Methods: This cohort study used data collected from common data model database at a single tertiary center in Seoul, Korea during 2004-2019. All patients with indication of gestational diabetes were included in the study. Cases were all women who experienced severe maternal morbidity using the ICD-10 codes identified by the Centers for Disease Control and Prevention. We assessed associations between representative biomarkers and severe maternal morbidity, using t-test and multivariable logistic regression models.
Results: Among 15,096 women who gave birth, the prevalence of gestational diabetes was 9.19% (n=1,388). Among those, 329 (23.7%) developed severe maternal morbidity during pregnancy. HbA1c, triglyceride, and fasting blood sugar were higher among women with severe maternal morbidity ($p<0.05$) and younger age showed association ($p<0.01$) with severe maternal morbidity.
Conclusion: This study showed that gestational diabetes was highly associated with severe maternal morbidity. Blood glucose and lipid metabolism were shown to be associated factors with severe maternal morbidity among women with gestational diabetes.

Diabetes Mellitus and Glucose Metabolism

TYPE 2 DIABETES MELLITUS

Diabetic Retinopathy in Latinos with Type 2 Diabetes: Temperance Is Protective

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SUN-686

Diabetic retinopathy (DR) is a duration-dependent complication of diabetes (DM). Yet some people with DM do not develop DR despite long disease duration. We evaluated such a group in search of novel factors that might signal protection from DR, using a large cohort of Latinos with type 2 DM and readable retinal images in the GOLDR study (n=614). Participants were phenotyped and 7-field retinal images were evaluated using Airlie House criteria. We identified 90 participants with DM>10y without evidence for DR (NoDR). We compared this group of patients with another group more susceptible to DR with evidence for earlier onset DR, in DM <10y duration (EoDR, n=103). Duration of diabetes in NoDR was [x+SEM] 14.2+ 0.6y, and in EoDR, 4.3+ 2.9 y ($p<0.001$), a 10-y spread. We found that most of the typical DR-associated risk factors could not explain DR protection in NoDR, including age, sex, age at DM onset, systolic blood pressure (SBP), percent insulin users, duration of hypertension, fasting plasma glucose, A1C, urine albumin/creatinine ratio and estimate glomerular filtration rate; these parameters were not significantly different in the two groups. Protective factors that did emerge were female sex ($p=0.02$), lower diastolic BP 69.1+0.9 vs. 72.5+0.9 ($p<0.01$) and lower alcohol intake 3.1+0.8 vs. 7.8+2 de/w (14g drink equivalents/week; $p=0.025$). In a sensitivity analysis to determine whether sex accounted for the apparent effect of alcohol on DR, we evaluated the men in the study, who were more likely to be drinkers. Alcohol consumption was compared in men with DR who reported drinking alcohol (n=93) compared to men without DR who also reported drinking (n=53). Men without DR reported significantly less alcohol intake, 14.8+2.4 vs. 25.9 +3.3 de/w in those with DR ($P<0.01$), suggesting that a possible protective benefit of lower alcohol consumption observed in NoDR was not likely to be mediated by the presence of fewer men in that cohort. In summary, type 2 diabetic patients with no evidence of DR after 10y were more likely to be women, have a lower diastolic BP, and who imbibed less alcohol when compared with a more accelerated DR subgroup with <10yrs duration of DM. We conclude that in type 2 DM Latino patients, a focus on alcohol intake may be a useful management strategy in addition to traditional medication-based BP control and renal protection, as well as a pathophysiological pathway for DR worthy of investigation.

Thyroid

THYROID NEOPLASIA AND CANCER

Suppressing the Growth of Human Medullary Thyroid Cancer Cells Using FDA-Approved Drug

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MON-513

Medullary thyroid carcinoma (MTC) is a solid tumor of the parafollicular cells in the thyroid gland. MTC has worse prognosis, when compared with other differentiated thyroid cancers, and MTC patients with distant metastases have a low survival rate unless thyroidectomy is performed at an early stage. Furthermore, conventional treatments have only marginal benefits. Therefore, there is a need to develop novel therapeutics for MTC. Several drugs that are developed and tested in preclinical trials fail in clinical trials. Therefore, repurposing the already US Food and Drug Administration (FDA)-approved drugs towards the treatment of cancers may have potential benefits, like saving the lives of cancer patients and lowering the investment cost of drug development. Here, we explored a novel precision treatment for thyroid cancers by repurposing the FDA-approved small molecule anti-parasitic drug Nitazoxanide (NTZ). In our study, we examined the anticancer effects of NTZ on human MTC cells using the TT cell line. We treated the TT cells with different concentrations of NTZ and assessed the cell proliferation by water-soluble tetrazolium salt (WST-1) assay and oxygen consumption rate (OCR) by Seahorse extracellular flux analysis (Seahorse XFe24 Analyzer). Additionally, we determined the effects of NTZ on the protein expression of key signaling molecules that regulate MTC cell growth by western blot analysis. Our results indicated that NTZ significantly suppressed the growth of TT cells at 24 h treatment. Very importantly, NTZ reduced the basal OCR demonstrating the inhibition of mitochondrial respiration. Moreover, protein expression studies revealed that NTZ markedly reduced the key Hippo

signaling pathway effector molecule TAZ and the oncogene c-myc. Interestingly, NTZ decreased the expression of epidermal growth factor receptor (EGFR) that plays an important role for RET activation in MTC. Importantly, NTZ increased the expression of p53 upregulated modulator of apoptosis (Puma). Taken together, our findings demonstrate for the first time that NTZ inhibits the growth of MTC cells and decreases the cancer cell metabolism. The mechanisms by which NTZ targets the MTC cells involve the suppression of key oncogenic proteins and upregulation of tumor suppressor molecule. Thus, our study highlights that repurposing this FDA-approved currently used drug may have a greater advantage of being tested in preclinical models of MTC, and therefore, for the rapid consideration of NTZ as a potential therapeutic drug to treat MTC patients in the near future.

Adrenal

ADRENAL MEDICINE — CLINICAL APPLICATIONS AND NEW THERAPIES

Increased Overall Mortality and Cardiovascular Morbidity in Patients with Adrenal Incidentalomas and Autonomous Cortisol Secretion: Results of the ENS@T NAPACA-Outcome Study

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OR25-05

Objective. Several smaller studies on adrenal incidentalomas (AI) suggested an association between autonomous cortisol secretion (ACS) and mortality (Di Dalmazi Lancet Diabetes Endocrinol 2014, Debono J Clin Endocrinol Metab 2014, Patrova Endocrine 2017). However, a recent meta-analysis (9 studies, 1356 patients) could not confirm these findings (Elhassan Ann Intern Med 2019). **Aim.** To investigate the effects of ACS on mortality, prevalence of cardiovascular (CV) risk factors, and (CV) morbidity, in a representative cohort of AI. **Design.** Retrospective observational study conducted at 27 ENS@T centers from 15 countries. **Methods.** Inclusion criteria: AI diagnosed 1996-2015, 1 mg dexamethasone suppression test, follow-up (FU) of ≥36 months, known survival status. Exclusion criteria: clinically relevant adrenal hormone excess (i.e. Cushing's syndrome, pheochromocytoma, primary hyperaldosteronism), known malignancy. Patient stratification: serum cortisol after dexamethasone (>5 µg/dl, ACS; 1.9-5 µg/dl, possible ACS (PACS); ≤1.8 µg/dl, non-functioning adenoma (NFA)). Definition of CV events (CVE): hospitalization due to myocardial infarction and related interventions (PTCA, surgical bypass), stroke, deep vein thrombosis, pulmonary embolism. **Results.** 3640 patients (57% NFA, 36% PACS, 7% ACS) were considered eligible: 64% females; median age 61 years (range 18-91); median FU 84 months (36-277) (distribution between subgroups n.s.). 352 patients died during FU. Age- and sex adjusted overall survival was significantly reduced in patients with PACS (HR 1.55; 95%CI 1.24-1.94) and ACS (1.84; 1.29-2.61). Prevalence of CV risk factors were significantly higher in PACS and ACS than in NFA (hypertension: 72, 73, 57%, p<0.0001; dyslipidemia: 42, 49, 35%, p<0.0001; diabetes: 22, 25, 17%, p<0.0001) When adjusted to relevant confounders (i.e. age, sex, CV risk factors), time to first CVE was shorter in PACS (HR 1.36; 1.07-1.73) and ACS (HR 1.62; 1.10-2.40) compared to NFA. **Conclusion.** PACS and ACS are associated with increased overall mortality and CV morbidity. However, to prove causality a large randomized intervention trial is required.

Reproductive Endocrinology

CLINICAL STUDIES IN FEMALE REPRODUCTION II

Variable Presentation of Two Patients with Gestational Trophoblastic Disease and Hyperthyroidism.

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SUN-009

Background: Gestational trophoblastic disease (GTD) represents a group of tumours caused by abnormal proliferation of trophoblastic cells, including molar pregnancy. Elevated β-hCG levels are an established marker for the presence of the disease and useful for monitoring. Due to the shared structural homology of β-hCG and TSH, hyperthyroidism can occur.

Clinical Cases: We present two patients with GTD associated with hyperthyroidisim. Case 1, a 20 year old female (G1P0) presented to the emergency department complaining of vaginal bleeding associated with abdominal pain. She was estimated to be 13 weeks. Laboratory