

Cancer Guidelines (ATA Guidelines) and the 2017 ACR TIRADS system (ACR Guidelines). The nodules were divided into benign or malignant categories based on surgical pathology. Noninvasive follicular thyroid neoplasms with papillary like nuclear features (NIFTP) were categorized as benign. **Results:** A total of 22 nodules were identified to have a RAS mutation. NRAS mutated nodules, all with the same point mutation (pQ61R c.182A>G), were most common 14/22 (63.6%). There was no significant difference in clinical features, ultrasonographic appearance or histopathologic outcomes between NRAS- and HRAS-mutated nodules. 12/22 (54.4%) were low risk by ATA Guidelines and 11/22 (50%) were TIRADS 4 (moderately suspicious) by ACR Guidelines. There was no significant difference in predictive value of ATA Guidelines vs ACR Guidelines. The prevalence of malignancy was 45.4% (only slightly lower than the general risk for a suspicious GSC). Invasive follicular variant papillary thyroid cancer (FVPTC), was the most common malignancy, 4/10 (40%). 6/10 (60%) were classified as low risk of recurrence post-operatively. All malignant RAS-mutated nodules (10/10) had at least one other non-cystic nodule present on ultrasonography whereas only 4/9 (44%) of RAS-mutated benign nodules did [P=.006]. RAS-mutated malignant nodules had significantly more nodules with irregular borders compared to RAS-mutated benign nodules (4/10 and 0/10, 40% and 0% respectively) [P=.03]. **Conclusions:** This is the first study to observe higher rates of malignancy in RAS-mutated indeterminate nodules when other non-cystic nodules are present. A lobectomy is the preferred surgical approach for RAS-mutated nodules, however a total thyroidectomy may be considered in patients with other non-cystic nodules or irregular nodules borders. Overall, RAS-mutated nodules have a low risk of recurrence post-operatively.

## Thyroid THYROID CANCER

### *Interobserver Variability in Ultrasound Reporting - Tertiary Hospital Radiologists Do Better*

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**Introduction:** Thyroid Imaging Reporting and Data System (TI-RADS) was developed to provide a standardized risk-stratification system for patients with thyroid nodules. Single-center studies have demonstrated an acceptable level of interobserver agreement in applying TI-RADS in clinical practice, however data regarding consistency among different centers is limited. In Israel, thyroid nodules are initially evaluated by ultrasound performed by radiologists at the health maintenance organization (HMO) and then patients are referred to tertiary hospitals for ultrasound-guided fine needle aspiration (FNA) biopsy when indicated. **Objective:** To evaluate the interobserver concordance in TI-RADS classification system reporting between the HMO and a tertiary hospital. **Methods:** We performed a retrospective analysis of the sonographic features of 370 thyroid nodules TI-RADS category 2 or higher, from 350 patients

evaluated by ultrasound at the HMO and at Hadassah Medical Center from January 1, 2018 to December 31, 2019. The primary outcome was concordance between the TI-RADS classification at the HMO compared to the hospital. Additional endpoints included correlation of TI-RADS to the Bethesda category following FNA, and correlation of TI-RADS with malignancy on final pathology. **Results:** Of 370 nodules, only 73 (19.8%) demonstrated concordance between the HMO and the hospital. The level of agreement was poor, with 277 (74.8%) nodules demonstrating higher TI-RADS at the HMO compared to the hospital, and 20 (5.4%) with lower TI-RADS at the HMO compared to the hospital ( $p<0.001$ , weighted Kappa = 0.120). Of the nodules referred to the hospital, 241 (65.1%) were selected for FNA. A strong correlation between the hospital TI-RADS and Bethesda category was demonstrated ( $p<0.001$ ). Furthermore, 60 (16.2%) nodules were surgically removed. A strong correlation was identified between the hospital TI-RADS and malignancy on final pathology ( $p<0.001$ ), yet there was no correlation with the TI-RADS of the HMO ( $p=0.346$ ). **Conclusions:** There is poor concordance between TI-RADS classification on ultrasound performed in the HMO compared to a tertiary hospital. In patients who underwent FNA and eventually surgery, the hospital TI-RADS strongly correlated with Bethesda category and final risk of malignancy. Standardization of thyroid ultrasound terminology and dedicated training in thyroid imaging are needed to improve the interobserver concordance in clinical practice.

## Thyroid THYROID CANCER

### *Is Metformin Use Associated With Decreased Thyroid Cancer Risk in Patients With Acromegaly?*

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**Context:** Acromegaly has long been blamed to portend an increased risk for benign and malignant thyroid neoplasia. Growth hormone (GH) and consequent insulin-like growth factor 1 (IGF-1) hypersecretion are implicated in cancer promotion. Metformin, a biguanide derived from the French lilac, is gaining considerable interest because of its plausible anti-tumor properties. Besides, metformin has been shown to inhibit somatotroph proliferation and decrease GH secretion in *in vivo* studies. Patients with acromegaly have high incidence of diabetes and were thereof treated with metformin. We hypothesized metformin use may be linked to decreased thyroid cancer incidence in patients with acromegaly. **Study Design and Methods:** The medical records of 508 patients with acromegaly followed at our tertiary referral center between 1969 and 2019 were retrospectively reviewed. The inclusion criteria were having a follow-up duration for at least 12 months and being regularly screened for nodular thyroid disease and thyroid cancer by ultrasonography as indicated in respective guidelines. Patients with acromegaly were evaluated based on ongoing or prior history of metformin use or thyroid cancer diagnosis. Metformin exposure was defined