

RESEARCH ARTICLE

Is Level V Dissection Necessary for Low-risk Patients with Papillary Thyroid Cancer Metastasis in Lateral Neck Levels II, III, and IV

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Abstract

Whether it is beneficial to dissect level V in papillary thyroid cancer (PTC) patients with positive lateral neck lymph nodes at levels II-IV is still controversial, especially for low risk cases. In this study, we reviewed the medical records of 47 patients who underwent 47 ipsilateral selective lateral neck dissections (levels II-IV) for previously untreated papillary thyroid carcinomas between October 2006 and October 2008 to assist in establishing the optimal strategy for lateral neck dissection in low risk PTC patients with clinically negative level V nodes. All 47 patients were confirmed to have positive lymph nodes pathologically. Seventeen (36.12%), 36 (76.6%), and 34 (72.34%) patients had positive lymph nodes in levels II, III, and IV, respectively. The mean number of pathologically positive lymph nodes was 1.7 in level II, 2.9 in level III, 2.8 in level IV. No death and distant metastasis were recorded during follow up period. Just 2 patients exhibited recurrence to lymph nodes, and only one showed nodal recurrence in ipsilateral level V, who had positive lymph nodes in all of levels II, III, and IV at initial neck surgery. In conclusion, for PTC low risk patients with clinically negative lymph nodes in level V, non-performance of level V dissection would still achieve good survival results as traditional modified radical neck dissection, with a "wait and see" strategy to be recommended.

Keywords: Papillary cancer - lymph node dissection level V - thyroid

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Introduction

Thyroid cancer ranks among the 10 most common malignancy in populations around the world (Cooper et al., 2006), epidemiological data from USA have shown a 2.4-fold increase between 1973 and 2002 (Davies and Welch, 2006). Papillary thyroid cancer (PTC) accounts for more than 80% of all thyroid cancers, Lymph node metastases develop in 30%–90% of patients with PTC (Caron and Clark, 2005), depending on which diagnostic modalities are employed to assess for potential metastases. therapeutic neck dissection is usually performed in patients with positive lateral neck lymph nodes, while the extent of neck dissection is still controversial. Therapeutic neck dissection for patients with PTC includes berry picking, selective neck dissection, and a formal modified radical neck dissection in which all lymphatic tissue within the cervical lymph node levels II, III, IV, and V are removed (Sivanandan and Soo, 2001), the uncertainty of the prognostic impact of lymph node metastases on overall patient survival contributes to these diversity of options for neck dissection. Currently, most surgeons recommend formal modified radical neck dissection, sparing the spinal accessory nerve, internal jugular vein, and the sternocleidomastoid muscle (Kupferman et al., 2008), while in recent years, some surgeons take selective neck dissection cautiously to decrease complications after neck

dissection. Whether it is beneficial to dissect level V in PTC patients with positive lateral neck lymph nodes is still controversial, especially for low risk PTC patients (Lundgren et al., 2006), dissection of level V may lead to clinically important postoperative morbidities (shoulder dysfunction, neck numbness, and neuropathic pain) because of injury to the spinal accessory nerve or the cervical plexus, despite gross preservation of these nerves (Laverick et al., 2004).

This study is a small scale and prospective study, the purpose of this study was to introduce our experience about neck dissection not involving level V in low-risk patients with papillary thyroid cancer for metastasis in other lateral levels. Our information will assist in establishing the optimal strategy for neck dissection in low risk PTC patients with Clinically negative level V nodes.

Materials and Methods

This prospective study enrolled 47 patients who underwent 47 ipsilateral lateral neck dissections (levels II-IV) for previously untreated papillary thyroid carcinomas between October 2006 and October 2008. All diagnoses of papillary thyroid carcinoma were confirmed pathologically. all the patients belong to low risk group (<45 years old, T1, T2, M0) (Shaha, 2006). Of those patients, the following were excluded: patients

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with non-papillary cancer and poor differentiated types, patients with distant metastasis at initial presentation, patients with a clinically positive node in neck level V and contralateral lateral neck, and patients who had a history of thyroid or neck surgery for nonthyroidal head and neck cancers. Lateral neck dissection was performed when physical examination and ultrasonography (US) were suspicious for metastatic neck nodes in the lateral neck except level V. All patients underwent a thyroidectomy and a therapeutic neck dissection of both the central and lateral compartments simultaneously. Local approval by our institutional review board was obtained for this study. The clinical, radiologic, and pathologic data of 47 patients were reviewed. Clinically negative level V nodes were defined as no palpable cervical lymph nodes and having no suspicious metastatic lymph node on US in level V. There were 7 males and 40 females, with a mean age of 37.9 years (range, 18-45). The T stage of the patients were T1, 11; T2, 36. The TNM stages of all the patients were I. All the patients underwent US and found suspicious metastatic nodes, and 19 patients found palpable cervical lymph nodes in lateral neck except level V.

Central neck dissection was carried out in all 47 patients. Its superior border is the hyoid bone, the inferior border is the suprasternal notch, and the lateral borders are the common carotid arteries. Central lymph nodes include pretracheal and paratracheal nodes, the precricoid (Delphian) nodes, and the perithyroidal nodes (White et al., 2007). All the patients underwent ipsilateral lateral neck dissections encompassing levels II-IV. Its superior border is the skull base and mandible, the inferior border is the subclavian vein, the lateral border is posterior margin of sternocleidomastoid muscle. Neck dissection spares the internal jugular vein, spinal accessory nerve, and the sternocleidomastoid muscle. During neck dissection, the specimens were labeled. They then cut along this landmark and labeled the specimen accordingly. All surgical procedures were performed by the same surgeon team.

All the patients received thyroid hormone suppression therapy postoperatively, none of the patients underwent RAI ablation (we do not undertake RAI ablation in low risk PTC patients).

The frequency and pattern of lymph node metastases in the lateral compartments were analyzed. The timing and rate of recurrence, especially in level V, and mortality were collected.

Results

The mean size of the primary thyroid cancer was 2.1 cm (range, 0.3-4 cm). Forty-one (87.23%) patients had thyroid cancer with the primary tumor size greater than 1 cm. The number of patients with multifocalities in the thyroid gland was 15 (31.91%). Direct invasion to the recurrent laryngeal nerve, trachea, and tracheoesophagus was found in 2, 2 and 1 patients, respectively.

All 47 lateral neck dissection samples were confirmed to have positive lymph nodes pathologically. The mean number of harvested lymph nodes in the lateral neck dissection was 22.7 (range, 13; 45). According to neck level, level II averaged 9.7, level III 7.3, level IV 7.9

nodes. The largest positive nodes ranged in size from 0.5 to 3.2 cm, with a mean 1.3 cm.

Of the 47 lateral neck dissection samples, 30 (63.83%) showed nodal diseases at multiple levels, and 17 (36.17%) had just one level disease. Seventeen (36.12%), 36 (76.6%), and 34 (72.34%) patients had positive lymph nodes in levels II, III, and IV, respectively. Six and 11 patients had positive lymph nodes in levels III, and IV, respectively. The mean number of pathologically positive lymph nodes was 1.7 in level II, 2.9 in level III, 2.8 in level IV.

After the initial surgery, patients were followed up once per three months in our clinic

Ultrasonography was performed to detect lymph nodes suspected to have metastasis when follow-up, average duration of patient follow-up was 48.2 months (range, 36--60). No death and distant metastasis were recorded in follow-up period. To date, just 2 patients have shown recurrence to the lymph node within 2 year of the initial neck dissection, the overall neck recurrence rate is 4.26% (2/47), and the recurrence rate in level V is 2.13% (1/47), one patient showed nodal recurrence in contralateral level VI (8.3 month postoperatively), another patient showed nodal recurrence in ipsilateral level V (17.2 month postoperatively). Both patients had nodal diseases in initial neck surgery, and the patient with level V recurrence had positive lymph nodes in all of levels II, III, and IV in initial neck surgery. Both two patients received salvage neck dissection.

In this series, 2 of 47 patients showed chyle leakage that was cured by a fat-restricted diet and local compression. Temporary accessory nerve paralysis was detected in one patient. Postoperative bleeding was seen in one patient.

Discussion

Because of postoperative morbidity associated with nerves (the spinal accessory nerve and cervical plexus) and uncertainty of the prognostic impact of lymph node metastases on prognosis, dissection of level V is still controversial. The superior boundary of level V is formed by convergence of the sternocleidomastoid and trapezius muscles, the inferior boundary is the clavicle, the anterior (medial) boundary is the posterior border of the sternocleidomastoid muscle, and the posterior (lateral) boundary is the anterior border of the trapezius muscle (Robbins et al., 2002), dissection of this large extent is closely associated with postoperative morbidity. Our opinion is that the principles of management of level V are to develop an evidence-based strategy, give the better outcome (relatively lower recurrence and better prognosis) with the lower morbidity, and avoid over-treatment in most of the patients, especially in the low-risk patients who would be expected to have good prognosis. Unfortunately, no studies offer level I evidence about the treatment of level V. Recent guidelines from the American Thyroid Association (ATA) note that functional compartmental en bloc lateral neck dissection in patients with metastatic lateral cervical lymphadenopathy, but offer no official recommendation concerning the dissection extent

(Doherty et al., 2009). Guidelines from NCCN (2011) tend to be conservative, which stated that Lateral neck dissection (levels III and IV, consider levels II and V depending on clinical and ultrasound findings) should be done if lymph node(s) palpable or biopsy positive. Our opinion tends to be closer with NCCN, but still some difference exists: level V would be spared when no palpable cervical lymph nodes and having no suspicious metastatic lymph node on US in level V. This small scale prospective study examined the recurrence in level V in 47 new patients with papillary thyroid cancer and clinical positive lateral neck nodes in levels II-IV. All patients underwent ipsilateral lateral neck dissections (levels II-IV) in a uniform. This study significantly differs from other studies, just explore the experience in low risk PTC patients.

When level V was included in the extent of neck dissection, postoperative morbidity was usually emphasized, leading to shoulder dysfunction, neck numbness, and neuropathic pain, and has a negative impact on patients' social activities (Terrell et al., 2000; Cappiello et al., 2005; Inoue et al., 2006). Despite attempts to preserve the spinal accessory nerve and cervical plexus during neck dissections. Terrell et al found that less shoulder and neck pain, and fewer physical problems achieved when the spinal accessory nerve was spared during lateral neck dissection not involving level V, patients maintained better quality of life (Terrell et al., 2000). When the spinal accessory nerve tried to be preserved, its function still decreased (Laverick et al., 2004). As a result, selection of suitable patients to spare the nerves is urgent and necessary to achieve lower recurrence and better prognosis, and avoid most of the patients to undergo unnecessary level V dissection.

In general, for patients with lateral cervical metastasis, most institutions prefer the modified radical neck dissection (level II-V) to attain regional control (Shaha et al., 1996; Kupferman et al., 2008), modified radical neck dissection once became the standard treatment for cervical disease. While morbidities accompanied by this dissection disturbs both the surgeons and patients. Though the prognostic significance of lymph node metastases for overall patient survival remains controversial (Machens et al., 2002; Bhattacharyya et al., 2003), while many large retrospective studies had consistently failed to identify lymph node metastasis as an important prognostic factor for survival (Sato et al., 1998; Sugitani et al., 2004), the dissection extent in patients with positive lateral neck lymph nodes has been argued. Detailed studies demonstrated that lymph node metastasis in older patients and those with poorly differentiated histology (high risk patients) has major implications on prognosis (Shaha, 2004). As a result, for low risk PTC patients (<45 years old, T1, T2, M0) with positive lateral neck lymph nodes (Shaha, 2006), such extent of level II-V is also argued. Evidence exists that cervical lymph node metastasis has no major impact on survival in low-risk patients (Lundgren et al., 2006). Turanli demonstrated that no survival advantage was gained by modified radical neck dissection (level I-V) compared to more selective neck dissection (level II-IV) (Turanli et al., 2007). Caron stated that routine modified

radical neck dissection can be successfully replaced by a selective approach (Caron et al., 2006). We agree with the opinions of Caron, in this study, for PTC low risk patients with clinically negative lymph node in level V, dissection of level V was ignored, and low recurrence rate was achieved (4.26%, 2/47). No death and distant metastasis were recorded in follow-up period, though a long follow-up period was required further for survival analysis, the average duration of patient follow-up still reached 48.2 months, we could come to the preliminary conclusion that selective neck dissection (level II-IV) could at least reach the same results as the reported results of modified radical neck dissection (level I-V).

Thus, no survival benefits would be gained to perform prophylactic level V dissection for patients without a clinically evident level V lymph node. There are two kinds of lateral lymph node metastases, namely, clinically positive metastasis detected by palpation and on preoperative imaging studies such as ultrasonography (cN1b), and metastasis detected only on postoperative pathological examination (pN1b). pN1b does not independently affect the cause specific survival of patients (Ito et al., 2007), as a result, prophylactic lateral neck dissection was not recommended (Doherty et al., 2009), this is also applied to level V. When study population was restricted to patients without a clinically evident level V lymph node, pN1b were present in a number of level V specimens (16-20%) (Roh et al., 2008). Noguchi reported that at least 75% of patients with PTC have occult lymph node metastases, but only about 20% become clinically evident, which means pN1b occasionally developed to be evident (Noguchi et al., 1987). Carton reported a recurrence rate of 3% at level V, and they thought that recurrence rarely recurred at level V regardless of whether this lymphatic region had previously been found to be positive for metastatic disease, negative for metastatic disease or simply not dissected (Caron et al., 2006). In our study, 2 patients have shown recurrence to the lymph node, and just one patient showed nodal recurrence in ipsilateral level V. Hence, patients with a clinically negative level V lymph node and occult lymph node metastases would be expected to have lower recurrence rate.

Formerly, we confirmed clinically positive lymph node metastasis by palpation (Moley et al., 1999). As the wide use and satisfactory diagnostic efficacy, high resolution ultrasonography has been used to detect lateral positive lymph node (Robbins et al., 2002; Caron et al., 2005; Ito et al., 2005; Cooper et al., 2006; Doherty et al., 2009). Nowadays, clinically positive lymph node metastasis includes the nodes detected both by palpation and ultrasonography (Caron et al., 2006), and ultrasonography is more sensitive than palpation, the proportion of clinically positive lymph node detected by ultrasonography becomes greater, we would think that the severity of cN1b detected by ultrasonography is less than that by palpation, and would be expected to have lower recurrence and better survival. In our study, all the patients underwent US and found suspicious metastatic nodes, and only 19 patients found palpable cervical lymph nodes. No death and distant metastasis were recorded in follow-up period. Node metastasis overlooked by ultrasonography (pN1b)

has only limited clinical importance (Ito et al., 2007). Most of node metastasis at level V belong to pN1b, so prophylactic dissection of level V also has only limited clinical importance.

levels II, III, and IV were the most frequent with clinically positive lymph node (Caron et al., 2006), our study also have the similar results, Seventeen (36.12%), 36 (76.6%), and 34 (72.34%) patients had positive lymph nodes in levels II, III, and IV, respectively. Some studies evaluated the potential predictor factors (Caron et al., 2006), revealed that patients with simultaneous metastases to levels II, III, and IV had greater node metastasis at level V (Caron et al., 2005; Roh et al., 2008), these node metastasis at level V all belong to pN1b, the clinical benefits from level V dissection guided by simultaneous metastases is still controversial. And more patients would not benefit from this dissection while would face postoperative morbidity. For patients without a clinically evident level V lymph node, this dissection would be considered unreasonable.

Above all, for PTC low risk patients with clinically negative lymph node in level V, ignorance of level V dissection would get good survival results as traditional modified radical neck dissection, "wait and see" strategy for negative level V is acceptable and low recurrence and morbidity are expected. As a result, we take selective neck dissection (level II-IV) as standard treatment for low risk PTC patients with positive lymph node in lateral neck (level II-IV except level V). This study is a preliminary report to introduce the recurrence and mortality, we are taking more patients into this study and long time follow up are on the process.

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