

# Response to Letter to the Editor From Green and Gosmanov: “Tall Cell Percentage Alone in PTC Without Aggressive Features Should not Guide Patients’ Clinical Management”

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**Key Words:** papillary thyroid carcinoma, prognosis, recurrence-free survival, tall cells

**Abbreviations:** ATA, American Thyroid Association; PTC, papillary thyroid carcinoma; RAI, radioactive iodine; RFS, recurrence-free survival; TCPTC, tall cell variant of papillary thyroid carcinoma.

We thank the Editor for the opportunity to answer the letter by Green and Gosmanov (1), and the latter for the interest in our study (2).

In our retrospective study on papillary thyroid carcinoma (PTC) with any tall cell feature we tried to understand what could happen, following the diagnostic criteria of the WHO 2017 guidelines, with the decrease from 50% to 30% in the threshold of the tall cell percentage within PTC required for the diagnosis of tall cell variant of PTC (TCPTC).

First, we demonstrated that following the new definition of the WHO some patients shifted from low to intermediate risk of recurrence according to the American Thyroid Association (ATA) guidelines (3). This change may induce a more aggressive treatment in this subgroup of patients and represents a step back in the decision to treat low-risk patients less aggressively.

Second, we observed that the recurrence rates of the patients who were upgraded from low to intermediate risk according to the new WHO guidelines did not differ from the recurrence rate of low-risk patients and was much lower than the recurrence rate of intermediate-risk PTC. This observation demonstrates that this change in the definition may have non-negligible consequences. In fact, a significant proportion of patients with an actual low risk of recurrence but defined as intermediate risk according to the new definition could be at risk for overtreatment.

Third, we found that there were no differences in the clinicopathological features of aggressiveness among PTC with less than 30%, between 30% and 49%, and more than 50% of tall cells. Moreover, no differences were found in recurrence-free survival (RFS) and distant RFS among the 3 groups with different prevalence of tall cells suggesting that aggressive disease is driven by the classical clinicopathological

features of aggressiveness and that the clinical impact of tall cell percentage alone is negligible.

As reported in the manuscript discussion section, the retrospective nature of the study made it infeasible to directly evaluate the effects of different treatments on the outcomes. We agree that recommendations for doses of radioactive iodine (RAI) employed have varied over the years in parallel with the ATA guidelines in some centers, and that this could have an impact on the study results. However, the data collection was intentionally performed between 2001 and 2017, before some of the suggestions of ATA guidelines of a more conservative approach regarding surgery and RAI use were embraced. To respond to Green and Gosmanov and to add important details in this large cohort study, we examined RAI use and found that 131-iodine was administered to 1246 out of 1278 (97.5%) patients with no difference across the 3 groups ( $P = .8$ ); in addition, there was no difference in RAI cumulative activities ( $P = .1$ ).

In conclusion, considering the increase of prevalence of TCPTC (4), the change in the WHO criteria for its diagnosis, and that aggressive disease is driven by the classical clinicopathological features of aggressiveness, we think that the presence of tall cells per se should not guide patient management.

## Financial Support

None.

## Disclosures

All authors have no disclosures to declare.

Received: 11 January 2022. Editorial Decision: 25 January 2022. Corrected and Typeset: 11 February 2022

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## References

1. Green M, Gosmanov AR. Letter to the editor from Green and Gosmanov: tall cell percentage alone in PTC without aggressive features should not guide patients' clinical management. *J Clin Endocrinol Metab.* 2022;dgac053. doi:[10.1210/clinem/dgac053](https://doi.org/10.1210/clinem/dgac053).
2. Poma AM, Viola D, Macerola E, *et al.* Tall cell percentage alone in PTC without aggressive features should not guide patients' clinical management. *J Clin Endocrinol Metab.* 2021;106(10):e4109-e4117.
3. Haugen BR, Alexander EK, Bible KC, *et al.* 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid.* 2016;26(1):1-133.
4. Kazaure HS, Roman SA, Sosa JA. Aggressive variants of papillary thyroid cancer: incidence, characteristics and predictors of survival among 43 738 patients. *Ann Surg Oncol.* 2012;19(6):1874-1880.