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Quantitative Analysis of Osteoporotic Vertebral Fracture Risk on Pre-Existing CT

Önceden Var Olan CT'de Osteoporotik Vertebral Kırık Riskinin Kantitatif Analizi

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Abstract

Aim: Recent research has shown that the measurement of vertebrae bone density on computed tomography for diagnosis of osteoporosis is associated with dual energy X-ray absorptiometry. Our aim was to compare vertebra bone density on pre-existing CT images (CTd) between patients with and without osteoporotic vertebral fracture (OVF) for predicting OVF.

Methods: Fifty patients with OVF and age and gender-matched 50 controls were included in this retrospective case-control study. All measurements were taken from transverse sections passing through the center of the vertebrae (L5-T10), and Hounsfield units (HU) values were recorded. Using receiver operating characteristics analysis, cut-off point values for different levels were determined.

Results: CTd measured at each vertebra was significantly lower in the case group than in controls (p<0.001). In increased risk of OVF, the cut-off value was 90 HU for each lumbar vertebra, and 100 HU for T12-T11-T10 vertebrae, sensitivity is over 90%, positive predictive values for lumbar vertebrae, and T12-T10 were 96% and 92%, respectively.

Conclusions: Vertebral bone density measurement on pre-existing CT images is an easy method demonstrating the risk of OVF, without additional cost and radiation exposure. CTd value below 100 HU on lower thoracic and below 90 HU on lumbar vertebrae indicates a high risk of OVF.

Keywords: Osteoporotic compression fracture, computed tomography, osteoporosis, density

Öz

Amaç: Son araştırmalar, osteoporoz tanısı için omurga yoğunluğunun bilgisayarlı tomografide (BT) ölçülmesinin, çift enerjili X-ışını absorbsiyometrisi ile ilişkili olduğunu göstermektedir. Bizim amacımız önceden var olan BT'de osteoporotik vertebra kırığını (OVF) tahmin etmek için OVF olan ile olmayan hastalarda omurga yoğunluğunun karşılaştırılmasıdır.

Yöntemler: Retrospektif olgu kontrol çalışması, 50 OVF ve 50 kontrol grubu dahil edildi. Kontrol hastaları yaş ve cinsiyet için eşleştirildi. Tüm ölçümler, vertebraların (L5-T10) merkezinden geçen enine kesitlerden alınmış ve Hounsfield birimleri (HU) değeri kaydedilmiştir. Alıcı işletim karakteristiği analizi kullanılarak farklı seviyeler için kesme noktası değerleri belirlendi.

Bulgular: Olgu grubunun tüm vertebralarında vertebra yoğunluğu kontrol grubuna göre anlamlı derecede düşüktü (p<0,001). OVF riskinde, her bir lumbar vertebra için kesme değeri 90 HU, T12-T11-T10 vertebraları için 100 HU, duyarlılık %90'ın üzerindedir, pozitif prediktif değerler lomber vertebralar için %96 ve T12-T10 için %92'dir.

Sonuç: Mevcut BT'deki vertebral yoğunluk ölçümü, ek maliyet ve radyasyon maruziyeti olmaksızın OVF riskini gösteren kolay bir yöntemdir. Radyolog, farklı amaçlar için yapılmış BT tetkiklerinde OVF riskini değerlendirmelidir. Vertebral dansite değerlerinin alt torasik vertebralarda 100 HU, lumbar vertebralarda ise 90 HU'nun altında ölçülmesi OVF açısından yüksek risklidir.

Anahtar Sözcükler: Osteoporotik kompresyon kırığı, bilgisayarlı tomografi, osteoporoz, dansite

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Introduction

Osteoporotic vertebral fracture (OVF) is a health problem and the prevalence of OVF increases with age (1-3). The incidence of OVF has been reported to be 5-50% in women aged 50-85 years (2). An increase is observed in both sexes with increased age (1,2). A detected OVF is the best indicator of increased OVF risk in other vertebrae. Detected OVF increases the risk for subsequent vertebral fracture by about five times, and hip fracture risk by three times (4-6). OVF is usually observed in earlier ages, compared to hip fracture. Despite the importance of OVF, clinicians usually fail to detect it (7,8), and it is frequently underdiagnosed by radiologists (9,10). Presence of an OVF is the most important criteria in the treatment of osteoporosis (11-14). Dual-energy X-ray absorptiometry (DXA) and quantitative computed tomography (QCT), with additional cost and radiation risk, are used to diagnose osteoporosis. Is it possible to detect an increased fracture risk on a pre-existing computed tomography (CT) scan? In this study, we aimed to evaluate increased risk of OVF using vertebral bone density measurement on pre-existing CT scans (CTd).

Methods

This study was planned as a case-control retrospective study. Approval of the ethics committee was received, and informed consent was waived. We conducted the study of lumbar CT or abdominal CT examinations at the Department of Radiology at our hospital between August 2016 and January 2018.

Case group (n=50); case group consisted of 50 patients who had a compression fracture, radiologically and clinically known OVF, in at least one of the vertebrae between T10 and L5.

Control group (n=50); this group consisted of 50 patients without compression fractures. Control subjects, who have been examined with CT for an abdominal pain or back pain, were matched with each patient for age and sex.

Exclusion criteria were presence of a known traumatic vertebral fracture, intra-abdominal malignancy, vertebral metastasis, and vertebral mass. Furthermore, patients for whom IV-contrast matter was used were excluded considering that it may affect the bone density measurements.

128-slice CT (Optima CT660, GE Healthcare; USA) was used in all scans. Lumbar CT and abdominal CT images were used for measurements. The average kV preferred for the abdominal and lumbar CT was 120-130, and the average mAs was 100-130. All measurements were taken from transverse sections passing through the center of a vertebra in the bone window, using trabecular bone region of interest (ROI). Cortex was not included in the area of measurement. ROI width was held approximately 1 cm^2 that taken from each vertebra from L5 to T10, and average Hounsfield units (HU) value was recorded. Focal vertebral lesion and artifact areas that could affect ROI measurements, such as posterior venous plexus or hemangioma, were avoided. In addition, presence or non-presence of OVF in each vertebra was noted.

Evaluation of compression fracture: Genant's visual semiquantitative method (15), defined and widely accepted for vertebral fracture in conventional radiography, was preferred due to its easy application on CT. Moderate (grade 2, 26-40%) and severe (grade 3 >40% loss of height) compression deformities were recorded. CTd measurement could be taken from a moderate compression fracture, but since correct measurements were not possible in severe vertebral fractures, density measurements could not be conducted in these vertebrae and were recorded as "severe compression fracture." Mild compression deformity (grade 1, 20-25%) was not reported since it could be interpreted differently.

Statistical Analysis

Normality test was conducted using the Shapiro-Wilk test, histogram, Q-Q plot, and box plot graphics. Data were provided in terms of mean, standard deviation, median, minimum, maximum, frequency, and percentage. Variables that displayed a normal distribution in case and control groups were analyzed using the independent samples t-test, whereas variables without a normal distribution were analyzed with the Mann-Whitney U test. Nominal variables were evaluated with a chi-square test with Yates' correction. Spearman's correlation coefficient was used for the link between age and CTd. Using ROC analysis, cut-off point values for different levels were determined, compatibility of which was evaluated with Kappa analysis. Diagnostic test values and 95% confidence interval (sensitivity, specificity, positive predictive value, negative predictive value, accuracy) were calculated. The significance level was pre-determined as $p<0.05$ and two-tailed. Analyses were conducted using NCSS 10 (2015. NCSS, LLC. Kaysville, Utah, USA).

Results

Case group consisted of 31 females, 19 males and the mean age of the case group was 66.8±9.18 years. The mean age of the females and males was 67.13±8.94 and 66.26±10.27 years, respectively. There was no significant difference in age between females and males (p=0.73).

Control group consisted of 31 females and 19 males and the mean age of the controls was 67.12±9.37 years. The mean age of females and males was 67.13±8.77 and 66.26±10.03 years, respectively. There was no significant difference in age between females and males (p=0.75).

Age was found to be similar between case and control groups (p=0.863). All comparisons were conducted between case and control groups (Table 1, 2). CTd measured at each vertebra was significantly lower in the case group (p<0.001).

In evaluations of case group, OVF was not detected in any of the patients who had a CTd measurement over 123 HU. Among patients with CTd measurement below 100 HU, OVF was present in 40 patients, but not detected in 10 patients. OVF was observed most frequently in the first lumbar vertebra (13 severe, 15 moderate OVF) (Figure 1).

In increased risk of OVF, the cutoff value is 90 HU for each lumbar vertebra, and 100 HU for T12-T11-T10 vertebrae, sensitivity is over 90%. There was a significant difference in CTd between case and control groups (p<0.001). CTd for each vertebra is presented in Table 3 and Figure 2 shows the ROC curve and AUC results for predicting OVF based on density measurement on CT images. For OVF, the AUC range was 0.96 to 0.97 on T10-T11-T12 levels and AUC range was 0.96 to 0.98 on L1 to L5 levels.

Discussion

DXA T-score, used for the diagnosis of osteoporosis, is affected by the degenerative changes. This is an important limitation of DXA (16,17). Marinova et al. (18) reported that more than half of all fractures were detected in patients with non osteoporotic DXA T-scores. In other studies as well, in OVF-detected patients, osteoporosis was not present, based on the WHO criteria (T score >-2.5) (19-21). In order to avoid such disadvantages of DXA, some centers use QCT. QCT is a three-dimensional technique that measures bone mineral density in spinal-femur-forearm and tibia, while by differentiation of the trabecular bone, eliminating density differences that can

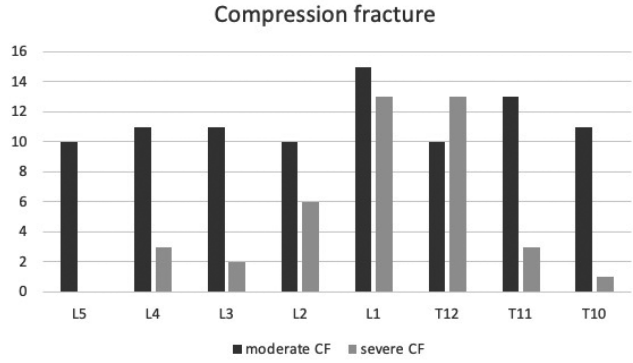

Figure 1. Frequency of compression fracture based on vertebral levels
CF: Compression fracture

Table 1. Analyses of L2-L3-L4-L5 vertebral density for the groups. P, Mann-Whitney U test

	L5	L4	L3	L2
Case group (n=50)	(n=50) 71.5 (15-120)	(n=47) 69 (2-112)	(n=48) 64 (2-100)	(n=44) 66 (10-100)
Control group (n=50)	(n=50) 133.5 (90-215)	(n=50) 125 (90-204)	(n=50) 128.5 (89-198)	(n=50)139 (87-192)
p	<0.001	<0.001	<0.001	<0.001

Table 2. Analyses of L1-T12-T11-T10 vertebral density for the groups. P, Mann-Whitney U test

	L1	T12	T11	T10
Case group (n=49)	(n=37) 74 (13-110)	(n=37) 85 (20-123)	(n= 47) 80 (34-120)	(n=49) 80 (10-120)
Control group (n=50)	(n=50) 142 (87-205)	(n=50) 145 (90-220)	(n=50) 157 (90-234)	(n=50) 158 (90-226)
p	<0.001	<0.001	<0.001	<0.001

Table 3. Cutoff points of osteoporotic compression fractures are shown based on vertebra level

Level	Cut-off	Sensitivity	Specificity	PPV	NPV	Accuracy
L5	90	0.93 (0.82-0.98)	1 (0.69-1)	1	0.71(0.49-0.87)	0.94 (0.85-0.98)
L4	90	0.93 (0.82-0.98)	1 (0.69-1)	1	0.71(0.49-0.87)	0.94 (0.85-0.98)
L3	90	0.94 (0.84-0.99)	0.92 (0.62-0.99)	0.98 (0.88-0.99)	0.79 (0.55-0.92)	0.94 (0.85-0.98)
L2	90	0.94 (0.84-0.99)	0.85 (0.55-0.98)	0.96 (0.87-0.99)	0.79 (0.54-0.92)	0.92 (0.83-0.97)
L1	90	0.94 (0.84-0.99)	0.92 (0.62-0.99)	0.98 (0.88-0.99)	0.79 (0.55-0.92)	0.94 (0.85-0.98)
T12	100	0.96 (0.86-0.99)	0.75 (0.48-0.93)	0.92 (0.83-0.96)	0.86 (0.6-0.96)	0.91 (0.81-0.97)
T11	100	0.96 (0.86-0.99)	0.8 (0.52-0.96)	0.94 (0.85-0.98)	0.86 (0.6-0.96)	0.92 (0.83-0.97)
T10	100	0.92 (0.81-0.98)	0.71 (0.42-0.92)	0.92 (0.83-0.96)	0.71 (0.48-0.87)	0.88 (0.77-0.94)

PPV: Positive predictive value, NPV: Negative predictive value

result from degenerative changes (22). On the other hand, QCT is an expensive method requiring additional costs. Recently, various studies were conducted by measuring CTd for the diagnosis of osteoporosis on non-calibrated CT ordered for different reasons. Density measurements are taken from the vertebral trabecular structure on the axial plan on CT images, in order to eliminate cortex and cortical degenerative changes. In this way, degenerative changes do not affect the measurement, and this is the main advantage of CT over DXA. Furthermore, unlike DXA, other pathologies, such as vertebral mass and metastasis, could be observed on CT, so that suitability of vertebra for the measurement of osteoporosis can be evaluated.

Pickhardt et al. (16), in their comprehensive series using CT and DXA, determined their threshold values for osteoporosis and osteopenia in vertebra L1 as 160 HU and 110 HU, respectively, whereas normal CTd was determined as 200 HU or higher. In this study, CTd values below 100 HU were determined to require osteoporosis treatment. In contrast, values over 200 HU are reported to be accepted as normal, and not requiring DXA. The authors suggested

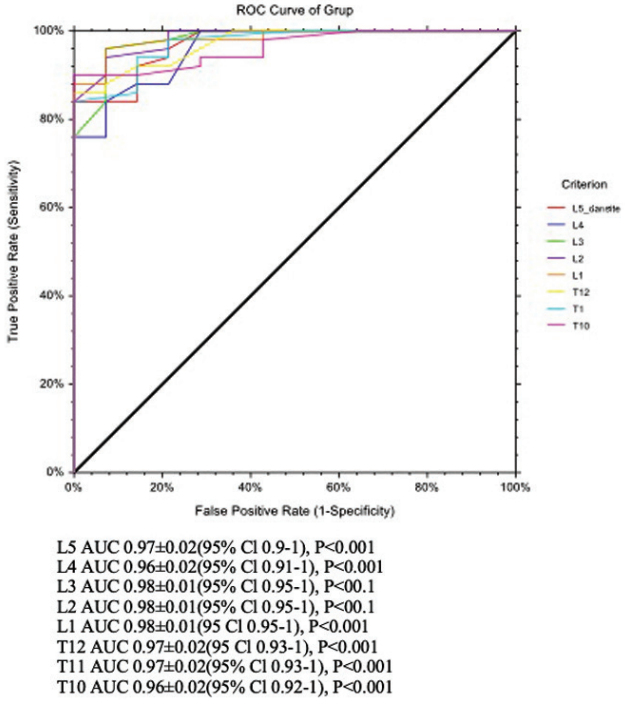

Figure 2. ROC curves for increasing risk of osteoporotic compression fracture with density measurement on CT AUC: area ± standard error (95% confidence interval)

AUC: Area under receiver-operating characteristic curve, ROC curves for increasing risk of osteoporotic compression fracture with density measurement on CT. The AUCs were similar at each vertebra

CT: Computed tomography, AUC: Area under the curve, ROC: Receiver operating characteristic

that patients with a detected OVF in a single vertebra had lower CT density values in other vertebrae as well, and this is compatible with our findings. Furthermore, it is also suggested that OVF could develop in patients in whom osteoporosis was not detected with DXA, due to which CT-attenuation is more accurate as a fracture risk indicator. False-negative DXA evaluation was emphasized to be the result of degenerative changes. In a study by Pickhardt et al. (16), DXA was used as a reference for osteopenia-osteoporosis values. Possible misleading results of DXA in patients with degeneration were reported as a limitation of the study. Alacreu et al. (23) conducted a study with oncologic patients, comparing vertebral bone density measurements using CT and DXA. They reported L1 CTd values to be more significant. Lee et al. (24) compared CTd measures of axial and sagittal reconstruction images on CT, and reported them to be similar. In another study, Pickhardt et al. (25) evaluated the effects of IV-contrast on density measurements, and the contrast-enhanced CT shows an average increase of 11 HU over the unenhanced series for L1 trabecular attenuation. In their study, Marinova et al. (18) reported that abdominal and particularly thoracic CT scans obtained for other clinical indications can sensibly be used in detecting osteoporosis and risk of fracture, superiorly to DXA. Li et al. (26) recommended that radiologist should consider and report findings of osteoporosis in patients undergoing abdominal CT for other indications. And the last review about this subject, Zaidi et al. (27) published that HU value measurement was a useful and also practicable technique to assess bone quality that should be reported by a radiologist in all patients with pre-existing abdominal CT scans. All these studies have gained momentum in the last four years and mainly focused on correlation between CTd measured on routine CT and DXA scores. The answer to the question of whether it is possible to diagnose osteoporosis using CT density value is sought. Bringing a different perspective to the literature by comparing patients with and without OVF, our study contributes to this issue. This study provides similar results in a different way to the literature and confirms the knowledge. In our study, eight vertebrae, between L5 and T10, were measured for each patient. Among the examined vertebrae, compression fractures were detected most frequently on the L1 level. CTd values in the patient group were significantly lower than in the control group ($p<0.001$). CTd value below 100 HU in the lower thoracic spine and below 90 HU in the lumbar vertebra is associated with high risk of OVF, sensitivity is over 90%, and OVF was detected in almost every patient with values below 80 HU (Figure 3). OVF was not detected in any patients who had attenuation over 123 HU. However, in patients with a density value below 100 HU, 10 patients did not have OVF. Briefly, we do not expect OVF if the CTd

value is over 100 HU. We suggest that CTd evaluation in patients with a detected vertebral fracture could be useful especially for differentiating pathological-OVF on CT scans (Figure 4). In the differential diagnosis of vertebral fracture, CTd values over 100 HU decrease the possibility of OVF, and pathological fracture should be considered. However, since patients with osteoporosis could have metastatic fractures, values below 100 HU does not differentiate between OVF and pathological fracture.

This study has the following limitations: OVF diagnosis and trauma exclusion were based on patient reports, clinical information, and radiological findings. Using the cut-off values determined for OVF, further studies could monitor patients to evaluate how long it takes to develop a vertebral fracture.

Conclusion

In conclusion, vertebra bone density measurement using a pre-existing abdominal CT is an easy method that provides information about the risk of osteoporotic compression fractures, without requiring any additional costs. Even if ordered for different purposes, it may be useful to evaluate CTd for risk of OVF on CT images. CTd values below 100HU on lower thoracic and below 90 HU

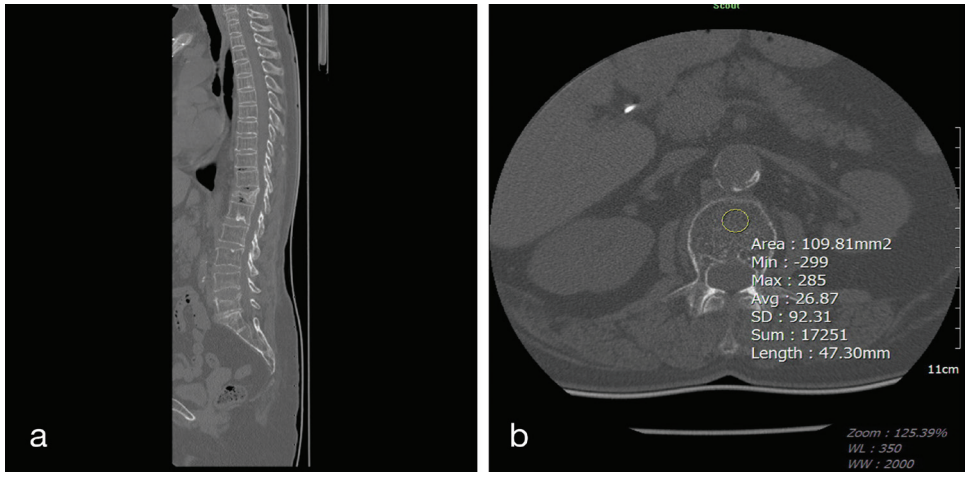

Figure 3. Midsagittal reformat CT scan of a 78 year-old female patient (a) shows osteoporotic compression fractures; moderate OVF on L5 vertebra, severe OVF on T12 vertebra. In addition, different levels of spondylosis are observed (b) In the same patient, on the transverse CT section passing through the central of L2 vertebra, density measure taken from the trabecular bone was 26.8 HU, and highly osteoporotic

CT: Computed tomography, OVF: Optical viewfinder, HU: Hounsfield unit

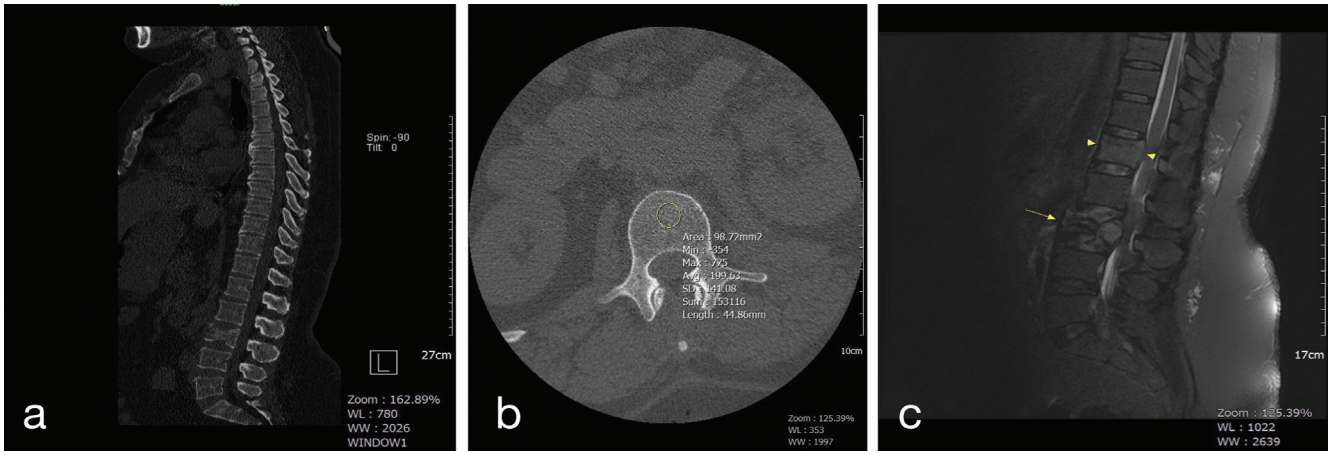

Figure 4. Fifty four year-old female patient with suffering from lower back pain (a) diagnosed compression fractures on L3 vertebra on mid-saggital CT (b) However, since density measure was 199 HU on adjecent vertebras, for this reason, OVF was excluded. A full-body scan was recommended for pathological fracture evaluation. Breast cancer and vertebral metastases were diagnosed by hystopathologically (c) four months later, mid-saggital STIR MRI image shows that another vertebral metastases occured on L2 vertebrea (arrow head)

CT: Computed tomography, OVF: Optical viewfinder, MRI: Magnetic resonance imaging, STIR: Short T1 inversion recovery, HU: Hounsfield unit

on lumbar vertebrae indicate high risk in terms of OVF. In the differential diagnosis of vertebral fracture, values over 100 HU decrease the possibility of OVF, and pathological fracture should be examined in these patients.

Authorship Contributions

Surgical and Medical Practices: E.E.E., M.E.A. Concept: M.E.A. Design: E.E.E. Data Collection or Processing: E.E.E. Analysis or Interpretation: E.E.E. Literature Search: M.E.A. Writing: E.E.E., M.E.A.

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