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OUTCOMES OF MANAGEMENT OF THYROID NODULES DIAGNOSED AS FOLLICULAR NEOPLASM ON CYTOLOGY: INSIGHTS FROM A SPECIALIZED HOSPITAL FOR THYROID DISEASES

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Backgrounds

The management for thyroid nodules cytologically diagnosed as follicular neoplasm (FN) based on the Bethesda System often annoys both patients and attending physicians. Recently, gene panel testing is reported to be useful to diagnose whether the nodules are malignant or benign, but in Japan, these testing systems are not covered by national insurance and no laboratories are available for performing the testing. In this study, we investigated how we have managed FN tumors and how their clinical outcomes were.

Methods

We enrolled 1,412 tumors of 1,353 patients, which were cytologically diagnosed as FN between 2012 and 2018 at Kuma Hospital (Kobe, Japan) by one pathologist (M.H.). He also checked whether each FN tumor has any cytological findings favoring malignancy as per the previous study (Hirokawa et al. 2021). All patients underwent surgery (Total thyroidectomy for 216 patients and others for 1,137 patients). N1 or M1 patients and patients having other thyroid malignancy were deleted from our series. Three hundred and thirty-six patients underwent conversion surgery after active surveillance for >1 year. The change in tumor volume was evaluated by tumor-volume doubling rate (TV-DR) (Miyauchi et al. 2019)

Pathological examination
All surgical specimens were pathologically studied by one pathologist (M.H.). He pathologically diagnosed as the tumors as benign, low-risk neoplasm, or malignant based on the newest WHO classification.

Statistical analysis
StatFlex (Artec, Osaka, Japan) was adopted for univariate and multivariate logistic analyses. A p-value <0.05 was regarded as being statistically significant. Receiver operating characteristic (ROC) curve analysis was performed using R software. Five factors were assigned 1 score or 2 scores (Table 1).

Fig. 1
A receiver operating characteristic curve with the six scores for diagnosing pathological malignancy
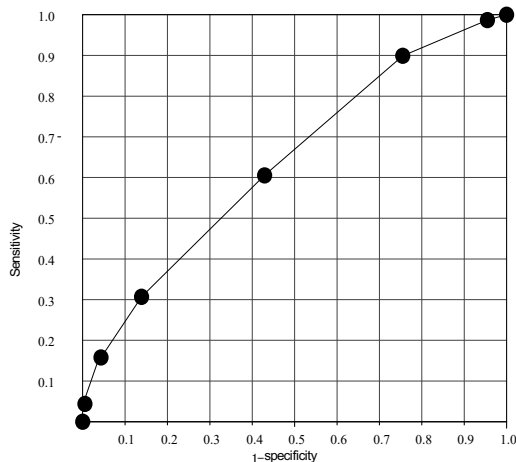
Area Under the Curve (AUC) 0.637 (0.598-0.676)

One score; non-oncocytic cytology, non-benign US findings serum Tg ≥1000 ng/mL, tumor size ≥3 cm
Two scores; Presence of cytological findings favoring malignancy

Conclusion
A high enlargement activity was not related to malignant pathology.
   The scoring system is helpful to predict malignant pathology of FN tumors to some extent, but AUC is still low. There are limitations to accurately predict the pathological malignancy of FN tumors based only on imaging studies and clinical and cytological examinations. Early induction of gene panel testing is expected, especially for tumors with high scores.

Table 1. Relationships between various factors and pathological findings

Variables	Non-malignant	Malignant	Total	p-values
Sex Male	229 (81.5%)	52 (18.5%)	281 (100%)	0.555
Female	904 (79.9%)	227 (20.1%)	1131 (100%)	
Age ≥55 years	515 (81.0%)	121 (19.0%)	636 (100%)	0.531
<55 years	618 (79.7%)	158 (20.3%)	776 (100%)	
Oncocytic Yes	326 (84.7%)	59 (15.3%)	385 (100%)	0.010 (1 score for ROC curve)
No	807 (78.8%)	220 (21.4%)	1027 (100%)	
US findings Non-benign	846 (77.9%)	240 (22.1%)	1086 (100%)	<0.001 (1 score for ROC curve)
Benign (Unknown 2)	286 (88.3%)	38 (11.7%)	324 (100%)	
Serum Tg level ≥1000 ng/mL	113 (71.1%)	46 (28.9%)	159 (100%)	0.001 (1 score for ROC curve)
<1000 ng/mL (Unknown 231)	839 (82.1%)	183 (17.9%)	1022 (100%)	
Cytological findings favoring malignancy Yes	105 (59.7%)	71 (40.3%)	176 (100%)	<0.001 (2 scores for ROC curve)
No	1028 (83.2%)	208 (16.8%)	1236 (100%)	
Tumor size ≥3 cm	639 (77.3%)	188 (22.7%)	827 (100%)	<0.001 (1 score for ROC curve)
<3 cm	494 (84.4%)	91 (15.6%)	585 (100%)	
Multiplicity Yes	102 (85.7%)	17 (14.3%)	119 (100%)	0.117
No	1031 (79.7%)	262 (20.3%)	1283 (100%)	
TV-DR ≥0.5 /year	79 (79.8%)	20 (20.2%)	99 (100%)	0.922
<0.5/year (unknown 1076)	188 (79.3%)	49 (20.7%)	238 (100%)	
Total	1133 (80.2%)	279 (19.8%)	1412 (100%)	