

achieve satisfactory rates of detection of relevant mutations. In this study, we examined a newly developed approach for ultrasensitive detection of oncogenic mutations in thyroid cancer using BRAF mutation as a proof-of-concept. In an exploratory analysis, we also correlated our findings with clinical outcomes and with levels of standard of care biomarkers. **Methods:** We included a group of patients with metastatic thyroid carcinoma. Cell free DNA (cfDNA) was isolated from an average of 2 ml of plasma and from matched formaldehyde fixed paraffin tissue blocks (FFPB) that were obtained from prior surgery. Extracted DNA was subject to preamplification of mutant copies using Q5 High-Fidelity PCR kit. Digital droplet PCR was performed on pre-amplified purified DNA where BRAF mutated allele frequencies (AF) were measured using BioRad ddPCR Qx200. **Results:** Thirty-three patients were included in our study with a median age at diagnosis of 62. Our method achieved a sensitivity of detection of 47.6% and a specificity of 80%. Mutant BRAF V600E was detected in cfDNA of 54.5% of patients (n=18) compared to 80.8% in isolated DNA from matched FFPB. Median overall survival (OS) was shorter in patients with wild type (WT) BRAF in both ctDNA and tissue (127m vs 218m, p=0.015; 116m vs 223m, p=0.004). Thyroglobulin (Tg) levels did not correlate with BRAF mutations either quantitatively or qualitatively. In the papillary thyroid carcinoma-classic variant cohort (n=20), however, patients with cfDNA mutant BRAF were more likely to have elevated Tg (90.9% versus 44.4% respectively, p=0.05). **Conclusions:** Our study provided a proof of concept for a newly developed technique to provide high sensitivity of mutation detection in thyroid cancer. The achieved sensitivity of detection is the highest to date using liquid biopsy in this tumor type. While we addressed only BRAF mutations in our study, the same approach can potentially be used for other mutations as well, likely changing the paradigm for use of liquid biopsy in thyroid cancer.

Thyroid

THYROID CANCER

Ultrasound Guided Percutaneous Ethanol Ablation of Benign Thyroid Nodule: A Study From a Tertiary Hospital in Eastern India

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Introduction: Ultrasound guided percutaneous ethanol injection (PEI) of benign thyroid nodule is an easy and effective procedure particularly in cystic and predominantly cystic nodule. **Aims:** To evaluate efficacy and safety of PEI in managing purely cystic and mixed cystic and solid thyroid nodules. **Materials and Methods:** Patients of either sex presented with solitary purely cystic benign thyroid nodule, solitary benign mixed with predominantly cystic (>50% of total volume) thyroid nodule, solitary benign mixed with predominantly solid (>50% of total volume) thyroid nodule, solitary solid thyroid nodule were included in this study. Patients who had a nodule BETHESDA 3 and above, pregnancy, patients with critical or terminal illness, patients with other malignancies, multinodular lesions of thyroid, patients with raised T3, T4 and/ or suppressed TSH level were excluded from the study. One hundred

sixty patients presenting with thyroid nodule were initially evaluated with thyroid function test and USG. Only those patients with euthyroid solitary thyroid nodules are subjected for fine needle aspiration (FNA). Nodules under BETHESDA 2 are considered for US guided percutaneous ethanol injection (PEI). One hundred twenty-three patients were excluded because of various reasons. Finally ethanol ablation was done in 37 patients. Benign, purely cystic and mixed thyroid nodules were aspirated under ultrasonography guidance. Sterile absolute alcohol (99.99%) (50% of volume aspirated/ maximum 10 ml) was injected and reviewed after 2, 5 and 7 months. In case of solid nodule alcohol (50% of nodule volume) was injected. A reduction in volume is calculated at each follow up visit. An adequate response is considered as ≥ 50 percent reduction in size from baseline after 7 months. If the reduction is $< 50\%$, then a second session of absolute ethanol injection is given. Again, patients were similarly followed up after 2, 5 and 7 months. **Results:** Thirty seven patients underwent PEI. Thirty three patients were considered for final analysis (4 lost to follow up). Response rate of PEI for purely cystic nodule was 100.0% and the overall response rate for mixed nodule was 53.57%. None of the solid nodule responded to PEI even after second session. Among the responder in the mixed nodules, 93.33% responded after first session of PEI. Minor complications like headache occurred in 54.1% patients in the first session. Transient pain at injection site were complained by 86.5% and 37.8% patients in the first and second session respectively. Nausea and vomiting were complained by 18.9% and 16.2% patients in the first and second session respectively.

Conclusions: PEI is an effective and safe for purely cystic and mixed thyroid nodules. It is a relatively safe and less invasive procedure from management of benign solitary cystic and mixed thyroid nodules.

Thyroid

THYROID CANCER

Unmet Information Needs Among Hispanic Women With Thyroid Cancer

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Background: Despite thyroid cancer being the second most common cancer in Hispanic women, little is known about access to and utilization of medical information resources by Hispanic women with thyroid cancer. **Methods:** Hispanic women who had diagnoses of thyroid cancer reported to the Los Angeles Surveillance Epidemiology and End Results (SEER) registry in 2014-2015, and who had previously completed our thyroid cancer survey in 2017-2018, were offered follow-up surveys in both English and Spanish (N=273; 80% response rate). Acculturation, which is the process by which individuals adopt the language, values, attitudes, and behaviors of a different culture, was assessed with the Short Acculturation Scale for Hispanics (SASH). Health literacy was assessed with the validated single-item question of "How confident are you filling out

medical forms by yourself?” with response categories based on a five-point Likert scale from “extremely” to “not at all”. Patients were also asked about their internet access, information resources used, and ability to access medical information about thyroid cancer in their preferred language. We generated descriptive statistics for all categorical variables and used Rao-Scott adjusted chi-square tests to test for a relationship between level of acculturation and the following variables: health literacy, internet access, information resources used, and ability to access information. **Results:** Participants’ median age at diagnosis was 47 years (range 20-79); 49% were low-acculturated, 25% had low health literacy, and 14% reported no internet access at home. Low-acculturated Hispanic women reported using information resources in both English and Spanish whereas high-acculturated women used resources in English only. Hispanic women were more likely to report the ability to access medical information about thyroid cancer all of the time if they preferred information in English compared to if they preferred it in Spanish (89% vs 37%, $P < 0.001$). Low-acculturated (vs high-acculturated) Hispanic women were more likely to have low health literacy (47% vs 5%, $P < 0.001$) and to report use of in-person support groups (42% vs 23%, $P = 0.006$). Depending on their level of acculturation, Hispanic women accessed the internet differently ($P < 0.001$) such that low-acculturated women were more likely to use only a smartphone (34% vs 14%) or have no internet access (26% vs 1%), and less likely to use both a smartphone and home computer/tablet (28% vs 58%) or use only a home computer/tablet (10% vs 21%). **Conclusion:** Our findings demonstrate that low-acculturated Hispanic women with thyroid cancer have greater unmet information needs and access information differently compared to high-acculturated Hispanic women. This study emphasizes the importance of a patient-focused tailored approach to providing medical information to this understudied population.

Thyroid

THYROID CANCER

Utility of Stimulated Thyroglobulin in the Differentiate Thyroid Cancer

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Introduction: The treatment of differentiated thyroid cancer has changed considerably, total thyroidectomy and radioactive iodine ablation represented the initial treatment for these patients, currently with a great debate around the choice of which patient should undergo ablation with radioactive iodine in the post-surgical period. Objective: To determine the values of stimulated thyroglobulin (in hypothyroidism) in patients with differentiated thyroid carcinoma who have had surgery and its relationship with the ATA 2015 recurrence risk stratification and the presence of distant or locoregional metastasis in post ablative total body scan with I131 Methodology: Retrospective study, which included patients with differentiated thyroid carcinoma, patients who have had total thyroidectomy surgery and subsequent

ablation with I131 in 45 days at the Central Hospital of Instituto de Prevision Social, from 2011 to 2018. There were evaluated: post-surgical thyroglobulin dosage in hypothyroidism, antithyroglobulin antibody measurement, and total body scan results at 72 hours post ablation with I131. There were excluded: Patients with positive antithyroglobulin antibodies, eu /hyperthyroidism, or incomplete data.

Results: 100 patients conformed by women (88.0%), whose average age was 44.7 (± 16.1), intermediate risk 60%, high risk 31% and low risk 9%. According to the stimulated thyroglobulin values, 3 groups were classified: Group A thyroglobulin less than 1 ng/dl 32%, Group B 1 to 10 ng/dl 39%, Group C greater than 10 ng/dl 29%. Of the patients at intermediate risk n: 60, 23 (38%) belonged to group A, 27 (45%) to group B and 10 (17%) to group C. Of high-risk patients n: 31, 7 (22%) belonged to group A, 8 (26%) to group B, and 16 (52%) to group C. Of low risk patients n: 9, 2 (22%) belonged to group A, 4 (44%), group B, and 3 (33%) to group C. Post-ablative body scan detected locoregional or distant metastases in 23 (23%) patients, of which 2 (8.6%) belonged to group A, 6 (26%) to group B, 15 (65%) to group C. They were intermediate risk 10 (43%) and high risk 13 (57%) of them. No low-risk patient presented a positive RCT. There was found a relationship between thyroglobulin and high ATA risk ($p < 0.05$) with positive RCT. Association between thyroglobulin $> 10 \text{ ng/dL}$ and the presence of metastasis ($p = 0.0001$), Exp (B) 15.1 with R2 25 and 35%. **Conclusion:** A stimulated postoperative thyroglobulin dosage greater than 10 ng/dL increases the chances of recurrence 15 times, with 25 to 37% chance of it. So, it would be important to consider ablation with iodine 131 in this type of patients.

Thyroid

THYROID CANCER AND AUTOIMMUNITY

Cepharanthine Blocks the Presentation of Thyroid & Islet Peptides in a Novel Humanized Autoimmune Polyglandular Syndrome Type 3 Variant (APS3v)

Mouse Model

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Introduction: There is a strong genetic association between autoimmune thyroiditis (AITD) and Type 1 diabetes (T1D), and the co-occurrence of AITD and T1D in the same individual is referred to as Autoimmune Polyglandular Syndrome type 3 variant (APS3v). We previously discovered a unique amino acid signature of the HLA-DR pocket (designated APS3v HLA-DR pocket) that predisposes to APS3v, and we found that both thyroid (Tg.1571, TPO.758) and islet (GAD.492) peptides can bind to this flexible APS3v HLA-DR pocket. The goal of the present study is to identify small molecules that can block the presentation of these thyroid and islet peptides by the APS3v HLA-DR pocket as a potential therapeutic approach for APS3v. **Methods:** We screened a panel of small molecules using an *in vitro* screening assay we developed using Baculovirus-generated recombinant APS3v-DR. To validate “hit” compounds discovered by the *in vitro* assay in a mouse model we established