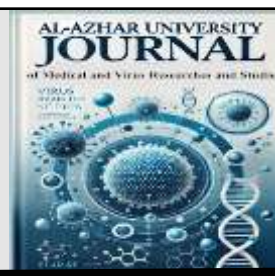




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Incidence of Error of Ultrasound in Comparison to Frozen Section in Suspicious Thyroid Nodule

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Abstract

Total thyroidectomy is the right treatment for people with thyroid cancer but not needed for people with non-cancerous nodules. while hemithyroidectomy (lobectomy and isthmectomy) may need more surgery if a nodule looks suspicious of cancer during the operation. So, malignancy will be assessed by frozen section intraoperative. The aim of the work is to evaluate the incidence of error of ultrasound in patients with suspicious thyroid nodules in comparison to frozen section. This study looked at 50 people with thyroid nodules. ultrasound preoperative revealed solitary suspicious thyroid nodule who underwent hemithyroidectomy while frozen section was done intraoperative to evaluate the ultrasound results. The initial study was conducted at General Surgery Department, Faculty of Medicine for Girls Al-Azhar University, Al-Zahraa University Hospital to evaluate the incidence of error of ultrasound in patients with suspicious thyroid nodules in comparison to frozen section. Using frozen section to distinguish between benign and malignant thyroid lesions is of accuracy 84% vs. 82%. However, ultrasound had higher Sensitivity 91.7% vs. 71.4% and frozen section had higher Specificity 100% vs. 76.9%. Also, malignant cases were statistically significant older, with higher number of solitary thyroid suspicious nodules, and more frequent complaints, progressive course, shorter disease duration and higher Bethesda score compared with benign cases. Based on our research, we can draw the inference that ultrasound goes with frozen section when distinguishing between benign and malignant thyroid growths. In recommendations, if possible, combined use of ultrasound and frozen section is advised to be used for better assessment of cases with suspicious thyroid nodules.

Keywords: Suspicious thyroid malignancy, Frozen section, Thyroid ultrasonography, Total thyroidectomy and hemithyroidectomy.

1. Introduction

The thyroid gland sits in front of the trachea within the muscular triangle. There are wing-shaped left and right lobes that flank the isthmus. Parathyroid glands are mainly found on the posterior surfaces of each of the thyroid lobes [1]. The secretion of T3 and T4 by the thyroid gland plays a significant role in regulating metabolism by interacting with nuclear receptors in target tissues, leading to the initiation of numerous metabolic pathways [2]. Recognizable enlargements of the thyroid gland, known as nodular goiter, are characterized by excessive growth and structural and/or functional changes in one or more areas within the normal thyroid tissue. When thyroid dysfunction, autoimmune thyroid disease, thyroiditis, and thyroid malignancy are absent, these enlargements are classified as simple multinodular goiter (SMG) [3]. The most crucial method for distinguishing between benign and suspicious nodules is performing an ultrasound of the thyroid and the adjacent neck structures. Both the American Thyroid Association (ATA) and the American College of Radiology Thyroid Image Reporting and Data System (ACR TI-RADS) help in this regard [4]. Thyroid nodules that are indeterminate fall into categories III (atypia of undetermined significance or follicular lesion of undetermined significance) and IV (follicular neoplasm or suspicious for a follicular neoplasm) as per the Bethesda system for reporting thyroid cytopathology. The malignancy risk for these nodules is 5–15% and 15–30% respectively, which leads to the need for surgical treatment for a conclusive diagnosis. Consequently, they pose a challenge for diagnosis and treatment due to the risk of over or under treatment. Some teams still conduct systematic intraoperative frozen sections (FS) to guide the initial extent of surgery and avoid a two-stage thyroidectomy. Frozen sections have a high specificity and positive predictive value for diagnosing malignancy, which permits a one-stage total thyroidectomy if the result is positive

[5]. The use of FS is a topic of much debate because of its low sensitivity and high rates of false negatives. It is essential to assess the tumor's capsule thoroughly and carefully to identify any signs of capsular or vascular invasion, which is crucial for diagnosing malignancy. Additionally, FS can identify indications of capsular invasion during the final pathological examination. While FS have limited utility in the Bethesda III and IV categories, they are valuable for guiding the preoperative management of nodules in the Bethesda V category. Intraoperative FS for ITNs is not usually recommended and is of minimal benefit. Their use should be limited to elderly individuals, those at a high risk of anesthesia, or patients who may not be compliant and may face challenges with potential subsequent surgeries [5]. Surgical removal of the entire thyroid gland, known as total thyroidectomy, can be carried out for various medical reasons such as multinodular goiter, cancer, noncancerous nodules, or cysts, concerning results from a fine needle aspiration biopsy, difficulty swallowing due to pressure on the cervical esophagus, or breathing difficulties due to compression of the airway [6]. The aim of the work is to evaluate the incidence of error of ultrasound in patients with suspicious thyroid nodules in comparison to frozen section.

2. Patients and Methodology:

There were 50 patients involved in the research with ultrasound preoperative revealed solitary suspicious thyroid nodule who underwent thyroidectomy while frozen section was done intraoperative to evaluate the ultrasound results.

Ethical concerns were considered: The research followed the guidelines approved by the Research Ethics Committee of Al-Azhar University. After a thorough explanation of the study details, all participants provided informed consent by signing.

2.1 Inclusion criteria

- Males and females.
- From 20 to 60 years.
- MNG with ultrasound preoperative reveals suspicion of malignancy.
- Solitary thyroid nodule with ultrasound preoperative reveals suspicion of malignancy.
- Recurrent goiter with ultrasound preoperative reveals suspicion of malignancy.

2.2 Exclusion criteria

- History of thyroid malignancy
- FNAS or True cut biopsy diagnosed thyroid malignancy.
- Thyrotoxicosis

2.3 Methodology

The patients chosen all had thyroid disease and their ages ranged from 20 to 60 years old. The diagnosis was made through a comprehensive history assessment, which included personal details such as age, gender, location, and specific habits. The main complaint was neck swelling. The assessment also covered the onset, progression, and duration of the thyroid disease, any related disorders, and history of medications. Past medical history encompassed any previous general or local ailments. Furthermore, both general and local examinations were conducted to identify any signs of systemic diseases and to examine the neck specifically. The study includes 50 patients.

- There is a total of 50 participants, and their ages range from 20 to 60 years.
- 92% of the patients were female.
- Every patient had neck swelling, which could be either painless or painful. They were evaluated for signs of pressure symptoms and symptoms of thyrotoxicosis or hypothyroidism, but these symptoms were not found.

- The vocal cords of these patients were assessed using flexible laryngoscopy. In all patients, the examination did not show any signs of vocal cord paralysis.
- Preoperative neck ultrasound was done to all cases.
- Hemithyroidectomy is done and the specimen is sent to the pathologist to start frozen section and till the surgeon there is malignancy or not.
- Intraoperative frozen section was done to all patients with thyroid nodules who did preoperative ultrasound and have suspicion of malignancy.
- Waiting for the result of FS: we proceed to total thyroidectomy if malignancy is confirmed as in figures 2,3&4. or we spare the healthy lobe and hemithyroidectomy is enough if the FS reveals benign lesion.

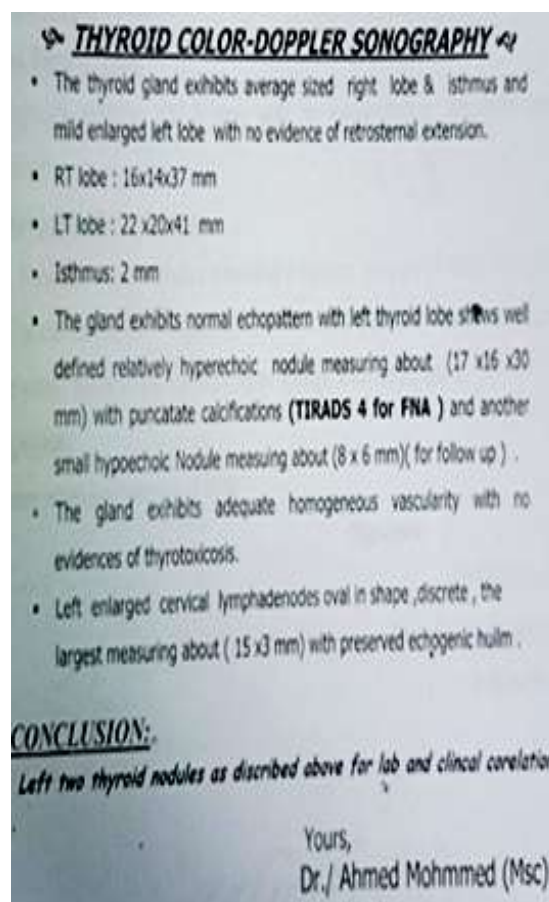


Figure (1): preoperative neck ultrasound revealed two left thyroid nodules, the largest is TIRADS 4

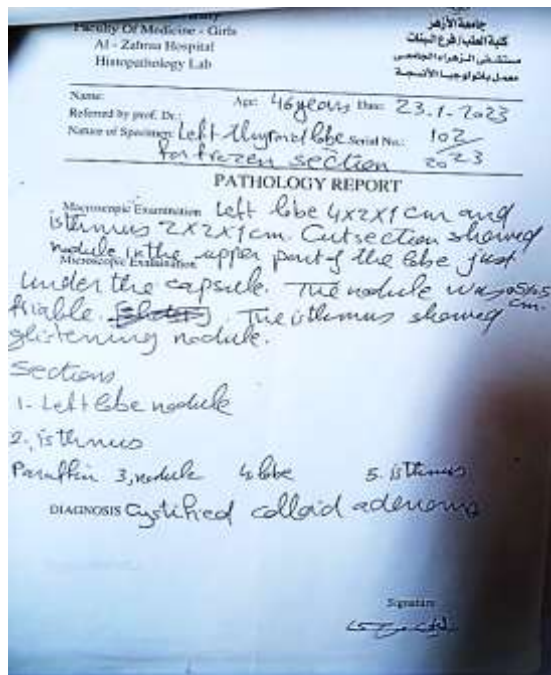


Figure (6): Frozen section revealed a denomatous goiter.

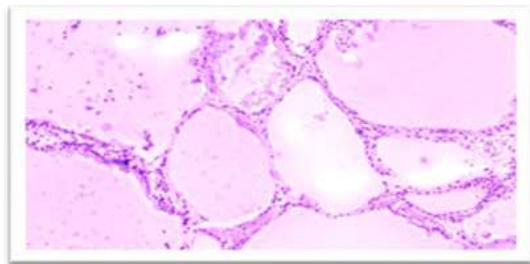


Figure (7): Adenomatous goiter frozen section: section showed variable sized thyroid follicles lined by bland

looking follicular cells. The lumens of follicles were dilated and filled with colloid (200x).

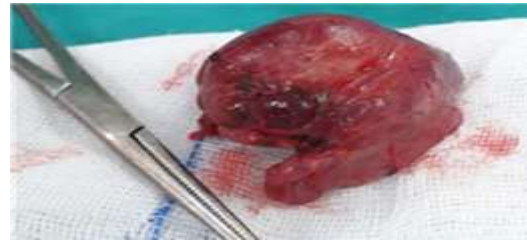


Figure (8): Right hemithyroidectomy is enough as the lesion is confirmed to be benign tax frozen section.

2.4 Statistical analysis:

The statistical analysis was performed using SPSS version 23.0 (SPSS Inc., Chicago, Illinois, USA). Mean, standard deviation, and ranges were used to present parametric data, while median and inter-quartile range (IQR) were used for non-parametric data. Qualitative variables were presented as percentages and numbers. Normality of the data was assessed using Kolmogorov-Smirnov and Shapiro-Wilk Test.

Statistical significance was set at $p < 0.0$

3. Results

Out of 50 patients, the gender distribution is as follows: 92% of the patients are female.

Table (1): Data regarding the demographics of the patients under study: illustrates the percentage of patients according to gender, 92% are females. Also, illustrates that 40% were at the age group of 30:40 years, 30% were at the age group of 40:50 years, 22% were at the age group of 20:30 years and only 8% were at the age group more than 50 years old.

Demographic Data		
Gender	No.	%
Male	4	8.0
Female	46	92.0
Total	50	100.0
Age group (in years)		
20 – 30 Y	11	22
30 – 40 Y	20	40
40 – 50 Y	15	30
>50 Y	4	8
Mean $\pm$ SD	42.42 $\pm$ 13.91	

Table (2): Diagnosis of the studied cases by ultrasound: Table illustrates that 18% of the studied cases by ultrasound have suspicious nodules.

Diagnosis	N=50	%
Solitary thyroid nodule	41	82
suspicious nodules	9	18

Table (3): Site of the nodules among the studied cases: Illustrates that 54% of studied cases have nodule at the right lobe, 34% at the left lobe and 12% at the isthmus.

Site of the nodules	N=50	%
Right lobe	27	54.0
Left lobe	17	34.0
Isthmus	6	12.0

Table (4): TIRADS classification among studied cases: Demonstrates that, 38% are TIRADS III, 50% TIRADS IV and 12% TIRADS V.

TIRADS	N=50	%
III	19	38.0
IV	25	50.0
V	6	12.0

Table (5): Frozen section results among studied cases: Frozen section illustrates that 50% adenomatous goiter, 18% nodular hyperplasia, 16% papillary carcinoma and 16% follicular carcinoma.

Frozen section	N=50	%
Adenomatous goitre	25	50.0
Nodular hyperplasia	9	18.0
Papillary carcinoma	8	16.0
Follicular carcinoma	8	16.0

Table (6): The TIRADS classification in ultrasound is valuable for distinguishing between benign and malignant lesions: Illustrates statistically significant difference between benign and malignant lesions as regards TIRADS classification. Among malignant lesions, 12.5% are TIRADS class III, 66.7% TIRADS class IV, 20.8% TIRADS class V and for benign lesions; 61.5% TIRADS III, 34.6% TIRADS IV and 3.9% TIRADS V.

TIRADS	Benign N=26(%)	Malignant N=24(%)
III	16(61.5)	3(12.5)
IV	9(34.6)	16(66.7)
V	1(3.9)	5(20.8)

Table (7): Value of frozen section in differentiating benign from malignant lesions: illustrates statistically significant difference between benign and malignant lesions. Frozen section demonstrates that true positive cases were detected among 15 cases, true negative cases among 29 cases, no false positive cases and 6 cases have false negative cases yielding sensitivity 62.5%, specificity 100%, Positive predictive value 100%, negative predictive value 74.3% and total accuracy 82%.

Frozen section	Benign N=29(%)	Malignant N=21(%)	of significance Test
Adenomatous goiter	17(65.4)	8(33.3)	MC=24.59 P=0.001*
Nodular hyperplasia	9(34.6)	1(4.2)	
Papillary carcinoma	0	8(33.3)	
Follicular carcinoma	0	7(29.2)	

4. Discussion

The preferred procedure for patients diagnosed with differentiated thyroid carcinoma before or during surgery is total thyroidectomy. Nonetheless, cytologic examination may not always provide a clear diagnosis. There is uncertainty about the most suitable surgical approach for cases where the cytologic diagnosis indicates suspicion but is not conclusively definitive for differentiated thyroid carcinoma, even though malignancy is the most probable outcome [7].

As far as we know, there have been no studies in literature that evaluate the outcomes of our study in the same population. So, we used in our discussion previous literatures that assessed ultrasound and frozen section in different populations.

In our research, we found that using ultrasound goes with frozen section in distinguish between benign and malignant thyroid lesions of accuracy 84% vs. 82%. However, ultrasound had higher Sensitivity 91.7% vs. 71.4% and frozen section had higher Specificity 100% vs. 76.9%.

Daimary et al., (2022) the patients in the report were between 15 and 69 years old, the mean age was 38.94 years. in our study the patients ranged from 20 to 60 years, and the mean age was 42.4 years [8].

But in Richards et al., (2002) the patients studied were between 8 and 86 years old and the mean age was (44.7 years) [9].

Daimary et al., (2022) Among the 53 patients, it was reported that 45 (84.9%) were females, while 8 (15.1%) were males. In our study males were (8%) and females were (92%) [8].

But in Richards et al., (2002) study data revealed involvement of 30 men (12.9%) and 201 women (87.1%) [9].

Daimary et al., (2022) Among 51 patients the site of nodules was in the right lobe in 25 cases (49%) and in left lobe in 26 cases (51%). In our study the site of nodules was in right lobe in 27 cases (54%), in left lobe in 17 cases (34%) and in the isthmus in 6 cases (12%) [8].

Daimary et al., (2022) Out of 53 patients, the largest group, which consisted of 48 patients (90.56%), were found to be euthyroid when they presented. A small percentage, 3 patients (5.66%), were diagnosed with hypothyroidism, while 2 patients (3.77%) were identified as hyperthyroid. Our findings revealed that 84% of the patients were euthyroid and 16% were hypothyroid [8].

Cetin et al., (2004) assessed the significance of intraoperative FS biopsy in individuals with thyroid gland nodular disease was questioned by a different group. They disputed our findings and stated that the sensitivity, specificity, and accuracy of FS were 87.1%, 100%, and 97.8%, correspondingly. Compared to our results, FS sensitivity, specificity and accuracy rates were 62.5%, 100% and 82%, respectively [10].

In the study by Daimary et al. (2022), the frozen section demonstrated a sensitivity of 85.71% and a specificity of 100%. The positive predictive value was 100%, the negative predictive value stood at 97.87%, and the diagnostic accuracy was 98.11%. In our research, the frozen section showed a sensitivity of 62.5% and a specificity of 100%. The positive predictive value was 100%, the negative predictive value was 74.3%, and the overall accuracy was 82% [8].

But Richards et al., (2002) The sensitivity and specificity rates for FS were reported to be 50% and 100% respectively and overall accuracy of FS is 90%. That agreed with our results regarding specificity and accuracy and disagreed about sensitivity [9].

Daimary et al., (2022) The frozen section reports categorized findings as either benign, deferred, or malignant. Out of the cases, 42 (79.3%) were determined to be benign, while 6 patients (11.3%) received a confirmed diagnosis of malignancy, and 5 cases (9.4%) had their diagnosis deferred. In our study 34 cases (68%) were reported as benign, while 16 cases were reported as malignant (32%) [8].

Shi et al., (2022) The available evidence indicates that ultrasound is capable of

accurately diagnosing both benign and malignant thyroid nodules, thus establishing a scientific foundation for evaluating and diagnosing thyroid conditions. The sensitivity, specificity and accuracy of ultrasound for the diagnosis of thyroid nodules were 88%, 86% and 87% respectively. Comparing to our results as regards sensitivity, specificity and accuracy 91.7%, 76.9% and 84% respectively [11].

Horvath et al. (2017) The analysis determined that a TIRADS 4 cut-off point for malignancy resulted in a sensitivity of 99.6%, specificity of 74.35%, positive predictive value (PPV) of 82.1%, and negative predictive value (NPV) of 99.4%. In our research, the sensitivity was 91.7%, the specificity was 76.9%, the PPV was 78.6%, and the NPV was 90.9% [12].

Daimary et al, (2022) The results showed that 43 patients (81.13%) had solid consistency on preoperative ultrasonography (USG), four patients (7.55%) had cystic consistency, and the remaining six patients (11.32%) had swellings with mixed consistency [8].

Horvath et al. (2017) In a study involving 210 patients, the distribution of TIRADS categories was as follows: 116 patients were classified as TIRADS II (23.11 %), 56 patients as TIRADS III (11.15%), 243 patients as TIRADS IV (48.41 %), and 87 patients as TIRADS V (17.33 %). In our study, the distribution of TIRADS categories 19 cases (28%) were TIRADS III, 25 cases (50%) were TIRADS IV and 6 cases (12%) were TIRADS V [12].

Horvath et al. (2017) The malignancy rate for each category was: TIRADS 3 had a 1.79% (1/56) malignancy rate, TIRADS 4 had a 76.13% (185/243) malignancy rate, and TIRADS 5 had a 98.85% (86/87) malignancy rate. And in our study 15.8% (3/19) in TIRADS 3, 64% (16/25) in TIRADS 4 and 83.3% (5/6) in TIRADS 5 [12].

Grani et al., (2019) and Li et al., (2021) The TIRADS score is known for its high accuracy in identifying suspicious thyroid nodules that warrant cytological examination, allowing for early detection

while minimizing unnecessary biopsies, as reported [13] & [14].

In summary

Our research findings indicate that ultrasound and frozen sections yield nearly similar results in distinguishing between benign and malignant thyroid lesions. of accuracy 84% vs. 82%. However, ultrasound had higher Sensitivity 91.7% vs. 71.4% and frozen section had higher Specificity 100% vs. 76.9%.

Also, malignant cases were statistically significant older, with higher number of solitary thyroid suspicious nodules, and more frequent complaints, progressive course, shorter disease duration and higher Bethesda score compared with benign cases.

In recommendations, if possible, combined use of ultrasound and frozen section is advised to be used for better assessment of cases with suspicious thyroid nodules.

The current research could contribute to the existing knowledge and provide insight for future studies with larger sample sizes and extended follow-up periods to validate our findings.

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