

To Establish the Normal Bone Mineral Density Reference Database for the Singapore Male

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Abstract

Introduction: The objective of this study was to establish the normal bone mineral density (BMD) reference curve for the Asian Singapore male. **Materials and Methods:** Three hundred and eighty-three male subjects were enrolled; comprising of 309 Chinese, 44 Malays and 30 Indians resident in Singapore. Bone mineral density was measured at the lumbar spine and left hip using a Hologic QDR 4500Elite dual-energy X-ray absorptiometry (DXA) scanner. **Results:** The mean peak BMD for the average lumbar spine and the neck of femur was 1.006 g/cm² and 0.97 g/cm², respectively. The mean peak BMD was taken at the 20 to 24 years age group at both the hip and spine based on data distribution for the various age groups. The BMD corresponding to -2.5 standard deviations from the peak adult value was 0.719 g/cm² for the average lumbar spine and 0.655 g/cm² for the neck of femur. **Conclusion:** This Asian male BMD reference database, which is 10% and 5% lower than corresponding values from the Caucasian reference database, allows for more accurate diagnosis of osteoporosis in Asian males.

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Key words: Bone mineral densitometry, Dual-energy X-ray absorptiometry scanner, Hologic scanner, Male osteoporosis

Introduction

Bone mineral densitometry was developed as a means to quantify the bone mineral content of the skeleton accurately¹ and has been used in the diagnosis of osteopenia and osteoporosis. Dual-energy X-ray absorptiometry (DXA) of the axial skeleton is one such technique² which is based on a subtraction method. The DXA scanner uses alternating X-ray pulses, for example at 70 and 140 kV. These 2 photoelectric peaks are used to separate bone from soft tissue for bone mineral content measurement. While DXA is generally reliable, vascular or soft tissue calcification, previous fracture, clothing and extremes of body weight may cause errors. The radiation dose from the central DXA scanner is small, the typical effective dose being 1 to 3 μ S per site. This is comparable to natural background radiation of 5 to 8 μ S per day.³

The T- and Z-scores are generated by the bone densitometer. These numbers allow the interpreter to relate bone density of the patient to the young normal person (T-

score) and age-matched (Z-score) person of the same sex and ethnic group respectively. The T-score is the patient's bone mineral density (BMD) expressed in standard deviations (SDs) or percentage above or below the average value found in healthy young adults at peak bone mass.

The World Health Organization (WHO) guideline for the diagnosis of osteoporosis is as follows:⁴

Normal = T-score $\geq$ -1.0 SD

Osteopenia = T-score $< -1.0 > -2.5$ SD

Osteoporosis = T-score ≤ -2.5 SD

Severe osteoporosis = T-score < -2.5 SD + fracture

WHO T-score values for osteoporosis were originally defined in 1994 by an expert panel for females and it is not entirely clear whether the same T-score values apply to males.⁵

The value below which BMD is defined as osteoporosis is dependent on the precision of the equipment applied and the range utilised to describe the normal population.

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Systematic differences are noted in measurements obtained for the same individual measured at the same site using different machines. The normal reference curve from one country may not be applicable to another because there are well-recognised differences in the reference ranges between communities from different regions or ethnic origins. It is also known that differences in the risk of hip fracture between communities are not attributed solely to BMD, so that different cut-off values may be necessary to capture the same degree of fracture risk. In view of these requirements, the use of a comparable and relevant reference database is crucial in the accurate diagnosis of osteoporosis. The reference curve for the resident Singapore Asian female is already in use. The purpose of our study was to establish the BMD reference database for the resident Asian male.

Materials and Methods

Participants in the study were Asian male volunteers resident in Singapore. Three hundred and eighty-three male subjects comprising of 309 Chinese (81%), 44 Malays (12%) and 30 Indians (8%) were enrolled for the study. This proportion is comparable to the 2000 resident Singapore population census comprising of 77% Chinese, 14% Malays, 8% Indians and 1% others. Their age range was 20 to 89 years.

The exclusion criteria for the selection of subjects were:

- interfering diagnostic studies (contrast examination within the last 5 days);
- conditions which precluded the measurement of BMD at the hip or lumbar spine (e.g. fracture or surgery to the lower back or hip region, metallic objects in the abdomen or spine);
- interfering drugs (steroids, calcium pills, Vitamin D, anticonvulsants, diuretics);

- chronic diseases (renal, hepatic, thyroid, adrenal or other endocrine diseases, diabetes, rheumatoid arthritis, hypogonadism, cancer); and
- occupation with predisposition to bone infarct (deep sea diving).

BMD was measured at the lumbar spine and left hip using the Hologic QDR-4500 densitometer (Hologic Inc, Waltham, MA, USA).

The precision error of Hologic Precision QDR4500 is approximately 1% for the lumbar spine and 2% for the proximal femur.⁶ Quality control with spine phantoms is performed routinely to ensure precision. The Hologic densitometers have an internal reference standard which continually calibrates the instrument during a scan.

The DXA machine calculates the bone mineral content (BMC) of the region of interest (ROI). BMD is derived based on BMC divided by the area of the ROI, that is $BMD = BMC/ROI$, and is measured in g/cm^2 .

BMD results from different Hologic models can vary by several percent and cross calibration is useful for increased accuracy.⁷ There are also formulas to convert BMD measurements from one manufacturer to another.⁸

The average SD of all age groups was used to derive the T-scores. The threshold BMD at -2.5 SD was calculated by subtracting 2.5 x average SD from the mean peak BMD.

Results

The mean BMD at various sites in the lumbar spine and hip, calculated for the various age groups in the local males, is shown in Table I. Data for the 70 to 89 years age group were not used to calculate the average SD due to the small sample size. The SDs calculated at each measurement site by age group are shown in Table II. From the data collected, the standard reference BMD curves were created. The

TABLE I: MEAN BONE MINERAL DENSITY (BMD) (g/cm^2) AT EACH MEASUREMENT SITE BY AGE GROUP

Age group (y)	No. of subjects	Measurement site							Total hip	Neck	Troch.	Inter troch.	Ward's
		L1	L2	L3	L4	L1 - L4	L2 - L4	L3 - L4					
20 to 24	54	0.954	1.009	1.022	1.029	1.006	1.020	1.025	1.065	0.970	0.813	1.240	0.900
25 to 29	44	0.925	0.997	1.024	1.024	0.996	1.015	1.024	0.985	0.898	0.733	1.161	0.804
30 to 34	50	0.908	0.968	0.988	0.989	0.966	0.982	0.989	0.962	0.845	0.709	1.151	0.748
35 to 39	58	0.943	1.017	1.033	1.033	1.009	1.028	1.033	0.974	0.859	0.732	1.152	0.746
40 to 44	44	0.876	0.946	0.963	0.956	0.938	0.955	0.960	0.918	0.821	0.691	1.084	0.661
45 to 49	26	0.890	0.955	0.968	0.963	0.946	0.962	0.965	0.938	0.822	0.713	1.105	0.653
50 to 54	36	0.887	0.932	0.945	0.952	0.932	0.943	0.948	0.877	0.758	0.673	1.031	0.581
55 to 59	18	0.922	1.003	1.014	1.022	0.993	1.013	1.018	0.900	0.759	0.685	1.065	0.552
60 to 69	34	0.899	0.947	0.997	0.993	0.970	0.977	0.992	0.898	0.778	0.709	1.043	0.587
70 to 79	17	0.891	0.924	0.876	0.938	0.947	0.913	0.907	0.860	0.724	0.651	1.026	0.501
80 to 89	2	1.017	1.060	1.007	1.036	1.030	1.035	1.022	0.782	0.606	0.647	0.916	0.366
Total	383												

Intertroch: intertrochanteric region; L: lumbar vertebra; Neck: neck of femur; Troch: trochanter; Ward's: Ward's triangle

TABLE II: STANDARD DEVIATION (g/cm²) AT EACH MEASUREMENT SITE BY AGE GROUP

Age group (y)	No. of subjects	Measurement site										Inter troch.	Ward's
		L1	L2	L3	L4	L1 - L4	L2 - L4	L3 - L4	Total hip	Neck	Troch.		
20 to 24	54	0.112	0.107	0.099	0.090	0.095	0.093	0.090	0.141	0.140	0.113	0.165	0.180
25 to 29	44	0.113	0.115	0.118	0.114	0.109	0.112	0.114	0.147	0.140	0.122	0.168	0.156
30 to 34	50	0.097	0.099	0.105	0.111	0.097	0.100	0.105	0.110	0.120	0.088	0.132	0.148
35 to 39	58	0.126	0.139	0.133	0.144	0.129	0.133	0.135	0.127	0.126	0.112	0.147	0.163
40 to 44	44	0.117	0.131	0.134	0.125	0.120	0.125	0.126	0.128	0.119	0.104	0.153	0.149
45 to 49	26	0.125	0.138	0.145	0.147	0.133	0.138	0.142	0.138	0.128	0.132	0.156	0.151
50 to 54	36	0.114	0.113	0.119	0.126	0.110	0.112	0.117	0.115	0.110	0.107	0.130	0.132
55 to 59	18	0.117	0.138	0.122	0.112	0.114	0.118	0.112	0.148	0.134	0.121	0.166	0.128
60 to 69	34	0.122	0.144	0.148	0.172	0.127	0.140	0.142	0.103	0.121	0.103	0.122	0.164
70 to 79*	17	0.170	0.148	0.275	0.306	0.150	0.203	0.289	0.133	0.147	0.102	0.156	0.155
80 to 89*	2	0.092	0.013	0.020	0.055	0.034	0.016	0.018	0.014	0.052	0.022	0.014	0.114
Average SD		0.116	0.125	0.125	0.127	0.115	0.119	0.120	0.129	0.126	0.111	0.149	0.152

* Due to the small sample size in the 70 to 89 years age group, data from these groups are not taken into the calculation of average SD.

Intertroch: intertrochanteric region; L: lumbar vertebra; Neck: neck of femur; SD: standard deviation; Troch: trochanter; Ward's: Ward's triangle

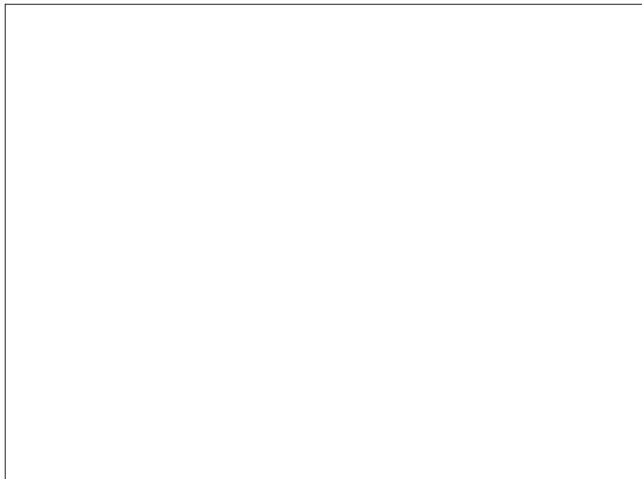


Fig. 1. Reference graph generated by the Hologic scanner for the average lumbar spine based on the Asian Singapore male database obtained from the study. The graph shows the BMD as a function of age. The middle line separating the two shaded areas represents the mean BMD value as a function of age. The light band above this line represents two standard deviations (SDs) above the mean; the dark band below represents two SDs below the mean. The dash line represents the BMD at -2.5 SD for young adult males.

standard reference curve based on this study for the average lumbar spine is illustrated in Figure 1, and that of the hip in Figure 2.

The mean peak BMD in the Singapore male for the average lumbar spine and the neck of femur was 1.006 g/cm² and 0.97 g/cm², respectively. The 20 to 24 years age group was utilised for the mean peak BMD at both the lumbar spine and femoral neck as the subsequent age groups of 25 to 29 years and 30 to 34 years showed a decrease in BMD values. The 35 to 39 years age group showed a slightly higher mean BMD value of 1.009 g/cm², but this was likely to be spurious based on the distribution curve. The mean BMD of 1.03 g/cm² for the 80 to 89 years

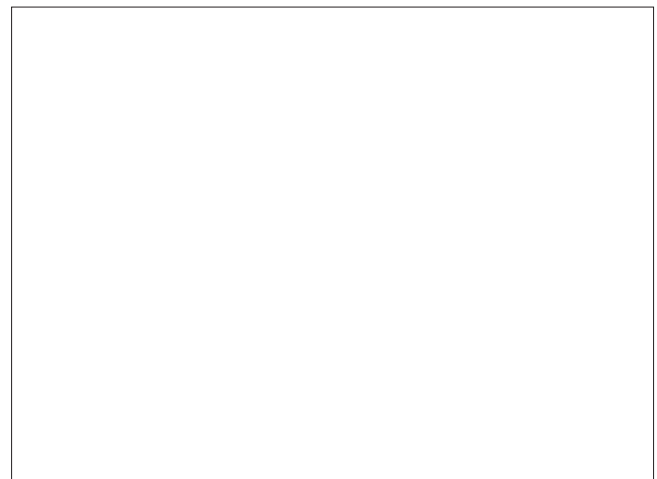


Fig. 2. Reference graph generated by the Hologic scanner for the hip based on the Asian Singapore male database obtained from the study.

age group was not considered in view of the small numbers (2). The corresponding values for the mean peak BMD in the United States (US) Caucasian male database (provided by Hologic Inc) for the average lumbar spine and the neck of femur were 1.091 g/cm² and 0.979 g/cm², respectively.

BMD at -2.5 SD from the peak adult value in the Singapore male database for the average lumbar spine and the neck of femur was 0.719 g/cm² and 0.655 g/cm², respectively. The corresponding values for the US male database were 0.816 g/cm² and 0.704 g/cm², respectively. BMD values for the Singapore male and the US male reference database are shown in Table III. The local male database shows that the BMD value utilised for the diagnosis of osteoporosis is lower compared to the US male database (a difference of 9.75% for the average lumbar spine and 4.9% for the neck of femur).

TABLE III: SINGAPORE ASIAN MALE REFERENCE BONE MINERAL DENSITY (BMD) DATABASE COMPARED TO THE UNITED STATES CAUCASIAN MALE REFERENCE DATABASE

	Measurement site					Total hip	Neck	Troch.	Inter troch.	Ward's
	L1	L2	L3	L4	L1 - L4					
Singapore male reference BMD (g/cm ²)										
Mean BMD (peak)	0.954	1.009	1.022	1.029	1.006	1.065	0.97	0.813	1.24	0.9
SD	0.116	0.125	0.125	0.127	0.115	0.129	0.126	0.111	0.149	0.152
2.5 SD	0.29	0.313	0.313	0.318	0.288	0.323	0.315	0.278	0.373	0.380
BMD at -2.5 SD	0.664	0.697	0.710	0.712	0.719	0.743	0.655	0.536	0.868	0.520
USA male reference BMD (g/cm ²)										
Mean BMD (Peak)	1.008	1.094	1.103	1.145	1.091	1.072	0.979	0.797	1.243	0.832
SD	0.11	0.11	0.11	0.11	0.11	0.13	0.11	0.11	0.15	0.12
2.5 SD	0.275	0.275	0.275	0.275	0.275	0.325	0.275	0.275	0.375	0.300
BMD at - 2.5 SD	0.733	0.819	0.828	0.870	0.816	0.747	0.704	0.522	0.868	0.532
Percentage difference (Singapore-USA)	-6.90%	-12.25%	-11.85%	-15.85%	-9.75%	-0.45%	-4.90%	1.35%	-0.05%	-1.20%

Intertroch: intertrochanteric region; L: lumbar vertebra; Neck: neck of femur; SD: standard deviation; Troch: trochanter; Ward's: Ward's triangle

Discussion

The current recommendation from the International Osteoporosis Foundation⁹ is to use the female reference for the diagnosis of osteoporosis. This is supported by studies which have shown that males fracture at the same BMD as females.¹⁰ However, other studies have shown that males fracture at a higher BMD than females.¹¹ For this reason, it may be appropriate to use a separate reference for the male population. At present, all central DXA manufacturers use a male reference for calculating T-scores in male patients.

There is no previously published study to establish the BMD reference database for the local Singaporean male. Prior to this, the local male T- (number of SDs from the peak adult BMD) and Z- (age-matched control) scores were based on the reference database from the US. As the mean peak BMD was higher and SD lower in the US database, the percentage of persons in the local population with osteoporosis tended to be overestimated.

As shown in our study, the BMD value utilised for the diagnosis of osteoporosis is lower in the local male population compared to the US male database. This suggests the potential of over diagnosing osteoporosis in the local male, when using the US male reference curve. We believe the use of a local male reference database will allow for more accurate diagnosis of osteoporosis in the local population.

The spike in the mean lumbar spine BMD in the 35 to 39 years age group above the mean peak BMD of the 20 to 24 years age group is possibly related to the increased physical activity among subjects in that age group. The secondary BMD rise after the age of 55 years in the lumbar spine may be spurious, related to increasing extraskelatal calcification

with age. The spike in the mean total hip and neck of femur BMD measurements in the 45 to 49 years age group and the increase in BMD after the age of 55 are possibly related to the onset of hip joint degeneration and sclerosis in older patients.

Some limitations of this study include the small number of subjects in the older age group (70 to 89 years). The 70 to 79 years age group has 17 recruits and the 80 to 89 years age group has 2 recruits. This is likely the reason why there is a slightly higher mean BMD value of 1.03 g/cm² for the average lumbar spine in the 80 to 89 years age group as shown in Table I. The small number has also limited the ability to compare among ethnic groups.

Bone mineral apparent density (BMAD) was not evaluated in this study. This could be calculated for the spine but not the hip measurements in the Hologic QDR 4500Elite model. Studies have shown that area BMD is lower in Asian than Caucasians but when corrected for size, the BMAD becomes more similar between Asian and Caucasians.¹²

Conclusion

This BMD reference database study performed on the local male population allows for more accurate diagnosis of osteoporosis in male Asian subjects. This enables fracture risk to be more accurately assessed for the local population.

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