

62.5% [60.3 – 64.6]), and total BMD (1.11 [1.08 – 1.14] vs. 1.17 [1.14 – 1.20] g/cm²) compared to Controls. Women with PCOS also had decreased upper (0.72 [0.70 – 0.74] vs. 0.73 [0.71 – 0.76] g/cm²) and lower (1.13 [1.10 – 1.16] vs. 1.15 [1.12–1.18] g/cm²) limb BMD compared to the HA group. Insulin sensitivity evidenced by Matsuda index was declined in PCOS group compared to Controls, yet was positively associated with SMI% in all groups (All: P ≤ 0.05). The OA group exhibited exaggerated insulin-like-growth-factor-1 (IGF-1) compared to Controls (P = 0.01) that had negative associations with LESMI% (r = -0.90; P < 0.01). Only Controls showed positive associations between IGF-1 and upper (r = 0.84) and lower (r = 0.72) limb BMD (All: P < 0.01). Unlike PCOS group, estradiol (r = 0.64) and the ratio of luteinizing hormone to follicle-stimulating hormone (r = 0.54) were positively associated with BMD (All: P < 0.05) in OA group. Also, unlike PCOS group, IGF binding protein-2 (IGFBP-2) was positively associated with muscle or bone mass in other groups. Specifically, IGFBP2 was associated with SMI% in Controls (r = 0.45) and HA (r = 0.67), with LESMI% in OA (r = 0.91), and with upper limb BMD (r = 0.98) in HA groups (All: P < 0.05). Reproductive-aged women with PCOS exhibited early signs of osteosarcopenia likely owing to their unique metabolic and endocrine alterations. Perturbations in insulin signaling and function may drive muscle and bone loss in PCOS. Understanding the biological mechanisms and management strategies that may delay or prevent the development of osteosarcopenia is recommended to improve the musculoskeletal health and associated long-term comorbidities of PCOS.

Neuroendocrinology and Pituitary

PITUITARY TUMORS I

Relationship Between Clinicopathological Aspects and MSH6/MSH2 and PD-L1 Expressions in Clinically Nonfunctioning Pituitary Adenomas

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Introduction: Mismatch repair (MMR) genes are associated with the MMR mechanism that corrects DNA polymerase misincorporation errors. We analyzed the aggressive pituitary adenomas (PAs) associated with Lynch syndrome due to germline mutation in the MMR gene. Reduced expression of MMR genes *mutS homologs 6/2 (MSH6/2)* directly promotes PA growth (1, 2). MMR gene expression and programmed cell death 1 ligand 1 (PD-L1) expression are involved in tumor immunity

with immune checkpoint inhibitors, but the direct association in PAs is not fully understood. **Hypothesis and Objectives:** MSH6/2 and PD-L1 expression could affect PA proliferation and invasion by pathological classification of nonfunctioning (NF) PAs because the proliferation and invasiveness differ depending on the PA histological subtype. In this study, we therefore analyzed the correlation between MSH6/2 and PD-L1 mRNA expression levels and clinicopathological factors related to tumor proliferation using human NFPAs. **Experimental Design:** We performed immunohistochemistry to classify the NFPAs into gonadotroph adenomas (GAs), silent corticotroph adenomas (SCAs), null cell adenomas (NCAs) and pituitary transcription factor 1 (PIT1) lineage PAs according to 2017 WHO classifications. Quantitative analyses were by real-time PCR to detect MSH6/2 and PD-L1 mRNA expressions in NFPAs (n = 89). We also performed statistical analyses of the expressions and clinicopathological factors such as Knosp Grade and histological subtypes. We investigated the effect of MSH6 knockout on cell proliferation and PD-L1 expression in AtT-20ins cells. **Major Results:** MSH6/2 expression was positively associated with PD-L1 expression. MSH6/2 and PD-L1 expressions are significantly lower in invasive NFPAs with Knosp Grade 3–4 or recurrence than in non-invasive NFPAs with Knosp Grade 1–2. Their expression is significantly lower in SCAs and NCAs than in GAs. Although MSH6/2 expression also tends to be lower, the PD-L1 expression tends to be higher in PIT1 lineage PAs, which is unlike SCAs and NCAs. MSH6 knockout in AtT-20ins significantly decreased PD-L1 expression with cell proliferation promotion. **Interpretation of results and Conclusion:** MSH6/2 and PD-L1 expressions of SCAs, NCAs, and PIT1 lineage PAs compared to GAs were thought to contribute to their clinically aggressive behaviors. The molecular mechanism of the difference in clinical features of NFPAs was partially elucidated. In particular, reduced expressions of MSH6/2 were thought to be useful for predicting the proliferation and invasiveness of NFPAs.

References: (1) Uraki S et al., *Endocr J.* 2017;64(9):895–906 (2) Uraki S et al., *J Clin Endocrinol Metab.* 2018;103(3):1171–1179. **Declarations of conflicts of Interest:** No authors declare any conflicts of interest.

Thyroid

THYROID NEOPLASIA AND CANCER

Quantitative Characteristics and Sonographic Patterns Before and After Thyroid Radiofrequency Ablation

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Although most thyroid nodules (TNs) are benign and require only serial observation, some may need treatment for symptoms. Radiofrequency ablation (RFA) has been used and shown to be a promising and well-tolerated new approach. The efficacy of RFA is evaluated by using parameters such as volume reduction ratio (VRR), and cosmetic or symptomatic improvement. However, no index is now available to predict the therapeutic success before