

remission state. **Methods:** Our study was a cross-sectional study performed at the outpatient endocrinology clinic of Dr. Cipto Mangunkusumo Hospital, a tertiary care hospital in Jakarta, Indonesia. Graves' disease subjects were recruited, of whom then grouped into overhyperthyroidism (clinical signs and symptoms of hyperthyroidism, low THS, high thyroxine levels, treatment naïve of within 3 months of treatments) and remission state (no clinical signs and symptoms of hyperthyroidism, normal THs and thyroxine levels, without any anti thyroid drugs for at least 6 months). CIMT measurements were performed by trained physician on both right and left artery carotid arteries using an ultrasound equipped with software that automatically measured the CIMT. We also measured lipid profile, fasting blood glucose, and ECG. **Results:** We recruited 49 Graves' disease subjects, of whom 32 and 17 subjects were in overt hyperthyroidism and remission state respectively. Median CIMT in overhyperthyroidism and remission state were 0,473 mm and 0,488 mm respectively,  $p:0,109$ . Among clinical and laboratory risk factors, only age which had an independent correlation with CIMT in Graves disease. ( $r: 0,371$ ;  $p:<0,0001$ ). **Discussion:** Our is the first study that measured CIMT among subjects with Graves' disease in remission and overt hyperthyroidism state, of which we observed no differences. This might be due to the fact that the atherosclerosis risk factors were not distributed evenly on both group, of which subjects were older in the remission group. It has been reported that there are increasing CIMT along with aging (0,003-0,010 mm per year). Furthermore, in remission state we need to take metabolic and physical changes into consideration, such as increasing weight as much as 2,5% from prior weight along with increasing total cholesterol and LDL-cholesterol which both can affect CIMT levels. **Conclusions:** There are no significant differences in CIMT between overt hyperthyroid and remission state in Graves' disease. **Keywords:** carotid intima media thickness, Graves' disease, overt hyperthyroid, remission.

## Cardiovascular Endocrinology

### CARDIOVASCULAR ENDOCRINOLOGY

#### *Carotid Intima Media Thickness in Young Peruvians With Onset of Type 2 Diabetes Mellitus, an Early Marker of Vascular Compromise*

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**Objective:** To evaluate the relationship between the thickness of the carotid intima media (GIMT) with clinical and laboratory parameters in young people to identify asymptomatic endothelial dysfunction and prevent future vascular complications. **Methods:** This is a cross-sectional study of 81 adolescents from 10 to 18 years of age distributed in three groups: (i) 27 with onset of type 2 diabetes (DM2), (ii) 22 were non-diabetic obese; and (iii) 32 with normal weight, non-diabetic BMI from a National Reference Hospital in Lima, Peru. Laboratory evaluation consisted of fasting glucose levels, HbA1C, lipid profile, us-CRP, and Doppler ultrasound for measurement of the common carotid artery (right and left, both?). **Results:** In total 81 participants, 27 of them with a previous diagnosis

of type 2 diabetes mellitus, of which 22 obese patients without the onset of type 2 diabetes mellitus and 32 normal weight without onset of type 2 diabetes mellitus, the median for age was 20, 19.5 and 20 years respectively, with a predominance of the female sex in the three groups; the median time of illness in years for the study group was 6 years (IQR 3–8) with DM2; Regarding treatment, metformin was the main drug used (20 patients) followed by sulfonylureas (glimepiride and glyburide, 9 patients), insulin (7 patients) and DPP4 inhibitors (vildagliptin and sitagliptin, 06 patients); Differences were found between the groups of patients with DM2, obese patients without DM2, and normal weight subjects without DM2, this difference being stronger in terms of body mass index (26.29, 31.35, 23.73 kg / m<sup>2</sup>, respectively); abdominal girth (91, 97.25, 78 cm, respectively); fasting blood glucose (126, 87.5, 94 mg / dl, respectively); glycosylated hemoglobin (7.77, 4.85, 4.97%, respectively), all of these with a  $p: 0.001$ ; diastolic blood pressure (74, 68, 64 mmHg, respectively); and triglycerides (112, 112.5 and 65.5 mg / dl, respectively); The median IMT  $\pm$  iqr was 0.430  $\pm$  0.08 mm in adolescents with DM2; 0.420  $\pm$  0.03 mm, in non-diabetic obese adolescents; and 0.405 mm  $\pm$  0.02 mm, in non-diabetic adolescents with normal weight. In general, lean, non-diabetic adolescents had a lower IMT than adolescents with DM2 ( $p = 0.003$ ) and obese adolescents ( $p = 0.006$ ). **Conclusions:** Adolescents with DM2 had a higher median IMT compared to lean, non-diabetic adolescents that reflect the onset of early vascular damage due to DM 2.

## Cardiovascular Endocrinology

### CARDIOVASCULAR ENDOCRINOLOGY

#### *Effect of Chronic Kidney Disease on Outcome of Adult Patient Admitted With Hyperthyroidism: Analysis of the National Inpatient Sample 2016–2017*

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**Introduction:** Kidney and thyroid function and dysfunction are interrelated through several mechanisms. Thyroid hormones can also have significant impact on kidney disease so it is important to consider the physiological association of thyroid dysfunction in relation to chronic kidney disease (CKD). Research shows that hyperthyroidism is usually not associated with CKD but is known to accelerate it. We sought to determine the effect of chronic kidney disease on patient admitted with hyperthyroidism.

**Methods:** We queried the National Inpatient Sample (NIS) databases from 2016 to 2017 for adults aged 18 and above with hyperthyroidism as a principle diagnosis with and without hypertriglyceridemia using ICD-10 codes. Multivariate logistic and linear regression analysis was used accordingly to adjust for confounders

**Results:** There were over 71 million discharges in the combined 2016 and 2017 NIS database. Out of 17,705

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:  $41844 \pm 263.2$  vs.  $44522 \pm 275.6$ ;  $p<0.0001$ ). 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  $\geq 0.5$  %. **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 ( $\geq 1.5$ -fold change, ANOVA,  $p \leq 0.05$ ) 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