



The ambiguity of intermediate risk thyroid cancer: multifocality as a risk factor

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Thyroid cancer is projected to be the fourth leading cancer diagnosis by 2030 (1,2). In general, these patients have an excellent prognosis with an overall long-term survival greater than 90% (2). The American Thyroid Association (ATA) updated their guidelines in 2015 to better inform clinical decision-making and management of thyroid nodules and cancer (3). In these updated guidelines, patients are categorized into three risk groups at the time of diagnosis: low, intermediate, and high. The three categories are based on the characteristics of the thyroid cancer (nodule size, presence or absence of aggressive variants, presence of large lymph nodes with cancer involvement, invasion of blood vessels and metastasis). Previous studies have supported the utility of the ATA classification system in avoiding unnecessarily aggressive therapies (4).

Patients with intermediate risk differentiated thyroid carcinoma (DTC) present with factors that include microscopic invasion in perithyroidal tissue, aggressive variants or cN1, and multifocal papillary microcarcinoma with extrathyroidal extension. The implication of multifocal disease is not well researched; some studies report an association with higher rates of disease recurrence and a poorer prognosis when compared to patients with unifocal disease (5,6). Other studies have published no difference in outcomes or disease recurrence (7). Notably, Harries *et al.* examined a cohort of over 6,000 patients and found that multifocal disease was not associated with poorer outcomes (8). In fact, there were comparable local recurrence rates compared to patients with unifocal disease. This study concluded multifocal disease should not

be an indication for completion thyroidectomy (8). The ATA guidelines also support these findings recommending a thyroid lobectomy as an acceptable initial procedure for unifocal intrathyroidal carcinomas in lieu of a total or near-total thyroidectomy. The current ATA guidelines do not separate multifocal from unifocal disease presence in its risk stratification system. Instead, the guidelines group this intermediate group as one inclusive category with a risk of recurrence ranging from 4–6% (3).

In the work of Curto *et al.*, their study aim was to investigate and delineate further the surgical management for patients with unilateral multifocal intermediate-risk DTC (9). The authors examined 92 DTC patients classified as intermediate risk in a retrospective single institution study. They categorized patients based on multifocal or unifocal disease and examined predictive factors to assist in developing a surgical management paradigm for whether patients should undergo hemi or total thyroidectomy.

In this Curto *et al.* cohort, 67% of patients with DTC underwent total thyroidectomy and 33% underwent a hemithyroidectomy (9). The authors found no association between gender, histological type and multifocality. This group found that multifocal disease is more common in patients <50 years old ($P=0.02$) which has not been previously described by the literature. The authors concluded hemithyroidectomy is sufficient in older patients without extrathyroidal extension, angioinvasion and with N0 disease. Total thyroidectomy should be considered for patients with risk factors, such as extrathyroidal extension

and the presence of angioinvasion.

There are important considerations to reckon when deciding between total thyroidectomy and hemithyroidectomy. The advantages of a hemithyroidectomy include lower complication rates, which include lower rates of temporary or permanent vocal fold paralysis, temporary hypoparathyroidism, and permanent hypoparathyroidism (10). There is also decreased (though not zero) risk for lifelong hormonal replacement. Disadvantages of hemithyroidectomy include potentially needing to remove the contralateral lobe at a future time. If the contralateral lobe is not removed, thyroglobulin evaluation cannot be used during follow-up and radioiodine cannot be utilized if indicated.

This study is limited by the small cohort size, and it is also difficult to know the true extent of multifocality when not all cases underwent total thyroidectomy. The current ATA guidelines encourage individual case-by-case approach for intermediate-risk DTC surgical approach. This study attempts to focus on the gray zone surrounding multifocal disease and intermediate risk, given the surprising paucity of data in this area. Studies in this area should continue to better inform treatment guidelines and improve perioperative discussions with patients on whether hemithyroidectomy or total thyroidectomy is the better treatment option.

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