Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2022;47(4):1471-1476
DOI: 10.17826/cumj.1152618

ARAŞTIRMA / RESEARCH

Comparison of thyroid fine needle aspiration cytology results before and during the COVID-19 pandemic: the impact of the pandemic

COVID-19 pandemisi öncesinde ve sırasında tiroid ince iğne aspirasyon sitolojisi sonuçlarının karşılaştırılması: pandeminin etkisi

Süleyman Altıntaş[1], Mehmet Bayrak[2]

[1]Health Sciences University, Adana City Training and Research Hospital, Pathology Clinic, Adana, Turkey
[2]Private Middle East Adana Hospital, General Surgery, Adana, Turkey

Cukurova Medical Journal 2022;47(4):1471-1476

Abstract

Purpose: The aim of this study was to compare the Bethesda classification to report the distribution of thyroid cytology diagnostic categories and total thyroid fine needle aspiration cytology numbers before and during the pandemic.

Materials and Methods: This study was planned in two phases: (1) before the pandemic, from March 15, 2018, and 29 February 2020, and during the pandemic period, from 1 March 2020 to 12 March 2022. Each period consisted of 24 months. The total number of thyroid fine needle aspiration cytology performed before the pandemic and during the pandemic dates and histopathological data were obtained from the hospital database.

Results: 432 thyroid fine needle aspiration biopsies were performed in the pre-pandemic period and 351 during the pandemic. There was no significant difference considering age and gender in patients who underwent thyroid fine needle aspiration cytology before and during the pandemic. According to the Bethesda classification, those who were benign were 70.8% (n:306) and 59.0% (n:207) respectively before pandemia and during the pandemia. According to the Bethesda classification, malignant lesions were 4.4%(n:19), and 9.1%(n:32) before and during the pandemia, respectively. During the pandemic, malignant lesions were detected significantly more than before the pandemic.

Conclusion: Malignant lesions were detected significantly more in the thyroid fine needle aspiration cytology results according to the Bethesda classification during the pandemic period compared to before the pandemic period.

Keywords:. Thyroid FNA, Bethesda classification, COVID-19

Öz

Amaç: Bu çalışmanın amacı pandemi öncesi ve pandemi sırasında tiroid sitolojisi tanı kategorilerinin dağılımını ve toplam tiroid ince iğne aspirasyon sitoloji sayılarını Bethesda sınıflaması kullanılarak karşılaştırmaktır.

Gereç ve Yöntem: Bu çalışma iki dönem olarak planlanmıştır: (1) pandemi öncesi 15 Mart 2018 -29 Şubat 2020; (2) pandemi dönemi ise 1 Mart 2020-12 Mart 2022 tarihlerini içermekte idi. Her dönem 24 aydan oluşuyordu. Pandemi öncesi ve pandemi döneminde yapılan toplam tiroid ince iğne aspirasyon sitolojisi sayısı ve histopatolojik veriler hastane veri tabanından elde edildi.

Bulgular: Pandemi öncesi dönemde 432, pandemi sırasında 351 tiroid ince iğne aspirasyon biyopsisi yapıldı. Pandemi öncesi ve pandemi sırasında tiroid ince iğne aspirasyon sitolojisi yapılan hastalarda yaş ve cinsiyet açısından anlamlı bir fark yok idi. Bethesda sınıflamasına göre pandemi öncesi ve pandemi sırasında benign sitolojiler sırasıyla %70.8 (n:306) ve %59,0 (n:207) idi. Bethesda sınıflamasına göre, malign lezyonlar pandemi öncesi ve pandemi sırasında sırasıyla %4.4(n:19) ve %9.1(n:32) idi. Pandemi sırasında, pandemi öncesine göre anlamlı olarak daha çok malign lezyon tespit edildi.

Sonuç: Pandemi döneminde, pandemi öncesi döneme göre Bethesda sınıflamasına göre tiroid ince iğne aspirasyon sitolojisi sonuçlarında malign lezyonlar anlamlı olarak daha fazla saptandı.

Anahtar kelimeler: Tiroid FNA, Bethesda sınıflaması, COVID-19

Yazışma Adresi/Address for Correspondence: Dr. Süleyman Altıntaş, Health Sciences University, Adana City Training and Research Hospital, Pathology Clinic, Adana, Turkey E-mail: suleymanveysmn@yahoo.com
Geliş tarihi/Received: 01.07.2022 Kabul tarihi/Accepted: 19.08.2022

INTRODUCTION

The restrictions due to the COVID 19 pandemic have had a great impact on our healthcare system. Lockdown and restrictions resulted in the delay of non-emergent elective medical and operational processes, including fine needle aspiration (FNA) cytology for thyroid nodules[1,2]. The approach to thyroid nodules should be multidisciplinary, and communication between endocrinologists and pathologists is essential[3]. When FNA cytology of nodules with high-risk ultrasonographic features is requested by the endocrinologist, diagnostic technical workup performed by experienced cytopathologists is of great importance. On the other hand, if thyroid FNA requests are not performed properly, it causes unnecessary thyroid surgeries and reduces diagnostic efficiency[4,5]. To reduce the number of unnecessary FNAs, especially for nodules with low-risk ultrasonographic characteristics, new guidelines have reviewed and established criteria for performing FNAs for the handling of thyroid nodules [6,7]. However, this is not always possible in clinical routine application. A few studies have been conducted by American and European endocrinologists to determine the criteria for requesting FNA, and as a result of these studies, fewer rules than generally accepted recommendations have been requested for FNA[8,9]. Unnecessary FNAs can be safely delayed during the COVID 19 pandemic, as well as because aspirating material poses a risk of COVID 19 transmission to personnel. In such a critical scenario, radiologists and cytopathologists do not routinely address FNA because they have to minimize contact with patients and reliably prevent the infection potential of the fresh specimen[10,11].

Ultrasonography-guided thyroid FNAs were performed by an experienced interventional radiologist in Private Ortadogu Hospital located in Adana, according to the latest thyroid FNA trends. Patients were referred from the endocrinologist and general surgery department at the Hospital and other nearby community hospitals.

This study aims to reveal whether the COVID 19 pandemia has altered our FNA experience for thyroid nodules. For this purpose, we compared the Bethesda system for reporting thyroid cytology diagnostic categories distribution and total FNA numbers before and during the pandemic. We also investigated whether our study complied with the FNA guideline criteria of FNAs, especially from February 2020 to March 2022 time frame and whether FNA for high-risk patients was performed by our routine clinical practice. We predict that this study will contribute to the literature in the development of clinical and diagnostic guidelines on performing thyroid FNA in a crisis scenario similar to COVID-19.

MATERIALS AND METHODS

The present cohort was approved by the Cukurova University Clinical Ethical Board with reference number 121, 8 April 2022. All features of the study were held concerning the principles of the Declaration of Helsinki (64th, 2013). After fully explaining the purpose and content of the procedure, the consent form was obtained from each patient. This cohort was retrospective in nature. The study was held in Adana Private Ortadogu Hospital.

Sample

The total number of thyroid FNA performed in the pre-pandemic and during the pandemic dates and cytopathological data were obtained from the hospital database. This study was planned in two phases: (1) before the pandemic, from 15 March 2018, and 29 February 2020, and during the pandemic period, from 1 March 2020 to 12 March 2022. Each period consisted of 24 months. Inclusion criteria consisted of 17 years of age and older patients of both genders, new and non-diagnosed patients. Exclusion criteria were patients presenting with thyrotoxicosis and/or hypothyroidism (n: 17) and patients with coagulopathy disorders (n: 4). Before and during the pandemia 432 and 351 US-guided FNA were applied respectively.

Procedure

Ultrasonography-guided FNA was performed by two interventional radiologists. Generally, before the pandemic thyroid, FNAs were performed from each nodule, if possible, using the Zajdela procedure (with no suction) to prevent contamination of blood elements. Before the pandemia, air-dried smears were examined with hematoxylin-eosin stain. However, when the pandemic period began, we gave up the air drying technic of ethanol fixation because the air drying slides can generate aerosols and their droplets can carry the viable and transferable virus. Instead, a rapid on-site inspection method was used when certainly needed, choosing immediate methanol fixation. PAP dye was used to examine the fixed

smears. All cytopathologists and technicians were wearing masks and used face protection shields. All thyroid FNAs was classified according to the Bethesda system for thyroid diagnostic category.

The Bethesda System initially founded a standardized reporting framework for thyroid fine needle aspiration samples with a limited number of diagnostic categories. Using The Bethesda System, cytopathologists can convey their comments to the referring physician in concise, clear, and clinically beneficial terms The Bethesda Thyroid Cytopathology Reporting System has accepted a standard, category-based reporting framework for thyroid fine needle aspiration samples. The 2017 review states that each thyroid FNA record must start with one of six diagnostic categories whose names have stayed unaltered since they were first subjected: (i) non-diagnostic or inadequate; (ii) benign; (iii) atypia of indeterminate significance or follicular lesion of indeterminate significance; (iv) follicular neoplasm or a suspected follicular neoplasm; (v) suspicion of malignancy; and (vi) malignant[12-13].

Statistical analysis

Statistical analysis was performed using SPSS software (Version 25.0, SPSS Inc., Chicago, IL, USA). The age was compared by the use of the Student t-test depending on parametric values; respectively. The categorical variables between the groups were analyzed by using Fisher's exact test. The level for statistical significance was predetermined at $p < 0.05$.

To identify trends in FNA demands for low-risk and high-risk, clinical, and ultrasonographic thyroid nodules, we assessed the proportions of benign, suspected malignancy, and malignant fine needle aspirations detected during the cohort period. These Bethesda systems diagnostic categories show a sufficiently low (benign) and high (suspected malignancy and malignant) risk of malignancy and can be considered an indicator.

When we calculate the power with a 95% confidence interval retrospectively according to benign results, the power of the study was found to be 93%. On the other hand, as we calculate the power with a 95% confidence interval retrospectively according to the malignant results, the power of the study was determined as 74% [7,14].

RESULTS

All FNA and Bethesda classifications before and during the pandemic are shown in Table 1. From 15 March 2018, and 29 February 20201, 432 FNAs were performed before the pandemic. During the pandemic period, from March 2020 to 12 March 2022, the total count of FNAs was 351. The mean age of the patients before and during the pandemic was 46.6±14.9, and 48.2±14.4 respectively. Sex distribution of female and male before the pandemic and during the pandemic were 51.6%(n:223) 49.3%(n:173); 48.4%(n:209) 50.7%(n:178), respectively. There was no significant difference considering age and gender in patients who underwent FNA before and during the pandemia. Nondiagnostic or unsatisfactory results before and during pandemic were 12.7%(n:55), 12.0% (n:42) respectively. There was no significant association (p:0.416). According to the thyroid FNA results, the rates of benign and malignant changed before and during the pandemic. Those who were benign were 70.8% (n:306) and 59.0% (n:207) respectively before pandemia and during the pandemia (p:0.001).

Benign diagnoses include colloidal nodular goiter, colloidal nodular goiter with cystic changes, Hashimoto thyroiditis, lymphocytic thyroiditis, de Quervain thyroiditis, and hyperplastic thyroid nodules were shown in Table 1and statistically no significant correlation was detected during the pandemic and before pandemic period.

There was no significant association in terms of atypia of undetermined significance or follicular lesion of undetermined significance before and during the pandemia. There was no significant relation for follicular neoplasm or suspected follicular neoplasm before and during the pandemic (p:0.056).

According to the Bethesda classification, malignant lesions were 4.4%(n:19), and 9.1%(n:32) before and during the pandemia, respectively. During the pandemia, malignant lesions were detected significantly more than before the pandemia (p:0.009). Malignant conditions consisting of papillary carcinoma, medullary carcinoma, anaplastic carcinoma, and lymphoma were shown in table 11and statistically no significant associations were detected between during the pandemic and before the pandemic period.

Table 1. Patients characteristics and Bethesda classifications before and during the pandemic period

	Before pandemic		During pandemic		p
Patient number	432		351		
Age	46.6±14.9		48.2±14.4		* 0.133
	%	n	%	n	
Gender					
Female	51.6	223	49.3	173	#0.519
Male	48.4	209	50.7	178	
I. Nondiagnostic or unsatisfactory	12.7	55	12.0	42	#0.416
II. Benign	70.8	306	59.0	207	#0.001
Colloidal nodular goiter	26.9	116	21.9	77	#0.114
Colloidal nodular goiter with cystic changes	28.9	125	28.0	99	#0.874
Hashimoto thyroiditis	6.9	30	4.0	14	#0.086
Lymphocytic thyroiditis	5	21	3	13	#0.539
De Quervain thyroiditis	1.9	8	1.1	4	#0.562
Hyperplastic thyroid nodules	1.4	6	0.0	0	#0.036
III. Atypia of undetermined significance or follicular lesion of undetermined significance	3.9	17	7.1	25	#0.056
IV. Follicular neoplasm or suspicious for a follicular neoplasm	6.0	26	8.8	31	#0.166
Follicular neoplasm	4.9	21	8.0	28	#0.077
Hurtle cell neoplasm	1.2	5	0.8	3	#0.737
V.Suspicious for malignancy	2.1	9	4.0	14	#0.138
VI.Malignant	4.4	19	9.1	32	#0.009
Papillary carcinoma	2.1	9	4.0	14	#0.138
Medullary carcinoma	1.2	5	3.1	11	#0.073
Anaplastic carcinoma	1.2	5	1.1	4	#1.000
Lymphoma	0.0	0	0.9	3	#0.090

*Student test, # Fisher's exact test

DISCUSSION

In this cohort, FNA numbers and the Bethesda system were compared before pandemia and during the pandemia. FNA plays an important role in determining whether there is a presence of cancer in the detected thyroid nodule. Generally, FNA is performed by interventional radiologists or interventional cytopathologists, by ultrasonography-guided. Because it is performed with ultrasonography-guided, it is important in terms of being cost-effective, saving time, and reducing inadequate or non-diagnostic samples. US-guided FNA establishes a better specimen of smaller and multiple nodules than free-hand FNA[15-18].

Clinical guidelines for the management of European endocrine conditions during COVID-19 and the US endocrinology division of Phoenix Veteran Affairs Healthcare Management have made it clear that FNA of most thyroid nodules can be safely delayed. Although many healthcare professionals could not provide adequate healthcare service during the pandemic process, our clinic continued to provide diagnostic support throughout the pandemic[1,2].

The number of FNAs during the pandemic was slightly lesser than before the pandemic. In a study conducted by Palladino Raffaele et al., they stated that the number of FNA procedures decreased rapidly during the pandemic period [19]. In addition, other recent studies have also revealed that the number of FNA has decreased significantly during the COVID-19 pandemic[20,21]. Diagnosis and treatment support continued in our country, as no restrictions were imposed on those who had an appointment at the hospital even during the lockdown period.

Benign FNAs were significantly less during the pandemic period than the before pandemic period. Whereas, during the pandemic period, malignant FNA was higher than before the pandemic period (table 1). In the study of Rafaella et al., the number of FNA detected cancer was statistically higher during

the pandemic compared to the before pandemic period [19]. Consequently, during the pandemic period, FNAs requests were higher in cases at high cancer risk, consisting of cases with breast masses, than in cases with thyroid nodules [22].

During the pandemic, stringent procedures suggested by local healthcare institutions were performed in our clinic. Each patient undergoing FNA was investigated for COVID-19 symptoms. Temperature measurements were taken for each patient in the waiting room. Those who were positive and suspicious according to the rapid serology test were referred to the infection unit. Face masks and hand disinfection with hydroalcoholic solutions were required throughout the entire procedure.

Inadequate or unsatisfactory samples were not significantly different before and during the pandemic. (p:0.416). In one study, it was determined that inadequate or unsatisfactory examples were lower before the pandemic period[19]. This condition may have resulted from the application of FNA as an on-site application during the pandemic period.

The COVID-19 pandemic has brought about many changes in our personal and professional lives. This study showed that during the pandemic period, endocrinologists refer to higher-risk nodules for FNA. Despite protocols developed to prevent the outspread of COVID-19 infection, interventional radiologists and cytopathologists continued to accomplish thyroid FNAs.

One of the limitations of this study was retrospective in nature. Another limitation could be a multicentric study rather than a single hospital. Other limitation could be the number of cases included in the study.

In this cohort, benign cytopathologic results were significantly higher in cases with thyroid FNA before the pandemic compared during the pandemic period. Although the thyroid FNA numbers were similar, malignant lesions were detected at a significantly higher rate during the pandemic period than before the pandemic period. This may be due to endocrinologists delaying low-risk patients for FNA during the pandemic. We consider that this study will contribute to the literature in the development of clinical and diagnostic guidelines for thyroid FNA by endocrinologists and cytopathologists in a crisis scenario.

Yazar Katkıları: Çalışma konsepti/Tasarımı: SA, MB; Veri toplama: SA, MB; Veri analizi ve yorumlama: SA, MB; Yazı taslağı: SA, MB; İçeriğin eleştirel incelenmesi: SA, MB; Son onay ve sorumluluk: SA, MB; Teknik ve malzeme desteği: SA, MB; Süpervizyon: SA, MB; Fon sağlama (mevcut ise): yok.
Etik Onay: Bu çalışma için Çukurova Üniversitesi Tıp Fakültesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulundan 08.04.2022 tarih ve 121/53 sayılı kararı ile etik onay alınmıştır.
Hakem Değerlendirmesi: Dış bağımsız.
Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.
Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.

Author Contributions: Concept/Design : SA, MB; Data acquisition: SA, MB; Data analysis and interpretation: SA, MB; Drafting manuscript: SA, MB; Critical revision of manuscript: SA, MB; Final approval and accountability: SA, MB; Technical or material support: SA, MB; Supervision: SA, MB; Securing funding (if available): n/a.
Ethical Approval: Ethical approval was obtained for this study from the Ethics Committee of Non-Interventional Clinical Trials of the Faculty of Medicine of Çukurova University with the decision dated 08.04.2022 and numbered 121/53.
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support

REFERENCES

1. Li M, Marquez RC, Vinales KL, Reaven PD, Behari G, Dildeep Aet al. Considerations for thyroid fine needle aspiration biopsies during the covid-19 pandemic. Clin Thyroidol. 2020;32:156–58.
2. Vrachimis A, Iakovou I, Giannoula E, Giovanella L.. Endocrinology in the time of covid-19: management of thyroid nodules and cancer. Eur J Endocrinol. 2020;183:41-8.
3. Poller DN, Johnson SJ, Bongiovanni M. Measures to reduce diagnostic error and improve clinical decision making in thyroid FNA aspiration cytology: a proposed framework. Cancer Cytopathol. 2020;128:917-27.
4. Russ G, Bonnema SJ, Erdogan MF, Durante C, Ngu R, Leenhardt L. European Thyroid Association Guidelines for Ultrasound Malignancy Risk Stratification of Thyroid Nodules in Adults: The EU-TIRADS. Eur Thyroid J. 2017;6:225-37.
5. Lee YK, Park KH, Song YD, Youk T, Nam JY, Song SO et al. Changes in the diagnostic efficiency of thyroid fine-needle aspiration biopsy during the era of increased thyroid cancer screening in Korea. Cancer Res Treat. 2019;51:1430–6.
6. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid. 2016;26:1-133..
7. Peng JY, Pan FS, Wang W, Wang Z, Shan QY, Lin JH et al.. Malignancy risk stratification and FNA recommendations for thyroid nodules: A comparison of ACR TI-RADS, AACE/ACE/AME and ATA guidelines. Am J Otolaryngol. 2020;41:102625.

8. Burch HB, Burman KD, Cooper DS, Hennessey JV, Vietor NO. A 2015 survey of clinical practice patterns in the management of thyroid nodules. J Clin Endocrinol Metab. 2016;101:2853-62.
9. Negro R, Attanasio R, Grimaldi F, Frasoldati A, Guglielmi R, Papini E. A 2016 Italian survey about guidelines and clinical management of thyroid nodules. Eur Thyroid J. 2017;6:75–81.
10. Bellevicine C, Vigliar E, Troncone G.. Thyroid FNA in the time of coronavirus: the interventional cytopathologist point of view. Cancer Cytopathol. 2020;128:589.
11. Troncone G. Thyroid cytology in the times of coronavirus. Diagn Cytopathol. 2021;49:467-68.
12. Cibas ES, Ali SZ . The Bethesda system for reporting thyroid cytopathology. Thyroid. 2009;19:1159–65.
13. Cibas ES, Ali SZ. NCI Thyroid FNA State of the Science Conference. The Bethesda System For Reporting Thyroid Cytopathology. Am J Clin Pathol. 2009;132:658-65.
14. Bellevicine C, Migliatico I, Sgariglia R, Nacchio M, Vigliar E, Pisapia P et al. Evaluation of BRAF, RAS, RET/PTC, and PAX8/ PPARg alterations in different bethesda diagnostic categories: a multicentric prospective study on the validity of the 7-gene panel test in 1172 thyroid FNAs deriving from different hospitals in South Italy. Cancer Cytopathol. 2020;128:107–18.
15. Poller DN, Stelow EB, Yiangou C. Thyroid FNAC cytology: can we do it better? Cytopathology. 2008;19:4-10.
16. Cai XJ, Valiyaparambath N, Nixon P, Waghorn A, Giles T, Helliwell T. Ultrasound-guided fine needle aspiration cytology in the diagnosis and management of thyroid nodules. Cytopathology. 2006;17:251-6.
17. Robinson IA, Cozens NJA. Does a joint ultrasound-guided cytology clinic optimize the cytological evaluation of head and neck masses? Clin Radiol. 1999;54:312–6.
18. Kojic Katovic S, Halbauer M, Tomic-Brzac H. Importance of FNAC in the detection of tumors within multinodular goiter of the thyroid. Cytopathology. 2004;15:206–11.
19. Palladino R, Migliatico I, Sgariglia R, Nacchio M, Iaccarino A, Malapelle U et al. Thyroid fine-needle aspiration trends before, during, and after the lockdown: what we have learned so far from the covid-19 pandemic. Endocrine. 2021;71:20-5.
20. Zhang D, Fu Y, Zhou L, Liang N, Wang T, Del Rio P et al. Thyroid surgery during coronavirus-19 pandemic phases I, II and III: lessons learned in China, South Korea, Iran, and Italy. J. Endocrinol. Investig. 2021;44:1065-73.
21. Tsang VHM, Gild M, Glover A, Clifton-Bligh R, Robinson BG. Thyroid cancer in the age of COVID-19. Endocr Relat Cancer. 2020;27:R407-16.
22. Vigliar E, Iaccarino A, Bruzzese D, Malapelle U, Bellevicine C, Troncone G. Cytology in the time of coronavirus disease (COVID-19): an Italian perspective. J Clin Pathol. 2021;74:261-63.