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Abnormal subchondral bone remodeling and its association with articular cartilage degradation in knees of type 2 diabetes patients

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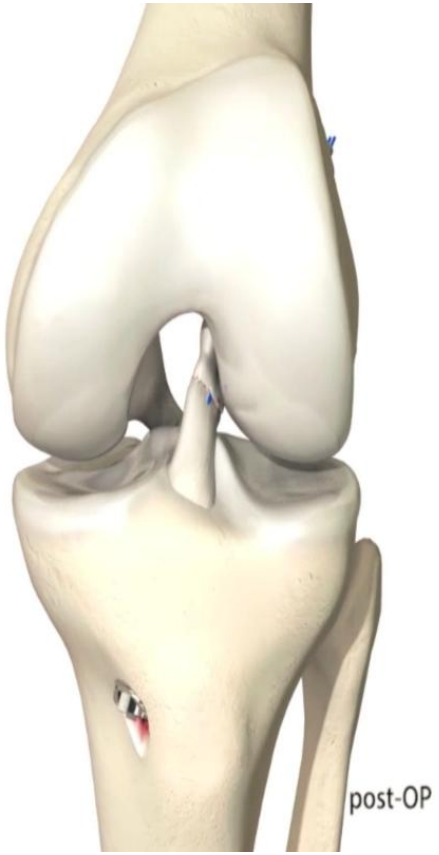
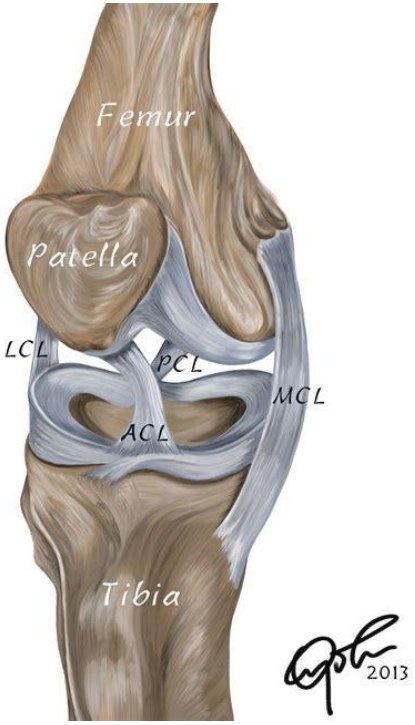
INTRODUCTION

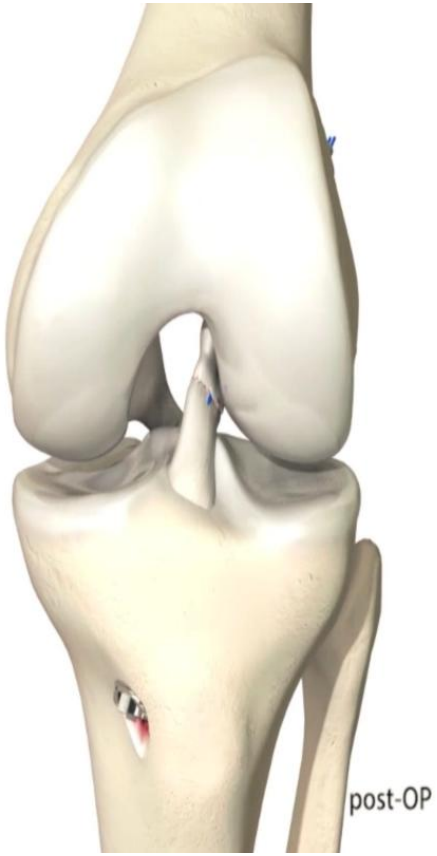


T2D patients have increased fragility fracture (for example, at femoral neck, distal radius, and tibia) induced by bone loss and deficits of bony microarchitecture and strength. It was evident that bone loss was attributable to increased bone resorption and decreased osteoblastogenesis.In addition, the disruption of bony microarchitecture partly accounts for strength deficits in T2D patients.



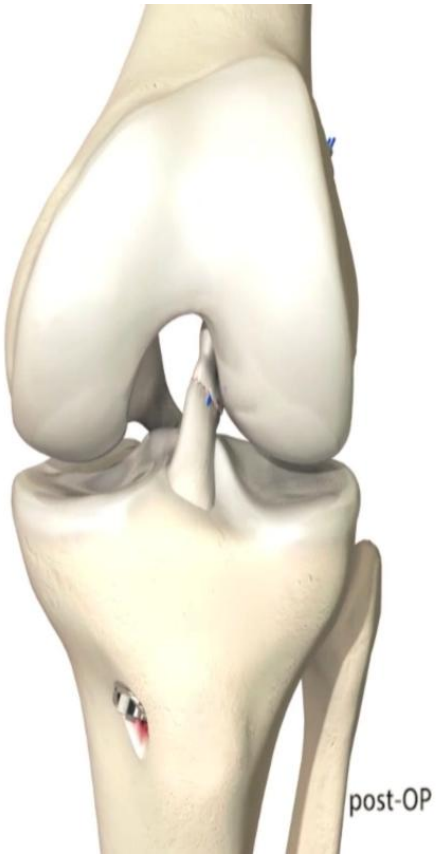
. It was reported that focally increased subchondral bone remodeling and impaired structure of lead to altered mechanical properties, thereby adversely affecting the overlying cartilage. Subchondral bone sclerosis, characterized by increased bone density, is associated with OA cartilage degradation.

the aims of this study



(1) to determine whether subchondral bone remodeling, microstructure and strength and cartilage morphology are altered in knees from patients with T2D.

the aims of this study



(2) to examine the associations of the bony alterations with cartilage degradation. It was hypothesized that increased subchondral bone remodeling led to deterio rated microstructure and strength, which in turn aggravated cartilage degradation in T2D patients.

MATERIALS AND METHODS

Clinical data
1.control（n=20）2.non-diabetic(n=70)
3.diabetes(n=51)

Micro-computed tomography (Micro-CT)

Micro-finite element analysis (FEA)

Histology

Immunohistochemistry

Statistical analysis

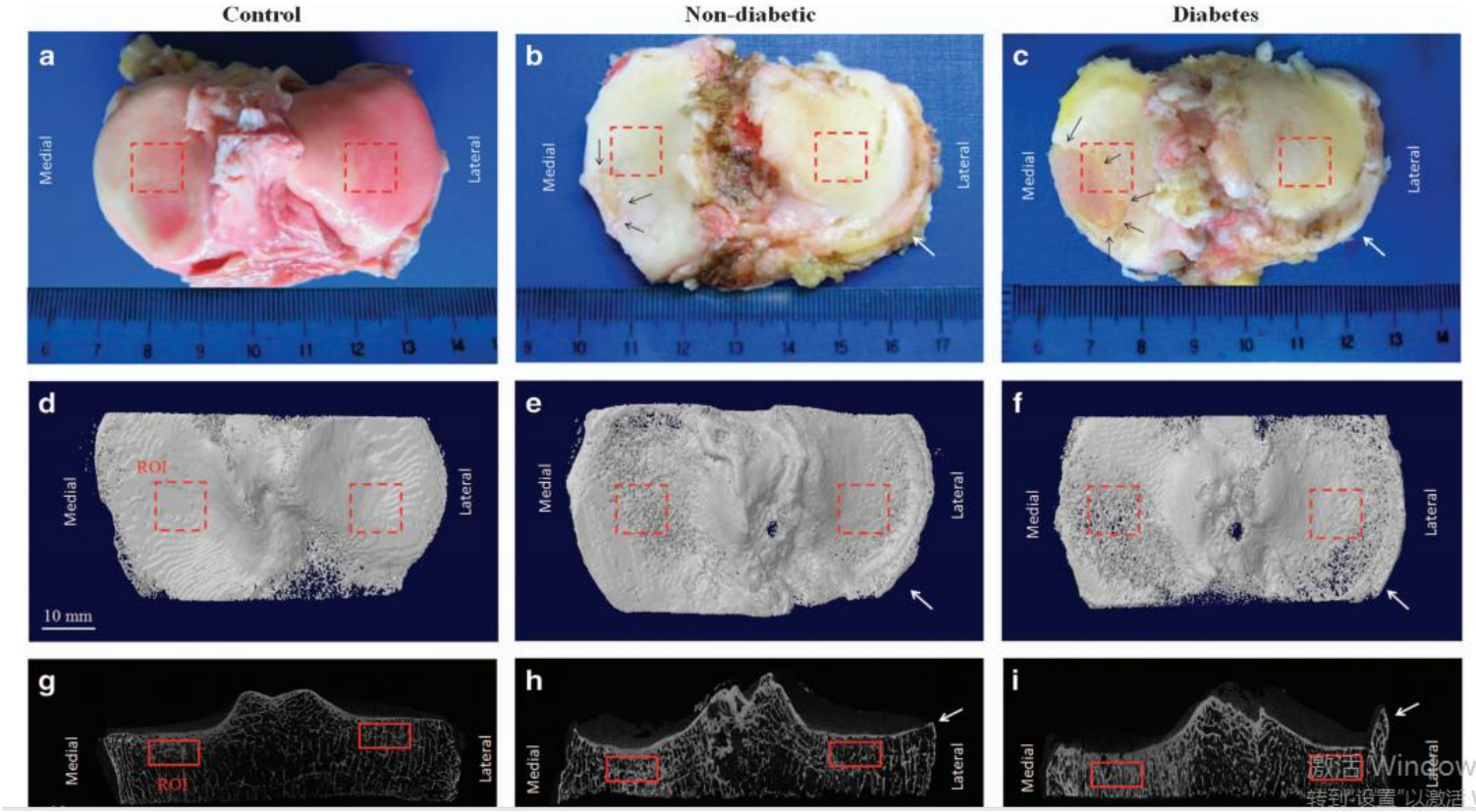


Figure 1. Macroscopic and micro-CT images of tibial plateaus from non-diabetic and diabetes patients. Macroscopic images were shown in (a–c). Black arrows (b,c) indicated edges of the remained cartilage in OA specimens. The corresponding micro-CT images were displayed in (d–f) (top view) and (g–i) (coronal view), with the red rectangles indicating the ROIs of subchondral bone (solid lines) and subchondral plate (dashed lines) on medial and lateral sides. White arrows (b,c,e,f,h,i) indicate osteophytes in non-diabetic and diabetes groups.

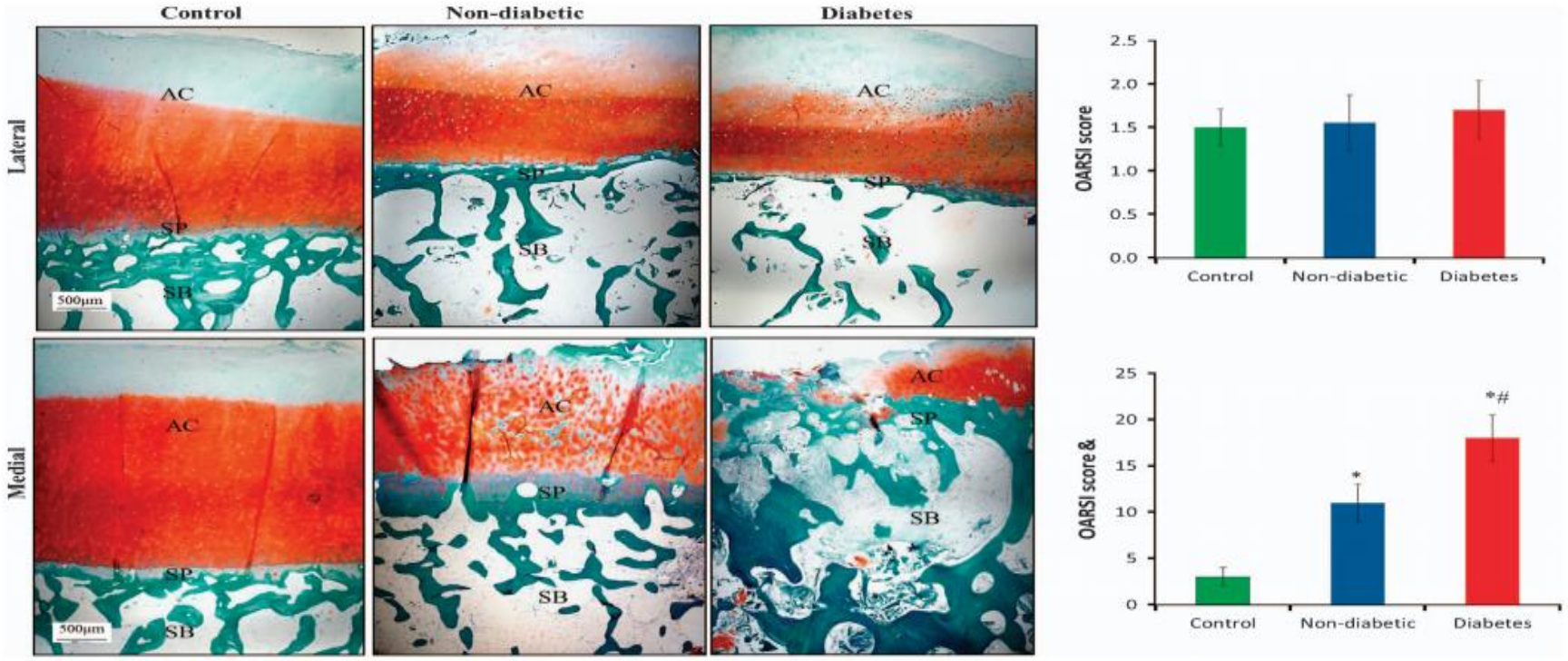


Figure 2. Histological changes of cartilage and subchondral bone from non-diabetic and diabetes patients. Cartilage damage was not obviously observed in all the groups on lateral tibial plateau. The analysis showed that there were no statistically significant differences in OARSI score among groups. On medial side, diabetes group showed more obvious disruption of cartilage surface and loss of proteoglycans, and these degenerative changes extended into deeper zone than non-diabetic group. Post-hoc tests revealed a significantly higher cartilage OARSI score in diabetes group when compared with non-diabetic group.

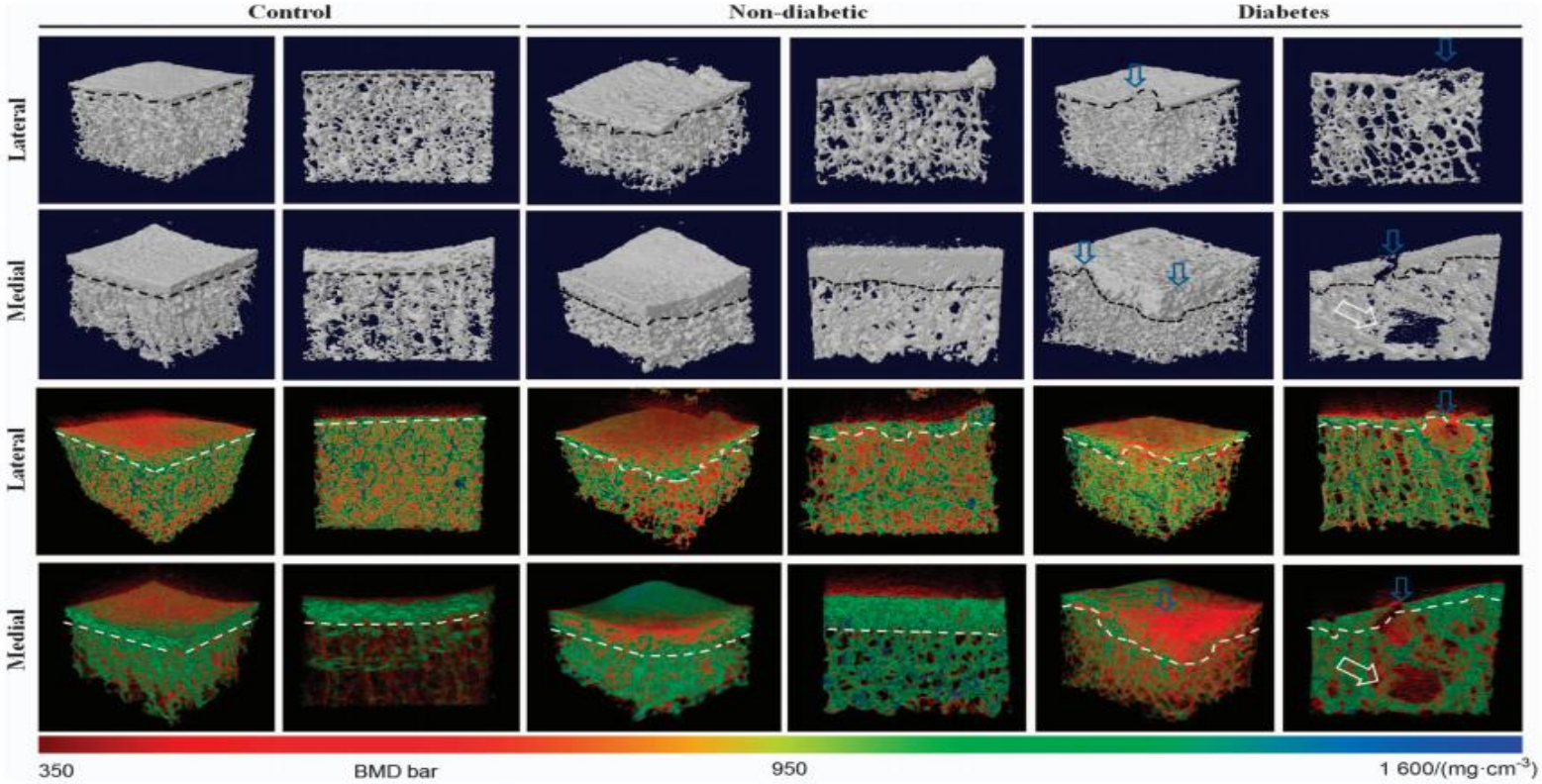


Figure 3. Micro-CT three-dimensional images and BMD maps of subchondral bone from non-diabetic and diabetes patients. The dashed black and white lines indicate the boundaries of subchondral bone. Note the bone lesions (white arrows) at subchondral bone and disruption (blue arrows) of subchondral plate in diabetes group. The BMD bar is displayed in the bottom.

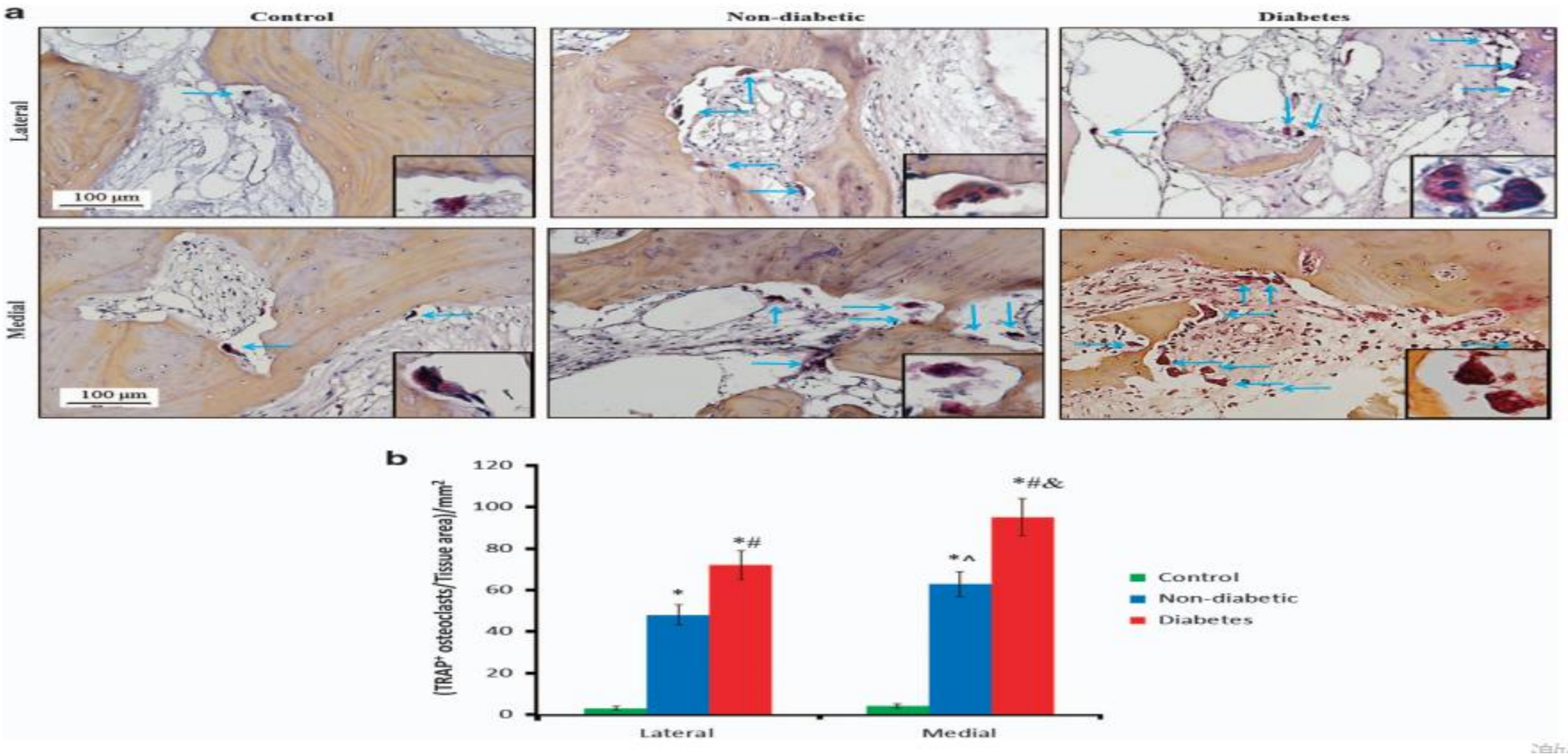


Figure 4. Activity of TRAP+ osteoclasts in subchondral bone from non-diabetic and diabetes patients. (a) Diabetes group generated larger bone marrow cavities than non-diabetic group on both lateral and medial sides. (b) One-way ANOVA analysis showed that there were significant differences in TRAP+ osteoclasts among groups on both sides. Of note, the number of TRAP+ osteoclasts in diabetes group was higher than non-diabetic group. In addition, the numbers of TRAP+ osteoclasts on medial sides were higher than lateral sides in both non-diabetic and diabetes group. Insert: morphology of TRAP+ osteoclasts.

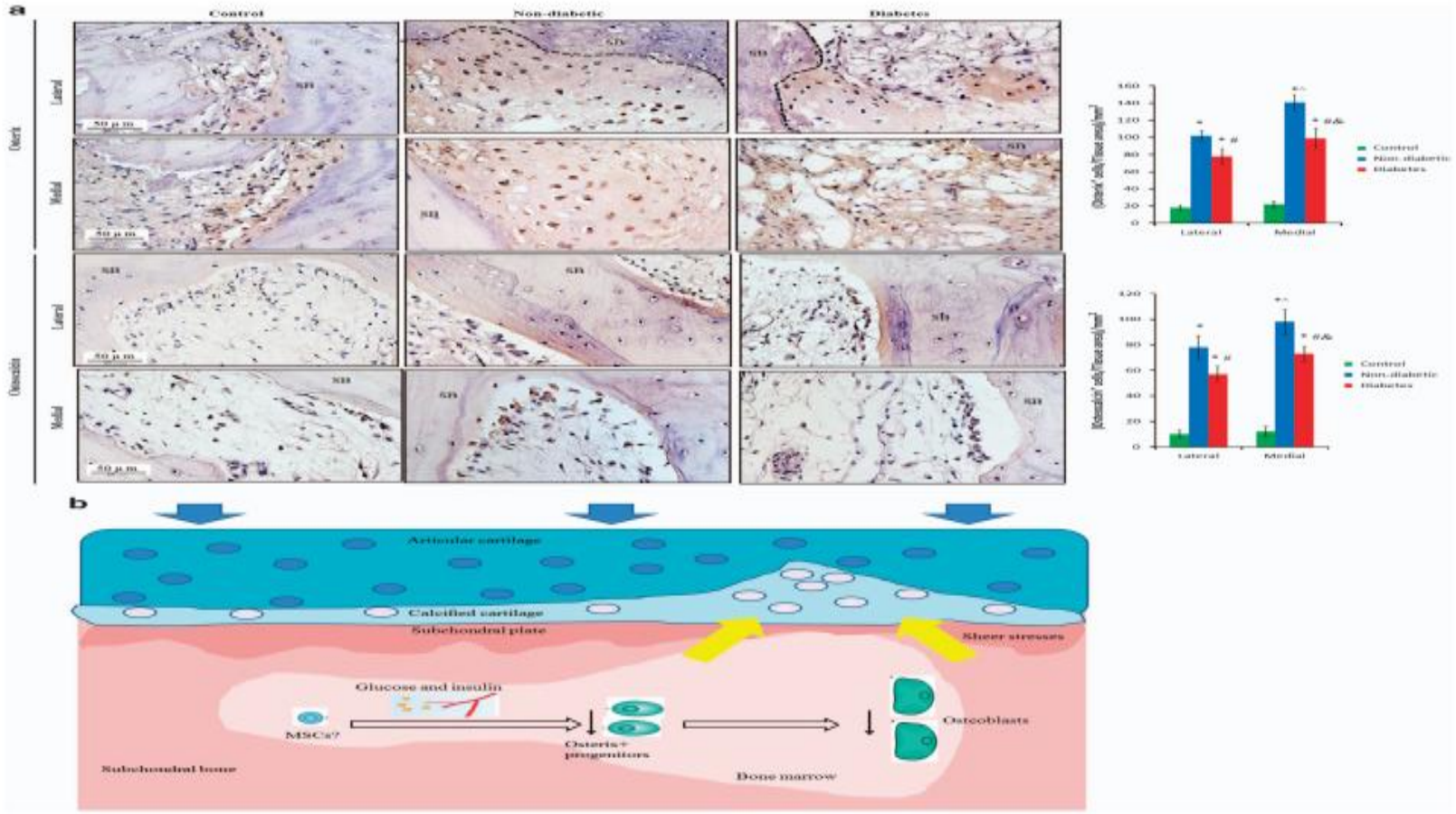


Figure 5. Activity of Osterix+ osteoprogenitors and Osteocalcin+ osteoblasts in subchondral bone from non-diabetic and diabetes patients.(a) The expression of Osterix+ osteoprogenitors and Osteocalcin+ osteoblasts was weaker in diabetes group than non-diabetic group on bothlateral and medial sides.
(b)Schematic figure of the potential mechanism of abnormal subchondral bone remodeling in pathogenesis of T2D-induced knee OA:

conclusion

researchers found that T2D patients had abnormal bone remodeling and microstructural deterioration and decreased strength. These bony changes were related with aggravated cartilage degradation. Furthermore, the bony changes have occurred in regions with intact cartilage. These findings suggest that abnormal subchon dral bone remodeling may account for the exacerbation of cartilage damage when T2D and knee OA co-exist simultaneously in the same individuals.

Discussion

First, this is a cross-sectional study. Thus, the causality between impaired bony and cartilagi nous structure in knee joints and T2D remains unclear, which could only be ascertained in future longitudinal study. Second, our specimens of tibial plateau were collected from knee OA patients, and we could not investigate specimens from individuals with T2D only. Nevertheless, it is generally difficult to attain tibial plateaus from patients with T2D only. Third, our study population was primarily consisted of patients with moderate-to severe knee OA defined by K-L grade, the results of this study hence could not represent the conditions of early OA.

thanks