accessibility to osteoporosis care while maintaining quality. At our Osteoporosis Centre, we have implemented a group counseling model for this purpose: the Patient-Centred Educonsult Program for Osteoporosis (PEP-OP). Each two-hour PEP-OP session - co-facilitated by an osteoporosis physician and a nurse - provides up to 10 patients (the equivalent to 3–5 half-day physician clinics under the TC model) with a combined consultative and educational experience consisting of an individualized fracture risk assessment and extensive review of medications available to lower fracture risk. Patients are then encouraged to make an informed, autonomous decision about osteoporosis treatment initiation. Although the PEP-OP can accommodate a greater patient volume than the TC, and we have previously reported that the PEP-OP results in high patient satisfaction, it is not known whether PEP-OP produce similar results compared to TC in terms of treatment decisions. In this cohort study, we compared decisions to initiate osteoporosis therapy in PEP-OP (N=100) and TC (N=43) attendees. Ten-year risk of major osteoporotic fracture was estimated for each participant using the FRAX calculator, and participants were stratified based on whether their ten-year risk was ≥20% or <20%. Proportion of participants in each risk category who decided to initiate treatment were compared between the PEP-OP and TC groups. PEP-OP and TC groups were comparable in terms of age (63.3 vs 64.9 years), BMI (24.4 vs 24.9 kg/m^2), previous fragility fractures (35 vs 25%), parental hip fractures (19 vs 23%), lumbar neck T-score (-2.5 vs -2.3), femoral neck T-score (-2.1 vs -2.1) and average FRAX estimate (13.1 vs 13.3%). The proportion of participants at high ten-year risk of major osteoporotic fracture (≥20%) who decided to initiate treatment was similar in both the PEP-OP (7/16, 44%) and TC (5/10, 50%) groups, according to the Chi Square Test (p=0.76). Among those with FRAX estimate of <20%, a similar proportion of patients in the PEP-OP (15/84, 18%) and TC (4/33, 12%) groups chose to undergo treatment (X^2, p=0.45). In summary, decisions to initiate pharmacologic therapy were similar for the PEP-OP and the TC. Considering that the PEP-OP is acceptable to patients and is more efficient than the TC, this care model should be considered by other centers wishing to improve access to high-quality osteoporosis care.

Reproductive Endocrinology

CLINICAL STUDIES IN FEMALE REPRODUCTION II

Loss of Antimullerian Hormone Immunoreactivity Due to a Homozygous AMH Gene Mutation Rs10417628 in a Woman with Classical Polycystic Ovary Syndrome

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Anti-Müllerian hormone (AMH), an inhibitor of primordial/small antral follicle development and Leydig cell androgen synthesis in mice, could exaggerate the polycystic ovary syndrome (PCOS) phenotype, given reports of PCOS-specific AMH loss-of-function mutations (1–3). This report describes a normal-weight PCOS woman with severely reduced AMH levels (index PCOS woman). It examines the molecular basis for her reduced serum AMH levels and also compares her endocrine characteristics to similar-weight PCOS women with detectable AMH. Twenty normo-androgenic ovulatory (control) and 13 age- and body mass index-matched PCOS women (19–35 years; 19–25 kg/m^2) underwent transvaginal sonography and serum hormone measures. Wilcoxon rank-sum test compared clinical features of control and PCOS women with detectable AMH, which were then individually ranked by magnitude in all PCOS women. DNA analysis was performed by PCR amplification with direct gene sequencing. The identified mutation was introduced in hAMH-expression plasmids for functional analysis of AMH processing in HEK293 cells by Western blot and ELISA (pico-AMH assay, Ansh Labs, Webster, TX), and for bioactivity in KK-1/AMHR2 cells using a luciferase reporter. Unpaired t-test compared AMH-induced luciferase activity between wild type and mutant AMH. A homozygous AMH gene mutation rs10417628 involving a single base pair substitution in exon 5 (NG_012190.1:g.7705C>T, p.(Ala515Val)) was identified in the index PCOS woman. PCOS women with detectable AMH had higher serum AMH (10.82 [6.74–13.40] ng/mL, Median [IQR]), total/free testosterone (T) (total T: 55.5 [49.5–62.5] ng/dL; fT: 5.65 [4.75–6.6] pg/mL) levels and greater total antral follicle numbers (AFNs) (46 [39–59] follicles) than controls (AMH: 4.03 [2.47–6.11] ng/ml; total T: 30 [24.5–34.5] ng/dL; fT: 2.2 [1.8–2.45] pg/mL; AFNs 16 [14.5–21.5] follicles, P<0.05, all values), along with a trend toward LH hypersecretion (P=0.06). The index PCOS woman with the lowest AMH levels (0.1 ng/ml) did not have the highest serum total T/fT (total T: 89 ng/dL; fT: 7 pg/mL,) or LH levels nor the greatest AFN (43 follicles). In vitro analysis of cells expressing hAMH-^{515}Val or hAMH-^{515}Ala showed that hAMH^{515}-Val, in contrast to hAMH^{515}-Ala, was undetectable and severely reduced in the pico-AMH assay in cell lysates and supernatants, respectively. AMH protein processing and AMH-induced luciferase activity, however, did not differ between hAMH^{515}Val and hAMH^{515}Ala. Thus, homozygous *AMH* mutation rs10417628 in a PCOS woman can impair serum AMH immunoreactivity without affecting AMH bioactivity, perhaps because of conformational changes from the mutation that only interfere with its immunodetection but not its function. **References**: 1. Teixeira J, et al. Endocrinology 1999;140:4732 2. Gorsic LK et al. JCEM 2019;104:2855 3. Broekmans FJ, et al. Trends Endocrinol Metab 2008;19:340

Thyroid

BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID I

Evaluation of the Siemens Thyroid Stimulating Immunoglobulin (TSI) Assay for Diagnosis and Prognosis of Graves' Disease

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SAT-422

Background: Hyperthyroidism due to Graves' disease (GD) is an autoimmune condition caused by thyroid stimulating hormone receptor (TSHR) autoantibodies. Autoantibodies to the TSHR can stimulate or block thyroid hormone production, therefore testing specifically for stimulating antibodies would be beneficial for diagnosis of GD.
Objectives: The primary objective of the first phase of this trial is to assess the diagnostic capability of the Siemens Thyroid Stimulating Immunoglobulin (TSI) immunoassay in diagnosing GD and to compare it with the Roche TSH Receptor Antibody (TRAb) assay.
Design and Methods: Two hundred patients with suspected GD are being enrolled in this single-center multiphase prospective cohort study. Consenting patients undergo biochemical testing including thyroid stimulating hormone (TSH), free T3 (FT3) and T4 (FT4), TRAb and TSI measurements. GD diagnosis was confirmed by endocrinologists that were blinded to TSI results.
Results: To date, 85 patients were included in the analysis, of which 66 were diagnosed with GD. For the primary analysis, all patients taking anti-thyroid drugs (ATD) at time of sample collection (n=14) were removed. The respective sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) for TSI was 98, 84, 94 and 94%, which were comparable to those generated by TRAb (98, 95, 95, and 98%). In patients with clinical findings of GD (ie. orbitopathy or goiter, n=33), both the TSI and TRAb assays had identical sensitivity and specificity at 96% and 80% respectively. In patients without orbitopathy or goiter (n=38), the TSI assay had perfect sensitivity and excellent specificity of 100% and 86% respectively (TRAb had 100% sensitivity and specificity). Sensitivity, specificity, NPV, and PPV were slightly lower for both TSI and TRAb in patients treated with ATDs compared to patients without treatment (TSI: 85, 84, 62, 95%; TRAb: 91, 95, 75, 98%). Of ten patients with GD and false negative TSI results, nine were on ATDs. Of this subset, four patients had discordant results between TSI (negative) and TRAb (positive). Notably, one of these patients had normalization of their FT3 and FT4 on the day of sample collection.
Discussion and Conclusion: Based on our preliminary results, TSI is an excellent marker for diagnosing GD, particularly in untreated GD patients. The performance of the TSI assay has been comparable to the TRAb assay and correlates well with clinical findings. Discordant false negative results were only seen in patients on ATD. One potential explanation is that the TSI assay is detecting a decrease in stimulating autoantibodies when there is normalization of FT3 and FT4. Importantly, all discordant samples will be tested by a TSI bioassay to confirm diagnosis. Further patient enrollment is occurring, and prognostic assessment of these assays will soon be possible.

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS I

High Enhancement Washout by CT Imaging Does Not Exclude Pheochromocytoma/Paraganglioma: Review of Two Cases.

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SUN-910

Background:
It is well known that delayed images from contrast-enhanced CT are useful in distinguishing adrenal adenomas from non-adenomas, with an absolute washout that exceeds 60% being most consistent with a lipid rich adenoma. We present two cases of an adrenal mass that met the criteria for a lipid rich adenoma by CT imaging, but found to be a pheochromocytoma (PCC) and paraganglioma (PGL).
Clinical Case
Case#1
An 82 yo woman presenting with tachycardia was found to have a 2.4 cm heterogeneously attenuating, left adrenal nodule with an absolute washout of 61% and a relative washout of 45%. The right adrenal was normal. Urinary catecholamine levels were elevated with an epinephrine (E) 38 mcg (2–24), norepinephrine (NE) 388 mcg (15–100), dopamine (DOPA) 175 mcg (52–480), metanephrine (MN) mcg 620 (90–315), normetanephrine (NMN) 1553 mcg (122–676) and vanillylmandelic acid 12.5 mg (< 6) on a 24h collection. Due to a cardiac resynchronization therapy device, an MRI could not be obtained. MIBG imaging was obtained and showed increased uptake in left adrenal gland, corresponding to the lesion identified on CT. The patient underwent laparoscopic adrenalectomy and the pathology confirmed a PCC.
Case#2:
A 74 yo man was found to have an incidental right adrenal nodule on CT imaging measuring 2.4 cm. Absolute washout was 83% and relative washout 68%. The left adrenal gland was normal. A follow up MRI obtained showed slight increase in T2 weighted images and no drop out on out of phase imaging, raising concern for a PCC. Urinary catecholamines were elevated including E 12 mcg (2–24), NE 280 mcg (15–100), DOPA 246 mcg (52–480), MN 175 mcg (90–315) and NMN 1298 mcg (122–676) on a 24-hr. collection. MIBG imaging further confirmed the diagnosis with increased uptake in the right adrenal gland. The patient underwent laparoscopic adrenalectomy then, converted to open right adrenalectomy through an anterior approach due to adherence of the tumor to the renal vein. The pathology revealed a PGL.
Conclusion:
PCC/PGL are rare but life-threatening neuroendocrine tumors that require early detection to reduce associated morbidities and mortality and improve surgical outcomes. CT is commonly used to characterize adrenal lesions and an absolute washout of >60% is most consistent with an adenoma. However, as demonstrated by these two cases, washout exceeding 60% can also be seen in non-adenomas, perhaps secondary to degeneration of the nodule causing necrotic or cystic changes or uncommonly, the presence of a high lipid content in the tumor [1]. Thus, when clinical suspicion is strong and/or there is a positive biochemical workup, confirmatory imaging should be considered to establish the diagnosis.
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