Nodules with nondiagnostic results on repeat fine needle aspiration biopsy (FNAB): Which nodules should be considered for repeat biopsy or surgery rather than follow-up?

Na Lae Eun

Department of Medicine

The Graduate School, Yonsei University

Nodules with nondiagnostic results on repeat fine needle aspiration biopsy (FNAB): Which nodules should be considered for repeat biopsy or surgery rather than follow-up?

Directed by Professor Eun Ju Son

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Na Lae Eun

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This certifies that the Master's Thesis of
Na Lae Eun is approved.

Thesis Supervisor : Eun Ju Son

Thesis Committee Member#1 : Hang-Seok Chang

Thesis Committee Member#2 : Hee Jung Moon

The Graduate School
Yonsei University

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<TABLE OF CONTENTS>

LIST OF FIGURES

LIST OF TABLES

ABSTRACT

Nodules with nondiagnostic results on repeat fine needle aspiration biopsy (FNAB) : Which nodules should be considered for repeat biopsy or surgery rather than follow-up?

Na Lae Eun

Department of Medicine
The Graduate School, Yonsei University

(Directed by Professor Eun Ju Son)

Objective: To assess the clinicopathologic and ultrasonographic features of thyroid nodules with nondiagnostic results on repeat ultrasound (US)-guided fine-needle aspiration biopsy (FNAB) and to determine proper management of nodules with consecutive nondiagnostic results.

Materials and Methods: This retrospective study included 297 nodules with nondiagnostic results on repeat FNAB that underwent at least 12 months follow-up US, follow-up biopsy or operation. We compared clinical and ultrasonographic variables between benign and malignant nodules according to size in nodules with repeat nondiagnostic results.

Results: Comparison of benign and malignant nodules with repeat nondiagnostic results revealed that age, marked hypoechogenicity, irregular or

microlobulated margins, microcalcification, and nonparallel shape were significantly associated with malignancy (p <0.05). Multivariate logistic regression analysis in malignant nodules revealed that microcalcification (odd ratio, 3.241; 95% CI: 1.504, 6.985, p =0.003) and irregular or microlobuated margins (odd ratio, 2.35; 95% CI: 1.003, 5.539, p =0.049) were independently associated with malignant nodules with nondiagnostic results.

Microcalcification was also independently significant in repeat nondiagnostic nodules measuring ≤10 mm. In contrast, nodules >10 mm showed significant differences with microlobulated or irregular margins.

Using the receiver-operating characteristic analysis, the best cutoff value for the "number of suspicious findings" between benign and malignant nodules were greater than 2 in all sizes, greater than 2 in nodules measuring ≤10 mm and greater than 1 in nodules measuring >10mm..

Conclusions: US findings of microcalcification and irregular or microlobuated margin and number of suspicious findings are predictive of malignancy in thyroid nodules with repeated nondiagnostic cytology. Among them, irregular or microlobulated margins were most significant in nodules larger than 10 mm. Repeat FNAB or surgery should be performed for repeat nondiagnostic thyroid nodules with irregular or microlobuated margin or two or more suspicious US features.

Keywords: US-guided fine needle aspiration biopsy (FNAB), repeat biopsy, follow-up US, nondiagnostic, thyroid nodule

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I. Introduction

Fine-needle aspiration biopsy (FNAB) is considered the standard first-line method to evaluate thyroid nodules, offering high accuracy and low invasiveness.[1-3] This method has significantly reduced operation rates for benign nodules. Unfortunately, unsatisfactory or nondiagnostic results present a dilemma for clinicians and radiologists managing thyroid nodules, particularly nodules with high nondiagnostic rates in repeat biopsy or high malignancy rates. The Bethesda System for Reporting Thyroid Cytopathology[4] recommends nondiagnostic rates ideally less than 10% of all FNABs; however, up to 21% of nodules have nondiagnostic results in initial FNAB and up to 50-63% in repeat biopsies.[5-9] The recommended risk of malignancy of nondiagnostic nodules in

the Bethesda system is 1-4%; however, malignancy rates ranging from 2%-51% have been reported.[3,7,10-13]

Upon nondiagnostic initial FNAB findings, the American Thyroid Association (ATA), American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association[14,15] recommend repeat FNAB or resection for repeat nondiagnostic nodules. If initial nondiagnostic nodules still shows nondiagnostic results after repeat FNAB, surgery is recommended for solid nodules, and surgery or close observation is recommended for cystic nodules.[14,15] However, surgery for all solid nodules are not cost-effective and can cause patient's postoperative morbidity. To avoid unnecessary operations, several reports have suggested that conservative management rather than surgery should be considered in low-risk groups because most repeatedly nondiagnostic nodules have benign outcomes.[7,16] Moon et al.[17] suggested that surgery is recommended for nondiagnostic nodules in repeat biopsies showing one or more suspicious features.

The aim of our study was to investigate the clinicopathologic and US features of thyroid nodules with repeated nondiagnostic results and to determine proper management of nodules with consecutive nondiagnostic results.

II. MATERIALS AND METHODS

1. Study population

This retrospective study was performed from January 2009 to December 2013 at a referral tertiary center. Our institutional review board approved the study without requirement of informed consent or patient approval. During that period, 13,193 nodules underwent US-guided FNAB at our institution. Of these, 1517 nodules (11.5%) were reported as having nondiagnostic results according to Bethesda category. Among them, 772 underwent a 2nd FNAB and 477 nodules (61.8%) once again showed nondiagnostic results. Thyroid nodules were classified as benign or malignant after pathological confirmation during surgery or repeat FNABs. Thyroid nodules without significant changes or that decreased in size during at least 12 months of follow-up US were considered clinically benign.

Among 477 nondiagnostic nodules with repeat FNABs, 180 were excluded due to the absence of follow-up at least 12-months with US or repeat FNAB. A total of 297 nodules with repeat nondiagnostic results were included in this study.; among these, 153 were benign results after repeat biopsies, 74 showed no changes during at least 12 months of follow-up US and 7 decreased in size (mean follow-up, 23 months; range, 12-70 months), and 63 underwent operation (Figure 1). Of total 297 nodules, 68 were men and 229 were women. The mean patient age was 52 years ±11 months (range:-23-77). The mean nodule size was 9.8 mm (range: 3-81 mm). Clinical information (patient sex and age at the time of FNAB, and the dates of US), US findings, and cytopathologic records were reviewed for all nodules.

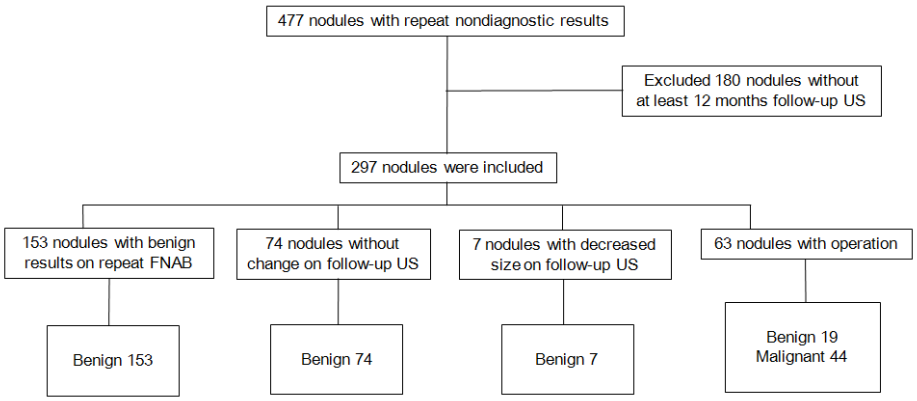


Figure 1. Study group flow chart.

2. Imaging methods and US-guided FNAB

US and FNA were performed using 7–15 MHz (HDI 5000; Philips Medical Systems, Bothell, WA) and 5–12 MHz linear array transducers (iU22; Philips Medical Systems). Real-time US examinations were performed by one of six radiologists with 1–16 years of thyroid imaging experience. Nodule size was defined as the maximum diameter on US. US findings of thyroid nodules that underwent FNAB were prospectively analyzed according to internal composition, echogenicity, margin, calcifications, shape, and vascularity at the time of US. Internal composition was divided into solid and cystic portions of 50% or less and over 50%. The nodules were classified as hyperechoic, isoechoic, or hypoechoic compared to normal thyroid parenchyma; marked hypoechogenicity was defined as hypoechoic findings compared to those of the strap muscles. Margins were categorized as circumscribed, microlobulated, and

irregular. Calcifications were classified as micro (tiny or punctuate foci measuring less than 1 mm), macro and no calcifications. Shape was designated as parallel or nonparallel (taller than wide or greater anteroposterior than transverse direction). Vascularity was divided into peripheral (flow during Doppler US only at the periphery of the nodule), central (flow during Doppler US only in the central portion), both (flow in both sides of the central and peripheral portions), and no vascularity. Suspicious malignant US findings were solidity, marked hypoechogenicity, microcalcifications, microlobulated or irregular margins, and taller than wide shape as described previously.[18]

The same radiologist who performed the thyroid US performed all US-guided FNABs. FNABs were performed using a free-hand technique and 23-gauge needle attached to a 2-mL disposable syringe without an aspirator. Each sample smeared onto different glass slides and immediately alcohol-fixed for Papanicolaou staining. The sample remaining in the syringe was rinsed in saline for cell blocking. Cytologists did not routinely perform on-site evaluation. Pathologists evaluated all nodules according to the Bethesda system.

3. Data and statistical analysis

Categorical data were classified according to percentages and frequencies. We compared malignancy rates, patient characteristics (sex and age), and US characteristics (nodule size, composition, echogenicity, margin, calcification, shape, vascularity, and number of suspicious findings) between benign and

malignant nodules in repeat nondiagnostic thyroid nodules. Continuous variables including patient age and nodule size were analyzed using Student's t-test, while categorical variables including sex, malignancy rates, and US features were compared with $\chi 2$ and Fisher's exact tests. To assess independent variables of malignancy in repeat nondiagnostic nodules, multivariate logistic regression analysis with a forward stepwise selection method and odds ratios (ORs) were performed. These methods were also used to assess nodules of all sizes, 10 mm or less, and larger than 10 mm.

In addition, receiver operating characteristic (ROC) curves were performed to assess diagnostic value of "number of susicious findings". The cutoff point was analyzed by a ROC curve so that sum of sensitivity and specificity was maximized. Then, the diagnostic sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were determined by ROC curves. These methods were also used to assess nodules of all sizes, 10 mm or less, and larger than 10 mm.

Statistical analysis was performed using SAS (version 9.2; SAS institute, Cary, NC, USA). $P < 0.05$ was considered statistically significant.

III. RESULTS

Among 297 nondiagnostic nodules with repeat FNAB, 44 (14.8%) were diagnosed as malignant on operation, while 253 (85.2%) were diagnosed as benign. Of 253 benign nodules, 153 were pathologically confirmed as benign on the 3rd through sixth repeat FNABs. Eighty-one nodules showed no change or decreased in size during follow-up US; the other 19 were confirmed on operations.

Marked hypoechogenicity, microlobulated or irregular margins, microcalcifications, and taller-than-wide shape occurred significantly more often in malignant nodules than in benign nodules (p = <0.001, <0.001, <0.001, and 0.0215 respectively) (Table 1). Composition and vascularity did not differ significantly between benign and malignant nodules. However, the number of suspicious findings did differ significantly between benign and malignant nodules (1.95±1.12 vs. 2.82±1.32, respectively; p <0.001) (Table 1).

Table 1. Comparison of malignancy rates, clinical and ultrasonographic features of repeat nondiagnostic thyroid nodules according to malignancy and benignity

	Malignant nodules (n =44)	Benign nodules (n = 253)	*p*-value
Age (years), mean ± SD	49 ± 10	53 ± 11	0.032
Sex			0.676
Male	35/44(79.55%)*	194/253(76.68)	
Female	9/44(20.45%)	59/253(23.32%)	
Nodule size (mm), mean ± SD	9.89 ± 8.55	10 ± 8.46	0.935
Composition			0.3804
Solid	39/44(88.64%)†	202/253(79.84%)	
Cystic portion ≤50%	5/44(11.36%)	41/253(16.21%)	
Cystic portion >50%	0/44(0%)	110/253(3.95%)	
Echogenicity			<0.001
Hyperechogenicity	0/44 (0.0%)	0/253 (0.0%)	
Isoechogenicity	3/44(6.82%)	51/253(20.16%)	
Hypoechogenicity	30/44(68.18%)	175/253(69.17%)	
Marked hypoechogenicity	11/44(25%)	27/253(10.67%)	
Margin			0.0008
Well defined	9/44(20.45%)	118/253(46.64%)	
Microlobulated	6/44(13.64%)	43/253(17%)	
Irregular	29/44(65.91%)	92/253(36.36%)	
Calcification			
No calcifications	14/44(31.82%)	31/253(12.25%)	0.0004
Microcalcifications	5/44(11.36%)	85/253(33.6%)	
Macrocalcifications	25/44(56.82%)	137/253(54.15)	
Shape			0.0215
Wider than tall	19/44(43.18%)	156/253(61.66%)	
Taller than wide	25/44(56.82%)	97/253(38.34%)	

Vascularity			0.7985
Peripheral	13/44(29.55%)	85/253(33.6%)	
Central	1/44(2.27%)	6/253(2.37%)	
Both	8/44(18.18%)	33/253(13.04%)	
No	22/44(50%)	129/253(50.99%)	
Number of suspicious finding	2.82±1.32	1.95±1.12	<0.001

*Number of patients / total patients

†Number of nodules with the feature/ total nodules

The results of multivariate logistic regression analysis of clinical and US findings in malignant nondiagnostic nodules with repeat nondiagnostic results are shown in Table 2. Microcalcification (OR, 3.241; 95% CI: 1.504, 6.985, p = 0.003) and irregular or microlobuated margins (OR, 2.35; 95% CI: 1.003, 5.539, p = 0.049) were independent factors associated with malignant nodules with nondiagnostic results.

Table 2. Multivariate analysis of clinical and ultrasound characteristics for predicting malignancy of repeat nondiagnostic nodules

	OR (95% CI)	*p*-value
Echogenicity (marked hypoechogenicity)	2.034 (0.862-4.800)	0.105
Microcalcification	3.241 (1.504-6.985)	0.003
Margin (irregular/microlobulated)	2.35 (1.003-5.539)	0.049
Shape (nonparallel)	1.412 (0.003-5.539)	0.348

CI, Confidence interval; OR, odds ratio.

Of 216 nodules measuring 10 mm or less, 187 (88.6%) and 24 (11.4%) were benign and malignant, respectively. Marked hypoechogenicity, margin, calcification, and shape differed significantly between benign and malignant nodules (p = 0.004, 0.005, 0.001,and 0.005, respectively). The number of suspicious findings also differed significantly between benign and malignant nodules (2.14±1.12 vs. 3.24±1.02, respectively; p <0.001) (Table 3).

Table 3. Comparison of malignancy rates, clinical and ultrasonographic features of repeat nondiagnostic nodules measuring 10mm or less according to malignancy and benignity

	Malignant nodules (n =29)	Benign nodules (n = 187)	*p*-value
Composition	27/29(93.1%)*	158/187(84.5%)	0.399
Solid	2/29(6.9%)	22/187(11.8%)	
Cystic portion ≤50%	0/29(0%)	7/187(3.7%)	
Cystic portion >50%			
Echogenicity	0/29(0.0%)	0/187(0.0%)	0.004
Hyperechogenicity	0/29(0.0%)	28/187(15.0%)	
Isoechogenicity	20/29(69.0%)	137/187(73.3%)	
Hypoechogenicity	9/29(31.0%)	22/187(11.8%)	
Marked hypoechogenicity			
Margin			0.005
Well defined	3/29(10.3%)	73/187(39.0%)	

Microlobulated	5/29(17.2%)	34/187(18.2%)	
Irregular	21/29(72.4%)	80/187(42.8%)	
Calcification			0.001
No calcifications	11/29(37.9%)	24/187(12.8%)	
Microcalcifications	5/29(17.2%)	66/187(35.3%)	
Macrocalcifications	21/29(72.4%)	97/187(51.9%)	
Shape			0.005
Wider than tall	8/29(27.6%)	104/187(55.6%)	
Taller than wide	21/29(72.4%)	83/187(44.4%)	
Vascularity			0.854
Peripheral	9/29(31.0%)	47/187(25.1%)	
Central	1/29(3.4%)	5/187(2.7%)	
Both	2/29(6.9%)	20/187(10.7%)	
No	17/29(58.6%)	115/187(61.5%)	
Number of suspicious finding	3.24±1.02	2.14±1.12	<0.001

*Number of nodules with the feature/ total nodules

The results of the multivariate logistic regression analysis of clinical and US findings in malignant nondiagnostic nodules measuring 10 mm or less are shown in Table 4. Only microcalcification (OR, 4.715; 95% CI: 1.841, 12.079, p = 0.001) was an independent factor associated with malignant nodules measuring 10 mm or less with repeated nondiagnostic results.

Table 4. Multivariate analysis of clinical and ultrasound characteristics for predicting malignancy of repeat nondiagnostic nodules measuring 10mm or less

	OR (95% CI)	*p*-value
Echogenicity (marked hypoechogenicity)	2.509 (0.919-6.846)	0.073
Microcalcification	4.715 (1.841-12.079)	0.001
Margin (irregular/microlobulated)	3.414 (0.907-12.851)	0.069
Shape (nonparallel)	2.140 (0.826-5.545)	0.117

CI, Confidence interval; OR, odds ratio.

Of 81 thyroid nodules larger 10 mm, 66 were benign (81.5%) and 24 were malignant (18.5%). Only irregular or microlobulated margins were significant US findings (p = 0.017). Other findings, such as composition, echogenicity, calcification, shape, and vascularity did not differ significantly between benign and malignant nodules larger than 10 mm. The number of suspicious findings were not significantly different between benign and malignant nodules (1.38±1.12, vs. 2.±1.46, respectively; p =0.071) (Table 5). But considering the small number of group, we were willing to accept that p value 0.071 for number of suspicious findings can be regarded as a tendency in differentiating between benign and malignant nodules because p-value less than 0.1 means that a tendency of probability exists statistically. [19,22]

Table 5. Comparison of malignancy rates, clinical and ultrasonographic features of repeat nondiagnostic thyroid nodules measuring larger than 10mm according to malignancy and benignity

	Malignant nodules (n =15)	Benign nodules (n = 66)	*p*-value
Composition			
Solid	12/15(80.0%)*	44/66(66.7%)	0.511
Cystic portion ≤50%	3/15(20.0%)	19/66(28.8%)	
Cystic portion >50%	0/15(0%)	3/66(4.5%)	
Echogenicity			0.477
Hyperechogenicity	0/15(0.0%)	0/66(0.0%)	
Isoechogenicity	3/15(20.0%)	23/66(34.8%)	
Hypoechogenicity	10/15(66.7%)	38/66(57.6%)	
Marked hypoechogenicity	2/15(13.3%)	5/66(7.6%)	
Margin			0.017
Well defined	6/15(40.0%)	45/66(68.2%)	
Microlobulated	1/15(6.7%)	9/66(13.6%)	
Irregular	8/15(53.3%)	12/66(18.2%)	
Calcification			0.355
No calcifications	3/15(20.0%)	7/66(10.6%)	
Microcalcifications	2/15(13.3%)	19/66(28.8%)	
Macrocalcifications	10/15(66.7%)	40/66(60.6%)	
Shape			0.646
Wider than tall	11/15(73.6%)	52/66(78.8%)	
Taller than wide	4/15(26.7%)	14/66(21.2%)	

Vascularity			0.145
Peripheral	4/15(26.7%)	38/66(57.6%)	
Central	0/15(0.0%)	1/66(1.5%)	
Both	6/15(40.0%)	13/66(19.7%)	
No	6/15(33.3%)	14/66(21.1%)	
Number of suspicious finding	2.±1.46	1.38±1.12	0.071

*Number of nodules with the feature/ total nodules

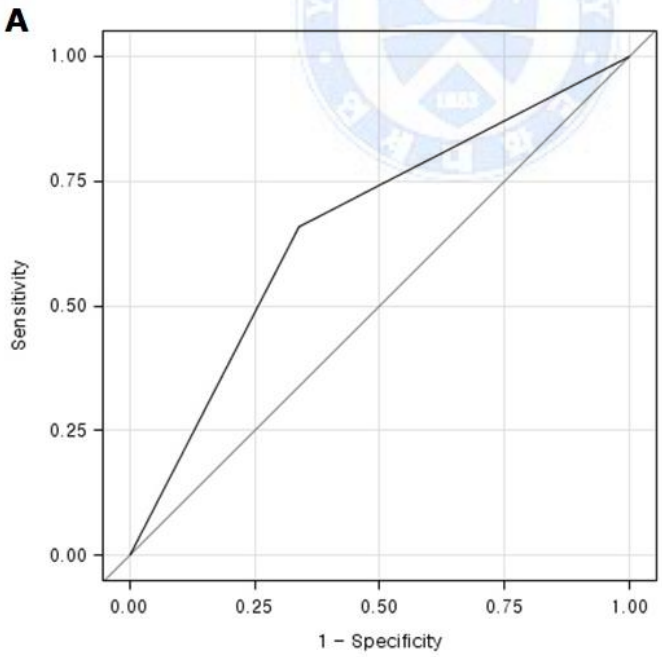
Using the ROC analysis, the best cutoff value for the "number of suspicious findings" between benign and malignant nodules was greater than 2 in nodules with all sizes (Table 6) and the area under the curve (AUC) was 0.66 (Fig. 2A). Using the best cutoff point, the sensitivity, specificity, PPV, NPV, and accuracy were 65.9%, 66.0%, 25.21%, 91.76% and 65.99%, repectively.

The best cutoff values were greater than 2 in nodules ≤10mm and greater than 1 in nodules > 10mm (Table 6). The AUC were 0.70 and 0.61, respectively (Fig. 2B, 2C). The sensitivity, specificity, PPV, NPV, and accuracy were 79.31%, 60.43%, 23.71%, 94.96% and 62.96% in nodules ≤10mm and 60%, 62.12%, 26.47%, 87.23% and 61.73% in nodules >10mm, respectively (Table 6).

Table 6. Optimal cutoff values, sensitivity, specificity, predictive values and accuracy using number of suspicious findings for differentiation of malignancy and benignity in repeat nondiagnostic thyroid nodules.

Size	Cutoff	Sensitivity , %	Specificity , %	PPV , %	NPV , %	Accuracy , %
All	>2	65.90	66.00	25.22	91.76	65.99
≤ 10mm	>2	79.31	60.43	23.71	94.96	62.96
>10mm	>1	60	62.12	26.47	87.23	61.73

Figure 2. Receiver-operating characteristic curves for number of suspicious findings in differentiation of malignancy and benignity in repeat nondiagnostic thyroid nodules. A. Nodules with all sizes (AUC = 0.66). B. Nodules measuring 10mm or less (AUC = 0.70). C. Nodules measuring larger than 10mm (AUC = 0.61)



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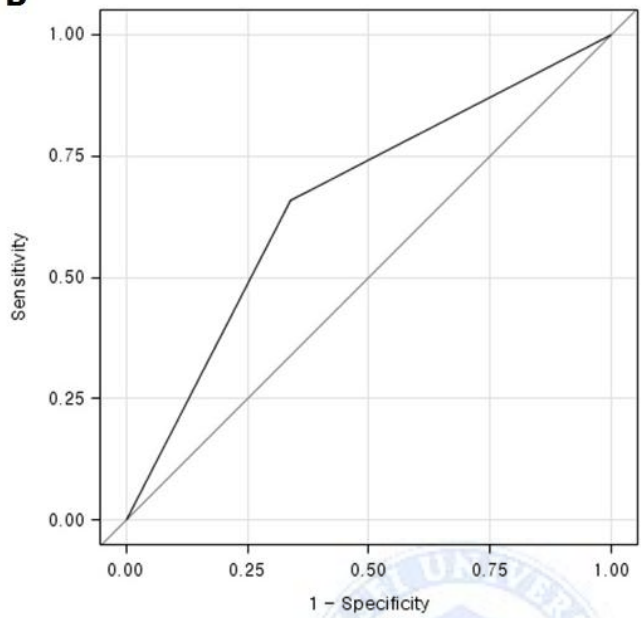
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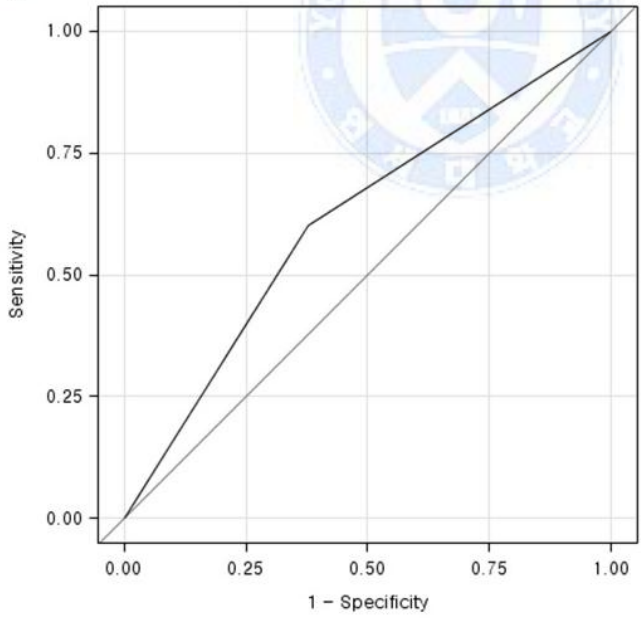
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IV. DISCUSSION

On initial US-guided FNABs, 11.5% of patients had nondiagnostic nodules. The nondiagnostic rate in repeat FNABs was 62%, higher than that of the initial FNAB group. The malignancy rates of nondiagnostic nodules on repeat FNABs (14.8%) were higher than the recommended rate in the Bethesda system,[4] but nondiagnostic nodule malignancy rates widely ranging from 2.3-51% have been reported.[3,7,10-13]

High nondiagnostic and malignancy rates of repeatedly nondiagnostic nodules often cause a diagnostic dilemma for clinicians and radiologists, who must decide whether to continue repeat FNABs (or surgical intervention) or perform follow-up US. According to the ATA and AACE guidelines, surgery is recommended for solid nodules and surgery or observation for cystic nodules.[14,15] However, surgery for all solid nodules are not cost-effective and can cause patient's postoperative morbidity.

Several studies and guidelines have suggested that nondiagnostic nodules with some specific US features be followed up with US rather than repeat biopsy. Yoon et al.[12] proposed that nodules with no suspicious features, especially mainly cystic nodules, be followed up with US. In our study, none of the nodules with greater than 50% cystic portions was malignant, consistent with the previous study. However, only 21 of 519 benign nodules were mainly cystic in our study, which indicates that mainly cystic nodules rarely undergo surgery or repeat FNAB in our institution. Woo et al[20] recently suggested that

hypoechogenicity was a independently significant factor in repeated nondiagnostic cytology, however, no significant correlation was found in our study.

The results of our study showed that US features including marked hypoechogenicity, microlobulated or irregular margins, microcalcification, and nonparallel shape, reported to be significant in a previous study,[18] differed significantly between benign and malignant nodules in repeat nondiagnostic nodules. Microcalcification (odds ratio [OR], 3.241; 95% confidence interval [CI]: 1.504, 6.985, p = 0.003) and microlobulated or irregular margins (OR, 2.35; 95% CI: 1.003, 5.539, p = 0.049) were independent factors predicting malignancy in multivariate regression analysis. Among them, only microcalcification was significant between benign and malignant nodules measuring 10 mm or less (OR, 4.715; 95% CI: 1.841, 12.079, p =0.001). In nodules larger than 10mm, however, only microlobulated or irregular margins differed significantly between benign and malignant groups (p =0.014). These results suggest more selective FNABs are done in nodules 10 mm or less based on US findings and that the most significant factor of malignancy differs according to nodule size. Current guidelines recommend FNAB for nodules larger than 10 mm;[14,15] therefore, we should consider margin to be the most significant factor for evaluation of repeat nondiagnostic nodules.

Some authors have proposed follow-up US to be preferable to repeat FNAB and surgery for nondiagnostic nodules;[7,16] Several reports suggest that diagnostic

options should be decided according to US findings.[10,12,17,20] Moon et al.[17] suggested that surgery is recommended for repeat nondiagnostic nodules showing one or more suspicious features. Recently, Moon et al.[10] proposed that TIRADS, developed by Kwak et al.,[21] can be used to stratify the malignant risks for initial nondiagnostic nodules. They concluded that nondiagnostic thyroid nodules without suspicious US features or one suspicious feature can be followed up by US, but those with two or more suspicious features should undergo repeat US-guided FNAB. Our study also showed that the number of suspicious features (including solidity, marked hypoechogenicity, microcalcifications, microlobulated or irregular margin, and taller than wide shape[18]) differed significantly between benign and malignant nodules with repeat nondiagnostic findings (2.82±1.32 vs. 1.95±1.12, respectively; p <0.001), which supports that the number of suspicious US findings is an important factor for deciding whether to perform follow-up examinations on thyroid nodules with repeatedly nondiagnostic results. In nodules measuring larger than 10mm, however, the number of suspicious findings were not significantly different between benign and malignant nodules (1.38±1.12, vs. 2.±1.46, respectively; p =0.071). But considering the small number of group, we decided to accept that a tendency exists for number of suspicious findings differentiating benign and malignant nodules.[19,22]

In our study, the cutoff values for number of suspicious findings were greater than 2 in nodules with all sizes and measuring 10mm and less and greater than 1

in nodules measuring larger than 10mm. The sensitivity, specificity, PPV, NPV, and accuracy were 65.9%, 66.0%, 25.21%, 91.76% and 65.99% in nodules with all size, 79.31%, 60.43%, 23.71%, 94.96% and 62.96% in nodules ≤10mm and 60%, 62.12%, 26.47%, 87.23% and 61.73% in nodules >10mm, respectively. Even the diagnostic performance was not optimal, we can recommend repeat biopy or surgery in nodules with two or more suspicious findings to detect malignancy in repeat nondiagnostic nodules.

To our knowledge, the current study is one of the largest population-based studies of repeated nondiagnostic cytology. However, our study has several limitations. First, there is a selection bias since 180 nondiagnostic nodules were excluded due to the lack of at least 12 months of follow-up US data. Second, nodules showing no interval changes in size or decreased size during at least 12 months that underwent only follow-up US were considered benign nodules in this study. Third, there might have been some errors in malignancy rates because surgery or repeat biopsies were decided by clinicians or patient preferences. Fourth, in nodules measuring larger than 10mm, p value 0.071 was regarded that a tendency exists in number of suspicious findings between benign and malignant nodules,considering the small number of group. Further study with larger population group should be followed.

V. CONCLUSION

In conclusion, US findings of microcalcification and irregular or microlobuated margin and number of suspicious findings are predictive of malignancy in thyroid nodules with repeated nondiagnostic cytology. Among them, irregular or microlobulated margins were most significant in nodules larger than 10 mm. Repeat FNAB or surgery should be performed for repeat nondiagnostic thyroid nodules measuring larger than 10mm with irregular or microlobuated margin or two or more suspicious US features.

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ABSTRACT (IN KOREAN)

미세침흡인생검술에서 불충분검체의 반복된 결과를 얻은 갑상선 결절 : 어떤 결절에 추적검사보다 반복 생검술이나 수술을 시행해야 하는가?

<지도교수 손 은 주>

연세대학교 대학원 의학과

은 나 래

서론: 초음파유도하 미세침흡인생검술을 시행하여 반복된 불충분검체의 결과를 얻은 갑상선 결절의 임상병리적, 초음파 소견을 알아보고 반복된 불충분 결과를 보이는 결절을 어떻게 관리해야 하는지를 알아보고자 하였다.

대상 및 방법: 반복 생검술을 시행하여 불출분 검체로 진단을 받은 297개의 갑상선 결절을 대상으로 한 후향적 연구이다. 불충분 검체를 얻은 결절 중 반복 생검술에서 진단적 결과가 나오거나, 12개월 후 추적 초음파를 시행했거나 수술을 시행하여 결과가 나온 결절을 대상으로 하였다. 초기에 불충분 검체로 진단받은 그룹과 반복해서 불충분 검체로 진단받은 그룹, 반복해서 불충분 검체로 진단받은 결절에서 양성과 악성으로 진단된 그룹 사이에 악성률, 임상적 그리고 초음파

소견을 크기에 따라 비교하였다.

결과: 양성과 악성 결절 사이에는 나이, 악성 의심 소견 (현저한 저에코, 불규칙하거나 미세소엽경계, 미세석회화, 앞뒤로 긴 모양) 그리고 악성 소견의 개수가 악성의 가능성과 유의하게 관련이 있었다 (p <0.05). 다변량 분산 분석에서는 미세석회화 (p =0.003) 와 앞뒤로 긴 모양 (p =0.049)가 악성과 관계가 있었다. 그 중에서 미세석회화가 10mm 보다 크기가 작은 결절에서 독립적으로 유의한 변수였으며 (p =0.001), 불규칙하거나 미세소엽경계가 10mm보다 큰 결절에서 유의한 변수였다 (p =0.017). 수신기작동특성곡선에서의 악성소견개수의 가장 좋은 절단점은 모든 크기의 결절에서는 2 초과, 10mm 그리고 그 이하의 결절에서는 2 초과, 10mm 이상일 경우는 1 초과 였다.

결론: 미세석회화가 10mm보다 크기가 작은 반복된 불충분 결과를 얻은 결절에서 가장 유의한 초음파 소견이었으며 불규칙하거나 미세소엽경계가 10mm보다 큰 결절에서 유의한 변수였다. 10mm 이상의 크기를 보이는 반복된 불충분 결과를 얻은 결절에서 불규칙하거나 미세소엽 경계를 보이는 결절 혹은 악성 소견이 2개 혹은 그 이상일 경우 반복 생검술 혹은 수술을 시행해야 할 것이다.

핵심되는 말: 초음파 유도하, 미세침흡인생검술, 반복 생검술, 추적 검사, 불충분검체, 갑상선 결절