

# Hormon Replasman Tedavisi ile Vertebralarda Homojen Olmayan Osteoporotik Değişiklikler

*Inhomogeneous Osteoporotic Changes of Vertebrae With Hormone Replacement Therapy*

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## Özet

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**Amaç:** Manyetik rezonans (MR) görüntüleme kullanarak menapoz sonrası hormon tedavisi ile bel omurgasında oluşan fizyolojik değişiklikleri incelemek  
**Gereç ve Yöntem:** Menopoz sonrası 110 kadın hastaya kemik mineral yoğunluğu (KMY) ölçümü ve standart lomber MRG tetkiki yapıldı. Hastalar KMY ölçümüne göre normal, osteopeni ve osteoporoz olarak gruplara ayrıldı. Ayrıca bu hastalar hormon tedavisi alan ve hormon tedavisi almayan olarak da iki gruba ayrıldı. Lomber MR tetkikinde orta sagittal düzlemde T1 ve T2 ağırlıklı sekanslardan her lomber vertebraanın merkezine ilgili alan birimi (ROI) yerleştirilerek sinyal değerleri ölçüldü ve ortalamaları hesaplandı. Lomber MR verilerinden elde edilen ortalama sinyal değerleri ile yaş ve KMY değerleri Pearson korelasyon katsayısı kullanılarak incelendi.w  
**Bulgular:** Tüm menapoz sonrası ve hormon tedavisi almayan olgularda lomber vertebra MR sinyal değerleri ile KMY değerleri arasında korelasyon bulunmamıştır. Ancak hormon tedavisi alan menapoz sonrası kadınlarda minimal korelasyon saptanmıştır. KMY değerleri ile yaş arasında negatif korelasyon varken T1 ve T2 ağırlıklı sinyal değerlerinin yaş ile ilişkili olmadığı bulunmuştur.  
**Sonuç:** Bel omurlarının merkezinin daha fazla vasküler yapı içermesi nedeniyle HRT alanların osteoporozdan daha geç ve az etkilendiği düşünülmüştür. Bu çalışma, hormon tedavisinin menapoz sonrasında kompresyon kırıklarından koruyabileceğini gösterebilir.

**Anahtar Kelimeler:** osteoporoz, osteopeni, manyetik rezonans görüntüleme, vertebra, kırıklar

## Abstract

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**Background and Aim:** To evaluate postmenopausal physiological bone marrow changes with hormone replacement therapy(HRT) of the lumbar spine using magnetic resonance (MR) imaging.  
**Materials and Methods:** BMD measurement and lumbar spine MR imaging performed in 110 postmenopausal women (PW). Women were classified as normal, osteopathic and osteoporotic. These patients grouped according to women who were and women who were not receiving HRT. Mean intensity from the center of each lumbar vertebrae at the mid-sagittal plane in a region of interest (ROI), measured and calculated from MR image data. Correlation between T1 and T2 intensities with age and BMD evaluated using Pearson's correlation coefficient.  
**Results:** No significant positive correlation found between BMD and T1, T2 intensity among all PW and PW who were not using HRT. However there was a correlation between T1,T2 intensities and BMD in PW receiving HRT. BMD was inversely correlated with age. No significant correlation found between the T1, T2 intensities of bone marrow at the center of the vertebrae and BMD.  
**Conclusion:** The center of the lumbar vertebrae is probably less and lately affected from fatty transformation by the help of HRT. This study may Show that postmenopausal hormone therapy may protect vertebrae from compression fractures.

**Keywords:** osteoporosis, osteopenia, magnetic resonans imaging, lumbar vertebrae, fractures

## Introduction

Osteoporosis is a metabolic disease of bone tissue characterized by reduced bone strength and predisposing those affected to fracture. Disease pathology includes not only a decrease in bone mass but micro architectural collapse<sup>(1,2)</sup>. Fracture risk is dependent on bone mineral density and bone quality, both influencing bone strength. Features of bone quality are trabecular architecture, connectivity, and repair capability after fatigue damage. Osteoporotic fractures are fairly common; almost half of caucasian women will develop osteoporotic fractures during their lifetimes<sup>(3)</sup>.

Many factors associated with osteoporosis including advancing age, female sex, smoking, excessive alcohol intake, family history of fracture, estrogen deficiency, low calcium intake, low body weight, some drugs and health conditions<sup>(4)</sup>. The incidence of osteoporosis increases significantly following menopause<sup>(5,6)</sup>.

The mortality and morbidity are high in osteoporosis if not treated. The single best predictor of osteoporosis and fracture risk identification is bone densitometry<sup>(7-9)</sup>.

There is an increase in fatty marrow correlated with reduced BMD. MR imaging reveals changes in bone physiology including increased marrow fat content. Studies of MR imaging of the lumbar spine have showed that, marrow fat increases as bone density decreases<sup>(9,10,11,14)</sup>. Techniques developed for detection of osteoporosis including diffusion MR imaging, MR perfusion MR relaxometry, high-resolution MR imaging and MR spectroscopy. Presence of fat in osteoporotic marrow affects MR relaxation times by decreasing T1 and by increasing T2 and T2\*<sup>(9,12)</sup>. MR spectroscopy studies have shown that bone weakness correlated with an increase in fatty marrow content<sup>(9,13,14)</sup>.

The aim of this study was to find the amount of osteoporosis at the center of lumbar vertebrae using T1 and T2 signal intensities using traditional lumbar MR imaging. We decided to compare T1, T2, intensities of each vertebra with BMD calculated by DEXA.

## Materials and methods

A total of 125 postmenopausal women (age range, 41–90 years average age  $\pm$  standard deviation, 59.3  $\pm$ 9.3 years) consecutively enrolled over one year period from September 2010 to October 2011. All women with lumbar pain referred for confirmation of the degree of osteoporosis. We excluded 15 women with history of previous spinal pathology, acute fracture, scoliosis, kyphosis or surgery. 110 women (mean age  $\pm$  SD, 59.3 years  $\pm$  9.3) were in the analysis. We gave information about the procedures and patients signed an informed consent form. Thirty four postmenopausal women had received HRT for more than a year. Each subject underwent both BMD and MR imaging of the spine at the same week.

### a. Bone Density Measurements (BDM)

BDM made with dual energy absorptiometry using a fan-beam bone densitometer (Lunar, GE Healthcare, Madison, WI). T and z-scores were calculated by Lunar software. The World Health Organization excepted t score of less than -2.5 as osteoporosis, osteopenia in the range of -1 to -2.5 and considered healthy above -1.

### b. Measurements of Lumbar MR Imaging

Spine imaging had done by using a 1.5-T MR system (Siemens Magnetom Essenza, Erlangen, Germany) with spinal coil. Both T1 and T2 weighted images were in the midsagittal plane from the level of L2 to L5.

The mean and SD of the signal intensity values of operator-defined regions of interest on T1 and T2-weighted images of the spine were measured by an experienced radiologist. We excluded the pathologies like neoplasm, compression fracture, or infection from the study.

### c. Data Analysis

The radiologist (A.R.A. with 11 years of experience) measured signal intensity values in operator-defined regions of interest (ROI) at the center of each vertebral body separately for each lumbar vertebrae (L2 through L5) in each subject (As shown in Figure 1 and Figure 2).

### d. Statistical Methods

All statistical analysis were performed using SPSS for Windows

18.0 statistical package. One-way ANOVA used to compare the T1, T2, T1/T2 and T1-T2 variables among normal, osteopenia and osteoporosis groups. The correlations between variables analyzed using the Pearson's correlation coefficient. We used the ROC curve for performance evaluation of T1 and T2 values in discriminating normal and osteopenia or normal and osteoporosis groups. P value less than 0.05 were statistically significant.

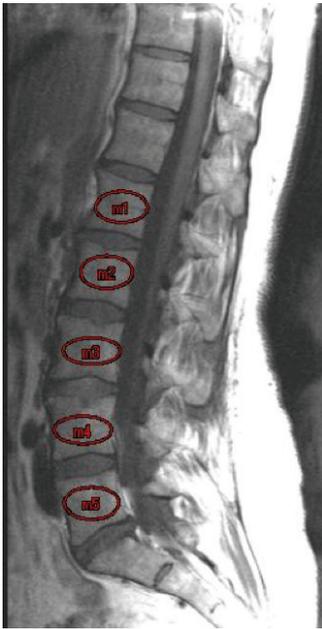


Figure 1: Vertebral intensity measurements from sagittal T1 weighted images

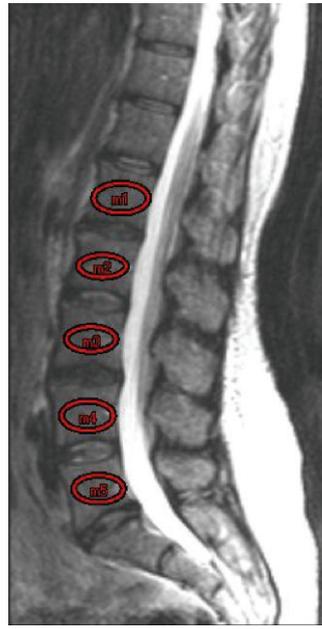


Figure 2: Vertebral intensity measurements from sagittal T2 weighted images

## Results

Fifteen premenopausal women were excluded from the initial group of 125 women. This resulted in a final cohort of 110 women (mean age, 59.3 years; age range, 46-90 years). The L2-L5 vertebral body was analyzed in all women. 78 (70,9%) postmenopausal women were not and 32(29,1%) were receiving HRT (Table 1).

Bone density was abnormal in nearly half (44%) of women who have osteopenia in 39(35.5%) and osteoporosis in 10(9%) according to t-scores (Table 2).

No significant positive correlation found for BMD with T2 intensity of lumbar vertebrae among all women (n =109, r = -0,09, p< 0.306) women who were not receiving HRT (n = 78,

r = -0.13, p< 0.274), and weak positive correlation was found in postmenopausal women receiving HRT (n =31, r = 0.36, p< 0.050). Correlation between BMD and T1 intensity of lumbar vertebrae MR imaging was evaluated among all women (n =109, r = -0.11, p< 0.243). Postmenopausal women receiving HRT(n =31, r = 0.22, p< 0.239) and postmenopausal women who were not receiving HRT (n = 78, r = -0.17, p< 0.133). BMD was inversely correlated with age (n=110, r=-0.38, p < 0.001), and T2 and T1 intensities were not correlated with age (n=109, r= 0.17, P< 0.073 and r=0.06, p< 0.546, respectively).

Mean intensities of T1 and T2 were strongly correlated with each other at the center of the vertebrae (n=109, (r=0.79, p<0.01)) The effect of age on these parameters was assessed by using Pearson correlation analysis. There were low negative relationship between age and BMD (r=-0.38, p<0.01). The signal intensities on lumbar MR imaging and the BMD for anteroposterior projections decreased significantly with increasing age (P < 0.001) (Table 3).

Table 1: Postmenapausal women with and without hormone therapy

Hormone	Frequency	Percent
Negative	78	70.9
Pozitive	32	29.1
Total	110	100.0

Table 2: Number of groups after DEXA examination according to t-score

	Frequency	Percent
Normal	61	55.5
Osteopenia	39	35.5
Osteoporosis	10	9.0
Total	110	100.0

In addition, one-way ANOVA revealed no difference between normal, osteopenia and osteoporosis groups according to mean T1, mean T2, T1/T2 or T1-T2 variables (P>0.05) (Table 4). According to the ROC curve analysis we were unable to distinguish the osteoporosis using mean T1 and mean T2 intensity values (P>0.05). Area under the curve is less than 0.50 so that normal or osteoporosis groups can not be distinguis-

hed with T1 or T2 intensities when ROI was at the center of the vertebrae. (As shown in Figure 3 and Table 5). The same was also true for osteopenia; T1 and T2 intensities has low performance on distinguishing the normal and osteopenia at the center of the vertebrae( $P>0.05$ ) (As shown in Figure 4 and Table 6).

**Table 3:**  
Pearson Correlations of lumbar MR mean T1, T2 intensities with age and bone mineral density(bmd)

		age	bmd	mean T2 int	mean T1 int
age	Pearson Correlation	1		0.172	0.059
	Sig. (2-tailed)		0.000	0.073	0.546
	n	110	110	109	109
bmd	Pearson Correlation		1	-0.099	-0.113
	Sig. (2-tailed)	0.000		0.306	0.243
	n	110	110	109	109
mean T2int	Pearson Correlation	0.172	-0.099	1	
	Sig. (2-tailed)	0.073	0.306		0.000
	n	109	109	109	109
mean T1 int	Pearson Correlation	0.059	-0.113		1
	Sig. (2-tailed)	0.546	0.243	0.000	
	n	109	109	109	109

**Table 4:**  
Comparison of BMD measured with anteroposterior and T1 and T2 signal intensities of lumbar MR imaging according to groups

Variables	Groups	n	Mean	F	P
mean T1 int	Normal	60	28.29±8.96	2.351	0.100
	Osteopenia	39	29.70±11.11		
	Osteoporosis	10	35.70±11.76		
mean T2int	Normal	60	23.96±7.31	0.883	0.417
	Osteopenia	39	25.38±7.83		
	Osteoporosis	10	27.03±9.81		
T1/T2	Normal	60	0.864±0.157	1.220	0.299
	Osteopenia	39	0.883±0.168		
	Osteoporosis	10	0.788±0.259		
T1-T2	Normal	60	-4.60±5.42	2.044	0.135
	Osteopenia	39	-4.32±5.74		
		10	-8.67±11.49		

When we selected half of the patients randomly, remeasured and calculated the mean T1 and T2 intensities, intraobserver

correlation coefficient was as high as 0,99. Using regression analysis there was no correlation between T1 and T2 intensities as dependent, HRT and age as an independent variable.

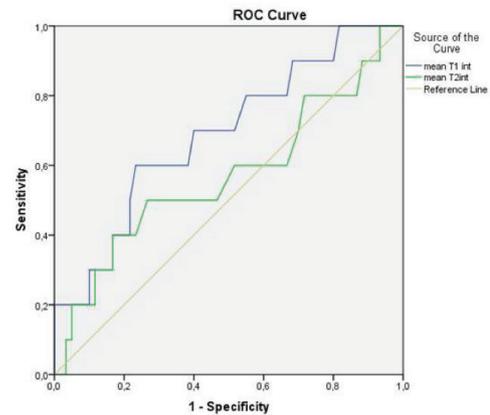


Figure 3:ROC curve of osteoporosis with T1 and T2 intensities

**Table 5:**  
Area Under the ROC Curve of osteoporosis for mean T1 int and mean T2 int

Variables	Area	Std. Error	P
mean T1 int	0.688	0.091	0.058
mean T2int	0.569	0.110	0.486

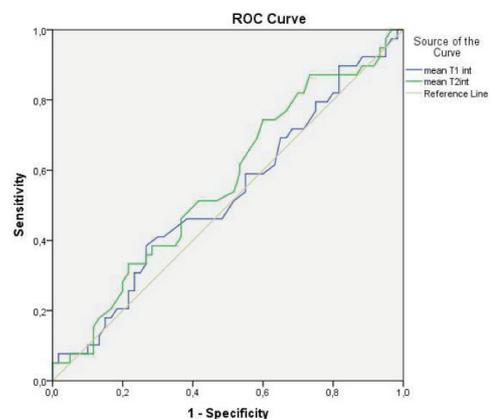


Figure 4: ROC curve of osteopenia with mean T1 and T2 intensities

**Table 6:**  
Area Under the ROC Curve of osteopenia for mean T1 int and mean T2 int

Variables	Area	Std. Error	P
mean T1 int	0.526	0.060	0.657
mean T2int	0.561	0.059	0.309

## Discussion

The pathogenesis of osteoporosis is complex. There are many contributing factors including genetic conditions, nutrition, and hormonal status. BMD correlates with age and in the spine decreases by about 20% between 40 and 70 years<sup>(7,15)</sup>. Histomorphometric studies have shown that skeletal blood flow is correlated with output rate of osteoblasts<sup>(6,16,17,18)</sup>. Atherosclerosis causes endothelial dysfunction, which can reduce the release of endothelial nitric oxide synthase, limiting osteoblast formation or decreasing the anabolic effect of bone<sup>(19,20)</sup>.

BMD loss is well known in osteoporosis and DEXA is the most commonly used and least expensive method of evaluation<sup>(2,8,9)</sup>. There may be qualitative and architectural changes in aging bone. The spaces of vertebrae with decreased BMD contain fatty bone marrow<sup>(6,13)</sup>. In aging bone marrow, osteoclast activity increases and adipocytes appear in locations where osteoblast function declines, resulting in osteoporosis<sup>(19)</sup>. MR spectroscopy shows increases in fatty bone marrow, in patients with osteoporosis<sup>(3,9,17)</sup>.

It has recently been identified that there are different rates of response to bone active agents in the inner and external aspects of the bone cortex<sup>(2)</sup>. This means different parts of vertebrae have different responses to osteoporosis. There is a significant increase in signal intensity among the osteoporotic group<sup>(6,14)</sup>. The rise in signal intensity in the osteopenia and osteoporotic groups might be explained by increases in fatty marrow content. In a variety of studies, the measurements were from the entire vertebral body (center and edges) on the axial plane. The edge of vertebrae is less vascular and probably much more fat transformation occurs in this place. In our study, we found no significant increase in T1 and T2 signal intensities at the center of the vertebrae and also no difference according to the ROC curves. This is because the center of the vertebrae is abundantly rich in vascular supply and less affected from the fatty transformation. We propose that the center of the lumbar vertebrae is not sensitive to the atherosclerotic process and osteoporosis or osteopenia. We demonstrated no significant correlation between MR bone marrow signal intensities at the center of the lumbar vertebrae and BMD. Both signal intensities and BMD were inversely

correlated with age ( $p < .001$ ). We believe this is one of the few reports on the quantitative analysis of osteoporosis only at the center of vertebrae.

This study has several limitations. First, women were not aware of their bone density results prior to MR examination. This may cause attendance of more normal women than women with osteopenia or osteoporosis. Second, participating women were not know the results of MR imaging, which may have prompted more women with back pain, to endure MR imaging. In addition, DEXA is less sensitive, and BMD may not show real BMD status. The study group consisted of only postmenopausal women. Another limiting factor is that we did not normalize the groups according to body weight and body fat level. Measurements were only at the center of the vertebrae which is not the case in the literature. Most studies calculated the MR signals from the whole vertebrae including the periphery of vertebrae. In osteoporosis, there is a total fat signal change like signal intensity increase in both T1 and T2 sequences. In this study, we demonstrated that osteoporosis and fatty change do not arise from the center of the vertebrae which is vascular.

The centre of the vertebrae which is highly trabeculated and less sensitive to osteoporosis because of large vascular supply. Fatty transformation of bone marrow occurs after demineralization. We have detected fatty transformation on MRI demineralization on DEXA, but MRI is much sensitive for detection of osteoporosis at the center of the vertebrae. There was a weak positive correlation between BMD and T1 signal intensity in postmenopausal women without HRT ( $n = 31$ ,  $r = 0.36$ ,  $P < 0.050$ ). This may also show that osteoporosis affect the center of the vertebrae late in disease pathogenesis.

## Conclusion

In this study, we have not observed bone marrow T1 or T2 signal increase at the center of L2-L5 lumbar spine of postmenopausal women. Signal intensities of lumbar vertebrae for bone marrow fatty change is correlated with age. Fat deposition is less at the center in postmenopausal women using HRT probably because of a vascular component in the pathogenesis of osteoporosis.

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