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Assessment of the Role of Intraoperative Frozen Section in Confirmation of Papillary Thyroid Carcinoma Metastasis during Thyroidectomies

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ABSTRACT

Background: When papillary thyroid cancer is first found, it often has lymphatic spread. However, there is still disagreement about the value of preventative central cervical lymph node removal in people with papillary thyroid cancer. Most doctors agree that when there is cervical lymphadenopathy, the first thyroidectomy should include removal of the central cervical lymph nodes. This needs a correct proof of the papillary thyroid cancer spread diagnosis during surgery using a frozen piece. **Objective:** This study aimed to figure out what part and how important it is to use a surgical frozen section biopsy to find metastases in papillary cervical lymph nodes so that needless central cervical lymph node neck dissections don't happen.

Patients and methods: Forty patients from the General Surgery Department and the Endocrine Unit at Ain Shams University Hospitals took part in the study. Examinations for diagnosis and grading were done according to the usual procedure used at Ain Shams University Hospitals.

Results: About 40 of the patients in our study who had negative fine needle aspiration cytology (FNAC) from lymph nodes had a frozen section done during surgery. About 21 patients tested positive for cancerous lymph nodes (52.5%) and had a central neck dissection. On the other hand, 19 patients tested negative for malignant lymph nodes (47.5%) and the central neck dissection was not done. This means that the procedure was 87.5% sensitive and 100% specific. After surgery, a paraffin slice showed that 24 patients had cancerous lymph nodes and 16 patients did not. This means that the test was 87.5% sensitive and 100% specific. So, the frozen section of the cervical lymph nodes during surgery is still very important for cutting down on the number of useless central neck dissections and the problems that can come up with them.

Conclusion: The frozen section of the lymph nodes during surgery's main purpose was to sort patients into those who really need surgery, lowering the number of useless central neck dissections and the risks that come with them. Along with that, frozen section had a high sensitivity and specificity rate that helped keep interventions from being too strong. The study's biggest flaw was that there were no enough subjects. A study with a bigger group of people would help us understand this similarity better.

Keywords: Papillary thyroid cancer, Lymph node metastasis, frozen section.

INTRODUCTION

Thyroid cancer is the most common cancer of the endocrine system. It has got a lot of attention around the world because it is becoming more common so quickly, but the death rate has stayed the same [(1)]. About 580,000 new cases of thyroid cancer were diagnosed around the world in 2020, making it the 11th most common type of cancer in the world [(2, 3)]. A little more than a third of the new cases were papillary thyroid cancer (PTC) [(4)]. Most of these cancers don't spread and have a good outlook. Because of this, there are more and more less invasive treatments being used beside of total thyroidectomies (TTs) [(5, 6)].

PTC spread to the LN mostly happens in the middle part of the neck, which is called neck level VI. There are a number of standards that suggest different node factors for figuring out how much PTC surgery is needed, but they all follow the current trend towards less aggressive surgery [(7, 8)].

Surgery is the main way that thyroid cancer is treated [(9, 10)]. But there is still debate about the extent of surgical resection and neck lymph node dissection. This is because, even if the treatment works, the more extensive the surgery, the more likely it is that there will be complications afterward. Some of these complications may last a patient's whole life or even change the course of his life [(11, 12)].

Metastasis to cervical lymph nodes (LNs) is an important factor in deciding how much surgery is needed. LN metastasis happens in 40–90% of PTC cases and is a strong indicator of local recurrence. Diagnosing and removing metastatic LNs are very important for treating PTC [(13, 14)]. However, not all LN metastases are found before surgery because ultrasound (US) and computed tomography (CT) aren't very good at diagnosing them. This is especially true if the metastases are small or in a hard-to-reach part of the neck. A quick-frozen clinical examination during surgery is a key way to limit the extent of the surgery and avoid too much removal [(15-17)].

Rapid frozen section pathology analysis during surgery is preferred in thyroid cancer surgery departments [(18)]. This method can tell the difference between thyroid tumours that are normal and those that are cancerous. It can also find lymph node spread, which is a key part of deciding whether to have surgery [(19, 20)]. As a result, this study aimed to find out how useful intraoperative frozen lymph node biopsy is for finding metastases in cervical lymph nodes in PTC. The goal was to lower the number of unnecessary central cervical lymph node neck dissections during

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thyroidectomies so that patients don't have to deal with the problems that come with these surgeries.

Aim of the work: Evaluation of the role of frozen section in patients with suspicious PTC, along with the surgical outcomes, postoperative complications, and survival rate aiming to prevent unnecessary neck dissection.

PATIENTS AND METHODS

Type of study: This was a prospective cross-sectional study.

Study setting: The work was done at Ain Shams University Hospitals in the General Surgery Department and the Endocrine Unit. Examinations for diagnosis and grading were done according to the usual procedure used at Ain Shams University Hospitals.

Study period: Between December 2024 and May 2025

Inclusion criteria: Patients with proven PTC with inconclusive or negative preoperative cytology from lymph nodes. Male and female patients, 25 to 75 years of age and fit for surgery.

Exclusion criteria: High-risk patients unfit for surgery. Old age (over 75 years old). Young age (below 25 years old). Patients with proven malignancy in lymph nodes in preoperative cytology. Patient refusal to enroll in the study.

Sample Size: The required sample size has been estimated to be 40 patients

Study tools: Intraoperative lymph nodes frozen section in pathology department Ain Shams University

Preoperative work-up: History taking stressing on the complaint and its analysis (Neck swelling, pressure symptoms, symptoms of hypothyroidism or hyperthyroidism).

Full clinical examination: General examination: Full general examination was done, to assess general body system, thyroid functions and presentation of metastasis: Head was examined for protrusion of eyes, fullness of the thyroid region, pale puffy face with protruding tongue and thick lips and waxy yellow complexion with puffy eye lids. Eye was examined for staring look, lid lag, lid retraction, exophthalmos and power of accommodation. Buccal examination for tremors of the tongue and septic focus. Hands were examined for tremors of the outstretched hands and sweating. Chest and heart examination for arrhythmia, heart failure, lung metastasis and mediastinal syndrome. Abdominal examination for hepatomegaly, splenomegaly and ascites.

Local examination: A full check-up of the neck was done. Check the spot, how it moves when you swallow, its size, shape, border, enlarged veins, whether they pulse or not, and any scars from earlier thyroid or central neck surgeries. Palpation to find out how big the gland was, whether the swelling was warm, painful, smooth, or lumpy, and to check if the trachea was in the middle or off-center, lymph nodes examination in the neck compartments, the carotid artery pulse, its attachment to the trachea and nearby structures, and the tracheal shift. For retrosternal extension, the sternum was used for percussion. Auscultation to hear if there was a bruit or not.

Full pre-operative investigations

Laboratory: Full blood count (CBC). Tests of thyroid activity. Tests of liver function. Renal function tests (urea & creatinine). Profile of coagulation. What is fasting blood sugar (FBS)? Calcium level in the blood. Tests for viruses (HIV, Hepatitis C, and Hepatitis B)

Radiological: Neck ultrasound (US) with TIRADS score. Neck computerized tomography (CT) (when indicated).

Examination of vocal cords by indirect laryngoscopy.

Cytology: Fine needle aspiration cytology (FNAC) with Bethesda scoring.

How surgery is done: A medical check, high-resolution US, and thoracocervical CT were all done on the patient before surgery. Before surgery, all of the patients were told they had either PTC (Bethesda category VI) or possible PTC (Bethesda category V) using a US-guided fine-needle aspiration biopsy. The initial US and thoracocervical CT were used together to look at the tumor's size and location, as well as its degree of extrathyroidal growth, node involvement, and any other abnormalities found in the neck and chest. Clinical LN metastasis (cN1a) was described as a change in the LN that was harmful and was seen in both tests.

Surgery: Prophylactic antibiotic (amoxicillin-clavulanic acid) was taken with induction of anesthesia

Patient positioning: A general anesthetic is given to the patient while they are lying on their back on the operating table. The anesthesiologists made sure that all of the tubes and lines they used were securely fastened on top so that they wouldn't fall onto the operating area. A ring was put under the head and a sandbag roll was put under the shoulder to make the neck longer. The person was put in a Trendelenburg position backwards. The neck and upper torso were cleaned up, and a towel was put on the head.

Skin preparation and draping: Betadine, a sterile substance, was used to clean the skin on the neck and upper chest. So that the side of the neck stayed clean, folded towels are put there. After that, four towels are put down and held in place with towel clips. The surgeon stands on the side that is not connected to the lobe that was being cut out.

Skin incision and dissection: Two finger widths above the sternal notch is where the cut should be made. Along a skin seam, the cut was made 2 to 3 cm above the sternal notch. The cuts on the sides of the body must be uniform and bent to follow Langer lines. The cut should be the same length on both sides of the midline, and it usually goes past the front edge of the sternocleidomastoid muscle. The skin and internal tissues are cut cleanly with a No. 15 blade, and the platysma is found. The platysma was then cut in half using electrocautery. Once the platysma is split, the helper pulls the skin and the platysma up so that a

subplatysmal flap can be made. Make sure that the cervical tissue is not part of the flap by keeping the incision close to the platysma. Lift the upper flap to the notch in the thyroid cartilage and the lower flap to the notch in the sternum. Stay stitches were used to fix the head flap in place. A hook retractor was used to pull the caudal flap down, which gave the strap muscles the best possible view.

Exposing the thyroid gland: After the flaps were made, the investment fascia was cut open in the middle, between the anterior jugular veins. This cut goes from the thyroid cartilage on top to the suprasternal notch on the bottom. The surgeon gently places his or her middle finger between the thyroid and the muscles to expose and move the gland. All of the strap muscles are lifted and pulled back. As the gland was being lifted to the side, any lingering muscle or diseased links were broken. This allowed the surgeon to see overall the gland's disease. Sometimes, the strap muscles should be split. If this is necessary, it should be done at the level of the thyroid cartilage so that the muscles' nerves from the ansa-cervicalis stay intact. A small loop retractor was used to tightly pull back the strap muscles while the thyroid gland was moved to the middle of the body. The next step is to divide the middle thyroid vein after tying it off with 3-0 vicryl sutures. This lets the thyroid gland move more medially.

Dissection of the upper pole: To find the superior thyroid pole, the thyroid was pulled down below the sternohyoid and the sterno-thyroid was pulled up above it. The better pole was stripped down to its bones by blunt surgery. The superior pole was cut from the trachea using a right-angled clamp going from the middle to the side. The superior thyroid veins were then cut with ultrasonic sheers or tied off and cut. This was done over and over until the whole top pole was free. It protects the external vocal nerve this way.

Dissection of the recurrent laryngeal nerve (Local identification of RLN): Once the thyroid gland was fully moved and turned to the medial side, the recurrent laryngeal nerve should be found in the tracheo-oesophageal groove or next to the airway, across from the inferior thyroid artery. The nerve looked like a white line that was usually connected to a small artery. The nerve can be found by carefully cutting through the areolar tissue, which is just below the inferior thyroid artery and to the side of the trachea with artery forceps and non-toothed forceps. The surgeon should know about the rare cases of the vocal nerve coming back. For most people, the hardest part of the surgery was the incision, which is when the RLN went through the Berry ligament. A small artery ran through the muscle that held the nerve in place. If there was bleeding at this spot, it should be stopped with gentle pressure before the nerve is found to keep it from getting hurt. After that, all of the vessels are tied off. It is very important not to use electrocautery to stop bleeding.

Handling of the parathyroid glands (local identification of the PTGs): The parathyroid glands were small, soft, and yellowish brown. They are not hard like lymph nodes or thyroid lumps. The upper parathyroid gland was always found next to the cricothyroid junction, behind the upper third of the thyroid gland. All parathyroid tissue that has been found should be kept alive by its own blood flow. It was common to find the superior parathyroid gland after moving the upper part of the thyroid. On the side of the thyroid gland, above the inferior thyroid artery, there is generally a fat pad where the parathyroid is located. You should move this fat pad, which includes the parathyroid gland, away from the side of the thyroid by starting at the top middle edge and moving it down and to the side. To protect its blood flow, it is important not to cut through the fat pad or the gland any further than the edge of the thyroid. Most of the time, the inferior parathyroid gland was located at the bottom of the thyroid or in the tongue of the thymus. Once it was found, it was taken off the inferior pole in the same way that the superior gland was.

Dissection of the lower thyroid pole: Most of the time, the veins going to the lower pole were cut after the RLN was properly exposed. There were veins from the front of the superior mediastinum that were shown and split up very close to the thyroid gland. These blood vessels could cause bleeding during surgery, especially if a big goiter in the back of the sternum was moved roughly.

Removal of the lobe: In the last few steps of the thyroidectomy, the lobe was cut away from the airway while the RLN was kept open and exposed. Most of the time, sharp cutting was needed to get rid of the thick attachments at the level of the posterior suspensory ligament (Berry). The other lobe of the thyroid was operated on with the same method.

Lymph node biopsy: Intraoperative Lymph node biopsy was taken from lymph nodes which was inconclusive or negative by preoperative FNAC and was sent as a frozen section intraoperatively to be studied in pathology department Ain Shams University

According to the results of these frozen sections: If it revealed malignancy or raised suspicion; central lymph node dissection is completed. If it revealed no malignancy, only total thyroidectomy was completed without central lymph nodes dissection. These frozen sections were to be sent to be studied by paraffin wax postoperatively to compare sensitivity of preoperative FNAC, intraoperative frozen section and post-operative paraffin.

Closure: Meticulous hemostasis was then assured after irrigating the space previously occupied by the thyroid gland with saline to identify small bleeding points, which were secured with either bipolar diathermy or the ultrasonic sheers. Closure was performed by re-approximation of the strap muscles using interrupted vicryl 3/0 sutures after insertion of haemovac drain in the space of the thyroid gland taking care not to apply the tip of the drain onto the

recurrent laryngeal nerves or the major vessels of the neck. The platysma was then re-approximated by interrupted inverted simple sutures using vicryl 2/0 and the skin was closed by subcuticular sutures using prolene or monocryl 3/0. The skin was then cleaned and the wound sweeped with the antiseptic solution and covered by a sterile dressing.

Postoperative: After surgery, care included checking the vocal cords. Clinical evaluation of problems that happen after surgery. Blood Ca levels (Total blood Ca and Ionised Ca) were checked 24 hours after surgery and then every 24 hours until the patient was sent home with normal levels. Then, one week after being sent home. The amount of albumin and phosphorus, the amount of parathyroid hormone after surgery (PTH) and Kidney health (amount of creatinine in the blood) were investigated. In the days after surgery and during follow-up, any signs and symptoms of low calcium levels were recorded. These included stiffness in the face or mouth, muscle cramps, confusion, delirium, seizures, positive Chvostek or Trousseau signs, and muscle spasms. Anything that could mean an injury to the RLN, like changes in voice, trouble breathing, dyspnea, and the need for a tracheostomy or not in cases of severe oxygen loss and choking.

Ethical considerations: The Ethical Committee of Ain Shams University gave its approval. Patients who took part in the study gave their informed permissions. All information about the patients was kept secret, and their names were not used in any written work. Patients can refuse to take part in the study or withdraw at any time, and it will not affect their chances of getting the surgery they need. The study adhered to the Helsinki Declaration throughout its execution.

Statistical analysis

The Statistical Package for Social Science (IBM SPSS) version 23 was used to enter, review, code, and store the data. Means, standard deviations, and ranges were used to show the numeric statistics. Qualitative factors were also shown as counts and percentages. When there was a predicted count of less than 5 in any cell, the Chi-square test or the Fisher exact test was used to compare the groups' qualitative data. We used an independent t-test to see how two numeric factors with a parametric distribution compared to each other.

The ROC curve was used to test the area under the curve, if the test comes back positive, the positive likelihood ratio tells you how much more likely it is that you have the condition. If the test comes back negative, it tells you how much less likely it is that you have the condition. 0.9 to 1.0 is great, 0.8 to 0.9 is great, 0.7 to 0.8 is good, 0.6 to 0.7 is enough, 0.5 to 0.6 is bad, and less than 0.5 is not a useful test. The allowed mistake was set to 5%, and the confidence range was set to 95%. This is why the p-value was thought to be important: If the P-value is greater than 0.05, it means that the result is not significant (NS). P-value $\leq$ 0.05: was deemed significant. (HS) when P-value $\leq$ 0.01.

RESULTS

The study cohort was relatively young–middle aged (mean 38.6 years; 18–62) with a marked female predominance (80%), which is consistent with the known gender distribution of papillary thyroid disease. Medical comorbidity was present in roughly two thirds of patients: Diabetes mellitus in 30%, hypertension in 22.5%, and both conditions in 12.5%, leaving 35% without major chronic illness (Table 1).

Table (1): Patient demographics and comorbidities (n = 40)

		Studied Patients (n=40)	
		N	%
Age (year)	**Mean± SD**	38.61 ± 8.18	
	Range	18 – 62	
Gender	**Male**	8	20.0
	Female	32	80.0
Complication	**None**	14	35.0
	Diabetes mellitus	12	30.0
	Hypertension	9	22.5
	DM & HTN	5	12.5

All sampled nodes were FNAC-negative preoperatively, yet intraoperative frozen section identified metastatic disease in 21/40 patients (52.5%), converting over half the "negative" cases to positive. Consequently, FNAC showed 0% sensitivity, 100% specificity, and 47.5% overall accuracy relative to frozen findings, insufficient for surgical decision-making on its own (Table 2).

Table (2): Correlation between Preoperative FNAC and Intraoperative Frozen Section

		Frozen Section			
		Negative (n=19)		Positive (n=21)	
		N	%	N	%
FNAC	**Negative (n=40)**	19	100	21	100
FNAC Accuracy		47.5%			

Final paraffin confirmed nodal metastasis in 24 patients; frozen section correctly identified 21 of these (sensitivity 87.5%) and produced no false positives (specificity 100%), yielding an overall accuracy of 92.5%. Only 3 paraffin-positive nodes were missed intraoperative, indicating that frozen section provided highly reliable real-time guidance for cervical lymphadenectomy (Table 3).

Table (3): Correlation between paraffin histopathology and Intraoperative frozen section

		Frozen Section			
		Negative (n=19)		Positive (n=21)	
		N	%	N	%
Paraffin	Negative (n=16)	16	84.2	0	0
	Positive (n=24)	3	15.8	21	100
Accuracy		92.5%			

All cervical nodes entered the study because FNAC was non-diagnostic/negative. Final paraffin later showed metastasis in 24/40 cases (60%). Thus, FNAC demonstrated 0% sensitivity, detecting none of the metastatic nodes, while correctly classifying all 16 benign nodes (specificity 100%). The resulting overall accuracy was only 40% (Table 4).

Table (4): Correlation between preoperative FNAC and paraffin histopathology

		Paraffin			
		Negative (n=16)		Positive (n=24)	
		N	%	N	%
FNAC	Negative (n=40)	16	100	24	100
Accuracy		40.0%			

Paraffin histopathology showed excellent agreement (AUC = 0.947, p < 0.001). Paraffin confirmed all frozen-positive nodes (sensitivity 100%) and was negative in most frozen-negative cases (specificity 89.47%), giving a PPV of 100% and NPV of 83.9%.

These data indicated strong concordance while highlighting that paraffin may occasionally upgrade nodes called negative on frozen (accounting for the <100% specificity) (Table 5).

Table (5): ROC curve analysis showing the diagnostic power of paraffin against the frozen section

	AUC	Sensitivity	Specificity	PPV	NPV	P-value
Paraffin	0.947	100%	89.47%	100%	83.9%	<0.001 **

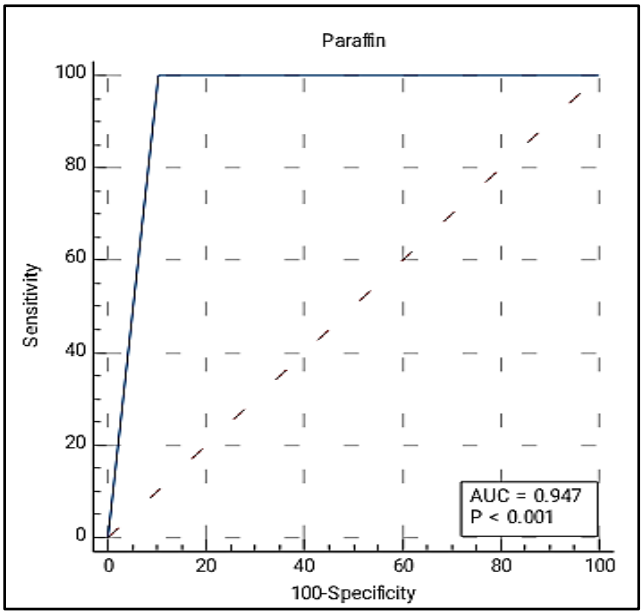

Figure (1): ROC curve analysis showing the diagnostic power of paraffin against the frozen section.

DISCUSSION

This is a prospective cross-sectional study that looks at how intraoperative frozen lymph node biopsy can help find cervical lymph nodes metastasis so that surgeries for differentiated thyroid carcinoma don't have to remove unnecessary central cervical lymph nodes from the neck, which can lead to complications.

There were 40 patients in this study, and all of them had negative fine needle aspiration cytology before surgery, as well as negative frozen sections during surgery and wax assessments after surgery.

People who took part in this study were between the ages of 18 and 62. It turned out that 42.5% of the patients were in their 40s or 50s. This is different from **Gupta *et al.*** [21], where most of the patients (44% of them) were in their 30s. The people in the study were between the ages of 18 and 62, with a mean age of 38.6 years and a standard deviation of 8.177 years. The studies by **Srirangaprasad *et al.*** [22] and **Ibrahim *et al.*** [23] both with a mean age of 39.6 years, agree with what we found. Eight (20%) of the people in this study were men, and 32 (80%) were women. The number of women to men in our study was 4:1. According to **Harshvardhan *et al.*** [24], the number of females to males was 7.5:1.

Surriah *et al.* [25] also found that females were more likely than males to have thyroid tumors (6:1). **Haider *et al.*** [26] on the other hand, found that women made up more of the population (11.5:1).

In 2011, **Basharat *et al.*** [27] found a ratio of 4.6 females to males.

In our review, all of the patients had a FNAC done before surgery, and those with a clean FNAC were chosen to be part of our study. About 21 patients had positive lymph nodes for cancer and had a neck dissection. On the other hand, 19 patients did not have any cancerous lymph nodes and the neck dissection

was not done. This means that the test was 87.5% sensitive and 100% specific. **Gupta *et al.* [21]** is a better example. The sensitivity in their study was 86.4%, which is the same as the sensitivity in **Keh *et al.*'s [28]** study (88%).

After surgery, a paraffin slice was used to find that 24 patients had cancerous lymph nodes and 16 patients did not. The specificity was 100% and the sensitivity was 87.5%. In our study for frozen, the rate of false negatives was 12.5%, while A study was carried out by **Dantanarayana *et al.*[29].** They found an 8.6% false negative rate. The diagnostic reliability was 92.5%, which is the same as what **Gupta *et al.*[21]** found (84%).

CONCLUSION

To sum up, the intraoperative frozen section of the lymph nodes' main job is to sort patients into those who really need surgery, which lowers the number of needless central neck dissections and the risks that come with them. Also, frozen section had a high sensitivity and specificity rate, which helps keep people from getting too much treatment. The study's biggest flaw was that there aren't enough subjects. A study with a bigger group of people would help us understand this similarity better.

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