Universität Basel

Research Project

Microarchitecture, Bone Strength and Fracture Risk in Type 2 Diabetes: the DiabOS Study

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Project title Microarchitecture, Bone Strength and Fracture Risk in Type 2 Diabetes: the DiabOS Study
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Fracture risk is increased in patients with type 2 diabetes mellitus (T2DM) despite preserved bone mineral density. Skeletal sites may variably be affected by T2DM with trabecular bone mass and structure being largely intact, whereas the cortical bone structure may be preferentially impaired mirrored by the occurrence of fractures at predominantly non-vertebral sites. The exact mechanisms accounting for bone fragility in diabetes are not known, however and among others, hyperglycemia-induced glycosylation of bone proteins may impair bone quality. Recent small cross-sectional studies investigating peripheral bone microarchitecture and strength indicate that increased cortical porosity may be responsible for decreased bone strength in postmenopausal diabetic women. Yet, data on cortical bone in diabetic men, data on longitudinal changes in bone microarchitecture in both diabetic women and men, as well as the influence of diabetes duration and severity on microstructural changes (and ultimately fracture risk) are not known. Hypothesis: Long-standing, poorly controlled T2DM results in significant and progressive deterioration of peripheral and central bone microarchitecture (at distal radius/tibia, femoral shaft and mid-tibia) with increased cortical porosity and decreased cortical strength in both, women and men.Aims: Based on cross-sectional and longitudinal approaches we are aiming a) to assess microstructural, biochemical and densitometric bone differences in postmenopausal women and men of comparable age with T2DM with and without fragility fractures, b) to examine longitudinal changes in microstructural, biochemical and densitometric measures and to compare the corresponding changes among each other with age and sex-matched non-diabetic controls, and c) to determine whether cortical microstructure is associated with incident osteoporotic fractures in patients with longstanding and more progressive T2DM, and whether any such effect is independent of BMD or other parameters related to fracture risk.Endpoints: Primary outcome variable: Cortical volumetric BMD at the femoral shaft and mid-tibia (HR-QCT) and cortical porosity at the distal radius and tibia (HR-pQCT). Secondary outcome variables include aBMD and TBS of the spine (DXA), vBMD of the proximal femur (QCT), cortical thickness at the mid-tibia (ultrasound), bone turnover markers, advanced glycation endproducts (pentosidine, CML), and occurrence of fractures during follow-up.Design: Multicenter, prospective, observational cohort study.Patient population: Consecutive patients with T2DM (n=245; incl. 140 without [DM] and 105 with [DMFx] prevalent fractures) and age-and sex-matched non-diabetic controls (n=245; incl. 140 without [CO] and 105 with [COFx] prevalent fractures).Procedures: Study participants will be assessed at baseline and at follow-up visits in years 2 and 3 (clinical, biochemical, DXA and ultrasound assessment). Radiological assessment (QCT, HR-QCT, HR-pQCT) is scheduled twice (at baseline and for a follow-up visit in year 3). Longitudinal follow-up is limited to study participants without fragility fractures at baseline (n=280; DM, CO).Statistical considerations: Our sample sizes of 140 for DM, 105 for DMFx, 140 for CO and 105 for COFx were chosen such as to guarantee at least 85% power both for detecting a signifi-

cant effect of a history of fracture (a) and a significant effect of diabetes (b) on the natural logarithm of porosity volume of the distal radius (LNPVDR), if the true effect sizes of both factors after adjustment for age are at least 0.45 and 0.4, respectively. These effect sizes correspond to AUCs between 61% and 63% under the ROC-curve describing the predictive power of LNPVDR for diabetes and fracture history, respectively. Analogous statements are valid if LNPVDR is replaced by its change between baseline and follow-up, even when allowing for 25% loss to follow-up, with the power staying above 85% for an effect size of 0.45.Collaborators and setting: Study participants will be recruited at the Medical Universities of Basel and Aarau and the Medical Departments of Hospitals in Lucerne and Bruderholz. We will collaborate with the Departments of Radiology at the University Hospitals in Basel and Kiel (Germany). The Public Health Institute (Basel) and Clinical Trial Unit (University Hospital Basel) will provide logistic and statistical support.

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