Sentinel lymph node biopsy: Is it a reliable indicator of lateral nodal involvement in papillary thyroid carcinoma?

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Abstract

Aim: Is to evaluate the role of sentinel lymph node biopsy (SLNB) in diagnosis of lateral nodal involvement in N0 papillary thyroid cancer patients.

Methods: 20 patients were included in this study; total thyroidectomy with dissection of the central neck compartment was done in all patients. 0.5 ml of 2% methylene blue dye was injected into the primary tumour; blue stained SLN in lateral neck was identified and examined by frozen section. If any of the SLNs were positive on the frozen section, selective neck dissection (levels II-IV) was performed during same operation. In false-negative cases of SLNs reoperation was carried out after 1 week.

Results: There were 6.7% false-negative rate; 100% specificity; 80% sensitivity, 93% negative predictive value; 100% positive predictive value, with 94.7% overall accuracy. Postoperative transient recurrent laryngeal nerve palsy occurred in 2 patients; but none of the patients had permanent nerve palsy. One patient required calcium supplement on discharge; however, no patient developed permanent hypocalcaemia.

Conclusion: SLNB is an easy and accurate method for assisting the diagnosis of metastasis in the lateral neck compartment, and it could reduce the risk of complications of thyroid surgery. We recommend this technique to support the decision to perform selective neck dissection in N0 papillary thyroid cancer patients.

Key words: Papillary thyroid cancer, sentinel lymph node, lateral neck compartment.

Introduction:

Management of occult lymphatic disease in papillary thyroid cancer (PTC) is controversial. While occult regional lymph node involvement ranges from 25% to 90% and is associated with increased tumor recurrence, there is no evidence that removal of these nodes confers a survival advantage.[1–5]

American Thyroid Association 2006 guidelines,[6] specify that the primary disease and involved lymph nodes should be removed and, additionally, that the operation should facilitate radioactive iodine administration, permit accurate surveillance, and minimize the risk of disease recurrence. To these ends, they recommend the following steps: (a) preoperative neck ultrasound; (b) either near-total or total thyroidectomy; (c) routine central compartment neck dissection; and (d) lateral neck compartment lymph node dissection for either clinical or image-identified lymph node metastasis.

The extent of lateral neck dissection for fine-needle aspiration-confirmed disease in the lateral neck remains a controversial and hot topic for debate.[7-12]

Intra-operative lymphatic mapping with sentinel lymph node biopsy (the first lymph node draining into a lymphatic basin) has become a revolutionary concept in the management of solid malignancies and can be adopted also in thyroid carcinoma, especially in patients N0 at clinical and ultrasound examinations as an alternative to elective lymph node dissection.[13-15]

In the case of positive sentinel lymph node (SLN) findings, it seems wise to extend lymph node dissection to the level to which the

positive node belongs, which may even be the laterocervical compartment. This helps to avoid a high incidence of node recurrence and the risks of prophylactic node dissection or reoperation.[16,17]

The aim of this non-randomized, prospective study is to evaluate the role of sentinel lymph node biopsy (SLNB) in diagnosis of lateral nodal involvement in N0 papillary thyroid cancer patients.

Patients and methods:

From June 2008 to May 2011, 20 patients, diagnosed as having PTC without lymph node metastasis based on finding from preoperative ultrasonography and fine needle aspiration, were included in this study. Patients with locally invasive tumours, distant metastases, and previous head and neck surgery were excluded off the study.

With Ethics Committee approval, all patients were informed and consented before surgery after explanation & discussion of the procedure and possible surgical options.

Surgical technique:

A standard collar incision was made approximately 2 finger-breadths above the sternal notch. After dissection of the subplatysmal flap, the infrahyoid muscles were divided in the midline and separated laterally from the thyroid gland and before mobilization of the gland; 0.5 ml of 2% methylene blue dye was injected into the primary tumor with a 25-gauge needle, taking care not to stain the surrounding tissue.

Immediately after the lobe was stained, the plane between the sternocleidomastoid muscle and the strap muscles was opened by dissecting the entire medial border of the sternocleidomastoid muscle, which was retracted laterally throughout the dissection. The omohyoid muscle was identified, encircled, dissected superiorly and laterally, thereby exposing the internal jugular vein and common carotid artery looking for the blue-stained lymphatic vessels and lymph nodes in the jugulo-carotid chain and recognized as SLNs. If there were no stained nodes, the closest node to the blue-stained lymphatic vessels was considered to be the SLN.

The dissected nodes were examined by frozen section histopathological examination. Meanwhile, total thyroidectomy with dissection of the central neck compartment and clearance of pretracheal and paratracheal nodes was routinely performed. Prior to total thyroidectomy, all parathyroid glands were preserved and both recurrent laryngeal nerves were identified and followed to the entrance into the larynx.

If any of the SLNs were positive on the frozen section, selective neck dissection (levels II-IV) was performed in the same operation via a vertical extension of the incision superiorly along the anterior border of the sternocleidomastoid muscle, **Figure(1-8)**.

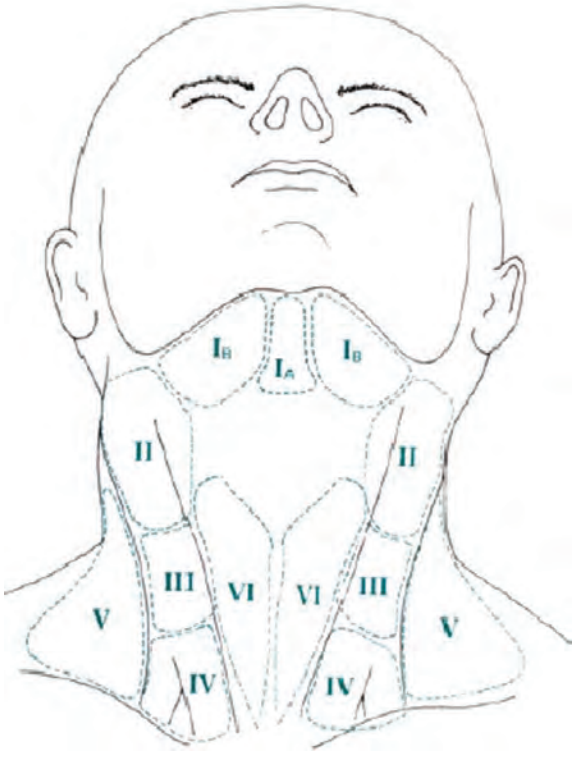
All thyroid glands and lymph node specimens were sent for paraffin section examination. In false-negative cases of SLNs (negative findings on frozen-section examination but positive on paraffin section examination), selective neck dissection was performed as a reoperative procedure after 1 week.

Postoperative complications including affection of vocal cord mobility, hoarseness of voice, appearance of manifestations of hypoparathyroidism in the form of tingling sensation around the lips or in fingertips, muscle cramps, carpopedal spasms and the need for supplemental calcium treatment were recorded.

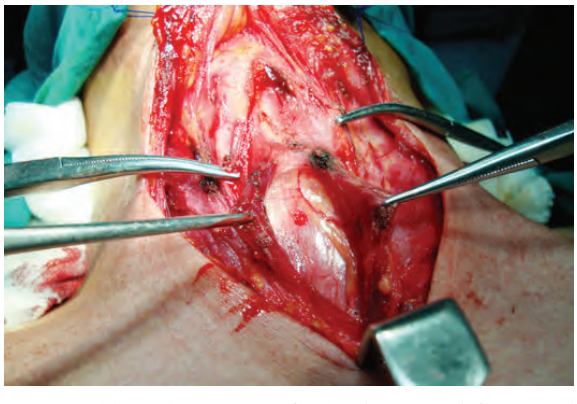
The validity of the test was estimated regarding the identification rate, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy.

Statistical analysis:

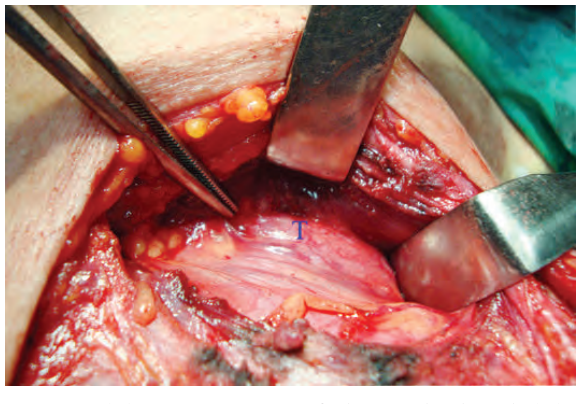
The collected data were tabulated and analyzed using t-test and Z-test. Statistical analysis was conducted using the SPSS (Version 16) for Windows statistical package. Values of $P < 0.05$ were considered significant.



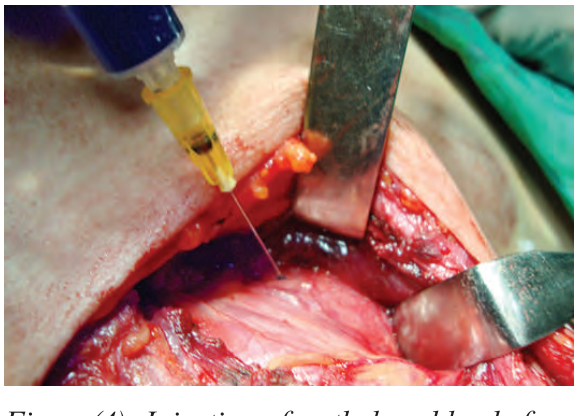
Figure(1): Level designations of lymph node groups in the neck.[18]



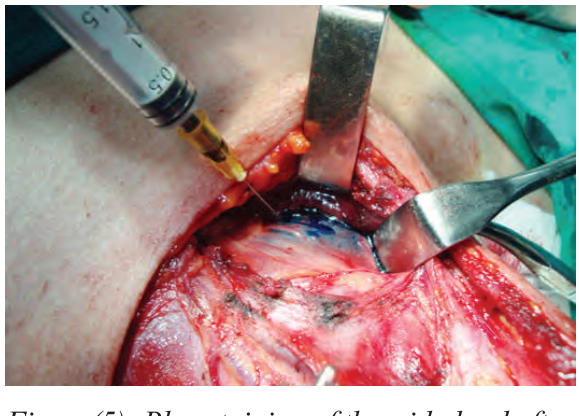
Figure(2): Elevation of subplatysmal flap and cutting of the cervical fascia in the midline.



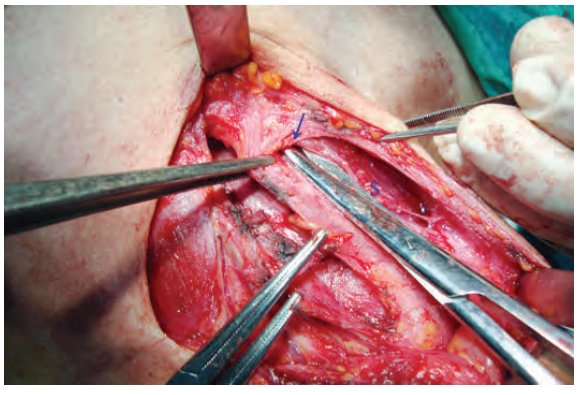
Figure(3): Exposure of thyroid gland (T).



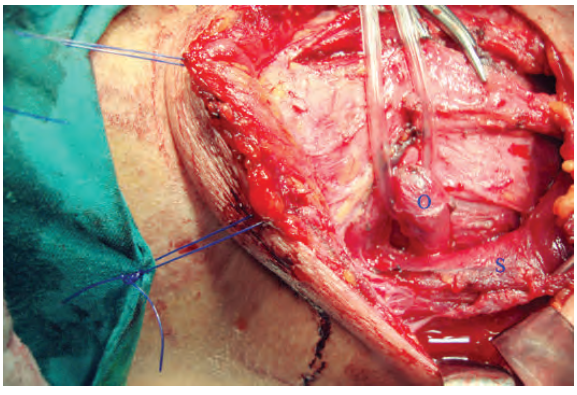
Figure(4): Injection of methylene blue before mobilization of the gland.



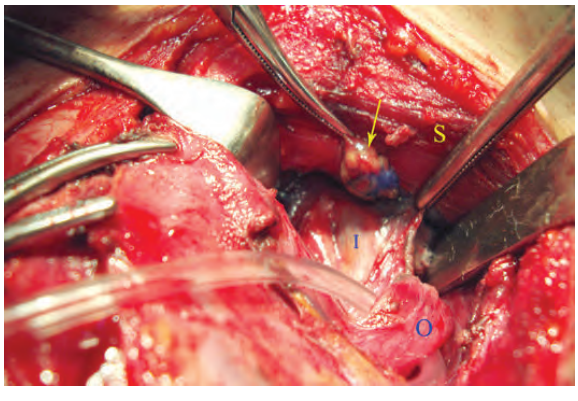
Figure(5): Blue staining of thyroid gland after methylene blue injection.



Figure(6): Cutting of the fascia (arrow) along the medial border of sternocleidomastoid muscle (S).



Figure(7): Isolation of omohyoid muscle (O) after dissection between sternocleidomastoid muscle (S) and strap muscles.



Figure(8): Identification of blue-stained sentinel lymph node (arrow). S indicates sternocleidomastoid muscle; O (omohyoid muscle); I (internal jugular vein).

Results:

The study comprised 20 patients; 14 (70%) females and 6 (30%) males, with mean age 46.9±12.7 years; range 26-65 years. The median tumour size was 1.6cm. 7 patients had tumours less than 1cm in diameter, 9 patients had tumours measuring 1-2cm and 4 patients had tumours measuring 2-3cm in diameter. Of 20 patients, thyroid tumours were solitary in 16 cases while multifocality was found in 4 cases. Of 16 cases with solitary thyroid tumour, the tumour was found in one lobe in 15 cases while in one case the tumor was found in the isthmus, **Table(1)**.

Identification and biopsy of blue-stained SLN in the jugulo-carotid chain was successful in 19 out of 20 cases while in one patient no lymphatic channels were visualized and he was excluded off the study. The identification rate of SLN was 95%. The median number of SNLs per draining area was 2 (mean 3.05). Frozen section examination of SLNS revealed metastasis in 4 cases for whom selective neck dissection was performed during the first operation. Paraffin section examination of the excised specimen showed metastasis in 5 cases including the 4 positive cases by frozen section examination. For the 5th case selective neck dissection was performed after one week.

Regarding the validity of the test, we found a false-negative rate of 6.7% (1 out of 15). The specificity of the method was 100%, the sensitivity was 80%, the negative predictive value was 93% (14 out of 15), and the positive predictive value was 100% (4 out of 4), while overall accuracy was 94.7% (18 out of 19), **Table(2)**.

Postoperative transient recurrent laryngeal nerve palsy occurred in 2 patients; but none of the patients had permanent nerve palsy. One patient required calcium supplement on discharge; however, no patient developed permanent hypocalcaemia, **Table(3)**.

Table(1): Characteristics of the patients.

Characteristics	No.
Gender (female :male)	14:6
Tumor size (mm)	
<10	7
10–20	9
20-30	4
Localization	
Solitary	16
Lobe	15
Isthmus	1
Multifocal	4

Table(2): Validity of the method.

Positive : True	4
False	0
Negative : True	14
False	1
Sensitivity	80%
Specificity	100%
Negative predictive value	93%
Positive predictive value	100 %
Accuracy	94.7 %
Identification rate	95 %

Table (3): Complications among the study group.

Complications	No.	%
Recurrent laryngeal nerve injury:		
Transient nerve palsy	2	10.0
Permanent nerve palsy	0	0.0
Hypocalcaemia:		
Transient hypocalcaemia	1	5.0
Permanent hypocalcaemia	0	0.0

Discussion:

Papillary thyroid carcinoma is the most common thyroid malignancy, accounting for 80% of all thyroid cancers.[19] It has been reported that 70% to 90% of patients with PTC had no evidence of lymph node metastasis but had micrometastases in adjacent lymph nodes.[20-22] Therefore, at the time of initial treatment for PTC, patients may already have regional lymph node metastasis, and a treatment policy should be established accordingly.

There are two representative regional compartments of lymph nodes to which PTC frequently metastasize. One is the central compartment, and the other is the lateral compartment. Goropoulos et al.,[23] and Greene et al.,[24] believed that metastases first involve the nodes in the central compartment and then the lateral compartment of the neck. However, skip metastasis leaping the central lymph node compartment has been reported in PTC.[25-28] Moreover in a large series by Ito and Miyauchi,[29] they demonstrated that of 694 papillary carcinoma patients who underwent dissection not only of level VI but also level II–IV, 11% were level VI-negative and level II–IV-positive and 15% were level VI-positive but level II–IV-negative. This finding strongly suggests that PTC initially metastasizes to either level VI or level II–IV with similar incidences.

Gimm et al.[27] and Machens et al.,[5] demonstrated that the central compartment is the most commonly involved with metastases. However, central node metastasis is more difficult to be detected by ultrasound than lateral node metastasis, probably due to disturbance from the air-filled trachea and from the thyroid itself.[30] Since this compartment can be dissected through the same wound as thyroidectomy, and re-operation is very hazardous in recurrence with increased risk of permanent hypoparathyroidism and recurrent laryngeal nerve injury, these nodes have been routinely dissected by most endocrine surgeons according to the American Thyroid Association guidelines.[1]

Since wound extension and a wide range of tissue peeling leading to postoperative discomfort in the neck and shoulder are unavoidable in the dissection of the lateral nodes, routine prophylactic modified radical lateral neck dissection for patients without preoperatively positive nodes in the lateral compartment is not usually performed in Europe and the United States. Most Western guidelines agree on performing therapeutic dissection only when metastatic cervical lymphadenopathy is evident.[31] However, some reports have referred to the usefulness of prophylactic lymph node dissection under specific conditions.[13] In Japan, several institutions have been performing prophylactic modified radical lateral neck dissection for all patients with PTC due to the high prevalence of pathological lymph node metastasis.[30] Also, Machens et al.[26] claimed that patients with tumours more than 1cm represent candidates for prophylactic lateral neck dissection. The argument supporting prophylactic lymph node dissection is that locoregional recurrence "which increase the psychological and financial burdens on the patient" and even distant metastasis can be prevented. Conversely Ito et al.,[32] reported that prophylactic modified radical neck dissection does not improve disease-free survival.

So far the most useful tool for detecting metastatic lateral nodes is ultrasonography as it shows a very high positive predictive value and specificity, even greater than 90%. However, it often misses small metastases with many false negatives; low negative predictive value and low sensitivity (21.6%).[29,33]

Radioactive iodine ablation following total thyroidectomy in patients with well-differentiated thyroid cancer has been shown retrospectively to decrease the incidence of regional recurrence.[34,35] This benefit is believed to be secondary to the destruction of occult micrometastases in clinically negative nodes. Since not all patients with well-differentiated thyroid cancer have lymph node involvement, not all patients would benefit from postoperative radioactive iodine ablation, which may account for the discrepancy in the literature as to the benefit of ^{131}I ablation.[36] There is therefore a reasonable rationale for exploring the use of SLNB for thyroid malignancy to identify those who harbor occult lymph node metastases in the lateral compartment. Thus help selection of patients who would benefit from, a more extensive procedure through modified radical neck dissection, and

postoperative radioactive iodine ablation. Moreover, Toniato[14] reported that SLN procedure may be considered a criterion to select patients in view of ablative ^{131}I therapy; indeed, patients classified N0 after the SLN technique could avoid ablative ^{131}I therapy, while N1 patients should have ^{131}I therapy.

In the current study, we used 0.5 ml of 2% methylene blue dye for intraoperative lymphatic mapping in 20 cases of PTC. There were 95% identification rate; 100% specificity; 80% sensitivity; 93% negative predictive value; 100% positive predictive value, with 94.7% overall accuracy. However, the accuracy of detection of SLN in the central neck compartment was not evaluated as total thyroidectomy with central compartment dissection was routinely performed in all patients of the study. These results go in hand with that reported by Bae et al.,[13] who reported 88.9% diagnostic accuracy and the sensitivity and specificity were 83.3% and 100%, respectively. The positive predictive value and negative predictive value were 100% and 75%, respectively. Also Wiseman et al.[37] summarized the results of several studies and found that the average rate of SLN identification was 91% (66%–100%) and when identified, the SLN accurately predicted the disease status of the neck in most patients (80%–100%). Moreover, Catry et al.,[38] reported that false negative rate for SLN detection is the single most important quality item for the SLN technique. In the current study we reported false-negative rate of 6.7%. This is better than 12.5% and 22% reported by Takami et al.,[4] and Roh and Park[39] respectively.

In our study, there was no meaningful time loss consumed for identification of SLN. This agreed with other studies.[13,37,40] All patients in the current study had smooth postoperative course with no permanent recurrent laryngeal nerve injury or permanent hypoparathyroidism. This coincides with that reported by other series.[13,40-42] This could be attributed to the use of methylene blue which stained the majority of nodes in the central neck compartment facilitating their removal and also simplified discrimination from parathyroid glands.

It could be concluded that SLNB is an easy and accurate method for assisting the diagnosis of metastasis in the lateral neck compartment, and it could reduce the risk of complications of thyroid surgery. We recommend this technique to support the decision to perform selective neck dissection in N0 papillary thyroid cancer patients.

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