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Effect of nodule size on the reliability of fine-needle aspiration biopsy in thyroid nodules

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Background/aim: To investigate the reliability of fine-needle aspiration biopsy (FNAB) in thyroid nodules and benign/malignant discrimination, particularly in large nodules.

Materials and methods: A retrospective analysis of 1466 nodules in 402 patients with thyroid nodules who underwent thyroid surgery was made. The pathologic results of the thyroid nodules from preoperative FNAB and postoperative surgical pathology results were compared.

Results: FNAB was found to be in accordance with the postoperative pathologic results. A concordance between the FNAB and postoperative pathologic results, particularly in nodules less than 3 cm in size, was detected. However, a similar finding was not detected in nodules larger than 3 cm in size. The rates, calculated without taking into consideration the nodule dimensions, were found to be: sensitivity, 47.65%; specificity, 93.98%; false-negative, 52.35%; and false-positive 6.02%

Conclusion: In our experience, the false-negative rate of FNAB in nodules larger than 3 cm was high. Therefore, we have concluded that in the event of malignant FNAB, this rate is significant; however, in the event of benign FNAB, it should not be trusted too much.

Key words: Thyroid nodules, thyroid cancer, surgery

1. Introduction

Thyroid nodules are commonly detected in the general population, with an incidence of 17% to 67% found in adults during ultrasonography. The incidence of thyroid cancer is generally low. It was shown that thyroid carcinoma frequency is higher in large thyroid nodes. Fine-needle aspiration biopsy (FNAB) is the gold standard initial step for the evaluation of thyroid nodules and has significantly reduced the number of surgeries performed unnecessarily for diagnostic purposes (1,2). Unfortunately, FNAB cytology seems to have a high false-negative rate in large nodules.

2. Materials and methods

In this study, the FNAB pathology results and the postoperative pathology results of patients who underwent thyroidectomy due to a nodular goiter were compared and, additionally, we investigated whether the dimension of the thyroid nodule had an impact on the FNAB results.

This study was performed retrospectively by evaluating the records of patients who underwent thyroidectomy due to nodular goiter in the Second Department of General Surgery of the Ankara Training and Research Hospital of the Ministry of Health between July 2006 and August 2008.

Overall, 487 patients who underwent thyroidectomy with the diagnosis of nodular goiter were evaluated. Of those, 402 patients whose age, sex, symptoms, physical examination findings, and ultrasonography, free triiodothyronine (T_3), free thyroxine (T_4), total T_3, total T_4, and thyroid-stimulating hormone (TSH) results were available and who had had a FNAB procedure were included. Eighty-five patients with cystic nodules, who had previously had a thyroidectomy and a relapsed thyroidectomy, were excluded from the study.

Serum T_3, T_4, and TSH levels were checked in all patients included in the study, and all patients underwent thyroid ultrasonography and ultrasound-guided FNAB. Nodule dimensions, number of nodules, FNAB pathology results, and postoperative pathology outcomes were recorded according to the results of thyroid ultrasonography.

All euthyroid patients and those with hypothyroidism who were included in the study underwent ultrasound-guided FNAB. Patients who had toxic and/or had laboratorial hyperthyroidism underwent the same

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procedure after becoming euthyroid following medical antithyroid treatment. The results of the FNAB pathology were divided into 4 groups as malignant, benign, suspicious, and insufficient material in terms of malignancy. The FNAB procedure was repeated in patients whose pathology results were found to be insufficient. The pathology reports in which malignancy was suspected and those that were reported as insufficient material again after the third repeat were included in the malignant group. The results of these 4 groups were collected into 2 groups as benign and malignant to be used in statistical analysis in this study.

Hurthle cell carcinoma, medullar carcinoma, follicular carcinoma, papillary carcinoma, and undifferentiated thyroid carcinoma were considered as malignant thyroid diseases. Remaining diseases, reported as Hurthle cell adenomas, diffuse hyperplasia, follicular adenoma, granulomatous thyroiditis, Hashimoto's thyroiditis, lymphocytic thyroiditis, nodular hyperplasia, nodular colloidal goiter, and Riedel thyroiditis, were grouped as benign.

Statistical analysis in this study was performed based on the data collected, including FNAB pathology results, postoperative pathology outcomes, and nodule dimensions.

2.1. Statistical analysis

The SPSS (SPSS Inc., Chicago, IL, USA), was used in the statistical analysis. In addition to the descriptive statistical methods (mean, standard deviation), Student's t-test was used for comparison of the descriptive data with normal distribution when the study data were evaluated. For comparison of the qualitative data, chi-square, McNemar, and kappa goodness-of-fit tests were used. Results were evaluated at the 95% confidence interval and the $P < 0.05$ significance level.

3. Results

A total of 1466 nodules were identified in patients by ultrasonography. Of the patients, 313 (77.86%) were female and 89 (22.14%) were male. Mean patient age was 47.67 ± 12.82 years (range: 17–79). Median patient age was 47 years. The women's ages ranged between 17 and 79, with a mean age of 46.96 ± 12.89 and a median of 46. The men's ages ranged between 19 and 75; their mean age was 50.18 ± 13.30 and the median was 50. The female-to-male ratio was found to be 3.52:1.

In terms of the distribution of nodules by sex, the number of nodules was 1139 (77.70%) in female patients and 327 (22.30%) in male patients (Table 1).

Regarding nodule dimensions measured according to ultrasonography, the smallest nodule was measured as 2 mm in size and the largest nodule size was 100 mm. When we classified nodules according to their sizes as 0 to 9 mm, 10 to 19 mm, 20 to 29 mm, 30 to 39 mm, and larger than 40 mm, the majority of the nodules (39.56%) were found to be in the small nodule group of 0–9 mm. There were also patients with more than 1 nodule.

According to the results of FNAB, the patients were grouped into 4 groups as benign, malignant, suspicious, and insufficient material in terms of malignancy, respectively. The ultrasound-guided FNAB procedure was repeated if insufficient material was reported. Nodules were grouped as malignant or benign according to the final results. Distribution of the nodules according to the results of FNAB is shown in Table 2.

Table 1. The distribution of patients and nodules by sex.

	Male		Female		Total
Patients	89	22.14%	313	77.86%	402
Number of nodules	327	22.30%	1139	77.70%	1466

Table 2. Distribution of the FNAB results to the number of nodules as benign/malignant.

FNAB by the number of nodules	Male		Female		Total	
	n	%	n	%	n	%
Benign	71	24.07	224	75.93	295	73.38
Malignant	5	13.51	32	86.49	37	9.20
Suspicious	6	12.50	42	87.50	48	11.94
Insufficient	7	31.82	15	68.18	22	5.47
Total	89	22.14	313	77.86	402	100

In the postoperative pathologic evaluation, 103 (25.62%) patients were reported as malignant and 299 (74.38%) as benign cases (Table 3).

Similarly, the postoperative pathology results were reviewed on the basis of nodules, and 170 (11.60%) nodules were reported as malignant and 1296 (88.40%) as benign (Table 4). According to our results, distributions of the postoperative pathology results by sex did not significantly differ (chi-square, $P > 0.05$). When the nodule dimensions were taken into account from the postoperative pathology results (Table 5), the number of malignant nodules was found to be higher in the group including 10–19 mm lesions, although the number of benign nodules was higher in the group of 0 to 9 mm.

From the pathology results and nodule dimensions it was seen that the larger the nodule dimension was, the higher the rate of malignancy was (Table 5). The malignancy rate, which was 11.60% in total, reached up to 19.57% in the 30–39 mm nodule size group. A significant difference between malignancy rates among the groups was detected (Table 5) (chi-square, $P < 0.05$). Thereafter, the nodules were grouped into 2 groups, as less than 30 mm in size and larger than 30 mm in size, and the malignancy rate was found to be increased in the group with thyroid nodules of >30 mm (Table 6). This difference was statistically significant (chi-square, $P < 0.05$).

In Cohen's kappa analysis performed between the results of FNAB and the postoperative pathology, while the kappa coefficient (κ) value of the group below 30 mm was 0.50, the κ value in the group above 30 mm was calculated as 0.16.

According to the kappa analysis, the values are considered as follows: 0 to 0.20, very weak; 0.21 to 0.40, weak; 0.41 to 0.60, moderate; 0.61 to 0.80, good; and 0.81

Table 3. Distribution of the postoperative pathology results to sex by the number of patients.

FNAB by the number of patients	Male		Female		Total	
	n	%	n	%	n	%
Benign	69	77.53	230	73.48	299	74.38
Malignant	20	22.47	83	26.52	103	25.62
Total	89	22.14	313	77.86	402	100

Table 4. Distribution of the postoperative pathology results to sex by the number of nodules.

By the number of nodules	Male		Female		Total	
	n	%	n	%	n	%
Benign	288	88.07	1008	88.50	1296	88.40
Malignant	39	11.93	131	11.50	170	11.60
Total	327		1139		1466	

Table 5. Distribution of the postoperative pathology results by nodule dimension.

Dimension	Benign		Malignant		Total
	n	%	n	%	n
1 to 9 mm	536	92.41	44	7.59	580
10 to 19 mm	401	87.94	55	12.06	456
20 to 29 mm	172	86.43	27	13.57	199
30 to 39 mm	74	80.43	18	19.57	92
>40 mm	113	81.29	26	18.71	139
Total	1296	88.40	170	11.60	1466

Table 6. Postoperative pathology results in the groups of 0 to 29 mm and above 30 mm.

Dimensions	Benign		Malignant		Total
	n	%	n	%	n
1 to 29 mm	1109	89.80	126	10.20	1235
>30 mm	187	80.95	44	19.05	231
Total	1296	88.40	170	11.60	1466

to 1.00, excellent. Accordingly, while the concordance in the group above 30 mm is very poor, this value is moderate in the group below 30 mm.

When we grouped nodules as below 30 mm and above 30 mm in size and examined their postoperative pathologic distributions, the rate of benign nodules was 89.80% (1109 nodules) and the rate of malignant nodules was 10.20% (126 nodules) in the group of nodules smaller than 30 mm in size (Table 6), while the rate of benign nodules was 80.95% (187 nodules) and the rate of malignant nodules was 19.05% (44 nodules) in the group of nodules larger than 30 mm in size. There was a statistical difference between these 2 groups (chi-square test, $P < 0.05$).

In order to judge the capability and performance of these diagnostic tests, a control test must be carried out by a proven method and the results compared. This control was performed by a McNemar statistical test, and if the diagnostic test results were found to be identical to the results of the actual diagnosis, then the validity of the diagnostic test was approved (1). For this reason, the McNemar test, performed for the results between the FNAB and the postoperative pathology, showed that the FNAB was in concordance with the postoperative pathology ($P < 0.05$). The rates, calculated without taking into consideration the nodule dimensions, were found as sensitivity, 47.65%; specificity, 93.98%; false-negative, 52.35%; and false-positive, 6.02%. However, significant changes in nodules of below 30 mm and above 30 mm were observed in the evaluation performed based on the nodule dimension (Table 7).

The results obtained when nodules were grouped as above 30 mm and below 30 mm in dimension are shown in Table 8. There is a statistically significant difference between the results obtained from the group below 30 mm and the results obtained from the group above 30 mm in size (chi-square, $P < 0.05$).

Table 7. Sensitivity, specificity, false-negative, and false-positive rates of the tests by nodule dimensions.

Dimensions (mm)	0–9	10–19	20–29	30–39	>40	All
Sensitivity	61.36%	56.36%	48.15%	22.22%	23.08%	47.65%
Specificity	96.08%	93.52%	91.28%	91.89%	91.15%	93.98%
False-negative	38.64%	43.64%	51.85%	77.78%	76.92%	52.35%
False-positive	3.92%	6.48%	8.72%	8.11%	8.85%	6.02%

Table 8. Sensitivity, specificity, false-negative, and false-positive rates of nodule dimensions below and above 30 mm.

	<30 mm	>30 mm	All
Sensitivity	56.35%	22.73%	47.65%
Specificity	94.41%	91.44%	93.98%
False-negative	43.65%	77.27%	52.35%
False-positive	5.59%	8.56%	6.02%

4. Discussion

Thyroid nodules are a common clinical problem. In epidemiological studies palpable thyroid nodules were detected in approximately 5% of women and in 1% of men in regions where enough iodine could be taken up. On the other hand, thyroid nodules were detected in 19% to 67% of randomly selected individuals (more often in women and elderly people) by high-resolution ultrasonography (2). In studies carried out in Turkey, this rate has been reported as higher than 2.8% (3). In autopsy series, thyroid nodules were detected in 35%–50% of thyroid glands, and it was possible to detect small nodules in most of the glands that were found normal in palpation (4–6). Ultrasound helps to demonstrate the prevalence of nodular goiters (4–6).

Although nodular thyroid diseases are relatively common, thyroid cancers are relatively rare and account for less than 1% of all malignant neoplasm. Between 3% and 5% of thyroid nodules are malignant (7–9). When a nodule is detected in the thyroid gland, it is important to differentiate between benign and malignant nodules with FNAB, as that will have an impact on the type of surgical approach. However, it is also important not to waste time or perform unnecessary investigations. Although medical history, age, sex, radiation history, and family history are helpful in evaluating nodules, they are not certainly diagnostic. However, approximately 6% of the patients treated with radiotherapy for upper chest and neck diseases at an age of younger than 5 years carry an increased risk of developing carcinomas (7).

While the annual incidence was 3.6/1000 in 1973, this rate reached 8.7/1000 in 2002, an increase of 2.4 times (for increase trend, $P < 0.001$). This increase trend is continuous. Almost all of this increase can be attributed to papillary thyroid cancer, whose incidence almost increased 2.9 times between 1988 and 2002. Moreover, 49% of this increase is due to cancers of 1 cm or smaller in size and 87% is due to cancers of 2 cm or smaller in size. The change in tumor dimensions may be due to the increase in the use of neck ultrasonography, early diagnosis and treatment, and changes in initial treatment and follow-up trends in many patients (2).

There are no precise criteria for differentiating malignant and benign thyroid nodules ultrasonographically or scintigraphically. The criteria for diagnosing malignancy in ultrasonography includes the presence of microcalcification, solid or predominantly solid internal structure, irregular contour, hypoechoic internal structure, and larger front and rear diameter than transverse diameter (10). The presence of lymphadenopathy and adjacent organ invasion are findings with a high specificity for malignancy. The number of nodules, nodule dimensions, and growth rate interval are nonspecific features for thyroid malignancies (10). The most specific ultrasonography finding for thyroid malignancies is microcalcification. It is observed in 29% to 59% of primary thyroid carcinomas and especially in papillary thyroid carcinomas (11–13). However, small anechoic cystic nodules, smaller than 4 cm in size, which include microparticles and do not contain a solid structure, usually with regular edges of the regular and thin hypoechoic halo around it, are considered as benign. Therefore, FNABs of thyroid nodules guided by ultrasonography, scintigraphy, and physical examination along with cytological evaluation of the materials have become standard diagnostic tools in the diagnosis of these lesions (14,15).

FNAB is the most convenient and economical method for the evaluation of thyroid nodules. Retrospective studies revealed that the rates for both false-negative results and failure to diagnose in ultrasound-guided FNABs performed with ultrasonography are much lower when compared to palpation. For this reason, ultrasound-guided FNAB should be preferred in thyroid nodules with a high nondiagnostic cytology (cystic component of >25%–50%) or with a high probability of sampling error (difficult to palpate or posterior nodules) (Table 3). If ultrasonography confirms the presence of a nodule in a palpated region, FNAB can be conducted, accompanied by palpation or ultrasound-guided. The results of FNAB are divided into 4 categories as follows; nondiagnostic, malignant (with 95% probability of malignancy after surgery), indeterminate or neoplasia suspected, and benign. To these categories were added 2 more categories at the latest National Cancer Institute Thyroid Fine-Needle Aspiration State of the Science Conference: follicular neoplasm with unidentified malignancy suspicion (50% to 75% risk of malignancy) and importance (5% to 10% risk of malignancy). In addition, at the conference both follicular and Hurtle cell neoplasms were proposed to be identified as 'uncertain' (15%–25% risk of malignancy) (2).

Patients with multiple thyroid nodules are also at risk of malignancy, as much as patients with solitary nodules. Despite the risk of malignancy being the same in each patient regardless of nodule number, there is a larger study that reports that the risk of solitary nodules for malignancy is higher than nonsolitary nodules. The performance of ultrasonography is required to identify the nodules. However, if only the 'biggest' or 'dominant' nodule is aspirated, a thyroid cancer can remain undetected. Radionuclide examination should be considered in patients with low or low–normal ranges of serum TSH. Patients diagnosed as hypofunctional after such an examination should have FNAB performed (2).

The main problem, when thyroid nodules are detected is to make a benign/malignant differentiation of nodules. The most valuable method for benign/malignant differentiation of thyroid nodules is FNAB (16). The presence of sufficient sampling and an experienced cytopathologist are 2 major factors for the success of FNAB (11). It is reported that false-negative and false-positive rates must be used instead of sensitivity and specificity rates for evaluating the success of FNAB. Some researchers found the false-negative rate of FNAB as 0%–1% and false-positive rate as less than 5% (17). Furthermore, 99% of nodules diagnosed benign as a result of FNAB have been shown to remain benign for 10 years (18). However, imaging of the thyroid gland periodically is recommended due to the adjacent nodules in the thyroid that did not have FNAB applied (19). Situations that require reevaluation in the follow-up are nodule shape change, growth in dimension, and development of new nodules. The follow-up interval must be a minimum of 6 months and a maximum of 18 months (20).

It is well understood that larger thyroid nodules have a higher risk of cancer (21–27). In the guidelines issued by the American Thyroid Disease Society in November 2009 it was said that thyroid nodules reported as benign, especially those above 4 cm in size, require follow-up due to the possibility of a false-negative rate (5%) that cannot be ignored (2).

In a study conducted by Hamming et al., the malignancy rate was found as 27% in a group of patients with solitary nodules, in which the longest diameter of the dominant nodule in the multinodular goiter was a minimum of 40 mm and the solid component of the nodule was 75% and above (14,15,28).

In 1995, Meko and Norton (22) reported that nodules larger than 3 cm and solid/cystic lesions had a higher rate of cancer compared to those smaller than 3 cm and solid nodules. This finding led to the proposal of clinical diagnostic lobectomy for nodules larger than 3 cm. The rate of malignancy in nodules larger than 3 cm was found as 19% in our study. When we grouped the thyroid nodules by their dimensions, similar to the study conducted by Meko and Norton, there was a statistically significant difference between the malignancy rate in the group with nodules of 30 mm and above and the malignancy rate in the group with nodules of below 30 mm (chi-square, $P < 0.05$) (Table 6). In addition, there was also a statistically significant difference between the false-negative rate of nodules above 3 cm (77.27%) and the calculated false-negative rates of nodules below 3 cm (43.65%) in our study (chi-square, $P < 0.05$). In addition, while we found the kappa coefficient as 0.50 between FNAB and postoperative pathology in the nodule group smaller than 3 cm during the statistical evaluations, this value in the group with nodules larger than 3 cm was found as 0.19, which could be regarded as incongruous. This supports our initial thesis.

Meko and Norton evaluated the characteristics of thyroid nodules associated with false-negative cytology in a series of 90 patients. The false-negative FNAB rate in 30 patients with lesions above 3 cm was 5 in their study (false-negative rate: 16.67%). On the other hand, the false-negative rate in patients with lesions below 3 cm was 0%. One of the 5 patients with a false-negative FNAB result had multiple micropapillary carcinoma foci detected outside the lesions assessed by FNAB, and another patient had a cancer of larger than 3 cm outside the nodule of 1 cm (22). The sample size was larger in our study, and the case as to whether the presence of thyroid cancer was inside or outside a malignancy or mass of 3 cm or larger could not be specifically examined and evaluated. However, the rate of malignancy of 19.05% in nodules above 3 cm in our study confirms the high cancer rate found by Meko and Norton for large thyroid nodules.

The sensitivity of FNAB was reported as ranging from 58.3% to 98% and the specificity of FNAB as ranging from 72% to 100% in the retrospective analysis of 37,895 patients issued by Ravetto et al. in 2000, and in studies by Cap et al., Mandell et al., Sankhla et al., and Bennedbaek et al. (22–26). The calculations in the majority of these publications were performed by excluding suspicious lesions from the studies. In our study, the cases reported as suspicious lesions after FNAB were analyzed in positive FNAB results. One of the reasons for this is that we perform surgeries on patients with suspicious lesions identified by FNAB in accordance with the principles of oncologic surgery, and the other reason is that the definitive pathologies of suspicious lesions are shown to be malignant in between 20% and 50% of cases in various publications (29,30).

McCoy et al. stated that they do not recommend FNAB as a routine in patients scheduled to undergo total thyroidectomy in the first place independently of cancer diagnosis (31); however, as mentioned above, all the preoperative tests create adverse effects for patients' mental state, increase the financial burden, and lead to loss of time, as well as harming the temporary well-being of patients and damaging their trust in health care professionals. Therefore, when we evaluate suspicious and benign FNAB results in patients with nodules above 3 cm in size, we think that it would be appropriate to follow-up at more frequent intervals, and even to strongly advise surgery, for patients with malignant findings, such as receiving radiation to the head and neck in childhood or whole-body irradiation history for bone marrow transplantation, the presence of thyroid cancer or thyroid cancer syndrome in first-degree relatives (Cowden's syndrome, familial polyposis, Carney complex, multiple endocrine neoplasia type 2, Werner syndrome, etc.), exposure to ionizing radiation fall-out in childhood and adolescent periods, rapid growth of the lesion, hoarseness, vocal cord paralysis, lateral cervical lymphadenopathy, invasion of the nodule to surrounding regions and hypoechoic nodules in ultrasonography according to the normal thyroid parenchyma, increase in internal nodule vascularity, irregular infiltrative borders, presence of microcalcifications, absence of halo, and higher nodule height than transverse size suggestive of malignancy, which was also specified in the guidelines issued by the American Thyroid Disease Society in November 2009. False-negative FNAB results may be secondary to the problems of sampling, processing, scanning, interpretation, or clinical correlation. A false-negative result can significantly delay the appropriate surgical treatment in patients with thyroid cancer. Therefore, we think that the assessment of FNABs by expert cytopathologists is important.

Follicular lesions typically appear to be follicular epithelial cells that create microfollicles with a minimal colloid floor in FNAB, and they are the cause of about 20% of nodule biopsies. Screening of malignancy in follicular lesions is usually not possible only on the basis of cytology; it requires diagnostic lobectomy (23).

It is understood that what is ultimately important is the overlooked cancer rate rather than any overlooked follicular lesions, but the malignant potential of follicular adenomas is not clear. However, the situation whereby 8 of 9 cancer cases (88.9%) overlooked in the study performed by McCoy et al. were follicular pattern neoplasms reveals that this group of lesions causes a false-negative cytology rate in terms of cancer. This situation is perhaps not surprising because moderately large follicular cell-lined structures filled with colloid, such as large follicular variant papillary thyroid cancers, follicular carcinomas, and follicular adenomas, can display significant intratumoral heterogeneity or cystic degeneration, and this makes sampling for a follicular lesion or malignancy diagnosis difficult (31).

In our study, the sensitivity of FNAB was calculated as 47.65% and the specificity as 93.98% when the nodule dimensions were not taken into account. However, when the nodule dimensions were taken into account, while the sensitivity for dimensions of less than 30 mm increased to 56.35%, the specificity increased to 94.41%, a value consistent with the literature. The sensitivity with nodules above 30 mm decreased to 22.73% and the specificity to 91.44%. The conclusion to be drawn here is that sufficient cytological samples must be obtained by performing FNAB more carefully, samples must be delivered to the pathology laboratory as soon as possible in an appropriate manner, and, most importantly, cytological samples must be examined by expert and experienced cytopathologists and the false-negative rate in suspicious lesions must be reduced to the acceptable limits defined in the literature.

The false-positive rate is reported as 1% to 8% in several publications (32–38). This rate in our study was found as 6.02%, taking all the patients into account, and in the patients with nodules above 3 cm in size it was found as 8.56%. These rates are consistent with the rates in the literature.

We agree with the recommendations in the study performed by McCoy et al. (31). Molecular tests can provide additional guidance in the evaluation of benign or large thyroid nodules with indeterminate cytology as their clinical roles continue. For example, the presence of BRAF, RET, RAS, and PAX8-PPAR gamma mutations may allow further characterization of FNAB cytology samples (39,40). The patient subgroup with large thyroid nodules or benign or indeterminate cytology can benefit potentially from molecular analysis as these analyses become more widespread and guidelines are developed from evidence-based data.

In conclusion, the incidence of cancer is high in thyroid nodules of 3 cm or larger (19.05%). Benign FNAB cytology of large thyroid nodules has a false-negative rate unacceptably high in terms of overlooked follicular lesions (77.21%). FNAB may be useful in larger lesions, especially if the cytology is malignant, because it can provide opportunity for preoperative counseling. However, it should not change the decision to progress to surgery for a thyroid nodule of 3 cm or larger as a result of a benign FNAB.

New prospective studies should be carried out on this subject in order to help us gather more reliable information. After new studies, we predict that nodule dimension will be accepted as a criterion for performing FNAB, and the decision for surgery for nodules above an estimation value can be taken directly.

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