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Endocrinology & Metabolic Syndrome

Commentary

Application of Cytopathology for Thyroid Nodules Diagnosis

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DESCRIPTION

Genetic and gene expression-based assays for thyroid fine-needle aspirations have been developed as a result of improvements in the molecular characterization of thyroid malignancies. These tests are intended to work together to increase thyroid cytology's.

The cancer in aspirates classified as follicular neoplasm/suspicious for a follicular neoplasm ranges from 15% to 30%. Patients are typically recommended for a diagnostic thyroid lobectomy at this risk category. In contrast, diagnostic lobectomy may be considered for nodules with repeatedly inconclusive FNA cytology. Repeat FNA is the typical approach for aspirates in the category of atypia of unknown significance/follicular lesion of undetermined importance due to a 5% to 15% risk of cancer.

Opportunities for improvement exist in management strategies that incorporate diagnostic lobectomy for thyroid nodules with uncertain cytology. The majority of AUS/FLUS or FN/SFN cytology nodules are ultimately determined to be histologically benign, making diagnostic lobectomy for these nodules excessive. On the other hand, a second visit to the operating theatre for a complete thyroidectomy may be required for the subset of patients for whom a malignancy in the lobectomy material was discovered. The knowledge that these surgical choices are influenced in part by cytologic interpretative categories with a high propensity for interobserver variability comes along with these difficulties.

With the goals of 1) reducing the overtreatment of benign nodules and 2) increasing the preoperative detection of malignant nodules that should be treated by a single surgery rather than a two-step procedure, molecular testing has emerged over the past few years as a promising method for elucidating the grey area of indeterminate thyroid FNAs (diagnostic lobectomy and completion thyroidectomy). The strengths, weaknesses, ideal application, and interpretation of the commercially available molecular assays for indeterminate thyroid FNAs will be highlighted in this review along with an analysis of their methodology and validation data.

There are two strategies to deal with the uncertainty of ambiguous thyroid FNAs: by "ruling in" or "ruling out" malignancy. The positive predictive value and negative predictive value of a clinical test determine whether it can "rule in" or "rule out" cancer. The clinical test's predictive values are dynamic and change according to the likelihood of the disease existing prior to the test. Bayes' theorem can be used to extrapolate PPV and NPV for any given pretest likelihood of disease based on the specificity and sensitivity properties of a test from a validation study. The pre-test likelihood of cancer in cytological ambiguous nodules for thyroid FNAs can vary depending on the thresholds used by cytopathologists to interpret AUS/FLUS or FN/SFN results. For instance, a test may have an NPV high enough to rule out malignancy in a cohort with a 15% to 30% pretest likelihood of malignancy; nevertheless, in a different cohort with a higher pretest probability of malignancy, the NPV of the same test may not be high enough to do so. It may not always be possible to apply the significance of a positive or negative test result reported by a validation study. Each end-user of these molecular tests should, ideally, ascertain whether the pretest probability of cancer in their patient population falls within the range for which positive and/or negative test results have clinical significance. The pretest probability can be approximated by the prevalence of malignancy for a specific cytologic interpretative category.

An auxiliary test that can preoperatively rule out malignancy has the potential to patients surgical operation because the majority of nodules with ambiguous cytology are proven to be benign on surgical resection. This strategy is adopted by the veracyte product afirma Gene Expression Classifier, which analyses the mRNA expression profiles of thyroid nodules with uncertain cytology using microarray technology.

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