ORIGINAL ARTICLE

Preoperative Diagnosis of Benign Thyroid Nodules with Indeterminate Cytology

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ABSTRACT

BACKGROUND

Approximately 15 to 30% of thyroid nodules evaluated by means of fine-needle aspiration are not clearly benign or malignant. Patients with cytologically indeterminate nodules are often referred for diagnostic surgery, though most of these nodules prove to be benign. A novel diagnostic test that measures the expression of 167 genes has shown promise in improving preoperative risk assessment.

METHODS

We performed a 19-month, prospective, multicenter validation study involving 49 clinical sites, 3789 patients, and 4812 fine-needle aspirates from thyroid nodules 1 cm or larger that required evaluation. We obtained 577 cytologically indeterminate aspirates, 413 of which had corresponding histopathological specimens from excised lesions. Results of a central, blinded histopathological review served as the reference standard. After inclusion criteria were met, a gene-expression classifier was used to test 265 indeterminate nodules in this analysis, and its performance was assessed.

RESULTS

Of the 265 indeterminate nodules, 85 were malignant. The gene-expression classifier correctly identified 78 of the 85 nodules as suspicious (92% sensitivity; 95% confidence interval [CI], 84 to 97), with a specificity of 52% (95% CI, 44 to 59). The negative predictive values for "atypia (or follicular lesion) of undetermined clinical significance," "follicular neoplasm or lesion suspicious for follicular neoplasm," or "suspicious cytologic findings" were 95%, 94%, and 85%, respectively. Analysis of 7 aspirates with false negative results revealed that 6 had a paucity of thyroid follicular cells, suggesting insufficient sampling of the nodule.

CONCLUSIONS

These data suggest consideration of a more conservative approach for most patients with thyroid nodules that are cytologically indeterminate on fine-needle aspiration and benign according to gene-expression classifier results. (Funded by Veracyte.)