CLINICAL **THYROIDOLOGY** FOR THE **PUBLIC**

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THYROID NODULES

Ultrasound and molecular marker analysis for diagnosing cancer in indeterminate thyroid nodules

BACKGROUND

Thyroid nodules are common. Although thyroid biopsy is the "gold standard" for diagnosing thyroid cancer, some biopsies come back as "indeterminate", meaning that they cannot be diagnosed as benign or cancerous on the basis of the cells alone. The practice used to be for all patients with an indeterminate nodule to have surgery, but now there are some tests available that can help assess the risk of cancer. Testing for molecular markers (mutations in genes that are expressed in either benign or cancerous cells) can be used in thyroid biopsy specimens to either to diagnose cancer or to determine that the nodule is benign. However, these tests check for many cancer mutations and can be expensive (if you have an insurance that doesn't cover it). Ultrasound is also an important and useful tool to try and determine a nodule's risk of being cancer. This study looked at using a combination of ultrasound characteristics and checking for the 2 most common molecular mutations, BRAF and NRAS, for determining thyroid cancer in patients that had a thyroid nodule that was "suspicious for a follicular neoplasm" and then had surgery.

THE FULL ARTICLE TITLE

De Napoli L et al. Indeterminate single thyroid nodule: synergistic impact of mutational markers and sonographic features in triaging patients to appropriate surgery. Thyroid 2016;26:390-4. Epub December 9, 2015.

SUMMARY OF THE STUDY

At total of 258 patients with thyroid nodules that on biopsy had lesions "suspicious for a follicular neoplasm" and then had their entire thyroid removed. They recorded ultrasound features of the suspicious nodule and tested the tissue samples for BRAF and NRAS. About 35% of the nodules were cancerous. Of 8 nodules that had a BRAF mutation, all were cancer. Of 31 nodules that had NRAS mutations, 22 were cancer (70%). No nodules had both mutations. Patients that had 2 malignant-type features on ultrasound had cancer. Adding positive ultrasound features to mutation positivity for a nodule increased the prediction for cancer.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that combining ultrasound features and limited molecular marker testing with BRAF and NRAS could help in the diagnosis of thyroid cancer. Further studies are needed to confirm these finding but this may lead to a less expensive way to evaluate whether a nodule needs to be removed by surgery or can be monitored without surgery.

— Ronald Kuppersmith, MD

ATA THYROID BROCHURE LINKS

Thyroid Cancer: http://www.thyroid.org/thyroid-cancer/

Thyroid Nodules: http://www.thyroid.org/thyroid-nodules/

ABBREVIATIONS & DEFINITIONS

Thyroid nodule: an abnormal growth of thyroid cells that forms a lump within the thyroid. While most thyroid nodules are non-cancerous (Benign), ~5% are cancerous.

Thyroid Ultrasound: a common imaging test used to evaluate the structure of the thyroid gland. Ultrasound uses soundwaves to create a picture of the structure of the thyroid gland and accurately identify and characterize nodules within the thyroid. Ultrasound is also frequently used to guide the needle into a nodule during a thyroid nodule biopsy.

Thyroid biopsy: a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancer. The doctor uses a very thin needle to withdraw cells from the thyroid nodule. Patients usually return home or to work after the biopsy without any ill effects.

THYROID NODULES, continued

Indeterminate thyroid biopsy: this happens usually when the diagnosis is a follicular or hurthle cell lesion. Follicular and hurthle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or hurthle cell cancer from noncancerous adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule.

Molecular markers: genes and microRNAs that are expressed in benign or cancerous cells. Molecular markers can be used in thyroid biopsy specimens to either to diagnose cancer or to determine that the nodule is benign.

Cancer-associated genes: these are genes that are normally expressed in cells. Cancer cells frequently have mutations in these genes. It is unclear whether mutations in these genes cause the cancer or are just associated with the cancer cells. The cancer-associated genes important in thyroid cancer are BRAF, RET/PTC and RAS.

BRAF gene: this is gene that codes for a protein that is involved in a signaling pathway and is important for cell growth. Mutations in the BRAF gene in adults appear to cause cancer.

Thyroid Awareness Monthly Campaigns

The ATA will be highlighting a distinct thyroid disorder each month and a portion of the sales for Bravelets™ will be donated to the ATA. The month of July is **Graves' Disease Awareness Month** and a bracelet is available through the ATA Marketplace to support thyroid cancer awareness and education related to thyroid disease.