

Evaluation the Relationship Between Thyroid Nodule Size with Malignancy and Accuracy of Fine Needle Aspiration Biopsy (FNAB)

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ABSTRACT

Introduction: Some studies have shown largest thyroid nodule size, especially ≥ 4 cm that can predict malignancy and reduce fine needle aspiration biopsy (FNAB) accuracy. Therefore, this study is designed to evaluate relationship between thyroid nodule sizes with malignancy and its effect on FNBA accuracy. **Materials and Methods:** a retrospective analytical study design aims to investigate all patients with thyroid nodules who referred to surgery department of Imam-Khomeini Hospital of Mazandaran University of Medical Sciences in Sari from 20 March 2008 to 22 March 2014. We collected patient's demographic data, nodules size, FNAB reports and final pathology (after surgery) reports from their medical records. All data were analyses performed by SPSS18. **Results:** 167 patients (153 women) with mean age of 41.56 ± 13.24 years old were enrolled for this study. In final pathology; 38 patients (22.8%) had malignant nodules. The mean age of patients with or without malignant nodules were 34.93 ± 11.86 and 42.37 ± 12.26 years old, respectively ($P=0.002$). The mean size of benign and malignant nodules were 2.91 ± 1.29 cm and 3.38 ± 1.86 cm, respectively ($P=0.15$). 25.2% of < 4 cm nodules and 17.9% of ≥ 4 cm nodules were diagnosed as a malignant ($P=0.29$). FNAB was done on 95 patients that reported benign in 60 patients (63.2%), malignant in 18 patients (18.9%) and suspicious in 17 patients (17.9%). Positive and negative results of FNAB in all nodules were 3.5% and 6.3%, in < 4 cm nodules were 5.8% and 6.2% and in ≥ 4 cm nodules were zero and 6.7%, respectively. The sensitivity, specificity, Positive predict value (PPV), negative predict value (NPV) and overall accuracy (OA) of FNAB in all nodules were 76.19%, 96.49%, 88.88%, 91.66% and 91.02%, and in < 4 cm nodules were 78.57%, 94.11%, 84.61%, 91.42% and 89.58%, and in ≥ 4 cm nodules were 71.4%, 100%, 100%, 92% and 93.33%, respectively. **Conclusion:** the results of this study revealed that the size of the thyroid nodules is not reliable at predicting malignancy and should not be applied in medical decision making. FNAB showed good specificity but the sensitivity was low in our study. In ≥ 4 cm nodules; FNAB sensitivity was decreased and accompanied by higher false-negative results. Furthermore, FNABs with suspicious results were associated with high probability of malignancy.

Key words: Thyroid cancer, thyroid nodules, Fine needle aspiration biopsy.

1. INTRODUCTION

Thyroid nodules are very common and can be found clinically in 4-7% of general population (1). However, it seems that the true prevalence of thyroid nodules is higher. For example this prevalence is from 8 to 65% in autopsy and from 19 to 35% in ultrasound survey (2). According to retrospective studies, only 4-5% of thyroid nodules are malignant (3-5). Several risk factors have been reported for the presence of carcinoma in thyroid nodules, and one of them is the size of the thyroid nodules (6). Recent studies have shown that thyroid nodule exceeding 4cm could increase risk of malignancy,

thereby size can be considered as an independent indication to predict the risk of malignancy in people with thyroid nodules (7-9). But, some other studies did not support these data and even reported against their results (10-13).

FNAB procedure is one of the preliminary diagnostic procedures for detecting malignant thyroid nodules. Recently, some studies have reported that the diagnostic accuracy of FNAB is limited in large thyroid nodules (6, 9) while other studies disaffirm these results (12, 14, 15). Thus, whether the increased size of thyroid nodules is associated with higher risk of malignancy and lower diagnostic accuracy of

FNAB and whether the size of nodules can be considered as an important indication for therapeutic decision making are not certain. Therefore, the purpose of this study was to investigate the relationship between the size of thyroid nodules and malignancy risk and the diagnostic accuracy of FNAB in patients with thyroid nodules.

2. MATERIALS AND METHODS

A retrospective analytical study that was performed on all patients with thyroid nodules (single or multiple) presented and put underwent surgery at Imam-Khomeini Hospital of Mazandaran University of Medical Sciences (north of Iran) from 20 March 2008 to 22 March 2014. Exclusion criteria were patients with cystic nodules or complex nodules.

The records of the patients were used to extract demographic data (age, sex) from history of radiation exposure, nodules size, FNAB results and final pathology. The size of nodules was recorded in centimeter using patients' ultrasonography reports. In patients with multiple thyroid nodules, the risk of malignancy is as high as patients with single thyroid nodules (16). Thus, in patients with multiple nodules, every nodule should be evaluated individually and if the nodules are ultrasonographically consistent, FNAB procedure should be performed for the largest nodule (17). Thereby, we considered the largest nodule as the main nodule. FNAB results were extracted from the patients' records and assigned into 4 groups: malignant, benign, suspicious, and insufficient. The meaning of suspicious cases were follicular and Hurthle cell adenoma/carcinoma that can be differentiated using final pathology. Also, the final pathology of patients has been studied.

Statistical analysis

This data was collected and analyzed by SPSS version 18. Chi-Square and Fisher's exact tests were used to analyze the qualitative data. For analysis of the quantitative data, Student's t-test was performed. A P value of 0.05 was considered statistically significant.

3. RESULTS

Amount of 167 patients with thyroid nodules put underwent thyroidectomy. The mean ages of the patients were 41.56 ± 13.24 years old (between 13 and 86 years old). 14 of 167 patients were male with mean ages of 48.72 ± 12.86 years old, and 153 were female with mean age of 40.28 ± 12.23 years old ($P=0.03$). 88 (52.7%) cases had multiple thyroid nodules, and 79 (47.3%) cases had single thyroid nodules. The average sizes of the nodules were 3.17 ± 1.76 cm (between 0.4cm and 10cm). In terms of size, 115(68.9%) cases had nodules in size of 4cm, and 52 (31.1%) cases had nodules in size of ≥ 4 cm.

Postoperative pathologic examination revealed that 129 (77.2%) patients had benign thyroid nodules, and 38 (22.8%) patients had malignant thyroid nodules. The malignant thyroid nodules were papillary carcinoma in 35 (92.10%) patients and follicular carcinoma in 3 (7.9%) patients. The mean ages of the patients with malignant and benign thyroid nodules were 34.93 ± 11.86 (median=33) and 42.37 ± 12.26 (median=43) years old respectively. The mean ages of the patients with malignancy were significantly less compared with other patients ($P=0.002$). 3 (21.4%) males and 35 (22.9%) females were diagnosed having malignant thyroid nodules. The average sizes of

		sensi- tivity	speci- ficity	PPV	NPV	Overall ac- curacy
FNAB	4cm	78.57%	94.11%	84.61%	91.42%	89.58%
	≥ 4 cm	71.4%	100%	100%	92%	93.33%
	total	76.19%	96.49%	88.88%	91.66%	91.02%

Table 1. Sensitivity, specificity, PPV, NPV, and overall accuracy of FNAB based on final pathology

the malignant and benign thyroid nodules were 2.91 ± 1.29 cm and 3.38 ± 1.86 cm, respectively ($P=0.15$). 29 patients (25.2%) with < 4 cm thyroid nodules and 9 patients (17.3%) with ≥ 4 cm thyroid nodules diagnosed having malignancy. There were no significant differences to observe in the malignancy potential under and over 4cm thyroid nodules ($P=0.29$). Among the 79 patients with single nodules; 14 (17.7%) patients, and among the 88 patients with multiple nodules; 24 (27.3%) patients had thyroid cancer ($P=0.14$).

Of the total amount of 167 patients, 95 patients had FNAB and the results were reported as benign in 60 cases (63.2%), malignant in 18 cases (18.9%), and suspicious in 17 cases (17.9%). In patients with multiple thyroid nodules, FNAB results were interpreted as benign in 25 cases (60.97%), malignant in 10 cases (24.39%), and suspicious in 6 cases (14.63%). In the patients with single thyroid nodules, FNAB results were interpreted as benign in 35 cases (64.81%), malignant in 8 cases (14.81%), and suspicious in 11 cases (20.37%) ($P=0.44$).

FNAB results of 62 patients with 4cm nodules were reported as benign in 36 cases (58.04%), malignant in 13 cases (21%), and suspicious in 13 cases (20.96%). Also, FNAB results of 33 patients with ≥ 4 cm nodules were reported as benign in 24 cases (72.72%), malignant in 5 cases (15.2%), and suspicious in 4 cases (12.12%) ($P=0.35$). According to postoperative pathologic survey of the nodules that put underwent FNAB; 16 patients (25.8%) with 4cm nodules and 8 patients (24.2%) with ≥ 4 cm nodules were diagnosed having thyroid cancer. Pathological examination of 17 cases that were diagnosed suspicious in FNAB revealed that 4 cases (23.5%) were malignant (3 cases with 4cm nodules and 1 case with ≥ 4 cm nodules). After exclusion of suspicious cases that were reported by FNAB, 16 patients of 21 patients pathologically diagnosed as malignant were malignant on FNAB and 55 of 57 patients pathologically diagnosed as benign were benign on FNAB. False-positive and false-negative rates of FNAB for all nodules were 3.5% and 6.2%, respectively. The sensitivity, specificity, PPV, NPV, and overall accuracy of FNAB were 76.19%, 96.49%, 88.88%, 91.66%, and 91.2%, respectively (Table 1).

In 4cm thyroid nodules, 11 patients of 14 patients pathologically diagnosed as malignant were malignant on FNAB and 32 patients of 34 patients pathologically diagnosed as benign were benign on FNAB. In 4cm thyroid nodules, false-positive rate and false-negative rates of FNAB were 5.8% and 6.2%, respectively. Furthermore the sensitivity, specificity, PPV, NPV, and overall accuracy were 78.57%, 94.11%, 84.61%, 91.42%, and 89.58%, respectively (Table 1).

In ≥ 4 cm thyroid nodules, 5 patients of 7 patients pathologically diagnosed as malignant were malignant on FNAB and 23 patients of 23 patients pathologically diagnosed as benign were benign on FNAB. In ≥ 4 cm nodules, false-positive and false-negative rates of FNA were 0% and 6.7%, respectively. Also the sensitivity, specificity, PPV, NPV, and overall accu-

racy of FNAB were 71.4%, 100%, 100%, 92%, and 93.33%, respectively (Table 1).

4. DISCUSSION

Some studies shown that thyroid nodule size can be considered as an independent indication to predict the risk of malignancy in people with thyroid nodules (7-9) But other studies did not support these data and even reported against their results (10-13). Furthermore, diagnostic accuracy of FNAB in large thyroid nodules is still controversial (6, 9, 12, 14, 15). Therefore, this study is designed to investigate the relationship between the size of thyroid nodules and malignancy risk and its effect on diagnostic accuracy of FNAB.

Different studies shown different results about the role of age as a risk factor of thyroid malignancy. Pinchot et al. reported that thyroid carcinoma prevalence was higher in the elderly compared with others while Rosario and et al. did not observe a significant difference between the age of the patients (6, 18). Nevertheless, some studies including ours, revealed that the prevalence of thyroid carcinoma is higher in the younger patients (19, 20).

Kamran et al. reported that increasing thyroid nodule size had an influence on cancer risk in a nonlinear fashion, and there was no increase in the risk beyond the 2cm threshold (14). While, Berker et al. reported no significant difference between 1cm nodules and 1cm in malignancy risk (21). Some studies have shown higher prevalence of thyroid carcinoma in ≥ 4 cm nodules (8, 9). Conversely, Rausei et al. and McHenry et al. reported higher prevalence of thyroid carcinoma in smaller nodules (12, 22). In this study, there was no statistically significant difference between malignant and benign nodules size. These contradictory results show that the size of the nodule is not reliable at predicting malignancy and should not be applied for medical decision making (12, 13, 22-24).

Our results revealed that in all nodules, false-positive and false-negative rates of FNAB were 3.5% and 6.3%, respectively. In 4cm nodules false-positive rate was higher while in ≥ 4 cm nodules false-negative rate was higher. Kuru et al. reported that in all nodules, such as 4cm nodules and ≥ 4 cm nodules false-negative rates of FNAC were 2%, 1.3%, and 4.3% respectively (15). But, McCoy et al. shown a high rate of (16%) false-negative FNABs in ≥ 4 cm nodules and suggested that FNAB is not a reliable procedure on these patients and diagnostic lobectomy is required too (9). Bestepe et al. reported the rate of false-negative FNAB in nodules ≥ 4.0 cm was twice as high as in nodules 1.0–3.9 cm (24). In addition, in different studies false-negative rate of FNAB has been reported between 4 and 21% (25-28); and false-positive rate of FNAB has been reported between 0 and 28% (27-29).

In this study, the specificity of FNAB was acceptable, but sensitivity was low, especially in ≥ 4 cm nodules. Conversely, kuru et al. reported that sensitivity and specificity of FNAB were 90% and 79%, respectively (15). Sinna et al. reported that sensitivity, specificity, PPV, NPV, and overall accuracy of FNAB were 92.8%, 94.2%, 94.9%, 91.8%, and 93.6%, respectively; these results were almost in concordance with our results, except sensitivity (30). Also, Kulstad reported Sensitivity/specificity for detecting malignancy by FNA was ~80%; PPV was just below 60%; NPV was 93% (31). gener-

ally, in different studies, FNAB results were sensitivity between 65% and 98%, specificity between 72% and 100%, PPV between 34% and 100%, and NPV between 83% and 100% (15, 30, 32). these reasons might be different number of participants, inclusion criteria, and classification of suspicious cases (32, 33).

In our study, the data showed the malignancy prevalence in suspicious cases on FNAB to be 23.52% which is almost comparable with the results of Pinchot et al. (27.3%) (6). According to the high prevalence of malignancy in non-diagnostic FNABs, it is preferable to perform diagnostic thyroidectomy in addition to rebiopsy (34).

5. CONCLUSIONS

Finally, the results of this study revealed that the size of the thyroid nodules is not reliable at predicting malignancy and should not be applied for medical decision making. FNAB showed a good specificity but low sensitivity in our study. In ≥ 4 cm nodules; FNAB sensitivity was decreased and accompanied by higher false-negative results. Furthermore, FNABs with suspicious results were associated with high probability of malignancy.

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