doi: 10.5505/abantmedj.2019.76258

Abant Tıp Dergisi

Özgün Makale / Cilt 8 Sayı 3 Yıl 2019

Abant Medical Journal

Original Article / Volume 8 Issue 3 Year 2019

Tiroid Nodüllerinin İnce İğne Aspirasyon Biyopsisinde İkili Enjektör Modelinin Geleneksel Teknik ile Histopatolojik Sonuçlarının Karşılaştırılması

A Comparison of The Histopathological Results of Thyroid Nodule Biopsy Applied with Ultrasound-Guided Traditional Technique Fine Needle Aspiration and A Novel Dual-Injector Model Fine Needle Aspiration

Çağlayan Çakır

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Öz

GİRİŞ ve AMAÇ: Çalışmamızda Ultrasonografi (USG) kılavuzluğunda geleneksel ince iğne aspirasyon biyopsisi (İİAB) ve yeni geliştirmiş olduğumuz ikili enjektör modeli ile İİAB işleminin başarı düzeyinin ölçülmesi çalışmamızın amacını oluşturmaktadır.

YÖNTEM ve GEREÇLER: Aralık 2017-Mayıs 2018 tarihleri arasında klinisyen istemiyle tarafımıza yönlendirilen tiroid nodülü olan hasta grubunda bilgisayar ortamında tasarladığımız ve 3 boyutlu yazıcıdan çıktısını aldığımız ikili enjektör modeliyle USG klavuzluğunda aynı anda iki iğne ile 130 nodülden (Grup 1) ince iğne aspirasyon biyopsisi yaptık. Alınan materyallerin histopatolojik sonuçlarını geleneksel yöntem olan tek iğne kullanılarak yine USG eşliğinde yapılan 169 (Grup 2) adet İİAB sonuçları ile istatistiksel olarak karşılaştırdık. Sitolojik tanılar Bethesda sınıflaması baz alınarak yapılmış olup olguların ultrasonografi bulguları belirlenen kriterler dahilinde kaydedilmiştir.

BULGULAR: Değerlendirilen olguların malign (pozitif)/benign (negatif) oranları, Grup 1 (4/99) ile Grup 2 (5/133) arasında farklı değildi (p= 0,581). Değerlendirmeye alınan Grup 1 olgularının %14,62 (19/130)'i yanlış, %85.38 (111/130)'u doğru, Grup 2 olgularının 12,43 (21/169)'ü yanlış, %87.57 (148/169)'si doğru, toplam %13,4 (40/299) yanlış, %86,6 (259/299)'i doğru bulunmuştur.

TARTIŞMA ve SONUÇ: Çalışmamızda ikili enjektör modeli kullanılarak yapılan tirod biyopsisi başarılı bir metod olarak bulunmuştur.

Anahtar Kelimeler: Tiroid, Aspirasyon biyopsisi, Tiroid nodülü

Abstract

INTRODUCTION: To compare the cytological aspects of traditional ultrasound-guided fine needle aspiration biopsy (FNAB) with the newly developed dual injector model, as the measurement of success.

METHODS: A total of 130 thyroid nodules (Group 1) were applied with ultrasound-guided fine needle aspiration biopsy with two needles at the same time. This technique was designed in a computer environment and a 3D printed dual injector model was applied to the patient group between December 2017-May 2018. The histopathological results of the obtained materials were statistically compared with the results of 169 (Group 2) thyroid nodule FNAB biopsies using a single needle, which is the ultrasound-guided traditional method. Cytological diagnoses were based on the Bethesda classification and ultrasonography findings of the cases were recorded within the specified criteria.

RESULTS: No difference was determined in the malignant (positive)/benign (negative) ratios of the evaluated cases in Group 1 (4/99) and Group 2 (5/133) (p = 0.581). In Group 1, the diagnosis was incorrect in 14.62% (19/130) and correct in 85.38% (111/130) of cases. In Group 2, the diagnosis was incorrect in 12.43 (21/169) and correct in 87.57% (148/169) of cases. For the whole sample, these rates were 13.4% (40/299) incorrect and 86.6% (259/299) correctly. No statistically significant difference was determined between the groups in respect of inadequate material and diagnostic material distribution in both groups. (p = 0.581).

DISCUSSION AND CONCLUSION: The results of this study showed succesful method in the results of biopsies made using the binary injector model that was developed in a computer.

Keywords: Thyroid, Aspiration biopsy, Thyroid nodules

INTRODUCTION

Thyroid nodules, which have been described as lesions that can be differentiated from normal thyroid tissue with radiological imaging, constitute an important clinical problem as they are frequently seen in daily practice. The purpose of diagnosis is to exclude malignancy. High resolution ultrasound is a cheap and effective imaging method used in diagnostic evaluation and can also be a guide in tissue sampling. With

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Geliş tarihi / Received: 09.11.2018 **Kabul tarihi / Accepted:** 10.10.2019 **Çıkar Çatışması / Conflict of Interest:** Yok / None

the current innovations of 3D printers, it is now possible to implement computerized drawings and designs, and in this way, we produced a new model to improve diagnostic rates and facilitate the process of FNAB. Ultrasound-guided FNAB is the gold standard for tissue sampling with the success rate reported to be 85-94% (1).

Using a newly-developed model, histopathologic sampling was made from different locations of the nodule at the same time. The aim of this study was to compare this new dual injector model with the traditional method in terms of cytological accuracy, from the results of a total of 299 patients with thyroid nodule.

METHODS

Innovations in computer technology are now widely available in both daily life and medical fields, with computerised designs implemented with 3D printers. The model presented in this study was designed in a computer environment for FNAB. It was designed by our clinical team and produced on 3D printer.

In the Radiology unit, the biopsy procedure made by one radiologist with 12 years of experience. In the traditional FNAB procedure, when the needle enters the nodule, the 5 ml injector is withdrawn with a pumping movement and the procedure is repeated 2 or 3 times. In the new model, 2 injector needles are entered into the nodule at the same time and the FNAB process is applied. The model combines two 5 ml injectors into a single instrument (Fig. 1). The tips of both injectors and pistons are within this model, so the piston movements were made at the same time and the reverse motion was performed with a single biopsy. In all cases, high resolution thyroid US was performed prior to the biopsy procedure.

Patients with a thyroid nodule or thyroid nodules were included in this study. All thyroid nodules were evaluated in respect of size, internal structure, contour structure, and

***Figure 1**. The model combines two 5 ml injectors into a single instrument*

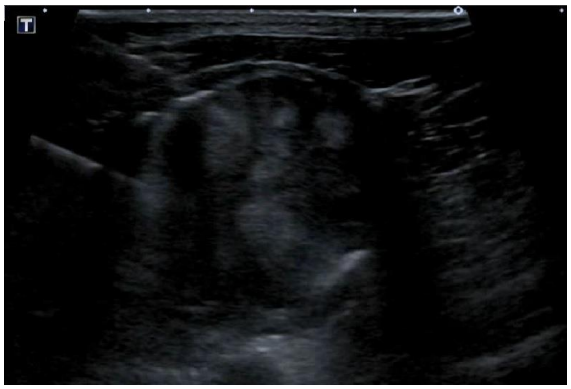

***Figure 2.** Image showing the hyperechoic solid nodule in the right lobe of the thyroid gland and the appearance of two needles inside. The pathology was reported as benign Bethesda 2.*

microcalcification. The three dimensions of nodules were also measured, with the largest diameter considered in the evaluation. The inner structure of the nodule was classified as solid or cystic components, with particular attention paid to the solid part of semi-solid nodules. Only nodules identified as cystic rarities were excluded from the research.

The echogenicity of the nodule was reported as hyperechoic, isoechoic or hypoechoic based on normal thyroid tissue. Microcalcifications were classified as either present or absent in the thyroid nodules. If the patient was being

followed up for a diagnosis of multinodular goiter and the clinician had not specified a particular nodule, FNAB was applied to the largest nodule. Before the biopsy, patients were questioned in detail in terms of contraindications (use of anticoagulant etc.).

Informed consent was obtained from all patients before the procedure. The biopsies were taken under US guidance (Toshiba Aplio 500, Japan) using a 7.5 MHz linear probe, covered with a sterile sheath and 23G needles and 5 ml injectors. The area to be processed was cleaned at least twice with povidon-iodine. The biopsy procedure was performed with the patient in the supine position and the neck in hyperextension.

Group 2 patients were applied with single needle FNAB under US guidance. When the needle tip was observed to be in the nodule, negative pressure was applied with a 5 ml injector. The needle was moved back and forth on the same axis at least 20-25 times. After the final application of negative pressure, the needle was withdrawn at the end of the process. This procedure was repeated twice in each patient.

Group 1 patients were applied with FNAB using the newly-designed model. Two 5 ml injectors were combined in this model. When the needle tips were observed to be in the nodule, negative pressure was applied to the 5 ml injectors. The pins were moved back and forth at least 20-25 times on the same axis. This procedure was performed once only in each patient. (Fig. 2)

In both methods, the material obtained on the needles was sprayed into mini-tubes containing alcohol, and the needles were placed in the same tubes and sent to the pathology unit. After the biopsy, hemostasis was achieved.

The results of the biopsy were evluated as unsuccessful when insufficient material was obtained, and correct positive and negative cases were considered successful.

Statistical analyses of the data obtained in the study were made using NCSS 11 software (Number Cruncher Statistical System, 2016 Statistical Software).

Continuous variables were stated as mean±standard deviation (SD) and median values, and categorical variables were stated as number (n) and percentage (%). Conformity of the continuous variables to normal distribution was tested using the Kolmogorov Smirnov test. Relationships between categorical data were examined using Chi-square analysis and the Fisher Freeman Halton test where appropriate.

Two groups of independent variables with normal distribution were compared using the Independent Samples t-test, and the Mann-Whitney U test was applied to two groups of independent variables not showing normal distribution. A value of $p<0.05$ was considered statistically significant.

RESULTS

We obtained informed consent forms from all patients for the FNAB procedure. The ratio of male / female cases was 12.8% (34/265) in the whole study sample, as 5.8% (11/190) in the new dual injector model (Group 1) and 15.7% (23/146) in the traditional method (Group 2). The mean age of the patients was 51.5 ± 12.3 years in the whole group; 51.71 ± 12.68 years in Group 1 and 51.38 ± 12.06 years in Group 2, with no statsitically significant difference determined between the groups ($p>0.05$) The mean nodule size was determined as 18.85 ± 6.25 mm in the whole group, 21.83 ± 5.4 mm in Group 1 and 17.25 ± 6.74 mm in Group 2. The median nodule size was determined to be statistically significantly greater in Group 1, applied with the standard method compared to Group 2 with the double injector model ($p <0.0001$) (Table 1).

The distribution of echogenicity change was significant in both groups of patients ($p = 0.013$).

Table 1*. To compare the age and size of traditional fine needle aspiration biopsy (FNAB) with the newly developed dual injector model*

	Traditional fine needle aspiration (n=169)	Newly developed dual injector model (n=130)	
	Ort.+SS Med. (Min.-Maks.)	Ort.+SS Med. (Min.-Maks.)	p
Age	51,38±12,06 51- (24-80)	51,71±12,68 51- (20-79)	0,819*
Size (mm)	17,25±6,74 16- (8-45)	21,83±5,4 22- (8-36)	<0,0001**

* Independent Sample t Test **Mann Whitney U Test

When the distribution of the parameters was examined, 55 (65.48%) cases were hypoechoic and 14 (77.78%) isoechoic in Group 2 (traditional method thyroid FNAB). No statistically significant differences were determined in respect of the other variables of microcalcification and solid / semisolid distribution (p> 0.05) (Table 2).

Table 2. *To compare the variables of traditional fine needle aspiration biopsy (FNAB) with the newly developed dual injector model*

		Traditional fine needle aspiration	Newly developed dual injector model	
		N(%)	N(%)	p
Gender	Male	23(67,65)	11(32,35)	0,165
	Female	146(55,09)	119(44,91)	
Echogenicity	hypoechoic	55(65,48)	29(34,52)	0,013
	hyperechoic	100(50,76)	97(49,24)	
	isoechoic	14(77,78)	4(22,22)	
Microcal-cifications	-	136(54,4)	114(45,6)	0,095
	+	33(67,35)	16(32,65)	
Solid/Semi-solid	solid	76(62,81)	45(37,19)	0,071
	semisolid	93(52,25)	85(47,75)	
Bethesda	1	21(52,5)	19(47,5)	0,974**
	2	133(57,33)	99(42,67)	
	3	6(50)	6(50)	
	4	4(66,67)	2(33,33)	
	5	4(57,14)	3(42,86)	
	6	1(50)	1(50)	

**Ki-Kare* Analysis ***Fisher Freeman Halton Test*

(malignant) in 4 cases, Grade 4, (Hürthle cell-oncocytic type) in 4 cases, Grade 3 (atypical) in 3 cases, and Grade 2 (benign) in 99 cases. A total of 11 samples of blood components and 8 samples of materials were evaluated as inadequate.

In Group 2, the cytological evaluation according to the Bethesda classification was Grade 5-6 (malignant) in 5 cases, Grade 4, (Hürthle cell-oncocytic type) in 4 cases, Grade 3 (atypical) in 6 cases, and Grade 2 (benign) in 133 cases. A total of 11 samples of blood components and 10 samples of materials were evaluated as inadequate.

Malignant (positive) / benign (negative) ratios of the evaluated cases showed no difference between Group 1 (4/99) and Group 2 (5/133) (p = 0.581). In Group 1, diagnosis was incorrect in 14.62% (19/130) of cases and correct in 85.38% (111/130). In Group 2, diagnosis was incorrect in 12.43% (21/169) of cases and correct in 87.57% (148/169). In the total of the two groups, 13.4% (40/299) of diagnoses were incorrect and 86.6% (259/299) were found to be correct. There was no significant difference between the groups in respect of inadequate material distribution (p = 0.581). Complications related to the procedure were not seen in either group.

DISCUSSION

Thyroid nodule is a common endocrine pathology both in Turkey and throughout the world. The prevalence of thyroid nodule has been reported as 50% in postmortem examinations and as 50-70% using high resolution US (2). The main clinical problem of thyroid nodules is to exclude malignancies, as most patients are asymptomatic. In the United States, the annual incidence of thyroid malignancies has been steadily increasing over the years, reaching 14.3 per 100,000 in 2009 (3).

There are important current guidelines on the approach to thyroid nodules, and these published guidelines are followed as the main

source in almost all countries worldwide. The primary source was published by the American Thyroid Association (ATA) in 2006 and revised in 2015. The guidelines of the American Association of Clinical Endocrinologists (AACE), the Associazione Medici Endocrinologi (AME) and the American College of Endocrinology (ACE) were updated in 2016 (4).

Thyroid nodule management includes high resolution ultrasonography, sensitive thyrotropin (thyroid stimulating hormone), FNAB and clinical findings.

High resolution ultrasonography of the thyroid gland is used to assess the presence, size, characterization, composition (solid / semisolid / cystic structure) of a nodular structure and its relation to the thyroid gland. When a nodule is detected, assessment is made of the malignancy criteria of microcalcification, a predominantly solid internal structure, irregular contours, hypoechoic internal structure, and anterior-posterior diameter > transverse diameter. Nodule count, size, and rapid growth are non-specific features for thyroid malignancies (5).

The most specific US finding for thyroid cancer is nodule microcalcification. Primary thyroid carcinomas occur in 29%-59% of undilated and especially papillary thyroid carcinomas (6-8). In the current study, the majority of malignant cases (77.7%) were papillary carcinoma. Microcalcification was observed on US in 55.5% of the nodules reported as papillary carcinoma. Of the malignant nodules, 88.8% were reported as hypoechoic, which was similar to findings in literature.

In the current study, the nodule size of the malignant cases was measured as 12-25 mm, with no statistically significant correlation determined between nodule size and malignancy positive results ($p > 0.05$). The cancer risk has been shown to be similar in studies of solitary thyroid nodules and multinodular goiters (9,10). The majority of thyroid cancers (82-91%) are solid (11-15). In a Mayo Clinic study of 360 cases, malignancy was determined in 88% of lesions that were solid or minimally cystic (<5% cyst), in 9% of leasions that were <50% cystic, and in 3% of those that were >50% cystic (16). In the current study, all the nodules reported as papillary carcinoma were solid.

FNAB is the most valuable current method for the differentiation of benign / malignant thyroid nodules (17). Surgical planning and treatment are performed according to FNAB cytology results and accurate results have been shown to decrease the number of operations and increase the malignancy rates in thyroidectomy plaques (18).

When FNAB is applied under US guidance, the diagnosis criteria and false negative cytology rates have been shown to be lower compared to FNAB with palpation (19, 20). When the FNAB procedure is performed in the thyroid nodules, usually needle aspiration and core biopsy studies of different thicknesses are available. There are no different models or methods used outside these. It has been reported in literature that thyroid core-needle biopsy provides a higher level of diagnostic ability compared to the conventional FNAB method (21). However, greater levels of pain are felt in trucut biopsy than in FNAB procedure and there is increasing concern about the seriousness of procedure-related complications (21, 22).

Newly-developed diagnostic and treatment methods in the health sector continue to facilitate the fight against diseases. With the advances in computer technology, it is now possible to create new models that can solve difficult situations and put them into daily practice using 3D printers. In daily interventional radiology practice such as thyroid FNAB, technological advances have made it possible to increase the number of diagnoses, which has previously been a laborious and time-consuming process, and decrease operating times. The new

model described in this study was designed in a computer environment and made from Acrylonitrile Butadiene Styrene (ABS) material, which is currently used for Lego ®, using a 3D printer. With FNAB using the dual injector system, described here for the first time in literature, it was considered that higher rates of complications could be diagnosed, and thus it was aimed to reduce gross complications which can develop with the use of conventional FNAB and thyroid thick needle biopsy.

Two important factors for the success of FNAB are the availability of an adequate sample and the experience of the cytopathologist (6). With the newly-developed model, multiple samples were taken from different locations of the nodule with 23 G needles. Thus, the diagnosis rate is predicted to be higher than in the conventional method. In addition, the biopsy procedure was shorter than the conventional method. The proportion of the nodule obtained was 87.6% in Group 2 with the standard method and 85.4% in Group 1 with the new model, which was consistent with rates of 77% - 96% reported in literature (4). Biopsy failure may be due to inadequate material intake, patient position and immobilization of the nodule, insufficient negative pressure and inadequate movement of the long axes of the needles. False negative and false positive rates have been used to evaluate the success of FNAB. Some studies have reported a FNAB false negative rate of 0-1% and false positive rate of <5% [23]. It has also been shown that 99% of nodules, which are benign at the end-stage of FNAB, remain benign within 10 years (24).

In the current study, thyroid nodules were more common in females than in males with thyroid malignancy, which was similar to literature (25). There was no relationship between age and gender and the FNAB results in both groups ($p > 0.05$). In both groups, nodules of Bethesda Grade 5 and 6 were surgically removed as a result of FNAB, and 7 of the total pathological malignancies were reported as papillary carcinoma, 1 as follicular neoplasm, and 1 as Hurthle cell neoplasm. These rates were 3.07% in Group 1, 2.95% in Group 2, and 3.01% in the whole group. All Bethesda Grade 4 nodules were reported to be Hürthle cell (oncocytic type), and these were found in Group 1 at 1.53%, in Group 2 at 2.36% and in total at 2.01%. Bethesda Grade 3 atypical nodules were determined at 4.60% in Group 1, 3.55% in Group 2, and 4.01% in total. The rates of benign thyroid nodule lesion, defined as Bethesda Grade 2, were slightly higher in Group 1 (76.15%), Group 2 (78.69%) and in total (77.59%) compared to rates previously reported in literature (46%-83%).

In both groups, the great majority of the pathology results were reported as benign follicular nodule, cystic degenerated nodule, and lymphocytic thyroiditis. These ratios suggested that the indication for FNAB in our hospital is sometimes unnecessary. As mentioned in the guidelines, unnecessary operations can be avoided by performing benign / malignant differentiation with FNAB and the surgical technique should be selected according to the Bethesda pathology classification as the result of biopsy.

The distance between the two needles is at least 0,5 cm in the newly-developed model. Therfore, it can be used larger than 1 cm size in nodules. The currently increasing use of FNAB is due to increased sensitivity and specificity rates and low false positive and false negative results. This is supported by the results of this FNAB series, using the newly-developed dual injector model.

The success rate of the new model was seen to be similar to that of the traditional method, with no statistically significant difference. In thyroid gland FNAB, it can be considered that the newly developed model, using more nodules and needles at different thicknesses may increase the success rate significantly.

CONCLUSION

New studies using this design and development may be able to perform stylographic sampling from axillary, or inguinally located lymphadenopathies. There may be some advantages compared to conventional methods even in benign and malignant breast lesions.

Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Acknowledgments

The authors declared that this study has received no financial support.

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