DescriptionResearchers at the University of Toledo have found that thyroid nodule microenvironment cell profiling can be used as a predictive and prognostic marker for thyroid cancer. This approach uniquely focuses on the phenotype, rather than the genotype, of the microenvironment. Recently described Double Negative (DN) T-cells were significantly more abundant in lymphocytic infiltrates of thyroid cancer. They were shown to downregulate proliferation and cytokine production of activated effector T cells present in the tumor microenvironment and contribute to tumor tolerance and active avoidance of tumor immunity. If the quantify of DN T cells exceeds the defined threshold, it indicates a likelihood of cancer presence. Aside from immune cell profiling, our approach further establishes an integration of the information derived from transcriptome/meta-analysis of the genome and cytokine/chemokine signal analysis all from thyroid FNA. Applications[[Unsupported Character - Symbol Font •]] Diagnosis of thyroid cancer from FNA samples[[Unsupported Character - Symbol Font •]] Predictive tool of severity of disease Advantages[[Unsupported Character - Symbol Font •]] Microenvironment profiling can provide a unique way to diagnose and assess disease progression[[Unsupported Character - Symbol Font •]] Sheds light on cellular crosstalk; more accurate diagnose; can prevent unnecessary surgery IP Status:Patent Pending

Adrenal

ADRENAL - TUMORS

Frailty in Patients With Mild Autonomous Cortisol Secretion Is Higher Than Patients With Nonfunctioning Adrenal Tumors.

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SAT-LB37

Background: Mild autonomous cortisol secretion (MACS) affects up to 50% of patients with adrenal adenomas. Frailty is a syndrome characterized by diminished strength and endurance and serves as a marker of declining health and dependency. We hypothesized that patients with MACS are more frail when compared to patients with nonfunctioning adrenal tumors (NFAT).

Methods: This is a retrospective study of adult patients with adrenal adenoma evaluated at a tertiary center from 2004 to 2018. MACS and NFAT were defined as cortisol after 1 mg overnight dexamethasone suppression (DST) between 1.8-5 mcg/dl and <1.8 mcg/dl, respectively. Frailty index (FI, range 0-1) was calculated using a 47 variables -deficit model (20 comorbidities, 14 activities of daily living, and 13 symptoms). Patients were excluded if treated with exogenous glucocorticoids, if diagnosed with overt adrenal hormone excess, another adrenal disorder, or if missing variables of interest.

Results: MACS was diagnosed in 168 patients (67% women) at a median age 65 (30-91) years and NFAT in 275 patients (61% women) at a median age of 59 (21-84) years. Patients with MACS demonstrated higher prevalence of hypertension (73% vs 62%), cardiac arrhythmias (50% vs 40%), and chronic kidney disease (25% vs 17%), but lower prevalence of asthma (5% vs 14%), when compared to patients with NFAT, p<0.05 for all. Patients with MACS reported more symptoms of weakness (21% vs 11%), falls (7% vs 2%), and sleep difficulty (26% vs 15%) as compared to patients with NFAT, p<0.05 for all. Age, sex and BMI-adjusted FI was higher in patients with MACS vs patients with NFAT (0.17 vs 0.15, p=0.009). Using cut-off FI of 0.2, 42% of patients with MACS were frail, versus 30% of patients with NFAT (p=0.01).

Conclusion: Higher frailty in patients with MACS supports a more aggressive management, such as adrenalectomy over conservative follow up. Future prospective studies are needed to characterize frailty in greater detail in patients with MACS, as well as to examine frailty reversal by adrenalectomy.

Neuroendocrinology and Pituitary

PITUITARY TUMORS II

Poor Response to Pre-Surgical Treatment With Somatostatin Receptor Ligands Is Associated With Diabetes Mellitus in Patients With Acromegaly.

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MON-LB50

Introduction: somatostatin receptor ligands (SRL) represent the first-line medical therapy in acromegaly patients who were not cured by surgery and in those where surgical remission is unlikely. It is well known that SRL may negatively act on insulin secretion, with consequent hyperglycemia and diabetes mellitus (DM). **Purpose:** To evaluate whether the degree of response to surgical pre-treatment with SRL predicts alterations in blood glucose levels.**Patients and Methods:** We retrospectively studied 181 patients attending the Unit of Neurosurgery of our Hospital prior to transsphenoidal surgery. All patients had a biochemical and radiological diagnosis of acromegaly (nadir GH during OGTT >0.4 ng/mL; IGF-I above age-standardized UNL and pituitary adenoma at MRI scans); diagnosis of DM and impaired fasting glucose (IFG) was performed on fasting blood glucose (FBG) according to the American Diabetes Association guidelines; all parameters of the pituitary axes were determined. The response to SRL treatment was determined as percent change of GH levels. Data are presented as mean±SD; Continuous data normally distributed were analyzed using a two-tailed Student's t-test to compare two groups, and one-way ANOVA to compare several groups, followed by the Bonferroni post-hoc procedure for pairwise comparison of groups after the null hypothesis was rejected (p<0.05); categorical data were analyzed by chi-squared test.**Results:** 97 (54%) patients with acromegaly underwent pre-surgical treatment with SRL; we found no difference in age (53±11 vs. 51±12 years; p=NS) and sex (M/F: 51/46 vs. 43/41; p=NS) between SRL treated and non-treated patients. We found no difference in FBG between SRL treated vs. non-treated

patients. In contrast, we found increased proportions of IFG and DM patients in SRL treated when compared to non-treated patients (euglycemic: 45%, IFG: 42%, DM: 13% vs. euglycemic: 70%, IFG: 22%, DM: 8%, respectively; p=0.006). In addition, SRL treatment increased the odds ratio of IFG and DM (OR 4.7; 95%CI 2.1-10.3). When considering the degree of response to SRL pre-surgical treatment, we found that poor responders displayed at the time of surgery glycemias diagnostic of DM; whereas, good responders displayed glycemias in the range of IFG (percent change in GH levels 50±35% vs 79±22%, respectively; p<0.05).**Conclusions:** Our findings show that the proportion of patients with acromegaly undergoing surgery with glycemic levels diagnostic of DM, is modest. Interestingly, pre-treatment with SRL represents an independent risk factor for high glucose levels. Moreover, among patients on SRL pre-treatment, the ones that respond poorly are the ones that at the time of surgery display glycemias diagnostic of DM. Our findings suggest that SRL pre-treatment may predispose to worsened glucose metabolism but selectively affecting those patients in whom biochemical control is not reached.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

The Testosterone-To-Estradiol Ratio, Rather Than Testosterone or Estradiol Alone, Is a More Precise Marker of Metabolic-Related Outcomes in Males: Insights From a Systematic Review.

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SAT-LB8

Background: Estradiol (E2) has been shown to exert beneficial effects on males, particularly for metabolic outcomes. However, these benefits tend to be more evident when accompanied by concurrent increase in testosterone (T) levels, when the increase of E2 is secondary to the increase of T. Oppositely to its benefits in healthy males, when under metabolic and inflammatory diseases, E2 has been reported to be a marker of worse prognosis, once E2 is unproportionally high compared to testosterone in pathological conditions, which results in hypogonadism. The collective analysis of T and E2 shows that the balance between these two hormones determines whether increase in E2 levels is physiological or pathological, demonstrated by balanced T and E2, i.e., intact T:E2 ratio compared to healthy males, and
disrupted balance between T and E2, with impaired T:E2 ratio, respectivey. Hence, it seems that the dual relationship between E2 and health markers in males is based on the balance, or ratio, between T and E2. The objective of the present study is to propose a ratio between T and E2(testosterone-to-estradiol ratio, or T:E ratio) as a better predictor of health outcomes than testosterone or estradiol alone, and to differentiate health from pathological states within this single marker, from a review of the literature. **Methods:**We systematically searched for articles using the following criteria: 1. Any of the combinations of the expressions “testosterone” (AND) ”estradiol” (AND) “male(s)” (OR) ”men” (OR) “masculine”, or “testosterone-to-estradiol” (OR) “testosterone:estradiol” (OR) “estradiol-to-testosterone ratio” (OR) “estradiol:testosterone” (AND) “male(s)” (OR) ”men” (OR) “masculine”, to be present in the title and/or abstract; 2. Fully written in English; 3. Performed in humans; 4. Throughout the literature until Jan 30th 202020; and 5. Original researches.**Results:**We selected 39 articles, from which 27 were performed in healthy males, and 11 under metabolic or inflammatory conditions. Benefits of E2 in healthy males occurred irrespective of T for bone mass and quality, and anger levels. Benefits that were better identified when E2 and T were evaluated together include better libido, improved cognitive functions, improved well-being and other mood states, increased muscle mass, enhanced loss of fat mass, quality, increased basal metabolic rate, increased fat oxidation, and reduced cardiovascular markers, including reduced maximal intimal-media carotids thickness, when T:E ratio was > 13.7. In pathological states, increased estradiol was associated to increased risk of disease-specific complications, and worse quality of life, particularly when T:E was < 9.5. T:E ratio was also able to accurately identify healthy athletes from those affected by any sport-related metabolic conditions.**Conclusion:**Testosterone-to-estradiol (T:E) ratio is likely a more precise predictor of metabolic-related health outcomes in both healthy and pathological states, compared to testosterone or estradiol alone.

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS III

Concurrent Peri-Adrenal Paraganglioma and Renal AngiomyolipomaComplicated by Toxic Multinodular Goiter

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SAT-LB305

Concurrent Periadrenal Paraganglioma And Renal Angiomyolipoma Complicated By Toxic Multinodular Goiter

Abstract: A 40 years old woman presented with headache, palpitation and diaphoresis by the past 3 months, and then developed progressive dyspnea on exertion and chest pain 2 weeks ago. She also lost 5 kg of her body weight during the past 6 months. She ever had multinodular goiter and lobectomy was done 12 years ago, after that she lost to follow up. At meantime, toxic multinodular goiter was suspected and high level of free T_4, T_3, and suppressed thyrotropin were demonstrated. Furthermore, thyroid scan revealed heterogenous tracer uptake at her thyroid bed. Methimazole was started, however her blood pressure and heart rate were all uncontrolled. Pheochromocytoma was suspected and markedly elevated of both urinary normetanephrine and metanephrine were confirmed. Computed tomogram revealed a huge, right supra-renal mass. In addition, hypodensity mass were found at upper pole of right kidney, and the results of ^{131}I-Metaiodobenzylguanidine