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EFFICACY OF ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION BIOPSY OF THYROID NODULES <10 MM IN THE MAXIMUM DIAMETER

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Abstract:
Purpose: *Ultrasound Guided Fine Needle Aspiration (US-FNAB) is a safe and effective method of screening for malignant thyroid nodules such as papillary thyroid cancer. However, there is little data on the diagnostic efficacy of US-FNAB in papillary thyroid microcarcinoma (≤10 mm in diameter). We aim to compare the diagnostic efficacy of USFNAB on thyroid nodules between two groups divided by a diameter of 10 mm by correlating the cytological results of US-FNAB with the histopathologic diagnoses in selected patients.*
Place and Duration: *In the Surgical Unit-II of Services Hospital Lahore for one-year duration from May 2019 to May 2020.*
Patients and Methods: *Eight hundred and twenty-two thyroid nodules (group A: diameter ≤10 mm, n = 620; group B: diameter> 10 mm, n = 202) from 797 patients treated between March 2014 and June 2017 were evaluated retrospectively. Only nodules with categories 4-6 Thyroid Imaging Reporting and Data System (TIRADS) were qualified and collected by the US-FNAB, and then surgically resected.*
Results: *According to the diagnostic categories,94 thyroid nodules were classified as I, III, and IV and were excluded from the analysis. 728 thyroid nodules from 721 patients were analyzed. The malignancy rates in the US-FNAB were 88.2% and 84.6% (p = 0.202) in groups A and B, respectively, and the malignancy rates were 89.5% and 86.9% (p = 0.330), respectively in histopathology. There was a high agreement between the cytological and histopathological diagnoses (kappa value = 0.797) and no statistical difference in the accuracy of US-FNAB was found between the two groups (p = 0.533).*
Conclusion: *In the case of thyroid nodules of the category 4-6 TIRADS, the diagnostic efficacy of US-FNAB is similar in the case of thyroid nodules smaller or larger than 10 mm in diameter.*
Key words: *ultrasound guided fine needle aspiration biopsy, thyroid nodules, microcarcinoma, histopathology, cytopathology.*

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INTRODUCTION:

Thyroid nodules are common entities that are detected in 19-68% of the population by high-resolution (US) ultrasound. Nevertheless, only a relatively small percentage (~ 5%) of thyroid nodules are malignant, and papillary thyroid cancer (PTC) is the most common pathological type. According to the WHO classification system, papillary thyroid microcarcinomas (PTMC) are PTCs <10 mm in diameter. Early detection and intervention of cancer has been suggested to reduce patient mortality and morbidity. Due to its minimal invasiveness and technical simplicity, ultrasound guided fine needle aspiration biopsy (US-FNAB) is widely used for the cytopathological characterization of thyroid nodules. The results of the cytology will help determine if a thyroidectomy is needed later. According to the American Thyroid Association (ATA) guidelines, US-FNAB is recommended for thyroid nodules> 10 mm in diameter with moderate or high suspicion of ultrasound. On the other hand, in patients with nodules ≤10 mm of a suspect ultrasound pattern, active ultrasound surveillance is recommended instead. Despite the fact that the prognostic advantage of PTMC has been debated in recent studies, early diagnosis and treatment of PTMC may be beneficial for patients' prognosis, as the small size alone does not guarantee a low risk in the case of accidentally detected thyroid cancer. There are several studies investigating the effectiveness of US-FNAB in small thyroid nodules. Here we have focused on the diagnostic efficacy of US-FNAB for ultrasonographic ally "suspects", ie category 4-6 Thyroid Imaging Reporting and Data System (TIRADS), and small ones, ie measuring ≤10 mm as the maximum diameter on ultrasound, thyroid nodules. To the best of our knowledge, our study is the first of its kind with the largest sample size. This knowledge is important to determine whether US-FNAB should be routinely performed in this subset of patients in future clinical practices.

PATIENTS AND METHODS:

Patient selection

We retrospectively assessed 721 patients who received thyroid ultrasound, US-FNAB of a thyroid nodule, and subsequent thyroid surgery at the Surgical Unit-II of Services Hospital Lahore for one-year duration from May 2019 to May 2020. Thyroid nodules were based on cytopathological and histopathological diagnosis with the criteria listed in the following sections and grouped according to their maximum diameter as measured in the US: Group A (≤10 mm) and Group B (> 10 mm). Written informed consents were obtained from all patients prior to US-FNAB and surgery. Patients' written consent was also obtained for reporting their medical data. Ethical approval for this retrospective study was obtained from the Ethics Committee.

Thyroid ultrasound assessment

Ultrasound examinations were performed in the Ultrasound Department with the Philips Q5 US apparatus and a 5–12 MHz linear probe. The reasons for the thyroid ultrasound are as follows: 1) palpable touch of the cervix and / or enlarged lymph nodes; 2) patients with known history of thyroid nodes and referred from other hospitals and 3) routine medical examinations including thyroid ultrasound. Ultrasound of thyroid lobes and nodules (e.g., calcification, echogenicity, volume, shape, dimensions, long-to-short axis ratio, vascularization) was recorded and all nodules were classified according to TIRADS using five ultrasound parameters (i.e., composition, echogenicity, shape, margins). and echogenic foci). Patients with TIRADS 4–6 thyroid nodules were enrolled in US-FNAB, and the exclusion criteria were: 1) patients who rejected US-FNAB or did not cooperate with the procedure; 2) with severe cardiovascular or pulmonary diseases and 3) with bleeding of unknown cause or history of coagulation disorders (prothrombin time> 18 seconds, platelet count <40%).

US-FNAB procedure for thyroid nodules

US-FNAB was performed by the same pair of experienced diagnostic ultrasound scanners who were licensed to perform the procedure to ensure the techniques used were similar. In particular, one was responsible for the US guidelines and the other for fine needle aspiration (FNAC). In accordance with the US guidelines, the target lump was punctured with a 24 G needle connected to a 5 ml syringe without local anesthesia. After confirming that the US needle tip had reached the target tubercle, the needle was moved forward and backward ten times under vacuum to aspirate the sample. The needle was then removed, the vacuum was released, and the sample in the needle was immediately transferred to a liquid-based cytology medium. In general, only one puncture was needed to sample each nodule, and in the case of unsatisfactory gross tissue yield from the first attempt, a second attempt could be made as judged by the aspiration sonograph as a precaution.

Pathological review of thyroid nodules

Cytological and histopathological diagnostics were performed by pathologists specializing in the treatment of thyroid cancer. Pap tests were made by

two independent specialist cytologists and the final report was approved.

Statistical analyzes

Data were analyzed using the SPSS 22.0 software package (IBM Corporation, Armonk, NY, USA). Continuous variables are presented as mean ± SD. Categorical variables are shown as a percentage. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) are given as percentages. The diagnostic efficacy of USFNAB was determined on the basis of consistency between cytological and histopathological results: US-FNAB was considered accurate when both results were consistent and vice versa. Data comparisons between groups were performed using the Mann-Whitney U test. Chi-square test or Fisher's exact test was used to compare categorical variables. Kappa statistics were used to measure agreement between US-FNAB and histopathological diagnoses. The kappa value can range from -1 to +1: values ≤0 indicate no agreement, and values 0.01-0.20 indicate no to little agreement, 0.21-0.40 mean fair agreement, 0.41-0, 60 moderate agreement, 0.61–0.80 average fair agreement, and 0.81–1.00 is almost perfect agreement. A p value of <0.05 was considered statistically significant.

RESULTS:

Demographic data, US and US-FNAB results

A total of 822 TIRADS category 4-6 thyroid nodules from 797 patients (772 had 1 nodule and 25 had 2) were initially analyzed during the study period. There were 620 nodules in group A and 202 nodules in group B. Cytologically, 94 thyroid nodules were classified as TBSRTC I, III and IV and excluded from further statistical analysis. Of these 721 patients, 557 (77.3%) were women and 164 (22.7%) were men. There were 553 nodules in group A and 175 nodules in group B. Median nodule size was 6 mm (range: 2–10 mm) in group A and 15 mm (range: 11–52 mm) in group B. significant difference in mean age between two groups (group A: 42.3 ± 15.4 vs group B: 48.9 ± 17.2, p = 0.018).

US-FNAB diagnostic performance

According to the US-FNAB cytology, the percentage of nodes belonging to diagnostic categories V (suspected of being malignant) and VI (malignant), which indicate a tendency to malignancy, was 88.2% in group A and 84.6% in the group B (P = 0.202), while the histological malignancy rate was 89.5% in group A and 86.9% in group B (p = 0.330). There was a good agreement between US-FNAB cytology and the final histopathology (kappa value = 0.797). There was no significant difference in sensitivity, specificity, accuracy, PPV and NPV US-FNAB between the two groups (Table 1). The US-FNAB diagnostic results also showed no significant difference between the two groups (P = 0.533).

Table 1 Sensitivity, specificity, accuracy, PPV and NPV of USFNAB for thyroid nodules of TIRADS categories 4–6

Diagnostic parameters	Group A (£10 mm), %	Group B (>10 mm), %	*P*-value
Sensitivity	96.8	96.7	1.000
Specificity	84.5	95.7	0.268
Accuracy	95.5	96.6	0.533
PPV	98.2	99.3	0.467
NPV	75.4	81.5	0.596

DISCUSSION:

Given its minimal invasiveness, technical simplicity, and high concordance with histological results, US-FNAB has become the routine biopsy method for many benign and malignant pathologies, including thyroid nodules. The current recommendations for the selection criteria for US-FNAB size of thyroid nodules have been established at a cut-off value of 10 mm with suspect sonographic features. The ATA guidelines recommend that nodules ≥10 mm with a high or medium suspect ultrasound image (or ≥15 mm with a low suspect pattern or ≥20 mm with a very low suspect pattern) be assessed by the US-FNAB.5 Similarly, the Society of Radiologists in Ultrasound recommends USFNAB is performed on thyroid nodules> 10 mm and in the case of suspicious USF features suggesting cancer. On the other hand, for nodules <10 mm, ATA recommends further evaluation only in patients with clinical symptoms or accompanying lymphadenopathy and no routine ultrasound monitoring in people with very low suspicion of ultrasound (weak recommendation, low-quality evidence). Therefore, for nodules ≤10 mm showing intermediate or highly suspect ultrasound

patterns, routine ultrasound examinations are warranted. However, the size of the nodule alone does not predict a malignant neoplasm in patients with Bethesda Category III, IV and V thyroid nodules, and due to the presence of thyroid microcarcinomas such as PTMC, early identification with US-FNAB and subsequent surgical intervention may have clinical benefits for these selected patients. Some US-B patterns have been linked to potential malignancy and therefore indicate the need for US-FNAB. For example, a recent meta-analysis suggested that American features such as microcalcification, taller than wide shape, irregular margins, and inflexibility are associated with a higher risk of cancer and have the most satisfactory diagnostic outcomes25. Likewise, the Revised Korean Society. Thyroid radiology statements and recommendations suggest that for nodules> 5 mm, FNAB should be performed if the target nodule is solid and hypoechoic, along with three of the following suspicious ultrasound features: microcalcification, non-parallel orientation (greater than wide), spicular, or microlobulated margin . According to the TBSRTC, the risk of malignancy is 60–75% for category V (suspected because of malignancy) and 97–99% for category VI (malignant). On the other hand, there are only a limited number of reports assessing the diagnostic efficacy of US-FNAB in thyroid nodules <10 mm in diameter. Also among these inconsistent cases (false negative: cytologic category benign but histologically malignant), PTMC accounted for the majority of cases. Rosario et al. Have recently specifically addressed the FNA scores for the subgroup of "highly suspect" thyroid nodules (≤10 mm, highly suspect ultrasound, thyroid restricted) in patients who are candidates for active surveillance according to ATA. They analyzed a total of 198 nodules and found a very high histology malignancy rate for nodules with suspect / malignant (100%) and indeterminate (81.4%) cytology results. Zhong et al. Compared the efficacy of US-FNAB for 344 thyroid nodules of various sizes (≤5.0, 5.1-10.0 and> 10.0 mm) and found similar diagnostic efficacy regardless of size. The main novelty of the current study is the focus on TIRADS 4-6 thyroid nodules and selecting the largest sample so far to compare the diagnostic performance of US-FNAB in nodules ≤10 or> 10 mm in diameter. Also, unlike previous studies where the benign nature of the nodule was verified by repeated cytology or simply by clinical observation, all nodes in our study were surgically removed with specific histopathological findings. Our results showed that the rate of inconsistency between US-FNAB and histology was significantly lower than previously reported: only 21 cytologically "benign" nodules identified by US-FNAB were later confirmed as postoperative PTC (false negative) and 10 cytologically nodules "Malignant" was later verified as benign (false positive). Of the 21 nodes with false negative US-FNAB results, 5 were> 10 mm and 16 were ≤10 mm. This may be due to taking a sample of healthy thyroid tissue during US-FNAB surgery. Additionally, both groups had false-negative US-FNAB results, implying the need to follow these patients with cytologically "mild" results. Given the slow-developing nature of PTC, there is still controversy about the clinical value of its early diagnosis by US-FNAB. It was reported that the autopsy showed a high frequency of latent papillary microcarcinomas (35.6%). In our study, the number of nodules ≤10 mm was three times greater than those> 10 mm, which suggests the importance of adequate clinical treatment of these nodules below the centimeter. However, the 2015 ATA guidelines do not recommend US-FNAB for nodules less than a centimeter, unless there is extra thyroid dilation or suspected lymphadenopathy. In addition, ATA also promotes active supervision in selected low-risk PTMCs rather than immediate surgery. These recommendations are largely based on observational studies by Japanese scientists that have suggested the relatively lazy nature of some PTMC subtypes. Nevertheless, metastasis to the parathyroid lymph nodes is a feature seen in some PTMC subtypes that show poor differentiation. However, without US-FNAB, there is no better way to divide patients with sub-centimeter thyroid nodules with intermediate or highly suspect features for active surveillance or surgery. Nor is there any reliable method of predicting which subsets of the PTMC will be more aggressive and therefore require faster operation. A recent study by Gweon et al. Found that among patients with sub-centimeter thyroid nodules with highly suspect ultrasound features, younger age (<45 years), male, and certain ultrasound features (microcalcification and tall shape) may not be good candidates for active surveillance as they are related to the degree of malignancy and aggressive biological behavior. Moreover, long-term active surveillance itself is not without its costs in terms of clinical, psychological and economic burdens for the healthcare system and patients. Therefore, continuous research is needed to provide evidence for the optimal management of patients with PTMC at the sub-centimeter level. A detailed discussion of the natural history of PTMC is beyond the scope of the current work, and the strength of our results is to demonstrate that US-FNAB is a convenient and reliable diagnostic procedure for these selected sub-centimeter pathologies. However, our study also has several limitations. First, as in the previous work,

patients with TIRADS category 4–6 nodules were offered US-FNAB and subsequent surgery. While this provides valuable information on the consistency of cytology and histology, some physicians would doubt the necessity of surgery in patients with mild US-FNAB cytology and suggest a continuation instead. This is at least partly due to the accompanying surgical complications. However, in our practice, we provided each patient with an explanation of the current ATA guidelines and related research by Ito et al. And proposed conservative options, including active surveillance. After careful consideration, some patients opted for follow-up visits to the US, while others continued to experience severe mental stress and underwent surgery despite our advice. Secondly, the analysis excluded thyroid nodes with TBSRTC I, III and IV cytology (11% of all cases), because according to the TBSRTC guidelines it is necessary to repeat the BAC in the case of category I and III nodules, while in the case of category IV (follicular or suspect nodules) is not the subject of this study. Therefore, our study only focused on thyroid nodules with specific cytological findings (benign or malignant but excluding follicular neoplasms) obtained in a single biopsy. However, this may lead to a selection error to some extent. Third, we did not exclude patients with a coexistence of diffuse thyroid disease such as thyroiditis or diffuse goiter, and these thyroid diseases may affect US-FNAB function, especially in small nodules. Last but not least, our study is retrospective, and a future prospective study will provide higher levels of clinical evidence to address the controversy over the benefits of surgery for the prognostic advantage of PTMC. Overall, US-FNAB is an effective diagnostic method for thyroid nodules with TIRADS categories> 4 regardless of their size. Prospective studies are needed to determine the natural history of thyroid cancer <10 mm and identify those at high risk of exhibiting aggressive behavior to further enhance the value of early diagnosis and surgical intervention, and to provide more optimal and personalized care.

REFERENCES:

1. Lyu, Yi-jun, Fang Shen, Yun Yan, Ming-zhu Situ, Wei-zhu Wu, Guo-qiang Jiang, and Ya-ya Chen. "Ultrasound-guided fine-needle aspiration biopsy of thyroid nodules< 10 mm in the maximum diameter: does size matter?." *Cancer management and research* 11 (2019): 1231.
2. Borges, Felipe Abrantkoski, Deolino João Camilo-Júnior, and José Cândido Caldeira Xavier-Júnior. "Thyroid nodules 1 cm or less are related to Bethesda System nondiagnostic and suspicious for malignancy categories." *Cytopathology*.
3. Wei, Pei-Ying, Nian-Dong Jiang, Jing-Jing Xiang, Chen-Ke Xu, Jin-Wang Ding, Hai-Bin Wang, Ding-Cun Luo, and Zhi-Jiang Han. "Hounsfield Unit Values in ACR TI-RADS 4-5 Thyroid Nodules with Coarse Calcifications: An Important Imaging Feature Helpful for Diagnosis." *Cancer Management and Research* 12 (2020): 2711.
4. Kaya, C., E. Bozkurt, D. Türkyılmaz Mut, M. Mihmanli, and M. Uludağ. "WHICH FACTORS ARE ASSOCIATED WITH MALIGNANCY IN THYROID NODULES CLASSIFIED AS BETHESDA CATEGORY 3 (AUS/FLUS) AND HOW DO THEY INFLUENCE THE PATIENT'S MANAGEMENT?." *Acta Endocrinologica (Bucharest)* 15, no. 4 (2019): 491.
5. Wu, Hao, Qin Chen, Yingxian Liu, Jidong Chen, and Wanyue Deng. "Optimized algorithm in solid thyroid nodule elastography." *Oncology Letters* 20, no. 5 (2020): 1-1.
6. Zhou, JianQiao, LiXue Yin, Xi Wei, Sheng Zhang, YanYan Song, BaoMing Luo, JianChu Li et al. "2020 Chinese guidelines for ultrasound malignancy risk stratification of thyroid nodules: the C-TIRADS." *Endocrine* (2020): 1-24.
7. Paja, Miguel, Jose Luis del Cura, Rosa Zabala, Igone Korta, Aitziber Ugalde, and José I. López. "Core-needle biopsy in thyroid nodules: performance, accuracy, and complications." *European Radiology* 29, no. 9 (2019): 4889-4896.
8. . Son, Donghoon, Hunter Gilbert, and Metin Sitti. "Magnetically Actuated Soft Capsule Endoscope for Fine-Needle Biopsy." *Soft robotics* 7, no. 1 (2020): 10-21.
9. Ito, Yasuhiro, and Akira Miyauchi. "Active surveillance as first-line management of papillary microcarcinoma." *Annual review of medicine* 70 (2019): 369-379.
10. Ito, Yasuhiro, and Akira Miyauchi. "Active surveillance of low-risk papillary thyroid microcarcinomas in Japan and other countries: a review." *Expert review of endocrinology & metabolism* 15, no. 1 (2020): 5-12.
11. Wei, Peiying, Niandong Jiang, Jinwang Ding, JingJing Xiang, Luoyu Wang, Haibin Wang, Ying Gu, DingCun Luo, and Zhijiang Han. "The Diagnostic Role of Computed Tomography for ACR TI-RADS 4–5 Thyroid Nodules With Coarse Calcifications." *Frontiers in Oncology* 10 (2020): 911.
12. Baek, Jung Hwan, and Auh Whan Park. "Radiofrequency and Laser Ablation of Thyroid

Nodules and Parathyroid Adenoma." In *Surgery of the Thyroid and Parathyroid Glands*, pp. 163-171. Content Repository Only!.

13. Kiković, Saša, Dejan M. Marinković, Petar Ristić, Jelena Karajović, Snežana Kuzmić-Janković, Zorana Đuran, Milica Čizmić, Božidar Kovačević, Nemanja Nenezić, and Zoran Hajduković. "Role and importance of elastography in the diagnosis of differentiated thyroid carcinomas regarding the clinical, echosonographic, biochumoral and cytological examination and correlation of these results with definitive pH finding.-retrospective study." *Vojnosanitetski pregled* 00 (2019): 109-109.
14. Angell, Trevor E., and Erik K. Alexander. "Thyroid nodules and thyroid cancer in the pregnant woman." *Endocrinology and Metabolism Clinics* 48, no. 3 (2019): 557-567.
15. Zhou, Liuhua, Qiaodan Zhu, Jincao Yao, Di Ou, Chen Yang, and Dong Xu. "Correlation Analysis of Papillary Thyroid Carcinoma on Sonographic Features and Cervical Lymph Node Metastasis." (2020).