

deficiencies with secondary AI including 6 with secondary hypothyroidism, 1 patient with hypogonadotropic hypogonadism and 1 with hypothyroidism and hypogonadism in addition to secondary AI. Despite development of irAEs, ICI therapy was continued in 59 pts (65%) who developed an endocrine irAE. **Conclusions:** In summary, this is one of the largest single institution retrospective studies on ICI related endocrinopathies. The majority of endocrinopathies were low grade, and most patients continued ICI treatment. Reference: Barroso-Sousa, Romualdo. Incidence of Endocrine Dysfunction Following the Use of Different Immune Checkpoint Inhibitor Regimens: A Systematic Review and Meta-analysis. JAMA, Sept 2017

Adrenal

ADRENAL - HYPERTENSION

Role of Female Gender and Subcutaneous Fat in the Positive Association of Obesity with Idiopathic Hyperaldosteronism

NAGISA SAWAYAMA, MD, Yu Hatano, MD, Ken Ebihara, MD,PHD, Chihiro Ebihara, MD,PhD, Manabu Takahashi, MD,PhD, Shuichi Nagashima, MD,PhD, Tomoyuki Kurashina, MD,PhD, Kenta Okada, MD,PhD, Shun Ishibashi, MD,PhD. Division of Endocrinology and Metabolism, Department of Internal Medicine, Jichi Medical University, TOCHIGI, Japan.

MON-210

Context: Primary aldosteronism (PA) is the most frequent cause of secondary hypertension. The relationship between PA and various metabolic disorders including obesity, diabetes mellitus and dyslipidemia has been reported. On the other hand, PA consists of two main subtypes: unilateral aldosterone-producing adenoma (APA) and the bilateral idiopathic hyperaldosteronism (IHA), which have different etiologies. Recently, it was reported that the prevalence of obesity was higher in patients with IHA than those with APA, suggesting that there is a link between obesity and the etiology of IHA (Ohno Y et al. *J Clin Endocrinol Metab* 2018). Furthermore, it has also been reported that female patients with PA are more likely to have IHA than male patients.

Objective: Our objective was to clarify the pathological role of female gender in the positive association of obesity with IHA. Because of the difference of body fat distribution between men and women, we also investigate the contribution of visceral and subcutaneous fats in the pathogenesis of IHA.

Design: This retrospective observational study comprised 117 PA patients (IHA: n = 73, APA: n = 44) diagnosed by adrenal venous sampling between January 2006 and July 2019 at Jichi Medical University Hospital. We compared prevalence of obesity and metabolic parameters including visceral and subcutaneous fat areas measured by computed tomography between patients with IHA and APA by gender. We also compared visceral and subcutaneous fat areas between patients with IHA and APA by the presence of obesity, BMI ≥ 25 kg/m² (the diagnosis criteria by Japan Society for the Study of Obesity).

Results: In consistent with previous reports, BMI was significantly higher in patients with IHA than those with APA. However, in male patients, no difference of BMI between IHA and APA was observed. By contrast, in female patients, not only BMI but also both visceral and subcutaneous fat areas were significantly higher in IHA than in APA. Next,

we investigated the contribution of visceral and subcutaneous fats in the positive association of obesity with IHA in female patients. Subcutaneous fat area but not visceral fat area was significantly higher in female obese patients with IHA. By contrast, visceral fat area but not subcutaneous fat area was significantly higher in female non-obese patients with IHA.

Conclusions: These results suggest that obesity, especially subcutaneous fat accumulation, contributes to the pathogenesis of IHA in female patients.

Thyroid

THYROID NEOPLASIA AND CANCER

Quality of Life in Patients with Papillary Thyroid Microcarcinoma According to the Treatment: Total Thyroidectomy Versus Total Thyroidectomy with Radioactive Iodine Remnant Ablation

Jonghwa Ahn, MD, Min Ji Jeon, MD, PhD, Eyun Song, MD, Tae Yong Kim, MD,PHD, Won Bae Kim, MD,PHD, Young Kee Shong, MD,PHD, Won Gu Kim, MD, PhD. Asan Medical Center, Seoul, Korea, Republic of.

MON-494

Background: Recently, the role of radioactive iodine (RAI) ablation in the treatment of low risk differentiated thyroid carcinoma (DTC), especially for papillary thyroid microcarcinoma (PTMC), is controversial. This study aims to compare quality of life (QoL) parameters in patients with PTMC underwent total thyroidectomy (TT) versus TT with RAI ablation.

Methods: In this cross-sectional study, patients with PTMC who underwent TT with/without RAI remnant ablation were prospectively enrolled between June 2016 and October 2017. All patients completed three questionnaires: 12-item short-form health survey (SF-12), thyroid cancer specific quality of life (THYCA-QOL), and fear of progression (FoP). **Results:** The TT and TT with RAI groups comprised 107 and 183 patients, respectively. The TT with RAI group had significantly lower serum TSH level than TT group. However, after matching of TSH level between the groups (TT with RAI = 100, TT = 100), there was no significant difference in baseline characteristics. According to the SF-12, the score for general health showed significantly lower in TT with RAI group than TT group ($p = 0.047$). The THYCA-QOL also showed statistically significant difference in felt chilly score between the groups ($p = 0.023$). No significant differences in FoP scores were seen between the groups.

Conclusion: Patients with PTMC underwent TT with RAI ablation experienced more health-related problems than those managed by TT alone. These findings support RAI ablation should be carefully determined in patients with low-risk DTCs.

Neuroendocrinology and Pituitary

NEUROENDOCRINOLOGY AND PITUITARY

Diagnostic Value of Copeptin in Central Diabetes Insipidus

Emma Boehm, MD¹, Julie Sherfan, MSci², Joel Smith, MBBS¹, James King, MBBS RACS¹, John Wentworth, MBBS PhD¹, Cherie Chiang, MBBS(Hons), MAACB, FRACP, FRCPA¹.

¹Royal Melbourne Hospital, Parkville VIC, Australia, ²Royal Prince Alfred Hospital, Sydney, Australia.

MON-270

Background: The diagnosis of diabetes insipidus (DI) relies on indirect measurement of serum and urine sodium and osmolality. Since the diagnosis can only be made when an inappropriately dilute urine is paired with a significantly concentrated serum, the process is tedious for the clinician and uncomfortable for the patient. Copeptin is the C-terminal portion of the anti-diuretic hormone (ADH) prohormone which correlates with the less stable ADH, therefore providing a direct measurement of posterior pituitary response to hyperosmolar stress. (1,2)

Aim: This study aims to assess the diagnostic accuracy of copeptin in patients with central DI compared with subjects who underwent pituitary surgery without developing DI.

Methods: Serum samples from subjects with central DI, control subjects post pituitary surgery with no DI (NDI) and control subjects with SIADH were collected and analysed on the BRAHMS KRYPTOR copeptin assay. Groups were compared using unpaired T-test and Levene's test for equal variance.

Results: 56 samples from 22 subjects (13 females, 9 males, mean age 53.9 ± 15.5 y.o.) were analysed. Two subjects had resolved DI (RDI) after copeptin analysis and were successfully weaned off DDAVP and reclassified as NDI. Of the DI subjects, 1 had acute and 5 had chronic DI. Copeptin was lower in DI compared to NDI group ($p = 0.013$), while serum sodium, osmolality, urine osmolality were similar. Copeptin did not differentiate between the SIADH and NDI groups. After exclusion of NDI samples with serum sodium ≤ 140 mmol/L, the area under the curve was 0.97 (95% CI 0.9 to 1.0), a copeptin cut-off of 2.9 pmol/L predicts DI with a sensitivity of 92% and a specificity of 90%.

Conclusion: Copeptin concentration of < 3.0 pmol/L concurrently with serum sodium concentration of > 140 mmol/L predicted central DI when using post pituitary surgery subjects without DI as controls.

1. Winzeler, B., Zweifel, C., Nigro, N., Arici, B., Bally, M., Schuetz, P., Blum, C., Kelly, C., Berkmann, S., Huber, A., Gentili, F., Zadeh, G., Landolt, H., Mariani, L., Müller, B. and Christ-Crain, M. (2015). Postoperative Copeptin Concentration Predicts Diabetes Insipidus After Pituitary Surgery. *The Journal of Clinical Endocrinology & Metabolism*, 100(6), pp.2275-2282.
2. Fenske, J., Refardt, I., Schnyder I., Winzeler, B., Drummond J., Ribeiro-Oliveira, Jr. A., Drescher, T., Bilz S., Vogt, D.R., Malzahn, U., Kroiss, M., Christ, E., Henzen, C., Fischli S., Tönjes, A., Mueller, B., Schopohl, J., Flitsch, J., Brabant, G., Fassnacht M., Christ-Crain, M. (2018). Copeptin in the Diagnosis of Diabetes Insipidus. *New England Journal of Medicine*, 379(18), pp.1784-1786.

Thyroid

HPT-AXIS AND THYROID HORMONE ACTION

Essential Role of GATA2 in the Negative Regulation of the Prepro-Thyrotropin-Releasing Hormone Gene by Liganded T3 in the Rat Paraventricular Nucleus.

Go Kuroda, MD, Shigekazu Sasaki, MD & PhD, Akio Matsushita, MD & PhD, Kenji Ohba, MD & PhD, Yuki Sakai, MD, Shinsuke Shinkai, MD, Hiroko Nakamura, BS, Yutaka Oki, MD & PhD.

Hamamatsu University School of Medicine, Hamamatsu, Japan.

SAT-450

T3 inhibits thyrotropin-releasing hormone (TRH) synthesis in hypothalamic paraventricular nucleus (PVN). Although T3 receptor (TR) $\beta 2$ is known to mediate the negative regulation of prepro-TRH gene, its molecular mechanism remains unknown. Our previous studies on the T3-dependent negative regulation of the thyrotropin β subunit (TSH β) gene indicate the tethering mechanism, where T3-bound TR $\beta 2$ interferes with the function of the transcription factor GATA2, which is essential for TSH β expression. Interestingly, the transcription factor Sim1, a determinant of PVN differentiation in hypothalamus, is reported to induce the expressions of TR $\beta 2$ and GATA2. Indeed, our immunohistochemistry revealed the expression of GATA2 in the TRH neuron of the rat PVN. According to the experimental report with transgenic mice, the DNA sequence from nt. -547 to nt. +84 is sufficient for the expression of the prepro-TRH gene in PVN. Using the CAT reporter gene harboring this region, we found that this promoter is activated by GATA2 approximately 6-fold in CV1 cells. The deletion and mutation analyses identified a functional GATA-responsive element (GATA-RE) between nt. -357 and nt. -352. When TR $\beta 2$ was co-expressed, T3 reduced GATA2-dependent promoter activity to approximately 30%. T3-dependent repression was maintained after the mutation of the putative negative T3 responsive element (site4). Although the melanocortin 4 receptor signaling is known to stimulate the prepro-TRH promoter via protein kinase A pathway in the PVN, inhibition by T3 was dominant over the 8-bromo-cAMP-induced activation. We observed the in vivo recognition of GATA-RE by GATA2 using chromatin immunoprecipitation assay with CA77 cells, which express endogenous TRH. The electrophoretic mobility shift assay also demonstrated that GATA2 bound to oligonucleotide containing the GATA-RE. These results suggest that, as in the case of the TSH β gene, GATA2 transactivates the prepro-TRH gene and that T3-bound TR $\beta 2$ interferes with its function, resulting in the negative regulation of this gene.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS II

Progesterone Receptor Membrane Component 1 Suppresses Lipid Accumulation and Lipotoxicity in Animal Model of Diabetic Cardiomyopathy (DCM).

Sang R. Lee, D.V.M., Eui-ju Hong, Ph.D., D.V.M.

Chungnam National University, Daejeon, Korea, Republic of.

MON-672

Progesterone receptor membrane component 1 protects heart from lipotoxicity and suppresses diabetic cardiomyopathy (DCM).

Abstract: Diabetic cardiomyopathy (DCM) is one of the complications triggered by type II diabetes (T2D) (1). When free fatty acids (FFA) are abundant in insulin resistant pre-diabetic patients because of adipose lipolysis, FFA tends to move toward heart (2). Lipid accumulation can cause cardiac lipotoxicity and exacerbate DCM (3). In previous