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Improving Thyroid Nodule Diagnosis: A Comprehensive Investigation Utilizing Ultrasonography and Fine-Needle Aspiration Cytology at Derna Hospital in Libya

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Abstract:

Thyroid nodules present a common clinical challenge, ranging from benign to malignant lesions, necessitating accurate diagnostic strategies for appropriate management. This retrospective study conducted at Derna Hospital, Libya, aimed to evaluate the predictive efficacy of ultrasonography and fine-needle aspiration cytology (FNAC) in determining histological outcomes of thyroid nodules. A cohort of 300 patients clinically diagnosed with thyroid nodules underwent thyroid function tests, ultrasonography, and FNAC. Histopathological examination was performed post-operatively for surgically managed cases. Data analysis involved comparing predicted and actual histological outcomes using various categories, assessing precision and overall accuracy. Initial evaluation showed an overall accuracy of 82%, with high precision for multinodular goiter, adenomatous nodules, and papillary thyroid carcinomas. Following re-categorization into clinically significant entities, expert ultrasound evaluation demonstrated an overall accuracy of 92% in distinguishing between colloid/adenomatoid nodules, follicular neoplasias, and papillary thyroid carcinomas, with precision values ranging from 70% to 98%. Notably, no cases of follicular, medullary, or neoplastic thyroid cancers were observed. Our findings underscore the pivotal role of ultrasonography in predicting histological outcomes of thyroid nodules, facilitating precise diagnosis and tailored management strategies. The high accuracy and precision values attained highlight the utility of expert ultrasound evaluation in enhancing diagnostic reliability, potentially reducing unnecessary surgeries and associated healthcare costs. However, challenges persist in differentiating indeterminate lesions and predicting the biological behavior of thyroid malignancies, warranting continued research efforts in thyroid pathology. Integration of advanced imaging modalities and artificial intelligence algorithms may further refine diagnostic algorithms, improving patient outcomes and optimizing clinical practice in thyroid nodule management.

Keywords: Thyroid nodules, Ultrasonography, Fine-needle aspiration cytology, Diagnostic accuracy, Histopathological outcomes, Diagnostic challenges.

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تحسين تشخيص عقد الغدة الدرقية: تحقيق شامل باستخدام الموجات فوق الصوتية وسيتولوجيا الحقن بالإبر الدقيقة في مستشفى درنة في ليبيا

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الملخص
تشكل العقيدات الدرقية تحديًا سريريًا شائعًا، يتراوح بين الآفات الحميدة والخبيثة، مما يتطلب استراتيجيات تشخيصية دقيقة للإدارة المناسبة. هدفت هذه الدراسة الاسترجاعية التي أجريت في مستشفى درنة، ليبيا، إلى تقييم كفاءة التنبؤ بالموجات فوق الصوتية وعلم الخلايا باستخدام الشفط بالإبرة الدقيقة (FNAC) في تحديد النتائج النسيجية للعقيدات الدرقية. خضع 300 مريض تم تشخيصهم سريريًا بالعقيدات الدرقية لاختبارات وظائف الغدة الدرقية، والموجات فوق الصوتية، و(FNAC). تم إجراء الفحص النسيجي بعد الجراحة للحالات التي أُديرت جراحياً. شملت تحليل البيانات مقارنة النتائج النسيجية المتوقعة والفعلية باستخدام فئات مختلفة، وتقييم الدقة والدقة العامة. أظهرت التقييمات الأولية دقة عامة بنسبة 82%، مع دقة عالية لتضخم الغدة الدرقية متعدد العقيدات، والعقيدات الغدية، وسرطانات الغدة الدرقية الحليمية. بعد إعادة التصنيف إلى كيانات ذات أهمية سريرية، أظهر تقييم الموجات فوق الصوتية من قبل الخبراء دقة عامة بنسبة 92% في التمييز بين العقيدات الغروانية/الغدية، والأورام الجريبية، وسرطانات الغدة الدرقية الحليمية، بقيم دقة تتراوح بين 70% و98%. لم تُلاحظ أي حالات لسرطانات الغدة الدرقية الجريبية أو النخاعية أو الأورام النسيجية.
تؤكد نتائجنا الدور المحوري للموجات فوق الصوتية في التنبؤ بالنتائج النسيجية للعقيدات الدرقية، مما يسهل التشخيص الدقيق واستراتيجيات الإدارة المخصصة. تبرز القيم العالية للدقة وفائدة تقييم الموجات فوق الصوتية من قبل الخبراء في تعزيز موثوقية التشخيص، مما يقلل من العمليات الجراحية غير الضرورية وتكاليف الرعاية الصحية المرتبطة بها. ومع ذلك، لا تزال التحديات قائمة في التفريق بين الآفات غير المحددة وتنبؤ السلوك البيولوجي لسرطانات الغدة الدرقية، مما يستلزم استمرار جهود البحث في أمراض الغدة الدرقية. قد يؤدي دمج تقنيات التصوير المتقدمة والخوارزميات الذكية إلى تحسين الخوارزميات التشخيصية، مما يحسن نتائج المرضى ويحسن الممارسة السريرية في إدارة العقيدات الدرقية.
الكلمات المفتاحية: عقد الغدة الدرقية، الموجات فوق الصوتية، سيتولوجيا الحقن بالإبر الدقيقة، دقة التشخيص، نتائج النسيجية، تحديات التشخيص.

Introduction

The thyroid gland plays a pivotal role in regulating metabolism, growth, and energy homeostasis through the synthesis and secretion of thyroid hormones. Despite its relatively small size, the thyroid gland is susceptible to a myriad of pathological alterations, ranging from benign nodular formations to malignant neoplasms. Thyroid nodules, discrete palpable or radiologically detectable lesions within the thyroid gland, represent a common clinical entity encountered in routine practice, with prevalence as high as 50% in certain populations [1-3]. While the majority of thyroid nodules are benign and asymptomatic, a subset harbors malignant potential, necessitating meticulous evaluation and management to differentiate between benign and malignant lesions. The clinical significance of thyroid nodules lies in their association with thyroid dysfunction, compression symptoms, and the risk of malignancy, thereby underscoring the importance of accurate diagnosis and appropriate therapeutic interventions [4,5].

Epidemiologically, thyroid nodules exhibit notable variations in prevalence based on factors such as age, gender, iodine intake, and geographical location. Females, individuals over the age of 60, and those with a history of radiation exposure are predisposed to a higher risk of thyroid nodules. Furthermore, iodine deficiency, autoimmune thyroid disorders (e.g., Hashimoto's thyroiditis), and genetic predispositions contribute to the pathogenesis of thyroid nodules, highlighting the multifactorial nature of thyroid gland pathology [6].Histologically, thyroid nodules encompass a diverse array of entities, including benign follicular adenomas, hyperplastic nodules, colloid nodules, and malignant neoplasms such as papillary thyroid carcinoma, follicular thyroid carcinoma, and medullary thyroid carcinoma. The morphological spectrum of thyroid lesions is characterized by architectural patterns, cellular composition, and stromal alterations, which are scrutinized through histopathological examination to delineate the underlying pathology and guide clinical management decisions [7,8].

Efforts to mitigate overtreatment of thyroid nodules have led to ongoing enhancements in diagnostic protocols. Ultrasound (US) has emerged as a pivotal tool for assessing thyroid nodules and has undergone significant advancements in technology [9].

While distinguishing between benign and malignant nodules was once deemed challenging using US alone, it now holds a central role in several risk stratification systems (RSS) for identifying thyroid malignancies. Various versions of Thyroid Imaging Reporting and Data Systems (TIRADS) have been introduced over the past five years, aiming to standardize and enhance radiological assessments. However, consensus on a unified

system is hindered by discrepancies in inter-rater reliability and the associated malignancy risks within each category.

Fine-needle cytology (FNC) guided by ultrasound is the gold standard for evaluating thyroid nodule cytology, in contrast to palpation-guided FNC. Despite the crucial role of US in identifying suspicious nodules, its characteristics are often considered nonspecific [10]. Consequently, the decision to proceed with surgery heavily relies on cytological assessment, with US evaluation itself not being emphasized in the diagnostic process. However, cytology's diagnostic accuracy stands at approximately 70%. Some studies suggest that in cases of uncertain cytology, US evaluation can aid in determining the necessity for diagnostic surgery. Furthermore, emerging research on artificial intelligence (AI) algorithms demonstrates that US images alone contain sufficient information to predict malignancy with diagnostic accuracy comparable to cytological evaluation [11]. Despite these advancements, challenges persist in differentiating indeterminate lesions and predicting the biological behaviour of thyroid malignancies, underscoring the need for ongoing research and clinical vigilance in the realm of thyroid pathology.

Against this backdrop, this study endeavors to provide a comprehensive overview of thyroid nodules pathology, encompassing their epidemiology, clinical significance, diagnostic evaluation, with a primary emphasis on histopathological evaluation as a cornerstone for discerning diverse thyroid disorders. By synthesizing current evidence and clinical insights, we aim to enhance understanding and foster advancements in the diagnosis and management of thyroid lesions, ultimately optimizing patient care and outcomes in clinical practice.

Material and methods

Patient inclusion and prospective diagnostic assessment: This retrospective study was conducted at Derna Hospital, Libya, spanning the period from 2012 to 2019. The inclusion criteria comprised patients clinically diagnosed with thyroid nodules and admitted to the surgery department. A total of 300 patients meeting these criteria were included in the study. To ensure consistency and accuracy in diagnosis, all patients underwent thyroid function tests to assess thyroid hormone levels as part of the initial evaluation. Subsequently, thyroid ultrasonography (USG) and fine-needle aspiration cytology (FNAC) of thyroid nodules were performed for further diagnostic assessment. Post-operative histopathological examination was conducted for all patients who underwent thyroid surgery.

Ethics approval: Ethical considerations were paramount throughout the study process. The research protocol was approved by the ethics committee of Derna Hospital, ensuring that the study adhered to ethical standards and guidelines for human research. Informed consent was obtained from all participants or their legal guardians before any procedures were conducted. Furthermore, strict confidentiality measures were implemented to protect the privacy of patients' personal and medical information. Patient data were anonymized and securely stored in compliance with data protection regulations.

Statistical analysis: All data were meticulously organized using Microsoft Excel, while statistical analyses were conducted utilizing SPSS Statistics (IBM) for rigorous testing and interpretation.

Results and discussion

Epidemiological overview of thyroid nodule characteristics and patient profiles

Out of the 300 patients included in the study, the age ranged between 18 and 67 years. Females comprised the majority, accounting for 80% of the study cohort. Thyroid function tests showed that 200 patients (67%) were euthyroid, 180 (60%) were hyperthyroid, and 120 (40%) were hypothyroid.

Moreover, upon reviewing all the thyroid nodules included in the study (Table 1), it becomes evident that approximately 4 out of 5 nodules were identified in female patients, highlighting a potential gender predilection in thyroid nodule occurrence. Interestingly, statistical analysis revealed no significant difference in the mean age between patients with benign and malignant disease ($P = 0.01$), suggesting that age may not be a distinguishing factor in determining nodule pathology.

Furthermore, an analysis of nodule size yielded intriguing findings. Benign nodules that underwent surgical intervention exhibited a larger average size compared surgically removed malignant nodules ($P < 0.001$).

Table 1: Overview of the characteristic of all thyroid nodules in the study.

	Malignant histology	Benign histology
Number of nodules	6	297
Females (%)	83.3%	78.3%
Males (%)	16.7%	19.7%
Age (years)	36 ± 6	47 ± 7
Nodule size (mm)	25 ± 6	35 ± 5

Histological classification of thyroid nodules based on ultrasonography confidence levels: a comparative analysis

Initially, we assessed the efficacy of expert ultrasonography (US) in distinguishing between benign and malignant thyroid nodules, without employing any Thyroid Imaging Reporting and Data System (TIRADS) scoring. Nodules were categorized into predicted histopathological entities, and the confidence level was graded into confidant benign, uncertain, and confident malignant. In the category of benign histology, the majority of nodules (206) were confidently classified as benign, indicating a high level of certainty in their non-malignant nature (**Figure 1A**). However, a notable number of nodules (90) were categorized as "Uncertain," suggesting some ambiguity in their histological characterization.

Conversely, in the malignant histology category, no nodules were confidently classified as malignant, indicating a lack of definitive identification of malignancy based on ultrasonography alone. However, there were 25 nodules confidently classified as malignant in the "Confident malignant" category, indicating a high level of certainty in their malignant nature (**Figure 1A**).

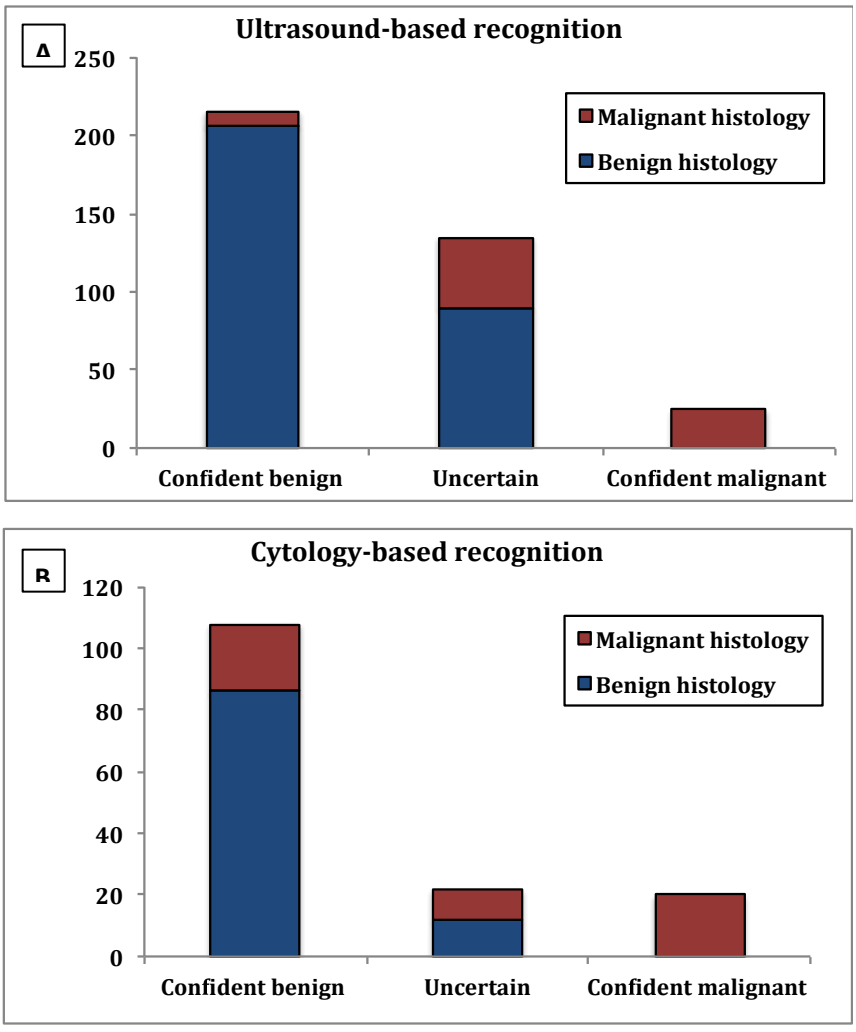

Figure 1: Classification of thyroid nodules based on recognition by ultrasound **(A)** and fine-needle aspiration cytology **(B).** For operated nodules, the final histopathology result is color-coded, representing the histological assessment.

Distribution of Thyroid Nodule Histological Classification by Confidence Levels in Fine-Needle Aspiration Cytology (FNAC) Examination

The distribution of thyroid nodules based on histological classification and confidence levels assigned during fine-needle aspiration cytology examination (FNAC) is depicted in Figure 1B. Among nodules categorized as

benign histology, 86 were confidently classified as benign, indicating a high level of certainty in their non-malignant nature. Additionally, there were 12 nodules categorized as "Uncertain," suggesting some ambiguity in their histological characterization. Conversely, in the category of malignant histology, no nodules were confidently classified as malignant, indicating a lack of definitive identification of malignancy based solely on FNAC. Among these cases, 2% were histologically proved to be malignant papillary carcinoma, and 12% were benign follicular neoplasms.

Surgical Procedures and Histopathological Patterns: Examination of Thyroid Lesions and Distribution

The surgical interventions conducted comprised lobectomy in 169 instances (56%), with 82 cases (27%) undergoing right lobectomy, 41 cases (14%) undergoing left lobectomy, and 46 cases (15%) undergoing isthmusectomy. Total thyroidectomy was performed in 6 cases (2%).

Histopathological examination of the specimens revealed that multinodular goitre was the most common non-neoplastic lesion, representing 36% of all cases, followed by adenomatous nodules (26%), colloid cysts (8%), Hashimoto's nodules (6%), hyperplastic nodules (5%), toxic nodules (5%), and lymphocytic thyroiditis (4%). Among neoplastic lesions, papillary carcinoma was the most common malignancy, representing 1% of cases, while benign lesions were diagnosed as follicular adenoma, representing 19% of cases. A female preponderance was observed for both non-neoplastic and neoplastic cases (**Figure 2)**.

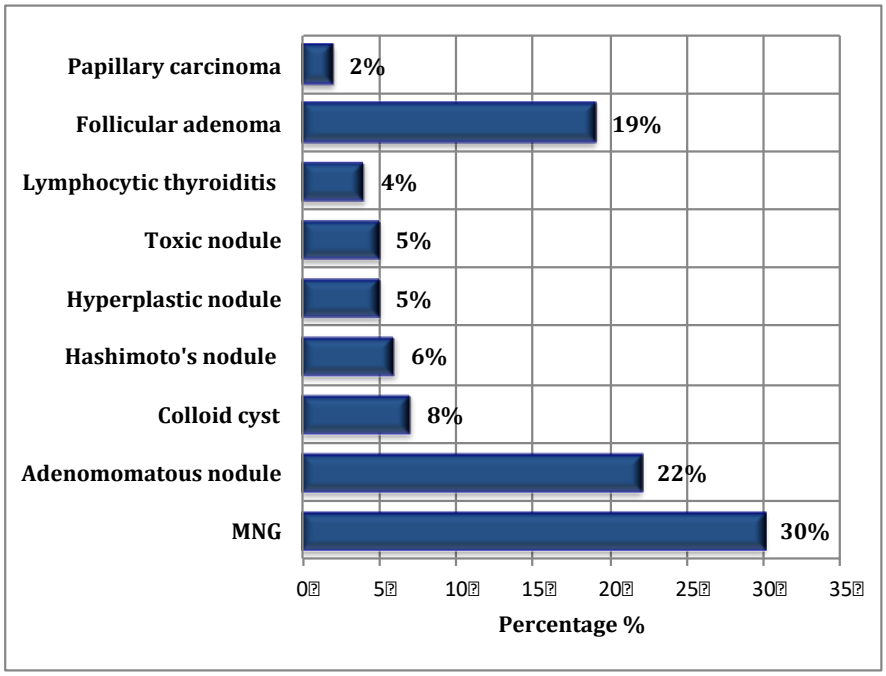

Figure 2: Histopathological analysis of thyroid specimens: distribution of lesions.

Non-neoplastic lesions included multinodular goitre (36%), adenomatous nodules (26%), colloid cysts (8%), Hashimoto's nodules (6%), hyperplastic nodules (5%), toxic nodules (5%), and lymphocytic thyroiditis (4%). Among neoplastic lesions, papillary carcinoma accounted for 1% of cases, while benign lesions were predominantly follicular adenomas, representing 19% of cases. A female preponderance was observed for both non-neoplastic and neoplastic cases.

Assessment of ultrasonography alone in predicting histological outcomes of thyroid nodules

To thoroughly assess the predictive ability of dedicated ultrasonography in determining histological outcomes, we conducted a detailed comparison between predicted and actual histological results using three benign and one malignant category, as illustrated in **Figure 3**. The overall accuracy of this evaluation was determined to be 82%.

The precision was notably high for multinodular goiter (MNG) at 71%, adenomatous nodules (76%), and papillary thyroid carcinomas (88%). However, statistical assessment for the remaining categories was not feasible due to the limited number of observations. In light of this, we re-categorized our dataset into broader categories representing clinically significant entities. Colloid and adenomatoid nodules were combined, while follicular neoplasias, including follicular cancers, were merged. Papillary thyroid cancers remained as distinct

categories. Our analysis demonstrated that expert ultrasound evaluation could reliably differentiate between these four categories, achieving an overall accuracy of 92%. Furthermore, the positive predictive value (precision) for each sub-category was determined to be 90% for colloid/adenomatous nodules, 70% for follicular neoplasias, and 98% for papillary thyroid carcinomas. Notably, no cases of follicular, medullary, or neoplastic thyroid cancers were observed during our study period.

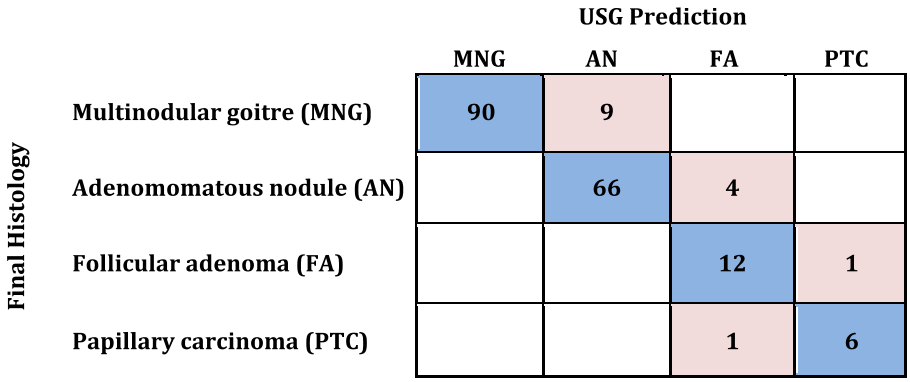

Figure 3: Confusion matrix comparing ultrasound predictions with actual histopathological diagnoses. Data are grouped into major clinically relevant entities. The overall accuracy of this comparison was determined to be 92%.

Discussion:

Thyroid nodules represent a significant clinical challenge due to their high prevalence and potential for malignancy. In this study, we aimed to evaluate the diagnostic performance of ultrasonography and fine-needle aspiration cytology (FNAC) in predicting histological outcomes of thyroid nodules [1-4, 7,9]. Our findings contribute to the existing body of literature on thyroid pathology and have implications for clinical practice.

Ultrasonography has emerged as a cornerstone in the evaluation of thyroid nodules due to its non-invasive nature, wide availability, and ability to provide detailed anatomical information [12]. Our study demonstrates the high overall accuracy of expert ultrasound evaluation in distinguishing between benign and malignant nodules, with precision values ranging from 70% to 98% for different histological categories. These results underscore the importance of skilled interpretation of ultrasound images by experienced radiologists in guiding clinical decision-making, assist in avoiding the need for invasive fine-needle cytology (FNC) procedures and minimizing the frequency of diagnostic thyroidectomis.

The diagnostic accuracy of ultrasound in this study appears to be comparable to or even superior to the published sensitivity and specificity of cytological evaluation for thyroid nodules [3,6,8,13-15]. However, directly comparing ultrasound and cytology may not be appropriate since the performance of cytology is heavily influenced by ultrasound evaluation [10]. Cytological sampling relies on ultrasound guidance and is thus greatly influenced by the quality of the ultrasound examination and the precision of ultrasound-guided fine-needle cytology (FNC) [11]. It is important to note that the accuracy of ultrasound is contingent upon the expertise of the operator and the quality of the equipment used. This consideration is particularly pertinent in clinical settings where access to expert high-volume ultrasound services may be limited. In such cases, thyroid ultrasound and FNC procedures may be performed by low-volume endocrine or ENT surgeons who may face challenges in adequately documenting images and needle positions during the procedures. [1-9, 12-15]

Fine-needle aspiration cytology (FNAC) remains the gold standard for evaluating thyroid nodule cytology, providing crucial information on cellular composition and morphology. While FNAC-guided by ultrasound has traditionally been the preferred approach, recent advancements in artificial intelligence (AI) algorithms suggest that ultrasound images alone may contain sufficient information to predict malignancy with comparable diagnostic accuracy [10,11].

However, challenges remain in differentiating indeterminate lesions, highlighting the need for continued research in this area. Our study also highlights the importance of accurate histopathological examination in confirming the diagnosis of thyroid nodules. The absence of follicular, medullary, or neoplastic thyroid cancers in our study cohort underscores the significance of precise diagnostic modalities in minimizing unnecessary surgical interventions and reducing patient morbidity [9,16].

Furthermore, our findings have implications for optimizing clinical management strategies for thyroid nodules. Accurate pre-operative diagnosis allows for tailored surgical approaches, such as lobectomy or total thyroidectomy, based on the nature and extent of the lesion. Additionally, the identification of specific

histological categories, such as papillary thyroid carcinomas or follicular adenomas, informs post-operative follow-up and surveillance protocols, facilitating early detection of recurrence or metastasis.
Limitations of our study include its retrospective design, reliance on data from a single centre, and the relatively small sample size. Additionally, the absence of long-term follow-up data precludes the assessment of patient outcomes beyond the initial diagnostic phase. Future studies incorporating larger, multicentre cohorts and long-term follow-up data are needed to further validate our findings and refine diagnostic algorithms for thyroid nodules.

Conclusion:
The study underscores the diagnostic utility of ultrasonography and FNAC in predicting histological outcomes of thyroid nodules. By leveraging these modalities in clinical practice, clinicians can achieve accurate pre-operative diagnosis, optimize surgical management strategies, and improve patient outcomes. Continued research efforts are warranted to address remaining challenges and further enhance diagnostic accuracy in thyroid nodule evaluation.

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