



THYROID CANCER

Should the noninvasive encapsulated follicular variant of papillary thyroid cancer be re-classified as benign?

BACKGROUND

The number of patients with thyroid cancer has been rising and more low risk papillary thyroid cancers are being diagnosed in recent years. The likelihood of low risk thyroid cancer causing death or coming back after initial treatment (cancer recurrence) is very low and some researchers have debated whether some of these tumors should still be called cancer. The current study goal was to define a subgroup of noninvasive papillary thyroid cancer that is associated with a very low risk of causing death or recurring in the future, after being removed after surgery. The noninvasive follicular variant thyroid cancers in this study were confined within a tumor capsule in the thyroid gland and did not spread to lymph nodes or other organs.

THE FULL ARTICLE TITLE

Nikiforov YE et al. Nomenclature revision for encapsulated follicular variant of papillary thyroid carcinoma: a paradigm shift to reduce overtreatment of indolent tumors. *JAMA Oncol.* April 14, 2016 [Epub ahead of print].

SUMMARY OF THE STUDY

In this study, the authors reviewed select thyroid surgical specimens from multiple institutions. The review included specimens from 109 patients with noninvasive encapsulated follicular variant papillary thyroid carcinoma that was confined to a thyroid capsule and who were not treated with radioactive iodine and observed for 10 to 26 years. These were compared to specimens from 101 patients with invasive follicular variant papillary thyroid carcinoma (presence of invasion of blood vessels and or thyroid capsular invasion) observed for 1 to 18 years. The patients were selected on a historical review of pathology records from 13 institutions. A total of 24 expert pathologists reviewed all of the specimen slides. The long-term outcomes of the two groups, based on chart review, was compared. In another phase of the study, 30 of the above cases were subject to molecular marker testing using ThyroSeq v2 panel and 23 pathologists who did not know the molecular results (blinded) reviewed the slides to develop a scoring system for evaluating the nucleus of the

cells. These data were compared to results from benign hyperplastic nodules. Furthermore, the newly developed nuclear scoring system was tested by 22 pathologists who reviewed tumors from 26 patients (validation phase).

This study showed that 12% (12/101) of the patients with invasive follicular variant papillary thyroid carcinoma had a recurrence of their cancer. However, none of the 109 patients with noninvasive encapsulated follicular variant papillary thyroid carcinoma died or had cancer recurrence. This led to the proposal to rename this latter cancer as noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP). NIFTP diagnostic criteria included all of the following: 1) the tumor being encapsulated or clear demarcated, 2) follicular growth pattern with specific features, 3) a nuclear score of 2 to 3, 4) no invasion of blood vessels in the thyroid, 5) no break-down (necrosis) of the tumor, and 6) no high mitotic (proliferative) activity.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that noninvasive encapsulated follicular variant papillary thyroid carcinoma should be re-named as the non-cancer NIFTP in the future. It is important to know that at present, a NIFTP diagnosis cannot be made before thyroid surgery, as the tumor needs to be completely removed for thorough examination. If this is confirmed, then such patients will require much less monitoring and testing after surgery than current cancer patients. More research is needed to confirm the results of this study, to evaluate the performance of the new classification system and to determine the implications on patient's long-term outcomes.

— Anna Sawka, MD

ATA THYROID BROCHURE LINKS

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

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

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

**THYROID CANCER**, 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.

Papillary thyroid cancer: the most common type of thyroid cancer. There are three variants of papillary thyroid cancer: classic, follicular and tall-cell.

Cancer recurrence: this occurs when the cancer comes back after an initial treatment that was successful in destroying all detectable cancer at some point.

Lymph node: bean-shaped organ that plays a role in removing what the body considers harmful, such as infections and cancer cells.

Lobectomy: surgery to remove one lobe of the thyroid.

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (Thyroid Scan) or to take pictures of the whole body to look for thyroid cancer (Whole Body Scan).

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.

