DOI: 10.4274/tod.galenos.2021.35403
Turk J Osteoporos 2022;28:125-30

The Effect of Type 2 Diabetes Mellitus on Osteopenia and Vertebral Fractures in Elderly Women

Tip 2 Diabetes Mellitusun İleri Yaş Kadınlarda Osteopeni ve Vertebral Kırıklar Üzerine Etkisi

Zeynep Koç

University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital, Clinic of Internal Medicine, İstanbul, Turkey

Abstract

Objective: In our study, we examined the effects of type 2 diabetes mellitus (DM) on the thoracic and lumbar vertebrae in patients with osteopenia.

Materials and Methods: Ninety patients had type 2 DM while 64 patients did not have any chronic disease. We analyzed the patients' total lumbar T-score with dual energy X-ray absorptiometry. We included patients with a T-score between -1 and -2.4 and evaluated the thoracic and lumbar vertebrae of the patients with dorsal and ventral X-ray imaging.

Results: In the results of the study in which we examined 154 osteopenic female patients, we found the mean osteopenia depth to be -1.52 in individuals with type 2 DM and -1.74 in the control group. We found the lumbar T value to be statistically significantly higher than the control group cases (p=0.001; p<0.01). However, the fracture rate was 21.9% in the control group, while it was 36.7% in type 2 DM. We found the fracture rate in patients with type 2 DM to be statistically significantly higher than that in the control group (p=0.049; p<0.05). In the control group, 64.3% of the fractures were grade 1, and 35.7% were grade 2, and there was no collapse fracture, while in the group with diabetes, we found grade 1 fractures 24.2%, grade 2 27.3%, and grade 3 collapse fractures 48.5%. Notably the incidence and severity of fractures was significantly higher than the control group, however, the lumbar T-score in the presence of type 2 DM was not as low as the control group in our study.

Conclusion: Although the lumbar T-score in the presence of the type 2 DM was not as low as the control group in our study, it is noteworthy that the incidence and severity of fractures was significantly higher than the control group.

Keywords: Osteopenia, elderly women, diabetes mellitus, vertebrael fracture

Öz

Amaç: Çalışmamızda osteopenili hastalarda tip 2 diabetes mellitusun (DM) torasik ve lomber vertebra üzerindeki etkilerini incelemeyi amaçladık.

Gereç ve Yöntem: Doksan hastada tip 2 DM varken 64 hastada herhangi bir kronik hastalık bulunmamaktaydı. Hastaların total lomber T-skoru dual-enerji X-ışını absorbsiyometri ile analiz edildi. Çalışmaya T-skoru -1 ile -2,4 arasında olan hastaları dahil edildi ve dorsal ve ventral X-ışını görüntüleme ile hastaların torasik ve lomber vertebraları değerlendirildi.

Bulgular: Osteopenik 154 kadın hastayı incelediğimiz çalışmanın sonuçlarında ortalama osteopeni derinliği tip 2 DM olan bireylerde -1,52, kontrol grubunda ise -1,74 olarak bulundu. Lomber T değeri kontrol grubu olgulara göre istatistiksel olarak anlamlı derecede yüksek bulundu (p=0,001; p<0,01). Ancak fraktür oranı kontrol grubunda %21,9 iken tip 2 DM'de %36,7 idi. Tip 2 DM'li hastalarda fraktür oranı kontrol grubuna göre istatistiksel olarak anlamlı derecede yüksek bulundu (p=0,049; p<0,05). Kontrol grubunda kırıkların %64,3'ü 1. derece, %35,7'si 2. derece olup kollaps kırığı yoktu, diyabetik grupta ise 1. derece fraktür %24,2, 2. derece fraktür %27,3 ve 3. derece fraktür %48,5 tespit edildi. Çalışmamızda fraktür insidans ve şiddetinin kontrol grubuna göre anlamlı derecede yüksek olması ancak tip 2 DM varlığında lomber T-skorunun kontrol grubu kadar düşük olmaması dikkat çekicidir.

Sonuç: Çalışmamızda tip 2 DM varlığında lomber T-skoru kontrol grubu kadar düşük olmasa da kırık insidansı ve şiddetinin kontrol grubuna göre anlamlı derecede yüksek olması dikkat çekicidir.

Anahtar kelimeler: Osteopeni, ileri yaş kadın, diabetes mellitus, vertebral fraktür

Address for Correspondence/Yazışma Adresi: Zeynep Koç MD, University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital, Clinic of Internal Medicine, İstanbul, Turkey
Phone: +90 537 207 95 63 **E-mail:** zynpkoc000@gmail.com **ORCID ID:** orcid.org/0000-0002-1393-4561
Received/Geliş Tarihi: 09.08.2021 **Accepted/Kabul Tarihi:** 26.10.2021

Introduction

The World Health Organization (WHO) defines a T-score between -1 and -2.5 as osteopenia. With the aging of the population and the prolongation of life expectancy, osteoporosis and osteopenia are emerging as more critical health problems. In the FRACTURK (1) study, the prevalence of osteoporosis in Turkey was 25% over the age of 50, while the prevalence of osteopenia was 50%. The United States expects the cost of care for direct and indirect fragility fractures to exceed $25 billion by 2025 (2). Osteopenia was shown to increase the risk of high fractures in many studies (3,4), just like in osteoporosis, and the risk of osteopenic and osteoporotic fractures is high, especially in elderly women (3). Fragility fractures are fractures that occur as a result of mechanical force, known as trauma with energy too low to normally cause a fracture. This mechanical power is the force equivalent to falling from standing height according to WHO (5). In the TURDEP 2 (6) study, the prevalence of diabetes in our population was 16.5%. Osteopenia isalso associated with type 2 diabetes mellitus (DM); however, the pathogenesis of diabetic osteopenia is unclear. In an experimental study evaluating bone mineral density (BMD) by dual energy X-ray absorptiometry (DEXA), bone metabolism in rats was evaluated 120 days later. In the study, the femoral trabecular distance increased approximately 3 times in rats with plasma glucose above 250 mg/dL compared to the non-diabetic control group, and the trabecular thickness decreased by 2 times and the bone trabecular volume by 77% (7). Type 2 DM increases the risk of fracture, and risk assessment is challenging in these individuals because BMD is often underestimated. Low bone turnover, accumulation of advanced glycation end products, and changes in bone micro and macro architecture impair bone strength and mass. Diabetic patients with impaired glycemic regulation, length of disease duration, -cell damage, and insulin therapy are at highest risk of fracture. Diabetes-induced complications such as sarcopenia, neuropathy, oculomotor problems, and frequent hypoglycemic episodes increase the risk of falling and the incidence of fractures (8). It was shown that white women with type 2 DM lose more BMD per year on average compared to acontrol group (9); however, post-fracture recovery is also impaired in these patients (10). Type 2 DM, metabolic bone diseases, including low BMD, fractures and falls in geriatric patients were associated with other bone-related events (11). Diabetes not only exacerbates low BMD but also causes osteopenia and osteoporosis (12). Mathen et al. (13) showed that BMD was significantly lower in both the lumbar vertebra and femoral neck in indians with type 2 DM compared to the control group and concluded that diabetes is an "overlooked complication" for osteopenia and osteoporosis.

Purpose of the Study

Fracture presence and degrees were compared by evaluating the lumbar T-score and thoracic and lumbar vertebrae in elderly osteopenic diabetic patients and patients with osteopenia who do not have any chronic disease. We evaluated whether the severity of osteopenia, frequency of fracture, and degree of fracture were higher in type 2 DM compared to the control group. In our study, the plan was to investigate how much attention should be paid to osteopenia in individuals with diabetes and how much antiresorptive therapy is required in the diabetic osteopenic population.

Materials and Methods

A total of 154 female patients aged between 48 and 74 years treated in the internal medicine outpatient clinic of a secondary health care institution were included. Cases were reviewed retrospectively. A total of 90 patients had type 2 DM, while 64 patients did not have any chronic disease. We analyzed the patients' total lumbar T-score with lunar DPX-L DEXA. The entire study was performed on patients evaluated with the same device. Patients with a T-score between -1 and -2.4 were included and the thoracic and lumbar vertebrae of the patients were evaluated with dorsal and lateral X-ray imaging. The presence of vertebral fractures in patients was examined and if present, fracture level was determined. The criterion by which Genant et al. (14) categorized vertebral fractures by fracture level was used. Mild fracture wascharacterized by the concavity of the vertebra and evaluated as stage 1 fracture, moderate fracture wascharacterized by wedging of the vertebra and evaluated as a stage 2 fracture, and severe fracture wascharacterized by vertebral crushing and collapse and evaluated as stage 3 fracture. The presence of vertebral osteophytes was excluded. Patients who exceeded the osteoporosis threshold and had a T-score of -2.5 and above were excluded from the study. Patients with diagnosis of osteoporosis and those receiving osteoporosis treatment were excluded from the study. The cases without major or minor trauma and the presence of fracture due to osteopenia were evaluated during outpatient follow-up. Medications used by patients were reviewed retrospectively. Patients who used antiepileptics, pioglitazone, anticoagulants, furosemide, glucocorticoids, and levothyroxine were excluded from the study because adequate standardization could not be achieved. Patients with hyperthyroidism, primary hypothyroidism, diagnosed with type 1 DM, malignancy disease, with rheumatic disease and using chronic steroids were excluded. We examined the fracture frequency, severity, and osteopenia severity in type 2 diabetic patients and the group without any chronic disease. Patients who were followed up due to the presence of metabolic bone diseases such as osteopetrosis and osteomalacia were excluded from the study. Patients with diabetic nephropathy were excluded because the presence of low glomerular filtration rate may affect bone metabolism at various levels.

Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee approval was obtained (decision no: 2021/514/200/2, date: 28.04.2021).

Statistical Analysis

Number cruncher statistical system 2007 (Kaysville, Utah, USA) program was used for statistical analysis. Descriptive

statistical methods (mean, standard deviation, median, frequency, percentage, minimum, maximum) were used when evaluating study data. Conformity of quantitative data to normal distribution was examined with the Shapiro-Wilk test and graphical examinations. The Mann-Whitney U test was used for comparisons between two groups of normally distributed and non-normally distributed quantitative variables. The Pearson chi-square test and Fisher-Freeman-Halton exact test were used to compare qualitative data. Statistical significance was accepted as $p<0.05$.

Results

Diabetes was observed in 58.4% (n=90) of the cases (Table 1).
Lumbar T measurements forthe cases ranged from -2.4 to -1.5, and the mean was -1.62±0.55.

Fractures were present in 30.5% of the cases (n=47). The fracture severity was grade 1 in 36.2% (n=17), grade 2 in 29.8% (n=14), and grade 3 in 34% (n=16) of the cases with fracture. When the fracture frequencies of the cases with fractures were examined, 36.2% (n=17) of the cases had concave, 29.8% (n=14) had wedge, and 34% (n=16) had crush fractures (Table 2).
The lumbar T value of patients with diabetes was statistically significantly higher than those in the control group. (p=0.001; p<0.01) (Figure 1).
The rate of fracture in patients with diabetes was statistically significantly higher than in the control group (p=0.049; p<0.05) (Figure 2).
No statistically significant difference was found between the diagnoses of the cases according to sex (p=0.004; p>0.01). Fracture frequencies of the cases in the DM group were

Table 1. Distribution of findings

n (%)		
Group	Control group	64 (41.6)
	DM's	90 (58.4)
Lumbar T	Mean ± SD	-1.62±0.55
	Median (min-max)	-1.6 (-2.4-1.5)
Fracture	No	107 (69.5)
	Exist	47 (30.5)
Fracture severity	Grade 1	17 (36.2)
	Grade 2	14 (29.8)
	Grade 3	16 (34)
Fracture frequency	Concave	17 (36.2)
	Wedge	14 (29.8)
	Crush	16 (34)

DM: Diabetes mellitus, SD: Standard deviation, min: Minimum, max: Maximum

Table 2. Comparisons by group

		Group		**p**
		DM's control group	**Control group**	
Lumbar T	Mean ± SD	-1.53±0.54	-1.74±0.54	[a]0.001**
	Median (min-max)	-1.4 (-2.4-1.4)	-1.8 (-2.4-1.4)	
Fracture	No	57 (63.3)	50 (78.1)	[b]0.049*
	Exist	33 (36.7)	14 (21.9)	
Fracture severity	Grade 1	8 (24.2)	9 (64.3)	[c]0.004**
	Grade 2	9 (27.3)	5 (35.7)	
	Grade 3	16 (48.5)	0 (0)	
Fracture frequency	Concave	8 (24.2)	9 (64.3)	[c]0.004**
	Wedge	9 (27.3)	5 (35.7)	
	Crush	16 (48.5)	0 (0)	

DM: Diabetes mellitus, SD: Standard deviation, min: Minimum, max: Maximum. [a]Mann-Whitney U test , [b]Pearson chi-square test, [c]Fisher Freeman Halton test, *p<0.05, **p<0.01

significantly lower than those in the control group. The incidence of grade 2 and grade 3 fractures was significantly higher in the type 2 DM group (Figure 3).

Discussion

Fractures can occur in osteopenic patients, just like osteoporotic patients (15). While the rate of vertebral fractures in women over 50 in the general population is between 20-30%, this rate is 40% over the age of 80. In our study, vertebral fractures were identified in 30.5% of all patients, and this result is consistent with literature data.

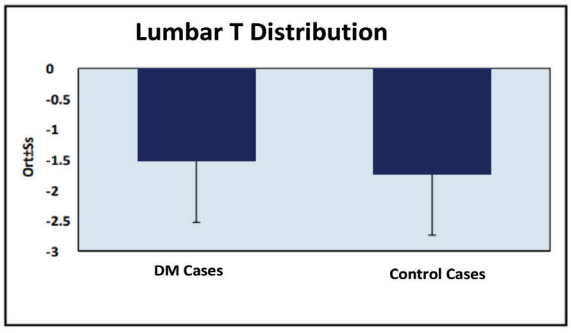

Figure 1. Lumbar T distribution by group
DM: Diabetes mellitus

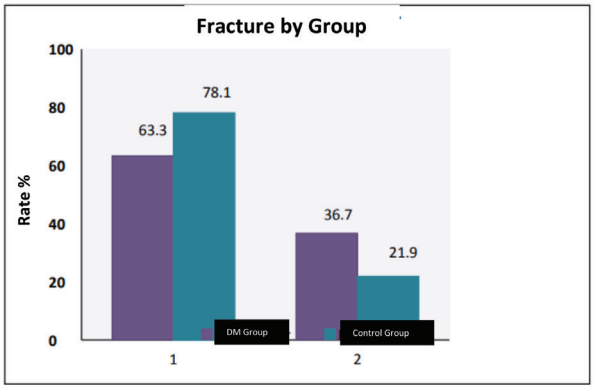

Figure 2. Fracture distribution by group
DM: Diabetes mellitus

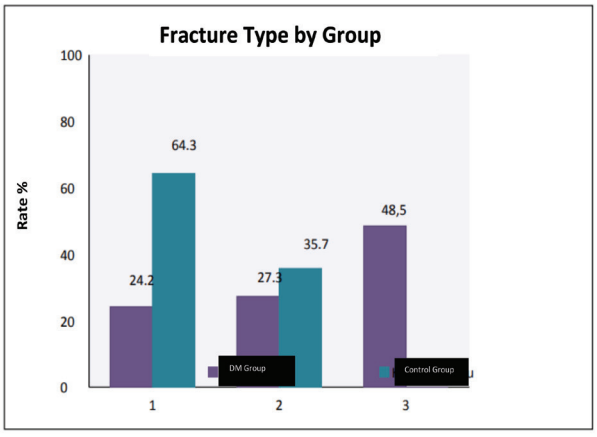

Figure 3. Distribution of fracture type by group
DM: Diabetes mellitus

There are studies showing that BMD is severely decreased in patients with uncontrolled type 2 DM (16,17). Yaturu et al. (18) found significantly deeper BMD in type 2 DM when they compared 2 groups in the same age group. Asokan et al. (19) showed an inverse correlation between the duration of diabetes and glycemic control with BMD. At the same time, the incidence of osteopenia was higher in the control group in this study and in 3 different studies conducted by Sosa et al. (20) and Wakasugi et al. (21). Petit et al. (22) reported better BMD values in elderly patients with type 2 DM compared to the same age group without chronic disease. In our study, when the patients with type 2 DM and the control group were compared forseverity of osteopenia, the severity of osteopenia was higher in the control group. While the mean T-score was -1.53 in the diabetic group, it was -1.74 in the control group. Contrary to the general literature and our initial expectations, BMD was better in individuals with type 2 DM. Our result, like the result by Petit et al. (22), gave a positive result for the T-score in favor of the group with diabetes. While there are studies reporting a lower incidence of fractures in patients with type 2 DM (23,24), there are also studies that correlate it with a high fracture risk (25). Jain et al. (26) also showed that the development of lumbar vertebral fracture increases if the T-score in diabetic osteoporosis and osteopenia falls below -1.5. Vestergaard (27) reported an increased risk of fracture in many regions, including the vertebrae and the femur. In our study, the incidence of fracture in the control group was 21.9%, while it was 36.7% in the diabetic group. While grade 1 fractures were more common in the control group, grade 2 and grade 3 fractures were significantly higher in the diabetic group. While the lumbar T-score gave a more positive result in the diabetic group, it is surprising that the incidence and overall severity of fractures were significantly higher in this group. While the incidence and severity of fractures are expected to be higher in the group with a lower T-score, the result is outside of expectations. This result leads to the consideration that there may be other factors that affect the development of fracture in diabetics besides BMD. However, the literature data aboutthis condition is limited and the pathogenesis of diabetic osteopenia is not clear. While osteoporosis is better known and treatable in the general population, osteopenic patients cannot benefit from antiresorptive treatments unless fracture assessment is performed. The FRACTURK study (1) showed the prevalence of osteopenia was twice that of osteoporosis in our population. In our study, in which patients with type 2 DM a type of chronic disease were evaluated, in the osteopenic groupthe results show that silent fractures can accompany type 2 DM more frequently compared to the control group, even with more positive T-score results. It was shown that when type 2 DM and osteopenia are comorbid, osteopenia progresses more catastrophically and fractures heal later.

Patients using pioglitazone, one of the thiazolidinedione group oral antidiabetic agents known to cause osteoporosis and osteopenia in type 2 DM cases, were excluded because adequate standardization could not be achieved. Other oral antidiabetic agents have no osteopenic effect.

When compared with the decrease in the treatment response with the progression of osteopenia accompanying fractures to osteoporosis and the cost of fractures due to the decrease in BMD, taking the necessary precautions and providing antiresorptive treatment for osteopenic fractures are cost-effective. Our study showed that diabetic osteopenics should be evaluated further in terms of fractures. If fractures are detected by X-ray evaluation of thoracic and lumbar vertebrae, antiresorptive treatment should be arranged immediately.

Since our study is retrospective, the inability to evaluate body mass index and the inability to make inquiries about smoking, alcohol use and caffeine consumption are limitations of our study.

Conclusion

Type 2 DM and osteopenia often accompany each other. Osteopenia is thought to be an "overlooked complication" of type 2 DM, but the underlying mechanism has not been elucidated. Studies show that diabetic patients with BMD values of -1 and below should be screened for fractures. In our study, although the severity of osteopenia was not as bad as the control group, it seems that the frequency of fractures is unexpectedly higher in diabetic individuals with higher T-scores. The presence of fracture should be investigated considering that the vertebrae of these patients are evaluated with X-rays and the healing of osteopenic fracture is impaired and delayed in type 2 DM. If we take into account the progression to osteoporosis and various mortality and morbidities if left untreated, detecting fractures in the osteopenic group and arranging antiresorptive treatment will be cost-effective. The aging population, long life expectancies, and increasing frequency of these problems are becoming increasingly crucial. The presence of diabetes should be an alarming finding especially in the osteopenic group in terms of the presence of vertebral fractures and fractures that can be detected in these patients should not be missed.

Ethics

Ethics Committee Approval: Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee approval was obtained (decision no: 2021/514/200/2, date: 28.04.2021).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Financial Disclosure: The author declared that this study received no financial support.

References

1. Tuzun S, Eskiyurt N, Akarirmak U, Saridogan M, Senocak M, Johansson H, et al. Turkish Osteoporosis Society. Incidence of hip fracture and prevalence of osteoporosis in Turkey: the FRACTURK study. Osteoporosis Int 2012;23:949-55.
2. Burge R, Dawson-Hughes B, Solomon DH, Wong JB, King A, Tosteson A. Incidence and economic burden of osteoporosis-related fractures in the United States, 2005-2025. J Bone Miner Res 2007;22:465-75.
3. Khosla S, Melton LJ 3rd. Clinical practice. Osteopenia. N Engl J Med 2007;356:2293-300.
4. Pasco JA, Seeman E, Henry MJ, Merriman EN, Nicholson GC, Kotowicz MA. The population burden of fractures originates in women with osteopenia, not osteoporosis. Osteoporos Int 2006;17:1404-9.
5. Papaioannou A, Morin S, Cheung AM, Atkinson S, Brown JP, Feldman S, et al. 2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary. CMAJ 2010;182:1864-73.
6. Satman I, Omer B, Tutuncu Y, Kalaca S, Gedik S, Dinccag N, et al. Twelve-year trends in the prevalence and risk factors of diabetes and prediabetes in Turkish adults. Eur J Epidemiol 2013;28:169-80.
7. Duarte VM, Ramos AM, Rezende LA, Macedo UB, Brandão-Neto J, Almeida MG, et al. Osteopenia: a bone disorder associated with diabetes mellitus. J Bone Miner Metab 2005;23:58-68.
8. Napoli N, Chandran M, Pierroz DD, Abrahamsen B, Schwartz AV, Ferrari SL, et al. Mechanisms of diabetes mellitus-induced bone fragility. Nat Rev Endocrinol 2017;13:208-19.
9. Schwartz AV, Sellmeyer DE, Strotmeyer ES, Tylavsky FA, Feingold KR, Resnick HE, et al. Diabetes and bone loss at the hip in older black and white adults. J Bone Miner Res 2005;20:596-603.
10. Schurman L, McCarthy AD, Sedlinsky C, Gangoiti MV, Arnol V, Bruzzone L, et al. Metformin reverts the deleterious effects of advanced glycation end-products (AGEs) on osteoblastic cells. Exp Clin Endocrinol Diabetes 2008;116:333-40.
11. Brown SA, Sharpless JL. Osteoporosis: an under-appreciated complication of diabetes. Clin Diabetes 2004;22:10-20.
12. Hamilton EJ, Rakic V, Davis WA, Chubb SA, Kamber N, Prince RL, et al. Prevalence and predictors of osteopenia and osteoporosis in adults with Type 1 diabetes. Diabet Med 2009;26:45-52.
13. Mathen PG, Thabah MM, Zachariah B, Das AK. Decreased Bone Mineral Density at the Femoral Neck and Lumbar Spine in South Indian Patients with Type 2 Diabetes. J Clin Diagn Res 2015;9: OC08-12.
14. Genant HK, Wu CY, van Kuijk C, Nevitt MC. Vertebral fracture assessment using a semiquantitative technique. J Bone Miner Res 1993;8:1137-48.
15. Siris ES, Chen YT, Abbott TA, Barrett-Connor E, Miller PD, Wehren LE, et al. Bone mineral density thresholds for pharmacological intervention to prevent fractures. Arch Intern Med 2004;164:1108-12.
16. Gregorio F, Cristallini S, Santeusanio F, Filipponi P, Fumelli P. Osteopenia associated with non-insulin-dependent diabetes mellitus: what are the causes? Diabetes Res Clin Pract 1994;23:43-54.
17. Krakauer JC, McKenna MJ, Buderer NF, Rao DS, Whitehouse FW, Parfitt AM. Bone loss and bone turnover in diabetes. Diabetes 1995;44:775-82.
18. Yaturu S, Humphrey S, Landry C, Jain SK. Decreased bone mineral density in men with metabolic syndrome alone and with type 2 diabetes. Med Sci Monit 2009;15:CR5-9.
19. Asokan AG, Jaganathan J, Philip R, Soman RR, Sebastian ST, Pullishery F. Evaluation of bone mineral density among type 2 diabetes mellitus patients in South Karnataka. J Nat Sci Biol Med 2017;8:94-8.
20. Sosa M, Dominguez M, Navarro MC, Segarra MC, Hernández D, de Pablos P, et al. Bone mineral metabolism is normal in non-insulin-dependent diabetes mellitus. J Diabetes Complications 1996;10:201-5.

21. Wakasugi M, Wakao R, Tawata M, Gan N, Koizumi K, Onaya T. Bone mineral density measured by dual energy x-ray absorptiometry in patients with non-insulin-dependent diabetes mellitus. Bone 1993;14:29-33.
22. Petit MA, Paudel ML, Taylor BC, Hughes JM, Strotmeyer ES, Schwartz AV, et al. Bone mass and strength in older men with type 2 diabetes: the Osteoporotic Fractures in Men Study. J Bone Miner Res 2010;25:285-91.
23. Forsén L, Meyer HE, Midthjell K, Edna TH. Diabetes mellitus and the incidence of hip fracture: results from the Nord-Trøndelag Health Survey. Diabetologia 1999;42:920-5.
24. Kwon DJ, Kim JH, Chung KW, Kim JH, Lee JW, Kim SP, et al. Bone mineral density of the spine using dual energy X-ray absorptiometry in patients with non-insulin-dependent diabetes mellitus. J Obstet Gynaecol Res 1996;22:157-62.
25. Yamamoto M, Yamaguchi T, Yamauchi M, Kaji H, Sugimoto T. Diabetic patients have an increased risk of vertebral fractures independent of BMD or diabetic complications. J Bone Miner Res 2009;24:702-9.
26. Jain RK, Lee E, Mathai C, Dako F, Gogineni P, Weiner MG, et al. Using opportunistic screening with abdominal CT to identify osteoporosis and osteopenia in patients with diabetes. Osteoporosis Int 2020;31:2189-96.
27. Vestergaard P. Discrepancies in bone mineral density and fracture risk in patients with type 1 and type 2 diabetes–a meta-analysis. Osteoporos Int 2007;18:427-44.