



# Repeat Fine Needle Aspiration Cytology (FNAC) in Thyroid Does Not Help in Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance (AUS/FLUS)

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Received: 31 May 2021 / Accepted: 16 July 2022  
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## Abstract

Although the current recommendation in the category of “Atypia of undetermined significance/follicular lesion of undetermined significance” (AUS/FLUS) is a repetition of fine needle aspiration cytology (FNAC), it does not solve the problems. Our aim is to analyze the effectiveness of FNAC repeat in AUS/FLUS cases by comparing it with clinical and ultrasonographic criteria and to contribute to patient management. In our institution, 138 patients’ results, of those who were operated with AUS/FLUS FNAC between 2014 and 2019 and who had definite pathological diagnoses with clinical-pathological-radiological data, were examined. We divided the AUS/FLUS cases in our center into those with and without repeat FNAC (rFNAC), and we evaluated those with definite pathological results of these nodules with all clinical radiological data. We found that the incidence of malignancy increased significantly as the nodule size increased (2.6 cm) and in the presence of microcalcification in all nodules whose initial biopsy result was AUS/FLUS ( $p=0.047$ ,  $p=0.019$ , respectively). The malignancy rate was 19.8% (18/91 cases) in cases without rFNAC and 23.4% (11/47 cases) in nodules with rFNAC. The incidence of malignancy was found to be higher in patients with nodules of 2 cm and larger in rFNAC cases ( $p=0.043$ ), and in patients with solid and microcalcified nodules in cases without rFNAC, and the results were significant ( $p$  values 0.037 and 0.046,  $p < 0.05$ , respectively). It was remarkable that the incidence of malignancy increased with advanced age ( $57.5 \pm 14.2$  years,  $p=0.017$ ) in rFNAC cases. No relationship was found between nodule size and advanced age in cases after rFNAC, and other clinical and radiological features other than the relationship between solid and microcalcified nodule and malignancy in cases without rFNAC. We found a significant correlation between a microcalcific and solid nodule larger than 2 cm and malignancy in elderly patients diagnosed with AUS/FLUS after the first biopsy. We recommend direct surgery without repeat FNAC in the management of cases with all of these criteria.

**Keywords** Thyroid · Bethesda Category · AUS/FLUS · Repeat FNAC

## Introduction

Thyroid nodules are very common. The frequency of random discovery has a wide range between 20 and 76% [1]. Thyroid cancer has the fastest increasing incidence rate of all cancers worldwide [2]. Fine needle aspiration cytology (FNAC) of the thyroid gland is a reliable diagnostic technique. The decision regarding treatment depends largely on the result of thyroid FNAC [3]. FNAC results have been standardized using the Bethesda System, which facilitates effective communication between clinics [4, 5]. However, uncertainties persist in the categories of “non-diagnostic” (ND) or “unsatisfactory” (UNS), which are Bethesda Category (BC)-1 and atypia of undetermined significance or follicular lesion of

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undetermined significance (AUS/FLUS), which are BC-3. Discussions and difficulties continue in these categories due to the nature of the disease or the problems experienced in its practical use worldwide [6]. AUS/FLUS is the most controversial category of the Bethesda System. The expected probability of malignancy in this category is 5–15% [7]. But in practice, the incidence range reported in the literature is very variable (0.8–28%) [1]. In the meta-analysis including 4475 AUS/FLUS cases, rates between 12.5% and 50% were reported [8]. In our institution, the incidence of malignancy in cases in this category is 20%.

Current Bethesda recommends FNAC repeat (rFNAC), molecular analysis, or lobectomy options for the management of AUS/FLUS nodules. The contribution of molecular tests is still unclear or not available in all institutions [5]. Apart from this, the benefit of the remaining 2 options can be determined according to the situation encountered. If the histopathology of the nodule results in malignancy after lobectomy, it can be interpreted as insufficient surgery, or unnecessary surgery if it is benign. The rFNAC preference will be beneficial if the cytology result is distributed into categories that lead to more precise judgments such as BC-2, 5, 6. Other categories mean continued uncertainty [2]. The recommendation for the management of AUS/FLUS lesions is the repetition of FNAC to reclassify the lesion, guide treatment, provide more precise risk stratification, and avoid unnecessary surgical procedure. There are also contradictions in the literature regarding the incidence of malignancy in cases with and without rFNAC in the AUS/FLUS category. Some authors have suggested that there is no difference in the rate of malignancy, and some authors have suggested the presence of higher malignancy rates in rFNAC results, thus repeating that FNAC is a guide [7]. Our study covers the AUS/FLUS category, which is full of contradictions, in which the incidence and frequency of malignancies are in a wide range, and which has been determined in previous studies and questioned the contribution of rFNAC. Therefore, we evaluated the status and clinical management of our patients in the AUS/FLUS category, who were operated and had a definite pathological definition. In particular, we planned the study to examine whether rFNAC has an effect by correlating it with clinical-radiological parameters and comparing it.

## Patients and Methods

The files of all thyroid FNAC patients conducted in our institution between January 2014 and December 2019 were scanned in the database. Our study, based on case series analysis, included patients with accrual/past patient records. The histopathological and clinical results of these patients obtained from all available sources were recorded. In our

study, 138 nodules with cytology, results of which were classified as AUS/FLUS were identified among 3270 nodules that were applied FNAC during this period. These 138 nodules belonging to 138 patients between the ages of 22 and 70 years who were operated and met the study criteria were identified from patients with these nodules.

The data belong to the patients who were followed up and operated in the AUS/FLUS group, which included 3270 cases. In our institution, patients with nodules larger than 3 cm and clinical complaints are operated regardless of the FNAC category. Ninety one patients who were directly operated on were patients with BC-3 FNAC results and were already to be operated. The fact that FNAC is not performed again in patients who will be operated anyway is a limitation of our study.

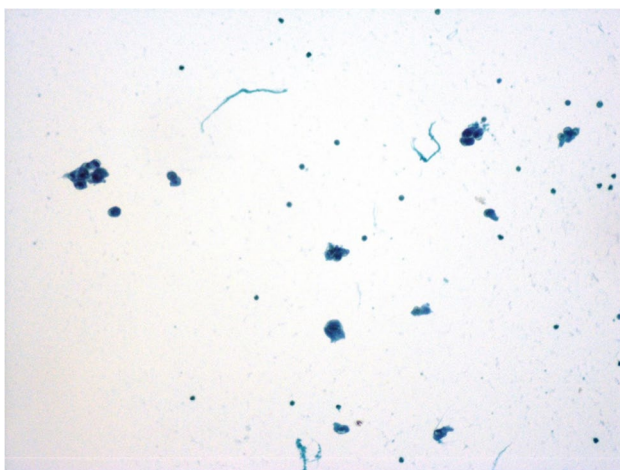
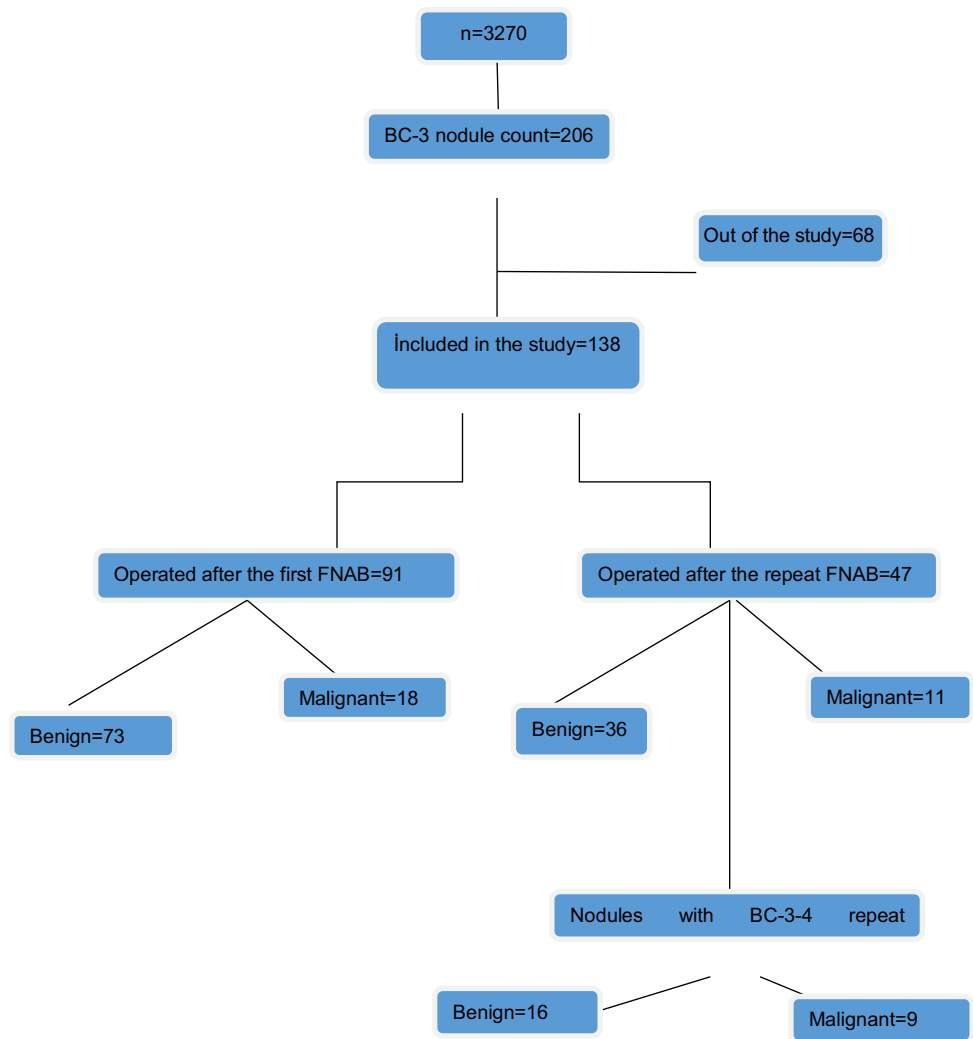
In our institution, our protocol in this category is performing FNAC again, but even if the second result is BC-2, rFNAC is not performed in patients who will be operated on. All preparations belonging to the cases were independently re-evaluated by 2 pathologists, one of whom was specialized in endocrinology. rFNAC was performed at a time interval of 2–3 months, with a minimum wait of 8 weeks. In the clinic, the algorithm was determined according to the ATA 2015 guidelines for the approach to nodules. In the FNAC evaluation, the Bethesda system 2017 criteria were used. In cases whose first FNAC result was BC-3, hyperfunctional and benign nodules were followed up by looking at TSH level and radiological features. The management was applied according to the rFNAC results of those in clinical follow-up. Those who were not hyperfunctional and had suspicious radiological features were operated on.

The cases with AUS/FLUS FNAC results among the definite histopathologically defined nodules subject to our study are summarized in Fig. 1.

Patients with a personal or family history of cancer, a history of irradiation to the head and neck region, who received thyroid hormone therapy, previously undergone thyroid surgery, and who had missing file information were not included in the study. The files of all patients were scanned and the results of age, gender, ultrasonographic nodule characteristics, FNAC repeat, type of surgery and postoperative pathology were recorded.

Neck Ultrasonography (USG) and FNAC of the patients were performed by a radiologist with at least 10 years of experience in this field. USG device with 5–12 MHz linear transducer and 23 G needle were used for the procedure. The preparations stained with routine PAP, prepared by conventional cytology and liquid-based cytology methods, were examined by pathologists experienced in this field (Fig. 2). Surgical resections were re-examined in detail by an experienced endocrine pathologist. In the evaluation, categorization was done in accordance with Bethesda 2017 criteria. USG features

**Fig. 1** Case selection and distribution in the study content



**Fig. 2** FNAB consisting of follicle groups poor in colloid and showing structural atypia, AUS/FLUS(BC-3), LBC, X40

such as nodule size, rim irregularity, internal structure, echogenicity, presence of calcification, vascularization, halo loss and benign/malign histopathology results of the cases were compared. Solid nodule structure; for nodules containing at least 90% solid components, hypoechogenicity; it was descriptive for those with low resolution compared to normal thyroid parenchyma. Border irregularity; clearly visible spiculation, microlobulated or jagged edge or poorly circumscribed margin not clearly distinguishable from adjacent thyroid tissue. Microcalcification; it was the presence of calcification spots 1 mm or less that appeared bright on an ultrasonographic image. Halo loss; it was defined as the loss of the thin or thick hypoechoic rim surrounding the nodule [9, 10]. Patients with large nodular goiter, patients with clinical complaints, and patients who did not accept repeat FNAC were operated without rFNAC. Apart from these patients, rFNAC was applied to the nodules diagnosed with AUS/FLUS, and patients whose consecutive FNAC results were not BC-2 were operated. Some patients with a sequential

FNAC result of BC-2 were operated at their own request. The indication for surgery of the nodules in the BC-2 group is generally the patient's request, and they prefer surgery without being followed up. Apart from this, it is also possible for the nodule characteristics to be guided by the preferences of the patients in our clinic.

SPSS 15.0 for Windows program was used for statistical analysis. Descriptive statistics; number and percentage for categorical variables, and numerical variables as mean, standard deviation, minimum, maximum, median. The rates in independent groups were compared using the chi-square test. Since the numerical variable did not the normal distribution condition, comparisons of two independent groups were made using the Mann–Whitney *U* test. Statistical significance level of alpha was accepted as  $p < 0.05$ .

## Results

Of the total 138 BC-3 cases, 91 were operated directly, and 47 were surgically performed after rFNAC. rFNAC was performed in 47 cases. The clinical and radiological features of all our BC-3 cases are shown in Table 1. Malignancy was found in 29 of 138 (21%) cases after surgery. Papillary carcinoma and its variants were the most common. In 109 benign cases, the most common diagnosis was nodular goiter. rFNAC changed the initial diagnosis in the majority of nodules (31/47, 66%), 16 nodules (34%) remained BC-3. The Bethesda distribution, which showed that 36 of 47 cases who underwent rFNAC, required surgical procedure (BC-1–3–4 cases). None of our patients had rFNAC result BC-5 and BC-6. And malignancy was detected in 10 of these 36 cases. In all of these cases,

**Table 1** Clinical-pathological-radiological features of all AUS/FLUS cases

n = 138	Total	Benign	Malignant	<i>p</i>
Age (Median/Standard Deviation)	46.4SD11.9	45.4SD11.0	50.0SD14.3	0.063
Female	55 (39.9%)	48 (44.0%)	7 (24.1%)	0.052
Male	83 (60.1%)	61 (56.0%)	22 (75.9%)	
Nodule size 1 cm and below	15 (10.9%)	13 (11.9%)	2 (6.9%)	0.737
Nodule size 2 cm and above	56 (40.6%)	40 (36.7%)	16 (55.2%)	0.072
Nodule size (Median/Standard Deviation)	21.5SD11.4	20.3SD9.8	26.0SD15.7	0.047
Echogenicity				
Hypoechoic	50 (36.2%)	39 (35.8%)	11 (37.9%)	0.830
Iso-hyperechoic	88 (63.8%)	70 (64.2%)	18 (62.1%)	
Irregular border				
+	9 (6.5%)	7 (6.4%)	2 (6.9%)	1.000
–	129 (93.5%)	102 (93.6%)	27 (93.1%)	
Solid	60 (43.5%)	44 (40.4%)	16 (55.2%)	0.153
Cystic-Solid	78 (56.5%)	65 (59.6%)	13 (44.8%)	
Microcalcification				
+	12 (8.7%)	6 (5.5%)	6 (20.7%)	0.019
–	126 (91.3%)	103 (94.5%)	23 (79.3%)	
Halo loss				
+	11 (8.0%)	9 (8.3%)	2 (6.9%)	1.000
–	127 (92.0%)	100 (91.7%)	27 (93.1%)	
Vascularization				
+	9 (6.5%)	9 (8.3%)	0 (0.0%)	0.204
–	129 (93.5%)	100 (91.7%)	29 (100%)	
Number of suspicious features (USG)*				
0	56 (40.6%)	48 (44.0%)	8 (27.6%)	0.374
1	34 (24.6%)	24 (22.0%)	10 (34.5%)	
2	36 (26.1%)	28 (25.7%)	8 (27.6%)	
3	12 (8.7%)	9 (8.3%)	3 (10.3%)	
4	-	-	-	
5	-	-	-	

\*Ultrasonographic suspicious features: Hypoechoic, Solid nodule, Microcalcification, Halo loss, Vascularization

classic and follicular variant papillary carcinoma were detected after surgical excision. Only 11 of the 47 rFNAC were renewed as BC-2, and malignancy was detected in 1 of these cases after surgical excision. In these, as in the BC-2 category, we determined a definite diagnosis of 10 benign and 1 malignant nodule. In addition, clinical-pathological-radiological characteristics of our patients whose rFNAC results were BC-3 and BC-4 (25 cases, 16 benign, 9 malignant) were compared. No statistically significant data was found (none shown in the table). Unfortunately, 11 cases had a BC-1 rFNAC result. FNAC was performed on all nodules under the guidance of USG. In our opinion, BC-1 result is high in 11 of the patients who underwent rFNAC. These data may also be evidence that the application of rFNAC is controversial. However, we will be able to see if future studies with case series support these results. In our cases, we found that as nodule size increased (mean 2.6 cm diameter), and in the presence of microcalcification, the incidence of malignancy increased significantly ( $p=0.047$ ,  $p=0.019$ , respectively). We could not find a significant relationship between the incidence of malignancy and age, nodule size smaller than 1 cm or greater than 2 cm, presence of irregular borders, echogenicity, structure of nodules, most of the suspicious radiological features (Table 1). Surgery was performed directly in 91 of 138 cases and after rFNAC in 47 cases. The malignancy rate was 19.8% (18/91 cases) in cases without rFNAC, and 23.4% (11/47 cases) in nodules with rFNAC. Malignant nodules in rFNAC cases were 2 cm and larger, and the incidence of malignancy increased as the size increased ( $p=0.043$ ,  $p=0.023$ , respectively, sensitivity 87%, specificity 84%). Twenty-one of the rFNAC cases had nodules 2 cm or larger and the incidence of malignancy was significantly higher. In addition, it was noteworthy that in our patients in this group, the incidence of malignancy increased with advanced age (57.5SD14.2 age,  $p=0.017$ ). No relationship was found between other clinical and radiological features and malignancy distribution of cases after rFNAC (Table 2). The incidence of malignancy was found to be higher in patients with solid and microcalcified nodules in whom rFNAC was not applied and the results were significant ( $p$  values, respectively, 0.037 and 0.046,  $p<0.05$ , sensitivity 94%, specificity 93%). No relationship was found between the other clinical and radiological features and the incidence of malignancy in 91 patients in this group who did not receive rFNAC (Table 2). In addition, we compared the clinical-pathological-radiological parameters of nodules with and without rFNAC. We could not find any statistically significant difference. In the cases that we performed rFNAC, the rate of malignant nodules was slightly higher (19.8% versus 23.4%), but there was no statistical significance (not shown in the table).

## Discussion

In practice, a precise histopathological definition of all nodules cannot be made, as nearly half of AUS/FLUS nodules are not resected [11, 12]. Our resection rate (67%, 138/206 nodules) was high (literature range is 43–64.7%) [11, 12] and had definite histopathological diagnosis. Since some of the AUS/FLUS cases are excised, it is difficult to calculate the risk of malignancy associated with this category [5, 7]. The malignancy detected in 21% of our cases (29/138 cases) was found within the ROM (10–30%) [5]. However, a 27% malignancy rate was reported in a meta-analysis study involving 4475 AUS/FLUS nodules with clinical follow-up [8]. Recent studies using Bethesda categories have found that the AUS/FLUS category exhibits significant differences in both cases. The incidence of AUS/FLUS is 0.8–28%, and resection specimens have a malignancy rate of 6–48% [1]. In previous studies, it has been reported that the incidence range of malignancy is much wider in resected cases (mean 34%, range 6–96.7%). The authors consider these wide ranges to be due to the heterogeneity of the AUS/FLUS category [13].

In our study, when we look at the properties of all AUS/FLUS nodules, we showed that the probability of malignancy increases as the nodule size increases (mean 2.6 cm diameter) with the presence of microcalcification. We could not find any relationship with other USG features (Table 1). This data about nodule size becomes meaningful with the recommendation to perform aspiration in nodules larger than 2 cm, albeit with low suspicious USG features specified in ATA guidelines [14]. However, it has been suggested that nodule size alone would not be predictive [15, 16]. In a study showing that many USG features are associated with malignancy, solid structure, microcalcification, increased nodule size (2 cm), and patient age (<65 years) were associated with triage to surgery [17]. In another study, microcalcification and rapid growth were found to be predictive factors for malignancy [18]. In the meta-analysis evaluation of 14 studies including 2405 AUS/FLUS nodules, it is suggested that any 2 or 3 suspicious USG features (hypoechoogenicity, microcalcification, irregular border) can be interpreted as an indicator of malignancy and it is stated that the probability of malignancy increases as the number of suspicious features increases [19]. The 2015 American Thyroid Association (ATA) guidelines recommend conservative management with repeat FNA or molecular testing for initial AUS/FLUS interpretation in most cases [14]. Although there is a molecular analysis unit in our institution, when the cost factor or clinical/radiological factors are evaluated together, molecular analysis is not performed in most cases. This, increases the importance of clinical/radiological factors, rFNAC and cytopathological examination. Therefore, we investigated the relationship between the clinical and



**Table 2** Comparison of clinical-radiological features and histopathological results of cases with & without rFNAC

n = 47	Total	Benign		Malignant		p	
Age (Median/Standard Deviation)	49.7SD12.4	<b>44.6 ± 11.3</b>	47.4SD11.0	<b>44.4SD11.0</b>	57.5SD14.2	<b>45.4SD12.7</b>	0.017 <b>0.730</b>
Female;	18 (38.3%)	<b>37 (40.7%)</b>	16 (44.4%)	<b>32 (43.8%)</b>	2 (18.2%)	<b>5 (27.8%)</b>	0.164
Male	29 (61.7%)	<b>54 (59.3%)</b>	20 (55.6%)	<b>41 (56.2%)</b>	9 (81.8%)	<b>13 (72.2%)</b>	<b>0.214</b>
Nodule size 1 cm and below	5 (10.6%)	<b>10 (11.0%)</b>	4 (11.1%)	<b>9 (12.3%)</b>	1 (9.1%)	<b>5.6%</b>	1.000 <b>0.680</b>
Nodule size 2 cm and above	21 (44.7%)	<b>35 (38.5%)</b>	13 (36.1%)	<b>27 (37.0%)</b>	8 (72.7%)	<b>27 (37.0%)</b>	0.043 <b>0.560</b>
Nodule size(Median/Standard Deviation)	21.7SD12.0	<b>21.4SD11.2</b>	19.4SD10.2	<b>20.7SD9.6</b>	29.0SD15.1	<b>24.2SD16.1</b>	0.023 <b>0.482</b>
Echogenicity							
Hypochoic;	19 (40.4%)	<b>31 (34.1%)</b>	15 (41.7%)	<b>24(32.9%)</b>	4 (36.4%)	<b>7 (38.9%)</b>	1.000
Isohyperechoic	28 (59.6%)	<b>60 (65.9%)</b>	21(58.3%)	<b>49(67.1%)</b>	7 (63.6%)	<b>11(61.1%)</b>	<b>0.630</b>
Irregular border							
+	-	<b>9 (9.9%)</b>	-	<b>7 (9.6%)</b>	-	<b>2 (11.1%)</b>	-
-	47 (100%)	<b>82 (90.1%)</b>	36 (100%)	<b>66 (90.4%)</b>	11 (100%)	<b>16 (88.9%)</b>	<b>1.000</b>
Solid	24 (51.1%)	<b>36 (39.6%)</b>	19 (52.8%)	<b>25(34.2%)</b>	5 (45.5%)	<b>11 (61.1%)</b>	0.671
Cystic-Solid	23 (48.9%)	<b>55 (60.4%)</b>	17 (47.2%)	<b>48 (65.8%)</b>	6 (54.5%)	<b>7 (38.9%)</b>	<b>0.037</b>
Microcalcification							
+	4 (8.5%)	<b>8 (8.8%)</b>	2 (5.6%)	<b>4 (5.5%)</b>	2 (18.2%)	<b>4 (22.2%)</b>	0.229
-	43 (91.5%)	<b>83 (91.2%)</b>	34(94.4%)	<b>69 (94.5%)</b>	9 (81.8%)	<b>14(77.8%)</b>	<b>0.046</b>
Halo loss							
+	6 (12.8%)	<b>5 (5.5%)</b>	4 (11.1%)	<b>5 (6.8%)</b>	2 (18.2%)	<b>0 (0.0%)</b>	0.614
-	41 (87.2%)	<b>86 (94.5%)</b>	32 (88.9%)	<b>68 (93.2%)</b>	9 (81.8%)	<b>18 (100%)</b>	<b>0.579</b>
Vascularization							
+	2 (4.3%)	<b>7 (7.7%)</b>	2 (5.6%)	<b>7(9.6%)</b>	0 (0.0%)	<b>0 (0.0%)</b>	1.000
-	45 (95.7%)	<b>84 (92.3%)</b>	34 (94.4%)	<b>66 (90.4%)</b>	11 (100%)	<b>18 (100%)</b>	<b>0.338</b>
Number of suspicious features (USG)*							
0	17 (36.2%)	<b>39 (42.9%)</b>	<b>15 (41.7%)</b>	<b>33 (45.2%)</b>	<b>2 (18.2%)</b>	<b>6 (33.3%)</b>	<b>0.064</b>
1	11 (23.4%)	<b>23 (25.3%)</b>	<b>5 (13.9%)</b>	<b>19 (26.0%)</b>	<b>6 (54.5%)</b>	<b>4 (22.2%)</b>	<b>0.565</b>
2	13 (27.7%)	<b>23 (25.3%)</b>	<b>11 (30.6%)</b>	<b>17 (23.3%)</b>	<b>2 (18.2%)</b>	<b>6 (33.3%)</b>	
3	6 (12.8%)	<b>6 (6.6%)</b>	<b>5 (13.9%)</b>	<b>4 (5.5%)</b>	<b>1 (9.1%)</b>	<b>2 (11.1%)</b>	
4	-	-	-	-	-	-	
5	-	-	-	-	-	-	

\*Ultrasonographic suspicious features: Hypoechoic, Solid nodule, Microcalcification, Halo loss, Vascularization  
Cases without rFNAC are highlighted in bold

ultrasonographic characteristics of the cases and the FNAC repeat results.

The malignancy rate was 19.8% (18/91 cases) in cases without rFNAC, and 23.4% (11/47 cases) in nodules with rFNAC. There was no statistically significant difference in these rates ( $p=0.620$ ). In 36 of 47 patients with rFNAC, there were new diagnoses in the uncertain category (BC-1–3-4) for the nature of the nodule, except for BC-2 (malignancy was also found in 1 nodule in this category), and malignant nodules were detected in 10 (10/36 cases, 27.8%) of them. However, we could not find a significant relationship between malignancy increase rate and rFNAC.

The increase in malignancy rate after rFNAC was a common feature of many studies. On the contrary, there are studies that find a high malignancy rate in nodules undergoing direct surgery and do not recommend rFNAC [18]. It has been suggested by some authors that rFNAC for the first AUS/FLUS category is associated with a significantly increased malignancy rate compared to those without rFNAC. They suggested repeating FNAC for nodules with AUS/FLUS in the first FNAC, considering that repeated FNAC would help the selection of patient with AUS/FLUS for triage for surgery [17]. On the contrary, there are some studies that found a high rate of malignancy after initial

diagnosis in AUS/FLUS nodules and recommended direct surgery [20]. Interestingly, there is a third approach to this discussion. There are also literature data reported by some authors that they found no difference in the incidence of malignancy in AUS/FLUS cases with and without rFNAC. According to them, rFNAC has no effect on the increase of the incidence of malignancy [7]. In the study they planned, inspired by this data, the authors found similar rates and reported that rFNAC did not increase the malignancy rate. And they argued that nodules with clinically and radiologically suspicious features should go directly to surgery [7]. In our cases, although a slight increase in malignancy was observed in the nodules to which we applied rFNAC, there was no statistical significance. Therefore, we interpreted this data as the result confirming the suggestion of these authors.

The literature is conflicting regarding the effects of age on thyroid malignancy risk. There are opposite publications reporting that young or advanced age is an important risk factor for malignancy in patients with AUS/FLUS nodules. In addition, it has been included in the literature in studies reporting that age is not associated with malignancy of AUS/FLUS nodules [1]. In our study, we found a significant correlation between older age (> 57.5 age, Table 2) and malignancy in our rFNAC cases. Therefore, we thought that surgical triage should be carefully evaluated in elderly patients with suspicious USG features. We thought that in elderly patients with AUS/FLUS diagnosis, larger than 2 cm, solid and microcalcific nodules, direct surgery could be performed. Already, in general, FNAC is recommended for nodules with suspicious USG features such as solid hypoechoic nodules larger than 1 cm, mixed solid/cystic nodules greater than 2 cm, and microcalcifications and irregular borders. In addition, personal characteristics (those with a family history of cancer or multiple endocrine neoplasia, and patients at high risk for thyroid cancer who were exposed to ionizing radiation early in life) are factors to be considered [21].

### Limitations

The study contains limitations due to its case series analysis nature and the presence of unoperated follow-up nodules suggesting selection bias.

### Positive Aspects of the Study

The presence of sufficient number of nodules with definite pathological results and patients with regular clinical follow-up, the ideal ratio of the number of AUS/FLUS nodules in all nodules and the cooperation of the pathologist-radiologist and surgeon experienced in this field are important factors.

## Conclusions

According to our data, we recommend direct surgery without repeat fine needle aspiration cytology in elderly patients with microcalcific and solid nodules larger than 2 cm, which we found to be significantly associated with malignancy in atypia of undetermined significance/follicular lesion of undetermined significance nodules. Repeat fine needle aspiration cytology can rather be used in the management of young patients with solid and cystic (mixed) atypia of undetermined significance/follicular lesion of undetermined significance nodules smaller than 2 cm.

## Declarations

**Ethics Approval** This study was approved by our hospital's institutional review board and ethics committee (No: 3027).

**Conflict of Interest** The authors declare no competing interests.

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