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BONE PROBLEMS DURING DIABETES MELLITUS

Abstract

The skeleton is recognized as an last damaged organ in diabetes. The effects of diabetes on bone are complex and an area of active investigation. While most studies demonstrate that fracture risk is increased in both type 1 and type 2 diabetes, bone mineral density (BMD), as measured by dual-energy x-ray absorptiometry (DXA), may not reflect bone fragility or accurately predict fracture risk.

This is particularly true in individuals with type 2 diabetes, in whom BMD is often normal or elevated compared with those without the disease.

Keywords: *bone, diabetes mellitus, fracture, hyperostosis*

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Şəkərli diabet zamanı sümük problemləri

Xülasə

Skelet diabetdə ən son zədələnmə yeri kimi tanınır. Diabetin sümüklərə təsiri mürəkkəbdir və aktiv araşdırma sahəsidir. Əksər tədqiqatlar həm 1-ci, həm də 2-ci tip diabetdə sınıq riskinin artdığını nümayiş etdirsə də, ikili enerjili rentgen absorbsiometriyası ilə ölçülən sümük mineral sıxlığı sümük kövrəkliyini əks etdirməyə və ya sınıq riskini dəqiq proqnozlaşdıra bilməz.

Bu göstərici xüsusilə 2-ci tip diabetli insanlar üçün doğrudur, onların sümük mineral sıxlığı adətən ya normal olur, ya da xəstəliyi olmayanlarla müqayisədə yüksəkdir.

Açar sözlər: *sümük, şəkərli diabet, sınıq, hiperostoz*

Introduction

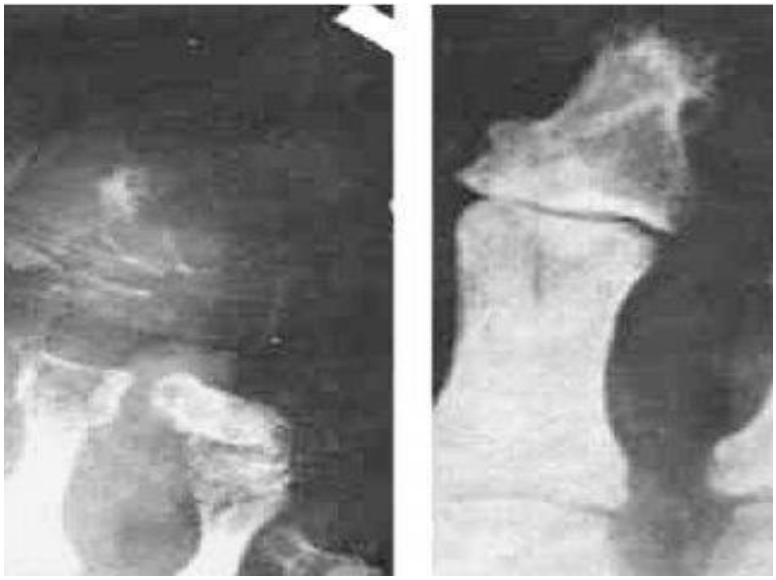
The osteoarticular complications of diabetes remain poorly understood, especially at the molecular level. They can be caused by changes in bone and connective tissue, joints and include osteopenia (in both children and adults), hyperostosis, osteoarthritis, rheumatoid arthritis, osteolysis, diabetic scleroderma, Dupuytren's disease, stiff hand syndrome, carpal tunnel syndrome, flexion synovitis (trigger finger syndrome, or stenosing ligamentitis), adhesive capsulitis, or frozen.

Osteolysis shoulder syndrome, a syndrome of limited joint mobility, which may be a marker of the risk of developing other complications of diabetes (Starup-Linde, Vestergaard, 2015: 99).

It is generally accepted that osteopenia, or decreased bone mineral density, occurs in diabetes mellitus. Secondary osteoporosis caused by diabetes, known as “diabetic bone disease”, can lead to long-term bone pain and impaired mobility in patients, increasing the risk of disability and disability.

The influence of both type - 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM)on the increased risk of bone fractures is undisputed, but the mechanisms of this influence are different. T1DM is characterized by almost complete insulinopenia (extremely low concentration of insulin in the blood),

which affects the anabolic tone of bones and leads to a decrease in their mineral density (Aung, Amin, Gulraiz, Gandhi, Pena, Malik, 2020:12). Whereas patients with T2DM in most cases have normal or even high bone mineral density, and their risk of fractures is due to changes in bone microarchitecture and the local humoral environment, which stimulates the activity of osteoclasts (cells that perform the function of destroying bone tissue) (Diabetes Atlas, 2021).

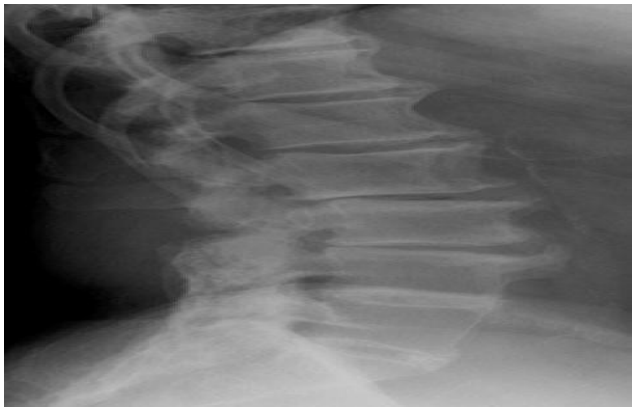


There is growing evidence that the high risk of fractures in T2DM is due to poor bone quality, despite high bone mineral density. Some authors call these disorders diabetic osteopathy (Napoli, Chandran, Pierroz, Abrahamsen, Schwartz, Ferrari, 2017:219).

It becomes obvious that the increased risk of fractures in patients with T2DM is due to a combination of factors, in particular, changes in bone metabolism, disruption of bone microarchitecture, accumulation of end products of gilding, muscle weakness, antidiabetic therapy and some other reasons.

According to the medical literature, diffuse idiopathic skeletal hyperostosis occurs in 25% of patients with diabetes, while in the general population its prevalence is about 2-4% (Si, Wang, Guo, Xu, Ma, 2019:48).

Experts associate the combination of type 2 diabetes mellitus and diffuse idiopathic skeletal hyperostosis with an increase in bone mineral density (Sato, Ye, Sugihara, Isaka, 2016:17). The pathological process may involve the spine, skull, pelvic bones, calcaneus and ulna. Patients may note mild stiffness when getting up in the morning, although the spine remains mobile. About a third of patients with hyperostosis due to diabetes develop heel and elbow pain due to heel and elbow spurs (Wang , Ba Y, Xing Q, Du, 2019:19).



Idiopathic spinal hyperostosis

The etiology of hyperostosis in diabetes mellitus is unclear. Its manifestations are fundamentally different from ankylosing spondylitis, which occurs at a younger age and causes more serious problems associated with morning stiffness and a disabling loss of spinal mobility (Kanazawa, Sugimoto, 2018: 57).

Type 2 diabetes mellitus can be combined with osteoarthritis due to a common pathogenetic factor, which is excess body weight.

Osteolysis (also known as diabetic osteopathy) of the forefoot is considered to be localized or generalized osteoporosis of the distal metatarsals and proximal phalanges. The severity of the pain syndrome varies, and erythema over the affected joint can be mistaken for phlegmon or osteomyelitis. Periarticular erosions may resemble manifestations of rheumatoid arthritis and gout (Poiana, Capatina, 2019: 15). The etiology of this bone lesion is unknown, and restoration of bone structure usually occurs spontaneously.

Other osteoarticular disorders are caused by connective tissue pathology that develops in patients with diabetes (Yoshida, Okumura, Aso, 2005: 54).

According to research, in almost 40% of patients, diabetes mellitus is combined with Dupuytren's disease (DD), a subcutaneous fibrosis of the palmar-aponeurotic space of the hands. Researchers from Finland found that the prevalence of BD is similar in T1DM and T2DM (~14%), but in T1DM the disease tends to manifest at a younger age (Grandhee, Monnier, 1991: 26). Dupuytren's disease (Dupuytren's contracture), which occurs in patients with diabetes, differs from the course of palmar aponeurosis disease in nondiabetic patients. Thus, patients with diabetes mellitus are less likely to experience contractures of the fingers that require surgical treatment. It is interesting to note that when Dupuytren's disease develops in people with diabetes, the third and fourth fingers are predominantly affected (without diabetes, the fourth and fifth fingers are affected).

Diabetes mellitus is the most common comorbidity with carpal tunnel syndrome. Carpal tunnel syndrome is caused by compression of the median nerve in the carpal tunnel and causes paresthesia of the thumb, index and little fingers with pain that is often worse at night. In diabetic patients, carpal tunnel syndrome may not simply be caused by nerve compression, but may also be a manifestation of diabetic neuropathy with reduced conduction of both the median and ulnar nerves. In addition to the typical atrophy of the thenar muscles of the hand, there is atrophy of the intrinsic and hypothenar muscles. Contractures of the metacarpophalangeal and proximal interphalangeal joints of all fingers develop equally.

The next joint pathology is flexor tenosynovitis, also known as trigger finger, trigger finger, and stenosing tenovaginitis. In adult patients, one third of multiple flexor tenosynovitis is associated with diabetes. In addition, among patients there is a predominance of women, as well as a tendency to affect the right hand and the predominant involvement of the thumb, middle and ring fingers in the pathological process. Fibrous tissue grows in the tendon sheath, especially where the tendon is narrowed as it passes through the annulus fibrosus (annular ligament). A palpable or audible click may be present when the finger is extended. When the finger is flexed or extended, the tendon becomes blocked as it passes through the thickened segment of the tendon sheath (Ferrari, Abrahamsen, Napoli, 2018: 29).

In patients with diabetes mellitus, frozen shoulder syndrome, or adhesive capsulitis of the shoulder, and shoulder-arm syndrome occur somewhat more often than in the general population. Patients with diabetes experience a loss of range of motion in the shoulder joint of more than 50%, and there are complaints of relatively mild discomfort around the shoulder joint due to pain. In addition, there is a combination of frozen shoulder syndrome with limited mobility of other joints (fingers, hip joint), caused by various reasons.

Another complication of diabetes is joint restriction syndrome. With this syndrome, changes usually begin in the metacarpophalangeal and proximal interphalangeal joints of the little finger and spread medially, and the distal interphalangeal joint may also be involved in the pathological process. Changes and limitation of mobility are described in the metatarsophalangeal joints and

larger joints (most often in the wrist and elbow, as well as in the ankle joint, in the cervical and thoracolumbar spine). Restriction of movement is not accompanied by pain, is resistant to physical therapy and does not lead to significant disability. However, limited mobility of the ankle and foot joints can contribute to the development of foot deformities and falls.

In hyperglycemic states, non-enzymatic glycation of proteins, phospholipids and nucleic acids leads to the formation of advanced glycation end products, which have a negative impact on the quality of bone tissue, tendons, and connective tissue.

It is known that advanced glycation end products have the ability to change the structure and properties of collagen due to the formation of covalent cross-links (so-called collagen cross-links). Type 1 collagen is also susceptible to this process. As a result, the adhesion of osteoblasts (cells that produce bone tissue) to the extracellular matrix is disrupted, which leads to bone fragility. These extracellular matrix changes also reduce alkaline phosphatase activity in mature osteoblasts, affecting bone mineralization. High levels of proinflammatory cytokines and reactive oxygen species trigger osteoclastogenesis and arrest osteoblast differentiation. Consequently, accumulation of advanced glycation end products contributes to chronic inflammation and bone resorption in diabetic patients.

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Conclusion

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References

1. Starup-Linde, J., Vestergaard, P. (2015). Management of endocrine disease: diabetes and osteoporosis: cause for concern? Eur J Endocrinol. Vol.173, pp.93-99.
2. Aung, M., Amin, S., Gulraiz, A., Gandhi, F.R., Pena, Escobar, J.A., Malik, B.H. (2020). The future of metformin in the prevention of diabetes-related osteoporosis, Cureus. Vol.12:0.
3. IDF Diabetes Atlas. (2021). March, 9th edition, 2019. Vol. 9.
4. Napoli, N., Chandran, M., Pierroz, D.D., Abrahamsen, B., Schwartz, A.V., Ferrari, A.L. (2017). Mechanisms of diabetes mellitus-induced bone fragility. Nat. Rev. Endocrinol. Vol.13, pp.208-219.
5. Si, Y., Wang, C., Guo, Y., Xu, G., Ma, Y.J. (2019). Prevalence of osteoporosis in patients with type 2 diabetes mellitus in the Chinese mainland: a systematic review and meta-analysis. Pub Health. Vol.48, pp.1203-1214.
6. Sato, M., Ye, W., Sugihara, T., Isaka, Y. (2016). Fracture risk and healthcare resource utilization and costs among osteoporosis patients with type 2 diabetes mellitus and without diabetes mellitus in Japan: retrospective analysis of a hospital claims database. BMC Musculoskelet Disord. Vol.17, 489 p.
7. Wang, H., Ba, Y., Xing, Q., Du, J.L. (2019). Diabetes mellitus and the risk of fractures at specific sites: a meta-analysis. BMJ Open. Vol.9:0.
8. Kanazawa, I., Sugimoto, T. (2018). Diabetes mellitus-induced bone fragility. Intern Med. Vol.57, pp.2773-2785.

9. Poiana, C., Capatina, C. (2019). Osteoporosis and fracture risk in patients with type 2 diabetes mellitus. Acta Endocrinol (Buc). Vol.15, pp.231-236.
10. Yoshida, N., Okumura, K., Aso, Y. (2005). High serum pentosidine concentrations are associated with increased arterial stiffness and thickness in patients with type 2 diabetes. Metabolism. Vol.54, pp.345-350.
11. Grandhee, S.K., Monnier, V.M. (1991). Mechanism of formation of the Maillard protein cross-link pentosidine. Glucose, fructose, and ascorbate as pentosidine precursors. J Biol Chem. Vol.266, pp.11649-11653.
12. Ferrari, S.L., Abrahamsen, B., Napoli, N. (2018). Diagnosis and management of bone fragility in diabetes: an emerging challenge, et al. Osteoporos Int. Vol.29, pp.2585-2596.

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