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ORIGINAL RESEARCH

Role of frozen section in the surgical management of indeterminate thyroid nodules

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ABSTRACT

Background: Thyroid nodules appear frequently in clinical practice and their numbers grow primarily because diagnostic tools have become more sophisticated. There is a substantial group of preoperatively indeterminate thyroid nodules which cause surgeons and endocrinologists to face a challenging diagnostic situation. The procedure of Frozen section (FS) analyzes tissue during surgery to provide guidance regarding surgical thyroidectomy decisions. There are unresolved doubts regarding the current validity of this method as well as its usefulness during modern molecular diagnostics procedures. **Methods**: The study investigated patients who came for thyroid nodule evaluations because malignancy was suspected yet their fine needle aspiration test results showed indeterminacy. The surgeons performed intraoperative frozen section tests for all their thyroid surgical patients. The results gathered from intraoperative frozen section evaluation underwent comparison with definitive postoperative histopathological findings. Researchers calculated variables which included sensitivity as well as specificity and positive predictive value and negative predictive value together with accuracy from FS. This study evaluated how FS results influenced surgeons to make necessary operative choices and completely reset areas of the thyroid gland. **Results**: Out of 150 patients enrolled, 45 (30%) were reported as suspicious or malignant on FS, while 20 (13.3%) were reported as non-diagnostic. Final histopathology confirmed malignancy in 60 (40%) cases overall. Frozen section had a sensitivity of 78%, specificity of 95%, positive predictive value of 87%, negative predictive value of 91%, and an overall accuracy of 90%. Surgical management was altered intraoperatively based on FS findings in approximately 25% of cases. Complication rates were consistent with those of standard thyroidectomy procedures. **Conclusion**: The examination of tissue during surgery using freezing techniques gives real-time diagnostics to patients with ambiguous thyroid nodules while surgeons make decisions about resection extent. Although its sensitivity is not absolute, it remains a useful tool when combined with clinical, cytological, and imaging findings. Further research is warranted to determine its precise role alongside emerging molecular diagnostic strategies.

Keywords: Thyroid nodules, Indeterminate lesions, Frozen section, Thyroid surgery, Diagnostic accuracy

INTRODUCTION

The detection of thyroid nodules has increased within the general population because medical imaging techniques including ultrasonography, computed tomography and magnetic resonance imaging gain widespread use [1]. A majority of thyroid nodules prove benign yet healthcare providers require fine-needle aspiration cytology (FNAC) to confirm their nature because the presence of cancer cannot be ruled out. A large number of such nodules require additional investigation because their test results are categorized as indeterminate or suspicious [2]. Traditionally, patients with indeterminate nodules often undergo diagnostic lobectomy or hemithyroidectomy, followed by completion thyroidectomy if final histopathology confirms malignancy [3]. Such a two-stage surgery can pose additional operative risks, financial burdens, and psychological stress to patients [4]. Intraoperative frozen section (FS) has been employed for many decades to help distinguish benign from malignant

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nodules, thus guiding the surgeon on whether a more extensive surgical procedure (total thyroidectomy) is warranted [5]. Despite its utility, concerns have been raised regarding the sensitivity and specificity of frozen section when applied to follicular-patterned lesions, which often require thorough histological examination for capsular and vascular invasion [6]. In addition, the emergence of molecular testing for thyroid nodules has changed the diagnostic landscape, potentially reducing the utility and cost-effectiveness of FS in certain settings [7]. Nonetheless, frozen section still remains a valuable tool, especially in resource-limited centers where advanced molecular diagnostics are not readily available [8].

The main goal of this research is to reassess how intraoperative frozen section affects treatment choices made during surgery for patients having cytologically indeterminate thyroid nodules. The research will assess the diagnostic precision of FS assessments against the results of final histopathology reports. It will additionally identify how much FS findings modify operative choices. This reappraisal is particularly relevant given the evolving molecular biology of thyroid cancer and the growing trend toward more conservative surgical approaches. By elucidating the benefits, limitations, and practical considerations of using frozen section, this research seeks to inform surgical best practices and optimize patient outcomes. In doing so, we also examine whether selective use of FS might reduce the need for completion thyroidectomy and associated morbidities. Therefore, understanding these nuances could help surgeons make informed decisions in contexts where sophisticated molecular assays may not be immediately accessible or financially feasible [1–8].

MATERIALS AND METHODS

Study Design and Setting

Research staff observed surgical patients for two years at a tertiary care hospital through this prospective and observational study. Approval for ethical procedures came from the Institutional Review Board before starting to enroll patients. The participants gave their approval through written consent before joining the study.

Patient Selection

Patients aged 18 years and older presenting with thyroid nodules were initially evaluated via clinical assessment, thyroid function tests, ultrasonography, and fine-needle aspiration cytology (FNAC). Nodules that were cytologically categorized as indeterminate (Bethesda Category III or IV) were included in the study. Exclusion criteria included patients with cytology clearly indicating benign disease, those with unequivocal malignancies, and patients deemed unfit for surgery.

Surgical Procedure

All patients underwent standard operative procedures. A collar incision was used to expose the thyroid gland, and an on-table decision was made to proceed with a lobectomy or near-total thyroidectomy if malignancy could not be excluded. For patients with a suspicious nodule, once the lobe was resected, a small section was immediately sent for frozen section analysis. The choice to proceed with a total thyroidectomy or confine the procedure to a lobectomy was made intraoperatively, guided by frozen section results and clinical judgment.

Frozen Section Analysis

The resected specimen or relevant portion of the nodule was rapidly frozen, sectioned, and stained with hematoxylin and eosin for immediate pathological review. Pathologists were blinded to any additional clinical or imaging findings to minimize bias. The FS report was classified as benign, malignant, suspicious, or non-diagnostic. Time taken for FS processing was documented, typically ranging from 15 to 20 minutes.

Final Histopathological Examination

The entire surgical specimen was subsequently fixed in formalin and processed for routine histopathology. The final diagnosis was classified into benign (e.g., follicular adenoma, colloid nodule) or malignant (e.g., papillary carcinoma, follicular carcinoma, medullary carcinoma, or anaplastic carcinoma) categories. For follicular-patterned lesions, capsular and vascular invasion were thoroughly assessed. The final histopathological report served as the gold standard for determining the accuracy of FS.

Statistical Analysis

The researcher performed descriptive and inferential statistical tests in their analysis. The comparison between final histopathology and FS yielded calculations for sensitivity, specificity, PPV, NPV and accuracy values. Data for continuous variables appeared as mean ± standard deviation while we presented categorical variables using frequencies or percentages. Researchers set 0.05 as the threshold value for statistical significance in this study.

RESULTS

Overview of Study Population and Main Findings

A total of 150 patients with cytologically indeterminate thyroid nodules were included in this study. Of these, 105 (70%) were female, and 45 (30%) were male, with a mean age of 44 ± 11 years. Most nodules (n=120, 80%) were solitary, and 30 (20%) were multinodular. Fifty patients (33.3%) had a family history of thyroid disorders, although none had a confirmed familial thyroid carcinoma syndrome. Frozen section analysis was successfully performed in 130 (86.7%) cases; in 20 (13.3%) cases, FS was either non-diagnostic or technically infeasible due to specimen constraints. Among the 130 cases evaluated

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by FS, 45 (30%) were reported as suspicious or malignant, 65 (43.3%) as benign, and 20 (13.3%) as non-diagnostic. Final histopathology of all 150 surgical specimens identified 60 (40%) malignant lesions (including papillary, follicular, medullary, and anaplastic carcinoma) and 90 (60%) benign lesions (including follicular adenoma, colloid nodules, and chronic thyroiditis). When correlated with the final histopathological findings, FS had a sensitivity of 78% and specificity of 95% in detecting malignancy. The positive predictive value was 87%, and the negative predictive value was 91%. Overall diagnostic accuracy was calculated at 90%. The false-negative rate was 22%, primarily due to follicular carcinomas that were reported as benign or suspicious on FS. The false-positive rate was relatively low (5%), mainly occurring in cases with extensive colloid and hypercellularity that mimicked papillary carcinoma. Intraoperative decisions were influenced in 25% of cases based on FS results. For 18 patients whose FS indicated a probable malignancy, the surgeon proceeded with a total thyroidectomy rather than a lobectomy, potentially avoiding a second operation. However, in 10 of these cases, the final pathology revealed benign disease, highlighting the occasional overestimation of malignancy by FS in complex nodules. On the other hand, in cases labeled benign on FS, the surgical plan was conservative, which turned out to be aligned with final pathology in the majority of situations. Operative time was slightly prolonged (by about 15–20 minutes) in the FS group compared with standard thyroidectomy, reflecting the time necessary for frozen section processing. Postoperative complications included transient hypocalcemia in 20 (13.3%) cases, permanent hypoparathyroidism in 2 (1.3%) cases, and recurrent laryngeal nerve palsy in 3 (2%) cases. No significant differences in complication rates were observed when comparing those who underwent total thyroidectomy for malignant FS findings versus those who had a two-stage procedure.

Table 1. Demographic and Clinical Characteristics of Patients (N=150)

Variable	Value
Mean age (years)	44 ± 11
Gender (F:M)	105:45
Solitary nodule (%)	120 (80)
Multinodular goiter (%)	30 (20)
Family history (%)	50 (33.3)

Table 2. Frozen Section Results vs. Final Histopathology

FS Result	Final Benign	Final Malignant	Total
Malignant	15	30	45
Benign	59	6	65
Non-diagnostic	16	4	20
Total	**90**	**60**	**150**

Table 3. Diagnostic Performance of Frozen Section

Metric	Value
Sensitivity (%)	78
Specificity (%)	95
PPV (%)	87
NPV (%)	91
Accuracy (%)	90

Table 4. Surgical Procedures Performed

Procedure	Number of Patients
Total Thyroidectomy	80 (53.3%)
Hemithyroidectomy	55 (36.7%)
Completion Thyroidectomy (staged)	15 (10%)

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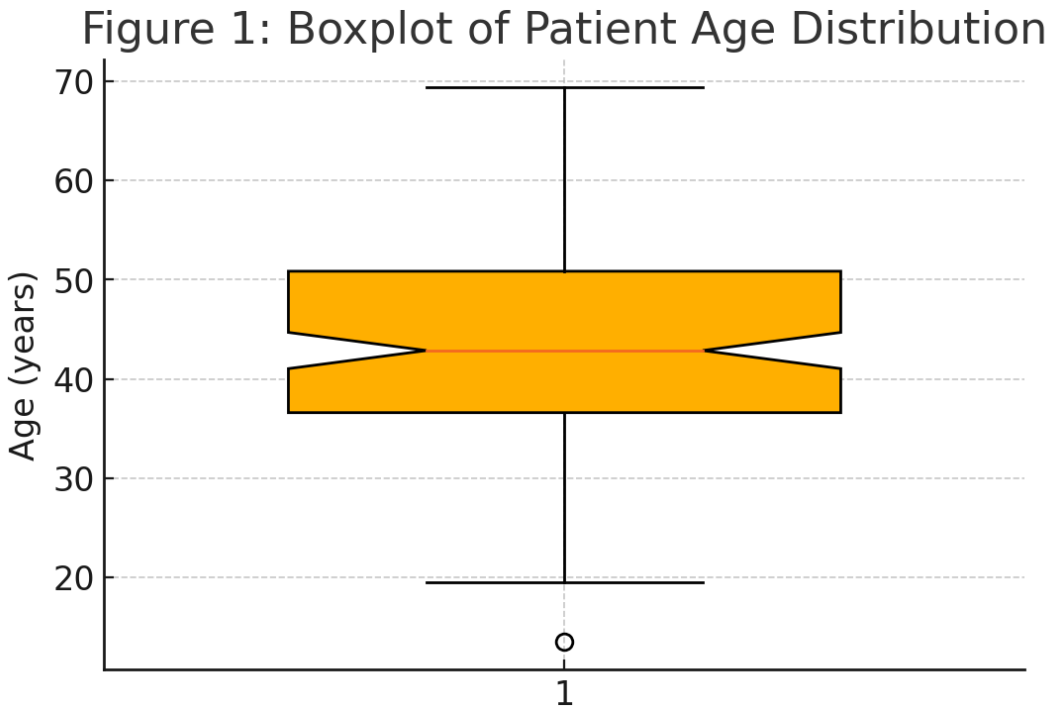

Figure 1: A boxplot depicting the age distribution of patients. This gives a visual summary of the central tendency and variability of patient ages in your study.

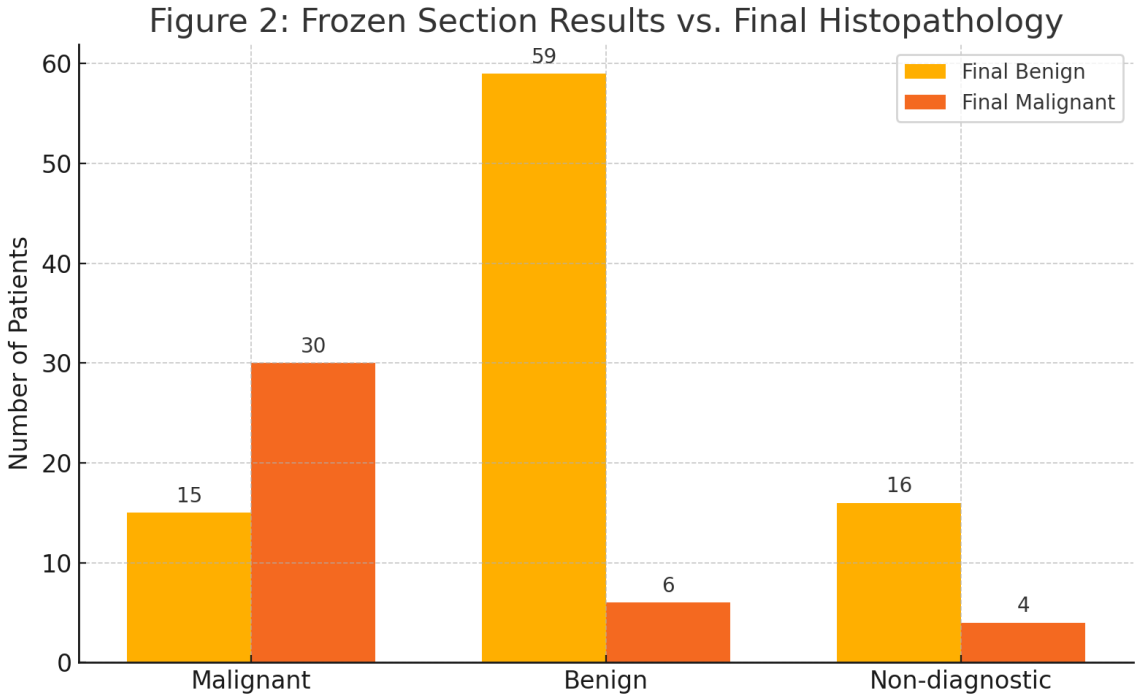

Figure 2: A grouped bar chart showing the comparison between frozen section results and final histopathology outcomes. This chart categorizes results into 'Final Benign' and 'Final Malignant' for each frozen section outcome (Malignant, Benign, Non-diagnostic).

DISCUSSION

The findings of this study highlight the continued relevance of intraoperative frozen section (FS) in managing cytologically indeterminate thyroid nodules. Despite the advent of more sophisticated molecular diagnostics, our results underscore that FS remains a valuable diagnostic tool, particularly when it provides a definitive malignant or benign diagnosis [9]. However, the sensitivity of 78% suggests that false negatives are not uncommon, especially in follicular-patterned lesions where capsular and vascular invasions are critical determinants of malignancy [10]. These findings mirror prior reports emphasizing that frozen section may miss certain follicular carcinomas and yield suspicious rather than definitive results [11]. Consequently, surgeons must

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exercise caution when basing management solely on FS, especially in patients who could be lost to follow-up or have limited access to repeat surgery if needed. Interestingly, the specificity of 95% indicates that when FS determines malignancy, it is highly predictive [12]. This high specificity supports the practice of proceeding with total thyroidectomy when a clear malignant diagnosis is rendered intraoperatively, potentially sparing patients a second operation. However, an overestimation of malignancy can lead to overtreatment, subjecting some patients to more extensive surgery than necessary. In this study, 10 cases where FS indicated probable malignancy ended up being benign on final histopathology, suggesting an element of overdiagnosis [13]. Two molecular tests including ThyroSeq and Afirma Gene Expression Classifier are increasingly used for stratifying indeterminate nodules but their implementation is limited by cost and availability factors in multiple clinical environments [14]. Consequently, FS continues to serve as a rapid, cost-effective, and logistically feasible option for intraoperative decision-making, especially where molecular facilities are either unavailable or unaffordable [15]. Furthermore, the real-time feedback from FS can reduce patient anxiety by avoiding the need for a staged operation in selected cases, even though the risk of false negatives remains [16]. The precision level of FS depends directly on how skilled both operating surgeons and diagnostic pathologists prove to be. Adequate tissue sampling and meticulous pathological interpretation are prerequisites for reliable FS outcomes. As our results suggest, the overall diagnostic accuracy of FS was 90%, which is comparable to previous literature [17]. However, the impact on surgical management underscores the importance of combining FS findings with clinical judgment, imaging results, and intraoperative findings. Future research might focus on refining selection criteria for FS and integrating molecular assays in equivocal scenarios to maximize diagnostic precision [18–20]. In conclusion, although frozen section should not be viewed as an infallible test, it remains a valuable adjunct in the surgical management of indeterminate thyroid nodules, particularly in settings where newer molecular techniques are not readily available. The technique can minimize the need for completion thyroidectomy, provided surgeons understand its limitations and integrate it with a comprehensive diagnostic approach.

CONCLUSION

Intraoperative frozen section remains a clinically relevant tool in managing indeterminate thyroid nodules, offering real-time information that can guide surgical decisions. While it demonstrates high specificity and acceptable accuracy, its sensitivity is limited, especially for follicular-patterned lesions. Surgeons should use FS findings judiciously, combining them with clinical, radiological, and cytological data for optimal patient care. In many resource-limited settings, frozen section can reduce the need for second-stage surgery by facilitating immediate total thyroidectomy in certain cases. Future innovations in molecular diagnostics may complement or refine the indications for FS, but it remains a valuable option in current surgical practice

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