Original Article

Role of Sentinel Lymph Node Biopsy in Well-Differentiated Thyroid Cancer – A Single Centre Observational Study

Uppari Azadh Chandrasekhar[1], Ravikumar Reddy Mandadi[2], Sandhya Rani Nippani[3], Tejaswi G[4]

[1&2]Associate Professor, Department of Surgical Oncology, Osmania Medical College/MNJ Institute of Oncology and RCC, Hyderabad, Telangana, India.
[3]Associate Professor, Department of Radiation Oncology, Osmania Medical College/MNJ Institute of Oncology and RCC, Hyderabad, Telangana, India.
[4]Senior Resident, Department of Surgical Oncology, Osmania Medical College/MNJ Institute of Oncology and RCC, Hyderabad, Telangana, India

Abstract

Background: Lymph node metastasis is a common feature of well-differentiated thyroid carcinoma (WDTC). This can influence tumor staging, prognosis, and surgical management. Routine central neck dissection remains controversial because of its associated morbidity. Sentinel lymph node biopsy (SLNB) can identify occult nodal metastasis and reduce the need for unnecessary lymph node dissection. This study aimed to evaluate the feasibility and clinical utility of methylene blue-guided SLNB in patients with well-differ differentiated thyroid carcinoma. **Material and Methods:** This prospective study included 15 patients with well-differentiated thyroid carcinoma who underwent thyroid surgery. Methylene blue dye was injected peritumorally into all four quadrants, and after 1 min, the site was explored to identify sentinel lymph nodes. Demographic, tumor, surgical, sentinel lymph node identification, localization, and pathological features were documented and analyzed. Appropriate statistical analyses were performed to determine the results. **Results:** The study population comprised predominantly females (80 %), with most patients aged 21–30 years (40 %). All tumors measured >1 cm, and multifocal disease was present in 40% of patients. Sentinel lymph nodes were successfully identified in of 8/15 patients, with an identification rate of 53.33%. Histopathological examination confirmed the metastatic involvement of all identified sentinel lymph nodes. Sentinel lymph node positivity was more frequent in patients with multifocal tumors (83.33%), clinically positive preoperative nodal status (83.33 %), and advanced T stage, increasing from (33.33%) in T1b tumors to 100% in T3 tumors. The right lateral compartment was the most common location of sentinel lymph nodes (26.66 %). **Conclusion:** Methylene blue-guided sentinel lymph node biopsy is a feasible, safe, and reproducible technique for nodal assessment in well-differentiated thyroid carcinoma. The procedure demonstrated acceptable sentinel node identification, with good histopathological correlation and no procedure-related complications. The absence of central compartment metastasis in patients with lateral sentinel node involvement suggests that SLNB may facilitate individualized neck dissection and reduce unnecessary central neck dissection. Larger prospective studies with long-term follow-up are required to validate these findings and establish the role of SLNB in routine surgical management.

Keywords: Well-differentiated thyroid carcinoma, Sentinel lymph node biopsy, Methylene blue, Neck dissection, Lymph node metastasis.

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Introduction

Thyroid cancer is one of the most common endocrine malignancies worldwide, and more than 90% of these cases are comprised of well-differentiated thyroid cancer (WDTC), papillary and follicular types.[1] Thyroid cancer is a steadily increasing cancer worldwide, especially among women. GLOBOCAN 2020 estimates suggest there are approximately 586,000 new cases of thyroid cancer worldwide, and that it is the ninth most common malignancy in the world.[2] In India, the incidence of thyroid cancer has been rising. The age-adjusted incidence rates in urban registries like the registries of Delhi and Chennai range from 3.5 to 6.5 per 100,000 population in females.[3] This increase is due to improved diagnostic skills and greater awareness, but it has led to discussions about the best management strategies, which take into account tumour control and minimization of surgical morbidity. WDTC is associated with a good prognosis, and a 10-year disease survival rate of >90% is present.[4] Regional lymph node metastasis is common in papillary thyroid carcinoma (PTC) and may be present even in clinically node-negative patients,[5] although the tumour is primarily indolent in nature. The role of central compartment neck dissection (CCND) in clinically node-negative patients is controversial. While some guidelines recommend prophylactic CCND, evidence indicates that it can potentially have no effect on survival rates and is linked to many postoperative complications like recurrent laryngeal nerve injury and hypoparathyroidism.[6,7] A more conservative strategy, however, would be a risk of failing to detect the occult nodal disease, and a risk of recurrence. In this context, sentinel lymph

Address for correspondence: Dr. Tejaswi G, Senior Resident, Department of Surgical Oncology, Osmania Medical College/MNJ Institute of Oncology and RCC, Hyderabad, Telangana, India, India.
E-mail: tejaa1094@gmail.com

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node biopsy (SLNB) has become an intermediate approach to determine the regional lymph node stage accurately without the morbidity associated with routine CCND. The sentinel lymph node concept was initially applied to the surgical treatment of melanoma and breast cancer, with the assumption that the sentinel node is the first lymph node to receive drainage from the tumor.[8,9] The use of this technique in thyroid cancer is relatively new and is increasingly being explored for its utility in evaluating for occult metastases and as a guide for extent of lymphadenectomy.[10,11]

Few studies have found the feasibility and accuracy of SLNB for detecting micrometastases in clinically node-negative WDTC patients. In papillary thyroid carcinoma, Roh et al. reported 88% sensitivity and 100% specificity when using blue dye-guided SLNB for the identification of metastatic central nodes.[12] In the same way, other prospective studies have proposed that SLNB could be used to avoid unnecessary CCND in some low-risk patients without compromising the surgical staging.[13,14] Nevertheless, widespread application of SLNB in thyroid surgery is limited; some of the reasons for this may be due to a lack of standardized techniques and a need for further studies to validate the procedure. The application of SLNB could be helpful in the Indian scenario as a decision-making tool because thyroid surgery is common in practice at tertiary care hospitals and there is variable thyroid surgical expertise and infrastructure available. The morbidity of routine CCND is high, and more accurate staging procedures are needed, making investigation into the role of SLNB in WDTC highly relevant. The novelty of this study is that it attempts to compare SLNB with no lymph node dissection (NOSLD) and routine CCND in patients with WDTC in order to determine whether SLNB offers a pathway between these two extremes. Such an approach could help optimize surgical approaches and tailor treatment strategies to individual patients, thereby enhancing outcomes and minimizing complications in a resource-limited health-care system.

Materials and Methods

This prospective study was done in the Department of Surgical Oncology, Osmania Medical College and Osmania General Hospital, Hyderabad. Institutional Ethical approval was obtained for the study with Reg. No. 22617001001D. The study was conducted over a period of 18 months, from July 2023 to January 2025. Written informed consent was obtained from all the participants of the study after explaining the nature of the study and possible outcomes in the vernacular language.

Inclusion criteria

1. Patients with cytologically proven well-differentiated thyroid carcinoma
2. Patients planned for thyroidectomy with sentinel lymph node biopsy as part of the surgical management.
3. Patients with primary, previously untreated thyroid malignancy.
4. Aged 18 years and above
5. Voluntary participation

Exclusion criteria

1. Patients with clinically or radiologically evident cervical lymph node metastasis (cN1).
2. Patients with poorly differentiated, medullary, anaplastic thyroid carcinoma, lymphoma, or metastatic thyroid tumors.
3. Patients with recurrent thyroid carcinoma or those who have undergone previous thyroid or neck surgery.
4. Patients who have received prior radiotherapy or chemotherapy to the neck region.
5. Patients with distant metastasis (M1) at presentation.
6. Patients with known allergy to the sentinel lymph node tracer (radioisotope, blue dye, or indocyanine green, depending on the study protocol).

The sample size was based on patients who met the inclusion criteria and were planned for total thyroidectomy with central neck dissection during the study period. The final number of participants depended on the patient load over the 18 months. A total of 15 samples were included in this analysis during the study period.

A consecutive sampling technique was employed for this study. All patients who presented to the department during the defined study period and fulfilled the inclusion criteria were consecutively recruited. Each patient who met the criteria and gave informed consent was included in the study without any exclusions based on demographic or clinical variables apart from the predefined criteria. This method ensured comprehensive inclusion of eligible cases for analysis without introducing selection bias.

Study protocol: Each patient underwent a standardized surgical procedure beginning with exposure of the thyroid gland by retracting the strap muscles. Methylene blue dye, 0.2 mL, was injected into the four quadrants surrounding the tumor using a tuberculin syringe. Care was taken to inject intraparenchymally without spillage into surrounding tissues. After the injection, a waiting period of approximately one minute was allowed for the dye to diffuse through lymphatic channels. The blue-stained lymphatic channels were visually traced, and the first and second blue lymph nodes identified within the central compartment were carefully excised as sentinel lymph nodes.

Data were collected prospectively using a structured case record form. Demographic information such as age and gender was documented. Clinical parameters including the size of the thyroid nodule, location within the lobe, presence of capsular invasion, and radiological assessment findings were recorded preoperatively. Intraoperative details such as dye diffusion, time to identification, number of sentinel lymph nodes identified, and intraoperative complications, if any, were documented meticulously. Postoperative data included the number of lymph nodes dissected, number of positive nodes among sentinel and non-sentinel groups, duration of hospital stay, and occurrence of postoperative complications such as hypocalcemia or recurrent laryngeal nerve palsy. Histopathological reports were collected and reviewed to confirm the presence or absence of metastasis in sentinel and non-sentinel nodes. Additionally, follow-up details including any need for re-intervention or adjuvant radioactive iodine therapy were recorded. The information was regularly updated in the master data sheet after patient discharge and during follow-up visits. Each data point was cross-verified from

operative notes, histopathology records, and follow-up outpatient notes to maintain accuracy and completeness.

Statistical analysis: All collected data were entered into Microsoft Excel and analyzed using SPSS software version 26 in Windows format. Categorical variables such as presence or absence of metastasis in SLNs were expressed as frequencies and percentages. Continuous variables such as age and tumor size were expressed as mean ± standard deviation. Fisher's exact test was used to determine differences between group values; $p<0.05$ was considered significant.

Results

The Baseline demographic and clinical characteristics of the study population are given in Table 1. Analysis of the table shows that among the 15 participants, 26.67% were aged below 20 years, 40.00% belonged to the 21–30 years age group, and 33.33% were older than 30 years, with the majority falling in the 21–30 years category. Females constituted 80.00%, while males accounted for 20.00% of cases. All patients had tumors measuring more than 1 cm in size. Multifocal disease was observed in 40.00%, whereas 60.00% had unifocal tumors. Thyroid-stimulating hormone (TSH) levels were normal in all study participants. Regarding tumor location, the right lobe was involved in 46.67%, both lobes in 6 patients (40.00%), and the left lobe in 13.33% of cases. Preoperative nodal disease was clinically present in 6 patients (40.00%) and absent in 9 patients (60.00%).

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population (N=15)

Characteristic	Category	Frequency (n)	Percentage (%)
Age Group	< 20 years	4	26.67%
	21 - 30 years	6	40.00%
	> 30 years	5	33.33%
Sex	Female	12	80.00%
	Male	3	20.00%
Tumor Size	> 1 cm	15	100.00%
	≤ 1 cm	0	0.00%
Multifocality	Present	6	40.00%
	Absent	9	60.00%
TSH Level	Normal	15	100.00%
	Abnormal	0	0.00%
Tumor Position	Right lobe	7	46.67%
	Left lobe	2	13.33%
	Both lobes	6	40.00%
Preoperative Nodal Status	Present	6	40.00%
	Absent	9	60.00%

Distribution of tumor characteristics and TIRADS stratification is given in [Table 2]. Analysis of the table showed that based on AJCC T-stage classification, 60.00% cases had T1b tumors, 26.67% cases had T2 disease, and 13.33% cases were classified as T3, making T1b the most common stage. Evaluation using the Thyroid Imaging Reporting and Data System (TIRADS) demonstrated that 20.00% had TIRADS 4 lesions, 8 patients (53.33%) had TIRADS 5 lesions, and 26.67% had TIRADS 6 lesions. More than half of the patients were categorized as TIRADS 5, indicating a high suspicion of malignancy.

Table 2: Distribution of Tumor Characteristics and TIRADS Stratification

Variable	Category	Frequency (n)	Percentage (%)
T stage	Tib	9	60.00%
	T2	4	26.67%
	T3	2	13.33%
TIRADS Score	TIRADS 4	3	20.00%
	TIRADS 5	8	53.33%
	TIRADS 6	4	26.67%

TIRADS: Thyroid Imaging Reporting and Data System; T stage as per AJCC staging system.

Surgical Procedures Performed and Sentinel Lymph Node Identification are depicted in [Table 3]. Total thyroidectomy with bilateral functional neck dissection and central neck dissection was the most commonly performed procedure, accounting for 40.00% of cases. Right hemithyroidectomy was performed in 33.33% cases, total thyroidectomy alone in 20.00%, and left hemithyroidectomy in 6.67% cases. Sentinel lymph node identification was successful in 8 patients (53.33%), while no sentinel node was identified in 46.67%. Among the identified sentinel lymph nodes, the right lateral compartment was the most frequent site (4 cases, 26.66%), followed by the central compartment in 13.33% of cases and the left lateral compartment in 13.33% of cases. Histopathological examination confirmed metastatic involvement in all identified sentinel lymph nodes.

Table 3: Surgical Procedures Performed and Sentinel Lymph Node Identification

Variable	Category	Frequency (n)	Percentage (%)
Surgery Performed	Left Hemithyroidectomy	1	6.67%
	Right Hemithyroidectomy	5	33.33%
	Total Thyroidectomy (TT) alone	3	20.00%
	Total thyroidectomy with bilateral functional neck dissection and central neck dissection.	6	40.00%
Sentinel Lymph Node Identified	Positive	8	53.33%
	Negative	7	46.67%
Level of Sentinel Node	Central Compartment	2	13.33%
	Left Lateral Compartment	2	13.33%
	Right Lateral Compartment	4	26.66%

TT: Total Thyroidectomy; B/L FND: Bilateral Functional Neck Dissection; CND: Central Neck Dissection.

Correlation of sentinel lymph node positivity with multifocality and nodal status is given in [Table 4]. Analysis of the table showed that among patients with multifocal tumors, 5/6 patients 83.33%) demonstrated positive sentinel lymph nodes, compared with only 3/9 patients 33.33%) with unifocal tumors. Similarly, sentinel lymph node positivity was observed in 5/6 patients 83.33% with clinically positive preoperative nodal status, whereas only 3/9 patients 33.33% without clinically detectable nodal disease had positive sentinel lymph nodes. With respect to tumor stage, sentinel lymph node positivity increased with advancing disease, being observed in 3/9 patients 33.33% with T1b tumors, 3/4 patients 75.00% with T2 tumors, and all 2 patients 100.00% with T3 tumors. Histopathological examination confirmed metastatic disease in all eight patients with positive sentinel lymph nodes.

Table 4: Correlation of Sentinel Lymph Node Positivity with Multifocality and Nodal Status

Variable	Category	Total Patients (N)	SLN Positive (n)	SLN positive (%)
Multifocality	Present	6	5	83.33%
	Absent	9	3	33.33%
Preoperative Nodal Status	Present	6	5	83.33%
	Absent	9	3	33.33%
T stage	T1b	9	3	33.33%
	T2	4	3	75.00%
	T3	2	2	100.00%

SLN: Sentinel Lymph Node. Note: All 8 SLN-positive patients had histopathologically confirmed metastasis on HPE.

Sentinel lymph node localization patterns and clinical implications are given in [Table 5]. Methylene blue dye was used in all patients and was injected peritumorally in four quadrants surrounding the tumor. Surgical exploration was initiated approximately one minute after dye injection. The overall sentinel lymph node identification rate was 53.33% (8/15 patients). Among the identified nodes, the right lateral compartment was the most common location (4 cases, 26.66%), followed by the central compartment (2 cases, 13.33%) and the left lateral compartment (2 cases, 13.33%). Notably, in all six patients with lateral compartment sentinel lymph node uptake, histopathological examination demonstrated the absence of central compartment lymph node metastasis. This finding challenges the routine practice of prophylactic central neck dissection in patients with lateral neck node involvement and suggests that sentinel lymph node biopsy may provide valuable guidance for tailoring the extent of cervical lymph node dissection in well-differentiated thyroid cancer.

Table 5: Sentinel Lymph Node Localization Patterns and Clinical Implications

Parameter	Category	Value
Dye Used		Methylene Blue
Injection Site		Peritumoral (4 quadrants)
Time to Exploration		1 minute
Overall SLN Identification Rate		53.33% (8/15)
SLN Localization	Right Lateral Compartment	4 (26.66%)
	Central Compartment	2 (13.33%)
	Left Lateral Compartment	2 (13.33%)
Lateral SLN Positivity Without Central Node Involvement		6/6 (100%)

Discussion

The present study evaluated the clinical utility of sentinel lymph node biopsy (SLNB) using methylene blue dye in 15 patients with differentiated thyroid carcinoma. The results showed predominance of female patients 80% and a higher proportion of individuals aged 21–30 years, which is consistent with the established epidemiology of thyroid carcinoma, which shows a greater incidence among young and middle-aged females.[2,15] Similar demographic trends have been reported globally and in Indian populations.[2–4] All tumors in the present study measured> 1 cm, supporting the accepted indication for surgical intervention because larger tumors carry a greater risk of nodal metastasis.[5] Multifocal disease was observed in 40% of patients, comparable to previous reports

demonstrating its association with aggressive tumor behavior, lymph node metastasis, and increased recurrence.[5,16] The relatively high proportion of bilateral tumors further emphasizes the importance of careful preoperative assessment and individualized surgical planning. All patients had normal preoperative TSH levels. Although elevated TSH has been associated with an increased risk of papillary thyroid carcinoma,[17] our findings indicate that thyroid malignancy may occur despite normal thyroid function, highlighting that TSH should be interpreted alongside imaging and cytological findings rather than as an independent predictor.[17] Tumors were more frequently located in the right lobe, similar to previous observations reported by Pelizzo et al,[12] although the clinical significance of this predominance remains uncertain.

Methylene blue proved to be a simple, inexpensive, and safe tracer for SLNB. The standardized peritumoral injection technique produced no dye-related complications, allergic reactions, parathyroid staining, or impairment of operative field visualization, findings consistent with previous reports supporting its safety and practicality.[12,14,18,19] These advantages make methylene blue particularly attractive for resource-limited settings where radiocolloid or fluorescence-guided techniques may not be available. The overall SLN identification rate was 53.33%, which is lower than rates reported with dual-tracer or radioguided techniques but comparable with studies using methylene blue alone.[12,13,19] Despite this modest identification rate, all identified sentinel nodes were confirmed positive on histopathology, supporting the diagnostic value of SLNB in detecting metastatic disease.[20] Sentinel node positivity was more common in patients with multifocal tumors, preoperative nodal disease, and advanced T stage, findings that agree with previous studies identifying these features as predictors of lymph node metastasis.[21,22]

An important observation was that sentinel nodes were identified not only in the central compartment but also in the lateral neck. Notably, all patients with lateral compartment sentinel node uptake showed no central compartment metastasis on histopathology. Although this finding should be interpreted cautiously because of the limited sample size, it raises questions regarding the routine practice of prophylactic central compartment dissection in selected patients with lateral nodal involvement. Accurate SLNB may therefore facilitate individualized surgical management while reducing unnecessary neck dissection and its associated complications, including hypocalcemia and recurrent laryngeal nerve injury.[6,21,23] The strengths of this study include its prospective design and the use of a standardized SLNB protocol for all patients, ensuring procedural consistency. However, several limitations should be acknowledged. The small sample size limits statistical power and generalizability. The absence of routine completion neck dissection in SLN-negative patients prevented assessment of sensitivity and false-negative rates.[13,20] In addition, the lack of long-term follow-up precluded evaluation of recurrence and survival outcomes.[14,24,25] Future studies involving larger cohorts, longer follow-up, and dual-tracer techniques may improve SLN identification and further establish the role of SLNB in differentiated thyroid carcinoma.

Conclusion

Sentinel lymph node biopsy using methylene blue dye is a feasible, safe, and reproducible technique for patients with differentiated thyroid carcinoma. Although the identification rate was 53.33%, all identified sentinel lymph nodes were confirmed metastatic on histopathology, supporting the value of SLNB for nodal staging. The absence of dye-related complications and the finding that patients with lateral sentinel node uptake had no central compartment metastasis suggest that SLNB may help individualize the extent of neck dissection and reduce unnecessary surgical morbidity. Larger prospective studies with long-term follow-up and comparison with standard neck dissection are required to validate these findings and define the role of SLNB in routine thyroid cancer surgery.

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Conflicts of interest

There are no conflicts of interest.

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