ACTA ORTHOPAEDICA et TRAUMATOLOGICA TURCICA
www.aott.org.tr

Research Article

Feasibility of diagnosing osteoporosis using routine computed tomography scans for hip fractures: Correlation with histopathological diagnosis of head and neck regions

Yunus Imren[1], Bulent Karslioglu[2], Suleyman Semih Dedeoglu[1], Ahmet Keskin[3], Ahmet Firat Berkay[1], Ali Cagri Tekin[2]

[1]Department of Orthopedics and Traumatology, Health Sciences University Baltalimanı Metin Sabancı Bone Diseases Training and Research Hospital, İstanbul, Turkey
[2]Department of Orthopedics and Traumatology, Health Sciences University Prof. Cemil Taşçıoğlu City Hospital, İstanbul, Turkey
[3]Department of Orthopedics and Traumatology, Health Sciences University Kartal Dr. Lütfi Kırdar City Hospital, İstanbul, Turkey

ARTICLE INFO

Article history:
Submitted May 16, 2023
Received in revised form November 13, 2023
Accepted December 1, 2023
Publication Date December 29, 2023

Keywords:
Dual-energy X-ray absorptiometry
Hounsfield unit
Osteoporosis
Proximal femoral fracture

ORCID iDs of the authors:
Y.I. 0000-0002-8056-6156;
B.K. 0000-0001-6127-9672;
S.S.D. 0000-0002-7441-5028;
A.K. 0000-0001-8627-5651;
A.F.B. 0000-0003-1566-8065;
A.C.T. 0000-0002-4308-8167.

ABSTRACT

Objective: The aim of this study was to demonstrate the feasibility of diagnosing osteoporosis through routine computed tomography (CT) by assessing the association between the histopathological assessment of femoral head specimens extracted from patients who underwent surgery for intertrochanteric fractures and the Hounsfield unit (HU) measurements derived from preoperative CT scans.

Methods: Forty-eight patients who presented to our clinic between November 2019 and May 2020 with hip fractures and underwent partial prosthesis fixation were included in this retrospective study. Hounsfield unit measurements were performed on the head and neck regions using dual-energy x-ray absorptiometry (DEXA) and CT scans, respectively. The trabecular ratio per unit area was calculated using the Nikon Imaging Software (NIS-Elements) program in the pathology laboratory from digitally captured images of the removed head and neck specimens.

Results: The mean HU receiver operating characteristic analysis had a sensitivity of 77% and a specificity of 87%, with a cutoff value of 77.68. There was a moderate correlation between the mean trabecular density and the mean HU of the femoral head (P=0.013, r=0.340). Additionally, there was a significant correlation between the mean HU and the T-score of the head, although this correlation was not found with the maximum–minimum HU. Although there was a significant correlation between trabecular density and mean HU, the correlation coefficient indicated a moderate relationship. This relationship was also observed between the inferior sections of the head and the trabecular density and HU (P=.018). However, no significant correlation was found between the T-score and the trabecular structure of the head (P=.977).

Conclusion: The results of the present study suggest that conventional CT has the potential to serve as a diagnostic tool for osteoporosis and may offer a more precise and accurate method for evaluating the success of intraosseous implants when compared to T-scores without the need for additional tests or procedures.

Level of Evidence: Level IV, Diagnostic Study.

Introduction

Osteoporosis is a growing social health concern that is characterized by low bone mass and changes in the microarchitectural environment of affected bone. Insufficiency fractures may occur even after low-energy traumas due to decreased bone strength.[1] More than 50% of patients who undergo orthopedic surgeries such as arthroplasty or spinal fusion surgery have osteopenia or osteoporosis.[2] Although some publications have reported a link between poor bone quality, unexpected postoperative effects, and the need for revision surgeries, there is insufficient attention paid to the diagnosis and treatment of osteoporosis.[2-4]

Due to the high incidence of morbidity and mortality and the economically catastrophic results of osteoporosis, dual x-ray absorptiometry (DEXA) measurements taken at the hip or lumbar spine have been chosen as a routine screening test to evaluate bone mineral density.[5-7] However, more than 80% of patients with osteoporotic fractures have not undergone bone mineral density (BMD) testing and/or pharmacological treatment to reduce the risk of fracture,[5] because nearly half of the women indicated for screening do not undergo testing,[8] due to insufficient information or test costs.

Although DEXA is accepted as the gold standard in bone density measurement, it has limitations such as reference standards that are not applicable to the whole population, not considering the width of the bone, and being a technician- and patient-dependent examination.[9] Unfortunately, DEXA may provide false results in degenerative joint disease, vascular calcifications, and vertebral compression fractures.[10] Hounsfield unit (HU) values, which can be measured from computed tomography (CT) scans taken for other reasons without additional cost or radiation, have been used instead of DEXA for these reasons.[9,11]

Although the correlation between HU and DEXA has been the subject of many studies, a study that demonstrates the histological effectiveness of HU

Corresponding author:
Yunus Imren
yunusimren@gmail.com

Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

Cite this article as: *Imren Y, Karslioglu B, Dedeoglu SS, Keskin A, Berkay AF, Tekin AC. Feasibility of diagnosing osteoporosis using routine computed tomography scans for hip fractures: Correlation with histopathological diagnosis of head and neck regions. Acta Orthop Traumatol Turc., 2023;57(6):384-388.*

DOI: 10.5152/j.aott.2023.23126

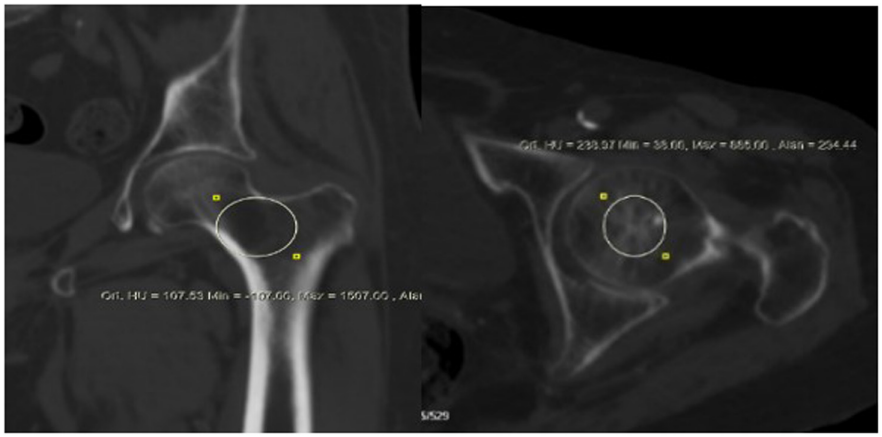

Figure 1. Hounsfield measurements were made with coronal and axial tomography sequences from the femoral head and neck.

measurement is not yet available in the literature, as far as we know. In our study, we aimed to reveal the correlation between the histological evaluation of femoral head samples taken from patients operated on due to intertrochanteric fracture and the HU measurements obtained from preoperative CT scans. Our hypothesis is that there is a correlation between preoperatively measured HU values and the histological evaluation of femoral heads, in favor of osteoporosis.

Materials and methods

Our study was a single-center retrospective study that included patients who underwent partial hip prosthesis surgery due to hip fracture and presented to the emergency department between November 2019 and May 2020. A total of 98 patients with hip fractures underwent DEXA measurements to diagnose osteoporosis or osteopenia, with measurements performed on the contralateral hip to avoid any potential inaccuracies due to the presence of a hip fracture. Patients with a T-score below −1.0 (27 patients), pathological femur fracture (2 patients), a history of cancer (2 patients), neurological disease (poliomyelitis) (1 patient), mobility impairment before the fracture, and those with implant and prosthesis application on their other hip (9 patients) were excluded from the study. The study included 48 patients (39 female and 9 male).

This single-center prospective study was approved by the institutional review board of Health Sciences University Prof. Cemil Taşçıoğlu City Hospital with the number E-48670771-514.10. Written informed consent was obtained from all patients, and the study was conducted in accordance with the ethical standards set forth in the 1964 Declaration of Helsinki and its later amendments.

HIGHLIGHTS

- The histological effectiveness of HU measurement for diagnosing osteoporosis remains a question. This study aimed to assess the relationship of the histological evaluation of femoral head samples from patients who underwent intertrochanteric fracture treatment and the HU measurements obtained from preoperative CT scans.
- Significant correlations were found between Hounsfield unit (HU), T-score, and bone mineral density (BMD). Moderate correlations were observed between trabecular density and HU, indicating a relationship that was also evident in the inferior sections of the head. Moreover, CT scans showed potential as a diagnostic tool for osteoporosis and provided a more precise method for evaluating the success of intraosseous implants compared to T-scores.
- The results demonstrated the feasibility of diagnosing osteoporosis through routine CT scans for hip fractures without the need for additional tests or procedures.

Hounsfield unit measurements were obtained for all patients using tomography sections. The Siemens ICT Elite CT scanner device was used to obtain 128 axial sections in the supine position with a setting of approximately 120 kVp in the iCT SP configuration. Mean HU values were measured using the INFINITT 3.0.11.4 (BN13) program. Axial sections were used for measurements of the femoral head, while coronal sections were used for measurements of the neck. Consistent with the study by Hyun Kyung Lim et al,[12] the intertrochanteric region was calculated in the area between the outer cortex and femoral neck, which contained the largest Ward triangle and the main compressive trabeculae. For measurement of the femoral head, an area of approximately 3 cm^2 was scanned, avoiding the outer cortex as specified by Narayanan et al[13] The Hounsfield measurement for the femoral head was based on the section measured for the neck. The lowest horizontal line, cutting the femoral neck in the coronal plane, was used. An area of 3 cm^2, which was central and away from the outer cortex, was scanned, and the average Hounsfield value was recorded (Figure 1). The highest and lowest Hounsfield values were excluded from the study, and mean HU measurements were calculated.

The femoral heads were extracted from patients who underwent partial hip replacement surgery without causing damage. The femoral head was coronally cut into 2 equal parts at the level of the fovea capitis, and the sections containing the cut femoral neck and head were sent for pathological investigation (Figure 2).

The femur samples were fixed in a 10% buffered formaldehyde solution for 24 hours. A 3 mm-thick coronal section was cut and decalcified in a 10% formic acid solution. The samples were checked every 24 hours to ensure complete decalcification and rinsed with running tap water to remove formic acid. The entire section was mapped and sampled. The samples went through standard tracking stages for 15 hours on a Shandon/Thermon Excelsior tracking device, and then were embedded in paraffin blocks using a SlEE MPS-C embedding device.

Sections of 3 μm thickness were cut from the paraffin blocks on a Shandon/Thermo Microm HM325 microtome and mounted on slides. The sections were then deparaffinized in an 85°C oven for 30 minutes and stained with hematoxylin and eosin (H&E) using a Sakura automatic staining device. The prepared H&E-stained sections were examined for histopathological changes under a Nikon Eclipse Ni microscope with an ocular scale at a magnification of ×100. Each section was evaluated in terms of the amount and thickness of trabeculae visible within the ×100 magnification field.

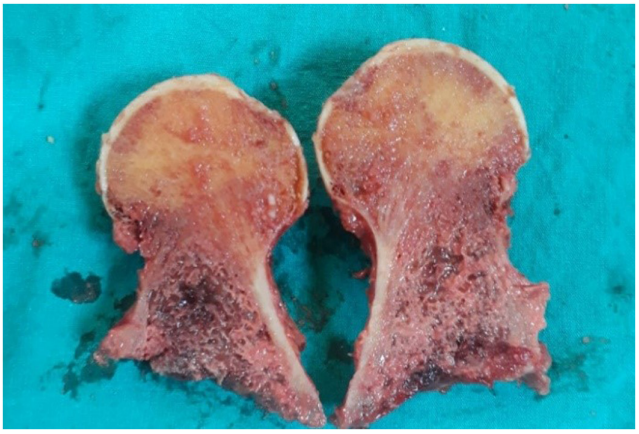

Figure 2. The femoral head was coronally cut into 2 equal parts at the level of the fovea capitis.

Furthermore, images were captured of all the samples at ×20 magnification, and the trabecular bone volume per unit area was calculated digitally using the NIS-Elements imaging software program (Figure 3).

Results

Among the 48 patients, 32 had neck fractures, whereas 16 experienced peri-trochanteric fractures. All study participants underwent T-score measurements of their intact hips using DEXA. The diagnostic criteria established by the World Health Organization (WHO)[14] were applied, with T-scores between −1 and −2.5 being classified as indicative of osteopenia and T-scores below −2.5 indicative of osteoporosis. Based on DEXA measurements, 18 participants with a mean total hip T-score of −3.17 ± 0.59 were assigned to the osteoporosis group, while 30 participants with a mean total hip T-score of −1.68 ± 0.5 were assigned to the osteopenia group (refer to Table 1 for details). The mean HU and mean trabecular density of the patients are presented in Table 1. Statistical analysis revealed a significant and strong correlation between HU mean, T-score, and BMD. The effectiveness of the mean HU value in predicting osteoporosis was evaluated through Receiver Operating Characteristic (ROC) curve analysis of variables correlated in a simple linear regression analysis. The curve passing through the top-left corner of this graph indicates that the model exhibits high levels of both sensitivity and specificity (Table 2). The mean HU receiver operating characteristic analysis showed a sensitivity of 77%, a specificity of 87%, and an HU cutoff value of 77.68 (Table 3). The study found a statistically significant correlation between the mean trabecular density of the femoral head and mean HU, with a moderate relationship (P=.013, r=0.340). Additionally, there was a statistically significant correlation between the mean HU of the femoral head and the T-score, but this correlation could not be determined with the maximum–minimum HU values.

Although a statistically significant value was found between trabecular density and mean HU values of the femoral head, the correlation coefficient indicated a moderate correlation. There was a correlation between trabecular density and HU in the sections taken from the inferior part of the head (P=.018). However, no significant relationship was found between the T-score and the trabecular density of the femoral head (P=.977).

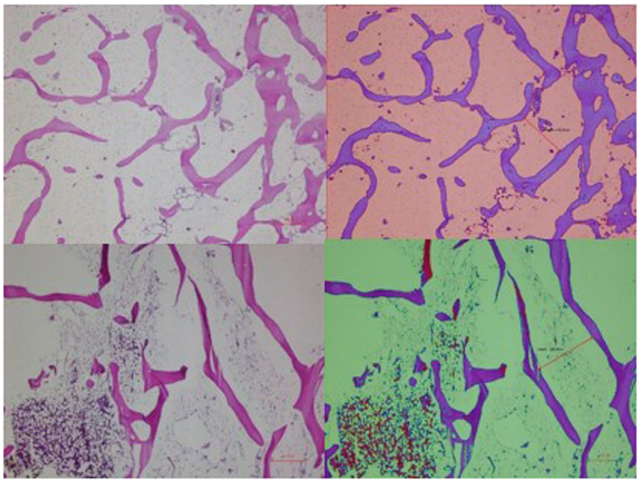

Figure 3. Images of all samples were captured at ×20 magnification, and the trabecular bone volume per unit area was calculated digitally using the NIS-Elements Imaging Software program.

Table 1. Information on demographic, surgical, and Hounsfield unit measurements of both groups

	Osteoporosis	Osteopenia
Patient (n)	18	30
Gender (m-f)	4-14	5-25
Age	82.4 ± 9.2	79.8 ± 8.3
Fracture site (c-h)	12-6	20-10
Operation side (r-l)	9-9	19-11
Average head HU	219.89	264.18
Average head trabecula Density	15.49%	16.28%
Average neck HU	66.28	110.54
Average neck trabeculae density	11.10%	12.50%
Average mineral density	0.48 ± 0.08	0.75 ± 0.1
Average T-score	−3.17 ± 0.59	−1.68 ± 0.5

c, collum; f, female; h, head; HU, Hounsfield unit; l, left; m, male; r, right.

Table 2. Receiver operating characteristic curves of maximum–minimum Hounsfield unit values

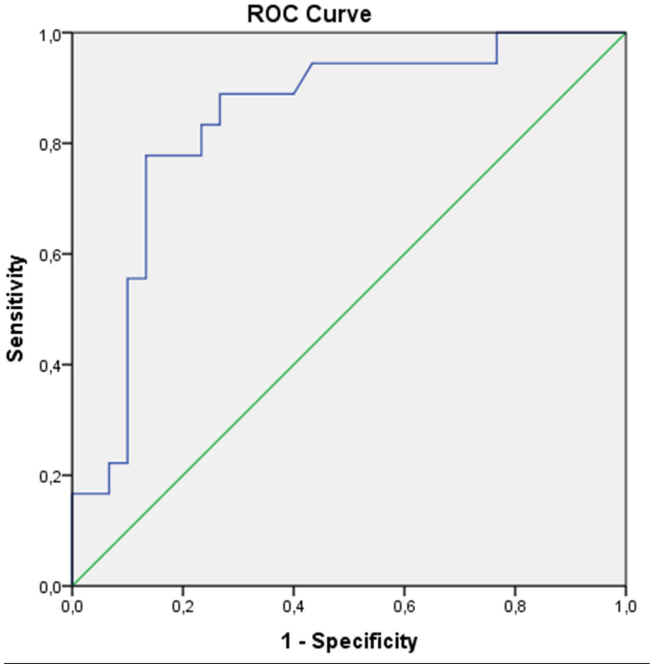

Table 3. The mean Hounsfield unit receiver operating characteristic analysis

	Cutoff (95%)	Sensitivity	Specificity	AUC (95% Cl)	*P*
Hounsfield unit average	77.68	78%	87%	0.840 (0.721-0.959)	<.001

AUC, area under the curve.

Statistical analysis

The statistical analysis conducted in the study involved several methods. Firstly, the chi-square test was used to compare the distribution of patients with neck fractures and peri trochanteric fractures. Secondly, independent t-tests were employed to compare the mean T-scores between different groups (the osteoporosis group and the osteopenia group). Additionally, correlation analysis, including Pearson's correlation coefficient, was conducted to examine the relationships between variables such as HU, T-score, and trabecular density. The significance of these relationships was determined using *P*-values, and the strength of the associations was assessed by examining correlation coefficients (*r*-values). All statistical analyses were performed using IBM's Statistical Package for Social Sciences Statistics for Windows, version 20.0 (IBM SPSS Corp.; Armonk, NY, USA). $P < .05$ was considered statistically significant.

Discussion

Hounsfield unit values obtained from preoperative CT scans in patients with hip fractures can provide information on bone quality similar to the T values obtained from BMD examinations. This information can be useful in determining the appropriate type of implant for the patient and in postoperative follow-up without requiring additional BMD testing.

Dual-energy x-ray absorptiometry is the most commonly used quantitative radiological technique for measuring BMD, which is a major determinant of bone strength.[15] Dual-energy x-ray absorptiometry measurements are used for diagnosing osteoporosis,[16] monitoring changes in BMD over time,[17] estimating fracture risk, and are often essential in therapeutic interventions.[5] Dual-energy x-ray absorptiometry is a noninvasive and x-ray-based absorptiometry technique with high precision (<1%) in normal weight populations. However, DEXA has some disadvantages, such as invalid reference standards for some patients and ignoring bone width in evaluating bone quality.[9] Variability in body composition can lead to errors of up to 20% in BMD measurements.[18] Despite all its advantages and disadvantages, screening and diagnosis of osteoporosis are limited, especially in low-income countries, due to the limited availability of DEXA.[19]

In the United States, around 80 million CT scans are performed annually, and using these scans to diagnose osteoporosis or insufficiency fractures can be advantageous for both the healthcare system and patients, as it can reduce the need for additional examinations.[11] The HU, which is a standardized linear attenuation coefficient of tissue measured in CT scans, can provide information about bone quantity without incurring additional costs, radiation exposure, or the use of phantoms.[9]

Hounsfield unit values can be easily obtained using radiology imaging programs in clinical CT examinations using the formula HU=([m − mw]/mw), where mw is the attenuation coefficient of distilled water and m is the measured attenuation coefficient of the tissue of interest.[9,20] The HU value for bone typically ranges from 300 to 3000[9], and a decrease in HU on CT scans is indicative of changes in the microstructure of trabecular bone due to osteoporosis.[12] Unlike DEXA, HU measurements are not affected by osteophytes, vascular calcifications, or compression fractures and can be performed without additional time, cost, or radiation exposure using opportunistic CT scans.[10]

Previous studies, such as the one conducted by Hyun Kyung Lim et al,[12] have used HU histogram analysis to predict osteoporosis on pre-contrast abdominal–pelvic CT scans. However, the histogram analysis method may be difficult for clinicians to use and analyze. In contrast, the single-center measurement method for HU via regions of interests (ROIs) used in our study is simple and easy to apply, and does not require histogram analysis. This is a significant advantage of our study.

There is currently no standardized method for measuring HU values in the proximal femur. Erhart et al[21] used 3 consecutive ROIs to measure HU values in the femoral neck, while Kim et al[22] used ROIs in both cortical and cancellous bone between the femoral head, femoral neck, and trochanters at the proximal end of the femur. In our study, we measured the average, lowest, and highest HU values within a 3 cm^2 area determined for each region of the femoral head and neck. The mean HU values were then determined for each anatomical region.

Our study suggests that the femoral head region may be less affected by HU values than other areas. HU measurements of the femoral head may be affected later in osteoporosis, as primary compressive trabeculae are affected later.[23] Dual-energy x-ray absorptiometry measurements are not taken from the femoral head but only from the femoral neck and intertrochanteric regions. Therefore, in our study, trabecular measurements of the femoral head and HU measurements were compared. Few studies have compared femoral head and HU values in the literature. Narayanan et al[13] found that the HU value of the femoral head was lower in fracture patients compared to the control group. In our study, there was a moderate correlation between HU measurements and the trabecular density of the femoral head.

Trabecular density decreases in osteoporotic patients, as shown in histomorphometric studies. However, the limited applicability of these studies and their dependence on the person making them reduce their use.[24] Our study, in which trabecular density was evaluated under the microscope, minimizes the possibility of individual dependency due to this feature. Although trabecular density decreases around the ward triangle of the femoral length due to osteoporosis, it seems difficult to standardize. The loss of isometry and connection of trabeculae due to osteoporosis makes measurement difficult. Additionally, trabecular size, length, and width become dependent on the histological section when considered in the three-dimensional plane. Therefore, trabecular density may not be correlated with the quantity of osteoporosis.

Based on our current knowledge, our study is the first of its kind to investigate the relationship between proximal femur trabecular density assessed through histopathological evaluation and HU values and DEXA measurements. Due to the limited number of patients used in our study, it is difficult to determine the cutoff value. A prospective study with a larger population is needed to determine

optimal cutoff ranges for the prediction of osteoporosis or osteopenia in the proximal femur.

In conclusion, this study aimed to demonstrate the feasibility of using routine CT scans for diagnosing osteoporosis in hip fracture patients and to investigate the correlation between HU measurements and histopathological diagnosis. The results showed significant correlations between HU mean, T-score, and BMD, as well as moderate correlations between the mean trabecular density and mean HU of the femoral head. The findings suggest that HU values derived from CT scans of the head region may provide a more accurate method for assessing the success of intraosseous implants compared to T-scores. Therefore, conventional CT scans may serve as a potential diagnostic tool for osteoporosis without the need for additional tests or procedures. However, measuring T-scores alone may not be sufficient for determining adequate anchorage for implants in the head and neck region. Further studies are needed to validate these findings and investigate the potential clinical implications.

Ethics Committee Approval: This study was approved by the Ethics Committee of Health Sciences University Prof. Cemil Taşçıoğlu City Hospital (Approval number: 1437, Date: November 5, 2019).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – Y.I., B.K.; Design – S.S.D., A.Ç.T.; Supervision – Y.I., B.K; Resources – A.K., A.F.B.; Materials – A.K., A.F.B.; Data Collection and/or Processing – A.K., A.F.B.; Analysis and/or Interpretation – Y.I., B.K.; Literature Search – A.K., A.F.B; Writing – B.K., Y.I.; Critical Review – S.S.D., A.Ç.T.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: The authors declare that this study has received no financial support.

References

1. Canbeyli İD, Çırpar M, Oktaş B, Çoban M. Analysis of factors among 30-day and 1-year mortality rates in patients with borderline stable-unstable intertrochanteric hip fracture. *Acta Orthop Traumatol Turc*. 2021;55(1):16-21. [CrossRef]
2. Teng S, Yi C, Krettek C, Jagodzinski M. Bisphosphonate use and risk of implant revision after total hip/knee arthroplasty: a meta-analysis of observational studies. *PLoS One*. 2015;10(10):e0139927. [CrossRef]
3. Labuda A, Papaioannou A, Pritchard J, Kennedy C, DeBeer J, Adachi JD. Prevalence of osteoporosis in osteoarthritic patients undergoing total hip or total knee arthroplasty. *Arch Phys Med Rehabil*. 2008;89(12):2373-2374. [CrossRef]
4. Ro DH, Jin H, Park JY, Lee MC, Won S, Han HS. The use of bisphosphonates after joint arthroplasty is associated with lower implant revision rate. *Knee Surg Sports Traumatol Arthrosc*. 2019;27(7):2082-2089. [CrossRef]
5. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. *BMJ*. 1996;312(7041):1254-1259. [CrossRef]
6. Fidan F, Polat A. The effect of preexisting radiographic hip osteoarthritis on the functional recovery after surgical treatment of intertrochanteric fractures in elderly patients. *Acta Orthop Traumatol Turc*. 2022;56(6):384-388. [CrossRef]
7. Biçen Ç, Akdemir M, Türken MA, Çekok K, Ekin A, Turan AC. Analysis of risk factors affecting mortality in elderly patients operated on for hip fractures: A retrospective comparative study. *Acta Orthop Traumatol Turc*. 2021;55(6):493-499. [CrossRef]
8. Amarnath ALD, Franks P, Robbins JA, Xing G, Fenton JJ. Underuse and overuse of osteoporosis screening in a regional health system: a retrospective cohort study. *J Gen Intern Med*. 2015;30(12):1733-1740. [CrossRef]
9. Schreiber JJ, Anderson PA, Rosas HG, Buchholz AL, Au AG. Hounsfield units for assessing bone mineral density and strength: a tool for osteoporosis management. *J Bone Joint Surg Am*. 2011;93(11):1057-1063. [CrossRef]
10. Zaidi Q, Danisa OA, Cheng W. Measurement techniques and utility of Hounsfield unit values for assessment of bone quality prior to spinal instrumentation: a review of current literature. *Spine*. 2019;44(4):E239-E244. [CrossRef]
11. Siris ES, Chen YT, Abbott TA, et al. Bone mineral density thresholds for pharmacological intervention to prevent fractures. *Arch Intern Med*. 2004;164(10):1108-1112. [CrossRef]
12. Lim HK, Ha HI, Park SY, Lee K. Comparison of the diagnostic performance of CT Hounsfield unit histogram analysis and dual-energy X-ray absorptiometry in predicting osteoporosis of the femur. *Eur Radiol*. 2019;29(4):1831-1840. [CrossRef]
13. Narayanan A, Cai A, Xi Y, Maalouf NM, Rubin C, Chhabra A. CT bone density analysis of low-impact proximal femur fractures using Hounsfield units. *Clin Imaging*. 2019;57:15-20. [CrossRef]
14. Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E. FRAX and the assessment of fracture probability in men and women from the UK. *Osteoporos Int*. 2008;19(4):385-397. [CrossRef]
15. Bouxsein ML, Seeman E. Quantifying the material and structural determinants of bone strength. *Best Pract Res Clin Rheumatol*. 2009;23(6):741-753. [CrossRef]
16. Kanis JA. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. WHO study group. *Osteoporos Int*. 1994;4(6):368-381. [CrossRef]
17. Miller PD, Bonnick SL, Rosen CJ. Consensus of an international panel on the clinical utility of bone mass measurements in the detection of low bone mass in the adult population. *Calcif Tissue Int*. 1996;58(4):207-214. [CrossRef]
18. Yu EW, Thomas BJ, Brown JK, Finkelstein JS. Simulated increases in body fat and errors in bone mineral density measurements by DXA and QCT. *J Bone Miner Res*. 2012;27(1):119-124. [CrossRef]
19. Amin MFM, Zakaria WMW, Yahya N. Correlation between Hounsfield unit derived from head, thorax, abdomen, spine and pelvis CT and t-scores from DXA. *Skelet Rad*. 2021;50(12):2525-2535. [CrossRef]
20. Orwoll ES, Bliziotes M. *Osteoporosis: Pathophysiology and Clinical Management*. Springer Science & Business Media; 2002.
21. Erhart S, Zegg M, Kralinger F, Kammerlander C, Roth T. Fast and easy preoperative estimation of cancellous bone mineral density in patients with proximal femur fractures. *Arch Orthop Trauma Surg*. 2015;135(12):1683-1689. [CrossRef]
22. Kim YS, Lee S, Sung YK, Lee BG. Assessment of osteoporosis using pelvic diagnostic computed tomography. *J Bone Miner Metab*. 2016;34(4):457-463. [CrossRef]
23. Singh M, Nagrath AR, Maini PS. Changes in trabecular pattern of the upper end of the femur as an index of osteoporosis. *J Bone Joint Surg Am*. 1970;52(3):457-467. [CrossRef]
24. Rehman MT, Hoyland JA, Denton J, Freemont AJ. Histomorphometric classification of postmenopausal osteoporosis: implications for the management of osteoporosis. *J Clin Pathol*. 1995;48(3):229-235. [CrossRef]