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

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THYROID CANCER

The combination of BRAF^{600E} mutation and TERT promotor mutations increases risk of recurrence and death in papillary thyroid cancer

BACKGROUND

Most patients with papillary thyroid cancer have an excellent prognosis, but predicting which patients do not do well has been an ongoing area of interest. Ideally, identifying those at higher risk of cancer recurrence would potentially allow the more aggressive therapies to be utilized when appropriate for patients with high risk papillary thyroid cancer. A lot of recent work has identified molecular markers, which are mutations in cancer-related genes that can help in the diagnosis of thyroid cancer on thyroid biopsy specimens. More recently, 2 specific molecular markers, BRAF^{v600E} and TERT promotor mutations have been associated with aggressive tumor behavior and worse outcomes in papillary thyroid cancer. The BRAF^{v600E} mutation is quite common in papillary thyroid cancer so using this mutation alone to predict outcome has been challenging, though it has been associated with poor prognosis. The TERT promoter mutation alone was not shown to cause adverse outcomes in some previous studies, though other studies suggested it was associated with a more aggressive clinical picture.

This study aimed to determine the prognosis of papillary thyroid cancer in patients with either of these mutations alone or in combination by a review of the current studies.

THE FULL ARTICLE TITLE

Moon S et al. Effects of coexistent BRAF^{V600E} and TERT promoter mutations on poor clinical outcomes in papillary thyroid cancer: a meta-analysis. Thyroid. March 7, 2017 [Epub ahead of print].

SUMMARY OF THE STUDY

A literature review was done to identify studies that included BRAF^{V600E} and TERT promoter mutations in thyroid cancer. A total of 13 studies were identified. Data was extracted and reviewed for clinical information to include the number of males and females, age at diagnosis, cancer stage, spread to lymph nodes, extrathyroidal extention, spread outside of the neck, cancer recurrence and death.

A total of 4347 patients with papillary thyroid cancer were evaluated in the study and 283 patients had both BRAF^{v600E} and TERT promoter mutations. A BRAF^{v600E} mutation alone was related to advanced age at time of diagnosis, advanced cancer stage, extrathyroidal extension of tumor, and spread to lymph nodes, compared with no mutation. A TERT promoter mutation alone was associated with older age at diagnoses, spread to lymph node and spread outside of the neck. The combination of BRAF^{v600E} and TERT promoter mutations together when compared with no mutations was associated with older age at diagnosis, male gender, advanced cancer staging, extrathyroidal extension, spread to lymph node and spread outside of the neck.

Overall, the combination of BRAF^{600E} and TERT mutations was associated with high recurrence rate when compared with no mutations. Further, it was noted that the combination of mutations also had a higher risk of death than no mutations or BRAF^{v600E} alone, although few patients were in this group.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that molecular marker analysis can be used to identify patients that have more aggressive thyroid cancer. The combination of BRAF^{v600E} and TERT promotor mutations worsens the prognosis for papillary thyroid cancer. Additionally, a limited data set suggested higher risk of death with the combination of BRAF^{600E} and TERT promoter mutations.

As we improve our understanding of the molecular changes in thyroid cancer, we will improve our ability to identify patients that have a more aggressive thyroid cancer. Ultimately this knowledge will lead to improved treatment options. Future studies must aim to determine if identifying these mutations at the time of diagnosis can lead to improved outcomes for patients at higher risk.

— Julie Hallanger Johnson, MD

ATA THYROID BROCHURE LINKS

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

THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

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™

Cancer-associated genes: these are genes that are normally expressed in cells. Cancer cells frequently have mutations in these genes. It is unclear whether mutations in these genes cause the cancer or are just associated with the cancer cells. The cancer-associated genes important in thyroid cancer are BRAF, RET/PTC, TERT and RAS.

BRAF gene: this is gene that codes for a protein that is involved in a signaling pathway and is important for cell growth. Mutations in the BRAF gene in adults appear to cause cancer.