SUN-622

Background Previous meta-analyses have reported an increase in the risk of hip fractures in diabetes, but the risk of non-vertebral fractures has not been investigated. In addition, it is not known how the risk of fractures is affected by age, body mass index, diabetes duration and insulin use. To investigate these features, we conducted a meta-analysis on the risk of hip and non-vertebral fractures in diabetes. MethodsWe selected a previously published review to be updated. Medline, Embase and Cochrane databases were searched in March 2018 and an update conducted in March 2019 (Pubmed) using relevant MeSH and free text terms such as "diabetes", "hyperglycaemia" and "fracture". We selected observational studies with data on the risk of fractures in adults ολδερ τηαν 18 years old with diabetes compared to people without diabetes. Study quality was assessed using the Newcastle Ottawa Scale. We used the random-effects model to calculate the risk estimates and 95% confidence intervals.Results Forty-nine studies were included. Forty-three studies were included in the hip fracture analysis, 40 cohorts and 3 case-control studies, reporting data from 17,575,873 participants, 2,387,899 with diabetes and 321,720 fractures. Eighteen studies reported the risk of fractures in two or more sites and were included in the non-vertebral fracture risk analysis. All but one study were cohorts. These studies reported data from 2,982,622 participants, 414,195 with diabetes and 185,363 fractures. In both analyses, age varies from 20 to 100 years old, including both type 1 and type 2 diabetes. Overall, the study quality was judged to be moderate to good.We found a significant increase in the risk of fracture in diabetes both for hip (RR 1.52, 95% CI 1.42-1.63) and for non-vertebral fracture (RR 1.20, 1.14-1.27). The increase in the risk was greater for insulin users and longer duration of diabetes, at both sites. At the hip, the risk was higher in the younger population, women, and those with T1D. ConclusionThere was an increase in the risk of hip and non-vertebral fractures in diabetes. Although the mechanisms are not established, patients with type 1 diabetes were the population at higher relative risk. The evidence suggest that the skeleton should be considered a site for diabetic complications.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

Free Testosterone and Cardiometabolic Parameters in Adult Men - Comparison of Algorithms for Calculation of Serum Free Testosterone

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SAT-045

Context. Determining the free or bioavailable testosterone level has gained increasing interest over the years and different indirect algorithms have been suggested.

Objective. To compare commonly used algorithms of calculation of serum free testosterone, specifically free androgen index (FAI), free testosterone estimated using the Vermeulen algorithm (cFTV) and the Zakharov algorithm (cFTZ) as well as total testosterone in relation to baseline and long-term cardiometabolic conditions.

Design. A prospective cohort study of men participating in four independent population-based surveys (MONICA I-III and Inter99) from 1982 to 2001 and followed until December 2012 with baseline and follow-up information on cardiometabolic parameters.

Setting and Participants. 5350 randomly selected men from the general population aged 30, 40, 50, 60, or 70 years at baseline participated.

Main Outcome Measures. Baseline cardiometabolic parameters and follow-up information on type 2 diabetes, ischemic heart disease, cardiovascular disease mortality, and all-cause mortality.

Results. Free testosterone levels calculated according to the two algorithms differed systematically but however correlated well (cFTV vs. cFTZ: r=0.9, p<0.01) and the relative standard deviations ranged from 37% to 41%. In general, men having cardiometabolic conditions at baseline had lower absolute levels of FAI, cFTV and cFTZ. However, when age-standardizing the hormone levels, FAI levels were higher in this group of men whereas cFTV and cFTZ remained lower compared to men without these conditions. The associations seen for cFTV and cFTZ were in line with the association seen for total testosterone. Cox proportional hazard models revealed that men in the highest quartiles of cFTV or cFTZ had lower risk of developing type 2 diabetes (cFTV: HR=0.74 (0.49-1.10), cFTZ: HR=0.59 (0.39-0.91)) than men in the lowest quartile. In contrast, men with highest levels of FAI had a 74% increased risk of developing type 2 diabetes compared to men in the lowest quartile (HR=1.74, 95% CI:1.17-2.59). In relation to all-cause mortality, FAI showed the strongest inverse association followed by cFTV, whereas cFTZ and total testosterone did not show any association.

Conclusion. Free testosterone estimated by the Vermeulen and Zakharov algorithms differed systematically. However, the computed values correlated well and showed similar associations to baseline and long-term cardiometabolic parameters; albeit with subtle differences. In contrast, an empiric ratio, FAI showed opposite associations to several of the examined parameters and may reflect limited clinical utility.

Genetics and Development (including Gene Regulation)

ENDOCRINE DISRUPTING CHEMICALS

Effects of Organohalogenated Endocrine Disrupting Chemicals on Cell Proliferation and Gene Expression in GH3 Somatolactotropes

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SAT-723

Endocrine Disrupting Chemicals (EDCs) are substances that have been increasingly implicated in many serious pathologies, such as tumor formation, metabolic, growth and reproductive disorders. The economic and health burden of exposure to these compounds has an annual predicted cost in excess of €150 billion, across the EU regions alone. Of the growing list of compounds that act as EDCs, the organohalogenated compounds (OHCs), polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) have been associated with an increased risk of pituitary disease. We have previously reported that feline patients with hypersomatotropism (acromegaly) are exposed to elevated levels of PBDEs and PCBs in their environment. However, the mechanisms by which these compounds might directly influence somatotroph function have yet to be established. In this study, we use the GH3 rat somatolactotrope cell line to investigate how two PCB congeners - 138 and 153 - influence cell proliferation (using a Crystal Violet assay) and somatotrope gene expression (using a multiplex RT-qPCR approach to examine expression of *Esr1, Esr2, Sstr1, Sstr2, Sstr3, Sstr4, Sstr5, Insr, Tshr, Pou1f1, Ghrhr2, Gh*). GH3 cells were treated with Phenol Red-free media in the absence or presence of either PCB138 or 153 (-10 to -6 M), or in combination (-10 to -6M) for up to 72h. Treatment with either PCB alone, or in combination, caused significant concentration-dependent, biphasic changes in cell proliferation at each time point, but with a different profile of response on each day (significantly increased at high pM/low nM concentrations); there was no evidence of toxicity at maximum concentrations (-6M). Gene expression changes were determined in GH3 cells treated in the absence or presence of either -8M or -6M PCB138 or 153 for 24h. Differential effects of these compounds were seen on the expression of *Sstr3, Sstr4, Sstr5* and *Insr*; all other gene transcripts were unaffected. These findings reveal that GH3 cells exposed to physiologically relevant concentrations of PCB138 and 153, alone or in combination, show concentration-dependent increases in cell proliferation; furthermore, the expression of genes associated with therapeutic targets for the treatment of acromegaly (i.e. SSTRs) are differentially affected by exposure to PCB138 and 153. Our data indicate a potential mechanism for EDCs in the onset of acromegaly, that require further, *in vivo*, investigations.

Adipose Tissue, Appetite, and Obesity

ADIPOSE TISSUE BIOLOGY AND OBESITY II

Micrornas in Brown and White Adipocytes

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SUN-584

Two types of adipose tissue exist: white (WAT) and brown (BAT). WAT stores energy while BAT consumes fatty acids and produces heat by non-shivering thermogenesis through Uncoupling Protein 1 (UCP1). BAT and WAT cooperate in maintaining energy homeostasis balance. Understanding their physiology is important for the development of treatments against diseases where this equilibrium is compromised, such as obesity and associated metabolic disorders. MicroRNAs (miRNAs) are potent gene regulators and an increasing body of evidence suggests their involvement in adipogenesis and adipose metabolism. MiRNAs can also be secreted into the extracellular environment and be taken up by distal cells, mediating cell-to-cell communication. However, very little is known about adipose tissue-derived circulating miRNAs. Through miRNA PCR array analysis we identified several miRNAs that are differentially secreted among undifferentiated and differentiated brown and white adipocytes, such as miR-196a, 378a-3p and miR-138-5p. Bioinformatics target prediction revealed that these miRNAs are potentially involved in important processes regulating the functioning of adipose tissue and its cross-talk with distal cells. Among the predicted targets of miR-196a, we identified ADAM10 (A Disintegrin And Metalloproteinase Domain-containing protein 10). This protein is responsible for the proteolytic release of several cell-surface proteins involved in numerous biological processes such as inflammation and its role could be of relevant importance in the physiopathology of the adipose tissues.

Adrenal

ADRENAL - TUMORS

High Prevalence Alterations on DNA Mismatch Repair Genes Related to Lynch Syndrome in Pediatric Patients with Adrenocortical Tumor Carried of the Germline Mutation on TP53

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SAT-155

Background: Adrenocortical cancer (ACC) is a rare malignant neoplasia associated with a variable clinical presentation. Pediatric patients generally have a better prognosis when compared to adults. In addition, unlike in adults where ACC which is usually sporadic, 50-80% of pediatric ACC is associated with genetic disorders such as Beckwith-Wiedemann and Li-Fraumeni syndromes. Recently, was