December 2015 Received in revised form 21 March 2016 Accepted 11 May 2016 Available online 13 May 2016

Keywords: Physical activity Age Bone mineral density Body mass index Percent fat mass Singaporean men

ABSTRACT

Purpose: The present study examined how age, bodyweight, body fat, regular exercise and some endocrine factors are associated with osteoporosis, spine bone mineral density (Sbmd) and femoral neck bone mineral density (Fnbmd) in Singaporean men.

Methods: Body composition and bone scans of lumbar spine at L2-L4 and hip were carried out with duel-energy X-ray absorptiometry (DXA). Anthropometric parameters were measured and demographic data, medical history and exercise schedule were collected via a questionnaire.

Results: Osteoporosis prevalence was higher and Sbmd and Fnbmd were lower in men with high percent body fat (PBF) and conversely osteoporosis prevalence was lower and Sbmd and Fnbmd were higher in men with higher body mass index (BMI). Age was negatively associated with Fnbmd but not Sbmd. On the other hand, PBF and insulin levels were negatively associated with both Sbmd and Fnbmd. Body mass index and exercise intensity were positively associated with both Sbmd and Fnbmd. Sex hormones were significantly associated with only Sbmd but not Fnbmd. Both estradiol and DHEAS were positively, while testosterone was negatively associated with Sbmd.

Conclusion: The study shows that the prevalence of osteoporosis and some of the determinants of bone mineral density (BMD) in Singaporean men was site-specific. Further, BMI and PBF are opposing predictors of BMD. Therefore, any strategy for improving bone health should include modalities that increase lean and bone mass and decrease fat mass. The bone health of Singaporean men is comparable to non-Hispanic whites and better than some other Asian men.

© 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Osteoporosis is known to be age- and gender-specific, affecting >40% of women and 20% of men at some point in their lifetime (Riggs et al., 2004; National Institutes of Health, 2001; Cooper et al., 2011; Kanis et al., 2000). Hormones and several behavioral and lifestyle factors including exercise and body composition are known to contribute to the bone health of men and women (TV et al., 2000; De Oliveira et al., 2012; Khosla, 2013; ES et al., 2009; Mosekilde et al., 2013; Orimo et al., 2012). Wide individual variations in some of these factors exist across different population and ethnic groups and these wide variations may account for the varying population-specific bone mineral density (BMD) and prevalence of osteoporosis (Kanis et al., 2000; Koh, 2002; Kruger et al., 2013). Most research into osteoporosis has been carried out in Caucasian populations, with fewer studies in Asian populations. It is therefore important to evaluate the major determinants of bone health in men in each population group.

The present study evaluated osteoporosis in Singaporean men, and how age, bodyweight, obesity and engagement in regular physical

exercise are associated with osteoporosis and with bone mineral density (BMD). It further examined whether there are gender-specific differences in how the major determinants are associated with BMD between Singaporean men and women. A comparison was made between BMD of Singaporean men and that reported for other population groups. A better understanding of the interrelationships of these factors with bone health will assist in the formulation of appropriate recommendations to delay or reduce the prevalence of osteoporosis in men.

2. Subjects, materials and methods

2.1. Subjects

This study was approved by the Institutional Review Board of the National University Hospital of Singapore and each volunteer gave his written informed consent. A total of 551 men were recruited from the general public through an open invitation, first through an announcement during the World Congress in Sexology held in Singapore. The announcement was included in the major newspapers in Singapore. Continual recruitment was assisted through word of mouth from volunteer to volunteer. A total of 551 men responded to the recruitment calls. Ethnic differences existed in the sample with the majority being ethnic

^{*} Corresponding author.

E-mail address: victor.goh@curtin.edu.au (V.H.H. Goh).

Chinese. The minority ethnic groups of Indians and Malays were too small to afford satisfactory statistical analyses, hence only 531 Chinese men were initially included. Out of the 531, only 482 Singaporean Chinese men, aged between 29 y and 71 y, had a whole body DXA and DXA scans of the spine at L2-L4 and at the hip were included in the analyses of this study. As the primary objective of the study was to evaluate the determinants of the aging process in normal healthy men, only community-dwelling healthy individuals with no known history of major medical illnesses such as cancer, hypertension, thyroid dysfunction, diabetes, and cardiovascular events nor major sleep disorders including sleep apnea requiring chronic treatment were included in the study. None of the subjects had a history of major joint surgery, or fracture. Subjects were not paid for their participation. They represented the diverse spectrum of men in Singapore, ranging from those with low to high levels of education, working and non-working men, and those in various types of vocations (Goh et al., 2007). Their profiles were typical of healthy Chinese men in Singapore, which is a highly urbanized citystate with no rural population.

2.2. Questionnaire

Each subject answered a self-administered and investigator-guided questionnaire to collect their demographic data, previous medical history and lifestyle factors. Anthropometric parameters were measured. The questionnaire allowed participants to record their physical exercise and/or sport as a lifestyle habit for each week. Only when an exercise regime was carried out for at least 6 months was the exercise considered a lifestyle habit. Participants recorded either no exercise or up to 4 different types of exercise/sport in which they were engaged in per week. For each exercise/sport type, they stated the duration and frequency per week. For example, a participant could record walking for 30 min 5 times a week and playing tennis for 60 min once a week.

2.3. Exercise/sport intensity and exercise groups (METGp)

The Metabolic Equivalent of Task (MET) scoring was used to normalize the different types of exercise/sport into a single common score. The total intensity of exercise/sport per week in MET minutes (METmin) was computed by taking into account the duration of each exercise episode and the frequency of the exercise per week in accordance with the exercise guidelines (Anon., 2015). For example, a participant reported that he walked for 30 min 5 times a week, played tennis for 60 min twice a week and did line dancing for 60 min once a week. Walking is assigned a MET of 3; tennis, a MET of 7; and line dancing, a MET of 5. His total physical/sports activities intensity per week will therefore be 1590 METmin $[(3\times30\times5)+(7\times60\times2)+(5\times60\times1)]$.

Participants were divided into three exercise intensity groups: METGp1, no exercise/sport with an assigned METmin score of "0"; METGp2, those with METmin from >0 to ≤1250; and METGp3, those with METmin of >1250. This classification of exercise intensity into 3 groups was based on an earlier report that showed regular physical exercise of intensity up to 1250 METmin, and those >1250 METmin have a dose-response relationship to health benefits (Goh & Hart, 2014).

2.4. Age groups

For comparisons, the men were divided into four age groups: AgeGp1: \leq 40 y; AgeGp2: 41–50 y; AgeGp3: 51–60 y; and AgeGp4: \geq 60 y.

2.5. Body mass index and BMI groups

As suggested earlier, body mass index (BMI) is more appropriately used as an index of bodyweight than of body fat (Goh et al., 2004). The BMI was computed by taking bodyweight in kilograms divided by

the square of height in meters measured using a stadiometer. Men were divided separately into three BMI groups: BMIGp1: (normal bodyweight - BMI $\leq 22~kg/m^2$); BMIGp2: (high bodyweight - BMI $> 22-27~kg/m^2$); and BMIGp3: (higher bodyweight - BMI $> 27~kg/m^2$). The cut off values were based on an earlier study which showed that for Singaporean men, instead of 30 kg/m², $27~kg/m^2$ was the more appropriate BMI index for obesity (Goh et al., 2004).

2.6. Bone density scans and osteoporotic groups

Each subject underwent a whole body scan and bone density scans of the lumber spinal at the L2-L4, and the hip (representing the femoral neck, shaft, and trochanter) using DXA (DPX-L, Lunar Radiation, Madison, WI, USA; software version 1.3z). Total percent body fat (PBF), spine bone mineral density (Sbmd, the average BMD of L2-L4) and femoral neck bone mineral density (Fnbmd) were computed automatically by the DXA scanner. The T-scores for the spine and femoral neck were computed with reference to the BMD for young men established for the local population. According to the WHO guidelines, a Tscore > -1.0 is normal, while T-scores < -1.0 to -2.5 denote osteopenia and T-scores of <- 2.5 denote osteoporosis (Anon., 1994). Hence, the following groups were identified: SOstGp1 (normal spinal BMD) and FnOstGp1 (normal femoral neck BMD) when the spine and femoral neck T-scores were >-1.0, and SOstGp2 (osteoporosis of spine) and FnOstGp2 (osteoporosis of femoral neck) where the spine and femoral neck T-scores were <- 2.5.

2.7. Body fat groups (OBGps)

All men were divided into three groups based on the percent body fat (PBF) with OBGp1: PBF of <20%, OBGp2: PBF >20–25% and OBGp3: PBF >25%.

2.8. Measurements of T, E2, SHBG, DHEAS, Insulin, IGF1 and BP3

An overnight 12 h fasting blood sample was collected in the morning between 9:00 am and 11:00 am and the sera were stored at $-80\,^{\circ}\mathrm{C}$ until analysis. Serum total testosterone (T) and estradiol (E2) concentrations were measured using reagents and methods recommended by the World Health Organization Matched Reagent Program (Sufi et al., 1992) with modifications into the scintillation proximity methods established in-house (Goh et al., 1990). Sex hormone binding globulin (SHBG) and dehydroepiandrosterone sulphate (DHEAS) were measured using methods reported earlier (Chia et al., 1997). The intraand inter-assay coefficients of variation were <15% over the effective concentration ranges for T, E2, SHBG and DHEAS.

Serum levels of insulin-like growth factor-1 (IGF1) and insulin-like growth factor binding protein-3 (BP3) levels were estimated using kits purchased from Diagnostic System Laboratories (Texas, USA) according methods reported earlier (Probst-Hensch et al., 2003; Goh et al., 1998). Serum insulin (INS) levels were measured using the kits from Abbott Diagnostic (USA). The inter-assay variations for all three assays were <15%.

2.9. Method of calculation of BioT

Bioavailable testosterone (BioT) was calculated using the computer formula of Vermeulen (Vermeulen et al., 1999). Total testosterone was computed as ng/dL while that for SHBG as nmol/L. Albumin level was assumed to be 44. BioT was expressed as ng/dL.

2.10. Comparisons of reference values with other population groups

The Sbmd and Fnbmd of Singaporean men aged between 20 and 29 y were compared with those of Europeans, Americans and Koreans

Table 1 Characteristics of men in the four age groups.

	AgeGp1 $29 -<40 y$ $n = 50$	AgeGp2 41–50 y n = 183	AgeGp3 51-60 y n = 171	AgeGp4 >60 y n = 76	P values
Age (y)	37.3 ± 0.039	46.0 ± 0.20	54.7 ± 0.21	64.7 ± 0.32	1 v 2, 3, 4 (<0.001, <0.001, <0.001), 2 v 3, 4 (<0.001, <0.001), 3 v 4 (<0.001)
METmin	551 ± 115	593 ± 60	648 ± 62	1046 ± 93	1, 2, 3 v 4 (0.005, <0.001, 0.003)
PBF (%)	16.4 ± 0.66	17.7 ± 0.34	18.6 ± 0.36	17.1 ± 0.53	1 v 3 (0.023)
Ht (cm)	170.4 ± 0.80	169.5 ± 0.4	167.6 ± 0.4	166.6 ± 0.7	1 v 3, 4 (0.014, 0.001), 2 v 3, 4 (0.009, 0.001)
Wt (kg)	68.4 ± 1.3	68.4 ± 0.7	67.9 ± 0.7	65.4 ± 1.0	NS
BMI (kg/m ²)	23.5 ± 0.4	23.8 ± 0.2	24.1 ± 0.2	23.5 ± 0.3	NS
W (cm)	82.9 ± 0.9	83.6 ± 0.5	85.4 ± 0.5	85.5 ± 0.8	NS
H (cm)	96.3 ± 0.8	95.5 ± 0.4	95.7 ± 0.4	94.0 ± 0.6	NS
W/H	0.861 ± 0.006	0.875 ± 0.003	0.892 ± 0.003	0.909 ± 0.005	1 v 3, 4 (<0.001, <0.001), 2 v 3, 4 (0.001, <0.001), 3 v 4 (0.026)
W/Ht	0.487 ± 0.005	0.494 ± 0.003	0.510 ± 0.003	0.514 ± 0.004	1 v 3, 4 (0.002, 0.001), 2 v 3, 4 (0.001, 0.001)

Statistical analyses on the various parameters among the 4 age groups were carried out using multivariate linear comparison of means using the General Linear Model coupled with the Bonferroni Post-Hoc test for multiple means. The values denote the mean + SE.

and Australians values reported earlier (Lee et al., 1997; Park et al., 2014; Kaptoge et al., 2008; Looker et al., 2012; Looker et al., 1998; Henry et al., 2010).

2.11. Statistical analysis

Statistical analyses were performed using SPSS for windows version 21.0. Basic descriptive statistics, as well as multivariate linear comparison of means using the General Linear Model coupled with the Bonferroni Post-Hoc test for multiple means were calculated for the bone parameters of Sbmd, Fnbmd, age, BMI, body fat, exercise groups. Where appropriate, the exercise intensity (METmin), BMI, PBF and age were analyzed as covariates in the comparison groups and all analyses of multiple means, except for BMI, were weighted for bodyweight. Linear regression analyses were carried out separately for Sbmd and Fnbmd using the stepwise method with age, METmin, PBF, BMI, T, E2, SHBG, BioT, INS, IGF1, BP3 and DHEAS. Cross-tab and Fisher's exact tests (Oyvind.Langsrud@ssb.no) were used to assess the prevalence of spine and femoral neck osteoporosis in the different age, BMI, body fat, and exercise groups.

3. Results

Table 1 shows the various parameters in the 4 age groups. The noticeable feature is that men in the oldest age group (>60 y) had significantly higher physical exercise intensity (METmin) than the 3 other younger age groups. In addition, the average height in the two older age groups (51-60 y and >60 y) were significantly shorter than those in the two younger age groups (Table 1). Consequently, the waist/hip and waist/height ratios in the two older age groups were higher than the two younger age groups (Table 1). The percent body fat in men in

the 51-60 y age group was significantly higher than men in the <40 y age group (Table 1).

Table 2 shows that femoral neck BMD, but not BMD of the spine, was significantly and negatively correlated with age. Both spine and femoral neck BMD were independently and negatively associated with percent total percent body fat, and significantly and positively correlated with body mass index, and exercise intensity (METmin) (Table 1). Only BMD of the spine but not the femoral neck BMD was significantly correlated to steroid hormones. Spine BMD was positively correlated to both estradiol and dehydroepiandrosterone sulphate (DHEAS), and negatively correlated to testosterone (Table 1). On the other hand, both spine and femoral neck BMD were significantly and negatively correlated with insulin level (Table 1). Serum levels of sex hormone binding globulin, bioavailable testosterone (BioT), insulin growth factor-1 and insulin growth factor binding protein-3 (BP3) were not independently correlated with either Sbmd or Fnbmd.

Table 3 shows the comparison of the values of Sbmd and Fnbmd of Singaporean men aged 20 to 29 y with corresponding values of those of Korean, European, American and Australian men. In general the Sbmd of Singaporean men was comparable to those of Europeans but higher than those in American and Korean men. The femoral neck BMD, on the other hand, was higher than all other groups (Table 2).

After adjusting for BMI, percent body fat and exercise intensity, spine BMD did not differ across age groups, with the exception that the spine BMD of men in the 7th decade was significantly higher than corresponding the spine BMD of men in the 6th decade (Table 4). In contrast, the age pattern of femoral neck BMD showed an age-dependent trend; Fnbmd was significantly lower after age 50 y (Table 4).

There was no relationship between age and spine osteoporosis but osteoporosis of the femoral neck was significantly higher in men in the 6th decade when compared to men in the 4th decade (Table 4).

Table 2Linear regressions of variables with spine bone mineral density (Sbmd) and femoral neck bone mineral density (Fnbmd).

Variables	Sbmd		Fnbmd	
	Standardized coefficients beta	P-value	Standardized coefficient beta	P-value
Age (y)	0.023	NS	-0.161	< 0.001
BMI (kg/m ²)	0.454	< 0.001	0.456	< 0.001
PBF (%)	-0.370	< 0.001	-0.300	< 0.001
METmin	0.148	0.001	0.149	0.001
INS	-0.103	0.039	-0.120	0.018
E2	0.112	0.006	0.013	NS
DHEAS	0.084	0.044	-0.021	NS
T	-0.099	0.024	0.020	NS
SHBG	0.013	NS	0.043	NS
BioT	-0.081	NS	-0.007	NS
IGF1	0.016	NS	0.060	NS
BP3	0.020	NS	0.039	NS

Table 3Young reference values for spine bone mineral density (Sbmd) and femoral neck bone mineral density (Fnbmd) in different population and ethnic groups.

	Sbmd	Fnbmd
Singapore (20-29 y) Korean (20-29 y) European (19-30 y) Americans (20-29 y) Australian (20-29)	1.176 ± 0.121 (Lee et al., 1997) 0.999 ± 0.140 (Park et al., 2014) 1.112 ± 0.150 (Kaptoge et al., 2008) 1.055 ± 0.119 (Looker et al., 2012)	1.052 ± 0.119 (Lee et al., 1997) 0.911 ± 0.168 (Park et al., 2014) 0.974 ± 0.159 (Kaptoge et al., 2008) 0.934 ± 0.137 (Looker et al., 1998) 0.934 ± 0.133 (Henry et al., 2010)

Overall, 2.9% and 8.5% of all men, regardless of age, had osteoporosis of the spine and femoral neck, respectively (Table 4). The prevalence of osteoporosis of both the spine and femoral neck was not significantly different between the four age groups except for a marginally higher prevalence of femoral neck osteoporosis in men above 50 y (AgeGp3) when compared to men above 40 y (AgeGp2) (Table 4).

Body mass index (BMI) was significantly and highly positively correlated with both Sbmd and Fnbmd (Table 2). Spine and femoral neck BMD were significantly higher, by 12.8% and 10.3% respectively, in BMIGp2 than corresponding levels in BMIGp1 and in BMIGp3 the levels were even higher, by 24.7% and 19.7%, respectively, than corresponding levels in BMIGp1 (Table 5). Thus there was lower osteoporosis prevalence in men with higher BMI (BMIGp2 & BMIGp3) (Table 5).

In contrast to BMI, percent body fat was significantly and negatively correlated to both spine and femoral neck BMD (Table 2). High percent body fat (OBGp2 and OBGp3) had about 10% higher spine and femoral neck BMD than men with normal percent body fat (OBGp1) (Table 6). However, the negative correlation of percent body fat with BMD was not reflected in significantly higher prevalence of osteoporosis (Table 6).

Exercise intensity (METmin) was independently and positively correlated with both Sbmd and Fnbmd (Table 2). Only men with high exercise intensity (METGp3) had significantly higher Fnbmd than those in the lower intensity (METGp2) or no exercise group (METGp1) (Table 7). No significantly different prevalence of spine and femoral neck osteoporosis was noted between the three exercise groups (Table 7).

4. Discussion

The present study showed that in highly urbanized Singapore, bone health is site-specific. Firstly, the prevalence of femoral neck osteoporosis (8.5%) in men is higher than in spine (2.9%). Furthermore, some determinants of BMD are site-specific being associated with Sbmd and not with Fnbmd. Both BMI and PBF are two major but opposite determinants of Sbmd and Fnbmd, while insulin (INS) was negatively correlated with both Sbmd and Fnbmd. On the other hand, E2, T and DHEAS, were significantly associated only with Sbmd but not with Fnbmd. What the

underlining mechanisms for the observed site-specificity are, remain to be elucidated.

The reference values for spine and femoral neck BMD of Singaporean men aged between 20 and 29 .y were comparable to those of European and higher than American, Korean and Australian men. These results appear to support the good bone status of Singaporean men when compared to others in South East Asian men reported earlier (Kruger et al., 2013; Vu et al., 2005; Lin et al., 2001; Thuy et al., 2003). The wide ranging prevalence seen in different Asian countries point, possibly, to population-specific factors at play in bone health. It is possible that the population-specific differences may be related to the many factors influencing BMD including nutritional habit, lifestyle factors such as bodyweight and adiposity and physical exercises. It is therefore important to evaluate which are the important determinants of BMD in order to establish the best strategies to improve bone health in each respective population group.

As with an earlier study, age was shown to be an important determinant of BMD (Mazess et al., 1990). It was noted that the age-related decline in BMD at the femoral neck was not observed at the spine, an observation similar to an earlier study (Rapado et al., 1999). In other studies, it was noted that when men with spinal abnormalities were excluded, an age-related decline in BMD at the spine was observed (Henry et al., 2010; Szulc et al., 2000). However, no men in the present study have had clinically diagnosed spinal abnormalities, hence the lack of age-related decline in BMD of the spine could not be explained by the presence of spinal abnormalities in men.

Apart from being site-specific, it was noted that Sbmd of men in the 7th decade tended to be higher and significantly so than that of men in the 6th decade. A similar trend of higher spine BMD in older men was also noted in American men (Looker et al., 2012). One possible reason is that, while the other factors of BMI, percent body fat and testosterone and estradiol levels were the same in all age groups of the Singaporean men, the exercise intensity of men in their 7th decade was significantly >40% higher than the average of those in the younger age groups. In addition, the femoral neck BMD of men in the 7th decade would be 1.3% higher, if it was not adjusted for exercise intensity. Therefore, it is possible that higher exercise intensity in older men may account for the

 Table 4

 Prevalence of spinal and femoral neck osteoporosis and spine bone mineral density (Sbmd) and femoral neck bone mineral density (Fnbmd) in the four age groups.

	$\begin{array}{l} AgeGp1 \\ \leq 40 \text{ y } (n = 51) \end{array}$	AgeGp2 41–50 y (n = 183)	AgeGp3 51-60 y (n = 171)	AgeGp4 >60 y (n = 77)
Age	37.4 ± 0.39	45.9 ± 0.20 Gp2 v Gp1, Gp3, Gp4 (<0.001, <0.001, <0.001	54.6 ± 0.21 Gp3 v Gp1, Gp4 (<0.001, <0.001)	64.6 ± 0.33 Gp4 v Gp1 (<0.001)
SOstGp1	40	141	113	59
SOstGp2	1 (2.0%)	6 (3.3%)	5 (2.9%)	2 (2.6%)
FnOstGp1	33	97	80	31
FnOstGp2	3 (5.9%)	10 (5.5%) Gp2 v Gp3 (0.041)	21 (12.3%)	7 (9.1%)
Sbmd	1.067 ± 0.022	1.059 ± 0.011 NS	1.026 ± 0.012 Gp3 v Gp4 (0.008)	1.100 ± 0.019
Fnbmd	0.862 ± 0.016	$\begin{array}{l} 0.881 \pm 0.008 \\ \text{Gp2 v Gp3, Gp4 } (0.011, 0.009) \end{array}$	0.839 ± 0.009	0.819 ± 0.015

 $SOstGp1 \ \& \ FnOstGp1 = groups \ with \ normal \ spine \ and \ femoral \ neck \ (T-scores \geq -1.00).$

 $SOstGp2 \ \& \ FnOstGp2 = groups \ with \ osteoporosis \ of \ spine \ and \ hip \ (T-scores < -2.5).$

Osteoporosis prevalence was tested for significance using the Fisher Exact Test.

Comparisons of Sbmd and Fnbmd among the 4 age groups were carried out using the multilinear regression analysis with, METmin, BMI, PBF as covariates.

 Table 5

 Prevalence of spine and femoral osteoporosis and spine bone mineral density (Sbmd) and femoral neck bone mineral density (Fnbmd) in the three BMI groups.

	BMIGp1 $\leq 22 \text{ kg/m}^2 \text{ (n} = 118)$	BMIGp2 > 22-27 kg/m ² (n = 305)	BMIGp3 > 27 kg/m ² (n = 57)
SOstGp1	70	233	49
SOstGp2	8 (6.8%)	6 (1.9%)	0 (0%)
-		Gp1 v Gp2 (0.031)	Gp1 v Gp3 (0.059)*
FnOstGp1	38	163	40
FnOstGp2	14 (11.9%)	27 (8.9%)	0 (0%)
		Gp2 v Gp3 (0.013)	Gp1 v Gp3 (0.006)
Sbmd	0.941 + 0.017	1.061 + 0.009	1.173 + 0.020
	Gp1 v Gp2, Gp3 (<0.001, <0.001)	Gp2 v Gp3 (<0.001)	
Fnbmd	0.780 + 0.013	0.860 + 0.007	0.934 + 0.015
	Gp1 v Gp2, Gp3 (<0.001, <0.001)	Gp2 v Gp3 (<0.001)	

SOstGp1 & FnOstGp1 = groups with normal spine and hip bone density, (T-scores ≥ -1.00).

SOstGp2 & FnOstGp2 = groups with osteoporosis of spine and femoral neck (T-scores < -2.5).

Osteoporosis prevalence was tested for significance using the Fisher Exact Test.

Comparisons of Sbmd and Fnbmd among the 3 BMI groups were carried out using the multilinear regression analysis with, age, METmin, PBF as covariates.

higher BMD in Singaporean men. We have reported that older men in Singapore tended to engage in more regular and intense physical exercise than their European counterparts (Goh & Hart, 2014).

Studies have shown that estrogen and testosterone as well as sex hormone binding globulin are associated with bone metabolism (Mosekilde et al., 2013; Khosla et al., 1998; Lormeau et al., 2004; Martinez Diaz-Guerra et al., 2001). In contrast to earlier studies, the present study showed that after adjusting for other determinants, testosterone has a negative correlation with Sbmd (Khosla, 2013; ES et al., 2009; Runolfsdottir et al., 2015). On the other hand, the observation that estradiol was positively correlated to Sbmd support the earlier suggestion that low levels of estrogen is possibly a risk factor for osteoporosis in men (ES et al., 2009; Runolfsdottir et al., 2015). It is possible that while testosterone per se has a negative correlation with Sbmd, it may still have an overall positive correlation with BMD via its aromatization to estrogen (De Oliveira et al., 2012; Khosla et al., 2001).

The present study showed that DHEAS has a positive correlation with spine BMD and therefore, it possibly has a role in bone metabolism in men

In contrast to an earlier study, insulin growth factor-1 and insulin growth factor binding protein-3 were not significantly correlated to BMD in men (Szulc et al., 2004). On the other hand, insulin levels were negatively correlated to both spine and femoral neck BMD in men. The mechanism governing insulin's role in bone metabolism is unclear.

One of the major contributions of this study is showing clearly a positive association of high bodyweight (BMI) but the negative association of high body fat with BMD. These observations reconfirmed earlier studies that indicate that bodyweight is a powerful predictor of BMD (Barrera et al., 2004; Tirosh et al., 2015), and on the other hand, percent body fat is a powerful, albeit negative predictor of BMD. While the mechanisms for the association of high bodyweight with higher BMD

remain unclear, the present studies and others support the notion that weight-related load and increased mechanical stress on bone improves bone density (Robling et al., 2006). Therefore, the results give credence to the strategy that avoiding a significant weight loss as one ages is a positive means of preserving bone health (Hannan et al., 2000; De Laet et al., 2005). Furthermore, the results suggest that a strategy to increase lean and bone mass while concurrently losing fat mass will be beneficial to bone health.

The strength of the study is the large number of normal healthy community dwelling men who did not have any major illnesses. Furthermore, we made used of BMI as an index of bodyweight and the use of DXA scan-derived percent body fat to clarify the independent association of bodyweight and body fat with BMD. The use of the METmin as the index of the intensity of physical exercise/sport allowed the normalizing of all physical activities and their frequency and duration to a single index for analyses. However, a limitation of this computed exercise intensity is that it reflects mainly the aerobic component and has lesser indication of the resistance or loading exercises which are more relevant to bone health.

In summary, the study shows that the prevalence of osteoporosis and some of the determinants of bone mineral density (BMD) in Singaporean men was site-specific. Further, BMI and PBF are opposing predictors of BMD. Therefore, any strategy for improving bone health should include modalities that increase lean and bone mass and decrease fat mass. The bone health of Singaporean men is comparable to non-Hispanic whites and better than some other Asian men.

Declaration of interest

The authors report no declaration of interest. This study was supported, in part, by funds from the Academic Research Fund of the National University of Singapore, Singapore.

Table 6Prevalence of spine and femoral neck osteoporosis and spine bone mineral density (Sbmd) and femoral neck bone mineral density (Fnbmd) in the three OB groups.

	OBGp1 (PBF \leq 20%) (n = 352)	OBGp2 (PBF > 20-25%) (n = 111)	OBGp3 (PBF > 25%) (n = 19)
SOstGp1	269	72	12
SOstGp2	11 (3.1%)	3 (2.7%)	0 (0%)
FnOstGp1	185	48	8
FnOstGp2	28 (8.0%)	11 (9.9%)	2 (10.5%)
Sbmd	1.086 + 0.009 Gp1 v Gp2, Gp3 (<0.001, 0.003)	0.978 + 0.016	0.963 + 0.036
Fnbmd	0.880 + 0.007 Gp1 v Gp2, Gp3 (<0.001, 0.028)	0.795 + 0.011	0.808 + 0.026

SOstGp1 & FnOstGp1 = groups with normal spine and hip bone density, (T-scores ≥ -1.00).

 $SOstGp2 \& FnOstGp2 = groups \ with \ osteoporosis \ of \ spine \ and \ femoral \ neck \ (T-scores < -2.5).$

Osteoporosis prevalence was tested for significance using the Fisher Exact Test.

Comparisons of Sbmd and Fnbmd among the 3 OB groups were carried out using the multilinear regression analysis with, age, METmin, BMI as covariates.

 Table 7

 Prevalence of spine and femoral neck osteoporosis and spine bone mineral density (Sbmd) and femoral neck bone mineral density (Fibmd) in the three exercise groups.

	METGp1 METmin = 0 (n = 123)	METGp2 METmin > 0-1250 (n = 151)	METGp3 METmin > 1250 (n = 208)
SOstGp1	82	104	167
SOstGp2	3 (2.4%)	6 (4.0%)	5 (2.4%)
FnOstGp1	50	73	118
FnOstGp2	13 (10.6%)	10 (6.6%)	18 (8.7%)
Sbmd	1.035 ± 0.014	1.038 ± 0.013	1.076 ± 0.011
Fnbmd	0.833 ± 0.010 Gp1, Gp2 v Gp3 (0.001, 0.001)	0.837 ± 0.010	0.883 ± 0.008

SOstGp1 & FOstGp1 = groups with normal spine and hip bone density, (T-scores ≥ -1.00).

SOstGp2 & FOstGp2 = groups with osteoporosis of spine and hip (T-scores < -2.5).

Osteoporosis prevalence was tested for significance using the Fisher Exact Test.

Comparisons of Sbmd and Fnbmd among the 3 MET groups were carried out using the multilinear regression analysis with, age, PBF, BMI as covariates.

Acknowledgments

We will like to acknowledge the technical assistance from staff of the Endocrine Research and Service Laboratory of the Department of Obstetrics and Gynaecology, National University of Singapore, Singapore. This study was designed, conducted and data collected while Prof. Victor H. H. Goh was at the Department of Obstetrics and Gynaecology, National University of Singapore, Singapore. Prof. William G. Hart was intimately involved in the interpretation of findings, drafting and critical revision of the article for submission.

References

- Riggs, B.L., Melton 3rd, L.J., Robb, R.A., Camp, J.J., Atkinson, E.J., Peterson, J.M., Rouleau, P.A., McCollough, C.H., Bouxsein, M.L., Khosla, S., 2004. Population-based study of age and sex differences in bone volumetric density, size, geometry, and structure at different skeletal sites. J. Bone Miner. Res. 19, 1945–1954.
- National Institutes of Health, 2001. Bone health information. Osteoporosis and related bone diseases from the Centers for Disease Control and Prevention. Prevalence of disabilities and associated health conditions among adults – United States 1999. JAMA 285, 1571–1572.
- Cooper, C., ZA, C., CR, H., SC, E., NC, H., EM, D., LJ, M., SR, C., JA, K., The IOF CAS Working Group on Fracture Epidemiology, 2011. Secular trends in the incidence of hip and other osteoporotic fractures. Osteoporos. Int. 22, 1277–1288.
- Kanis, J.A., Johnell, O., Oden, A., Sembo, I., Redlund-Johnell, I., Dawson, A., De Laet, C., Jonsson, B., 2000. Long-term risk of osteoporotic fracture in Malmo. Osteoporos. Int. 11, 669–674.
- TV, N., JR, C., JA, E., 2000. Osteoporosis in elderly men and women: effects of dietary calcium, physical activity, and body mass index. J. Bone Miner. Res. 15, 322–331.
- De Oliveira, D.H., Fighera, T.M., Bianchet, L.C., Kulak, C.A., Kulak, J., 2012. Androgens and bone. Minerva Endocrinol. 37 (4), 305–314.
- Khosla, S., 2013. Pathogenesis of age-related bone loss in humans. J. Gerontol. A Biol. Sci. Med. Sci. 68, 1226–1235.
- ES, L.B., CM, N., LM, M., JA, L., Barrett-Connor, E., KE, E., AR, H., Laughlin, G., Ohlsson, C., ES, O., Osteoporotic Fractures in Men Study Group, 2009. The effects of serum testosterone, estradiol, and sex hormone binding globulin levels on fracture risk in older men. J. Clin. Endocrinol. Metab. 94, 3337–3346.
- Mosekilde, L., Vestergaard, P., Rejnmark, L., 2013. The pathogenesis, treatment and prevention of osteoporosis in men. Drugs 73, 15–19.
- Orimo, H., Nakamura, T., Hosoi, T., Iki, M., Uenishi, K., Endo, N., Ohta, H., Shiraki, M., Sugimoto, T., Suzuki, T., Soen, S., Nishizawa, Y., Hagino, H., Fukunaga, M., Fujiwara, S., 2012. Japanese 2011 guidelines for prevention and treatment of osteoporosis executive summary. Arch. Osteoporos. 7, 3–20.
- Koh, L.K., 2002. An Asian perspective to the problem of osteoporosis. Ann. Acad. Med. Singap. 31 (1), 26–29.
- Kruger MC, Todd JM, Schollum LM, Kuhn-Sherlock B, McLean DW, Wylie K (2013) Bone health comparison in seven Asian countries using calcaneal ultrasound. BMC Musculoskelet. Disord. 14:81; http://www.biomedcentral.com/1471-2474/14/81.
- Goh, V.H.H., Tong, T.Y.Y., Mok, H.P.P., Said, B., 2007. Interactions among age, adiposity, bodyweight, lifestyle factors and sex steroid hormones in healthy Singaporean Chinese men. Asian J. Androl. 9, 611–621.
- Anon., 2015. Appendix 1. Translating scientific evidence about total amount and intensity of physical activity into guidelines http://:www.health.gov/PAguidelines/guidelines/appendix.aspx Accessed April 5, .
- Goh, V.H., Hart, W.G., 2014. Associations of physical exercise as a lifestyle habit with lean and fat body mass and handgrip strength and age in Asian men. Aging Male 17 (3), 131–135.
- Goh, V.H., Tain, C.F., Tong, T.Y., Mok, H.P.P., Wong, M.T., 2004. Are BMI and other anthropometric measures appropriate as indices for obesity? A study in an Asian population. J. Lipid Res. 45, 1892–1898.

- Anon., 1994. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. World Health Organ. Tech. Rep. Ser. 843. 1–129.
- Sufi, S., Donalson, A., Jeffcoate, S.L., 1992. Method Manual. WHO Special Programme of Research, Development and Research Training in Human Reproduction. Programme for the Provision of Matched Assay Reagents for the Radioimmunoassay of Hormones in Reproductive Physiology. World Health Organization, Geneva.
- Goh, H.H., Chow, A., Wang, F.L., Ratnam, S.S., 1990. Comparisons of a tritium labeled-based classical radioimmunoassay with a newly developed scintillation proximity assay for measurement of plasma oestradiol-17-beta. Med. Lab. Sci. 4, 33–35.
- Chia, S.E., Goh, V.H., Ong, C.N., 1997. Endocrine profiles of male workers with exposure to trichloroethylene. Am. J. Ind. Med. 32, 217–222.
- Probst-Hensch, N.M., Wang, H., Goh, V.H., Seow, A., Lee, H.P., Yu, M.C., 2003. Determinants of circulating insulin-like growth factor I and insulin-like growth factor binding protein 3 concentrations in a cohort of Singapore men and women. Cancer Epidemiol. Biomark. Prev. 12, 739–746.
- Goh, V.H.H., Mu, S.C., Gao, F.K., Lim, K.S., 1998. Changes in body composition and endocrine and metabolic functions in healthy elderly Chinese men following growth hormone therapy. Aging Male 1, 264–269.
- Vermeulen, A., Verdonck, L., Kaufman, J.M., 1999. A critical evaluation of simple methods for the estimation of free testosterone in serum. J. Clin. Endocrinol. Metab. 84, 3666–3672.
- Lee, S.T., Goh, J.C.H., Low, S.L., Bose, K., 1997. Bone mineral density in normal Chinese and women in Singapore. J. Musculoskelet. Res. 1 (1), 41–46.
- Park, E.J., Joo, I.W., Jang, M.J., Kim, Y.T., Oh, K., Oh, H.J., 2014. Prevalence of osteoporosis in the Korean population based on Korea National Health and Nutrition Examination Survey (KNHANES), 2008–2011. Yonsei Med. J. 55 (4), 1049–1057.
- Kaptoge, S., da Silva, J.A., Brixen, K., Reid, D.M., Kroger, H., Neilsen, T.L., Andersen, M., Hagen, C., Lorenc, R., Boonen, S., de Vernejoul, M.-C., Stepan, J.J., Adams, J., Kaufman, J.-M., Reeve, J., 2008. Geographical variation in DXA bone mineral density in young European men and women. Result from the Network in Europe on male osteoporosis (NEMO) study. Bone 43, 332–339.
- Looker, A.C., Melton III, L.J., Borrud, L.G., 2012. Lumber spine bone mineral density in US adults: demographic patterns and relationship with femur neck skeletal status. Osteoporos. Int. 23, 1351–1360.
- Looker, A.C., Wahner, H.W., Dunn, W.L., Calvo, M.S., Harris, T.B., Heyse, S.P., Johnston Jr., C.C., Lindsay, R., 1998. Updated data on proximal femur bone mineral levels of US adults. Osteoporos. Int. 8, 468–489.
- Henry, M.J., Pasco, J.A., Korn, S., Gibson, J.E., Kotowicz, M.A., Nicholson, G.C., 2010. Bone mineral density reference ranges for Australian men: Geelong Osteoporosis Study. Osteoporos. Int. 21, 909–917.
- Vu, T.T., Nguyen, C.K., Nguyen, T.L., Le, B.M., NguyenTrung Le, D., Bui, T.N., Nakamori, M., Kunil, D., Sakai, T., Yamamoto, S., 2005. Determining the prevalence of osteoporosis and related factors using quantitative ultrasound in Vietnamese adult women. Am. J. Epidemiol. 16 (9), 824–830.
- Lin, J.D., Chen, J.F., Chang, H.Y., Ho, C., 2001. Evaluation of bone mineral density by quantitative ultrasound of bone in 16862 subjects during routine health examination. Br. I. Radiol. 74, 602–606.
- Thuy, V.T., Chau, T.T., Cong, N.D., De, D.V., Nguyen, T.V., 2003. Assessment of low bone mass in Vietnamese: comparison of QUS calcaneal ultrasonometer and date-derived T-scores. I. Bone Miner. Metab. 21, 114–119.
- Mazess, R.B., Barden, H.S., Drinka, P.J., Bauwens, S.F., Orwoll, E.S., Bell, N.H., 1990. Influence of age and body weight on spine and femur bone mineral density in U.S. white men. J. Bone Miner. Res. 5, 645–652.
- Rapado, A., Hawkins, F., Sobrinho, L., Diaz-Curiel, M., Galvao-Telles, A., Arver, S., Melo Gomes, J., Mazer, N., Garcia e Costa, J., Horcajada, C., Lopez-Gavilanes, E., Mascarenhas, M., Papapietro, K., MB, L.A., MC, P., Martinez, G., Valverde, I., JJ, G., JJ, G., Garcia, I., 1999. Bone mineral density and androgen levels in elderly males. Calcif. Tissue Int. 65 (6), 417–421.
- Szulc, P., Marchand, F., Duboeuf, F., Delmas, P.D., 2000. Cross-sectional assessment of agerelated bone loss in men: the MINOS study. Bone 26, 123–129.
- Khosla, S., Melton 3rd, L.J., Atkinson, E.J., WM, O.'.F., GG, K., BL, R., 1998. Relationship of serum sex steroid levels and bone turnover markers with bone mineral density in men and women: a key role for bioavailable estrogen. J. Clin. Endocrinol. Metab. 83, 2266–2274.

- Lormeau, C., Soudan, B., d'Herbomez, M., Pigny, P., Duquesnoy, B., Cortet, B., 2004. Sex hormone-binding globulin, estradiol, and bone turnover markers in male osteoporosis. Bone 34, 933–939.
- Martinez Diaz-Guerra, G., Hawkins, F., Rapado, A., Ruiz Diaz, M.A., Diaz-Curiel, M., 2001. Hormonal and anthropometric predictors of bone mass in healthy elderly men: major effect of sex hormone binding globulin, parathyroid hormone and body weight. Osteoporos. Int. 12, 178–184. Runolfsdottir, H.L., Sigurdsson, G., Franzson, L., Indridason, O.S., 2015. Gender comparison
- Runolfsdottir, H.L., Sigurdsson, G., Franzson, L., Indridason, O.S., 2015. Gender comparison of factors associated with age-related differences in bone mineral density. Arch. Osteoporos. 10, 23. http://dx.doi.org/10.11007/s11657-015-0214-7.
- Khosla, S., Melton 3rd, L.J., Atkinson, E.J., WM, O.'.F., 2001. Relationship of serum sex steroid levels to longitudinal changes in bone density in young versus elderly men. J. Clin. Endocrinol. Metab. 86, 3555–3561.
- Szulc, P., Joly-Pharaboz, M.O., Marchand, F., Delmas, P.D., 2004. Insulin-like growth factor I is a determinant of hip bone mineral density in men less than 60 years of age: MINOS study. Calcif. Tissue Int. 74, 322–329.

- Barrera, G., Bunout, D., Gattas, V., de la Maza, M.P., Leiva, L., Hirsch, S., 2004. A high body mass index protects against femoral neck osteoporosis in healthy elderly subjects. Nutrition 20, 769–771.
- Tirosh, A., de Souza, R.J., Sacks, F., Bray, G.A., Smith, S.R., LeBoff, M.S., 2015. Sex differences in the effects of weight loss diets on bone mineral density and body composition: POUNDS LOST Trial. J. Clin. Endocrinol. Metab. 100 (6), 2463–2471.
- Robling, A.G., Castillo, A.B., Tumer, C.H., 2006. Biomechanical and molecular regulation of bone remodelling. Annu. Rev. Biomed. Eng. 8, 455–498.
- Hannan, M.T., Felson, D.T., Dawson-Hughes, B., Tucker, K.L., Cupples, L.A., Wilson, P.W., Kiel, D.P., 2000. Risk factors for longitudinal bone loss in elderly men and women: the Framingham Osteoporosis Study. I. Bone Miner. Res. 15 (4), 710–720.
- the Framingham Osteoporosis Study. J. Bone Miner. Res. 15 (4), 710–720.

 De Laet, C., Kanis, J.A., Oden, A., Johanson, H., Johnell, O., Delmas, P., Eisman, J.A., Kroger, H., Fujiwara, S., Garnero, P., McCloskey, E.V., Mellstrom, D., Melton 3rd, L.J., Meunier, P.J., Pols, H.A., Reeve, J., Silman, A., Tenenhouse, A., 2005. Body mass index as a predictor of fracture risk: a meta-analysis. Osteoporos. Int. 16 (11), 1330–1338.