

BRAF V600E Gene Testing Combined with Serum TSH, TGAb and TPOAb Testing for the Diagnosis of Malignancy in TI-RADS 4 Nodules

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Abstract

Background: To evaluate the diagnostic value of *BRAF V600E* gene testing combined with serum Thyroid Stimulating Hormone (TSH), Thyroid Peroxidase Antibody (TPOAb) and Thyroglobulin Antibody (TGAb) testing for malignancy in Thyroid Imaging Reporting and Data System (TI-RADS) 4 nodules.

Methods: This was a retrospective study of patients who were diagnosed with TI-RADS 4 nodules via ultrasound examination during an outpatient or inpatient visit who underwent *BRAF V600E* gene testing and who had histopathological results from June 2020 to June 2022 at Taizhou Cancer Hospital. We compared the baseline characteristics, namely, age, sex, presence of lymph node metastasis, tumour size, cytological results and *BRAF V600E* gene testing results, of the two patient groups according to their postoperative pathological results.

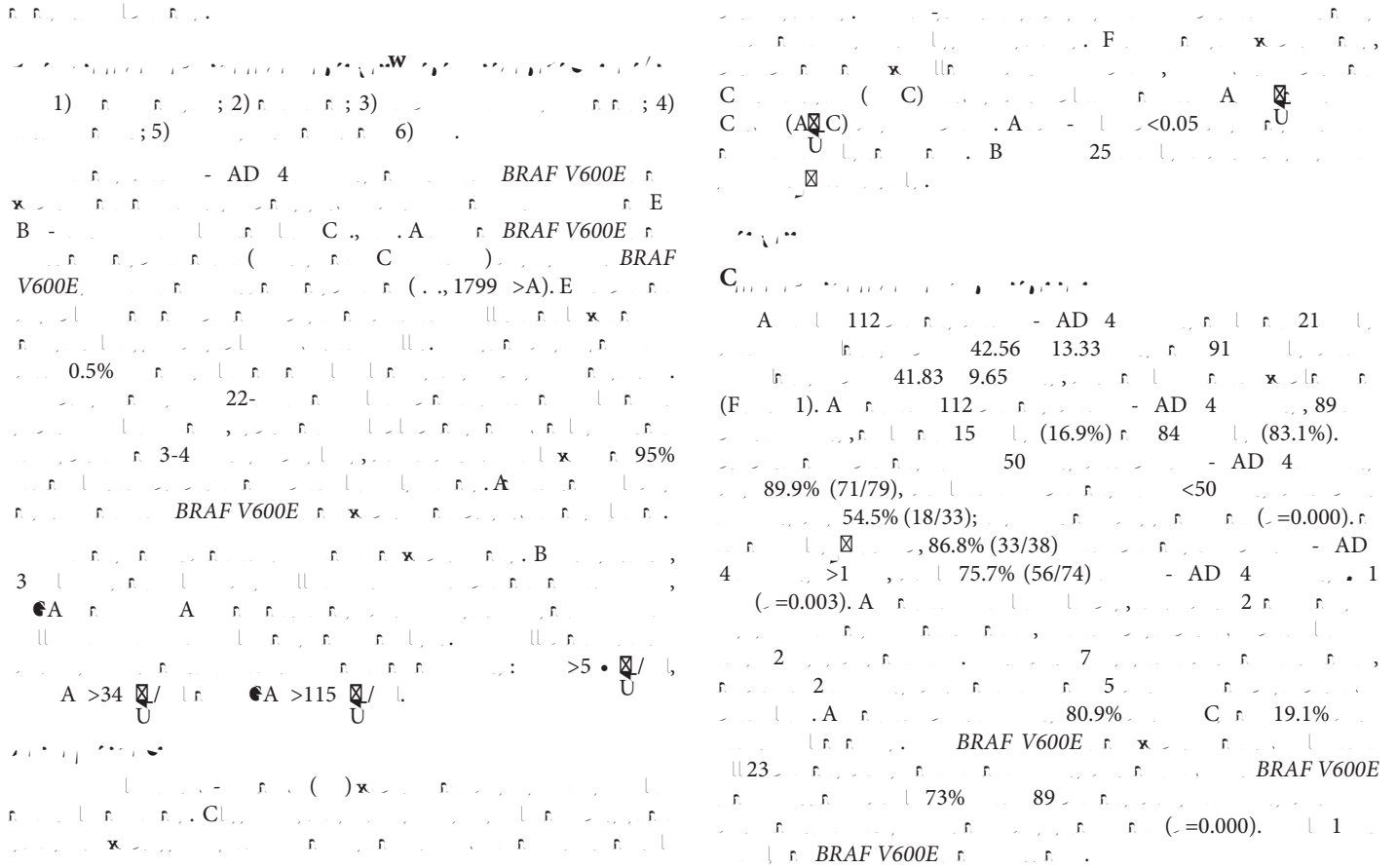


Figure 1: Kaplan-Meier survival curves showing overall survival (OS) for patients with BRAF V600E mutation. The figure is divided into two panels, A and B. Panel A shows OS for patients with BRAF V600E mutation (n=112) compared to those without (n=89). Panel B shows OS for patients with BRAF V600E mutation (n=25) compared to those without (n=89). The curves show that patients with BRAF V600E mutation have significantly better OS (p < 0.05).

Clinical characteristics	Postoperative pathology		X ² value	p-value
	Malignant (n=89)	Benign (n=23)		
Sex				
Men	51 (57.3%)	12 (52.2%)	0.213	0.213
Women	38 (42.7%)	11 (47.8%)		
Age				
≤40 years	31 (34.8%)	11 (47.8%)	0	0
>40 years	58 (65.2%)	12 (52.2%)		
Tumour size				
≤1 cm	31 (34.8%)	11 (47.8%)	0.003	0.003
>1 cm	58 (65.2%)	12 (52.2%)		
Cervical lymph node metastasis				
Yes	11 (12.3%)	1 (4.3%)	1.912	0.167
No	78 (87.7%)	22 (95.7%)		
Number of lesions				
Single	51 (57.3%)	11 (47.8%)	1.809	0.178
Multiple	38 (42.7%)	12 (52.2%)		
Sand granular calcification				
Yes	11 (12.3%)	1 (4.3%)	1.34	0.246
No	78 (87.7%)	22 (95.7%)		
Cytology results				
Lower puncture volume	11 (12.3%)	11 (47.8%)	1.809	0
Indeterminate lesions	11 (12.3%)	11 (47.8%)		
Other malignant lesions	11 (12.3%)	11 (47.8%)		
PTC	11 (12.3%)	11 (47.8%)		
Other benign lesions	11 (12.3%)	11 (47.8%)		
Histopathology				
Other malignant lesions	11 (12.3%)	11 (47.8%)	1.809	0
PTC	11 (12.3%)	11 (47.8%)		
Test indicators				
TSH (+)	11 (12.3%)	11 (47.8%)	1.809	0.318
TPOAb (+)	11 (12.3%)	11 (47.8%)		
TGAb (+)	11 (12.3%)	11 (47.8%)		
<i>BRAF V600E</i> gene				
Positive	11 (12.3%)	11 (47.8%)	40.029	0
Negative	78 (87.7%)	12 (52.2%)		

Table 1: Comparison of clinical characteristics between malignant and benign thyroid nodules.

A total of 112 patients with TI-RADS 4 nodules were included in the study. The mean age was 45.5 years (range 25-75), and 65 (57.9%) were female. The mean size of the nodules was 1.2 cm (range 0.5-2.5). The mean TSH level was 0.8 mIU/L (range 0.1-2.5), and 72 (64.3%) had elevated TSH. The mean TgAb level was 1.2 IU/mL (range 0-10), and 61 (54.5%) had elevated TgAb. The mean TPOAb level was 1.5 IU/mL (range 0-15), and 61 (54.5%) had elevated TPOAb. The mean follow-up time was 12 months (range 6-24). The mean size of the nodules was 1.2 cm (range 0.5-2.5). The mean TSH level was 0.8 mIU/L (range 0.1-2.5), and 72 (64.3%) had elevated TSH. The mean TgAb level was 1.2 IU/mL (range 0-10), and 61 (54.5%) had elevated TgAb. The mean TPOAb level was 1.5 IU/mL (range 0-15), and 61 (54.5%) had elevated TPOAb. The mean follow-up time was 12 months (range 6-24). The mean size of the nodules was 1.2 cm (range 0.5-2.5). The mean TSH level was 0.8 mIU/L (range 0.1-2.5), and 72 (64.3%) had elevated TSH. The mean TgAb level was 1.2 IU/mL (range 0-10), and 61 (54.5%) had elevated TgAb. The mean TPOAb level was 1.5 IU/mL (range 0-15), and 61 (54.5%) had elevated TPOAb. The mean follow-up time was 12 months (range 6-24).

Discussion
 All patients with TI-RADS 4 nodules were included in the study. The mean age was 45.5 years (range 25-75), and 65 (57.9%) were female. The mean size of the nodules was 1.2 cm (range 0.5-2.5). The mean TSH level was 0.8 mIU/L (range 0.1-2.5), and 72 (64.3%) had elevated TSH. The mean TgAb level was 1.2 IU/mL (range 0-10), and 61 (54.5%) had elevated TgAb. The mean TPOAb level was 1.5 IU/mL (range 0-15), and 61 (54.5%) had elevated TPOAb. The mean follow-up time was 12 months (range 6-24). The mean size of the nodules was 1.2 cm (range 0.5-2.5). The mean TSH level was 0.8 mIU/L (range 0.1-2.5), and 72 (64.3%) had elevated TSH. The mean TgAb level was 1.2 IU/mL (range 0-10), and 61 (54.5%) had elevated TgAb. The mean TPOAb level was 1.5 IU/mL (range 0-15), and 61 (54.5%) had elevated TPOAb. The mean follow-up time was 12 months (range 6-24).

Clinical characteristics	BRAF V600E gene		X ² value	p-value
	Positive (n=65)	Negative (n=47)		
Sex				
Men	17 (26.2%)	15 (31.9%)	0.941	
Women	48 (73.8%)	32 (68.1%)		
Age				
≤ 40 years	17 (26.2%)	15 (31.9%)	0.108	
> 40 years	48 (73.8%)	32 (68.1%)		
Tumour size				
≤ 1 cm	17 (26.2%)	15 (31.9%)	0.108	
> 1 cm	48 (73.8%)	32 (68.1%)		
Cervical lymph node metastasis				
Yes	17 (26.2%)	15 (31.9%)	0.009	
No	48 (73.8%)	32 (68.1%)		
Number of lesions				
Single	17 (26.2%)	15 (31.9%)	0.009	
Multiple	48 (73.8%)	32 (68.1%)		
Sand granular calcification				
Present	17 (26.2%)	15 (31.9%)	0.009	
Absent	48 (73.8%)	32 (68.1%)		

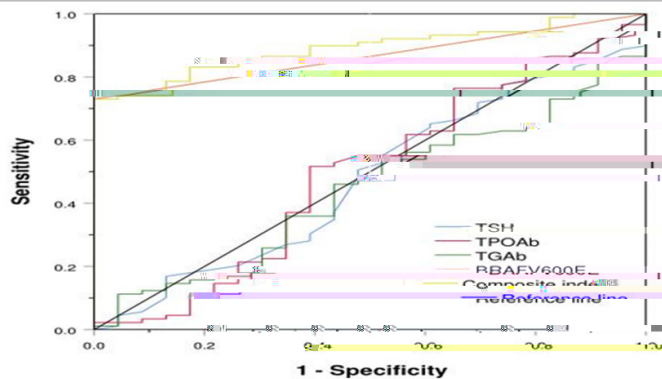


Figure 2: Receiver Operating Characteristic (ROC) curve analysis of the diagnostic performance of *BRAF V600E* gene testing combined with serum TSH, TPOAb and TGAb marker testing in distinguishing the nature of TI-RADS 4 nodules. **Note:** TI-RADS: Thyroid Imaging Reporting and Data System.

Index	AUC	SE	P	95% CI	Sensitivity	Specifcity
TSH	0.71	0.02	0.001	0.67-0.75	0.71	39.13
TPOAb	0.71	0.02	0.948	0.67-0.75	0.71	0.71
TGAb	0.71	0.02				

D. 结果

本研究旨在探讨 BRAF V600E 基因突变在甲状腺乳头状癌中的诊断价值。研究共纳入 112 例患者，其中 7 例为腺瘤，112 例为甲状腺乳头状癌。所有患者均接受了手术切除，术后进行了 BRAF V600E 基因检测。研究结果如下：

1. 在 112 例甲状腺乳头状癌患者中，BRAF V600E 基因突变的检出率为 84.7%。在 7 例腺瘤患者中，BRAF V600E 基因突变的检出率为 0%。

2. BRAF V600E 基因突变的检出率与肿瘤大小、淋巴结转移、远处转移等因素无显著相关性。

3. BRAF V600E 基因突变的检出率与甲状腺癌分期无显著相关性。

4. BRAF V600E 基因突变的检出率与甲状腺癌复发率无显著相关性。

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本研究旨在探讨 BRAF V600E 基因突变在甲状腺乳头状癌中的诊断价值。研究共纳入 112 例患者，其中 7 例为腺瘤，112 例为甲状腺乳头状癌。所有患者均接受了手术切除，术后进行了 BRAF V600E 基因检测。研究结果如下：

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10.1115/j.1524-6032.2022.00031.

Abstract

Background: The American Thyroid Association (ATA) guidelines for adult patients with papillary thyroid carcinoma (PTC) recommend total thyroidectomy (TT) and central lymph node dissection (CLND) for all patients with PTC. However, recent studies have shown that CLND is not necessary for all patients with PTC. All patients with PTC should undergo TT, but CLND should be performed only in patients with enlarged lymph nodes.

Keywords

1. Pæ~*^}ÁÓÜÉK|^\cæ}á^!ÁÓSÉÁÓià|^ÁSÓÉÁÖ[@^!c^"ÁÓTÉÁTæ}á^!ÁÜRÉÁ^cæ|ÉÁÇGÉFÍDÁ American thyroid association management guidelines for adult patients with cancer. *Thyroid* 2021;31(12):1983-1994.
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