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**Proceedings Paper:**
Vilaca, T., Schini, M. orcid.org/0000-0003-2204-2095, Harnan, S. orcid.org/0000-0002-9318-9206 et al. (3 more authors) (2020) SUN-622 The risk of hip and non-vertebral fractures in diabetes : a systematic review and meta-analysis update. In: Journal of the Endocrine Society. Annual Meeting of the Endocrine Society - ENDO 2020 (cancelled), 28-31 Mar 2020, San Francisco, CA, USA. The Endocrine Society .

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had when caring for individuals with cyanotic heart disease to pursue evaluation of these tumors. CASE: A 23-year-old man with a chief complaint of diffuse abdominal pain was found to have a 2.6 x 2.8 cm smoothly marginated soft tissue mass in the right lower quadrant on abdominal computed tomography. Patient had a known history of hypoplastic left heart syndrome (mitral atresia-aortic atresia) who had undergone a three-stage Norwood repair in childhood. In his adulthood was diagnosed with Central Adrenal Insufficiency, and Type 2 Diabetes Mellitus. At the time of presentation patient was short of breath, tachycardic (heart rate 115), and tender to palpation of his right lower quadrant. Plasma normetanephrines were 3.8 nmol/L (normal < 0.9 nmol/L), 24-hour urinary excretion of normetanephrine was 1117 mcg/24h (normal 103-390 mcg/24h). Plasma metanephrine levels were normal. A nuclear medicine whole body scan with metaiodobenzylguanidine (MIBG) scan confirmed a MIBG avid tumor in the right lower quadrant. Preoperative management was initiated with oral doxazosin. He underwent laparoscopic surgery with removal of a 3 cm pelvis mass resected from the retroperitoneal tissue deep to the peritoneum along the gonadal vein and ureter. Final pathology confirmed the diagnosis of a paraganglioma. Postoperatively, plasma normetanephrines were corrected at 0.86 nmol/L. Patient underwent genetic testing that was negative for FH, MAX, MEN1, NF1, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, TMEM127 and VHL. CONCLUSION: Multidisciplinary approach to these patients is essential given their complex hemodynamics. Long term follow up is necessary to monitor for tumor recurrence, review of case reports may suggest a higher risk of recurrence [1]. Of these case reports there has been no strong genetic association found, the most popular theory is a causal relationship from their cyanotic heart disease.

References:
Zhao B, Zhou Y, Zhao Y et al (2018) Co-occurrence of pheochromocytoma-paraganglioma and cyanotic congenital heart disease: A case report and literature review. Front Endocrinol. https://doi.org/10.3389/fendo.2018.00165

# Adrenal

## ADRENAL - CORTISOL EXCESS AND DEFICIENCIES

### *Evaluation of Adrenal Insufficiency and Recovery in Rheumatology Patients on Long-Term Glucocorticoid Therapy*

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**MON-189**

Background

Long-term glucocorticoid (GC) therapy is commonly used to treat rheumatological conditions. This may result in tertiary adrenal insufficiency, as a result of suppression of the HPA axis, when GC doses are weaned/withdrawn. There is little published data about tertiary adrenal insufficiency in this group. This study aims to further evaluate prevalence, characteristics and recovery of adrenal insufficiency in these patients at a large UK teaching hospital.

Methods

We retrospectively identified patients seen in outpatient clinics between January 2014 and September 2019 who had received tapering doses of long-term GC to treat their underlying condition (largely patients with polymyalgia rheumatica, giant cell arteritis or other vasculitis) and had either had a 9am cortisol or short synacthen test (SST). Data were collected using a standardised proforma.

Results

There was a total of 238 patients, median age of 71 years with a female preponderance (75%). Mean duration of glucocorticoid use was 63.3 months. Mean peak dose of glucocorticoid was 29.2mg.

142 patients had 9am cortisol as the first line test to assess adrenal function. 65% of these were considered suboptimal based on local protocol (cortisol <350nmol/L). 38% of these patients went on to have SST, of which 56% continued to show evidence of sub-optimal cortisol production. All patients where baseline 9am cortisol was <100nmol/L failed to reach stimulated cortisol of >500nmol/L on SST, whereas 31% failed SST if 9am cortisol was 250-350 nmol/L. In total 138 SSTs were performed of which 51% (n=70) were abnormal (cortisol <500nmol/L post synacthen). When baseline cortisol was <100nmol/L on SST, all patients had a suboptimal peak response. However, where baseline cortisol on SST was >350 nmol/L only 3% had a sub-optimal peak cortisol.

32 of these patients with an abnormal baseline SST went on to have a repeat SST within 2 years. 50% (n=16) continued to be suboptimal. Of the 32 patients, 38% (n=12) were switched to hydrocortisone with 33% showing complete adrenal recovery, average time to recovery of 25 months. 62% (n=20) patients did not switch, with 60% demonstrating recovery within the same time period ($p$=0.05). Mean ACTH levels in patients who had sub-optimal SST were 23.1 ng/L (n=19). ACTH levels were not different between those who recovered and those who did not ($p$=0.23).

Conclusion

Our study suggests that tertiary adrenal insufficiency is highly prevalent in this cohort of patients with rheumatological conditions requiring long-term glucocorticoid therapy. A 9am cortisol threshold of greater than 350nmol/L excludes most patients with adrenal insufficiency. These data also suggest no significant difference in adrenal recovery if switched to hydrocortisone versus continuing on prednisolone. ACTH levels were not fully suppressed in patients with adrenal insufficiency and did not predict recovery.

# Diabetes Mellitus and Glucose Metabolism

## DIABETES DIAGNOSIS, TREATMENT AND COMPLICATIONS

### *The Risk of Hip and Non-Vertebral Fractures in Diabetes: A Systematic Review and Meta-Analysis Update*

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**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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