hyperthyroidism hospitalizations, 4% had chronic kidney disease. Chronic kidney disease with hyperthyroidism had a similar odd of inpatient mortality (AOR 0.79, CI 0.34–4.52, P= 0.787) and cardiogenic shock (AOR 2.66, CI 0.35–20.50, P=0.347). There was a statistically significant increase in odds of acute kidney injury (AOR 2.77, CI 1.60- 4.80, P <0.001) in those hospitalized with hyperthyroidism and chronic kidney disease compared to those with hyperthyroidism alone

**Conclusion:** Chronic kidney disease is associated with similar odds of hospital mortality and cardiogenic shock among patients hospitalized for hyperthyroidism with increased odds of acute kidney injury compared to those without hyperthyroidism. It is very important to consider all clinical features and thyroid manifestations in those patients with CKD.

## Cardiovascular Endocrinology
### CARDIOVASCULAR ENDOCRINOLOGY

***Epigenetic Programming Reverses Cardiometabolic Dysfunctions and Modulates Hypothalamic Genes Involved in Oxidative Stress and Inflammation in Angiotensin II-Treated Male Mice***

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Cardiometabolic disease is a global health issue that affects millions of people worldwide. Environmental perinatal exposure affects the health outcomes of the offspring and determines their disease susceptibility later in life. Angiotensin-II (Ang-II) is a peptide known to cause vasoconstriction, elevated blood glucose levels and inflammation. Previously, we reported that perinatal exposure to a hypercaloric diet (HD) results in elevated blood pressure (BP), weight gain, fasting hyperglycemia and glucose intolerance only in male mice. In addition, subcutaneous infusion of a sub-pressor dose of Ang-II was associated with a normalization in fasting blood glucose levels and a reversal of glucose intolerance only in programmed male mice. We hypothesize that epigenetic programming blocks the deleterious effects of Ang-II by altering its inflammatory signaling pathway. C57BL6/J dams were fed HD or regular diet (RD) for 1 month before mating with RD-fed males. After weaning, offspring of HD dams (programmed) and of RD dams (controls) were maintained on RD until 3 months of age. Mice then underwent 24 h BP recording (telemetry) and were implanted with Ang-II osmotic pumps (200 ng/kg/min/2 weeks). BP (24 h) was recorded weekly for 2 weeks. Mice were then sacrificed and hypothalami were harvested for mRNA sequencing (Illumina NextSeq). Programmed mice had lower 24 h systolic BP levels compared to control males (area under the curve: 41844 ±263.2 *vs.* 44522 ±275.6; p<0.0001). For RNAseq analysis, data showed 62 differentially expressed genes (DEG) in programmed males compared to controls. Using iPathway analysis, we found that some of the DEG are correlated to cholinergic synapse pathway (p=0.005) and neuroactive ligand-receptor interaction pathway (p=0.003). Nicotinic acetylcholine alpha-7 receptor (Chrna7) gene, known for its anti-inflammatory and hypoglycemic effects was upregulated in programmed males (p=0.024). On the other hand, genes involved in metabolic pathways and oxidative stress were differentially expressed as well. Phospholipase A2 group 3 (Pla2g3) gene, known to be overexpressed in oxidative stress was downregulated in programmed males (p=0.04). Moreover, Thiosulfate sulfurtransferase (Tst) gene, an antioxidant enzyme and used as a marker for enhanced insulin sensitivity was upregulated (p=0.023) in programmed males. Interestingly, female mice did not show any changes in BP or gene expression between the two groups. In conclusion, perinatal exposure to HD alters the cardiovascular response to Ang-II possibly through the modulation of gene expression of Chrna7 gene and genes involved in oxidative stress. Future experiments will be investigating the signaling pathways used in epigenetic programming to affect inflammation and oxidative stress in male mice.

## Cardiovascular Endocrinology
### CARDIOVASCULAR ENDOCRINOLOGY

***Exploring Cardio-Metabolic Effects of Liraglutide in Patients With Type 2 Diabetes Through a Proteomic Approach***

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**Background:** Diabetes is associated with complications that increase the risk of cardiovascular events in diabetic patients by 3 folds compared to healthy population. Liraglutide is a GLP-1 receptors agonist that showed cardiovascular benefits beside its glycemic advantage and weight reduction. The cardioprotective benefit of liraglutide in diabetic patients is unclear. **Objective:** To explore potential cardiovascular-protective and metabolic effects of Liraglutide treatment in patients with T2DM, through evaluation of alterations in circulatory proteins using a proteomics approach. To relate the altered proteins to identify pathways using bioinformatics and network pathway analysis. **Methods:** Twenty adult patients with T2DM were recruited with HbA1c of 8–11 %, on oral anti-diabetic agents or insulin in whom liraglutide was indicated, after obtaining the consent. At baseline: anthropometric measurements, basal blood for HBA1c, Renal function, creatinine clearance, lipid profile and urine in the fasting state. Then Liraglutide 1.8 mg subcutaneous once daily injection was initiated as prescribed by the treating physician. AT 3 months follow up visit post-treatment, similar parameters were measured. Primary endpoint was the reduction from baseline in HbA1c for ≥ 0.5 %. **Results:** Alterations in the abundance of urinary proteins, analyzed by Progenesis software, revealed statistically significant differential abundance in a total of 80 spots corresponding to 71 proteins, 14 up and 57 down (≥1.5-fold change, ANOVA, p ≤ 0.05) in the post treatment group. The proteins identified in our study are known to regulate processes related to acute phase response (APR), cellular metabolism and transport. The post treatment group demonstrated an increased

abundance of proteins that included alpha-1-antitrypsin, alpha-1-antichymotrypsin, serotransferrin, transthyretin, plasma protease C1 inhibitor, adenosylhomocysteinase 3 and beta-2-glycoprotein 1. The proteins with a decrease in abundance following treatment included transthyretin, serotransferrin, haptoglobin, complement C3, retinol binding protein and ceruloplasmin. Bioinformatic analysis using Ingenuity Pathway Analysis (IPA) identified dysregulation of pathways related cellular compromise, inflammatory response, and neurological disease. It also identified the involvement of the inflammatory signalling pathways, NFκb, AKT, p38 MAPK via their interactions with interleukin 12 as the central nodes.

**Conclusion:** The altered proteins identified in the present study showed an increase in the APR in patients with diabetes before treatment with liraglutide which was significantly reduced in the post treatment group. Increase in the APR is known to lead to a state of chronic inflammation predisposing individuals to cardiometabolic stress and disease.

# Cardiovascular Endocrinology

## CARDIOVASCULAR ENDOCRINOLOGY

### *External Validation of Prediction Models for Unilateral Primary Aldosteronism*

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Primary aldosteronism (PA) is the most common cause of remediable hypertension. Treatment is informed by establishing whether disease is unilateral (localized to one adrenal gland) or bilateral. Adrenalectomy is the guideline-recommended treatment of choice for unilateral PA. However, the currently recommended subtyping test, adrenal vein sampling (AVS), is often limited in accessibility. Thus, prediction models have been developed to diagnose unilateral PA and therefore bypass AVS. However, their generalizability remains unknown. In this retrospective study, we aimed to externally validate the performance of prediction models for unilateral PA in a large population of PA patients at a Canadian referral center who underwent AVS during 2006–2018. The presence of unilateral disease was indicated by a lateralization index of >3 on AVS. We identified 6 clinical prediction models from the literature. The discrimination and calibration of each model were systematically evaluated. For the original models, the derivation cohorts were based out of Japan, France, Italy, and England, with mean age between 46–54 years and 43–56% being male. The derivation cohorts were generally small, with 4 of the 6 studies reporting less than 50 people with unilateral PA. Common variables reported to be predictive of unilateral PA included male sex, hypokalemia, elevated aldosterone-renin ratio, and the presence of a unilateral adrenal nodule on imaging. The validation cohort included 342 PA patients who underwent successful AVS (average age, 52.1 years; 58.8% male). Among them, 186 (54.4%) demonstrated unilateral disease, and the remaining 156 (45.6%) were considered to have bilateral disease. The baseline characteristics of the validation cohort were broadly similar to those of the derivation cohorts, except for potential differences in ethnicity. When applying the models to the validation cohort, subjects were excluded if any candidate variables were missing. All 6 models demonstrated poor discrimination in the validation set (C-statistics; range, 0.59–0.72), representing a marked decrease compared to the derivation sets where they were reported (range, 0.80–0.87). Assessment of calibration by comparing observed and predicted probabilities of the unilateral subtype revealed significant miscalibration. Calibration-in-the-large for every model was >0 (range, 0.36–2.23), signifying systematic underprediction of unilateral PA. Calibration slopes were all <1 (range, 0.35–0.85), indicating poor performance at the extremes of risk. These results suggest that the original models were optimistic due to overfitting in the derivation cohorts and therefore lack generalizability. This is primarily because these models were developed in small data sets. In conclusion, clinical assessment with prediction models for unilateral PA cannot be readily used to bypass AVS in the general PA population.

# Cardiovascular Endocrinology

## CARDIOVASCULAR ENDOCRINOLOGY

### *Feasibility of a Novel Nonhuman Primate Model of Age-Related Nonalcoholic Fatty Liver Disease*

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The objective of the proposed study is to investigate the feasibility of the marmoset as an animal model to study age-associated nonalcoholic fatty liver disease (NAFLD). This chronic liver disease includes a spectrum of disorders ranging from increased triglyceride accumulation in the liver or hepatic steatosis to the more severe inflammatory form nonalcoholic steatohepatitis that can lead to cirrhosis and even hepatocellular carcinoma in individuals who do not have a history of alcohol abuse. Aging increases the prevalence of NAFLD and is strongly associated with the progression and severity of this disease. End-stage hepatic failure and liver cancer resulting from advanced NAFLD are leading indications for liver transplantation enhancing the burden on our healthcare systems. Accumulating clinical evidence also suggests that patients with NAFLD have a higher prevalence of cardiovascular disease. Pathogenetic mechanisms involved in the development and progression of NAFLD are poorly understood and as such, there is a lack of effective therapies. The common marmoset is a relatively short-lived non-human primate that recapitulates many of the physiological changes that occur in human aging. We hypothesized an age-associated increase in hepatic steatosis and alterations in serum lipid profile in the marmoset model. An increase in triglyceride levels and oil red o staining in liver tissues of old marmosets compared to young animals was observed suggesting an age-associated