

**THYROID NODULES****Hürthle-Cell Nodules classified as suspicious by the Afirma gene expression classifier had a low cancer rate****BACKGROUND**

Thyroid nodules are common and may be found in up to 50% of people. While most nodules are benign (non-cancerous), up to 8% of nodules are cancers. Thyroid biopsy is the most commonly used method to distinguish cancerous from non-cancerous thyroid nodules. Although most thyroid biopsy results are either non-cancerous or cancerous, 15-30% of these results are in the gray indeterminate zone, when thyroid cancer cannot be excluded or confirmed. For example, Hurthle cell nodules yield indeterminate biopsy results. While surgery is recommended to remove thyroid nodules with indeterminate results, most of the excised nodules are found to be non-cancerous. Molecular genetic tests are currently available to further evaluate thyroid nodules with indeterminate biopsy results. The Afirma gene expression classifier (AGEC) examines possible mutations in 167 genes in the thyroid biopsy specimens to identify thyroid nodules with a low cancer risk. This test classifies thyroid nodules as “benign” with a cancer risk of less than 6% or “suspicious” with a cancer risk of 44%. A few prior small studies have showed an increased rate of suspicious AGEC results in Hurthle cell nodules, while most of these nodules proved to be non-cancerous after surgical removal. This is the largest study reported to date that evaluates the performance of the AGEC in patients with Hurthle cell nodules.

THE FULL ARTICLE TITLE:

Brauner E et al. Performance of the Afirma gene expression classifier in Hürthle cell thyroid nodules differs from other indeterminate thyroid nodules. *Thyroid* 2015;25:789-96. Epub June 4, 2015.

SUMMARY OF THE STUDY

The study included patients followed at three tertiary care centers who had HCNs with indeterminate biopsy results reported as suspicious for a Hürthle-cell nodule or with a predominance of Hürthle cells. The study included 62 patients with Hurthle cell nodules diagnosed during the 1-year period before the use of AGEC; among

the 50 patients who underwent surgery, 17 (27%) had cancerous nodules. The study also included 169 patients with Hurthle cell nodules who underwent repeat thyroid biopsy with AGEC after the initial biopsy showed indeterminate cytology. Among these patients, 97 were treated based on clinical and ultrasound features without using the AGEC result; 78 patients (80%) underwent surgery and 23 (29%) had cancerous thyroid nodules, the cancer rate being similar to the patients with HCNs treated prior to the use of AGEC. A total of 72 out of the 169 patients who had the AGEC were treated based on this test results; among these patients, 45 (63%) had suspicious AGEC results, 26 (36%) had benign results and one was non-diagnostic. Only 6 out of the 43 patients (14%) with suspicious AGEC results who underwent surgery had cancerous nodules. A total of 23 out of the 26 patients with benign AGEC results (88%) were followed clinically; only 3 patients had surgery and all 3 nodules were non-cancerous.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows a low AGEC performance for identifying Hurthle cell cancer. Although a large proportion of Hurthle cell nodules are classified as suspicious by the AGEC, only 14% of these nodules are cancerous. Further, only 32% of patients with Hurthle cell nodules avoided surgery based on a benign AGEC result. This study suggests that clinical judgment appears to better identify Hurthle cell cancer than the AGEC.

— Alina Gavrilă, MD, MMSC

ATA THYROID BROCHURE LINKS

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

Thyroid cancer: <http://www.thyroid.org/cancer-of-the-thyroid/>

Thyroid Surgery: <http://www.thyroid.org/thyroid-surgery/>

**THYROID NODULES**, continued**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), 5-10% are cancerous (malignant).

Hürthle cell nodule: thyroid nodule made of Hurthle cells, which are normal cells found in the thyroid together with the follicular cells. Hurthle cells have a distinctive appearance under the microscope.

Thyroid fine needle aspiration biopsy (FNAB): a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancerous. 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.

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 non-cancerous nodules. This occurs in

15-20% of biopsies and often results in the need for surgery to remove the nodule.

Non-diagnostic thyroid biopsy: this happens when not enough cells are obtained during the biopsy to provide a diagnosis. This occurs in 5-10% of biopsies. It often results in the need to repeat the biopsy.

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

Genes: a molecular unit of heredity of a living organism. Living beings depend on genes, as they code for all proteins and RNA chains that have functions in a cell. Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring.

microRNA: a short RNA molecule that has specific actions within a cell to affect the expression of certain genes.