TACSM Abstract

Trabecular and Cortical Bone and Ossified Vessel Alterations in Rat Tibiae with the Onset and Progression of Type 2 Diabetes Mellitus in a Novel, Transgenic Rat Model

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ABSTRACT

Type 2 Diabetes Mellitus (T2DM) is a metabolic disorder of systemic complications including increased fracture risk and microvascular pathology, suggesting a potential link between the two. **PURPOSE**: We determined how the onset and progression of T2DM affected bone and marrow vasculature in the University of California Davis T2DM transgenic rat model. **METHODS:** Forty-eight male T2DM rats were divided accordingly: pre-diabetes (12wks), diabetes onset (14wks), early-stage diabetes (20wks; 4wks post-onset), and late-stage diabetes (22wks; 12wks post-onset) matched with four healthy control (CTL; Sprague Dawley) groups. Body mass(g), HbA1c(%), and fasted blood glucose(g/dL) were measured at sacrifice. Tibiae were scanned via µCT (15µm) to assess trabecular volume-to-total volume ratio (BV/TV, %), trabecular thickness (Tb.Th, µm), trabecular number (Tb.N, /mm), trabecular separation (Tb.Sp µm), and density (mgHA/ccm) in the proximal metaphysis. Cortical thickness (Ct.Th, µm) and density (mmHg/ccm) were measured at the mid-shaft, and cortical porosity (%) was calculated (1-Ct.BV/TV). Ossified vessel volume (OsVV, %), ossified vessel thickness (OsV.Th, µm), and OsV density (mgHA/ccm) were analyzed in the diaphyseal marrow, representing conversion of blood vessels into bone-like tissue. A General Linear Model determined significance at $p<0.05$, a priori. **RESULTS**: Body mass (455-622g vs. 342-435g) and HbA1c (5-12% vs. 5%) was higher ($p<0.05$) in the T2DM vs. CTL groups, respectively. Blood glucose rose ($p<0.05$) in early- (113±9g/dL vs. 71±7g/dL) and late- (244±10g/dL vs. 68±2g/dL) stage diabetes vs. CTL. Trabecular BV/TV was lower ($p<0.05$) in pre- (4±1% vs. 9±2%) and late-stage (5±2% vs. 8±2%) diabetes vs. CTL, from reduced ($p<0.05$) Tb.N in pre- (2.5±0.1/mm vs. CTL, 3.8±0.2/mm) and late-stage (2.1±0.3/mm vs. CTL, 2.6±0.4/mm), and reduced ($p<0.05$) Tb.Th in late-stage (56±3µm vs. CTL, 67±4µm) diabetes. Trabecular separation increased ($p<0.05$) in pre-(407±23µm vs. CTL, 263±15µm) and late-stage (482±85µm vs. CTL, 406±85µm). Trabecular density and Ct.Th, density, and porosity did not differ. OsVV was lower ($p<0.05$) in early-stage diabetes (1.7±0.2% vs. CTL, 4.7±1.5%), OsV.Th was higher ($p<0.05$) in pre-(69±14µm vs. CTL, 56±13µm) and late-stage (80±10µm vs. CTL, 59±13µm) diabetes, and OsV density was higher ($p<0.05$) in late-stage diabetes (918±17mgHA/ccm vs. CTL, 891±31mgHA /ccm).**CONCLUSION**: T2DM developed in the transgenic rat model (i.e., increases in HbA1c, and blood glucose). Cortical bone parameters were not altered. Trabecular bone declined in pre- and late-stage diabetes, via reduced trabecular number and thickness. Ossified vessels were thicker at these stages. Thus, the observed trabecular bone and vascular pathologies coincided in the tibia with the onset and progress of T2DM.

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