

Treatment Outcome of Papillary Carcinoma Confined to the Thyroid Isthmus

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Abstract

Objective: The purpose of this study is to evaluate the clinicopathologic characteristics and treatment outcomes of Papillary Thyroid Carcinomas (PTC) of the isthmus and to establish an appropriate surgical strategy. **Methods:** Thirty-four patients with PTC in isthmus are managed by surgery in National Cancer Center/Cancer Hospital of Chinese Academy of Medical Sciences, Peking Union Medical College from 1985-2008. Demographic data, surgical procedures, pathological features, stages and outcomes are analyzed. **Results:** Seven patients were men and 27 were women. The median age was 41 years (range, 20 - 71). Twenty-five patients were treated with thyroid isthmusectomy or wide field isthmusectomy, five with hemithyroidectomy (lobectomy and isthmusectomy) and four with hemithyroidectomy and partial resection of the contralateral lobe. Twenty-eight patients had a pathologically T1 lesion (pT1); two patients had a pT2 lesion and four had a pT3 lesion. Five patients (14.7%) had papillary carcinoma detected in one of the pretracheal lymph nodes. Thirty-two patients had a solitary lesion confined to the thyroid isthmus. One patient had two lesions in the thyroid isthmus and another one had two lesions located in the thyroid isthmus and right lobe respectively. With a median follow-up of 94 months (range, 12 - 274), two patients had a recurrence and both survived after a re-operation. There was no regional lymph node or distant organ recurrences. No deaths occurred. **Conclusions:** Isthmusectomy or wide field isthmusectomy could be a sufficient treatment for PTC confined to the thyroid isthmus. We also recommend that pretracheal lymph node dissection be considered.

Keywords

Thyroid Tumor, Isthmus of Thyroid, Papillary Carcinoma, Surgery

1. Introduction

The frequency of papillary carcinoma arising in the thyroid isthmus only has been

demonstrated within a range of 1% to 9.2% [1] [2] [3] [4]. There have been no specific guidelines for the surgical treatment of patients with papillary carcinoma arising in the isthmus [5] [6] [7].

Most patients were treated with completion thyroidectomies after isthmusectomy for nodules [8] [9] [10]. PTCs located in the isthmus are more likely to be associated with multifocal disease, lymph node involvement and capsule invasion than carcinomas in other thyroid regions, and total thyroidectomy is to be considered as an appropriate surgical treatment [1] [4] [11]. However, Nixon *et al.* suggested that if the nodule was solitary and small in size and confined to the isthmus without evidence of extraglandular extension, the patient may be suitable for thyroid isthmusectomy or wide field isthmusectomy [2]. Sugeno *et al.* also recommended that isthmusectomy, including an adequate edge of surrounding normal thyroid tissues of each lobe, is sufficient and an appropriate primary surgical procedure for localized differentiated thyroid carcinoma of the isthmus [3]. Thyroid isthmusectomy is defined to remove the entire isthmus and wide field isthmusectomy is to remove the entire isthmus with surrounding thyroid tissues of each lobe. It should be noted that isthmusectomy or wide field isthmusectomy should encompass the lesion and a surrounding portion of normal tissue. Isthmusectomy has the benefit of avoiding dissection of the recurrent laryngeal nerve and parathyroid glands, thus limiting postoperative complications [2].

There is no consensus on the extent of lymph node dissection that should accompany treatment of isthmic PTC. Studies reported that central lymph node metastasis was present in 40.3% and 71.1%, and bilateral CND was considered to be needed for isthmic PTC due to the high rate of bilateral central lymph node metastasis especially involving the pretracheal and bilateral paratracheal lymph nodes [1] [12]. Delphian Lymph Node (DLN) metastasis was also reported a high metastasis rate in carcinomas located in the thyroid isthmus [13] [14].

This study is designed to analyze the outcomes of patients with papillary carcinoma in the thyroid isthmus treated with surgery at our institution. The aim is to demonstrate the role of thyroid isthmusectomy in the management of thyroid isthmus cancer.

2. Methods and Patients

34 patients with papillary thyroid carcinoma located in isthmus managed primarily by surgery in National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences, Peking Union Medical College from 1985-2008 were retrospectively analyzed. All the patients included were suspected with a malignant nodule in the isthmus by preoperative ultrasonography and any patients with suspected malignant nodule(s) in the lateral lobe were excluded. Data were collected from the electronic medical record on patient demographics, types of surgery, and the pathological characteristics. Pathological details included tumor histology, size, number and presence of microscopic extrathyroidal extension. Outcome data included local, regional, or distant recurrence. The presence of recurrence after treatment was based on cytological or histopathological evidence of disease. Distant disease was determined by imaging studies, including

chest X ray or CT scans. Statistical analysis was performed using SPSS version 20.0 software. Survival outcomes were analyzed using the Kaplan-Meier method.

3. Results

The clinical and pathological characteristics are shown in **Table 1**.

3.1. Patients and Treatment

Seven patients were men and 27 were women. The median age was 41 (range, 20 - 71) years. Twenty-five patients had a solitary nodule confined to the thyroid isthmus and nine patients with multiple nodules in thyroid lobes. All patients were with clinically negative lymph node(cN0) except one (2.9%) with clinically positive lymph node in left level IV (cN1b). All patients were free of distant metastases. Thirty-one patients (91.2%) were diagnosed with papillary thyroid carcinoma at frozen section pathological analysis and three patients (8.8%) were diagnosed at final histopathological analysis. Twenty-five patients were treated with thyroid isthmusectomy or wide field isthmusectomy, five with hemithyroidectomy (lobectomy and isthmusectomy) and four with hemithyroidectomy and partial resection of the contralateral lobe. Ten patients received pretracheal lymph node dissection (2 with DLN resected). The patient with cN1b received unilateral modified neck dissection and was confirmed with lymph node metastasis at final histopathological analysis (pN1b). No patients received postoperative

Table 1. Clinical and pathological characteristics.

Variables	Number (%)
Age (year)	
<45	19 (55.9)
≥45	15 (44.1)
Sex	
Male	7 (20.6)
Female	27 (79.4)
pT stage	
T1	28 (82.4)
T2	2 (5.9)
T3	4 (11.8)
pN stage	
N0	29 (85.3)
N1a	4 (11.8)
N1b	1 (2.9)
Capsular invasion	
No	18 (52.9)
Yes	16 (47.1)*

*Four of the 16 patients with extrathyroidal extension (ETE).

radioiodine treatment.

3.2. Pathology

All of the malignant nodules were diagnosed papillary carcinoma. Twelve patients accompanied with nodular goiter and two with chronic lymphocytic thyroiditis. Four patients were diagnosed with extrathyroidal extension after paraffin histopathologic analysis, and thirteen patients with microscopic capsular invasion. Thirty-two patients had a solitary lesion confined to the thyroid isthmus. One patient had two lesions in the thyroid isthmus and one had two lesions located in the thyroid isthmus and right lobe respectively. The median size of the lesion was 1 (range, 0.3 - 4) cm. Twenty-eight patients had a pathologically T1 disease (pT1), two patients had a pT2 lesion and four had a pT3 lesion. Five patients (14.7%) had papillary carcinoma detected in one of the pretracheal lymph nodes and one of them accompanied with metastatic lymph node in left level IV (1/7). All of the five patients with pretracheal lymph node metastasis had a solitary isthmus lesion and only one had a pT3 lesion.

3.3. Outcomes

There were no complications of recurrent laryngeal nerve palsy or hypocalcemia. One patient was lost-to-follow up. The median follow-up time of the other thirty-three patients was 94 months (range, 12 - 274). During the follow-up time, two patients had a recurrence and both survived after a re-operation. One who originally had two isthmus lesions (pT1N0) recurred at fifty-seven months and the histopathologic examination confirmed carcinosarcoma in left lobe after total thyroidectomy. Another patient (pT1N0) recurred at 101 months and the histopathologic examination confirmed papillary carcinoma after left lobectomy. Both patients survived to the follow-up deadline (67 and 274, respectively). There was no regional lymph node or distant organ recurrences. The 10-year recurrence-free survival rate was 89.4% (Figure 1). No deaths occurred. The 10-year overall survival rate was 100%.

4. Discussions

The frequency of papillary carcinoma arising in the thyroid isthmus is low (1% to 9.2%) [1] [2] [3] [4], and there are considerable literature debates on the extent of the surgical resection. No consensus existed on the appropriate management of thyroid cancer confined to the isthmus [5] [6] [7]. Papillary carcinoma arising in the isthmus has been reported more likely to be associated with multifocal lesions, lymph node metastasis and capsular invasion, and total thyroidectomy was considered as an appropriate surgical treatment [1] [4] [11]. A completion total thyroidectomy is normally performed in most studies [8] [9] [10]. Only a few studies advocated isthmusectomy or wide field isthmusectomy as a suitable and reasonable surgical procedure for isthmus PTC. In Sugeno *et al.*'s report on 19 well-differentiated thyroid isthmus malignancies, 4 patients were treated with isthmusectomy alone and all were alive with no evidence of recurrence 20 years after surgery [3]. Nixon *et al.* reported that if the nodule was solitary and

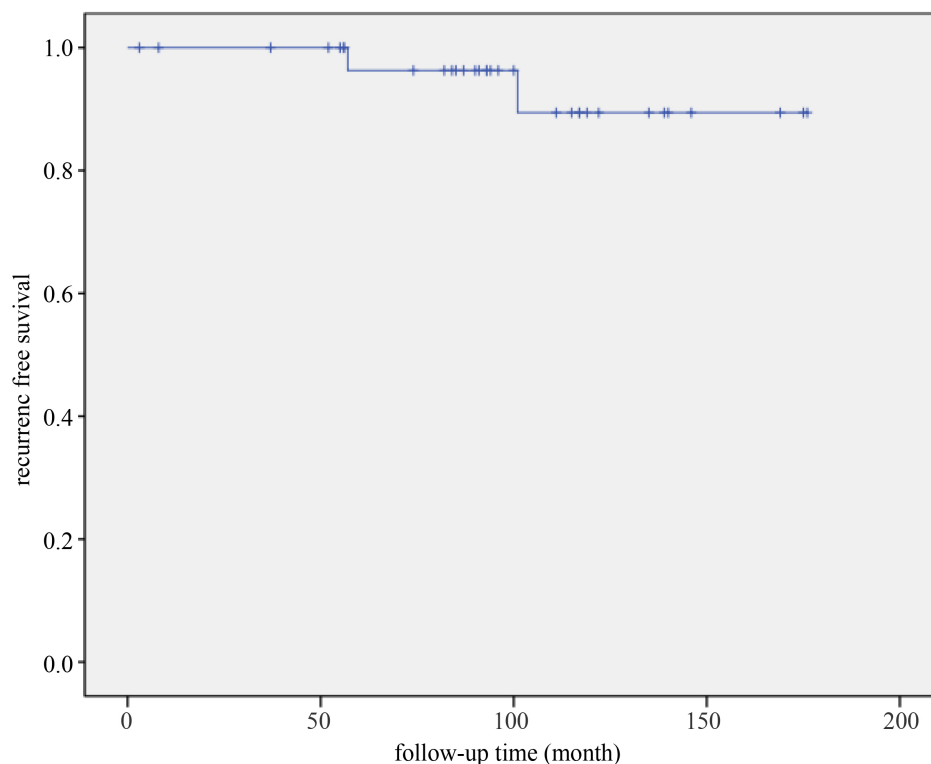


Figure 1. The 10-year recurrence-free survival of the patients.

small in size and confined to the isthmus without evidence of extrathyroidal extension, the patient may be suitable for thyroid isthmusectomy or wide field isthmusectomy with an excellent survival (10-year recurrence-free survival was 100%) [2]. The American Thyroid Association did not report isthmusectomy as an appropriate surgical procedure for papillary thyroid carcinoma [5]. In our study, only two of the patients treated with isthmusectomy had a recurrence and both survived after a re-operation. Most patients did not recur even with lymph node metastasis or extrathyroidal extension. Our results suggested that isthmusectomy or wide field isthmusectomy can be an effective treatment for isthmic PTC.

There is no consensus on the extent of lymph node dissection that should accompany with the treatment of isthmic PTC. The lymphatic system of the thyroid gland is parallel to the venous drainage system [15], and drains inferiorly into the pretracheal and paratracheal lymph nodes, and follows the inferior jugular lymphatics and superior mediastinal lymphatics [16], while the isthmus and upper lobes of the thyroid are drained superiorly to the prelaryngeal lymph nodes [13] [17]. In Song CM, *et al.*'s study, the most common subsite of central compartment metastasis in isthmic PTC was the pretracheal lymph node, and the isthmic PTCs had higher rates of metastasis to pretracheal and bilateral paratracheal lymph nodes than the non-isthmic PTCs, and complete bilateral central neck dissection should be considered [12]. In our study, only ten patients had pretracheal lymph node dissection done and no patients had bilateral paratracheal lymph node dissected. Though five patients had pretracheal lymph node

metastasis, no patient had a lymph node recurrence during the follow-up time. We suggest that pretracheal lymph node dissection is needed and also sufficient for most isthmic PTCs with clinically negative lymph node. The DLN is located in the fascia above the isthmus of the thyroid gland, between the cricoid and thyroid cartilage; it is also known as the prelaryngeal, precricoid, or cricothyroid node [18] [19]; is known to be predictive of a poor prognosis [20]. DLN metastasis was associated with tumor location in the isthmus or upper third of the thyroid, and with ETE [13]. DLN should be resected with pretracheal lymph node, especially for those with lymph node metastasis or with tumor ETE.

Our results suggest that isthmusectomy/wide field isthmusectomy could be sufficient treatment for PTC confined to the thyroid isthmus. We also recommend that the pretracheal lymph node dissection routinely be performed.

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