



ORIGINAL ARTICLE

Risk factors of distant metastasis in the follicular variant of papillary thyroid carcinoma



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KEYWORDS

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Background/Purpose: The follicular variant of papillary thyroid carcinoma (FVPTC) is the most common variant of papillary thyroid carcinoma (PTC). A previous population-based study revealed its clinical behavior as a mix of classic papillary thyroid carcinoma (C-PTC) and follicular thyroid carcinoma. Whereas locoregional extension was lower in FVPTC than in C-PTC, the distant metastasis rate was higher in FVPTC than in C-PTC. The aim of this study was to evaluate the risk factors of distant metastasis in FVPTC postoperatively.

Methods: A retrospective review of 359 patients with final pathological diagnosis of FVPTC treated at Chang Gung Memorial Hospital between January 2000 and January 2014 was performed. After excluding patients who had inadequate pathological data for analysis or did not attend regular follow up for >1 year, 346 patients were included in this study. Univariate and multivariate statistical analyses were performed to determine the significance of various factors.

Results: Of the 346 patients with FVPTC, 19 (5.5%) had lymph node metastases and 32 (9.2%) had distant metastases. Two positive and one negative risk factors were predictive for distant metastasis using multivariate analysis: angiolymphatic invasion [odds ratio (OR), 3.085; 95% confidence interval (CI), 1.008–9.442], extrathyroidal extension (OR, 3.929; 95% CI, 1.330–11.602), and encapsulation (OR, 0.361; 95% CI, 0.154–0.850).

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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Conclusion: The presence of angiolymphatic invasion, extrathyroidal extension, or nonencapsulation was associated with distant metastasis in FVPTC in this study. In FVPTC patients, postoperative investigation for distant metastasis may be warranted by the presence of these two positive risk factors or the absence of the one negative risk factor.

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Introduction

The follicular variant of papillary thyroid carcinoma (FVPTC) is the most common variant of papillary thyroid cancer (PTC) and accounts for approximately 10–15% of all PTC cases.^{1–3} The FVPTC was first defined in 1950 by Dailey et al,⁴ who observed that FVPTC was a neoplasm characterized by follicular architecture and the nuclear features of conventional PTC. According to past reports, in general, the long-term outcome of classic papillary thyroid carcinoma (C-PTC) and FVPTC are similar, and patients in both groups should be treated in the same way.⁵ However, the clinical behavior of FVPTC may be different from that of C-PTC. A previous population-based study revealed its clinical behavior as a mix of C-PTC and follicular thyroid carcinoma (FTC).⁶ Although locoregional extension was lower in FVPTC than in C-PTC, the distant metastasis rate was higher in FVPTC than in C-PTC.⁶ Unlike the indolent clinical course that most FVPTC patients experience, patients with distant metastasis, either at initial diagnosis or at recurrence, have a relatively poor outcome. The aim of this study was to retrospectively analyze the possible predictors of distant metastasis in FVPTC after thyroidectomy.

Patients and methods

A retrospective review of a total of 359 patients with final pathological diagnosis of FVPTC who were treated at Chang Gung Memorial Hospital (CGMH) between January 2000 and January 2014 was performed. After excluding patients who had inadequate pathological data for analysis or who did not attend regular follow up for >1 year, a total of 346 patients were finally included in this study. All patients were staged using the International Union Against Cancer Tumor–Node–Metastasis (TNM) criteria (6th edition).⁷ Permission was obtained from the Institutional Review Board (IRB) and ethics committees of CGMH for a retrospective review of the medical records of the study participants. The IRB waived the requirement for obtaining informed consent. Confidentiality of the research participants was maintained in accordance with the requirements of the IRB of CGMH.

Ultrasonographic features, including solid/cystic/mixed lesion, marked hypoechogenicity, taller-than-wide shape, infiltrative margin, and micro- or macrocalcification were recorded and classified into PTC-like or follicular neoplasm (FN)-like nodules according to their ultrasonographic features as described in a recent study.⁸ PTC-like nodules were

defined as having at least one of the following malignant features: marked hypoechogenicity, taller-than-wide shape, infiltrative margin, and micro- or macrocalcifications. Conversely, FN-like nodules revealed a lesion without malignant features.

Fine-needle-aspiration cytology (FNAC) was performed in suspicious nodules after thyroid ultrasonography. The aspirate was expressed on frosted-end glass slides, air-dried, and stained, using the Romanowsky-based method as described by Lin et al.⁹ Because a diagnosis of FVPTC is made according to finding the typical nuclear features in classic PTC, we reported preoperation cytology in three main categories for triage of treatment: benign, FN, and malignant for PTC. Intraoperative frozen section (FS) analysis was performed on the cut surface of the thyroid nodules, including the interface between the nodule and adjacent thyroid tissue. Two to three FSs were regularly analyzed according to the size of the nodules. In the majority of cases, 30 minutes was needed to complete the analysis of the FS. Specimens for permanent pathology were fixed in 10% buffered formalin followed by paraffin embedding. Serial sections were stained with hematoxylin–eosin, and the slides were analyzed by experienced pathologists at our medical center.

Postoperative serum thyroglobulin (Tg) levels were detected using an immunoradiometric assay kit (CIS Bio International, Codolet, France). In most high-risk patients who had incomplete tumor resection or complete tumor resection using a scoring system based on metastasis, age, completeness of resection, invasion, and size (MACIS scores) ≥ 6 , thyroid remnant ablation with radioactive iodide (¹³¹I) was performed 4–6 weeks after surgery. The ¹³¹I ablation dose for most patients was 1.1–3.7 GBq (30–100 mCi). A whole-body scan (WBS) was obtained 1 week after ¹³¹I administration using a dual-head gamma camera (GE Infinia Hawkeye 4, Haifa, Israel) equipped with a high-energy collimator. Cases where the foci of ¹³¹I uptake extended beyond the thyroid bed were classified as distant metastases, and further confirmatory study was performed. Patients diagnosed with distant metastasis would be administered with higher therapeutic doses of ¹³¹I [3.7–7.4 GBq (100–200 mCi)] with the following therapeutic WBS. Physiological uptakes including thymus, breast, salivary glands, liver, and gastrointestinal tract were excluded by experienced nuclear medicine specialists with the information obtained from clinical history, physical examination, serum Tg level, and appropriate second imaging investigations if indicated. A repeat therapeutic dose of 3.7–7.4 GBq was used at an interval of 6–12 months.

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