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Reliability of fine-needle aspiration for thyroid nodules greater than or equal to 4 cm

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ARTICLE INFO

Article history:
Received 7 January 2012
Received in revised form
25 May 2012
Accepted 15 June 2012
Available online 6 July 2012

Keywords:
Thyroid malignancy
Fine-needle aspiration
Thyroid nodules

ABSTRACT

Background: Fine-needle aspiration (FNA) is considered the diagnostic test of choice in the evaluation of thyroid nodules. Some practice recommendations, however, suggest surgical resection of larger thyroid nodules due to concerns of FNA unreliability in the diagnosis of thyroid malignancy. The purpose of this study was to determine the reliability of FNA in thyroid nodules ≥4 cm.

Methods: Retrospective review of prospectively collected data of 1068 consecutive patients who underwent FNA and thyroidectomy at a single tertiary medical center from 2003 to 2010 was performed. Patients were divided into two groups: those patients with a dominant thyroid nodule ≥4 cm ($n = 212$) and those patients with a dominant thyroid nodule <4 cm ($n = 856$). Sensitivity, specificity, and negative and positive predictive values were calculated for FNA results and final histopathology after thyroidectomy.

Results: Of 212 patients with lesions ≥4 cm, 35% had thyroid malignancy on final pathology. Conversely, 54% of 856 patients with dominant thyroid nodules <4 cm had a final diagnosis of thyroid cancer after thyroidectomy. FNA demonstrated similar test characteristics among patients with lesions ≥4 cm and <4 cm, with a specificity of 99% (CI: 96%–100%) and 98% (CI: 96%–99.0%), respectively, and a sensitivity of 35% (CI: 23%–49%) and 42% (CI: 37%–46%), respectively. The positive predictive value of FNA was 82% (CI: 75%–100%) for nodules ≥4 cm and 96% (CI: 92%–98%) for nodules <4 cm. Negative predictive value was significantly different, with a value of 82% (CI: 75%–87%) for lesions ≥4 cm and only 59% (CI: 55%–63%) for lesions <4 cm.

Conclusions: The reliability of FNA as a diagnostic test is not affected by the size of thyroid nodules. Routine surgical resection for all thyroid nodules ≥4 cm should not be used as the only independent factor in determining need for surgical resection.

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0022-4804/$ – see front matter © 2013 Published by Elsevier Inc.
http://dx.doi.org/10.1016/j.jss.2012.06.030

1. Introduction

Clinically palpable thyroid nodules are present in 4% to 7% of the adult population in the United States [1]. Furthermore, advanced diagnostic imaging has greatly increased the frequency of incidentally discovered thyroid nodules [1]. The clinical relevance of these nodules is related to the concern of underlying thyroid malignancy among patients and clinicians alike. The overall incidence of malignancy in a patient with thyroid nodules and no associated risk factors is 9% to 13% [1,2]. The incidence of thyroid cancer has increased sharply since the mid-1990s due in part to the discovery of incidental nodules in more frequent imaging studies [3].

Fine-needle aspiration (FNA) is a principal diagnostic test in the evaluation of thyroid nodules [4]. FNA is highly sensitive and specific in the diagnosis of thyroid cancer, with an accuracy approaching 98% [1,4]. The false-negative rate for benign FNA results is low, with reported rates between 1% and 5% [1]. Some studies, however, suggest routine surgical resection of larger thyroid nodules due to concerns of FNA unreliability in the diagnosis of thyroid malignancy.

There is conflicting evidence regarding the accuracy of FNA in the evaluation of large nodules for thyroid carcinoma. Some clinicians report a FNA false-negative rate as high as 30% in patients with large thyroid nodules [4]. Conversely, some authors report a false-negative rate of FNA in large nodules to be as low as 0.7% [5]. The purpose of this study, therefore, was to determine the reliability of FNA in the evaluation of thyroid nodules $\geq$4 cm.

2. Methods

A retrospective review of prospectively collected clinical and pathologic data of 1068 consecutive patients referred to a single institution for thyroidectomy from January 2003 to June 2010 was performed. All patients underwent FNA of dominant thyroid nodules either at another facility prior to referral or upon initial visit prior to surgical intervention. A dominant nodule was defined as the largest and/or most suspicious-appearing thyroid nodule by ultrasound (US). FNA of index thyroid nodules was performed under US guidance in 98% of patients.

All FNA slides, including those from outside institutions, were reviewed by four experienced cytopathologists at the University of Miami Health System and regrouped into four main categories: nondiagnostic, benign, indeterminate, or malignant. The indeterminate group included follicular neoplasm (FN), Hürthle cell neoplasm (HCN), and suspicious for papillary thyroid cancer (PTC). Papillary microcarcinomas, defined as malignant lesions <1 cm within the index thyroid nodules subjected to FNA, were considered in the final analysis of this study. All thyroid cancers in this analysis, therefore, were those malignancies found only within the index nodule subjected to FNA. Incidental thyroid cancers, defined as a focus of thyroid cancer less than 1 cm located outside dominant thyroid nodule on final histopathology, were excluded from statistical analysis.

All 1068 patients underwent thyroid lobectomy or total thyroidectomy in this surgical series. At this institution, the approach to all FNA-indeterminate thyroid nodules is surgical resection. Patients with FN or HCN underwent diagnostic thyroid lobectomy with isthmusectomy. However, total thyroidectomy was often performed in these indeterminate FNA patients with bilateral thyroid nodules, symptomatic goiters, concurrent hyperthyroidism, intraoperative findings suggestive of malignancy, suspicious ultrasonographic features for malignancy, history of head/neck radiation therapy, family history of thyroid cancer, and/or patient preference. Frozen section was not routinely performed unless intraoperative findings suggested malignancy. In patients with FNA results suspicious for malignancy and no other risk factors, intraoperative frozen section was performed. Total thyroidectomy with or without central lymph node dissection was performed if the diagnosis of cancer was confirmed on frozen section, or if gross intraoperative findings suggested malignancy. When final histopathology confirmed carcinoma in patients who underwent initial thyroid lobectomy, completion thyroidectomy was performed. Indications for thyroidectomy when FNA of the index nodule was benign or nondiagnostic included interval growth, obstructive symptoms, cosmetic reasons, suspicious findings on US (e.g., microcalcifications, irregular borders, hypoechogenicity), and patient preference.

Patients were divided into two groups based on the size of dominant nodule on ultrasound: those patients with a dominant thyroid nodule <4 cm and those patients with a dominant thyroid nodule $\geq$4 cm. Sensitivity, specificity, and negative and positive predictive values were calculated with FNA results of all types of thyroid cancer. FNA results were compared with final histopathology after thyroidectomy. All patient charts and information were reviewed in accordance with Institutional Review Board guidelines at the University of Miami Miller School of Medicine.

Statistical analyses were performed with SPSS version 18.0 (IBM Co, Somers, NY). Confidence intervals were defined using the Wilson-Score method. A $P < 0.05$ value was considered statistically significant.

3. Results

Of the entire study group, patient ages ranged from 10 to 87 years with a mean age of 50 years. There was a 5:1 female-to-male ratio. Overall, 6% of FNA results were nondiagnostic, 30% were benign, 43% indeterminate, and 21% malignant. Patients were divided into two groups: those patients with a dominant thyroid nodule <4 cm ($n = 856$) and those patients with a dominant thyroid nodule $\geq$4 cm ($n = 212$). There were significantly more patients with thyroid nodules $\geq$4 cm and benign FNA results than patients with thyroid nodules <4 cm ($P < 0.05$). Furthermore, malignant FNA results were almost three times more common in those patients with dominant thyroid nodules <4 cm (Table 1).

On final histopathology, there were 75 patients (35%) with nodules $\geq$4 cm and 459 patients (54%) with nodules <4 cm that had thyroid cancer. The most common malignancy was