Editorial

Comment on "Refining Dynamic Risk Stratification and Prognostic Groups for Differentiated Thyroid Cancer With TERT Promoter Mutations"

Ashok R. Shaha

Head and Neck Service, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Correspondence to: Ashok R. Shaha. Head and Neck Service, Memorial Sloan-Kettering Cancer Center, New York, NY, USA. Email: shahaa@mskcc.org.

Provenance: This is an invited Editorial commissioned by the Section Editor Dr. Yunjian Zhang (Department of Thyroid and Breast Surgery, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China).

Comment on: Kim TH, Ki CS, Kim HS, *et al.* Refining Dynamic Risk Stratification and Prognostic Groups for Differentiated Thyroid Cancer With TERT Promoter Mutations. J Clin Endocrinol Metab 2017;102:1757-64.

Submitted Jun 06, 2018. Accepted for publication Jun 20, 2018.

doi: 10.21037/gs.2018.06.02

View this article at: http://dx.doi.org/10.21037/gs.2018.06.02

Tae Hyuk Kim and Jae Hoon Chung from Sungkyunkwan University School of Medicine, Seoul, Korea have reported their experience with adjusted hazard ratio (AHR) for differentiated cancer based on telomerase reverse transcription (TERT) promoter mutations (1). At present, the risk analysis of differentiated thyroid cancer does not consider molecular testing as a major factor. The authors have developed an integrative prognostic system that incorporates TERT promoter mutation into the risk stratification system. This has been used to better categorize and predict outcomes.

The authors reviewed the experience of 357 patients, who had 90 recurrences and 15 cancer-related deaths. The median follow-up is 14 years. The results were reported in an article in the *Journal of Clinical Endocrinology and Metabolism*, May 2017. The authors calculated the AHRs and noted the AHR grouping system to be better at predicting structural recurrences and cancer-specific survival. This system has been reported to be much better than the dynamic risk stratification (DRS) and tumor, node, metastasis (TNM) system. In their 357 patients, they noticed higher risk of recurrence in those with higher AHR, which was proportionate to higher risk of recurrence and cancer-related deaths.

However, we do need to recognize that the TERT promoter mutation was noted only in 8% of the patients. This clearly is a small percentage of patients with TERT mutation positivity. Whether we can use this information for the larger denominator who are negative for TERT mutation remains unclear. The authors have defined AHR of 1, 2, 3 and 4 and showed the outcome differences in relation to relapse, survival, and cause-specific survival. They have also reviewed their experience with structural recurrences and cancer-specific survival. This was analyzed against the current DRS system and the TNM classification.

The authors stratified the patients per DRS as having excellent response, indeterminate response, biochemically incomplete response, and structurally incomplete response. The percentages of patients in these four categories were 35%, 47%, 9% and 10%, respectively.

It is interesting to note that when patients were stratified according to TERT mutation, the hazard ratio of structural recurrence increased with increasing DRS. There were 15 deaths in this group, and many of the deaths were in the higher AHR groups. Excellent survival was noted in AHR groups 1 and 2, while in AHR group 4 the highest mortality was noted as 23%. They have noted that the TERT promoter mutation has higher impact on recurrence and cause-specific survival. In summary, the authors in this interesting and innovative manuscript have shown the impact of TERT promoter mutation and that including the TERT promoter mutation in the prognostic grouping may better define cause-specific survival.

Whether TERT mutation has a direct impact on long-term outcome, survival, and decision making in the management of thyroid cancer remains somewhat unclear.

There are few reports in the literature, including initial work from Xing *et al.* from Johns Hopkins University about the TERT promoter mutation. What remains unclear is if the standard prognostic factors that we know have the same definition of outcome and survival as the TERT mutation. Additional studies from many different parts of the world and institutions are important, and it would be helpful to know whether TERT alone stands as an independent prognostic factor. Presently, we are not using TERT mutation alone as a decision maker in the management of thyroid cancer. However, the presence of TERT mutation in fine needle aspiration biopsy may contribute to not only a higher risk of thyroid cancer but also a more aggressive thyroid cancer.

The TERT promoter mutation was discovered in 2013, and subsequently, extensive research has been undertaken by Xing *et al.* from Johns Hopkins (2,3). In an excellent review by Liu *et al.* in 2016, they reported the presence of TERT as a more aggressive form of thyroid cancer (4). They also reported that a combination of BRAF V600E mutation and other genetic markers are proving to be clinically useful in the management of thyroid cancer. They have reported that the presence of TERT and BRAF have a robust synergistic impact on the aggressiveness of thyroid carcinoma, including increased tumor recurrence and mortality, while either mutation alone has modest impact. This information will clearly be of great benefit in the evaluation, management, and follow-up of patients with high-risk thyroid cancers. I would like to take this opportunity to congratulate these authors for their excellent work in reviewing a large series of patients. Even though the TERT positivity is small, I think this is an important contribution to the fields of oncology and molecular markers.

Cite this article as: Shaha AR. Comment on "Refining Dynamic Risk Stratification and Prognostic Groups for Differentiated Thyroid Cancer With TERT Promoter Mutations". Gland Surg 2018;7(5):426-427. doi: 10.21037/gs.2018.06.02

Acknowledgements

None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

References

1. Kim TH, Ki CS, Kim HS, et al. Refining Dynamic Risk Stratification and Prognostic Groups for Differentiated Thyroid Cancer With TERT Promoter Mutations. J Clin Endocrinol Metab 2017;102:1757-64.
2. Xing M, Liu R, Liu X, et al. BRAF V600E and TERT promoter mutations cooperatively identify the most aggressive papillary thyroid cancer with highest recurrence. J Clin Oncol 2014;32:2718-26.
3. Liu X, Qu S, Liu R, et al. TERT promoter mutations and their association with BRAF V600E mutation and aggressive clinicopathological characteristics of thyroid cancer. J Clin Endocrinol Metab 2014;99:E1130-6.
4. Liu R, Xing M. TERT promoter mutations in thyroid cancer. Endocr Relat Cancer 2016;23:R143-55.

