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ORIGINAL ARTICLE

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Bone mineral density and mandibular osteoporotic alterations in type 2 diabetes

Densidade mineral óssea e alterações osteoporóticas na mandíbula em pacientes diabéticos do tipo 2

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ABSTRACT

Objective: To assess the influence of type 2 diabetes on bone mineral density in a group of type 2 diabetic patients, in comparison with non-diabetic patients. Additionally, to evaluate the correlation between mandibular cortical index and bone mineral density. **Material and Methods:** 48 patients (24 diabetics and 24 non-diabetics) referred for femur and spine densitometry and panoramic radiograph examination were included in this study. Patients were diagnosed based on densitometric results of the total femur and total spine. All panoramic radiomorphometric measurements were performed by 3 observers. Differences in T and Z-scores between both groups were evaluated with Mann-Whitney test and non-parametric correlations between mandibular cortical index and T/Z-scores were carried out with Spearman's test. **Results:** Median T and Z-scores for total femur and total spine presented no statistical significant difference between diabetic and non-diabetic patients. In addition, only diabetics total femur and non-diabetics total spine T-scores were significantly correlated with mandibular cortical index. **Conclusion:** The present results suggest that type 2 diabetic patients have similar Z and T-scores in femur and spine when compared to non-diabetic patients. Mandibular cortical index, assessed on panoramic radiographs is inversely correlated with femur densitometry results in diabetics and spine bone mineral density in non-diabetic patients.

KEYWORDS

Bone Mineral Density; Dual X-Ray Absorptiometry; Panoramic radiography; Osteoporosis; Type 2 Diabetes.

RESUMO

Objetivo: avaliar a influência do diabetes tipo 2 na densidade mineral óssea em um grupo de pacientes diabéticos do tipo 2, em comparação com pacientes não diabéticos. Adicionalmente, analisar a correlação entre o índice cortical mandibular e a densidade mineral óssea. **Material e Métodos:** 48 pacientes (24 diabéticos e 24 não diabéticos) que realizaram densitometria óssea de fêmur e coluna vertebral e exame radiográfico panorâmico foram incluídos neste estudo. Os pacientes foram diagnosticados com base nos resultados densitométricos do fêmur total e da coluna total. Por meio das radiografias panorâmicas, 3 observadores avaliaram o índice da cortical mandibular. Diferenças em T e Z scores entre os dois grupos foram avaliadas com o teste de Mann-Whitney e as correlações não paramétricas entre o índice cortical mandibular e os scores da densitometria foram verificadas por meio do teste de Spearman. **Resultados:** A mediana dos T e Z-scores para fêmur total e coluna total não apresentaram diferença estatisticamente significante entre diabéticos e não-diabéticos. Além disso, houve correlação significativa com o índice da cortical mandibular somente os T-scores de fêmur total do grupo de pacientes diabéticos e de coluna total dos paciente não-diabéticos. **Conclusão:** Os resultados deste estudo sugerem que pacientes diabéticos tipo 2 tem densidade mineral óssea aferida por meio de densitometria óssea do fêmur e coluna total semelhantes aos não-diabéticos. O índice cortical mandibular, avaliado em radiografias panorâmicas, foi inversamente correlacionado com os resultados da densitometria do fêmur em pacientes diabéticos e da densitometria de coluna total de pacientes não diabéticos.

PALAVRAS-CHAVE

Densidade mineral óssea; Radiografia panorâmica; Osteoporose; Diabetes do tipo 2; Densitometria óssea.

INTRODUCTION

Osteoporosis is a metabolic disease which affects bone mineral density (BMD) leading to increased low-energy fracture risk [1]. Type 1 and type 2 diabetes are recognized as potential modifier diseases to BMD and osteoporotic fracture risk [2]. However, the osteoporosis risk among diabetic patients remains unclear.

In type 1 diabetes, the full insulin deficiency and the osteoblast deficit are associated with the reduced BMD [3]. However, in type 2 diabetes, the disease physiopathology is unclear [4] and the consensus on osteoporosis risk in diabetic patients has not been reached. Studies considering BMD in diabetic patients provide distinct results [5]: some studies verified increase [6,7] in BMD but others decreased [8] or BMD no difference between type 2 diabetics and non-diabetic patients [9]. It is uncertain whether the usually named as "diabetic osteopathy" disease actually affects diabetic patients [10].

The gold-standard examination to detect BMD alterations is dual x-ray absorptiometry (DXA), which allows high precision BMD measurement using minimal radiation. However, DXA is not broadly accessible in many countries [11]. Notwithstanding, it is possible to investigate osteoporotic alterations in mandibular cortical bone by using radiomorphometric indexes on panoramic radiographs [12], frequently requested in clinical dentistry practice mainly in oral and maxillofacial area. Unlike DXA, panoramic radiograph is a low-cost and easily accessible examination.

One of the most studied radiomorphometric index is the "Mandibular Cortical Index" (MCI) which was developed to assess the endosteal margin of the mandibular cortex [13]. It is a qualitative analysis, and the endosteal margin is classified as C1, C2 or C3 according to the apparent intracortical bone erosion pattern presented. MCI is supported to be effective in screening patients at low BMD risk, and it is inversely correlated with BMD in many distinct populations [1,7,13] as well as in diabetic patients [7].

Thus, this study objective is to assess the influence of type 2 diabetes on total femoral and total spine BMD in a group of type 2 diabetes patients, in comparison with non-diabetic patients. Additionally, we also evaluate the correlation between MCI and BMD from femoral and spine skeleton sites.

MATERIALS AND METHODS

Study participants, inclusion and exclusion criteria

All patients willing to participate in this study signed an informed consent form. The guidelines of Helsinki were followed in this investigation. Approval was obtained from university's ethics committee (number FR358902).

This retrospective study was initially conducted with 64 patients, referred to dental treatment at the University dental clinic (São Paulo, São Paulo State, Brazil) who had undergone panoramic radiographic examination and femoral and spine DXA (at a private medical imaging clinic in the same city) between 2010 and 2014. From this initial sample, 9 patients who did not undergo panoramic radiographic examination and DXA on the same day or who had no technically acceptable radiographs were excluded.

Presence of other metabolic bone diseases (such as thyroid diseases), or history of medication intake affecting bone metabolism (such as glucocorticoids or bisphosphonate) were considered as exclusion criteria. Considering the aforementioned, 7 patients were excluded.

The final sample included 48 patients. Then, patients were classified as either diabetics or non-diabetics, according to clinical history file and confirmed with blood examinations, which included glycated hemoglobin measurements. A flow chart detailing the inclusion and exclusion criteria is available on Figure 1.

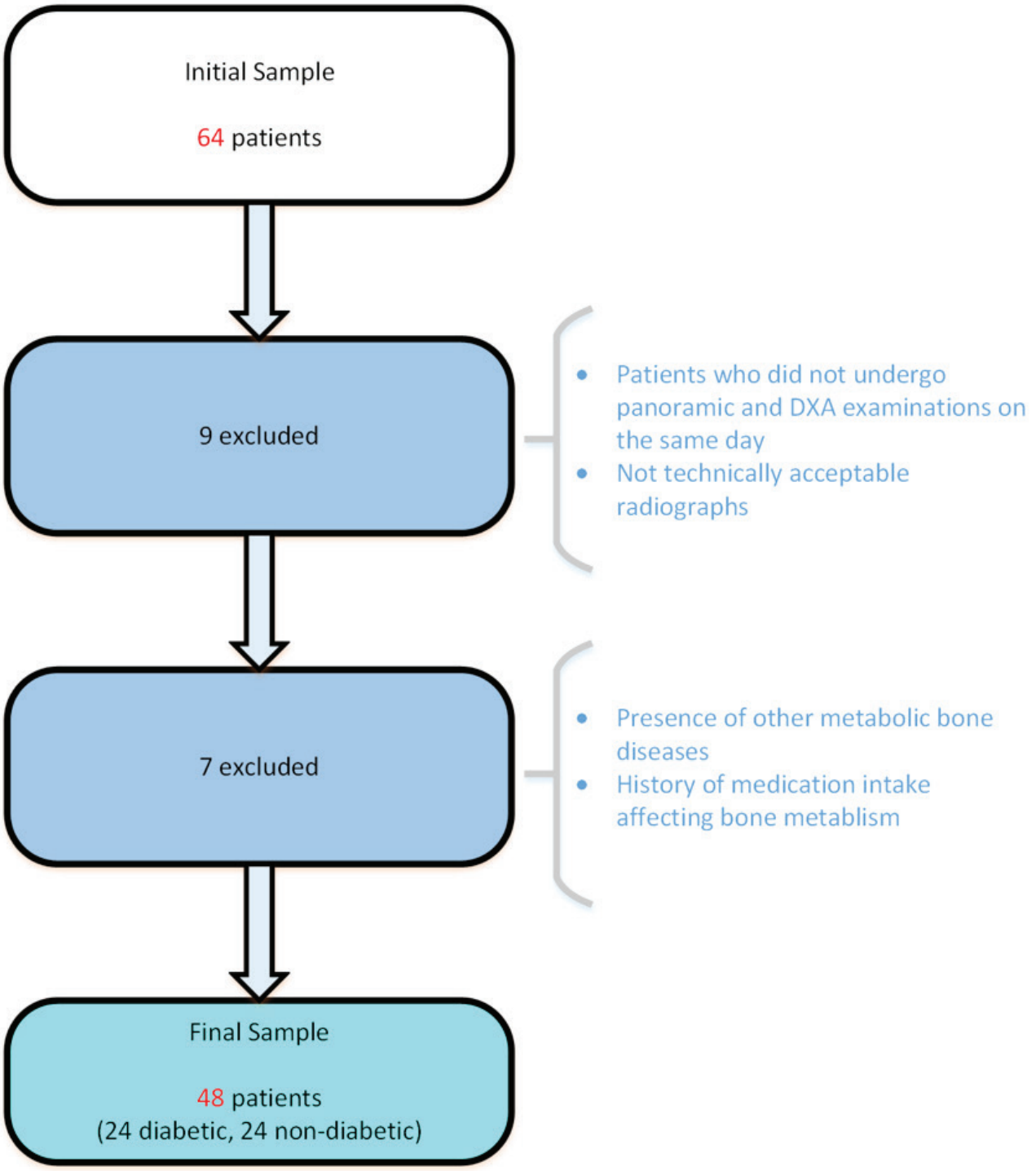

Figure 1 - Flow chart demonstrating inclusion and exclusion criteria.

Dual x-ray absorptiometry

Bone densitometry measurements were carried out with central dual energy X-ray absorptiometry (Hologic Discovery DXA system, Hologic Inc, Marlborough, MA, USA). The region of choice for scanning was the femur and spine. Patients were diagnosed based on BMD values of the total femur and total spine, measured according to World Health Organization (WHO) criteria, as normal (T score > -1.0), osteopenic (T score, -1.0 to -2.5) and osteoporotic (T-score ≤ -2.5 SD) [14]. Moreover, Z-score values were also recorded and used to classify the patients as either normal (Z score > 2) or with low bone density (Z score < 2).

Panoramic radiographs

All digital panoramic radiography images were taken using the same device (Kodak 8000 Digital Panoramic, Eastman Kodak Company, USA). All images were processed on the same software (ImageJ, National Institute of Health, Bethesda, MD, USA).

Mandibular Cortical Index (MCI)

The MCI was analysed by evaluating the appearance of the endosteal margin at the cortical bone below the mandibular foramen, using Klemetti classification [13]. The inferior mandibular cortex was classified as: C1 = normal, when presenting an even and sharp endosteal margin; C2 = moderately eroded, when presenting evidence of lacunar/linear resorption or endosteal cortical residues; and C3 = severely eroded, when porosity was markedly observed. All panoramic radiomorphometric measurements were performed in random order by three trained observers (i.e. dentists having expertise in oral radiology and previous experience with MCI classification). An example of MCI classification is available on Figure 2.

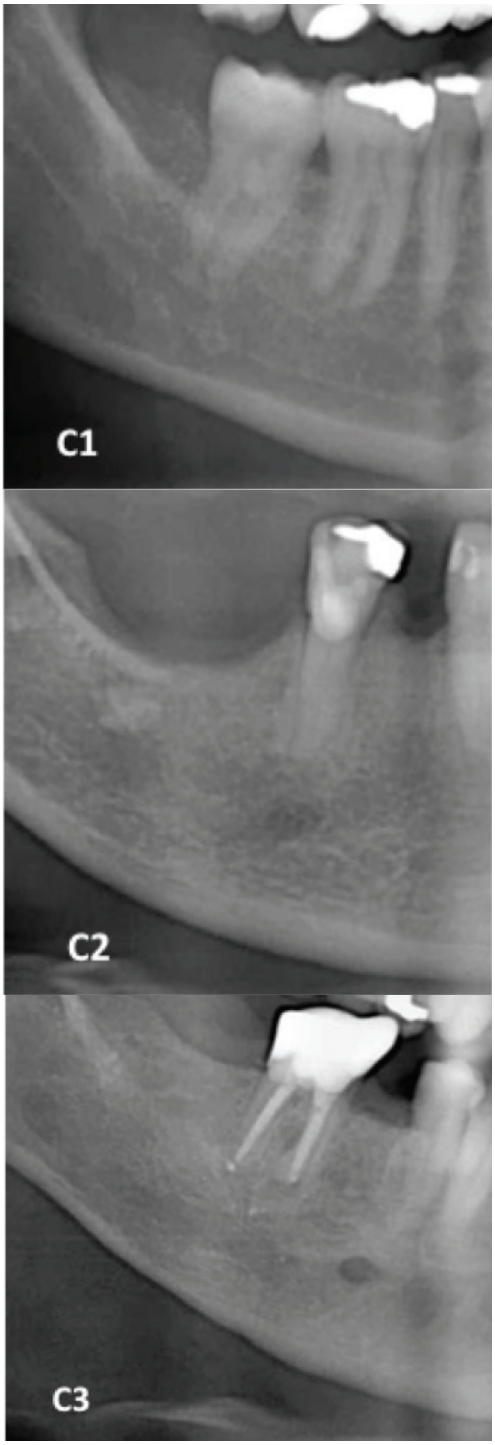

Figure 2 - Mandibular cortical index example: C1, C2 and C3 classifications.

Statistical Analysis

Intraobserver reliability was assessed between measurements performed 2 weeks apart to eliminate memory bias. Intra and interobserver agreement were assessed using the kappa test for MCI.

Normality was assessed for continuous variables using the Shapiro-Wilk test. Differences in T- and Z-scores between type 2 diabetic and non-diabetic patients were evaluated with the Mann-Whitney test. In addition, non-parametric correlations between MCI and T- and Z-scores were carried out with Spearman's test.

All statistical analyses were performed at a level of significance of 5%, using IBM SPSS Statistics 17, SPSS®, Inc, Chicago, IL.

RESULTS

A total of 48 patients was analysed, 24 non-diabetic and 24 diabetics (21 diabetic women; 21 non-diabetic women; 3 diabetic men and 3 non-diabetic men). None of the diabetic patients were insulin-dependent. Normality wasn't confirmed for MCI, T- and Z-scores, according to the Shapiro-Wilk test ($p<0.05$). Patients demographic data was described as median and interquartile range (IR) in Table 1.

Intraobserver reproducibility (kappa=0.82, 95% CI=0.76-0.89, $p<0.05$) and interobserver reliability were confirmed for MCI categorical measurements (kappa=0.80, 95% CI=0.74-0.87, $p<0.05$).

Median T-score values for total femur and total spine presented no statistically significant difference between diabetics and non-diabetics patients ($p=0.498$ and $p=0.642$ respectively, according to Mann-Whitney test), as presented in Figure 3.

Median Z-score values for total femur and total spine also presented no statistically significant difference between the two groups ($p=0.844$ and $p=0.842$ respectively, according to Mann-Whitney test). Figure 4 demonstrates Median Z-scores for total femur and spine in diabetics and non-diabetics patients.

In addition, only diabetic patient total femur T-score values was significantly correlated with MCI ($r=-0.554$, $p=0.05$) and non-diabetic total spine T-score values was significantly correlated with MCI. Non-parametric correlations results are available on Table 2. The two significant correlations found were also illustrated in Figures 5 and 6 (dispersion graphs considering T-scores and MCI).

Table 1 - Demographic data of the study. Number of participants, median age, bone mineral density, mandibular cortical index, total femur T and Z-scores, total spine T and Z scores

Group	Number of participants	Age (years)	BMI	MCI	Total Femur T-score	Total Spine T-score	Total Femur Z-score	Total Spine Z-score
Diabetics	24	67.00 (IR9.75)	29.27 (IR6.30)	2 (IR1)	-1.0 (IR1.48)	-1.3 (IR2.13)	0.2 (IR1.18)	0.0 (IR1.55)
Non-diabetics	24	69.50 (IR14.00)	27.65 (IR4.19)	2 (IR2)	-1.0 (IR1.85)	-1.5 (IR1.68)	0.35 (IR1.58)	0.30 (IR1.18)

Abbreviations: BMI: Bone Mass Index; MCI: Mandibular Cortical Index; IR: Interquartile Range.

Table 2 - Non-parametric correlations: MCI vs total femur and spine T/Z-scores of the participants, according to Spearman's test

Group	Femur T-score	Spine T-score	Femur Z-score	Spine Z-score
Diabetics	r = -0.554 p<0.001	r = -0.130 p = 0.546	r = -0.330 p = 0.115	r = 0.81 p = 0.707
Non-diabetics	r = -0.179 p = 0.403	r = -0.407 p = 0.049	r = 0.253 p = 0.233	r = -0.011 p = 0.961

* According to Spearman test, significant if $p<0.05$.

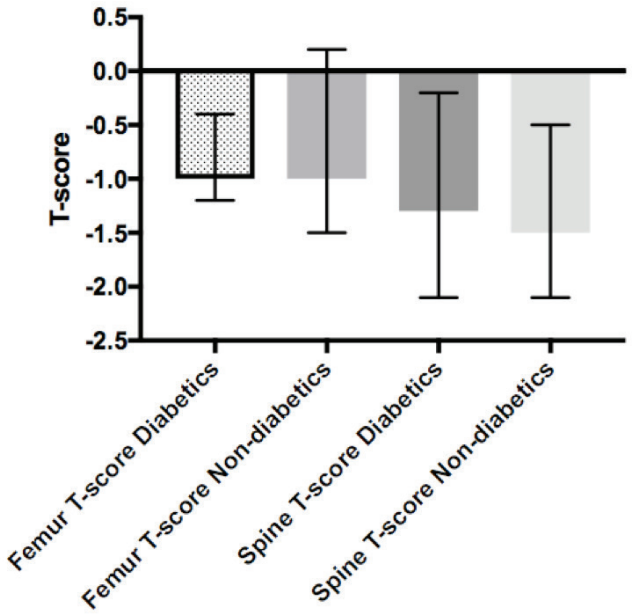

Figure 3 - Median T-score values: Total Femur and Total Spine in Diabetics and Non-diabetics.

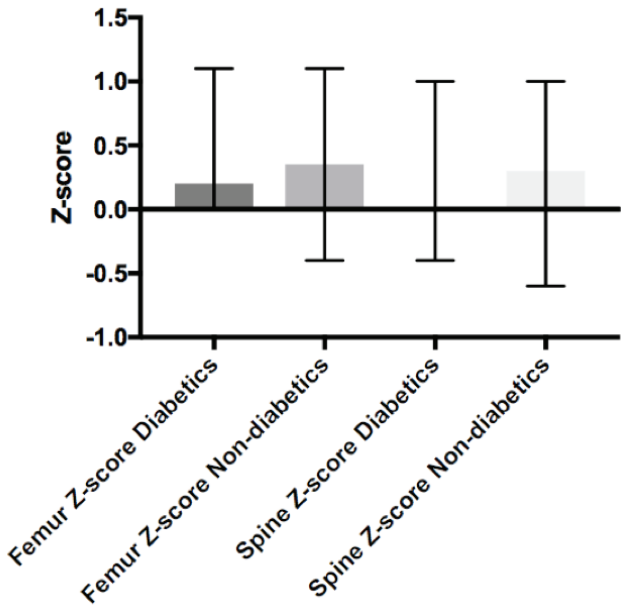

Figure 4 - Median Z-score values: Total Femur and Total Spine in Diabetics and Non-diabetics.

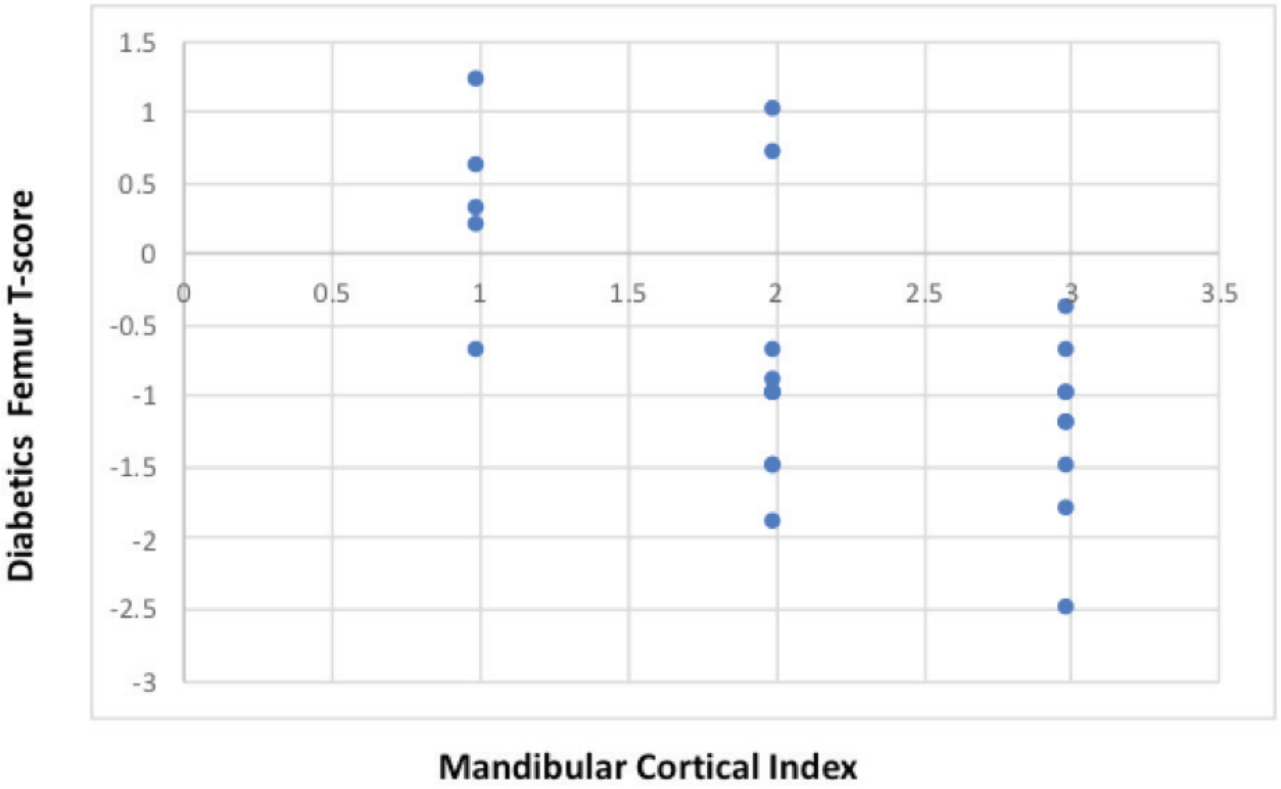

Figure 5 - Dispersion diagram representing the significant correlation found to Femoral T-scores in diabetic patients and MCI.

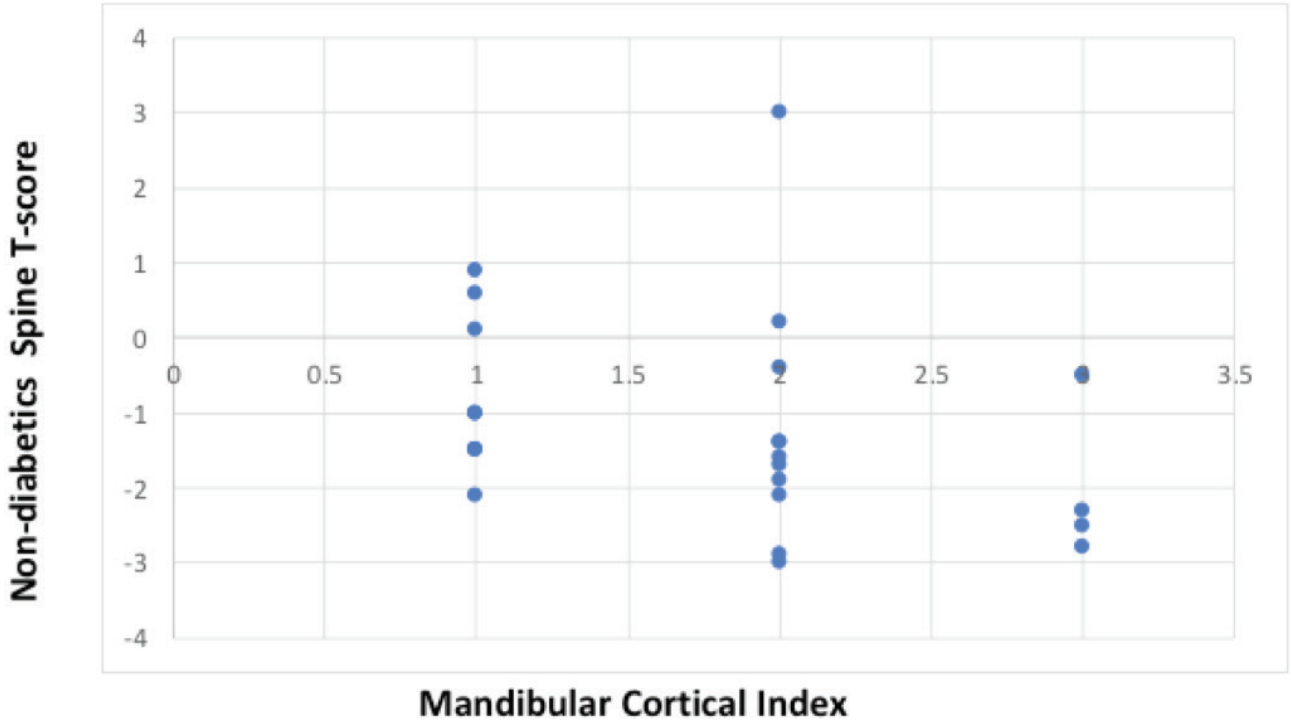

Figure 6 - Dispersion diagram representing the significant correlation found to Non-diabetic patients Spine T-scores and MCI.

DISCUSSION

In this study, we found no statistically significant differences between type 2 diabetic and non-diabetic patients in Z and T-scores at total femur and spine. Additionally, we have found an inverse correlation between total femur T-scores and MCI in diabetic patients. In non-diabetic patients, MCI was inversely correlated with spine T-scores.

The importance of assessing mandibular bone density, despite of the method applied, is appropriate prior to dental procedures such as treatment of periodontal diseases, osseointegrated implants or grafting [15], avoiding unsuitable post-procedures outcomes.

As aforementioned, there is an inconsistence about how type 2 diabetes influences BMD, due to the lack of information about the precise disease physiopathological mechanisms [15]. The disease usual feature is the altered glucose tolerance or impaired lipid associated to carbohydrate metabolism [15]. However, diabetes and osteoporosis are usually simultaneous conditions [16] and osteoporotic fractures are indeed more frequent in diabetic patients [5]. In type 2 diabetic patients, as previously observed, BMD might be increased [7,17,18] or even decreased [19,20] when compared to non-diabetics. In this study, type 2 diabetic patients showed a similar Z and T-score to non-diabetics, which is in agreement with preceding researches [21,22]. When considering only mandibular BMD measured by an appropriate DXA equipment, previous research found no statistically significant difference in BMD between diabetics and non-diabetics patients [15].

Possible reasons for this disagreement may not be related to osteoporosis itself, but other complications inherent to the diabetic condition, such as impaired eyesight, cerebral ischemia or inefficient balance resulting from neuropathy [16]. Furthermore, microvascular alterations may lead to reduced blood flow to the bones [16] and consequently affect bone remodeling.

Likewise, osteoporosis affects jawbones and results in visible modification in dental panoramic radiographs, these detectable modifications might potentially speed up periodontal bone resorption caused by periodontal disease [23]. Additionally, diabetes can also affect periodontal inflammatory diseases and, consequently, marginal bone loss. Periodontal diseases are worse among poorly controlled diabetic patients when compared to well-controlled diabetic patients or even non-diabetic individuals [24], essentially alveolar bone loss associated to periodontitis [25]. However, in diabetic patients with a good metabolic control, the degree of alveolar bone loss is similar than non-diabetic patients[26]; nevertheless, a peculiar result was found in another study which considered diabetes medication intake, and concluded that non-insulin dependent diabetic patients can have a more severe progression of alveolar bone loss when compared to health patients [27].

Notwithstanding, part of the divergence between results on the effects of type 2 diabetes on BMD may be as a consequence of heterogeneous study groups available in literature [9,15,28,29]. In this study, diabetic and non-diabetic groups were matched according to age, sex and body mass index (BMI).

Type 2 diabetes is routinely associated with overweight [30,31] and higher BMI is positively associated with BMD [32]. Nevertheless, overweight may be less protective against fractures than previously estimated [33,34] and recently it has been demonstrated that higher BMI did not modify BMD loss [2]. Ageing is also considered as an influencing factor for osteoporosis [35]: as the population ages, the number of individuals affected by the osteoporosis rises as well. We selected the matching non-diabetic group taking into account these arguments.

Albeit BMD is primarily measured by DXA, other imaging examinations, such as panoramic radiographs, have also been described as potential and reliable screening tools to screen patients at risk of low BMD [13]. As an additional objective of this study, we evaluated the correlation between MCI and DXA results. To our knowledge, this is the second study which correlates MCI with BMD in diabetic patients [7], but the first in identifying this correlation using total femur T-score results. Nonetheless, we have not found this correlation with total spine for diabetics and total femur for non-diabetic patients. The small sample size may be the reason for this lack of correlation. MCI has already been described as inversely correlated with BMD in other populations [1,13]. These results reinforce the affirmation that skeletal BMD reduction leads to alterations in mandibular BMD and shape [36,37], which can be detected by MCI.

The limitations of the present investigation are the small sample size and the retrospective design. Also, the lack of information about dietary conditions, time of diabetes diagnosis and glycated hemoglobin range. Larger population-based prospective investigations are recommended to verify the influence of type 2 diabetes on BMD, as well as to evaluate the correlation between MCI in distinct DXA skeleton sites.

CONCLUSION

In conclusion, the present results suggest that type 2 diabetic patients have similar Z and T-scores in total femur and spine when compared to non-diabetic patients. MCI, assessed on panoramic radiographs is inversely correlated with total femur DXA results in diabetic patients and spine in non-diabetic patients.

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