Long-Duration Type 1 Diabetes Reduces Resistance to Damage Accumulation in Femoral Cortical Bone in Older Adults

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While type 1 diabetes (T1D) is associated with an increased risk for hip fracture compared to non-diabetics, the factors contributing to skeletal fragility in T1D are not well understood. Previously we demonstrated a reduction in the post-yield properties of cortical bone, suggesting T1D may alter collagen and reduce the ability of cortical bone to resist damage accumulation. To test this hypothesis, cyclic cortical bone material properties and collagen crosslinks were assessed in the excised femora of older adults with T1D and non-diabetic controls.

Whole femora were acquired post-mortem from Joslin Medalists, a cohort of individuals with T1D ≥ 50 years (n=20); non-diabetic control femora of similar age and sex were obtained from a tissue bank (n=14). Impact microindentation (Osteoprobe, Active Life Scientific) was performed on the anterior diaphysis to quantify the Bone Material Strength index (BMSi). Cortical beams (2x2x40mm) were extracted from the midshaft for damage accumulation testing. Fluorescent advanced glycation end products (fAGEs) were quantified by a fluorometric assay and the crosslink pentosidine (PEN) was quantified by HPLC. For damage accumulation testing, beams were cyclically loaded in 4 point bending with incrementally greater displacements (i.e., damage cycles; from 75% to 200% yield displacement in 25% increments). Following each damage cycle, tangent stiffness and percent stiffness degradation relative to baseline were calculated. Mann-Whitney U tests assessed group differences.

The T1D group included 11 women and 9 men with an average (mean±SD) HbA1c=7.7±1.1%, T1D duration=67.5±6.0 years, age at onset=12.8±7.9 years, and age at death=80.3±8.2 years (range 68-92). The control group was 8 women and 6 men; age (p=0.58) and sex (p=0.90) did not differ between groups. BMSi and fAGEs did not differ between groups. PEN was greater by 17% in T1D (p=0.04). At 200% yield displacement, stiffness degradation from baseline was greater in T1D (14%) versus control (10%, p=0.06; Figure). Although no specimens failed in the control group, 25% of T1D specimens failed at or before 200% yield displacement (Figure). Stiffness degradation was not associated with fAGE (r^2=0.001, p=0.87) or PEN content (r^2=0.001, p=0.92).

Long-duration T1D altered the ability of cortical bone to resist damage accumulation induced by cyclic loading. Further investigation is necessary to determine the cause of reduced resistance to damage accumulation in T1D.

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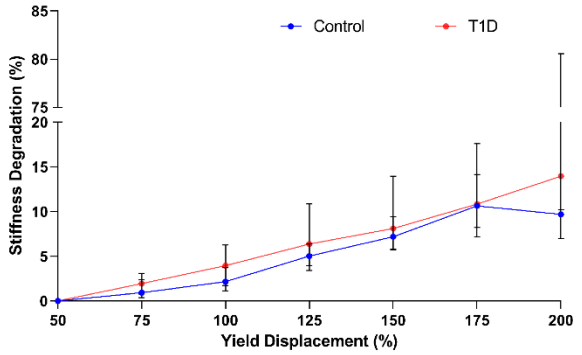

Survival Rate (%)						
Control	100	100	100	100	100	100
T1D	100	100	100	90	90	75

Figure. Stiffness degradation due to damage accumulation testing in T1D (red) and non-diabetic controls (blue). Data presented as median ± IQR. Survival rate at each damage step, or percentage of intact cortical beams at each damage step, shown in table below.