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Does bone mineral density change in polycystic ovarian syndrome?

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Abstract
Polycystic ovarian syndrome (PCOS), is the most frequent endocrine disorder in reproductive age and PCOS has effects on bone metabolism. There is conflicting data on the effect of PCOS on bone metabolism. The aim of this study to evaluate whether bone mineral density (BMD) changes in PCOS or not. Twenty-seven patients with PCOS for the study group and 27 patients for the control group were included in this retrospective study. BMD measurements with abdomen CTs were taken for each lumbar vertebra (from vertebra L1 to vertebra L5) and sacral 1st vertebra. BMD measurements were recorded as HU. The lumbar 5th vertebra's BMD was 238.70±47.80 HU in the PCOS group and 264.91±36.62 in the control group and the difference was statistically significant (P=0.033). BMD values of all vertebras were lower in the PCOS group than the control group, but statistically, significance was seen in only the lumbar 5th vertebra. BMD values were found to be lower in PCOS than the control group for all vertebras in this study. Even though there is no scanning method recommend to women in PCOS for BMD according to the current guidelines and literature, we think these patients should be evaluated more carefully in advanced ages in the light of the results of our study.

Keywords: Bone mineral density, CT, DEXA, PCOS, vertebra

Introduction

Polycystic ovarian syndrome (PCOS), is the most frequent endocrine disorder in reproductive age which is characterized by oligo/anovulation, hyperandrogenism, and hirsutism [1]. Although the exact cause of PCOS is still unclear unknown, and it is considered that the disease may be related to due to the hypothalamic-hypophyseal-ovarian axis dysfunction. In PCOS, it It is shown that hypophysis volume increases in PCOS and PCOS also have effects on the other endocrine organs other than pituitary glands, such as adrenal glands, fat cells and pancreas [2,3]. Moreover, PCOS has effects on bone metabolism, as well [4].

Bone mineral density (BMD) is evaluated with bone mineral densitometry (BD) and the most frequently used method is Dual-energy X-ray absorptiometry (DEXA). The World Health Organization (WHO) suggests DEXA for scanning and diagnosis osteoporosis [5,6]. Currently, BMD measurements with computerized tomography (CT) has shown that HU (Hounsfield unit) values are correlated with DEXA values and CT can be used in the differentiation of osteoporosis, osteopenia and normal bone density [7–9]. The evaluated BMDs with abdomen CTs taken for other reasons are defined as "opportunistic scans" and this is an alternative screening method which is speedy, reliable, not requiring extra costs and protecting the patients from additional radiation exposure [10,11].

It is known that androgens have positive effects on muscle mass and BMD [12,13]. There is conflicting data on the effect of PCOS on bone metabolism. It has been shown that there is no difference in terms of BMD, fracture incidence and muscle mass between PCOS and the control group in the postmenopausal period [14]. While it has been suggested that PCOS is protective against bone loss due to obesity, hyperandrogenemia and high estradiol level, in some studies BMD has been measured lower in PCOS despite the positive effect of hyperandrogenemia and hyperinsulinemia [4,15-18]. It has also been emphasized that body mass index (BMI) is the most important indicator in terms of BMD in PCOS patients [14,19].

In our study, we aimed to evaluate if there is a difference between PCOS and control groups in term of BMD by measuring the lumbar and sacral spine HU values with CT which is a contemporary approach with DEXA.

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Material and Methods

After obtained the ethical committee's approach from our center, 337 female patients diagnosed with PCOS in January 2015-January 2019 at our hospital were evaluated retrospectively. Data was collected in the electronic archive of our center. All of the subjects were diagnosed with PCOS according to the Rotterdam criteria. The Rotterdam Criteria require the presence of two of the following: oligo/anovulation, hyperandrogenism (clinical or biochemical) or polycystic ovaries on ultrasound [1]. Among 337 patients had abdomen CT for any kind of indication (n: 47) were defined and 27 patients were included in the study with unenhanced abdomen CT, since contrast media injection may have effects on bone density. Patients with lumbar CT were not included in the study due to the indications of lumbar CT may include some situations such as fractures or operative changes which can affect the density of vertebra corpus. Abdomen CTs with motion artifacts are not included in the study due to motion artifacts may alter the measurement of density. It is deleted from the text and mentioned as 27 patients included in the study)Totally, 27 female patients with unenhanced abdomen CT in the same time period and in the similar age with PCOS group it is mentioned in the results section) served as the control group.

Radiological Evaluation

All CT examinations were performed in a 256-slice multi-detector CT scanner (Somatom, Siemens Healthcare, Erlangen, Germany). BMD measurements with abdomen CTs were performed by the same radiologist for each lumbar vertebra (from vertebra L1 to L5) and first sacral vertebra in the sagittal plane, midline. ROI (region of interest) was drawn three times for each vertebra (Figure 1). BMD measurements were recorded as HU and the mean of the three measurements was calculated for each vertebra for each patient.

Statistical Analysis

For the statistical analysis, the SPSS 22.0 software was used (USA, Chicago). In order to determine whether the variables have a normal distribution, the Kolmogorov-Smirnov test was used. Since the number of patients in the groups was less than 30, the Mann Whitney U test was used. A p-value below 0.05 was accepted as statistically significant.

Results

The mean age of the PCOS group was 26.92±9.0 (15-50) and 26.96±8.8 (16-49) in the control group. The groups were matched in terms of age (p=0,945). The lumbar and sacral vertebra BMD values are given in Table 1. The mean BMD of a lumbar vertebra in the PCOS group was 233.49±40.43 HU, whereas 251.58±32.96 HU in the control group (p=0.095). The sacral vertebra density in the PCOS group was 289.96±96 HU and 303.45±55.56 HU in the control group (p=0.729). The lumbar 5th vertebra's BMD was 238.70±47.80 HU in the PCOS group and 264.91±36.62 in the control group and the difference was statistically significant (P=0.033). BMD values of all vertebras were lower in the PCOS group than the control group, but statistically significance was seen in only the L5 vertebra for groups. The highest density of was measured in the 1st sacral vertebra, whereas the lowest in the 4th lumbar vertebra.

Table 1. Bone mineral density values of groups

	Study group (n=27)	Control group (n=27)	P value
Lumbar 1st vertebra	232.76±42.58*	247.19±32.96*	0.513
Lumbar 2nd vertebra	233.06±42.79*	254.09±38.76*	0.088
Lumbar 3th vertebra	231.64±42.58*	243.24±33.71*	0.337
Lumbar 4th vertebra	231.29±41.11*	248.44±37.39*	0.172
Lumbar 5th vertebra	238.70±47.80*	264.91±36.62*	0.033
Lumbar mean	233.49±40.43*	251.58±32.96*	0.095
Sacral 1st vertebra	289.96±83.70*	303.45±55.56*	0.729

*: Values were given by Hounsfield unit (HU) ±standard deviation

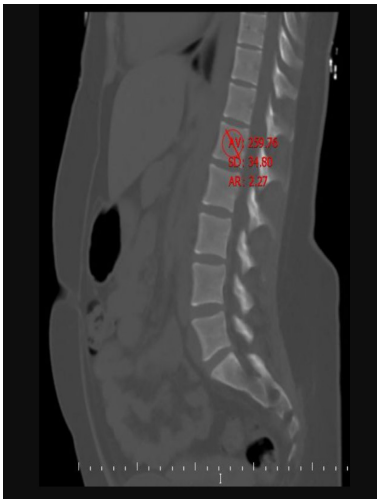

Figure 1. Midsagittal abdominal computed tomography image. Measurement of L1 vertebra bone mineral density with circle ROI is seen

Discussion

In our study, BMD was evaluated with CT and the BMD values in all vertebras were found lower in PCOS than the control group. Statistically significant difference was found in the L5 vertebra density values between groups. To the best of our knowledge, while there are some studies involving "BD" for the evaluation of BMD, our study is the first study in which BMD was evaluated with "CT" in PCOS.

Currently, osteoporosis and osteopenia can be evaluated in opportunistic scans with abdomen CTs in lumbar vertebras without additional DEXA [10,11,20,21]. In a study, 175 HU threshold value was determined to distinguish osteoporosis and osteopenia, whereas below 136 HU in the diagnosis of osteoporosis [21]. In our study, the mean of all vertebras' BMD values in groups was found higher than 175 HU. We are in the opinion that the main reason for this is our PCOS group consists of young patients.

Although BMD values are higher than the threshold for osteopenia and osteoporosis in PCOS, it is conspicuous that BMD values are quite lower in PCOS group than the control group.

There are some studies showing no differences for BMD values evaluated with DEXA in PCOS compared to the control group [14,22]. In a study carried out by Ganie et. al, it is emphasized that there is no difference in BMD in PCOS than the control group, BMD is higher in obese PCOS group compared to non-obese PCOS group and obesity is the most important determinant of BMD in women with PCOS [19]. It is shown in some studies that PCOS has a protective effect against to bone loss due to obesity, hyperandrogenism and high estradiol levels [15,16]. It has been claimed that obesity increases the stress forced on the skeletal system or increases the transformation of androgens into estrogens and thus becomes a protective factor against bone loss [23]. However, all PCOS subjects are not obese. Although it is known that a majority of the PCOS subjects are overweight or obese, there are lean PCOS subjects as well despite insulin resistance [24]. Due to the retrospective design of our study, we have done our evaluation regardless of the BMI of the patients in both the PCOS and control group. Even if it is assumed that a majority of the PCOS patients are obese, the PCOS group's average HU values were determined as 233.49±40.43 in our study, which is lower than the average of the control group (251.58±32.96) contrary to expected to be high due to obesity is a protective factor on bone metabolism hypothesis.

In a study involving PCOS subjects who were obese and normal weighted, it has shown that the lumbar BMD values in the PCOS group were lower than the control group, and also the BMD values in the group with normal weighted PCOS was lower compared to the control group but there was no difference between the obese PCOS group and the control group [17]. Parallel to this study, in our study, the BMD values in the PCOS group were found to be lower than the control group. In parallel to studies in which BMD was measured with DEXA and BMD was found to be lower in the PCOS group compared to the control group [4,18,25], in our study although there was no statistical significance out of L5 vertebra density values, it was shown that all vertebras' density values measured on CT images were lower than the control group. As these findings can point out that both there is no difference between the two groups in terms of BD and also the parameters such as BMI and hormonal values that we didn't evaluate might have an effect on this results.

The first limitations of our study were that due to the retrospective design of the study, we did not have information about the BMI states of the subjects and the control group. The second was that, since we used CT density measurements by opportunistic scans in the evaluation of BMD, due to the retrospective design of the study, our patient population was small because CT indication and CT scans were low in this age-group in which PCOS was seen. Despite the limited number of subjects, the strong side of our study was, this is the first study in which BMD was evaluated with lumbar vertebra density measurements on CT in PCOS subjects. In terms of understanding its effect on bone mineral density in PCOS, wide series of studies involving different age ranges and BMI values, considering laboratory data such as vitamin D, calcium, parathormone in which an effect on bone metabolism and hormonal data and DEXA and CT density values are compared is needed.

Conclusion

In conclusion, in this study, BMD was evaluated with abdominal CT images in PCOS patients for the first time and density of the vertebral corpora were found to be lower in PCOS than the control group for all vertebras. Even though there were no scanning method recommended to PCOS patients to evaluate BMD according to the current guidelines and literature, in the light of the results of our study, we think these patients should be investigated more carefully in especially advanced ages about bone mineral density.

Conflict of interest

The authors declare that there are no conflicts of interest.

Financial Disclosure

All authors declare no financial support.

Ethical approval

The study was approved by the local ethics committee.

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