# The Role of Sentinel Lymph Nodes Biopsy Using Blue Dye in the Management of Papillary Thyroid Carcinoma

Original Article

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## ABSTRACT

**Background:** The thyroid gland plays a pivotal role in regulating metabolism through the production of thyroid hormones. As the prevalence of thyroid carcinoma continues to rise globally, with varying histological subtypes such as papillary, follicular, medullary, and anaplastic thyroid cancers, the management landscape becomes increasingly intricate.

**Aim and Objectives:** In order to determine whether sentinel lymph nodes biopsy (SLNB) is a viable and effective method for treating papillary thyroid cancer that has not spread to regional lymph nodes, and to decrease the likelihood of needless lymph node distention in these patients, we will examine its practicality and clinical effectiveness.

**Patients and Methods:** Twenty (20) patients with a diagnosis of papillary thyroid cancer (PTC) participated in the current prospective study, which ran from November 2023 to November 2024 in the General Surgery Department of Al-Zahraa University Hospital.

**Results:** With a sensitivity of 92.3%(12/13*100), specificity of 100%(3/3*100), positive predictive value of 100%(12/12*100), and negative predictive value of 75%(3/4*100), SLN is a very successful model. Roughness level is 93.8%. Only 6 patients did not have true LN disease, whereas 14 patients did. There were a total of three instances of negative SNL and NSLN, with three, one, and zero cases of genuine negative, false negative, and false positive, respectively.

**Conclusion:** Using the blue dye technique for identifying sentinel lymph nodes in patients with non-metastatic papillary thyroid carcinoma has a 75% success rate (12/16). However, further studies on larger numbers of patients are needed to confirm the outcomes of this study.

**Key Words:** Blue dye; PTC; SLNB.

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## INTRODUCTION

The several subtypes of thyroid carcinoma offer a wide range of clinical manifestations, outcomes, and treatment options. Discussions on the best ways to diagnose, stage, and treat thyroid cancer continue, even though our knowledge and management of the disease have come a long way. This is especially true when lymph node involvement is an issue[1].

The standard surgical procedure for thyroid cancer usually includes removing the thyroid gland whole or in part, along with a thorough evaluation of the lymph nodes in the neck to find out how far the cancer has spread. The problem with this method is that it can't find the sentinel lymph nodes, which are the ones most impacted by metastasis[2].

Using blue dye in sentinel lymph nodes biopsy is one new method; this is a technique that has been used for different kinds of cancer, such as breast carcinoma and melanoma, in the past[3].

Blue dye has proven a game-changer in several cancer procedures by making lymphatic outflow and sentinel lymph nodes more visible. This method has shown potential in enhancing the accuracy of staging and directing treatment choices; it is commonly known as sentinel lymph node biopsy. Although it has been used mostly in the treatment of breast and melanoma cancers, there is growing interest in its possible use in thyroid carcinoma[4].

A growing number of researchers are looking into the sentinel lymph node (SLN) approach as a way to detect hidden lymph node metastases in cancer patients, with the hope of avoiding the risks and complications of total nodal dissection. The purpose of this study was to assess the predictive power of SLN for nodal status of extra central

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compartment lymph nodes in patients with PTC and to prospectively find out whether SLN biopsy is useful for detecting hidden metastases[5].

## PATIENTS AND METHODS

Twenty (20) patients with a PTC diagnosis were enrolled in the current prospective study, which ran from November 2023 to November 2024 in the General Surgery Department of Al-Zahraa University Hospital.

**Inclusion criteria:**

Patients with PTC confirmed by histology and at least 18 years of age.

**Exclusion criteria:**

Incomplete thyroidectomy, prior radiation or surgery on the neck, distant metastases, parathyroidectomy at the same time as thyroid cancer, benign pathologic signs (such as Grave's disease or chronic thyroiditis), cases of PTC with lateral LN metastasis, and undetected tumors.

**Pre-operative assessment:**

Before surgery, all patients in this study had their medical, surgical, family, and complaint histories reviewed. Serum electrolytes, coagulation profile, kidney function, liver function, and full blood picture are routine pre-operative blood testing. Thyroid nodule FNA for cancer confirmation; patient informed verbal and written permission outlining operation risks and benefits. ENT consultation for vocal cord examination, was also done.

**Method:**

**Surgical technique:**

Patient is placed in supine position with arms tucked at the side. A soft roll (or sand bag) is placed lengthwise beneath the shoulders to extend the neck to improve access, and a soft foam (donut-shaped) rest or head ring is used to stabilize the head.

Head of the bed at 30 degrees, the anterior surface of the neck is prepped and draped, exposing the anterior neck from sternal notch to chin and from both posterior borders of the sternocleidomastoid muscles.

A standard, transverse low-collar incision was performed, a subplatysmal skin flap was elevated, and the strap muscles were retracted laterally with minimal dissection to prevent any disruption of lymphatic vessels, and, before disruption of lymphatic vessels, and, before mobilization of the gland, 0.2-0.3ml of methylene blue dye 1%, was injected peritumorally into the thyroid parenchyma at the 3, 6, 9, and 12 o'clock positions or 0.5-1.0ml of methylene blue dye, 1%, was injected into the thyroid nodule using tuberculin syringe.

In cases of multiple tumor nodules, the predominant nodule was injected. Within seconds, the blue dye was seen spreading within the ipsilateral thyroid lobe and through lymphatic channels to the central compartment.

Injection required- 30s, and one more minute was permitted to allow lymphatic drainage. About 2min later, blue-stained lymph nodes were carefully identified in the central compartment by tracing the stained lymphatic vessels (Figure 1).

Thereafter, total thyroidectomy and bilateral central neck dissection were successfully carried out in all patients

Pretracheal nodes were found on anterior and lateral surfaces of the trachea, between the thyroid isthmus and the left brachiocephalic vein, the tissue containing the pretracheal lymph nodes may be partially or totally removed paratracheal lymph nodes were dissected away from the surface of the trachea.

Lymph nodes that stained blue were defined as SLNs. Central compartment lymph nodes that did not stain blue were defined as (NSLNs).

The SLN and NSLN samples were sent for permanent section and stained with hematoxylin and eosin in all patients was performed in negative patients only for detection of false-negative rate (FNR).

Patients and tumor characteristics were analyzed, and the locations, numbers, and frequency of detection of SLN were also investigated. FNRs of SLNB were analyzed Postoperative complications were also evaluated. Vocal cord paralysis was determined by postoperative flexible laryngoscopy in all patients.

Hypocalcemia due to hypoparathyrodism occur post operative was defined as any decrease in serum calcium level below the normal limit, either transiet less than 6 months or permanent after 6 months.

All patients were followed up regularly by clinical and US examination, whole-body radioiodine scanning, and serum thyroglobulin measurements.

**Central neck dissection:**

The SLN and NSNL samples were sent for permanent section and stained with hematoxylin and eosin in all patient.

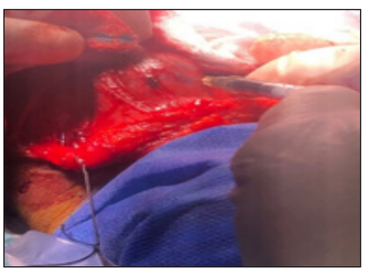

**Fig. 1:** Injection of methylene blue (MB) dye.

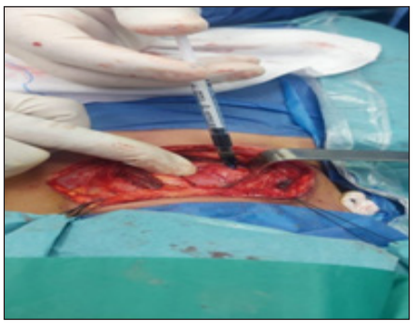

**Fig. 2:** Injection of methylene blue (MB) dye.

**POSTOPERATIVE CARE:**

It is recommended to assess total or ionized calcium levels on the morning of the first day after surgery. This is because, according to some reports, a small percentage of patients may experience transitory hypocalcemia in the first one to two days following surgery. If the patient had any tingling or numbness after surgery, or if their postoperative calcium level was dangerously low, they may be given calcium supplements.

To enable TSH increase prior to thyroid scanning, levothyroxine was prescribed and began 21 days following surgery. Ablation of RAI tissue is frequently advised in cases where RAI ablation in residual remnant tissue, nodal metastasis, exathyroid extension.

**Late postoperative complications and follow up:**

the recurrent laryngeal nerve injury that occur, bleeding after the operation, transient hypocalcemia, and wound problems are all examples of early postoperative complications. Any change in voice quality warrants a laryngoscopy to detect RLN or injury to the vocal cords.

Evaluation of parathyroid gland function (permanent hypoparathyroidism) is done by measuring serum calcium and parathyroid hormone levels. Repeated damage to the laryngeal nerve: assessment of vocal cord mobility using indirect laryngoscopy. In order to determine the likelihood of tumor recurrence and distant metastases, the following tests are used: computed tomography (CT) for patients with high serum thyroglobulin levels and negative radioiodine scanning; ultrasound (US) for the detection of residual, recurrent, or metastatic thyroid carcinoma; and 131 whole body scanning.

**The end point of the current study:**

The primary endpoints of this study are: the success rate of the blue dye technique in sentinel lymph node identification and the percentage of sentinel lymph node harboring metastasis. The secondary endpoints are the mean number of non-sentinel lymph nodes harvested and the rate of lymph node metastasis in non-sentinel lymph nodes.

**Ethical Consideration:**

Our investigation was authorized by the department's and college's ethical committee. The data was gathered solely for the purpose of study. At any moment, a patient is free to stop participating in the study. Permission to participate in the study was obtained from all patients.

**Data analysis:**

We used the SPSS application (Version 25) for Windows to code, process, and analyze the data that we collected. Means, standard deviations, medians, ranges, and percentages were computed as descriptive statistics. When comparing means of regularly distributed continuous variables, we used independent *t*-tests; for median differences of non-normally distributed data, we used Mann-Whitney *U* tests; and for categorical data, we used chi-square test. For the dependent groups, we utilized the *t*-test and the Wilcoxon test. For statistical significance, a *p*-value less than 0.05 is required.

## RESULTS

The average age of the patients who were part of the study was 42.6±9.94, with 6-men and 14-females making up 30% and 60% and 40% and 40% of the tumors, respectively, measuring 19.28±9.07 and 3.45±1.27, respectively, in the left and right lobes, (Table 1).

**Table 1:** Distribution of patient characteristics in the studied patients:

| | **Studied patients (*N*= 20)** | |
|---|---|---|
| | **Mean** | **±SD** |
| Age | 42.6 | 9.94 |
| Tumor size (mm) | 19.28 | 9.07 |
| Hospitalization (days) | 3.45 | 1.27 |
| | ***N*** | ***%*** |
| Gender | | |
| Male | 6 | 30% |
| Female | 14 | 70% |
| Tumor side | | |
| Tumor Left Lobe | 12 | 60% |
| Tumor Right Lobe | 8 | 40% |

The average number of LNs found in SLN was 2.67±1.7, 16 patients (80%) had Identification rate of SLN, 12-patients (75%) were positive and 4(25%) were negative, and in Non SLN mean number of LN detected was 6.37±2.4, 20-patients (100%) had Identification rate of SLN, 14-patients (70%) were positive, while 6-patients (30%) were negative, (Table 2,3 and Figure 3-5).

**Table 2:** Characteristics of sentinel lymph nodes(SLN) and non-sentinel lymph nodes(NSLN) in the group under study:

| | SLN | | Non SLN | |
|---|---|---|---|---|
| | **Mean** | **SD** | **Mean** | **SD** |
| Number of LN detected | 2.67 | 1.7 | 6.37 | 2.4 |
| | N | % | N | % |
| Identification rate of SLN | 16 | 80 | 20 | 100% |
| LN metastasis | | | | |
| Positive | 12 | 75% | 14 | 70 |
| Negative | 4 | 25% | 6 | 30 |

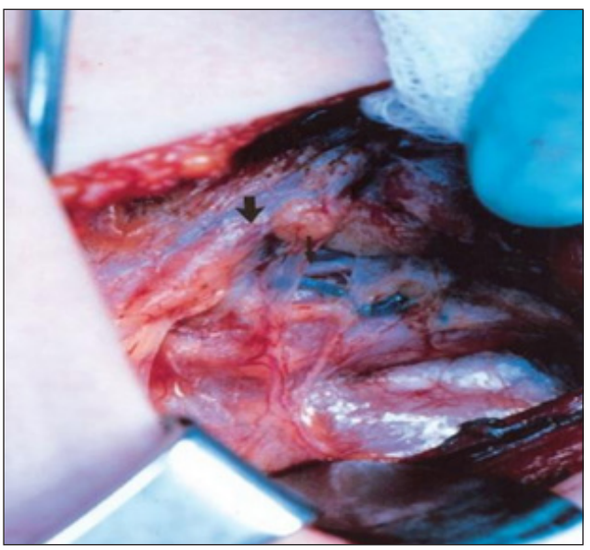

**Fig. 3:** Lymphatic channel staining is blue. A big arrow points to the inferior parathyroid, while a small arrow identifies the recurrent laryngeal nerve.

**Table 3:** Distribution of disease in the studied group

| | Disease present | Disease absent | Total |
|---|---|---|---|
| SLN +ve | 12(TP) | 0(FP) | 12 |
| SLN –ve | 1(FN) | 3(TN) | 4 |
| Total | 13 | 3 | 16 |

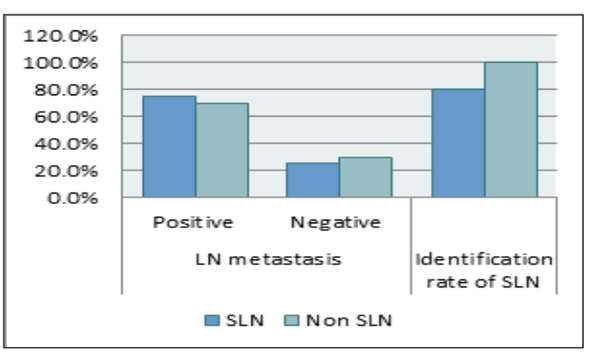


**Fig. 4:** Distribution of sentinel lymph node(SLN) and non-sentinel lymph node(NSLN) features among the individuals under study.

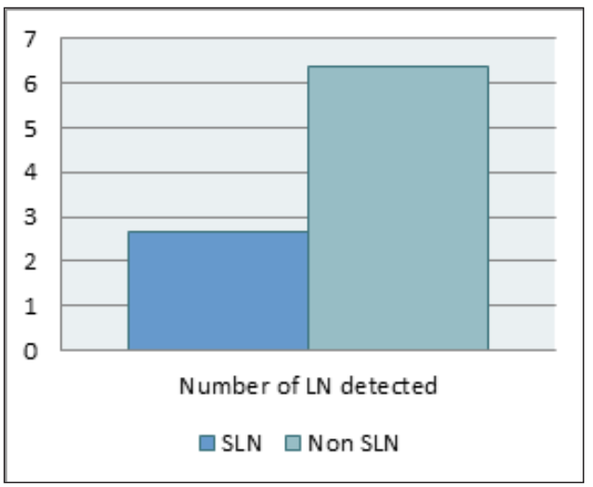


**Fig. 5:** Distribution of sentinel lymph node(SLN) and non-sentinel lymph node(NSLN) features among the individuals under study.

The sensitivity of SLN is 92.3%(12/13*100), the specificity is 100%(3/3*100), the positive predictive value is 100 %(12/12*100) and the negative predictive value is 75%(3/4*100). Accuracy is 93.8%, (Table 4).

**Table 4:** SLN accuracy in the group under study:

| | *N* | % |
|---|---|---|
| Sensitivity | 12/13 | 92.3% |
| Specificity | 3/3 | 100% |
| Negative predictive value | 3/4 | 75% |
| Positive predictive value | 12/12 | 100% |
| Accuracy | 15/16 | 93.8% |

## DISCUSSION

The thyroid gland is the primary target of endocrine system malignancies. However, accurate and specific markers for the diagnosis and stage of this illness are still lacking[6].

Over the past three decades, papillary thyroid carcinoma [PTC] has been the most prevalent kind of thyroid cancer due to an increase in its frequency worldwide[7].

The patients in the current study had a mean age of 42.6±9.94, a mean tumor size of 19.28±9.07, a mean hospitalization of 3.45±1.27, and twelve patients (60%) with left lobe tumors and eight patients (40%) with right lobe tumors. Six patients (30%) were male, and fourteen patients (70%) were female.

In the same line El-Tahan *et al*.,[8] aimed to discuss the validity of SLN biopsy in guiding Central Compartment Neck Dissection [CCND] in patients with papillary thyroid carcinoma and clinically negative lymph nodes [PTC cN0] using histopathology as a standard, patients aged 18-60

years old with PTC were enrolled in the study. Of the total 30-patients, 19 were female and 11 were male. All tumors were papillary carcinomas ranging in size between 0.5-4cm, with 12-patients experiencing malignancies in the left lobe and 18 in the right.

Also, Markovic *et al*.,[9] sought to determine whether methylene blue dye-assisted sentinel lymph node biopsy (SLNb) is a reliable method for detecting LNM in the lateral neck compartment of cN0 patients with PTC. 153 cN0 patients with PTC were included in the study; their mean tumor size was 14.4±3.3, their mean age was 47.5 years, with a range of 14–76years, and 85% of them were female and 15% were male. All had SLNb in the lateral neck compartment using methylene blue dye as a marker and a complete thyroidectomy with central neck dissection. In cases of metastatic SLNs, selective modified radical neck dissection was carried out.

In study of Ramadan *et al*.,[10] Following lymph scintigraphic imaging and colorimetric analysis using patent blue dye, thirty-seven patients with papillary thyroid carcinoma (8 men and 29 women) who met the selection criteria underwent sentinel lymph node biopsy using a radioactive technique using Technetium-99m-labeled dextran. The patients' mean age was 41.4 years, with a range of 19–51years.

In the same line Ji *et al*.,[11] discovered that out of the 196 SLN, 113(or 57.7%) were located in the ipsilateral paratracheal group, while the pretracheal group accounted for 24.5%, the prelaryngeal group for 14.8%, and the contralateral paratracheal group for 3.1%. Every single patient who had paratracheal SLN on one side also had it on the other.

The average of LN observed in SLN was 2.67±1, according to our findings.Seventeen patients (80%) had an SLN identification rate, twelve patients (75%) had a positive result, and four patients (25%) had a negative result. The mean number of LN found in non-SLN patients was 6.37±2.4. Of the patients, 20(100%) had an SLN identification rate, 14(70%) were positive, and 6(30%) were negative.

El-Tahan *et al*.,[8] noted that, the SLN identification rate was 80%, while the non-SLN rate was 93.3%. The number of LNs found was 0–6 in the SLN population and 0–9 in the non-SLN population. The percentage of cases with positive results for LN metastasis was 60% in SLN and 36.7 % in non-SLN.

In another study Markovic *et al*.,[9] found that 91.8% was the SLN identification rate (IR). The corresponding sensitivity, specificity, PPV, and NPV were 85.7, 96.7, 88.3, and 95.9%. The method's probability was 91.2% and its overall accuracy was 94.3% (ROC AUC, 95% CI: 84.2 to 98.3).

The present investigation has a 92.3% sensitivity, 100% specificity, 100% positive predictive value, and 75% negative predictive value for SLN. 93.8% accuracy.

In a previous study, Ji *et al*,[11] One hundred and fourteen individuals with papillary thyroid cancer that was clinically node-negative received SNB. After injecting 1% methylene blue around the tumors, blue-stained sentinel lymph nodes (SLN) were removed from the internal organs. The number of patients with SLN was 84(or 73.7%). The sensitivity, specificity, positive and negative predictive values, and overall performance of SLNB were 64.9, 100, 100, and 78.3%, respectively.

In agreement El-Tahan *et al*.,[8] SLN biopsy demonstrated a 91.6% sensitivity rate, a 100% specificity rate, a 100% positive predictive value, a 75% negative predictive value, and a 60% accuracy rate.

Garau *et al*.,[12] administered SNB to 111 patients using solely blue dye. While FNR was not applicable (NA), 111 SLNs were discovered with a Sentinel Node Detection Rate (SDR) of 100%, sensitivity of 57%, specificity of 100%, and accuracy of 97%.

Among the individuals surveyed, fourteen had confirmed cases of LN illness, while six did not. There were three cases of negative SNL and NSLN, three cases of false negative, and zero cases of false positive.

El-Tahan *et al*.,[8] 24 of 30-individuals had active lymph node disease. Out of a total of 30-instances, 3 were negative for both SNL and NSL, while 6 were negative for both SNL and NSL and 0 were positive for both.

According to our findings, 2-patients (10%) had temporary RLN paralysis, 2-patients (10%) had temporary symptomatic, 3-patients (15%) had temporary laboratory, and 1-patient (5%) had wound infection.

El-Tahan *et al*.,[8] found that, thirty percent of the cases had positive margins and underwent additional resections, 2-patients (6.7%) had temporary RLN paralysis, 4-patients (13.3%) had temporary symptomatic, and 2-patient (6.7%) had wound infection.

## LIMITATIONS AND RECOMMENDATIONS

The small sample size and the short period of follow-up were considered the main Limitations of the current study.

Further studies with larger sample size are needed to confirm the current results. Further studies with longer follow-up are needed to assess the feasibility and clinical efficacy of the SLNB in the treatment of clinically node negative PTC and avoid unnecessary LN dissection in patients with PTC who don't demonstrate spread to regional lymph modes.

It is recommended that future studies be conducted using well-designed randomized controlled trials or large, comparative observational studies and inclusion a representative sample of patients with similar age, gender, and disease severity.

## CONCLUSION

Using the blue dye technique for identifying sentinel lymph nodes in patients with non-metastatic papillary thyroid carcinoma has a 75% success rate (12/16). However, further studies on larger numbers of patients are needed to confirm the outcomes of this study.

## CONFLICT OF INTERESTS

There are no conflicts of interest.

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