
Prevalence of Contralateral Tumors in Patients with Follicular Variant of Papillary Thyroid Cancer



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BACKGROUND: Thyroid lobectomy alone is being performed increasingly for patients with encapsulated follicular variant of papillary thyroid carcinoma (fvPTC). However, the prevalence of contralateral disease in these patients is unknown. We investigated the presence of synchronous disease in fvPTC to improve decision making about the extent of surgical resection and need for surveillance.

STUDY DESIGN: We performed a retrospective review of patients who underwent thyroid surgery from October 2009 to February 2013 with a diagnosis of fvPTC as their primary lesion. We collected information on patient demographics, nodule size, multifocality, fine-needle aspiration results, lymphovascular invasion, extrathyroidal extension, and lymph node metastasis. Tumors were divided into noninvasive and invasive/infiltrative fvPTC categories. Characteristics of solitary and bilateral fvPTC were compared.

RESULTS: We identified 124 patients with final pathology demonstrating fvPTC. The most common fine-needle aspiration diagnosis was “suspicious for malignancy” (n = 53). Sixty-five contralateral tumors were identified in 44 of 124 patients (35.5%) and included fvPTC (n = 40), classical PTC (n = 22), tall cell PTC (n = 2), and follicular carcinoma (n = 1). Fifty contralateral tumors were 1 to 5 mm, 10 measured 6 to 9 mm, and 5 were ≥ 10 mm. Contralateral disease correlated significantly with lymphovascular invasion (p = 0.037) and larger primary lesions (p = 0.020). There was no significant difference noted in extrathyroidal extension or lymph node metastasis. Both noninvasive and invasive/infiltrative fvPTC demonstrated similar rates of contralateral disease.

CONCLUSIONS: Bilateral disease is common in fvPTC, primarily in the form of papillary microcarcinomas. Future monitoring of the contralateral lobe should be discussed with fvPTC patients who do not undergo completion thyroidectomy. (J Am Coll Surg 2017;224:1021–1027. © 2016 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Thyroid cancer incidence has risen in recent years, with approximately 63,000 new cases reported in the US in 2014.^{1–4} The majority of these malignancies are well-differentiated thyroid cancers, including papillary

thyroid carcinoma (PTC) and follicular thyroid carcinoma. After the classical type (cPTC), the follicular variant of papillary thyroid carcinoma (fvPTC) is the most common subtype, accounting for up to 41% of

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Abbreviations and Acronyms

cPTC	= classical type papillary thyroid carcinoma
FNA	= fine-needle aspiration
fvPTC	= follicular variant of papillary thyroid carcinoma
LVI	= lymphovascular invasion
NIFTP	= noninvasive follicular thyroid neoplasm with papillary-like nuclear features
PTC	= papillary thyroid carcinoma

all PTC cases.^{5,6} As such, understanding the clinicopathologic behavior of fvPTC is critical for optimizing patient treatment plans.

Histologically, fvPTC is distinguished from cPTC by a follicular architecture with nuclear features typical of papillary carcinoma. Cytopathologic interpretation of fine-needle aspiration (FNA) samples for fvPTC can be difficult due to the fact that fvPTC often has more subtle nuclear features of PTC compared with cPTC, and FNA accuracy varies widely in the literature.⁷⁻⁹ The follicular variant of PTC also demonstrates considerable histopathologic overlap with benign lesions, such as follicular adenoma, confounding the diagnosis. Consequently, indeterminate cytology results are not uncommon, and these cases are often treated by diagnostic lobectomy for definitive diagnosis.

Substantial variability exists in the behavior of fvPTC histologic subtypes, depending on the growth pattern of the tumor. Encapsulated or noninvasive fvPTC possess a molecular profile similar to follicular adenomas/carcinomas, frequently displaying *RAS* and lacking *BRAFV600E* mutations.¹⁰⁻¹⁴ These tumors are indolent compared with tumors with an infiltrative growth pattern, and have virtually no metastatic potential or recurrence risk in the absence of invasive growth.¹⁵⁻¹⁸ For example, Liu and colleagues¹⁸ found significantly greater rates of regional lymph node metastases among patients with infiltrative/diffuse neoplasms compared with their encapsulated counterparts (65% vs 5%; $p < 0.0001$). Recently, Nikiforov and colleagues¹⁹ proposed a nomenclature revision for patients with noninvasive fvPTC, suggesting these cases should be termed *noninvasive follicular thyroid neoplasm with papillary-like nuclear features* (NIFTP) to reflect a more indolent phenotype and reduce overtreatment of these lesions.

The diagnosis of fvPTC on final pathology of lobectomy specimens leads to uncertainty about whether completion thyroidectomy is necessary, especially in the presence of untested contralateral nodules or potential microcarcinomas not yet seen on ultrasound. Patients with fvPTC have historically been treated similarly to those with cPTC, including thyroidectomy and

radioactive iodine ablation, due in part to studies demonstrating equivalent prognosis.^{4,20-22} However, with the increased awareness about clinicopathologic differences in fvPTC subtypes, some authors have suggested that thyroid lobectomy alone might be appropriate for certain encapsulated tumors, such as NIFTP.¹⁷⁻¹⁹ In this study, we sought to define the prevalence of synchronous multifocal and bilateral disease in fvPTC to improve decision making about the extent of surgical resection.

METHODS

Under a protocol approved by the IRB at Brigham and Women's Hospital, we performed a retrospective review of all patients who underwent thyroid surgery at our institution between October 2009 and February 2013. For patients with a reported diagnosis of fvPTC for the index lesion, slides were re-reviewed by thyroid pathology subspecialists (JAB, BEH, and JFK). Tumors were categorized as fvPTC only if they had an entirely or almost entirely follicular architecture (<1% papillary architecture) in combination with nuclear features of PTC.¹⁶ Cases were further divided into noninvasive and invasive/infiltrative fvPTC groups, as described previously.²³ The noninvasive group would meet current diagnostic criteria of NIFTP, however, the diagnoses for all of these tumors were rendered before the proposed nomenclature revision.

Additional data, including patient demographics, FNA cytology results, extent of surgical resection; and histopathologic features, including nodule size, lymphovascular invasion (LVI), extrathyroidal extension, multifocality, and lymph node metastasis, were analyzed. Characteristics of fvPTC specimens with solitary vs bilateral disease were compared to define rates and features associated with bilateral disease. Solitary disease was defined as a single cancer identified in the entire thyroidectomy specimen; multifocal disease was defined as more than 1 cancer focus identified in either a single lobe or both thyroid lobes; and bilateral/contralateral disease was defined as more than 1 cancer focus identified in both thyroid lobes.

The majority of FNA specimens were obtained at Brigham and Women's Hospital by an attending endocrinologist under ultrasound guidance in our Thyroid Nodule Clinic. Preoperative ultrasound was performed by an attending radiologist using a 5- to 17-MHz transducer. Nodule size was reported in 3 dimensions (length, width, and depth). Ultrasound was used to guide the needle tip into the nodule and ensure an accurate specimen. Three (or rarely 4) needle sticks were obtained per nodule, constituting a single aspiration analysis. All aspirations were processed using the Thin Prep technique (Hologic, Inc).

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