The American Journal of Surgery (2016) 212, 419–425

The American Journal of Surgery®

Clinical Science

Recurrence in patients with clinically early-stage papillary thyroid carcinoma according to tumor size and surgical extent

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KEYWORDS:
Papillary thyroid carcinoma;
Surgery;
Recurrence;
Tumor size;
Risk factor

Abstract

BACKGROUND: To investigate whether post-treatment recurrence differs by tumor size or surgical extent in clinically early-stage papillary thyroid carcinoma (PTC) patients.

METHODS: A total of 1,041 surgical patients with PTC 4 cm or less and no clinical evidence of metastases to regional or distant sites were included. Cox proportional hazard models were used to identify the clinicopathological variables predictive of post-treatment recurrence.

RESULTS: Central nodal involvement was found in 313 (34.1%) of 918 patients who underwent prophylactic central lymph node dissection. For the median follow-up of 83 months, 25 (2.4%) of 1,041 patients had a regional recurrence and 12 (1.2%) patients died of other causes. Male gender, tumor size, extranodal extension, and positive resection margin remained independent variables predictive of recurrence by multivariate analysis ($P < .05$ each). There was no significant impact of age (<45 vs ≥45 years, $P = .944$) or surgical extent (unilateral vs bilateral thyroidectomy, $P = .776$) on recurrence.

CONCLUSIONS: Tumor size in patients with PTC of 4 cm or less is an important predictive factor for post-treatment recurrence.

The current American Thyroid Association (ATA) guidelines recommend total or near-total thyroidectomy for papillary thyroid carcinoma (PTC) greater than 1 cm, whereas thyroid lobectomy is reserved for PTC tumors 1 cm or less.[1] Thyroid lobectomy alone is sufficient for small, unifocal, intrathyroidal carcinomas in the absence of prior head and neck irradiation, familial thyroid carcinoma, or clinically positive lymph nodes (cN1).[1] This recommendation is reflected in the findings of several retrospective studies that contradict the results of Bilimoria et al[2] who concluded that tumors greater than 1 cm had a poorer overall survival outcome and, therefore, required a total thyroidectomy.[3–7] However, more contemporary studies have denied the findings of Bilimoria study by indicating no survival difference between thyroid lobectomy and total thyroidectomy.[8,9] These controversial findings have reopened the debate regarding the issue between the extent of surgery and survival.

There were no relevant financial relationships or any sources of support in the form of grants, equipment, or drugs.

The authors declare no conflicts of interest.

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Manuscript received August 14, 2015; revised manuscript November 2, 2015

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http://dx.doi.org/10.1016/j.amjsurg.2015.12.015

Along this line, the ATA are currently under review on the new guidelines for differentiated thyroid cancer: "for patients with thyroid cancer greater than 1 cm and less than 4 cm without extrathyroidal extension (ETE), and without clinical evidence of any involved lymph nodes or metastases (cN0), the initial surgery can be either a total thyroidectomy or a lobectomy. Thyroid lobectomy alone may be sufficient initial treatment for low-risk papillary and follicular carcinoma; total thyroidectomy can be chosen to enable radioactive iodine (^{131}I; RAI) therapy or to enhance follow-up based on disease features and/or patients references".[10] However, these changes along with the ATA recommendation still remain controversial in terms of selecting the optimal surgical extent and proper follow-up management for thyroid cancer patients.

The aim of this study was to analyze the rate of post-treatment recurrence in relation to tumor size and surgical extent in clinically early-stage PTC patients. We hypothesized that patients harboring PTC tumors less than 4 cm would show no recurrence or survival differences in accordance with tumor size and surgical extent.

Patients and Methods

Patients

After obtaining institutional review board approval, we retrospectively reviewed the electronic medical records of 1,807 consecutive PTC patients who underwent initial surgery in our department (2006 to 2009). We thereby identified 1,041 patients with a clinically node-negative PTC 4 cm or less that met our study inclusion criteria of early-stage thyroid cancer.[1] All the patients had preoperative neck ultrasound (US) examination. The clinical node-negativity was defined as the absence of abnormal lymph nodes from preoperative US and intraoperative examinations. Exclusion criteria included initial clinical T3–4, N1, or M1 lesions (n = 618); and a previous history of PTC (n = 98) or external beam irradiation of head and neck or upper chest (n = 13). Patients with incomplete clinical data (n = 37) were also excluded. All surviving patients in the study cohort had been followed for at least 2 years. Tumor sizes were measured from the surgical specimens. The median follow-up time was 83 months (range, 37 to 108).

Surgical strategy and postoperative follow-up

The aim of an initial surgery for PTC is a macroscopically complete resection of the tumor. When a tumor was restricted to 1 lobe and there was no evidence of intrathyroidal metastasis in the contralateral lobe, an ipsilateral lobectomy was performed. After thyroidectomy, prophylactic central lymph node dissection (CLND) was performed. In our institution, routine CLND occurred after the thyroidectomy regardless of whether there was any evidence of lymph node metastasis. Some patients did not undergo prophylactic CLND when the size of the tumor was less than 5 mm, or the results of the cytology were not determined, such as a suspicion of PTC or follicular neoplasm. Patients who underwent a completion thyroidectomy were considered as having undergone a total thyroidectomy.

Of the patients who underwent total thyroidectomy, most received a postoperative dose of RAI of either 30 mCi (n = 473, 45.4%), 80 mCi (n = 169, 16.2%), 100 mCi (n = 2, .2 %), or 150 mCi (n = 271, 26.0%); the RAI dose depended on the metastatic and residual diseases suspected or documented.[1] After considering a combination of age, tumor size, lymph node status, and individual histology; RAI ablation was performed for patients who had a 1 to 4-cm tumor and pathologically nodal metastasis (pN1), or microscopic ETE. Patients with unifocal cancer less than 1 cm, without any high-risk features, and those with a lobectomy did not receive RAI. Thyroid stimulating hormone suppression therapy was performed in most of the cohorts postoperatively, but the patient thyroid stimulating hormone and thyroglobulin levels were not analyzed in our present study. All patients underwent a routine neck US examination, chest radiography and in the case of total thyroidectomy, the measurement of serum thyroglobulin concentrations, and whole-body iodine scanning for detection of recurrence every 6 months or 1 year postoperatively. Whenever a recurrence in the remnant thyroid, resection bed, or lymph node was suspected, the diagnosis was confirmed by histologic examination from aspiration cytology or reoperation.

Postoperative complications

All patients were subjected to a laryngoscopic examination before and after operation and carefully observed for any complications. Patients were clinically evaluated for signs and symptoms of hypocalcemia. Hypocalcemia was defined by total calcium concentrations less than 8.0 mg/dL during the hospital stay or at any time after discharge from the hospital. Patients who developed hypocalcemia were started on oral calcium and vitamin D replacement and intravenous calcium gluconate for significant symptoms. Permanent hypoparathyroidism was diagnosed in patients with lower total calcium concentrations requiring calcium supplementation for more than 6 months.

Statistical analysis

The study end-points were an investigation of whether recurrence and survival outcomes varied in relation to tumor size, surgical extent, and other clinicopathological variables. Recurrence-free survival (RFS) was defined as the time from surgery until the 1st evidence of any recurrence. Continuous variables were expressed as the median and range, and categorical variables as a number