

# Malignancy risk of thyroid nodules with repeated “atypia of undetermined significance/follicular lesion of undetermined significance” diagnosis

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## OBJECTIVES

“Atypia of undetermined significance/follicular lesion of undetermined significance” (AUS/FLUS) is a heterogeneous diagnostic thyroid fine needle aspiration biopsy (FNAB) category. AUS/FLUS is comprised of cases that cannot be definitively diagnosed as benign, suspicious for/consistent with neoplasm, suspicious for malignancy or malignant. The recommended management strategy for these cases is to perform a repeat FNAB after an appropriate time course. Although the estimated risk of malignancy for AUS/FLUS is reported 5 – 15 % , there is growing evidence in the literature that suggest higher incidence of malignancy for this category. The purpose of this study is to estimate the malignancy risk of repeated AUS/FLUS diagnosis of thyroid fine needle aspiration biopsies.

## METHODS

We report retrospective analyzes of 56 cases with repeated AUS/FLUS diagnosis among 5396 thyroid FNABs. The demographic data and histologic follow-up were evaluated in the study. Histologic outcome was categorized as benign, malignant or well-differentiated tumors of uncertain malignant potential (WDT-UMP).

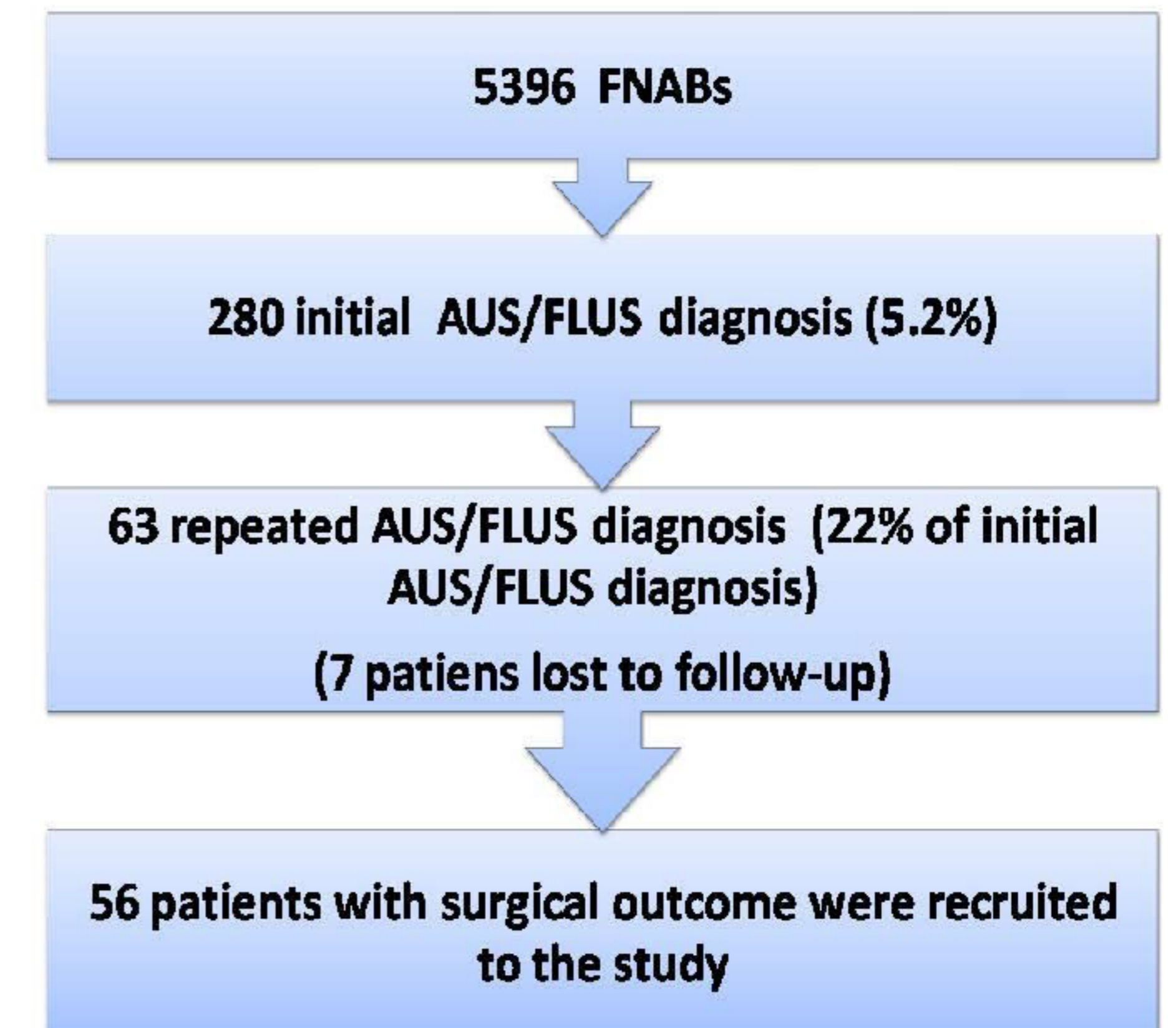


Table.1 Surgical outcome following a repeated diagnosis of atypia of undetermined significance/follicular lesion of undetermined significance in thyroid FNAB

Outcome	No. (%) of Cases
Benign	28 (50%)
Malignant	23 (41%)
Papillary Cancer	21 (95%)
Follicular Cancer	2 (5%)
Well-differentiated tumors of uncertain malignant potential	5 (9%)

Table.2 Surgical outcome of patients following a repeated diagnosis of atypia of undetermined significance/follicular lesion of undetermined significance according to gender

Outcome	No. (%) of Cases	
	Female	Male
Benign	26 (56%)	2 (22%)
Malignant	18 (38%)	5 (56%)
Papillary Cancer	16 (95%)	5 (100%)
Follicular Cancer	2 (5%)	0 (0%)
Well-differentiated tumors of uncertain malignant potential	3 (6%)	2 (22%)

## RESULTS

280 patients with AUS/FLUS diagnosis on initial FNAB were constituted 5.2% of all FNAB group, among them 63 (22%) was diagnosed again AUS/FLUS. A total of 56 cases with repeated AUS/FLUS diagnosis and surgical outcome were recruited to the study (figure.1). The study group included 47 (84%) females and 9 (16%) males with a mean age of 47.7 ( $\pm 13$ ) years. There was no difference between mean age in both groups, 48.4 ( $\pm 13$ ) for females, 44 ( $\pm 12$ ) for males ( $p > 0,05$ ). The nodule size ranged from 0.9 to 6 cm (mean, 1.8  $\pm$  1.0 cm). Among 56 cases with a repeated diagnosis of AUS/FLUS by FNAB, histologic follow-up revealed 28 (50%) patients were benign, 23 (41%) patients were malignant and 5 (9%) patients were WDT-UMP. These results are summarized in Table 1. Papillary thyroid carcinoma accounted for 95% of all malignant outcomes at surgical resection (beside WDT-UMP). The mean age of malignant and benign groups were similar in both groups, even in subgroup analysis according to gender. The results of the surgical outcomes according to gender revealed that, malignant outcome was higher in male patients although this difference was not statistically significant (56% in males and 38% of females) (table 2). If patients diagnosed with WDT-UMP were analyzed in malignant group, the malignancy outcome increased to 78% in males while 44,5% in females ( $p = 0,07$ ).

## CONCLUSIONS

AUS/FLUS is a heterogeneous FNAB category. The thyroid nodules in this category cannot be characterized as benign due to nuclear or architectural atypia of the follicular cells. However, the atypia is also insufficient to meet the criteria for diagnosing suspicious for malignancy, malignant or follicular neoplasm categories [2]. According to BS an AUS/FLUS diagnosis is obtained in 3% to 6% of thyroid FNABs [3,4]. The higher rates of this diagnosis might indicate overuse of this category. The incidence of AUS/FLUS diagnosis in our cohort was %5,2 which was consistent with the suggested incidence rate of BS.

The management recommendation of AUS/FLUS category according to BS is repeating FNAB at an appropriate interval, as the anticipated risk of malignancy is low, 5-15% [2]. However, the majority of the recently published data demonstrate higher malignancy risk than anticipated in BS [7,8]. The data concerning the malignancy risk of repeated AUS/FLUS diagnosis is controversial. Paul et al have showed no statistically significant difference in malignancy rate among patients who went directly to surgery after a single AUS diagnosis and patients having 2 successive AUS FNAB diagnoses (41-43% respectively) [7]. On the other hand, Wong et al reported the malignancy incidence of 25.6 % in single AUS/FLUS diagnosis while 38.8% after repeated AUS/FLUS diagnosis [8]. The malignancy rate among 56 repeated AUS/FLUS diagnosis in our study was 41% . This rate is three times higher than reported in BS but consistent with recent studies.

The evidence supporting higher malignancy rate of this category is increasing. Even the pathologic classification is not changed the clinical outcome data would be revised. The reported malignancy rate of follicular neoplasm or suspicious for a follicular neoplasm (FN/SFN) was 15%-30%, for whom surgery is recommended management. Therefore, the management strategy of AUS/FLUS should also be revised as the malignancy rate was same or even higher than FN/SFN.

## References

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