

Estimating the proportion of bone mineral density loss in patients with normal kidney function among South Indian population

Kevin Neil Aranha

Father Muller Medical College and Hospital, Mangalore

Dr. Rahul P Kotian (✉ kotian.rahul18@gmail.com)

College of Allied Health Sciences, Srinivas University, Mukka, Karnataka, India <https://orcid.org/0000-0003-2682-158X>

Arathy Mary John

Manipal College of Health Professions, Mangalore, Manipal Academy of Higher Education, Karnataka, India

Research Article

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Abstract

Background: Bone Mineral density (BMD) is considered as one of the golden tool to measure the bone quality in which two measurements namely T- Score and Z –score are used to report the BMD test results. Whenever there is deterioration of BMD it is associated with low skeletal mass. Creatinine is a chemical waste molecule that is generated from this muscle metabolism. Creatinine is a good marker for muscle mass. However, limited studies have been done which tell us the association between BMD loss and serum creatinine (SCr) levels.

Methodology: 200 participants who were referred for CECT abdomen and pelvis were scanned using 128 slice Philips Brilliance CT. Using BMD software, four different vertebral bodies from L1-L4 were taken and ROI was placed at the central portion of the trabecular bone, two reference ROI's, one in retro spinal muscle and one in fat tissue were also placed. To measure CT attenuation value, a ROI graphic tool was drawn at the trabecular bone. Average HU of BMD, T score and Z score values were taken from L1-L4.

Statistical Analysis: The data was analysed using SSPS version 16.0. For assessment of normal BMD values, the results of measurements were averaged for age, creatinine level, T score and Z score and descriptive statistics was calculated. Spearman's correlation coefficient was used to estimate the correlation between serum creatinine with T score and Z score.

Results: T Score and SCr correlated negatively at -0.25. The correlation between Z Score and SCr was also negatively correlated at -0.187.

Conclusion: It was evident from the study findings, that there is a non-association between SCr and T Score levels which showed that BMD of a person was not associated with normal kidney function. Thus, SCr levels cannot be used as a biomarker for osteoporosis or osteopenia.

Introduction

BMD reflects the bone rigidity which is a result of the calcium and phosphorus deposits. It is considered as one of the golden tool to measure the bone quality and density⁽¹⁾. Measuring the BMD from axial and appendicular skeleton helps to assess the reason for the shrinkage of bone with age⁽²⁾. Quantitative computed tomography (QCT) is a reputed technique used to measure the BMD in the axial skeleton which can be further used for the evaluation of risk with fractures in the vertebra, degree of bone loss, follow-up of osteoporosis and other bone related metabolic ailments⁽³⁾. The measurements named, T Score and Z Score are being used to report BMD test results. Deterioration of BMD is associated with low skeletal mass⁽⁴⁾. SCr levels can be used as a marker to assess muscle mass in subjects with normal renal function⁽⁵⁾. Therefore, SCr levels could be directly proportional to BMD⁽⁶⁾. Subjects with poor renal function have significantly lower BMD, than those with mild-to-moderate CKD who don't have a very significant loss⁽⁷⁾.

The relationship between SCr levels and BMD remains unexplored and its findings might help to test the efficiency of the QCT machine and its BMD software.

Methods

The study protocol followed was reviewed and approved by the Research Committee, and ethical clearance was also obtained. All the subjects provided written informed consent to participate after a detailed explanation about the study was given by the principal investigator.

Subjects

This was a cross sectional study. A total of 200 patients who were referred for CECT of abdomen and pelvis scans, were recruited. Patients above 20 and below 60 years of age with a creatinine level in the range of 0.7 - \leq 1.2 mg/dl were included in the study. Patients below 20 years and above 60, with fractures in spinal vertebra (L1-L5), implants in the spine, osteoporosis, osteopenia or any diseases which causes low BMD , consumption of calcium supplementation and CKD and renal insufficiency were excluded from the study.

Image Acquisition/SCr reading

Images were acquired using Phillips Incisive 128 slice MDCT. CT images were acquired using a standard CECT protocol using the following image parameters as depicted in table 1. The serum creatinine values of each patient was collected from their blood reports available in the patient's file obtained 4 days prior to CECT.

Table 1. BMD image acquisition protocol

Resolution	Standard
Scan type	Abdomen
Scan mode	Helical
Scan angle	180
Collimation	64x0.625
FOV	350
Thickness	5 mm
Increment	5 mm
Rotation time	0.75
KV	120
Mas	250
Matrix	512
Filter	Standard B
Window centre /width	60x360

Image analysis and post-processing

BMD and corresponding HU values were analysed using the BMD software and stored in the Philips intellectual space portal workstation. BMD of lumbar spine using ROI's at (L1-L4) was measured and averaged from the reconstructed plain scan images, using phantom less BMD application as shown in figure 1. ROI's were drawn on the vertebra avoiding any bony pathologies and two reference ROIs were used: one in retro spinal muscle (+40 HU to+120 HU) and one in fat (0 - to -100HU). The complete T score and Z score was then taken into consideration as shown in figure 2.

Statistical Analysis

All analyses were performed using the SPSS software package (version 16.0). The mean, standard deviation was calculated for Serum Creatinine, age, Z score and T score. Median, Q1 and Q3 of T Score and Z Score was also analysed. Spearman's correlation coefficient was used to find the correlation between SCr with T Score and Z Score respectively.

Results

Demographic characteristics of the participants

Out of the 200 participants aged between 20-60 years, mean age was 39 ± 11.6 and creatinine levels between 0.7-1.2 mg/dl with a mean of 0.87 ± 0.16 . 125 patients were males (62.5%) and 75 were females (37.5%).

Estimating the proportion of bone loss

105 patients had no bone loss (52.5%) and 95 had bone loss (47.5%). Out of the 95 patients with bone loss 74 (77.8%) patients had osteopenia and 21 (22.2%) patients had osteoporosis. All these values were recorded prospectively. The evaluation of normal vs bone loss was done according to world health organization (WHO) set guidelines, which states that a T score between -1 and +1 is reflected as a standard, a T score of -1 to -2.5 is considered osteopenic and if the T score is -2.5 or lower is considered to be osteoporotic. The frequency and percentage of bone loss where "positive" indicates the presence of bone loss and "negative" indicates no bone loss as depicted in table 2.

Table 2. Proportion of bone loss

Loss	Frequency	Percentage
Negative	105	52.5
Positive	95	47.5
Total	200	100.0

SCr in relation to T Score and Z score

A mean T Score of -0.84 ± 1.46 was found after analysing the BMD data. T Score and SCr showed negatively correlation at -0.25. SCr in relation to Z Score was also analysed with a mean of -0.08 ± 1.3 . The correlation

between Z Score and SCr was negatively correlated at -0.187 as depicted in table 3.

Table 3. SCr correlation with T score and Z score

Age-Mean ±SD	SCr- Mean ±SD	T score- Mean ±SD	Z score- Mean ±SD	Median T score	Median Z score	Q1 T score	Q3 T score	Q1 Z score	Q3 Z score
39±11.6	0.87±0.16	-0.84±1.46	-0.08±1.32	-1	-0.25	-1.9	-1	-0.2	-0.7

Discussion

Osteoporosis being the one of the most common bone ailment, it has been affecting our societies from a very long time and is mainly described as the disruption of the equilibrium between bone formation and resorption⁽⁸⁾. Subsequently this loss of bony constituent creates changes in bone microarchitecture which markedly favours the incidence of fractures, all of which makes it closely related with high morbidity and mortality rates⁽⁹⁾.

Reduction in skeletal muscle mass can be linked to decline BMD⁽¹⁰⁾. Since SCr can serve as an indicator for muscle mass, Huh et al assessed the association between SCr and BMD in an elderly population whose kidney function was normal and came to a conclusion that SCr imitated muscle mass, and low levels of SCr was related to low levels of BMD independently⁽¹¹⁾. Greater muscle mass is said to be related to better results and long life in people with CKD states⁽¹²⁾. Proper lifestyle choices, facilitated by choosing a balanced diet and regular exercise can help improve an individual's maximum bone potential at an early age⁽¹³⁾. If there is a vitamin D receptor genotype variant such patients are susceptible to low bone density⁽¹⁴⁾.

Robert H et al., evaluated the linkage between BMD and fractures in partakers with or without CKD by taking health, age and body composition into consideration. They came to a conclusion that BMD values provided information pertaining to fracture risk in the elderly with or without moderate CKD⁽¹⁵⁾. Therefore, by looking at the values we can predict the risk of future fractures in such individuals irrespective of their renal health. Simerjot K Jassal et al., conducted a study to determine the relationship between kidney function and BMD and related it to bone loss, and osteoporotic fracture. They found that measured renal function had declined with age. They concluded that there is an associations between kidney function and BMD which is the strongest when CKD is high, which shows that if a patient has declining renal function the BMD values may be low⁽¹⁶⁾.

Myong Jun-Pyo Myong et al., conducted a study in Korea to find the relationship between BMD and CKD among general population in Korea and concluded that there was a link between eGFR and BMD in men and women. This study shows that if GFR decreases, there can be a decline in BMD. Therefore, there's higher risk of osteoporosis or osteopenia in people with reduced renal function⁽¹⁷⁾. Using modern therapy for osteoporosis, it is important to use newer pathogenetic approaches which aim towards the elimination of any imbalances

between the relationship of osteoclast – osteoblast while using anabolic support of all bone cells. “Osteomed Forte” is a drug that complies these requirements⁽¹⁸⁾.

In this cross sectional study, 95 participants out of 200 were detected with bone loss (47.5%) and it was observed that most of the participants with bone loss were from the age range from (41-60) about 62.1%. Therefore, as age increases bone density decreases even with good renal health. We also evaluated the average of normal creatinine levels (0.87 ± 0.16) with BMD and independently associated it with the average values of T Score (-0.84 ± 1.46) and Z Score (-0.08 ± 1.32), and the principle finding was that T Score (-0.25) and Z Score (-0.187) were not associated with normal creatinine levels. A negative correlation between BMD and normal kidney function done by evaluating serum creatinine levels cannot give an explanation about the bone health of an individual.

QCT permits measurement of volumetric bone density without any superimposition of cortical bone and other surrounding soft tissue⁽¹⁹⁾. The site most commonly used to measure BMD using QCT is the lumbar spine. The trabecular bone is the main site for osteoporotic bone loss, therefore the density loss in that region is higher than that other sites like in cortical bone⁽²⁰⁾. Phantom-less CT scans can be used to estimate lumbar BMD with accuracy similar to that of dual energy x-ray absorptiometry (DEXA) scans which is considered a gold standard in detecting BMD. QCT is largely applied to both prospective and retrospective studies which can assess patient bone density and therefore can be helpful for research and clinical practice⁽²¹⁾. The QCT machine used for this study was Philips Incisive 128 slice CT. The Philips BMD software can therefore be used as an effective tool to diagnose osteoporosis/osteopenia. In this study we found that out of the 95 patients with bone loss 74 (77.8%) patients had osteopenia and 21 (22.2%) patients had osteoporosis. Moreover, we tested the efficiency of our MDCT system in evaluating BMD without any extra radiation, time and cost to the patient.

Conclusion

The present study has provided information about the relationship between Serum creatinine and T Score levels. It was evident from this study that there is a non-association between SCr and T Score levels which showed that BMD of a person was not associated with normal kidney function thus SCr levels cannot be used as a biomarker for osteoporosis or osteopenia. The results showed a loss in bone health in patients with good kidney function, this loss may be associated with other pathophysiological conditions other than normal SCr which weren't taken into account in this study.

Declarations

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CONFLICT OF INTEREST:

The authors declare no conflict of interest.

Abbreviations

BMD- bone mineral density

SCr- serum creatinine

ROI- region of interest

CECT- contrast enhanced computed tomography

HU- Hounsfield unit

QCT- Quantitative computed tomography

CKD- Chronic kidney disease

eGFR- estimated glomerular filtration rate

References

1. Paz ICL A, Ldg B, Bruno L. Bone mineral density: review. Brazilian J Poult Sci Rev Bras. 2006 [cited 2017 Nov 14];8(2):69–73.
2. Riggs BL, Wahner HW, Dunn WL, Mazess RB, Offord KP, Melton LJ. Differential changes in bone mineral density of the appendicular and axial skeleton with aging. Relationship to spinal osteoporosis. J Clin Invest. 1981;67(2):328–35.
3. Guglielmi G, Lang TF. Quantitative computed tomography. Semin Musculoskelet Radiol. 2002;6(3):219–27.
4. Carey JJ, Delaney MF. T-scores and Z-scores. Clin Rev Bone Miner Metab. 2010;8(3):113–21.
5. Huh JH, Choi SI, Lim JS, Chung CH, Shin JY, Lee MY. Lower serum creatinine is associated with low bone mineral density in subjects without overt nephropathy. PLoS One. 2015;10(7):1–11.
6. Perrone RD, Madias NE, Levey AS. Serum creatinine as an index of renal function: New insights into old concepts. Clin Chem. 1992;38(10):1933–53.
7. Rochester PL. Test Definition : CREA Z Creatinine with Estimated GFR (MDRD), Serum Result Codes : Supplemental Report : Test Definition : CREA Z. 2017;1–2.
8. Kong X, Tang L, Ma X, Liu W, Wang Z, Cui M, et al. Relationship between mild-to-moderate chronic kidney disease and decreased bone mineral density in Chinese adult population. Int Urol Nephrol. 2015;47(9):1547–53.
9. Celenk C, Celenk P. Bone Density Measurement Using Computed Tomography. In: Computed Tomography - Clinical Applications. 2008.; 123–36.
10. Mueller DK, Kutscherenko A, Bartel H, Vlassenbroek A, Ourednicek P, Erckenbrecht J. Phantom-less QCT BMD system as screening tool for osteoporosis without additional radiation. Eur J Radiol. 2011 Sep 1 [cited 2017 Oct 24];79(3):375–81.

11. Kaesmacher J, Liebl H, Baum T, Kirschke JS. Bone Mineral Density Estimations From Routine Multidetector Computed Tomography. *J Comput Assist Tomogr.* 2017;41(2):217–23.
12. Patel SS, Molnar MZ, Tayek JA, Ix JH, Noori N, Benner D, et al. Serum creatinine as a marker of muscle mass in chronic kidney disease: Results of a cross-sectional study and review of literature. *J Cachexia Sarcopenia Muscle.* 2013;4(1):19–29.
13. Suman VB, Pratik Kumar Chattterjee, Vinodini NA, Kunal K, Megha Gokul, Ramesh M Bhat. Effect of variable Diet and Physical Activity on Bone Mineral Density in Adults using Peripheral–Dexa Scan. *Research J. Pharm. and Tech* 2018; 11(6): 2404-2407.
14. Ainur Amanzholkyzy, Roza E. Nurgaliyeva, Aiman T. Kaldybayeva, Tamara Zh. Batyrova, Farida K. Balmaganbetova, Zhuldyz A. Aibassova. Biochemical variability of Vitamin D Receptor (Vdr) Gene and its Relationship with Bone Mineral Density in Children of the Western Region of the Republic of Kazakhstan. *Research J. Pharm. and Tech* 2019; 12(2):735-740.
15. Yenchek RH, Ix JH, Shlipak MG, Bauer DC, Rianon NJ, Kritchevsky SB, et al. Bone mineral density and fracture risk in older individuals with CKD. *Clin J Am Soc Nephrol.* 2012;7(7):1130–6.
16. Jassal SK, von Muhlen D, Barrett-Connor E. Measures of Renal Function, BMD, Bone Loss, and Osteoporotic Fracture in Older Adults: The Rancho Bernardo Study. *J Bone Miner Res.* 2006;22(2):203–10.
17. Myong J, Kim H, Koo J, Park CY. Relationship between Bone Mineral Density and Moderate to Severe Chronic Kidney Disease among General Population in Korea. 2013;569–74.
18. V. I. Strukov, A. I. Kislov, N. V. Eremina, G. P. Deriabina, M. Yu. Sergeeva-Kondrachenko, A. Yu. Antropov, Ya. V. Kuzmina, K. R. Tayrova, E. V. Petrova, D. G. Elistratov, O. V. Strukova-Jones. The use of Bone Tissue Non-Steroid Anabolizators in Treatment of Osteoporosis. *Research J. Pharm. and Tech.* 2019; 12(5):2195-2199.
19. Li N, Li XM, Xu L, Sun WJ, Cheng XG, Tian W. Comparison of QCT and DXA: Osteoporosis detection rates in postmenopausal women. *Int J Endocrinol.* 2013;2013:5–10.
20. Kinsella S, Murphy K, Breen M, O'Neill S, McLaughlin P, Coyle J, et al. Comparison of single CT scan assessment of bone mineral density, vascular calcification and fat mass with standard clinical measurements in renal transplant subjects: The ABC HeART study. *BMC Nephrol.* 2015;16(1):1–11.
21. Bone L, Density M, Measurements T, Incidence F. HHS Public Access. 2016;16(0 2):1–19.

Figures

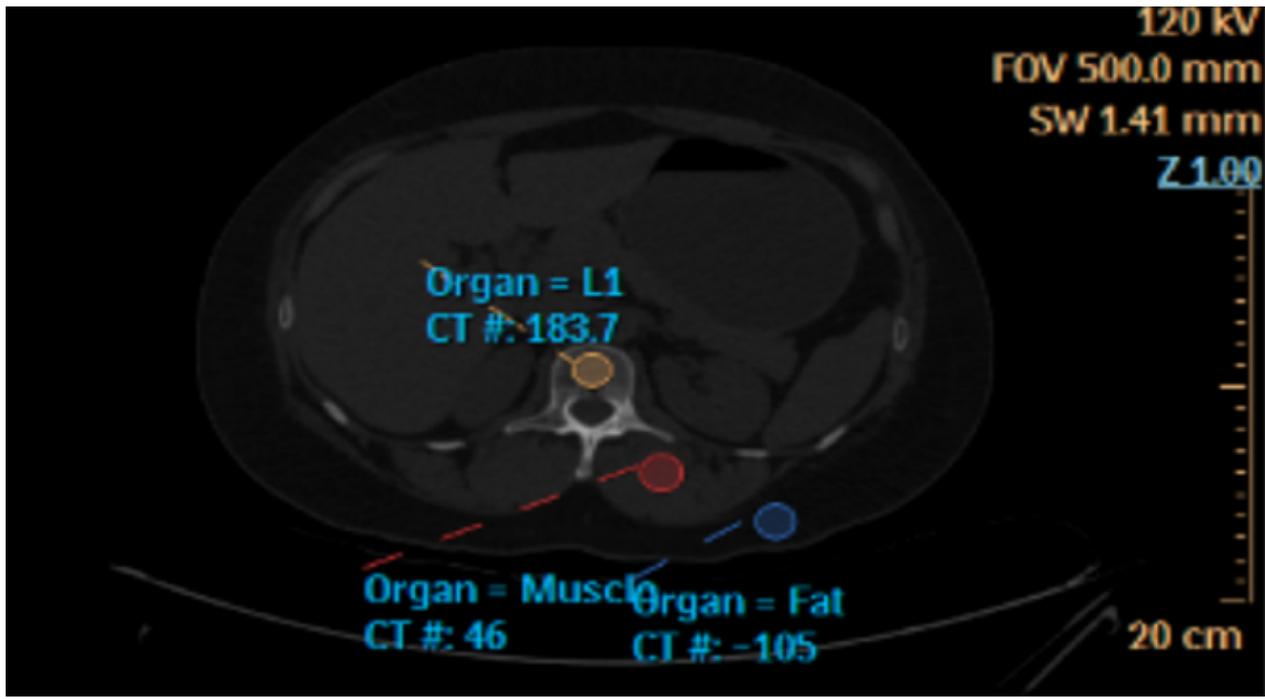


Figure 1

BMD analysis at the lumbar vertebra with subcutaneous fat and Para spinal muscle as calibration references

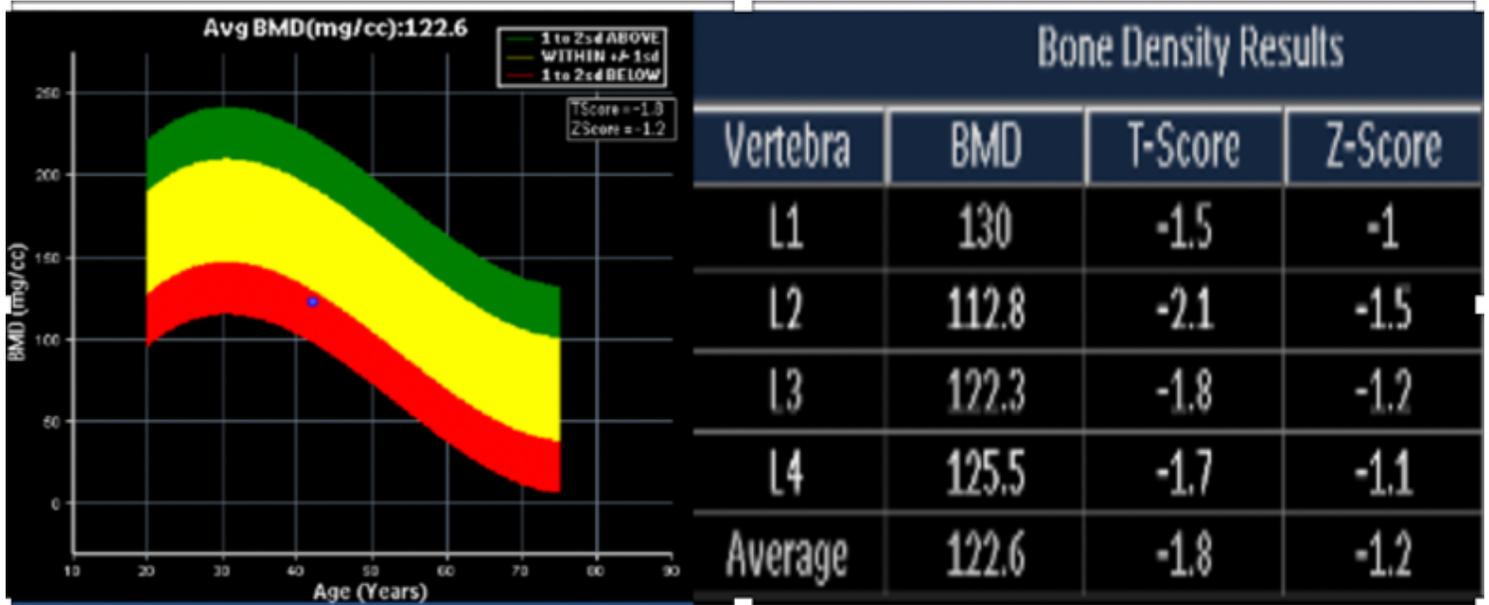


Figure 2

L1-L4 averaged BMD and their averaged Z score and T score

Supplementary Files

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