



THYROID NODULES

Evaluation of the Afirma™ Gene Expression Classifier to determine appropriateness of surgery in patients with indeterminate thyroid nodule biopsy results

BACKGROUND

Thyroid nodules are very common, occurring in 30-50 % of patients. The absolute risk of thyroid cancer is any one nodule is low (approximately 5%), but the possibility of cancer leads to thorough evaluation and much anxiety in patients and physicians alike. A thyroid biopsy can provide a diagnosis in most cases. The exception is with an indeterminate result, meaning that neither a diagnosis of cancer or benign (noncancerous) is made. Historically, patients with indeterminate biopsy results were sent to thyroid surgery to remove at least half the thyroid for diagnostic reasons. This was done despite a relatively low risk of cancer (15-20%) in these patients.

Recent studies have identified molecular markers in thyroid cells that may be predictive of cancer. These molecular markers are mutations in certain genes that are associated with cancer. While no single molecular marker is that helpful, a group of molecular markers may be useful in predicting cancer. One such panel of molecular markers is the Afirma™ Gene Expression Classifier (GEC) which, when used on thyroid biopsy specimens, has been reported to help make a diagnosis of benign vs cancer in cases of indeterminate cytology. This study was done to evaluate the Afirma™ GEC performance in an academic center (the Mayo clinic).

THE FULL ARTICLE TITLE

McIver B et al An independent study of a gene expression classifier (Afirma™) in the evaluation of cytologically indeterminate thyroid nodules. *J Clin Endocrinol Metab.* April 29, 2014 [Epub ahead of print]. jc20133584. PMID: 24780044.

SUMMARY OF THE STUDY

A total of 984 patients with 1207 nodules who underwent FNA at the Mayo Clinic during the study period were evaluated with thyroid biopsy. At the time of the procedure, samples were obtained for the GEC through the same method as the cytology and the samples were reserved. The patients were offered the Afirma™ GEC

test if their cytology results returned in the indeterminate category. If the GEC returned benign, the patients were offered serial ultrasounds and clinical follow-up. If suspicious by GEC, thyroid surgery was recommended.

Of 1207 nodules biopsied, 105 were reported as indeterminate (8.7%). Of these, 18 patients chose surgery, so 72 samples were obtained for analysis by GEC. In 12 samples (17%), there was not enough cellular material to analyze. Of the remainder, 17 (28%) were reported benign on GEC and 43 (72%) were reported as suspicious. A total of 4 patients with a benign GEC result went ahead with surgery anyway, with 1 cancer being found. A total of 32 patients with a suspicious GEC result had surgery with 5 cancers being found.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The use of the Afirma™ GEC at Mayo Clinic showed a lower than expected rate of benign results and a lower than expected rate of cancer at surgery in nodules that were noted to be suspicious on GEC. The authors of the paper suggest that the results of this assay may vary depending upon risk of cancer in the population studied. However, this study also raises questions as to the effectiveness of the GEC in preventing surgery for benign nodules, especially given the high cost of the test.

Cytology alone continues to be the best initial analysis for the evaluation of thyroid nodules. In cases where cytology is unclear (indeterminate cytology), analysis of molecular markers are helpful as another option in the evaluation of thyroid nodules. Further studies of molecular markers are needed to improve the prediction of cancer prior to surgery.

— Julie E. Hallanger Johnson, MD

ATA THYROID BROCHURE LINKS

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

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



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% are cancerous.

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 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.

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. These cytology results include Atypia of Uncertain Significance, Follicular Lesion of Undetermined Significance, Follicular Neoplasm and Hurthle Cell Neoplasm.

Cytology: the results of the review of the cells or tissue removed, often done by Pathologist physicians with special training in this area

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.

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.

Afirma™ Gene Expression Classifier: a test for a group of molecular markers in thyroid biopsy specimens in order to determine the likelihood that a thyroid nodule is benign or cancerous. This test is performed by the company Veracyte Inc.

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 October is **Thyroid Nodule Awareness Month** and a bracelet is available through the [ATA Marketplace](#) to support thyroid cancer awareness and education related to thyroid disease.

