



## BRAF Mutation Is Not an Independent Predictor of Central-Lymph-Node Metastases in the Classical Variant of Papillary Thyroid Cancer

When the bivariate analysis was performed for only the 315 classic variant PTCs, there was no significant association between BRAF mutation and lymph-node metastases or any of the other tumor variables. Multivariate logistic-regression analysis found that only age >45, tumor size >2 cm, and extrathyroidal extension were independent predictors of lymph-node metastases. There was no significant association between BRAF mutation status and lymph-node metastases in this group.

### Conclusions

Although BRAF mutation was found to be an independent predictor of central-lymph-node metastases in the overall cohort of patients with PTC, this relationship lost significance when only classical variant PTC was included in the analysis. Prospective studies are needed before BRAF mutation can be considered a reliable factor to guide the treatment of patients with PTC with regard to performing prophylactic central-lymph-node dissection.

### ANALYSIS AND COMMENTARY ● ● ● ● ●

This interesting study, concluding that BRAF mutation status is not a predictor of lymph-node metastasis for the classical variant of PTC, which occurred in 81% of the patients, is somewhat heretical with regard to the recent concern about the ominous prognostic value of this mutation. The finding that the BRAF mutation does not correlate with lymph-node metastasis is supported by a Japanese study of 613 patients with PTC of whom 38% had the BRAF mutation (2). In a meta-analysis of 32 studies including 6372 patients (written by some authors of the current study), BRAF mutation was associated with lymph-node metastases (3), but only 2 of the studies included prophylactic lymph-node dissection.

How can the contrary findings be reconciled? First, PTC has a very good prognosis in about 90% of patients, making it difficult to believe that the BRAF mutation indicates an ominous prognosis when it is currently found in such a high prevalence of PTC

patients. The finding that 80% of the classical variant PTCs had the mutation makes the statistical comparisons somewhat lopsided. If the large majority of patients with PTC have the BRAF mutation, then it becomes tough to prove that it predicts a poor outcome, including lymph-node metastases that correlates with more recurrence.

Second, the introduction of the current paper contains an excellent discussion about the controversial benefit of prophylactic central-lymph-node dissection, although it does not highlight the downside of the procedure, namely a higher incidence of surgical complications. It states that “most occult nodal micrometastases, although they occur in 31% to 62% of patients with PTC, remain clinically insignificant.” Perhaps the use of the BRAF mutation will be as a marker of more aggressive PTC that should be treated more aggressively in patients who have gross lymph-node macrometastases that have been detected preoperatively. These patients are probably more likely to benefit from central-lymph-node dissection.

### References

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