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Effects of Smoking and Hemoglobin Values on Femoral Bone Marrow Resonance Signal Intensity

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ÖZET

Sigara kullanımı ve hemoglobin değerlerinin femur kemik iliği manyetik rezonans intensitesi üzerine etkisi

Amaç: Bu çalışmanın amacı distal femur metafizindeki rezidü-rekonversiyone kırmızı kemik iliği alanlarının yaş, cinsiyet, kilo hemoglobn değerleri (hgb) ve sigara kullanımı ile korelasyonunu araştırmaktır.

Gereç ve Yöntem: 150 sigara içmeyen ve 62 sigara içen birey çalışmaya dahil edilmiştir. Distal femur metafizindeki rezidü-rekonversiyone kırmızı kemik iliği alanlarının Manyetik Rezonans Görüntüleme (MRG) bulguları 2 radyolog tarafından değerlendirildi. Rezidü-rekonversiyone kırmızı kemik iliğ alanları ile hasta yaşı, cinsiyeti, kilosu ve hemoglobin değerleri Oneway Anova Test, Tukey HSD Test, Fisher's Exact Test and Pearson Chi-Square Testleri kullanılarak karşılaştırıldı.

Bulgular: Çalışmamızda, rezidü-rekonversiyone kırmızı kemik iliği alanları sigara içen erkek ve kadın olgularda sigara içmeyen olgulara göre daha fazla bulundu. ($p=0.004$; $p<0.01$), ($p=0.026$; $p<0.05$). Rezidü-rekonversiyone kırmızı kemik iliği alanları kadın olgularda erkek olgulara göre daha fazla olarak bulundu. ($p=0.004$; $p<0.01$). Kilo ve hemoglobin değerlerinin ve yaşın bu alanlar üzerinde istatiksel anlamı olmadığı saptandı. ($p>0.05$).

Sonuç: Rezidü-rekonversiyone kırmızı kemik iliği alanları ile kadın cinsiyet ve sigara kullanımı arasında korelasyon tesbit ettik. Bu gruptakiler için bu alanlar fizyolojik olacağından MRG raporlarında belirtme taraftarı değiliz. Ancak bu alanlar komşu kas gruplarına göre T1 ağırlıklı sekansta (T1AS) hipointens ise, kemiğin büyük kesimini kaplamış ise ve ya eşlik eden yumuşak doku komponenti var ise raporda belirtilmelidir.

Anahtar kelimeler: Diz, MRG, kırmızı kemik iliği, rezidü, rekonversiyone

ABSTRACT

Effects of smoking and hemoglobin values on femoral bone marrow resonance signal intensity

Objective: The aim of our study is to evaluate the correlation of residual-reconverted red bone marrow areas of distal femoral metaphysis with the age, gender, weight and hemoglobin (hgb) values and smoking.

Material and Methods: 150 non smoking and 62 smoking patients were included in the study. The residual red bone marrow areas in the distal femoral metaphysis in MRI (Magnetic Resonance Imaging) images were examined by two radiologists. The size of the residual red bone marrow area and the age, gender, weight and hemoglobin values of the patients were compared by using the Oneway Anova Test, Tukey HSD Test, Fisher's Exact Test and Pearson Chi-Square Test.

Results: In our study, residual red marrow areas were detected higher in smoking male and female patients when compared to non-smoking patients ($p=0.004$; $p<0.01$), ($p=0.026$; $p<0.05$). Residual red marrow areas were more common in female patients when compared to male patients ($p=0.004$; $p<0.01$). We haven't seen significant effect of weight, hemoglobin values and age on these areas ($p>0.05$).

Conclusion: We have determined correlation between reconverted-residual red marrow areas, female sex and smoking behavior. In the correlation existing group; we are not in favor of mentioning these areas on MRI reports of the knee. But they should be phrased in reports considering the probability of malignancy if they are hypointense compared to adjacent muscle groups on T1-weighted sequences; if they are extensive involved in bone tissue; if they show epiphyseal extension or if there is accompanying soft tissue mass.

Key words: Knee, MRI, red bone marrow, residual, reconverted

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INTRODUCTION

Residual red marrow shows low signal intensity on T1-weighted sequence (T1WS) and high signal on Spair (spectral attenuated inversion recovery) sequences on Magnetic Resonance Imaging (MRI). Distinct areas of red marrow at birth, shows regression with the conversion into yellow bone marrow as aging goes on. The entire process is generally completed by the age of 25 (1). Depending on several reasons, MRI reveals residual or reconverted red marrow areas in distal femoral metaphysis. Although these findings are frequently seen on MRI under age of 25, they are considered as physiological and are not reported (1). On the contrary, these MRI findings are emphasized in radiological reports when they are detected over age of 25 (2). Reporting the signs which indicate physiological reconversion or residual red marrow by radiologists may reduce the clinicians ordering unnecessary tests and procedures. Previous studies have shown that reconverted red marrow areas were detected on MRI in anemic patients. (3). It was also reported that smoking has significant effects on bone marrow, bone and cartilage (4-8). However, no research exists addressing the correlation between hemoglobin levels, amount of smoking and reconverted-residual red marrow areas to our knowledge. In this study, we aim to investigate the correlation between gender, age, weight, hemoglobin levels and reconverted-residual red marrow areas.

MATERIAL AND METHODS

Patient population

Our study is a single-center retrospective clinical study performed between years 2012-2016 and was conducted in accordance with ethical principles of our institution. Signed consent was taken from the patients. This study is the continuation of the work that we have performed before (9). We have increased the sampling number by adding smoking patients to our previous patient population and evaluated whether there is difference in these areas between smokers and non-smokers.

Our patient group consisted of 120 women between the ages of 26 and 75, and 92 men between the ages of 27 and 72, who had lived in the city of Erzincan (with an altitude of: 1185 m, 3887 ft) for the last decade. 150 of them were non smokers and 62 of them were smokers. Patients were ordered knee MRI by the orthopedic surgeon because of meniscal/ligamentous complaints. The knee MRIs of the patients were performed and their hemoglobin values were measured in the following or previous week. We have chosen patients whom hemoglobin values were already ordered by the clinicians Patients did not have extra blood test done for this study.

Exclusion criteria

1- Cases under the age of 25 (since the adult bone marrow pattern is not formed until then);
2- Athletes (Hematopoietic bone marrow hyperplasia: High prevalence on MR images of the knee in asymptomatic marathon runners);
3- Patchy areas which were T1Ws hypointense when compared with the neighboring muscle tissue (10);
4- Cases with marrow edema due to contusion;
5- History of steroid use, osteonecrosis and fracture;
6- Cases with malignant or systemic diseases that might have affected the bone marrow.

Also 3 patients that MRI readers did not have a consensus on the grading were excluded. According to these criterias 12 patients were excluded.

Imaging and imaging analysis

The knee MR exams were conducted with a 1.5 Tesla Philips MRI (Intera, Philips Medical Systems, Best, The Netherlands) device by using an 8-channel knee coil. Coronal T1, sagittal-axial T2, and coronal spair sequences were performed without giving contrast agent. The following parameters were used for the T1-weighted coronal turbo spin-echo sequence: TR/TE 450/20;matrix size 256×192; section thickness 3 mm; FOV 16 cm; bandwidth 16. The following parameters were used for the spair coronal sequence: TR/TE 746/7, matrix size 256×192; section thicknes 4 mm; FOV 16 cm; bandwidth 19 cm. On knee MRIs, areas of residual red marrow of distal femoral metaphysis were interpreted by two radiologists experienced in musculoskeletal MR imaging. The areas which were hypointense relative to the neighboring bone tissue but hyper /isointense relative to the neighboring muscle tissue in T1WS, hyperintense relative to neighnoring tissues in the Spair sequence were defined as residual or reconverted red bone marrow.

The lesions that were more hypointense than the neighboring muscle tissue on T1WS were accepted as pathological (malignancy etc.) and were not included in the study. We have designed a grading system for the images. The patchy areas were defined as grade1 if mild and covering less than 30% of the metaphysis, grade 2 if moderate and covering between 30% and 60% of the metaphysis, and grade 3 if diffuse and covering more than 60% of the metaphysis. If there were no spair hyperintense area then it was graded as grade 0. (Figures 1,2,3,4a,4b). The measurements were repeated twice at different times in order to increase the accuracy of the grading system. There has been only 3 cases with disagreement and those patients were excluded. The correlation of the areas measured on the MR images of smoking and non smoking patients was made with the age, gender, weight, and hemoglobin values.

Statistical Analysis

NCSS (NumberCruncher Statistical System) 2007&PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) program was used for statistical analysis. Oneway Anova Test was used in comparing the normally distributed variables for three and more groups and Tukey HSD Test was performed to state significant difference among the groups in addition to the descriptive statistical methods (mean, standard deviation, median, frequency, ratio, maximum) used to evaluate data analysis of the study. Fisher's Exact Test and Pearson Chi-Square Test were performed to analyse qualitative data. Pearson Correlation Analysis and Spearman's Correlation Analysis were used to identify the relationship between parameters. Significance level was evaluated as $p<0.01$ and $p<0.05$.

RESULTS

The study was conducted on 212 patients and consisted of 92 males and 120 females. Their ages ranged from 26-75, with an average age of 45.39±12.36. Their weights ranged from 30 kgs to 110 kgs, the average being 75.41±13.80 kgs. Hemoglobin levels of the patients included in the study varied in the range of 9.10 mg/dl and 17.10 mg/dl with an average level of 13.66±1.66 mg/dl. It was observed that 70.8% (n=150) of the patients did not smoke while 29.2% were smokers (n=62). MR grades were grade 0-1, grade 2 and grade 3 in 80.2% (n=170), 11.7% (n=25) and 8.1% (n=17) of the patients, respectively (Table 1).

No significant difference was found between average ages, weight and hemoglobin values according to MRI Grades statistically ($p>0.05$). 70.8% of the patients (n=150) were non-smokers, while 29.2% (n=62) were smokers. Smoking pack years for male patients ranged from 0.50 pack years to 40 pack years, with an average of 11.16±8.88 pack years while it ranged from 0.25 to 32 for female patients with an average of 9.31±9.33 pack years.

Table 1: Distribution of descriptive statistics

	Min-Max	Mean±Sd
Age	18-75	45.39±12.36
Weight (kgs)	30-110	75.41±13.80
Hemoglobin (mg/dl)	9.10-17.10	13.66±1.66
	n	**%**
Gender		
Male	92	43.4
Female	120	56.6
Smoking		
Smoker	150	70.8
Nonsmoker	62	29.2
MRI Grading		
Grade 0	71	33.4
Grade 1	99	46.6
Grade 2	25	11.7
Grade 3	17	8.3

Table 2: Evaluation of MRI grades in male and female groups according to smoking

			Male n (%)	Female n (%)	[a]p
Nonsmoker	**MRI grade**	**Grade 0+1**	54 (98.2)	74 (77.9)	0.004**
		Grade 2	1 (1.8)	11 (11.6)	
		Grade 3	0 (0.0)	10 (10.5)	
Smoker	**MRI grade**	**Grade 0+1**	31 (86.1)	11 (42.3)	0.001**
		Grade 2	5 (13.9)	8 (30.7)	
		Grade 3	0 (0.0)	7 (27.0)	

[a]FisherFreemanHaltom Test **p<0.01

Table 3: Evaluation of age, weight and hemoglobin values according to MRI grades

	Grade 0 Mean±Sd	Grade 1 Mean±Sd	Grade 2 Mean±Sd	Grade 3 Mean±Sd	[c]p
Age	47.76±12.77	45.21±12.70	40.64±10.34	43.50±9.91	0.087
Weight (kgs)	78.51±13.89	74.27±13.29	72.24±15.63	72.93±12.04	0.110
Hemoglobin (mg/dl)	13.77±1.60	13.82±1.77	13.38±1.40	12.80±1.43	0.131

[c]OnewayAnova Test

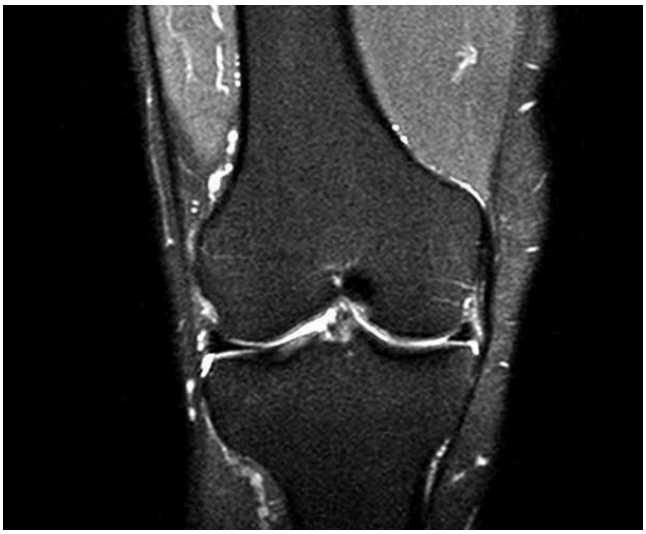

Figure 1: The pd tse spair sequence coronal plane of knee MRI. There is no residual red bone marrow area

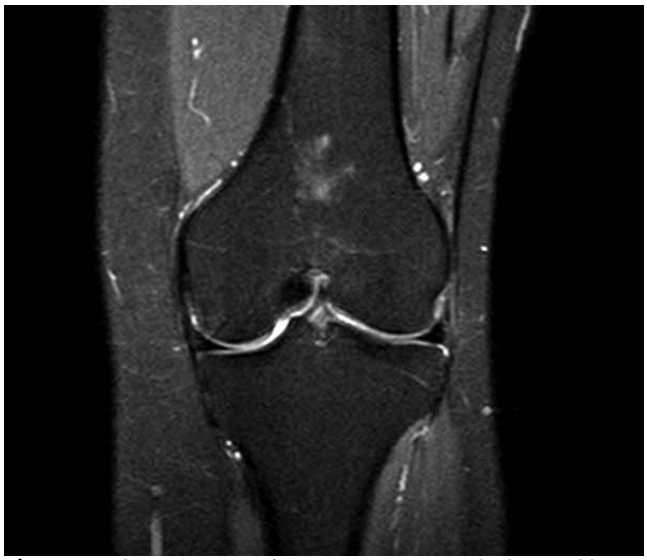

Figure 2: The pd tse spair sequence coronal plane of knee MRI. The residual red bone marrow areas were of grade 1 (covering less than 30% of the metaphysis)

According to smoking behaviors of male patients, no significant difference was detected between MRI grade areas statistically (p=0.004; p<0.01). While the ratio of MRI grade areas of 0 and 1 were significantly higher in non-smoking male patients (p=0.007; p<0.01); ratio of grade 2 was significantly higher in smoking male patients (p=0.034; p<0.05).

Statistically significant difference between the grade of areas was detected in female patients according to their smoking behaviors (p=0.026; p<0.05). The ratio of medium grade areas was significantly higher in smoking female patients when compared to non-smoking female patients (p=0.012; p<0.05) (Table 2).

Statistically significant difference between the grade of areas was detected in non-smoking patients according to their gender (p=0.004; p<0.01). The ratio of grade 3 cases were significantly higher in non-smoking female patients when compared to non-smoking male patients (p=0.014; p<0.05). The ratio of grade 2 cases was significantly higher in non-smoking female patients when compared to non-smoking male patients (p=0.002; p<0.01).

Statistically significant difference between MR grades areas was detected in smoking patients according to their gender (p=0.001; p<0.01). While the ratio of MR grades of 0 and 1 was significantly higher in smoking male patients (p=0.009; p<0.01); ratio of grade 3 cases was significantly higher in smoking female patients (p=0.019; p<0.05) (Table 3).

No significant difference between the quantity of smoking and MRI grades was found in male patients statistically (p>0.05). No significant difference between the quantity of smoking and and MRI grades was found in female patients statistically (p>0.05).

DISCUSSION

While almost the whole bone marrow in a newborn consists of the red bone marrow, conversion into the yellow bone marrow with age is seen. The conversion takes place from the peripheral to the center, and from the diaphysis into the metaphysis (11). The conversion is mostly completed until the age of 25, and only some residual red bone marrow remains in some areas such as

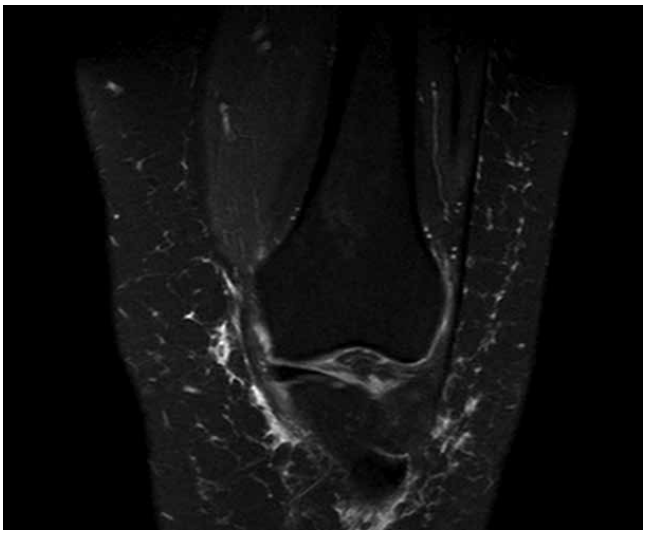

Figure 3: The pd tse spair sequence coronal plane of knee MRI. The residual red bone marrow areas were of grade 2 (covering almost half of the metaphysis)

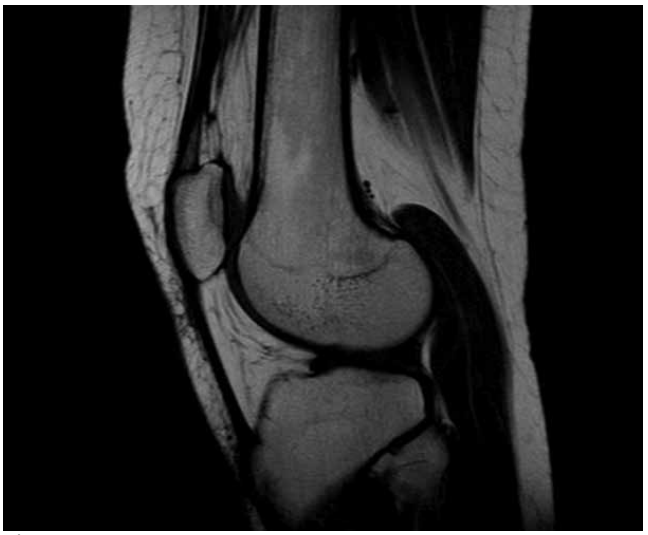

Figure 4b: The T1-weighted turbo spin echo sequence, sagittal plane of knee MRI. The residual red bone marrow areas were of grade 3 (covering almost all of the metaphysis)

Figure 4a: The pd tse spair sequence coronal plane of knee MRI. The residual red bone marrow areas were of grade 3 (covering almost all of the metaphysis)

the sternum, vertebra, ribs, pelvis, proximal femur, and humerus (12,13). With aging, according due to the need for blood cells of the body, the yellow bone marrow may be reconverted into the red bone marrow from the proximal to the dista, and this is called «reconversion». The situations that may cause reconversion include smoking, living in high altitudes and performing professional sports. Of the imaging methods, MRI is the choice for the investigation of bone marrow disorders (14). Fatty marrow appears hyperintense on T1-weighted sequences since lipid protons have short T1 relaxation times. Red marrow contains more water and has an intermediate T1 relaxation time, and appears to have a lower signal than subcutaneous fat, but a higher one than intervertebral discs or muscles (15,16). The physiological reconversion and pathological situations may easily be followed with MR imaging. In case of reconversion, the increase in the patchy hypointensities on T1WS. Which is limited to the distal femoral metaphysis without reaching the epiphysis is detected. Same areas appear hyperintense on spair sequences. In our study, we have investigated the correlation between age, gender, weight, hemoglobin values and the size of the area in distal femur metaphysis which is broadly similar with reconversion on MRI of knee. We have found that patients with grade 0 and 1 were most common among all smoking and non-smoking patients. We have found that grade 2 and 3 were more frequent in female patients when compared to male patients (17). We think that blood loss due to menstruation may lead to reconversion. We have seen that patients with Grade 2 and 3 were more common in smokers. (18). We have detected that these areas were increased in both male and female patients who were smokers. We think that smoking leads to this finding as a reason of reconversion. Nevertheless, we didn't observe correlation with amount of smoking. Poulton et al. have stated that these areas are more frequent in obese women (17). We have found that these areas are more common in women regardless of weight. Lowest hemoglobin value was 9.1 mg/dl in our

study. We didn't detect correlation between hemoglobin levels and these areas. According to the best of our knowledge, there is no previous report about the association between these areas and hemoglobin values. We think that there would be reconversion at lower hemoglobin values levels due to anemia and an increase in these areas would occur. But we didn't observe any increase in these fields due to reconversion unless hemoglobin count is less than a certain value. Relatively small number of smoking women involved in the study, subjective rather than quantitative characteristics of grading system and lowest hemoglobin count of 9 mg/dl among our patients were the limitations of our study. Also former hemoglobin values in the last 3 months could have been measured and used for the study as it might take time for the bone marrow react to anemia. Sampling of the patients within the population living at high altitude could also be considered as a limitation; but this variable was kept constant by selecting patients from the same region. The number of the patients in our sample groups were more than those who had been involved in previous studies (17,18).

Reconverted or residual red marrow areas may exist in female adults and smokers. They can be traced in proximal parts of axial skeleton such as like humerus and femur or in less frequently in distal parts. In our study, we have detected that these areas are seen more often in women and smokers. We think that it is important to distinguish these areas from pathological processes of bone marrow and we need to show due diligence in order to avoid unnecessary tests. If this area covers more than 60% of metaphysis, we may inquire the patients' gender, smoking behavior and hemoglobin levels. We are not in favor of reporting these areas in adult female patients and smokers. But we should not hesitate to define them considering the probability of malignancy if they are hypointense compared to adjacent muscle groups on T1-weighted sequences, they extensively involve the bone tissue, if they have show epiphyseal extension, or if there is an accompanying soft tissue mass.

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