1993 to 2014, previously diagnosed as NIFVPTC. The histological slides of these cases came from the Surgical Pathology files of the Pathology Department of UNICAMP, Brazil. After histological review, 14 cases reclassified as NIFTP were selected, all referring to female patients, of which 6 presented histological criteria of NIFTP associated with HT. Additionally, a histological and laboratory correlation of the 14 selected cases was performed through the dosages of relevant serum titers of antithyroid antibodies (anti-TPO and TgAb). Out of the 6 patients detected with association of NIFTP and TH, 5 had significant titers above 65IU/ml for anti-TPO and 120IU/ml for TgAb. Additional data from thyroid ultrasonography were collected and showed that cases of NIFTP without association with HT, presented nodules ranging from 1.5 cm to 5.1 cm, predominantly hypoechoic, solid, with regular contours, peripheral vascularization and located predominantly in the right lobe. In conclusion, 14 cases of NIFTP were detected, among 232 cases of PTC, with 6 cases being histologically associated with HT. Of these, 5 cases had laboratory tests with positive antithyroid antibody titers, proving this association, from a clinical point of view. All cases of NIFTP with and without HT association were female, with nodules ranging from 0.3cm to 5.0cm to ultrasound, predominantly in the right lobe.

Thyroid

THYROID CANCER

Impaired Sleep Influences Health Care Related Quality of Life in Patients With Well Differentiated Thyroid Carcinoma

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Background: Most patients with well differentiated thyroid carcinoma (WDTC) have a favorable prognosis but often report lower health care related quality of life (HRQoL). Sleep quality is one contributor to HRQoL that has also been reported to be impaired in WDTC patients. We evaluated patient reported outcome measures (PROM) of HRQoL and sleep quality in patients with WDTC, and compared them to patients with thyroid nodules.

Methods: This is a single institution cohort study utilizing data on consented adult patients with WDTC or thyroid nodules from an integrated cancer research database. We included participants with WDTC and thyroid nodules who completed the SF-36v2 HRQoL survey and the Pittsburgh Sleep Quality Index (PSQI). HRQoL was reported as a composite mental (MCS) and physical (PCS) component score that was compared with population-based norms and reported as the frequency of patients scoring below or well below the age-controlled reference population. Sleep quality was reported as PSQI raw score. Poor sleep quality was defined as a PSQI score >5. Cancer stage was calculated as American Joint Commission on Cancer (AJCC) 7th and 8th edition for each subject in the registry.

Results: We evaluated 727 patients and 424 (58%) had WDTC: 219 (72%) with papillary thyroid carcinoma (PTC), 28 (9%) with follicular variant of PTC, 53 (18%) with follicular thyroid carcinoma and 3 (1%) with Hurthle cell carcinoma. Of these, 208 (68.7%) were treated with radioactive iodine ablation with a mean cumulative dose of 197.7 (range 29-700) mCi. Mean age for WDTC was 42.7 years (standard deviation SD 15.4), and 53.4 years (SD 14.3) for nodules (p < 0.001). Eighty one percent of WDTC and 368 (87%) of nodules were female (p = 0.022). PSQI indicated worse sleep quality for WDTC patients with a mean of 6.85 (SD 3.97) and 174 (57.4%) reporting poor sleep quality with a PSQI > 5, compared with a mean score of 6.8 (SD 4.05) and 170 (40.1%) with PSQI > 5 for nodules (p < 0.001). WDTC diagnosis was associated with poor sleep quality with an odds ratio of 2.02 (95% confidence interval 1.48 - 2.75), p < 0.001. Poor quality sleep was also associated with WDTC stage using AJCC8 (0.017) but not AJCC7 (p = 0.067). Overall PCS, MCS, and HRQoL category were not significantly different between WDTC and nodule groups. When stratified by stage, MCS was inversely associated with cancer stage using AJCC7 (p = 0.035) but not AJCC8 (p = 0.96); PCS was associated with cancer stage using both AJCC7 (p = 0.003) and AJCC8 (p < 0.001).

Conclusions: Patients with WDTC report worse sleep quality than those with thyroid nodules and it is correlated with AJCC8 stage. HRQoL is similar between all WDTC patients and those with thyroid nodules in this cohort, though WDTC patients with higher stage reported worse physical function. The AJCC 8th was more sensitive to differences in sleep quality and physical function by stage than AJCC 7th.

Thyroid

THYROID CANCER

Indeterminate Thyroid Nodules With RAS Mutations Have Higher Rates of Malignancy When Multiple Non-Cystic Nodules or Irregular Borders Are Present

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Background: There is heterogeneity in positive predictive value for cancer in RAS-mutated cytologically indeterminate nodules and paucity of data with regards to specific ultrasound features that are associated with malignancy in these nodules. The goal of this study is to assess the ultrasonographic characteristics, in relation to clinical and histopathologic outcomes of thyroid nodules known to have a RAS mutation. Design and Methods: Cases were identified using our institutional Afirma® Genetic Sequence Classifier (GSC) database, and a retrospective review of electronic medical records for thyroid nodules biopsied between January 2018 and August 2020. Nodules categorized as Bethesda III or IV and harboring a RAS mutation by Xpression Atlas® were included. Thyroid ultrasound images were reviewed by the authors and were risk stratified according to the 2015 American Thyroid Association Thyroid Nodule and Differentiated Thyroid
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 ultrasound whereas only 4/9 (44%) of RAS-mutated benign nodules did [P=0.006]. 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=0.03]. 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 was 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 FNAs 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 \textit{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...