



Recurrence pattern after conservative surgery for papillary thyroid carcinoma



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ABSTRACT

Objective: Risk-based treatment represents the optimal management strategy for papillary thyroid carcinoma; however, the optimal extent of thyroidectomy and neck dissection remains controversial. This study aims to clarify the pattern of recurrence after conservative surgery in patients with papillary thyroid carcinoma.

Methods: We retrospectively reviewed 93 patients with papillary thyroid carcinoma treated with conservative surgery. We analyzed recurrence rate, recurrence pattern, risk factors for recurrence, salvage treatment, and disease-free survival (DFS) in patients stratified according to risk.

Results: The recurrence rate was significantly lower in the low-risk group compared with the high-risk group (14% vs 34%; $p < 0.01$). The recurrence pattern also differed between the two groups, with ipsilateral lateral neck recurrence being more common in the low-risk group (9%), while contralateral lateral neck recurrence was more common in the high-risk group (18%). Patients with contralateral thyroid lobe metastasis and/or direct contralateral thyroid lobe invasion showed a significantly higher rate of contralateral lateral neck metastasis than patients negative for both these features. The overall 5-year DFS was 81% in all patients. Advanced T and N classification, large primary tumor (≥ 4 cm), extrathyroidal invasion, and high-risk group were significantly associated with poorer 5-year DFS in univariate analysis.

Conclusion: Conservative surgery may represent a good treatment option for patients with low-risk papillary thyroid carcinoma. Tumor recurrence patterns differ between risk groups, with contralateral thyroid lobe lesions and direct contralateral lobe invasion being risk factors for contralateral lateral neck recurrence.

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1. Introduction

Papillary thyroid carcinoma (PTC) generally shows indolent characteristics, but is associated with a high incidence of regional lymph node metastasis and multifocal tumors. Although risk-based treatment represents the optimal management strategy, the optimal extent of thyroidectomy and neck dissection remains controversial.

According to the American Thyroid Association (ATA) guidelines, lobectomy may be sufficient for small (< 1 cm), low-risk,

unifocal, and intrathyroidal PTC in the absence of prior irradiation or clinically involved cervical nodal metastasis [1]. However, the indications for less-than-total thyroidectomy (lobectomy or subtotal thyroidectomy) are wide in Japan [2], because of the prevalence of low-risk PTC [3]. According to Japanese guidelines, lobectomy is recommended for intrathyroidal PTCs measuring < 2 cm without cervical node metastasis. In contrast, total thyroidectomy is strongly recommended for tumors > 5 cm in diameter and exhibiting extrathyroidal invasion, multiple cervical nodal metastasis, nodal metastasis ≥ 3 cm, and distant metastasis [4].

Although conservative surgery (lobectomy or subtotal thyroidectomy) may increase the risk of contralateral lobe, lymph node, and thyroid bed recurrences, such recurrences can be detected by adequate post-operative follow-up, with no adverse influence on survival rate [4]. Haigh et al. [5] also reported that survival rate was

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not influenced by the extent of thyroidectomy. Furthermore, preservation of the contralateral lobe decreases the risk of surgical complications such as recurrent nerve palsy, hypothyroidism, and hypoparathyroidism. Less-than-total thyroidectomy thus remains a treatment option for PTC in our institution.

In order to determine the optimal treatment strategy, it is necessary to determine the recurrence patterns and outcomes after conservative surgery. In this study, we therefore retrospectively review the treatment administered to 93 patients with PTC in our institution and analyze the recurrence rate, recurrence pattern, risk factors for recurrence, salvage treatment, and disease-free survival (DFS) in different risk groups.

2. Materials and methods

2.1. Study population

We analyzed data for 93 patients with histopathologically confirmed PTC who were treated in Takeda General Hospital from 1997 to 2007. The study population consisted of 33 men and 60 women with an age distribution of 17–85 years (average age, 58.8 years). The median follow-up period was 96 months (range, 37–164 months). All patients were previously untreated.

Clinical staging was performed according to the 2010 version of the TNM classification adopted by the UICC and AJCC. We also classified risk groups according to the report by Sugitani et al. [6]. Patients of any age with distant metastasis and those who were ≥ 50 years old with nodal metastasis ≥ 3 cm and/or extrathyroidal invasion were classified into the high-risk group; all others were classified into the low-risk group. The distributions of age, gender, TNM classification, and risk analysis are listed in Table 1.

2.2. Treatment strategy

The extent of thyroidectomy was determined by pre-operative ultrasonography (US). Lobectomy, sub-total thyroidectomy, and total thyroidectomy were performed according to the tumor location. Routine ipsilateral central compartment (level VI) neck dissection was performed; however, dissection of the lateral neck compartment was only mandatory in patients with clinical node metastasis. Total thyroidectomy was the recommended treatment for patients with high-risk PTC. However, less-than-total thyroidectomy was performed if the lesion was located in one lobe and

patients wished to preserve thyroid and parathyroid functions. Post-operative radioiodine (RI) therapy was administered in patients with distant metastases. Thyroid-stimulating hormone suppression was generally carried out in the high-risk group. After the initial treatment, patients were evaluated every 3 months for the first year, every 4 months for the next 2 years, and annually thereafter, by physical examination, US, computed tomography (CT), positron emission tomography (PET), and serum thyroglobulin (Tg) measurements to detect recurrences.

Definitions of clinical recurrence were cytologically proven lesions, high Tg levels in total thyroidectomy patients, and/or PET-positive lesions. Salvage surgery was performed for resectable recurrences. RI therapy was administered after complete thyroidectomy for unresectable recurrences, recurrences associated with severe dysfunction because of surgical resection, or distant metastases. The initial treatments according to risk analysis are shown in Table 2.

2.3. Statistical analysis

We analyzed recurrence rate, risk factors for recurrence, and DFS. DFS was calculated using the Kaplan–Meier method, and differences were analyzed using log-rank tests. χ^2 tests were used to evaluate differences between the two groups. A value of $p < 0.05$ was considered statistically significant. Analyses were conducted using Statmate Version 2 (GraphPad, La Jolla, CA, USA).

3. Results

3.1. Overall outcome

Of the 93 patients receiving definitive treatment, 20 (22%) exhibited recurrence after an average of 32 months (range, 6–82 months); the remaining 73 patients had no recurrence. The recurrence rate was significantly lower in the low-risk group compared with the high-risk group (14% and 34%, respectively; $p < 0.01$). Salvage treatment was performed in relapsing patients, including lateral neck dissection in 11 patients, remnant thyroidectomy in 6, lymph node resection in 5, central neck dissection in 2, and RI in 2. Finally, 12 resectable patients survived without disease. Distant metastasis and unresectable or extra-regional lymph node recurrence occurred in four and two patients, respectively and pre-treatment resectable cervical node recurrence occurred in two patients. These eight patients remained alive with disease.

Table 1
Patient characteristics.

Variable	No. of patients
Sex	
Male	33
Female	60
Median age (years)	58.8 (17–85)
Median follow-up period (months)	96 (37–164)
T classification	
T1a	2
T1b	30
T2	18
T3	34
T4a	9
N classification	
N0	47
N1a	22
N1b	24
M classification	
M0	88
M1	5
Risk analysis	
Low-risk group	65
High-risk group	28

Table 2
Distribution of primary surgery and neck dissection.

Treatment method	No. of patients
Low-risk group ($n = 65$)	
Type of thyroidectomy	
Lobectomy	53
Sub-total thyroidectomy	7
Total thyroidectomy	5
Extent of neck dissection	
VI	64
Ipsilateral II, III, IV, VI	1
High-risk group ($n = 28$)	
Type of thyroidectomy	
Lobectomy	10
Sub-total thyroidectomy	6
Total thyroidectomy	12
Extent of neck dissection	
VI	6
Ipsilateral II, III, IV, VI	16
Bilateral II, III, IV, VI	4
Ipsilateral II, III, IV, VI, VII	2

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