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Calculation of the reference bone mineral density values in North Indian population using phantomless quantitative computed tomography

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Abstract:

OBJECTIVE: The objective of the study is to generate reference values of bone mineral density (BMD) in north Indian population using phantomless quantitative computed tomography (QCT).

MATERIALS AND METHODS: Bone mineral densities were generated from the computed tomography (CT) scans of 691 patients (390 males and 301 females, ages 11–85 years) who underwent CT of the abdomen or thorax for indications unrelated to bone diseases. The individuals were divided according to age groups from 11–15 to 80–85 years. BMD was calculated by phantomless QCT software by assessing L1 and L2 vertebrae.

RESULTS: For females, the maximum BMD was observed for the age group of 21–25 years (144.67 mg/cc). The overall bone loss per year from 26 to 85 years was 1.62 mg/cc. Greater bone loss was seen from ages of 36–55 years which was 2.18 mg/cc. With bone loss per year being 0.99 mg/cc in ages from 26 to 35 years and 1.41 mg/cc from 56 to 85 years. Regression analysis gave a better fit using third order polynomial of age than did a linear regression line. For males, the maximum BMD was observed for the age group of 21–25 years (147.67 mg/cc). The overall bone loss per year from 26 to 85 years was 1.2 mg/cc. Regression analysis gave the best fit using linear regression.

CONCLUSION: In the study population, the males show a linear relationship between age and BMD with continuous bone loss after the age of 25 years while females demonstrate a more complex relationship between age and BMD with accelerated bone loss in perimenopausal age group.

Keywords:

Bone mineral density, epidemiology, osteoporosis, quantitative computed tomography

Introduction

Osteoporosis is a pathological condition resulting from abnormal bone loss and characterized by low bone mass and microarchitectural changes in cortical and cancellous bone. The quantification of osteoporosis can be done by various radiological modalities including dual-energy X-ray absorptiometry (DEXA), single energy X-ray absorptiometry, peripheral dual-energy X-ray absorptiometry (PDXA), (radiographic absorptiometry [RA], dual photon absorptiometry (DPA), single photon absorptiometry (SPA), magnetic resonance imaging, quantitative computed tomography (QCT), and ultrasound (US).[1]

Physical activity, optimal nutrition, and adequate sun exposure are the major factors required for attaining peak BMD.[2] BMD also varies according to the genetics and environment of the populations which are particular to the given geographic area, race, or sex.[3] Healthy males have been observed to achieve peak BMD in lumbar spine by the age of 30 years.[4] Osteoporosis is widespread in India with estimated more than 61 million affected individuals with

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80% being females. According to the National Health and Nutrition Examination Survey III (NHANES III) estimated 14 million women over the age of 50 years in the US have low BMD at hip.[5] In a large study, Patni *et al*. found that mean Indian BMD is about 2SD lower compared to the Western figures.[3] It has been observed that Indian migrant women in western countries are at a higher risk of accelerated bone loss and reduced BMD compared to natives of the west which has been attributed to factors such as darker skin, conservative clothing, and genetic differences.[6]

Other factors associated with a low BMD were observed to be low BMI, low calcium intake, lack of exercise, and advanced age; and moreover, Indian Council of Medical Research recommendation for calcium and Vitamin D for various populations in India is much lower when compared to the reference daily intake of developed nations.[7]

Materials and Methods

A total of 691 patients (390 males and 301 females) were included in this retrospective study who had undergone computed tomography (CT) scan of abdomen or thorax for indications unrelated to bone diseases (suspected alcoholic or biliary pancreatitis 202, suspected or sputum positive pulmonary tuberculosis 196, intestinal obstruction 117, suspected or localized abdominal or thoracic masses 86, abdominal or thoracic trauma 53, and miscellaneous 37). No additional exposure was given to the patients. Patients with known metabolic diseases, thyroid disorders, focal bone lesions (in vertebrae or elsewhere), disseminated malignancies, ongoing hormonal treatment (e.g., hormone replacement therapy), or anti-osteoporotic treatment and patients on diuretics were excluded from the study. Patients were included or excluded, based on their clinical records available.

The patients were scanned with Philips Brilliance 16-slice CT scanner (KVp = 120, mAS = 250, slice thickness = 2–3 mm). Standard soft-tissue convolution filter was used for reconstruction. Only noncontrast enhanced scans were utilized. Two vertebrae, L1 and L2, were selected for assessment. Patients with lesions in vertebrae, for example, compression fractures, hemangiomas, osteomas, or any lytic/sclerotic lesions were excluded. The sections for assessment of BMD were positioned parallel to vertebral endplates at the level of transverse processes. Regions of interest (ROIs) were placed over trabecular part of vertebrae, paravertebral muscles and subcutaneous fat [Figure 1]. Cortical bone or osteophytes were carefully excluded from ROI placement. BMD was calculated by phantom less QCT software of the Philips Brilliance CT workstation.

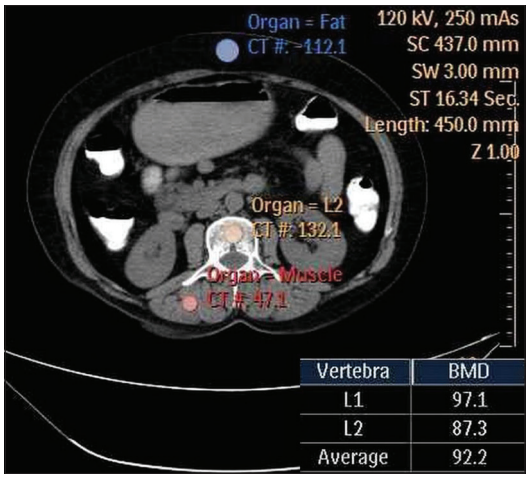

Figure 1: Placement of regions of interest on trabecular bone, paraspinal muscles and subcutaneous fat

Statistical analysis was performed using SPSS software. Values were rounded off to two digits after decimal point.

Results

Females

The mean BMDs of the females in different age groups were obtained [Table 1]. Figure 2a shows a scatter diagram of the studied females. The maximum BMD was observed for the age group of 21–25 years (144.67 mg/cc). The overall bone loss per year from 26 to 85 years was 1.62 mg/cc. Greater bone loss was seen from ages of 36–55 years which was 2.18 mg/cc. With bone loss per year being 0.99 mg/cc in ages from 26 to 35 years and 1.41 mg/cc from 56 to 85 years [Figure 2b]. Regression analysis gave a better fit using third order polynomial of age than did a linear regression line ($P = 0.05$, standard error = 27.07).

BMD for females = $75.858 + 5.819(\text{age}) - 0.155(\text{age})^2 + 0.001(\text{age})^3$.

Males

The mean BMDs of the males in different age groups were also obtained [Table 2]. Figure 3a shows a scatter diagram of the studied males. The maximum BMD was observed for the age group of 21–25 years (147.67 mg/cc). The overall bone loss per year from 26 to 85 years was 1.2 mg/cc [Figure 3b]. Regression analysis gave best fit using linear regression ($P < 0.001$, SE = 5.23).

BMD for males = 172.46–1.264 (age).

Discussion

QCT came into use in the mid-1970s.[8] It is a clinically proven method for measurement of bone mineral

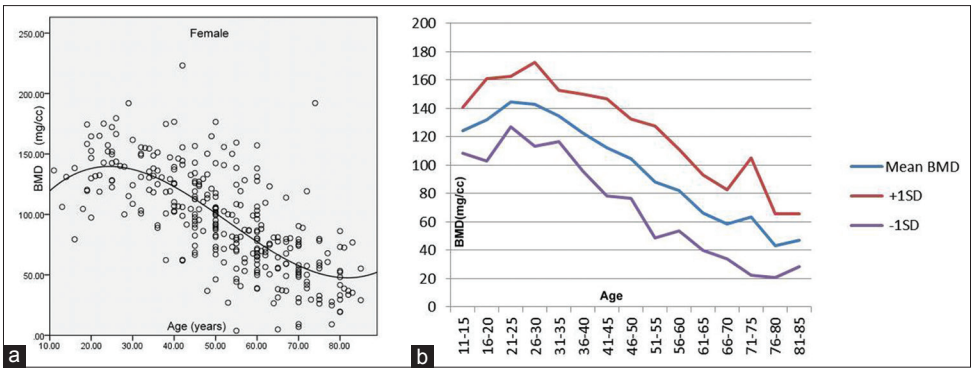

Figure 2: (a) Scatter diagram of the vertebral bone mineral density for females as a function of age and third-order regression line. (b) Age wise variation in mean bone mineral density in females in various age groups

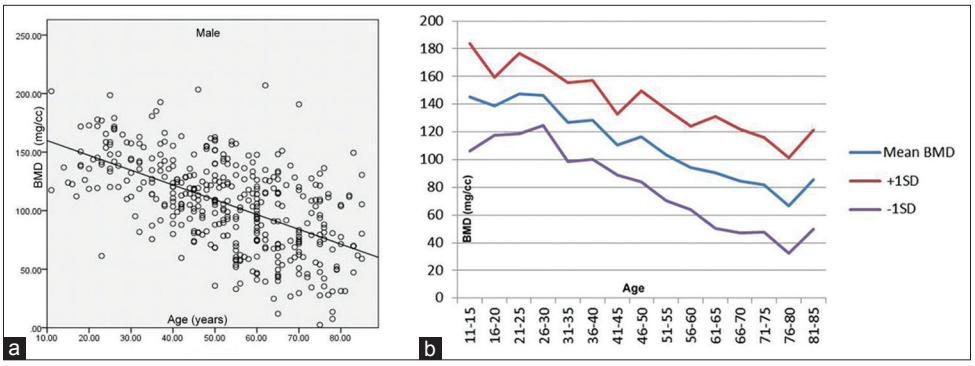

Figure 3: (a) Scatter diagram of the vertebral bone mineral density for males as a function of age and linear regression line. (b) Age wise variation in mean bone mineral density in males in various age groups

Table 1: Analysis of bone mineral density for females

Age group	*n*	Mean BMD	SD	Bone loss[a] (mg/cc/years)	Bone loss[b] (%/years)
11-15	3	124.53	16.11		
16-20	12	132.17	28.99	−1.53	−1.06
21-25	15	144.67	17.79	−2.5	−1.73
26-30	11	142.84	29.69	0.37	0.25
31-35	15	134.81	18.00	1.61	1.11
36-40	22	122.80	27.06	2.4	1.66
41-45	31	112.44	34.26	2.07	1.43
46-50	39	104.65	28.11	1.56	1.08
51-55	26	88.39	39.46	3.25	2.25
56-60	39	82.35	28.90	1.21	0.84
61-65	22	66.46	26.65	3.18	2.2
66-70	26	58.40	24.52	1.61	1.11
71-75	17	63.63	41.23	−1.05	−0.72
76-80	15	43.06	22.40	4.11	2.84
81-85	8	47.23	18.62	−0.83	−0.58
Total	301	97.90	35.82		

[a]Mean BMD for one age group minus the mean BMD for the previous age group/5 years, [b]Bone loss per year relative to the mean BMD value of the age group with highest BMD (21–25 years). BMD=Bone mineral density, SD=Standard deviation

density (BMD) in bones of axial and appendicular skeleton including the spine, proximal femur, and forearm. DEXA is currently the preferred method for estimation of BMD; however, it may be provide erroneous measurements in the presence of severe degenerative changes of spine or hip, calcified vessels, radiopaque orally administered contrast materials, for example, Barium solution and foods or other ingested materials with high radiopacity. It is also less accurate in presence of extreme obesity or low body mass index (BMI).[9]

In a study by Kroger *et al*. compared QCT and DEXA at various anatomic sites. They found that QCT of the spine has a high sensitivity of 94.2% for prediction of osteoporotic fractures in patients with T score −2.5 SD or lower and QCT of radius showed the highest specificity of 98.3%.[10] There is usually a threshold level for all BMD methods above which osteoporotic fractures are rarely seen while below this threshold prevalence of fracture rises. This threshold for QCT has been observed to be 100–110 mg/cc and below 50 mg/cc most patients already have vertebral fractures.[1] A threshold of 90 mg/cc showed 100% sensitivity for osteoporosis at L3 level.[11] According to the American College of Radiology guidelines a QCT trabecular spine BMD value of >120 mg/cc is considered normal, values from 80 to 120 mg/cc is considered osteopenia and <80 mg/cc is considered osteoporosis.[12] On QCT, a gradual decrease in the BMD value is observed from T1 to L3 levels with subsequent increase in L4 and L5 in both males and females.[13]

Table 2: Analysis of bone mineral density for males

Age group	*n*	Mean BMD	SD	Bone loss[a] (mg/cc/years)	Bone loss[b] (%/years)
11-15	4	145.075	38.80		
16-20	10	138.74	20.90	1.27	0.86
21-25	19	147.674	28.98	−1.79	−1.21
26-30	17	146.329	21.45	0.27	0.18
31-35	19	127.089	28.29	3.85	2.61
36-40	28	128.596	28.47	−0.30	−0.20
41-45	34	110.756	21.90	3.57	2.42
46-50	43	116.66	32.90	−1.18	−0.80
51-55	41	103.622	33.11	2.61	1.77
56-60	46	94.039	30.05	1.92	1.30
61-65	39	90.723	40.28	0.66	0.45
66-70	28	84.418	37.54	1.26	0.85
71-75	27	81.656	34.14	0.55	0.37
76-80	23	66.865	34.45	2.96	2.00
81-85	12	85.742	35.87	−3.78	−2.56
Total	390	111.20	26.77		

[a]Mean BMD for one age group minus the mean BMD for the previous age group/5 years, [b]Bone loss per year relative to the mean BMD value of the age group with highest BMD (21–25 years). BMD=Bone mineral density, SD=Standard deviation

Mehta *et al*. found paradoxically lower fracture rates in Indo-Asian women compared to Caucasian women despite lower BMD. This is assumed to be due to the difference in body sizes of the different populations which lead to lower BMD values on two-dimensional modalities such as DEXA due to different bone depths.[14] Three-dimensional methods such as QCT may be able to overcome this limitation.[8]

In a large prospective study, Budoff *et al*. concluded that phantomless BMD values show high correlation with standard phantom-based QCT BMD values.[15] Mueller *et al*. in their study concluded that phantom less Philips BMD option has high accuracy and sufficient precision for diagnosis of lowered BMD.[16] In contrast to phantom based QCT, phantomless QCT utilizes patient's paraspinal muscles and subcutaneous fat as the calibration references and assigns the mode to the resulting peak of the best fit Gaussian function for each component instead of only adopting an average CT attenuation value.[17]

Genant *et al*. in a large study found that among QCT, DPA, SPA, and combined cortical thickness methods QCT had the strongest correlation with vertebral fracture severity. They also concluded that single energy QCT is adequate and perhaps preferable over dual energy QCT for assessment of osteoporosis as the latter offers no additional improvement in correlation with facture index or DPA.[18]

Almost every radiological setup has a CT scanner while installation of DEXA requires extra space, maintenance, and dedicated staff which may not be economically feasible. A vast number of abdominal and thoracic CT scans are performed every day worldwide on patients who have a potential risk for having osteoporosis. At least, these many patients can be screened without additional radiation dose and with only little extra effort. However, usage of QCT for only diagnosis of osteoporosis is associated with significantly higher dose.[17]

Gudmundsdottir *et al*. calculated bone mineral densities of 187 healthy Icelandic women aged 35–64 years using phantomless QCT and provided reference BMDs for the population on QCT.[19] In a similar study, Manisal *et al*. provided reference data for BMD on QCT in healthy females of Turkey.[20] In a large study done at the University of California at San Francisco, Cann *et al*. provided reference data for the US population.[21] Firooznia *et al*. also calculated QCT values in individuals from New York.[22] Kalender *et al*. calculated the reference values in the European population.[23] Currently, there is no available data on BMD values of Indian population on QCT.

In our study, the results for males are as expected which is also consistent with majority of other such studies done so far.[9-11,14-16] However, the results for females are not in accordance with most of the current literature.[10,11,13,14,17-19] The authors propose that a different pattern/pathogenesis of osteoporosis may be implicated in females of north Indian population and also it may be attributed to the fact that our study included patients with a subset of population with risk factors (pancreatitis, alcohol consumption, and tuberculosis) which are known to themselves play a role in pathogenesis of osteoporosis.

Conclusion

The phantomless QCT is a clinically proven method for assessment of BMD; however, reference values of QCT BMD are not available till date for Indian population which has shown significant differences from western data on other modalities such as DEXA. In the study population, the males show a linear relationship between age and BMD on QCT with continuous bone loss after the age of 25 years while females demonstrate a more complex relationship between age and BMD on QCT with accelerated bone loss in perimenopausal age group. The values generated by the present study can be applied to the studied population as reference values and can be used for diagnosis of osteopenia and osteoporosis with phantomless QCT in patients undergoing CT of the abdomen and thorax without additional radiation exposure and patients with increased risk of vertebral fractures can be identified.

Limitations of study

Our study included patients with a subset of population with risk factors (pancreatitis, alcohol consumption,

and tuberculosis) which are known to themselves play a role in pathogenesis of osteoporosis. Hence, our population was not an entirely representative healthy population. Second, as suggested earlier, a different pattern/pathogenesis of osteoporosis may be implicated in females of north Indian population for which more studies with a larger female population are required.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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