disease including arrhythmia with high thyroid hormone level. Also a number of case reports have shown association with hyperthyroidism and pro-thrombotic state. Although there are scarce publications associating liothyronine or Armour Thyroid and hypercoagulable thrombotic event, significant drug interactions may exist with patient who are more vulnerable with inherited condition or other risk factors.

Diabetes Mellitus and Glucose Metabolism

ISLETS, LIVERS, PLACENTA, AND VASCULATURE — THE MULTITISSUE IMPACT OF DIABETES

Inhibition of Protein Kinase C-beta2 Phosphorylation Restores Nuclear Factor-Kappa B Activation and Improves Peripheral Arterial Disease in Diabetes

Satyanarayana Alleboina, PhD, Madhu V. Singh, MSc, PhD, Thomas Wong, BSc, Ayotunde Dokun, MD, PhD.
UNIVERSITY OF IOWA, Iowa City, IA, USA.

OR14-06

Peripheral artery disease (PAD) is atherosclerotic occlusion of vessel outside the heart and most commonly affects the lower extremities. Diabetes (DM) accelerates the course and severity of PAD. Studies have shown that vascular endothelial cell NF-κB activity is required for post ischemic adaptation in experimental PAD. To better understand how DM contributes to PAD severity, we investigated the role of DM hyperglycemia in the activation of NF-κB under ischemic conditions. Induced ischemia in human vascular endothelial cell (HUVEC) cultures increased components of both canonical and non-canonical NF-κB pathways in the nucleus (p65 1.0 ± 0.1 vs 1.5 ± 0.2, p< 0.05, RelB 1.0 ± 0.1 vs 1.5 ± 0.2, p<0.01). Similarly, HUVEC acutely exposed to high glucose (HG, 25 mM) activated both canonical (IκB-α degradation, normal vs. HG 1.25 ± 0.02 vs 0.9 ± 0.0, p<0.05) and non-canonical NF-κB (p100 degradation, normal vs HG 0.021±0.001 vs 0.016±0.000, p<0.05) pathways. Prolonged exposure (3 days) of HUVEC to high glucose before ischemia resulted in impaired NF-κB activation as evident from decreased IκB phosphorylation (pIκB/IκB in normal glucose and ischemia 1.56 ± 0.22 vs 1.12 ± 0.35, p<0.01). To understand the signaling pathways underlying the ischemic activation of the NF-κB pathway, we used an array of antibodies to phosphoproteins involved in the inflammatory pathway. Compared to the lysates from cells grown in normal glucose, the lysates from cells grown in prolonged high glucose had dramatically increased phosphorylation of PKC-β2 (PKC-$\beta2^{pSer661}$, 8-fold increase). To test whether this increase in PKC-$\beta2^{pSer66}$ impairs NF-κB activation by ischemia, we treated HUVECS with prolonged high glucose exposure and ruboxystaurin (Rbx) (20 nM), an inhibitor of PKC-β2 phosphorylation, prior to ischemic exposure. Immunoblotting results confirmed that inhibition of PKC-β2 phosphorylation enhanced the ischemia induced NF-κB activation in HUVEC in this condition. We then tested the effect of Rbx on PKC-β2 phosphorylation and NF-κB activation in vivo in Akita mice, a model for type 1 diabetes. Consistent with our in vitro findings, in experimental PAD, NF-κB activity in the ischemic hind limb of Akita mice was significantly lower than those of the wild type (WT) mice as measured by IκB-α degradation (WT ischemic vs Akita ischemic; 0.04 ± 0.03 vs 0.10 ± 0.04 p<0.05). However, treatment of Akita mice with Rbx increased NF-κB activation in the ischemic hind limb (Akita ischemic 0.10 ± 0.04 vs ischemic+ Rbx 0.05 ± 0.02, p<0.05). Moreover, compared to the WT mice, the untreated Akita mice showed an impaired perfusion in the ischemic limbs (% perfusion recovery, WT vs Akita; 80.1 ± 10.3 vs 55.7 ± 10.1, p<0.05, n=5-8) that was improved in Rbx treated Akita mice (96.3 ± 2.3, p<0.01). Thus, hyperglycemic conditions increase PKC-$\beta2^{pSer66}$ in endothelial cells attenuating salutary NF-κB activation contributing to poor PAD outcomes in DM.

Neuroendocrinology and Pituitary

PITUITARY TUMORS II

Inter-Rater Reliability of T2 MRI Intensity of Somatotroph Adenomas; Endocrinologists vs. Neuroradiologist Pilot Study

Elena V. Varlamov, MD[1], José Miguel Hinojosa-Amaya, MD[2], Dawn Lim Shao Ting, MD[3], Maria Fleseriu, MD[1], Joao Prola, MD[1].
[1]Oregon Hlth & Sci Univ, Portland, OR, USA, [2]Hospital Universitario "Dr. Jose E. Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico, [3]Singapore General Hospital, 31 Third Hospital Ave, Singapore.

MON-320

Background MRI T2 hypointensity of growth hormone (GH) secreting pituitary adenomas (PA) has been associated with better biochemical response to somatostatin receptor ligands and has been suggested to be useful in selecting patients with expected favorable response for pre- and post-surgery medical therapy. However, in most imaging centers, T2 intensity measurement is not part of standard neuroradiologist (NR) reporting. **Objective** To assess whether endocrinologists (Es) can reliably measure PA T2 signal intensity by calculating inter-rater reliability between Es and NR. **Methods** Retrospective review of MRI in 20 patients with pituitary somatotroph macroadenoma randomly selected from an IRB-approved PA database who had preoperative MRI available. T2 MRI intensity of the solid portion of the PA was compared to the temporal gray matter (GM) and white matter (WM): hypo- (PA< WM), hyper- (PA> GM), and isointense (WM <PA <GM). Measurements were performed separately by a NR and by two Es trained to take measurements by the same NR. Statistics: SPSS 25; Cohen kappa (κ). **Results** Patient mean age was 47 ± 20 years, with 12 females; mean largest PA diameter was 22.6 mm (range 11-45 mm). NR measured 12 hyper-, 7 iso- and 1 hypo-intense PA. Agreement was moderate between NR and E#1 (κ 0.72, 95%CI 0.751-1.0, p<0.001) and NR and E#2 (κ 0.638, 95%CI 0.351-0976, p<0.001) and strong between E#1 and E#2 (κ=0.90, 95%CI 0.309-0.903, p=0.001). Hypointense PA (by NR) was read by both Es as isointense. One hyperintense PA (by NR) was read by both Es as isointense. One isointense PA was read by E#2 as hypointense. Overall adenomas were; 9 densely granulated GH, 5 sparsely granulated GH, 3 mixed GH and prolactin, 1 plurihormonal, 1 not classified, and 1 no surgical intervention. **Discussion** Inter-rater reliability between the 2 Es was strong, however, it was moderate