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Surgical treatment of incidental and non-incidental papillary thyroid microcarcinoma

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Introduction

The World Health Organization (WHO) defined papillary thyroid microcarcinomas (PTMC) as tumors measuring 1.0 cm or less in diameter (1, 2). These tumors are often not detectable by clinical examination, and commonly found incidentally either after a total thyroidectomy is performed for other indications or during thyroid ultrasound. Incidental PTMC is defined as a postsurgical diagnosis of microcarcinoma with benign clinical course3. PTMC is also referred to as minimal, small, tiny, or minute carcinomas (4-7). Some authors suggest that small papillary carcinomas found at histology should be called occult papillary "tumors" instead of carcinomas to reflect its benignity and to avoid the culture stigma associated with a cancer diagnosis (8).

Discriminating between an incidental PTMC or invasive PTMC intraoperatively is essential. In this study, we analyzed the clinicopathology parameters between incidental PTMC and non-incidental PTMC study in order to test the hypothesis that less aggressive surgical treatments, such as lobectomy or subtotal thyroidectomy, are sufficient for incidental PTMC.

Although PTMC is considered a benign disease, it can have a variable biologic behavior. While the tumor cannot be palpated in the thyroid clinically, palpable lymph node metastasis may be found in a subset of patients. Nodal involvement rate is lower in PTMC compared to tumors larger than 1 cm. It has been reported that lymph node metastases were detected in 3.1–18.2% of patients with PTMC (9, 10). Lymph node metastasis at diagnosis is a predictive factor for loco-regional recurrence and distant metastasis for PTMC (11). In this study, we analyzed the factors predictive of central cervical lymph node metastasis from PTMC and tested the hypothesis that more aggressive surgical treatments such as near-total or total thyroidectomy with central cervical lymph node dissection are adequate procedures for non-incidental PTMC.

Materials and methods

Patients and operation

From December 1993 to October 2008, 588 papillary thyroid carcinoma patients underwent surgical treatment and were followed by our service at Shanghai Renji Hospital, China. Among them, 177 cases (30.1%) were PTMC as determined by histopathology. All patients received primary thyroid surgical resection and received follow-up care from service.

The 177 PTMC patients were divided into 2 groups. Fifty-four patients in group 1 were classified as incidental PTMC, while 123 patients in group 2 were classified as non-incidental PTMC. Incidental PTMC was defined as a postsurgical diagnosis of microcarcinoma with benign clinical course. Non-incidental PTMC was defined by histopathology before the operation by fine-needle aspiration biopsy or during the operation by frozen sections.

Patients in group 1 were diagnosed by palpation or neck ultrasound. No patient was found to have a suspicious cervical lymph node before operation. These patients received a subtotal thyroidectomy or lobectomy. Subtotal thyroidectomy was defined as removing more than 50% of the entire gland on abnormal lobe(s). Patients were treated with postoperative suppressive L-thyroxine (L-T4) therapy.

Patients in group 2 whose malignancy was confirmed by fine-needle aspiration biopsy or by frozen section

underwent a near-total or total thyroidectomy and a central cervical lymph node dissection. When the patient had the nodule(s) in only one lobe, he underwent a near-total thyroidectomy, when the patient had the nodule(s) in both lobes, he underwent a total thyroidectomy. Near-total thyroidectomy was defined as a total lobectomy in the lobe with the dominant nodule, with isthmectomy and near-total lobectomy on the contralateral side leaving thyroid posterior capsule, adjacent parathyroid glands, and blood supply. All the patients in group 2 received a central cervical lymph node dissection systematically. Fifty two patients in group 2 with concurrent neck lymphadenopathy by palpation or by neck ultrasound received a unilateral selective neck dissection, including level II-IV and VI. One patient with a suspicious cervical lymph node bilateral underwent a bilateral selective neck dissection. Patients were treated with postoperative suppressive L-thyroxine (L-T4) therapy as done in group 1.

Statistical analysis

Categorical variables were compared using the t-Test Procedure (**Table 1**), the FREQ Procedure (**Tables 1**, **2**), Fisher Exact Test (**Tables 1**, **2**) and the Logistic Procedure (**Table 3**). P values were two-sided. Differences were considered significant for $p<0.05$. Statistical analyses were performed using SAS version 6.12 software.

Results

Presentation of PTMC in 2 groups

The mean age of patients in group 1 is older than that in group 2 (49.6±8.9 versus 44.4±9.5, $p<0.01$)). Histological examination showed that patients in group 1 had a smaller tumor size than in group 2 (0.33±0.21 versus 0.71±0.23, $p<0.01$). No statistical difference of sex distribution, multifocal ratio or prognosis were noted between group 1 and 2. **Table 1** illustrated the age, gender, tumor size, multifocal and prognosis distribution of 177 PTMC patients in different groups.

Follow-up

No clinically important complications were found which defined as permanent hypocalcemia and permanent vocal paralysis. All patients received postoperative thyroid stimulating hormone suppression thyroxine therapy. No one received radioiodine, even for patients with known nodal metastatic thyroid disease. Patients were followed up until June 2009, prospectively from 11 to 188 months (mean: 59.73 months) according to Société Française d'Oto-Rhino-Laryngologie et de Chirurgie de la Face et du Cou Practice Guidelines (12). No mortality was recorded during the follow-up period. Ten-year disease-free and overall survival rates were 99.4% and 100%, respectively. No distant metastasis was determined during the follow-up period. The recurrence was defined by histopathology during the period. One patient in group 2 who underwent a near total thyroidectomy and right sided selective neck dissection for PTMC in the right lobe on November 1997 recurred in the left lobe 78 months after the initial operation. As we did not find the cervical lymph node metastasis, this patient underwent total thyoidectomy at May 2004. She was followed until now, no recurrence or distant metastasis was recorded.

Factors predictive of central lymph node metastasis in group 2

All patients in group 2 underwent central cervical lymph node dissection as routine surgical treatment. Thirty-two patients were level VI lymph node positive (26.0%) while 91 were negative. The FREQ Procedure and Fisher Exact Test analysis showed that all variables assessed, including sex, age and tumor size were not significantly predictive of central lymph node metastasis ($p>0.05$). However, multifocality of the tumor was found to be one of the factors significantly increasing the risk of central cervical lymph node metastasis ($p=0.013$)(**Table 2**). Multifocality was also found to be an independent risk factor for central cervical lymph node metastasis by logistic regression analysis (**Table 3**).

In group 2, 52 patients received a unilateral selective neck dissection and 1 patient received a bilateral selective neck dissection. Among the 54 cervical lymph node dissection,10 neck dissections were positive (18.5%) while 44 were negative. Among these 10 positive neck dissections, 8 were concurrent with central cervical lymph node positive, whereas other 2 dissections had a skip lateral nodal metastasis

without metastasis to the central compartment.

Surgical treatment of PTMC in our service

We have a routine treatment for the thyroid disease. We only operated on patients with thyroid nodules more than 10mm or whose fine-needle aspiration biopsy was positive. Patients diagnosed as PTMC before the operation or during the operation received a near total or total thyroidectomy with central cervical lymph node dissection. Patients with suspicious cervical lymph node by clinical palpation or by cervical ultrasound received a selective lymph node dissection. Patients who were diagnosed as PTMC postoperation underwent subtotal thyroidectomy or lobectomy and did not received more aggressive operation. All patients received postoperative thyroid stimulating hormone suppression thyroxine therapy for life. No one received radioiodine.

Discussion

The wide spread use of neck ultrasound has allowed the detection of non palpable thyroid nodules as small as 1-3 mm. When these nodules are included, the incidence of thyroid nodules may be as high as 70% in the general population (13, 14). In addition, ultrasound allows the biopsy of thyroid nodules that are difficult or impossible to palpate because of their size and location. The use of ultrasound-guided fine-needle aspiration biopsy has resulted in a marked increase in the diagnosis of patients with PTMC and in the number of patients operated on for small carcinomas. In 100% of subjects with PTMC in our study, frozen section was performed during thyroid operation. We found that the frozen section remains the most common determinant of surgical intervention, when not all the patients had to undergo fine-needle aspiration biopsy preoperatively.

Many researches (15, 16) have previously reported that a subtotal thyroidectomy is an effective surgical treatment for incidental PTMC. For nonincidental cases, aggressive treatment is essential for reducing the risk of cancer recurrence or mortality following surgery. Kalliopi (17) suggested when PTMC is diagnosed preoperatively, routine total or near-total thyroidectomy is the treatment of choice, therapy should not differ from that of larger tumors. In cases where a thyroid lobectomy for benign thyroid disease was performed, if a unifocal PTMC with favorable histological subtype, no extension beyond the thyroid capsule, no lymph node metastases, and normal contralateral lobe are found, completion thyroidectomy may be avoided and the patient's follow-up may be limited to periodical neck ultrasound while undergoing replacement L-T4 therapy.

In our study, we found that subtotal thyroidectomy is an effective surgical treatment for incidental PTMC, as no one recurred during the follow-up. Near total or total thyroidectomy with central cervical lymph node dissection is an adequate procedures for non-incidental PTMC, as ten-year disease-free and overall survival rates were 99.4% and 100%. Only one patient relapsed after first surgical treatment. Completion thyroidectomy is recommended in our service in case of multifocal disease, unfavorable histology, or lymph node metastases. In this study, patients were started on suppressive L-thyroxine (L-T4) therapy to achieve a low TSH level during follow-up. Because total thyroidectomy was not the routine surgical procedure in our series, patients did not undergo radioactive iodine ablation to achieve negative 131-I whole-body scan and undetectable Tg levels during follow-up. We found that our treatment was effective and consistent with China's national conditions in order to reduce the operative complications and to give patients proper not excessive treatment.

In group 1, the mean age of patients is older than that in group 2 and they had a smaller tumor size. A recent study (15) of 335 cases also showed that there was no statistically significant difference of the mean age between 2 groups and patients in incidental group had a smaller tumor size, few frequency of multifocal, better prognosis than that of non incidental group. As the prognosis of PTMC is related to the tumor size, Pelizzo (18) suggested that PTMC < 5 mm in diameter, without evidence of lymph node involvement, partial thyroidectomy may be a viable approach to treatment. In our study, the mean tumor size of group 1 is 0.33 cm, so our treatment for incidental PTMC is adequate.

We have systematically assessed the pattern of central cervical nodal metastasis in 123 patients. Multifocal PTMC was noted in 7.3% (9/123) of the patients in the group 2, in which 6 were central lymph node positive. A similar study (19) showed that of the 72 patients with PTMC, no clinicopathologic factor

predicted nodal metastasis. Despite the absence of palpable neck nodes, PTMC is associated with a high rate of central lymph node metastasis which was 26% (32/123) in our study. Since the central cervical lymph node dissection used the same incision as the original surgery, we suggested total thyroidectomy with central cervical lymph node dissection was more effective than the thyroidectomy alone for managing non incidental PTMC. It can improve the quality of life and survival by reducing cervical lymph node metastasis.

Ito (20) suggested if surgical treatment is performed for low-risk PTMC, prophylactic modified radical neck dissection is not necessary. In our study, 53 patients in group 2 with concurrent neck lymphadenopathy underwent cervical lymph node dissection, including level II–IV, 10 were (18.5%) positive. Although PTMC had high metastatic activity, prophylactic neck dissection had been discouraged for patients who present without palpable neck nodes because lymph node metastasis had not been considered prognostic for survival (21). So we thought if the patients without concurrent neck lymphadenopathy, it was unnecessary to undergo cervical lymph node dissection. According to our series, we considered that central cervical lymph node could also be regarded as the sentinel lymph node of PTMC.

Conclusion

Subtotal thyroidectomy is an effective surgical treatment for incidental PTMC. Patients with multifocal tumors may have more aggressive surgical treatment. Near total or total thyroidectomy with central cervical lymph node dissection is adequate procedures for non-incidental PTMC who without lymph node metastasis.

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