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Thyroid fine needle aspiration biopsy: The effect of radiological features of nodules on cytological adequacy

Tiroid ince iğne aspirasyon biyopsisi: Nodüllerin radyolojik özelliklerinin sitolojik yeterlilik oranına etkisi

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Abstract

Aim: Thyroid fine needle aspiration biopsy (FNAB) is an inexpensive and microinvasive procedure used in the diagnosis of thyroid nodules. However, cytology may be insufficient in up to 40% of biopsies. This study aimed to assess the effect of radiological features of thyroid nodules on cytological adequacy.

Methods: The patients who underwent thyroid FNAB between 2016 and 2019 in our clinic were reviewed in this retrospective cohort study. Diagnostic adequacy rate and radiological features of nodules (size, cystic component, calcification content, echogenicity, margin feature) were noted and their relationship was investigated.

Results: A total of 525 patients (77% female, 23% male; mean age 53.3 years; age range 14-87) had FNAB for 595 nodules. Mean diameter of the nodules was 20.1 mm (min: 4mm; max: 60 mm). Of the all biopsies, 25% were inadequate for diagnosis. Adequacy was significantly low in nodules containing macrocalcification (P=0.036). There was no significant relationship between adequacy and echogenicity, margin feature, solid structure or size of the nodules (P>0.05 for each).

Conclusion: Some radiological features may be predictive of inadequate sampling. Nevertheless, varied extrinsic factors affect cytopathological adequacy besides radiological features. Additional techniques may be required in these nodules.

Keywords: Thyroid nodule, Ultrasound, Biopsy, Radiology

Öz

Amaç: Tiroid ince iğne aspirasyon biyopsisi (İİAB), tiroid nodüllerinin tanısında kullanılan ucuz ve mikroinvaziv bir işlemdir. Bununla birlikte, biyopsilerin % 40'ına kadarında sitoloji yetersiz gelebilir. Bu çalışma, tiroid nodüllerinin radyolojik özelliklerinin sitolojik yeterlilik oranına etkisini değerlendirmeyi amaçlamıştır.

Yöntemler: Kliniğimizde, 2016-2019 yılları arasında tiroid nodul İİAB'si yapılan hastalar bu retrospektif kohort çalışmada incelendi. Nodüllerin tanısal yeterlilik oranı ve radyolojik özellikleri (boyut, kistik komponent, kalsifikasyon içeriği, ekojenite, sınır özelliği) not edildi ve aralarındaki ilişki araştırıldı.

Bulgular: Toplam 525 hastada (%77 kadın, %23 erkek; ortalama yaş 53,3; yaş aralığı 14-87) 595 nodüle İİAB yapıldı. Nodüllerin ortalama çapı 20,1 mm (min: 4 mm; maks: 60 mm) idi. Biyopsilerin %25'inde tanısal yetersizlik saptandı. Makrokalsifikasyon içeren nodüllerde yeterlilik anlamlı olarak düşüktü (P=0,036). Nodüllerin yeterlilik oranları ile ekojenite, sınır özelliği, solid yapısı veya boyutu arasında anlamlı bir ilişki yoktu (her biri için P>0,05).

Sonuç: Bazı radyolojik özellikler, yetersiz örneklemenin habercisi olabilir. Bununla birlikte, radyolojik özelliklerin yanı sıra çeşitli dış faktörler de sitopatolojik yeterliliği etkiler. Bu nodüllerde ek teknikler gerekebilir.

Anahtar kelimeler: Tiroid nodülü, Ultrason, Biyopsi, Radyoloji

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Introduction

Fine needle aspiration biopsy (FNAB) of thyroid nodules is a microinvasive, cost-effective and safe procedure that is mostly performed on an outpatient basis. The Bethesda system for reporting thyroid cytopathology has been used to classify nodules since 2007 [1,2]. FNAB findings are reported based on the risk of malignancy using 6 general diagnostic categories according to Bethesda. These categories are as follows: I: Nondiagnostic; II: Benign; III: Atypia of Undetermined Significance or Follicular Lesion of Undetermined significance; IV: Follicular Neoplasm or Suspicious for a follicular Neoplasm; V: Suspicious for malignancy; VI: Malignant according to Bethesda classification.

Approximately 5-15% of detected nodules are surgically confirmed to be malignant. Thus, US-guided FNAB is recommended as standard care by all guidelines to differentiate malignant and benign thyroid nodules, since results significantly affect treatment. However, about 0.4–40.7% of FNA results are insufficient for diagnosis [3]. Ultrasound (US) guidance allows the needle to be imaged real-time within the lesion, providing accurate biopsy of nodules [4]. Factors affecting material adequacy may be associated with intrinsic factors of the thyroid nodules such as echogenicity, structure (presence of macro or microcystic component), size, calcification content, margin features. Adequacy is not solely affected by intrinsic factors, it also depends on some extrinsic factors such as the experience of the radiologist and cytopathologist, presence of an onsite cytopathologist, number of needle passes during biopsy, type and size of the biopsy needle, biopsy technique (aspiration or capillary technique), poor specimen fixation or presence of an additional liquid-based cytology affect adequacy [5].

In this study, we aimed to assess the effect of intrinsic features of thyroid nodules on cytological adequacy rate.

Materials and methods

This retrospective cohort study was approved by the Ethics Committee of Sisli Hamidiye Etfal Training and Research Hospital (Date: 04.12.2018; Number: 2193). The patients who underwent thyroid FNAB between 2016 and 2018 were reviewed. Intrinsic factors of the nodules were noted. Echogenicity of the nodules were classified into four groups as isoechogenic, hyperechogenic, hypoechogenic, heterogeneous. Structure of the nodules was classified as ‘’solid’’ and ‘’semisolid’’ according to predominant internal component. Nodules containing micro or macrocystic areas were classified as semisolid. Pure cystic nodules were excluded from the study. Calcification content were classified into three groups as ‘’no calcification’’, ‘’micro‘’ and ‘’macrocalcification’’. Nodules were divided into 4 groups according to size as ‘’<10mm’’, ‘’11-20mm’’, ‘’21-40mm’’, ‘’41-60mm’’. The largest diameter of the nodules was considered as size. Margin of the nodules were classified into three groups as ‘’smooth-distinct’’, ‘’macro lobulated,’’ ‘’micro lobulated’’ (or indistinct).

Biopsy procedures were performed by two radiologists (with 10 and 2 years of experience). Informed patient consents were obtained before the biopsies from all patients. All patients were questioned about anticoagulant medication usage and appropriate procedures were applied before the biopsy if the patient had been under medication. All biopsies were performed under US (Mindray, China) guidance with a 14 MHZ linear array transducer. Local anesthetic medication was not routinely used except of a few patients who had high anxiety. Biopsies were performed under aseptic precautions. Twenty-two, 23- or 27-gauge needles were used as necessary according to the size and depth of the nodules; and aspiration technique was used during biopsy. Two needle passes were performed for each nodule. After biopsy, specimens were fixed in liquid-based cytology solution according to advice of our cytopathologists. Rapid onsite adequacy assessment by a cytopathologist was not available in our institution. Biopsy specimens were assessed by different cytopathologists in the pathology department, considering the radiological features of the nodules.

Cytopathological results were classified into 6 groups according to Bethesda (National Cancer Institute, Fourth Thyroid FNAB Guideline Committee) classification system [1]. Diagnostic adequacy rates and radiological features (echogenicity, structure, size, calcification content, margin feature) of the nodules were noted and the relationship between diagnostic inadequacy and radiological features of the nodules was investigated retrospectively.

Statistical analysis

For statistical analysis, Statistical Package for the Social Sciences (SPSS) for Windows (Version 21.0, Chicago, SPSS Inc.) program was used. The Pearson Chi-square test was used to analyze the specimen adequacy ratio. A *P*-value of 0.05 or less was considered statistically significant.

Results

A total of 525 patients (77% female and 23% male; mean age 53.3; age range 14-87) had 595 FNABs in our institution. Of the all biopsies, 75% were reported as adequate while 25% were inadequate (Bethesda I).

Mean diameter of the nodules was 20.1 mm (min: 4mm; max: 60 mm). Of all, 50% of the nodules were solid in structure. Thirty-one percent (31%) were isoechogenic, 13% hyperechogenic, 32% hypoechogenic and 24% were heterogeneous. Ratios of nodules in size groups of ‘’<10mm’’, ‘’11-20mm’’, ‘’21-40mm’’, ‘’41-60mm’’ were 9%, 52%, 35% and 4% respectively. Seventy-five percent (75%) of the nodules did not contain calcification while 12% had micro and 13% had macrocalcifications. Eighty-five percent (85%) had smooth-distinct margins, while 11% had macro-lobulated and 4% had micro-lobulated (or irregular) margins.

Isoechogenic nodules were more likely, while hyperechogenic nodules were less likely to be insufficient; but no statistical significance was found between echogenicity and inadequacy (P=0.05). Those with macrocalcifications had a higher rate of inadequacy (P<0.05). There was no statistically significant relationship between inadequacy rates and cystic-solid structure, size or border features of the nodules (P>0.05). The relationships between radiological features of the nodules and inadequate diagnostic sampling are listed in Table 1. There were no significant procedure-related complications according to Cardiovascular and Interventional Radiology Society of Europe (CIRSE) guidelines [6].

Table 1: Influence of echogenicity, internal structure (solid proportion), size, calcification, and margins on cytological inadequacy

	Inadequate sample n (%)	Adequate sample n (%)	Total n (%)	*P*-value
Echogenicity				
Isoechogenic	58 (31.2)	128 (68.8)	186 (100.0)	0.051
Hyperechogenic	13 (16.7)	65 (83.3)	78 (100.0)	
Hypoechogenic	46 (24.1)	145 (75.9)	191 (100.0)	
Heterogenous	30 (21.4)	110 (78.6)	140 (100.0)	
Structure				
Solid	76 (25.5)	222 (74.5)	298 (100.0)	0.651
Semisolid	71 (23.9)	226 (76.1)	297 (100.0)	
Size				
<10mm	8 (14.3)	48 (85.7)	56 (100.0)	0.210
11-20mm	83 (27.0)	224 (73.0)	307 (100.0)	
21-40mm	52 (24.6)	159 (75.4)	211 (100.0)	
41-60mm	4 (19.0)	17 (81.0)	21 (100.0)	
Calcification				
No calcification	104 (23.2)	345 (76.8)	449 (100.0)	0.036
Microcalcification	16 (22.5)	55 (77.5)	71 (100.0)	
Macrocalcification	27 (36.0)	48 (64.0)	75 (100.0)	
Margin				
Smooth-distinctive	129 (25.5)	377 (74.5)	506 (100.0)	0.160
Macrolobulated	11 (16.2)	57 (83.8)	68 (100.0)	
Microlobulated-indistinctive	7 (33.3)	14 (66.7)	21 (100.0)	

Categorical variables were compared using Qui square test.

Discussion

US-guided FNAB of thyroid nodules are recommended by all guidelines to differentiate malignant nodules from benign ones for management of thyroid nodules [7-10]. However, inadequate results of US guided FNAB are reported in about 0.4-40.7% of biopsies [3]. US guidance decreased the inadequacy rate compared to palpation-guided biopsies due to selective targeting of specific nodules and real time sampling. Nevertheless, inadequacy rate in US-guided biopsy is also reported up to 40% [5]. Since the Italian Societies of Endocrinology and Pathology (SIAPEC-IAP) consensus statement recommends that non-diagnostic results should not exceed 20% of the reports, being aware of the factors affecting adequacy is particularly important for the operators who perform the biopsies [11]. In the current study we aimed to demonstrate the intrinsic factors that affect diagnostic adequacy for achieving a successful biopsy.

Many of the studies have reported that specimen adequacy is not dependent on the echogenicity of the biopsied nodule [4,15]. In contrary to these studies, some other studies have reported that hypoechogenicity has a negative effect on adequacy [13,16]. Hypoechogenic nodules are more likely fibrotic in nature, which makes needle movement harder during aspiration. There was no negative correlation between hypoechogenicity and inadequate sampling rate in our study. On the other hand, we have demonstrated that hyperechogenic nodules were more frequently diagnostic compared to hypoechogenic and heterogenous nodules.

FNAB of solid nodules are expected to be more frequently adequate compared to cystic ones due to cellularity [12-14]. On the other hand, cystic areas may be related to hemorrhage in semisolid nodules which cause blood contamination and more frequently inadequate cytology. However, in our study, there was no significant relationship between the nodule structure and inadequacy rates. This may be due to exclusion of pure cystic nodules from the study. We included the nodules which the solid component composed at least one third of the nodule volume.

According to some studies, frequency of nondiagnostic cytology increases in nodules larger than 3 cm and smaller than 5 mm [12]. Although sampling of large nodules is easier than smaller ones, cytopathological results may be nondiagnostic. Large nodules tend to comprise necrotic-cystic-acellular areas. On the other hand, some studies have reported that size does not affect adequacy of biopsies [13,14]. American Thyroid Association (ATA) guidelines recommend the 1 cm cut-off size for nodules that are highly suspicious, since smaller nodules yield inadequate results more frequently. Nevertheless, smaller nodules should be sampled in case of high suspicion of malignancy [7]. In the current study, 56 (9%) nodules were smaller than 10 mm. In contrast with the results in some of these studies, we demonstrated no significant relationship between nodule size and inadequacy rate in our study.

Presence of an intra-nodular macrocalcification increases the possibility of inadequate results regarding the coarse structure of the nodules and restriction of the needle movement during FNAB [17-19]. As opposed to this, according to Moon et al. [13] and Grani et al. [16], presence of calcification is not associated with inadequate cytology. Consistent with Yi et al. [17], we demonstrated that there was a negative correlation with macrocalcification and diagnostic adequacy rate. However, it was not the case for presence of microcalcification.

Although it is known that irregular margins in a nodule is most likely related to malignancy, we could not find any study reports which reveal the relationship between specimen adequacy and margin features. In our study, there was no significant relationship between margin features of the nodules and specimen adequacy, either.

There are many extrinsic factors affecting the adequacy rates in FNAB of thyroid nodules. It is reported in the literature that rapid onsite adequacy assessment of thyroid FNABs have yielded conflicting results. [20-22]. Some studies have reported that rapid onsite adequacy assessment of thyroid FNABs reduce the frequency of nondiagnostic aspirates and thereby avoid the need for a re-biopsy [20]. However, some have reported that rapid onsite adequacy assessment does not provide a significant increase in the diagnostic adequacy rate of aspirates [21]. Since rapid onsite adequacy assessment was not available in our institution, we performed all the biopsies without an onsite cytopathologist. We think that rapid onsite adequacy assessment would reduce the rate of inadequacy, but it would require more needle passes and prolong the procedure time.

The experience of the operator in FNAB is another extrinsic factor affecting diagnostic yield. In their study, Ghofrani et al. [23] reported that the experience of the operator is a determining factor. They have noted that inadequacy rates may significantly reduce from 13.0% to 4.5% by an experienced operator. Nevertheless, we were not able to compare diagnostic yield rates between both the experienced and less-experienced operators in our study due to lack of information about the performing operator for each biopsy.

In the reported studies, a wide range of needle sizes between 20-25 Gauge were frequently used for thyroid FNABs [15]. Thinner needles such as 25 and 27 G were suggested to increase the diagnostic adequacy rate [24]. In the current study, 22, 23 and 27 Gauge needle were used as necessary, according to the size and depth of the nodules. Since 27 G needles tend to bend and get obstructed quickly, we preferred such a thin needle in limited number of cases, mostly for semisolid nodules with a

prominent cystic component or nodules that were smaller than 10 mm. We could not compare the role of needle size since we used them randomly. In our experience, we agree that thinner needles provide a higher diagnostic yield due to less contamination with blood.

Most of the studies recommend at least three needle passes per nodule to increase diagnostic yield rate [5,15,25]. Due to busy schedule of our outpatient clinic and the prominent level of anxiety of the patients, we performed two needle passes per nodule. The adequacy rate in the current study was 25% which was slightly higher than the suggested level in some reports [11]. This result might be due to performing less than 3 needle passes in our study. We agree that increase in the number of needle passes will result in an increase in adequacy rate.

Limitations

The most important limitation in this study was its retrospective design. Further research is needed to analyze the effect of radiological features of the nodules with combining more optimal extrinsic factors to investigate its presumed relation to the adequacy rate in our clinic.

Conclusion

Some radiological features may be predictive of inadequate sampling. Macrocalcification content increased the frequency of inadequate cytological result. On the other hand, echogenicity, inner structure (solid vs cystic), size and margin features of the nodules did not affect the yield of adequate sampling rate. Nevertheless, varied intrinsic and extrinsic factors affect cytopathological adequacy. None of them alone is enough to have a high diagnostic sampling. Some additional methods may be required in these nodules such as sampling with higher number of needle passes and using thinner needles. Patients must be notified that their biopsy report might be concluded as inadequate sampling or nondiagnostic before the biopsy.

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