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Ultrasound-guided thyroid nodule biopsy: outcomes and correlation with imaging features☆,☆☆

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ABSTRACT

Background and purpose: Thyroid nodules are ubiquitous on ultrasound but have a low risk of malignancy. Hence, risk stratification is essential before biopsying them. We aim to (a) determine the frequency and predictors of nondiagnostic fine needle aspiration biopsy (FNAB) of thyroid nodules and (b) seek correlation between sonographic features and biopsy outcomes.

Methods: Between January 2010 and April 2013, 559 thyroid nodules underwent ultrasound-guided FNAB. Demographic information was obtained. Prebiopsy ultrasound images were reviewed for size, multiplicity, echotexture, shape, margins, vascularity, calcifications, cervical lymphadenopathy, and extrathyroid extension. Univariate and multivariate logistic regression analyses adjusting for the correlation between multiple nodules obtained from the same patient were performed.

Results: A total of 10.6% of the biopsies were nondiagnostic. Male gender [adjusted odds ratio (OR)=3.78, 95% confidence interval (CI) 1.87–7.66, $P<.001$] and a taller-than-wide shape (adjusted OR=3.22, 95% CI 1.34–7.75, $P=.009$) were independent predictors of a nondiagnostic FNAB. There was no significant association with cystic echotexture or a smaller nodule size. Well-defined irregular margins, microcalcifications, and coarse calcifications were independent predictors of malignancy, with specificities above 96% but low sensitivities (59.3%, 44.4%, and 11.1%, respectively). All nodules with cervical lymphadenopathy were malignant. If biopsy is performed when at least one of the above four features are present, the sensitivity, specificity, positive likelihood ratio and negative likelihood ratio of predicting malignancy are 81.5%, 93.1%, 11.8 and 0.2 respectively. All purely cystic nodules and spongiform nodules were benign.

Conclusions: Male gender and taller-than-wide thyroid nodules are independent risk factors for a nondiagnostic FNAB. Prudent use of a combination of sonographic features can help to risk-stratify thyroid nodules for FNAB and may reduce unwarranted FNABs.

1. Introduction

The widespread use of imaging of the neck has led to a rise in detection of thyroid nodules. At sonography, their prevalence ranges between 10% and 67% [1,2]. Fine needle aspiration biopsy (FNAB) is the most reliable and commonly used method for further characterization of these lesions. However, only a minority (between 5.1% and 14.9%) of biopsied nodules are malignant [2–7]. Hence, it is highly desirable to risk-stratify these nodules for malignancy using noninvasive imaging features prior to biopsy, especially in patients with multinodular goiter. Several studies have been performed to elucidate sonographic predictors of malignancy or benignity [8–16]. However, there continues to be considerable variability in the reported value of some of these sonographic features [14,17]. The existing guidelines on when and which nodule to biopsy are also not entirely uniform [3,5,18]. Adding further complexity to the scenario is the problem of nondiagnostic biopsies. Between 9.5% and 20.4% of FNABs are nondiagnostic even under ultrasound guidance [19–23]. Currently, there is limited literature with varied results on the clinical and sonographic predictors of a nondiagnostic FNAB [22–24].

At our facility, patients referred for ultrasound-guided FNAB have most of their nodules that are more than 10 mm in size (regardless of sonographic appearance) or the largest of the nodules if all the nodules are subcentimeter in size biopsied. This cohort therefore forms a relatively unbiased sample to obtain a correlation between the different sonographic features and the FNAB outcomes. Based on this experience, we embarked on this study to (a) determine the frequency and predictors of nondiagnostic FNAB of thyroid nodules and (b) seek correlation between sonographic features and outcomes of biopsy, i.e., malignant or benign.

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2. Methods

Between January 2010 and April 2013, ultrasound-guided FNAB was performed for 559 thyroid nodules in 476 patients [104 male, 372 female; age ranging from 13 to 84 years; mean age: 53±14 (S.D.) years] at the radiology department of a university hospital. With formal approval from the institutional review board, the electronic medical records of these patients were accessed to determine the biopsy outcomes. Four hundred forty-eight of these nodules from 346 patients [71 male, 275 female; age ranging from 13 to 84 years; mean age: 54± 14 (S.D.) years] had a recent diagnostic ultrasound study (within the 3 months preceding the FNAB) available for review on the hospital picture archiving and communication system (PACS). The demographic profile (patient age and gender) and sonographic features of these nodules were correlated with the FNAB outcome.

2.1. Biopsy procedure and cytological evaluation

The thyroid nodule FNABs were performed using a 23G–25G needle under sonographic guidance by an interventional radiologist or a trainee in interventional radiology (under supervision). A cytotechnologist was present onsite to assess the adequacy of the biopsy sample. Up to a maximum of four passes were routinely made if the aspirate was deemed inadequate or unsatisfactory by the onsite cytotechnologist. The following were possible categories of diagnostic cytological results: benign (including colloid nodules, hyperplastic nodules, and thyroiditis), malignant, suspicious for malignancy, and indeterminate (including follicular or Hürthle cell neoplasm, atypia, or follicular lesion of undetermined significance) [25]. Histological results were used in lieu of cytology if the nodule underwent surgical resection. A final pathological diagnosis of benign or malignant was assigned to a nodule if it had a benign or malignant cytology (or histology if available).

2.2. Sonographic technique and evaluation

All prebiopsy diagnostic ultrasound studies were performed using a 5–12-MHz linear-array transducer. Grayscale and color Doppler examinations were performed using the standard equipment settings for thyroid gland evaluation. The examination included routine screening for cervical lymphadenopathy. The ultrasound images of the thyroid nodules were retrieved from the PACS database and retrospectively reviewed by an attending radiologist (with more 10 years' experience of reading thyroid ultrasound) who was blinded to the pathological diagnosis.

The following sonographic features were assessed: size, multiplicity, echotexture, shape, margins, vascularity and the presence of calcifications, cervical lymphadenopathy, and extrathyroid extension. Nodule size was recorded in the longest dimension. For nodule echotexture, the proportion of solid component in the nodule was assessed: purely or predominantly (≥50%) solid, purely or predominantly (<50%) cystic, or spongiform appearance (aggregation of multiple tiny cystic spaces occupying more than 50% of a nodule) [17]. The echogenicity of the solid component of the nodule with reference to the thyroid parenchyma (hyperechoic, isoechoic, or hypoechoic) was also evaluated. In addition, marked hypoechogenicity was defined as an echogenicity lower than that of the strap muscles [17]. The presence of a hypoechoic halo around a solid or predominantly solid nodule and the presence of colloid (tiny echogenic foci with posterior comet tail artifacts) [17] within the nodule were sought. Nodule shape was categorized into the presence or absence of a taller-than-wide shape (anteroposterior diameter more than transverse diameter on a transverse or longitudinal plane), while nodule margins were classified as well-defined regular, well-defined irregular (microlobulated or spiculated), or ill-defined. Nodules were classified into three vascularity patterns: absent, peripheral only, and central. Presence of chaotic internal vascularity was recorded separately. Intranodular calcification was classified into one of the following patterns: rim calcification, coarse calcification (a hyperechoic focus larger than 1 mm), or microcalcification (a hyperechoic focus of around 1 mm with or without acoustic shadowing but without posterior comet tail artifacts) [17]. Cervical lymphadenopathy was considered positive if any of the following features suspicious for metastasis was present: loss of reniform shape or fatty hilum, the presence of irregular margins, calcifications, cystic change, a heterogeneous or thyroid-like echotexture, and vascularity throughout the lymph node [17].

2.3. Data analysis

Each demographic and sonographic criterion was analyzed for its association with a nondiagnostic FNAB outcome and final pathological diagnosis using univariate and multivariable logistic regression, adjusting for the correlation between multiple nodules obtained from the same patient using a robust variance estimation approach by considering both variability between patients and within the same patient (at the nodule level) in the parameter estimation. Sensitivity, specificity, and positive and negative likelihood ratios were obtained for the predictors of malignancy. All statistical analyses were performed on a per-nodule basis using the STATA software (version 12.0; StataCorp, College Station, TX, USA), assuming a two-sided test with conventional significance level of .05.

3. Results

3.1. FNAB and histological results

The proportion of nodules that were nondiagnostic, benign, malignant, suspicious for malignancy, and indeterminate after FNAB was 10.6% (59/559), 75.0% (419/559), 3.6% (20/559), 1.4% (8/559), and 9.5% (53/559), respectively (Fig. 1).

Repeat biopsies were performed for eight nondiagnostic nodules, of which seven had a benign outcome and one was indeterminate (atypia of undetermined significance). A total of seven nondiagnostic nodules (including the nodule with an indeterminate repeat FNAB) were surgically resected, and all of them had benign histology. The remaining nodules showed interval decrease in size or stability at follow-up ultrasound until the writing of this article (minimum follow-up of 1 year).

There were 28 nodules that were malignant or suspicious for malignancy after FNAB. Twenty-one of the nodules underwent surgical resection, of which 19 had malignant histology (Fig. 1). The remaining seven nodules were from patients who declined surgery (three nodules), defaulted follow-up (three nodules), or underwent chemotherapy for a diagnosis of lymphoma (one nodule). Of the 25 resected nodules that were classified as benign on FNAB, only one had discordant histology (this was reclassified as malignant) (Fig. 1). Thus, in this subgroup of patients with surgical pathology available for correlation, the false-positive rate, false-negative rate, and diagnostic accuracy of FNAB were 7.7%, 5.0%, and 93.5%, respectively. Of the 25 indeterminate nodules that underwent surgical resection, 7 (28.0%) were malignant.

There were a total of 444 benign and 34 malignant pathological diagnoses, giving a malignancy rate of 7.1%. Of these, 29 were papillary carcinomas, 2 were medullary carcinomas, and 3 were lymphomas.

Further analysis was performed on the 448 nodules with recent prebiopsy diagnostic ultrasound imaging.

3.2. Demographic profile

There was no significant difference in the age of patients with diagnostic and nondiagnostic FNAB outcomes ($P=.139$) (Table 1). However, male gender was a significant independent predictor of a nondiagnostic FNAB outcome after multivariate analysis [adjusted odds ratio (OR)= 3.78, 95% confidence interval (CI) 1.87–7.66, $P<.001$]. There was no significant difference in the age ($P=.151$) and gender ($P=.937$) of patients with benign and malignant nodules.