

**THYROID CANCER****Genetic influence on outcomes in thyroid cancer****BACKGROUND**

Papillary thyroid cancer is increasing in frequency, especially in women. Fortunately, the vast majority of patients with papillary thyroid cancer do well. However, 5-10% of patients have persistent or recurrent thyroid cancer and some may die from their thyroid cancer. An improved method to determine the risk of recurrence and death for patients with thyroid cancer could help determine the extent of surgery, the use of additional treatment, and need for follow-up. This could potentially reduce the cost of treating thyroid cancer while maintaining or improving the effectiveness of treatment. The use of genetic molecular marker analysis in thyroid biopsy specimens has been suggested to help predict the aggressiveness of thyroid cancers. The aim of this study was to correlate thyroid cancer genetic molecular marker analysis with pathologic findings at surgery and disease-free survival.

THE FULL ARTICLE TITLE:

Yip L et al. Tumor genotype determines phenotype and disease-related outcomes in thyroid cancer: a study of 1510 patients. *Ann Surg* 2015;262:519-25.

SUMMARY OF THE STUDY

The authors examined a series of 1510 consecutive surgical patients diagnosed with thyroid cancer and treated at one medical center. Patients underwent preoperative ultrasound-guided needle biopsy. Genetic molecular marker analysis of the primary cancer was performed for genetic mutations. Total thyroidectomy was performed for all patients with abnormal lymph node removal as needed. The average follow-up was 33 months. More than 6 months of follow-up was available for 1349 patients.

Of 1510 tumors, 1039 (69%) had a genetic mutation identified. No tumor had more than one mutation.

Compared with cancers with mutations in the RAS-, PAX8/PPARG-, or BRAF K601E genes, those with mutations in the BRAF V600E or RET/PTC genes were more advanced and had a greater risk of early recurrence. The 5-year disease-free survival for patients with RAS-, PAX8/PPARG-, and BRAF K601E-positive cancers was 96%, 100%, and 100%, as compared with BRAF V600E- and RET/PTC-positive papillary thyroid cancer (80% and 77%). RET/PTC-positive papillary thyroid cancer had a high incidence of lateral neck lymph-node spread (35%) and distant spread (8%) at presentation. Recurrences were more frequent in patients with BRAF V600E (9.7%) or RET/PTC (9.4%). Overall survival was not affected by the mutation identified.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Specific genetic mutations or rearrangements are predictive of aggressiveness and a higher risk of distant spread and early recurrence for patients with papillary thyroid cancer. Determining genetic mutations prior to surgery could provide information to help determine the extent of surgery, the need for radioiodine treatment and the intensity of follow-up. More studies are needed to make specific and actionable recommendations.

— Ronald B. Kuppersmith, MD, FACS

ATA THYROID BROCHURE LINKS

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

Radioactive Iodine Therapy: <http://www.thyroid.org/radioactive-iodine/>

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

ABBREVIATIONS & DEFINITIONS

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.



THYROID CANCER, continued

Mutation: A permanent change in one of the genes.

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 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. Common thyroid cancer-associated genes include RAS, PAX8/PPARG, RET and BRAF

Papillary thyroid cancer: the most common type of thyroid cancer.

Thyroidectomy: surgery to remove the entire thyroid gland. When the entire thyroid is removed it is termed a total thyroidectomy. When less is removed, such as in removal of a lobe, it is termed a partial thyroidectomy.