MON-382

Background: Obesity and type 2 diabetes mellitus (T2DM) are both associated with normal to above average bone mineral density (BMD) but increased risk of fragility fractures. The impact of T2DM on bone mechanical and microarchitectural features in the obese population is unknown. We hypothesize that obese diabetics have lower bone quality compared to obese nondiabetic individuals. In this study, we investigated the microarchitectural features and mechanical properties of bone of obese men with and without T2DM along with the independent predictors of bone strength. **Methods**: Ninety-seven obese men (BMI >30) aged 35-65 years-old of which 38 had T2DM were included in the analysis. BMD and body composition were evaluated by DXA and bone microarchitecture of the tibia by high-resolution peripheral quantitative computed tomography. Bone strength was assessed by micro finite element analysis-derived parameters as failure load (f. load) and stiffness. Serum testosterone and estradiol were measured by LC-MS. Serum SHBG, osteocalcin (OCN), C-telopeptide (CTx) and sclerostin (SCL) were measured by ELISA. **Results:** OCN is lower in obese men with T2DM compared to those without T2DM (4.8 ± 2.8 vs 6.2 ± 2.6 ng/mL p=0.03, respectively), with also a trend for reduced CTx and SCL in the former. BMD at all sites was reduced in obese men with T2DM, but there were no differences in body composition. Obese diabetics also had lower tibial total volumetric BMD (vBMD) (p=0.04) and trabecular vBMD (p=0.01) with greater trabecular spacing (p=0.005). F. load (13.3 ± 2.1 vs 14.5 ± 2.3 kN, p= 0.02) and stiffness (24.7± 4.2 vs 27 ± 4.6 kN/mm, p=0.02) were reduced in men with T2DM relative to men without T2DM, respectively. F. load and stiffness were positively correlated with BMD at all sites, fat free mass (FFM), lean mass, free testosterone, free estradiol and SCL, but negatively correlated with % total body fat and visceral adipose tissue (VAT). FFM, BMD of the total hip, femoral neck and lumbar spine and free testosterone were significant independent predictors of bone strength in the entire group (model: R^2: 65.01 p< 0.0001 for f. load and model: R^2:63.21 p < 0.0001 for stiffness), whereas age and lumbar spine BMD were found to be independent predictors of bone strength in the non-diabetic group (model R^2: 54.6 p< 0.0001 for both f. load and stiffness). Analysis limited to the diabetic subgroup showed that BMD at the femoral neck and total hip, % total body fat, VAT volume, SCL and free estradiol were independent predictors of bone strength (model: R^2: 88.4 and p< 0.0001 for f. load and model: R^2: 85.3 and p<0.0001 for stiffness). Interleukin-6 was comparable between groups. **Conclusions**: Obese men with T2DM have lower bone formation and impaired bone quality and strength compared to those without T2DM. In addition to BMD and gonadal hormones, adiposity is an important predictor of bone strength in obese men with T2DM.

Reproductive Endocrinology

CLINICAL STUDIES IN FEMALE REPRODUCTION I

Adrenal Androgen Production Is Maintained While Ovarian Estrogens Fall Following the Final Menstrual Period in the Study of Women's Health Across the Nation (SWAN)

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The aim of this study was to clarify changes in sex steroids at the final menstrual period (FMP). We have shown previously that estradiol (E2) declines substantially in the 4-year period around the FMP, but hypothesize that testosterone (T) declines modestly and adrenal Δ5 androgens dehydroepiandrosterone (DHEA) and androstenediol (Adiol) remain unchanged. **Methods:** Liquid chromatography tandem mass spectrometry (LC-MS/MS) and immunoassay was used in approximately annual samples collected before and following FMP in 1490 women. We estimated time-related changes in each log-transformed androgen using piecewise linear mixed modeling, with knots (slope changes) at FMP-2 yrs and FMP+2 yrs as seen for E2. These models then were re-estimated for subgroups with different time courses identified using group-based trajectory modeling. **Results:** In the full sample, T was generally stable, although time course varied by subgroup, with a significant decrease of 5%/year in T in [FMP-2yrs, FMP+2yrs] only in the lowest T women. For DHEA and Adiol, declines were similar across all 3 time segments and across subgroups. Mean circulating androgen concentration declined modestly (P> 0.05) from five years before to five years following FMP. However, when stratified only the lowest 7% of circulating T declined significantly (p< 0.05) in the four years surrounding FMP when mean circulating E2 declined. This trajectory divergence of the lower circulating T suggests a different, non-adrenal source that is decreased at FMP which may be useful in clarifying ovarian versus adrenal testosterone production during the post-menopause. Paired results from samples collected before and following FMP in the same subjects indicate mean circulating E2 is less than 5% of mean circulating T suggesting that a relatively large portion of circulating E2 may be largely a result of peripheral conversion of adrenal androgens. Longitudinal LC-MS/MS analyses of circulating E2 and T indicate that the principal change in sex steroid influence at menopause is largely a decrease and dampening of ovarian and not adrenal steroid production.

Genetics and Development (including Gene Regulation)

GENETICS AND DEVELOPMENT AND NON-STEROID HORMONE SIGNALING I

Clinical and Genetic Features of Families with Maternally Inherited Central Precocious Puberty

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