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

A publication of the American Thyroid Association

AMERICAN THYROID ASSOCIATION
FOUNDED 1923
www.thyroid.org

THYROID NODULES

Mutational testing is helpful in identifying indeterminate thyroid nodules as benign

BACKGROUND

Thyroid nodules are very common, affecting up to 50% of people. Thyroid biopsy is an important test that is used to determine whether or not a thyroid nodule is cancerous. Patients whose biopsy result falls into a high risk category usually need surgery; whereas those in low risk categories are often followed clinically. However, a significant proportion of biopsy specimens fall into categories that are indeterminate – in other words a diagnosis of cancer cannot be made on examining the cells alone. Indeterminate nodules are further divided into atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS) and suspicious for follicular neoplasm (SFN). Indeterminate thyroid nodules have a 15-30% risk of being cancerous and some guidelines recommend surgery for these nodules in order to confirm the diagnosis.

Molecular markers are mutations in genes associated with cancer. Analysis of molecular markers in biopsy specimens can be used to determine the risk of cancer. The Thyroseq™ Next Generation panel developed by Nikiforov and colleagues at the University of Pittsburgh is a panel of molecular markers that has been available for a while to determine the risk of cancer in indeterminate nodules. Nodules with a negative Thyroseq™ panel are considered benign and surgery can be avoided. The purpose of the current study was to determine how accurate the Thyroseq™ Next Generation panel is in predicting the risk of cancer in indeterminate thyroid nodules.

THE FULL ARTICLE TITLE

Shrestha RT et al. Correlation between histological diagnosis and mutational panel testing of thyroid nodules: a two year institutional experience. Thyroid 2016;26:1068-76. Epub July 12, 2016.

SUMMARY OF THE STUDY

The authors examined biopsy specimens from 261 nodules that were operated on at the University of Minnesota Medical Centre between Jan 2013 and Dec 2014. A total of 125 nodules (48%) were found to be malignant. A total of 102 surgeries (39%) were performed on indeterminate thyroid nodules (73 ASUS/FLUS, 29 SFN). The cancer rate of ASUS/FLUS nodules was 30% and the cancer rate of SFN nodules was 28%.

The Thyroseq™ Next Generation panel testing was performed on 44 of the 73 nodules in the ASUS/FLUS category and was found to have a sensitivity of 85%, specificity of 65%, positive predictive value of 50% and negative predictive value of 91%. Mutational testing was performed on 12 of the 29 nodules in the SFN category and was found to have a sensitivity of 100%, specificity of 57%, positive predictive value of 63% and negative predictive value of 100%. Overall, Thyroseq™ Next Generation panel testing of biopsy specimens was more likely to be positive in nodules that were proven to be cancerous compared with those that were benign.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The results from this study indicate that mutational testing using the Thyroseq™ Next Generation panel may be helpful in managing indeterminate thyroid nodules. A negative test is very accurate in identifying a nodule as benign and, thus, avoiding surgery. The use of mutational testing on indeterminate thyroid nodules should be done on a regular basis to help determine the need for surgery in these nodules.

— Phillip Segal, MD

ATA THYROID BROCHURE LINKS

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

Thyroid Cancer (Papillary and Follicular): http://www.thyroid.org/thyroid-cancer/

Thyroid Cancer (Medullary): http://www.thyroid.org/medullary-thyroid-cancer/

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.

Indeterminate thyroid biopsy: this happens a few atypical cells are seen but not enough to be abnormal (atypia of unknown significance (AUS) or follicular lesion of unknown significance (FLUS)) or 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.

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.

Mutation: A permanent change in one of the genes.

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. The two most common molecular marker tests are the Afirma™ Gene Expression Classifier and Thyroseq™.

Negative predictive value: the likelihood that a patient does not have a disease when the test used to diagnose that disease is negative.

Positive predictive value: the likelihood that a patient has a disease when the test used to diagnose that disease is positive.

Test sensitivity: the proportion of patients with a certain disease in whom the test used to diagnose that disease is positive.

Test specificity: the proportion of patients without a certain disease in whom the test used to diagnose that disease is negative