

## Reply to “Differences in the Impact of Age on Mortality in Well-Differentiated Thyroid Cancer”

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To the editors:

We read with great interest the recent publication by Yan et al.<sup>1</sup> highlighting the important prognostic differences between follicular thyroid cancer (FTC) and the far more commonly encountered papillary thyroid cancer (PTC). FTC recurs rarely, but patients who have recurrences may die of metastatic disease in spite of otherwise favorable risk profiles. The different biology between the categories of well-differentiated thyroid cancer (i.e., PTC and FTC) is evident both clinically and in the laboratory.

Furthermore, our group recently published a whole exome-sequencing analysis of FTC that mapped the genetic landscape of these tumors, with a particular emphasis on the infrequent widely invasive (WIFTC) subtype.<sup>2</sup> Of 10 WIFTC patients studied, 5 experienced recurrence and died of FTC within 10 years. Of 6 thyroid cancer-specific deaths in our overall FTC cohort of 39 cases, half were classified as stage I or II by the American Joint Committee on Cancer (AJCC) eighth-edition staging system, mostly due to the increased age cutoff of 55 years.<sup>3</sup> Interestingly, we found that both genomic markers and traditional clinical and histopathologic factors predicted poor survival.

Unfortunately, the degree of FTC invasion is not well-captured in the national cancer registries, so a large-scale analysis of these high-risk subgroups is not possible using

these approaches. Prior studies have demonstrated the prognostic significance of the degree of invasion for FTC in smaller single-institution series.<sup>4</sup> Although the AJCC eighth-edition staging system provides accurate prognostic information for the vast majority of patients with well-differentiated thyroid cancer, certain high-risk histologic or molecular features may outweigh traditional tumor-node-metastasis (TNM) staging and should be considered when the risk of recurrence and death is evaluated for thyroid cancer patients.

### REFERENCES

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