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The utility of frozen section examination for determining the extent of thyroidectomy in patients with a thyroid nodule and "atypia/follicular lesion of undetermined significance"

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Frozen section examination;
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Abstract

BACKGROUND: The purpose of this study was to evaluate the role of frozen section examination (FSE) for determining the extent of thyroidectomy in patients with nodular thyroid disease and fine-needle aspiration categorized as atypia/follicular lesion of undetermined significance (AFLUS).

METHODS: A retrospective review of all patients operated on for a thyroid nodule and AFLUS was completed to determine the role of clinical examination and FSE in intraoperative decision making.

RESULTS: One hundred twenty patients with AFLUS underwent thyroidectomy; 18 (15%) had carcinoma. FSE altered management in 36 (62%) of the 58 patients—32 with benign disease and 4 with cancer who underwent lobectomy and total thyroidectomy, respectively. Total thyroidectomy without FSE was performed in 61 (51%) patients with sonographically confirmed bilateral disease. FSE had a 36.4% sensitivity, 100% specificity, 100% positive predictive value, 87% negative predictive value, and 88% accuracy.

CONCLUSION: Ultrasound in combination with FSE is of value for determining the extent of thyroidectomy in patients with AFLUS.

The National Cancer Institute introduced the Bethesda System for Reporting Thyroid Cytopathology (BSRTC) in 2008 to help promote more consistent management of patients with nodular thyroid disease.[1,2] The BSRTC standardizes the reporting of fine-needle aspiration biopsy (FNAB) results into 6 diagnostic categories, and provides an assessment of risk of malignancy and recommendations for clinical management for each cytologic category. Atypia/follicular lesion of undetermined significance (AFLUS) was introduced as a new cytologic category for nodules with cytologic features that are neither definitively benign nor definitively neoplastic. Although the implementation of the BSRTC has resulted in improved sensitivity of FNAB, it has raised questions about the operative management of patients with a thyroid nodule and persistent AFLUS. It was initially estimated that AFLUS would account for no more than 7% of thyroid FNABs; however, the published rates of AFLUS vary from 2.8% to 47% between institutions and individual cytopathologists at the

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same institution, creating ambiguity for the appropriate management of patients with AFLUS.[3,4]

The BSRTC estimates that the risk of malignancy is 5% to 15% for a thyroid nodule and an FNAB categorized as AFLUS.[1,2] In the absence of suspicious clinical and sonographic findings, the current recommendation for management of a patient with a thyroid nodule and AFLUS is to repeat the FNAB in 3 to 6 months.[1] In approximately two thirds of patients with AFLUS, repeat FNAB yields a definitive diagnosis with clear-cut recommendations for further management and treatment.[5] The reported rates of malignancy for AFLUS vary widely, from 6% to 48%.[5–7] Barring other indications for total thyroidectomy, such as radiation exposure, family history of thyroid cancer, or patient preference, the wide range of malignancy rates raises questions about the management of patients with nodular thyroid disease and AFLUS.[5]

Before the advent of FNAB, frozen section examination (FSE) was commonly used to help guide intraoperative management of patients with thyroid nodules. With the widespread use of FNAB, the role of FSE has been limited to patients with a thyroid nodule and an FNAB that is persitently nondiagnostic or suspicious for papillary cancer, for evaluation of abnormal lymph nodes, and to confirm the presence of parathyroid tissue before autotransplantation.[8,9] Although it is accepted that FSE is of no value in determining intraoperative management for nodules with an FNAB that is benign, suspicious for follicular or Hurthle cell neoplasm, or malignant, the role of FSE for management of patients with nodular thyroid disease and AFLUS has not been established.[8–10] Accordingly, we sought to investigate the usefulness of FSE in combination with clinical evaluation for determining the extent of thyroidectomy in patients with a thyroid nodule and AFLUS.

Patients and Methods

A retrospective review of all patients undergoing thyroidectomy for nodular thyroid disease and an FNAB classified as AFLUS was completed. FNAB was classified as AFLUS when variable degrees of nuclear or architectural atypia were present and the nodule could not be definitively diagnosed as benign or neoplastic. Fine-needle aspirates were classified as demonstrating nuclear atypia when one or more of the following were present: nuclear grooves, intranuclear inclusions, prominent nucleoli, or nuclear overlapping, crowding, pleomorphism, or hyperchromasia. AFLUS is used for specimens with various cytologic features that account for at least 8 different clinical scenarios described in the BSRTC.[1,2]

The study included patients operated on from 2010, when the BSRTC was introduced at our institutions, until 2013. Age, sex, history of radiation exposure, family history of thyroid cancer, compressive symptoms, personal history of hyper- or hypothyroidism, physical examination findings, serum thyrotropin (TSH) level, sonographic findings, and extent of thyroidectomy was collected for each patient. Pathology reports were reviewed for FSE diagnosis and final paraffin diagnosis. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of FSE were determined. The study was approved by the institutional review boards at MetroHealth Medical Center and University Hospitals Case Medical Center in Cleveland, OH.

The reference range for serum TSH level was .340 to 5.600 μIU/mL, which has been in use at our institutions since March 2009. Ultrasound reports were reviewed for specific features of the index nodule, including hypoechogenicity, irregular margins, micro- or macrocalcifications, increased vascularity, and the presence of nodular disease affecting the contralateral thyroid lobe. Significant contralateral disease was defined as the presence of one or more nodules greater than or equal to 1 cm in maximum dimension.

FNAB was performed as previously described.[11] All biopsies performed with ultrasound guidance by a radiologist were completed with an on-site assessment of adequacy. On-site assessment of adequacy was not utilized for FNABs performed by endocrine surgeons.

FSE results were classified as benign, indeterminate, or malignant. An FSE interpretation revealing thyroiditis, adenomatous nodule, colloid nodule, Hurthle cell nodule, or "benign with no evidence of malignancy" was classified as benign. An FSE result of "Hurthle cell neoplasm," "follicular neoplasm," or "follicular lesion" was considered inconclusive. Only FSE interpretations with a definitive diagnosis of cancer were classified as malignant. Intraoperative management of the patient was considered to be modified if a definitive decision regarding the extent of thyroidectomy was based on the results of FSE. Intraoperative management was not modified when FSE was inconclusive and definitive management was determined based on the examination of paraffin sections.

Demographic data were analyzed using descriptive statistics. FSE diagnosis was compared with the final paraffin diagnosis to determine the sensitivity, specificity, PPV, NPV, and accuracy of FSE. Sensitivity was defined as true positive results divided by the sum of true positive and false negative results. Specificity was defined as true negative results divided by the sum of true negative and false positive results. PPV was defined as the number of true positive results divided by the sum of true and false positive results. NPV was defined as the number of true negative results divided by the sum of true negative and false negative results. Diagnostic accuracy was defined as the sum of true positive and true negative results divided by the sum of true positive, false positive, true negative, and false negative results. For these calculations, malignant results were considered "positive," and benign results were considered "negative." Sensitivity, specificity, PPV, NPV, and accuracy were calculated in 2 ways: one by excluding inconclusive results and the second by grouping the