Effects of Implementing a Higher Threshold for Recommending Thyroid Biopsies on Malignancy Rates

Kori Higashiya, BS1; Liam Delgesso, BS2; Hyo-Chun Yoon, MD, PhD3

Perm J 2021;25:20.240
https://doi.org/10.7812/TPP/20.240
E-pub: 3/10/2021

ABSTRACT

Introduction: We implemented a new thyroid nodule classification system in which a biopsy was recommended for thyroid lesions ≥ 1 cm with at least 2 or more suspicious features.

Methods: Three consecutive years of thyroid biopsies using the new classification system were reviewed for patient demographics, biopsy recommendation based on nodule size and imaging characteristics, and pathology results. The primary outcome was malignancy rates for thyroid biopsies. These results were compared to a 3-year historical data set.

Results: Review of thyroid biopsies from 2010 to 2012, prior to the implementation of current recommendations, revealed 996 thyroid biopsies with a malignancy rate of 12.8%. Subsequent to the new classification system in 2017, 483 thyroid biopsies were performed over the next 3 years with a malignancy rate of 21.9%.

Discussion: Implementation of the new classification system with a higher threshold for biopsy reduced our yearly biopsy volume by approximately 50% while also increasing our malignancy rate from 12.8% to 21.9%, which is more in line with published rates of malignancy.

Conclusion: In a community setting performing less than 200 biopsies per year, the use of more stringent requirements for thyroid biopsy are necessary to achieve malignancy rates comparable to the published literature.

INTRODUCTION

The use of nodule size and suspicious characteristics to predict malignancy is well documented. Suspicious characteristics such as microcalcifications, irregular margins, marked hypoechogenicity, and taller than wide shape have been shown to have 87% sensitivity and 86.5% specificity for thyroid lesion malignancy.1 To standardize recommendations and reduce unnecessary biopsies, several professional societies have formed guidelines for the classification of thyroid nodules with corresponding targets for malignancy rates.

The 2015 American Thyroid Association (ATA) guidelines suggest that all solid thyroid nodules ≥ 1 cm should undergo a biopsy because of a risk of malignancy of 10% to 20% for nodules with no suspicious characteristics, and > 70% for nodules with at least 1 suspicious characteristic.2 The American College of Radiology–Thyroid Imaging Reporting and Data Systems (ACR-TIRADS) guidelines recommend biopsy for TR5 lesions that are ≥ 1 cm plus > 7 points based on suspicious characteristics due to an estimated risk of malignancy of > 20%.3

At our institution, we previously recommended biopsy for all lesions ≥ 1 cm with at least 1 suspicious characteristic. After getting agreement from the Departments of Endocrinology and Head and Neck Surgery, we instituted a more stringent classification system for thyroid ultrasounds similar to ACR-TIRADS. The classification system simplified ACR-TIRADS into 4 categories: #THY1 through #THY4. #THY1 recommends no further imaging unless clinical symptoms change for thyroid glands with no nodules, nodules with benign imaging characteristics, or nodules that have been stable for 1 year. #THY2 recommends 12-month follow-up imaging for thyroid nodules with no or 1 suspicious imaging feature. #THY3 recommends fine-needle aspiration (FNA)/biopsy for lesions with 2 or more suspicious features, and #THY4 recommends an endocrinology or head and neck surgery consult for abnormalities that do not fit into any of the other 3 categories.

We compared the volume of biopsy procedures and the prevalence of malignancy in the biopsy specimens for a 3-year period before and after the implementation of the more stringent biopsy threshold.

METHODS

The Institutional Review Board approved this study with a waiver of informed consent because this is a data-only retrospective investigation with no patient interaction. We reviewed the records of all patients who underwent a thyroid biopsy performed in our geographically isolated health maintenance organization that serves approximately 250,000 members, where all nonemergent care is provided within the organization and all patient encounters are included in a comprehensive electronic medical record. We reviewed the patient charts for all patients who underwent a thyroid biopsy for a full 3-year period before (January 1, 2010–December 31, 2012) and after (January 1, 2017–December 31, 2019) the implementation of our more stringent biopsy threshold.

Author Affiliations

1John A. Burns School of Medicine, University of Hawaii, Honolulu, HI
2University of British Columbia, Vancouver, Canada
3Hawaii Permanente Medical Group, Honolulu, HI

Corresponding Author

Kori Higashiya, BS (Kori.higashiya@hwmuc.edu)

Keywords: malignancy rate, thyroid, thyroid biopsy, thyroid cancer, thyroid malignancy
the implementation of the more stringent biopsy threshold. We recorded the age and gender of each patient as well as the pathology results of the biopsy specimens. For those patients who underwent subsequent surgical excision, the pathology results of the surgical specimen were used to determine whether the lesion was cancerous. For the latter study period, we also recorded thyroid classification (#THY).

Malignancy rates were determined based on the pathology results of the excised surgical specimens, or the biopsy results if the patient did not undergo surgical excision. Among patients who underwent a biopsy of multiple lesions, only the most suspicious pathological result was included in the analysis. For example, if a patient underwent 2 biopsies and 1 result was reported as benign follicular lesion and the other was a lesion suspicious for follicular neoplasm, then only the lesion suspicious for follicular neoplasm was included in the analysis for malignancy rate. Pathology results reported as suspicious for follicular neoplasm on biopsy did not undergo surgical excision, because the usual practice among our head and neck surgeons is to remove such lesions surgically. Lesions reported as follicular lesion of undetermined significance (FLUS) were not included in our calculation of malignancy rates because these lesions are usually followed by imaging or a repeat biopsy. Statistical analysis was performed on nominal variables with the \( \chi^2 \) test and continuous variables with 2-tailed \( t \)-tests assuming equal variance.

RESULTS

A total of 996 thyroid biopsies were performed during the 3-year period of 2010 through 2012 (Table 1). Of these 996 biopsies, 127 were found to be cancer or suspicious for follicular neoplasm on biopsy. Fifty-two lesions suspicious for follicular neoplasm on biopsy did not undergo surgical excision for definitive confirmation but were included in the total number of cancers. Seventy-five were confirmed papillary thyroid carcinoma or other cancer confirmed by biopsy or surgical excision. This resulted in a combined prevalence of 12.8%, with a surgically confirmed malignancy rate of 7.5%.

In the 3 years after the institution of the more stringent conditions for thyroid biopsy, 483 biopsies were performed. Of the 483 biopsies, 373 (77.2%) were the result of a prior thyroid ultrasound that was classified as #THY3 or #THY4. A total of 297 (79.6%) were classified as #THY3 (ie, a nodule \( \geq 1 \) cm and with 2 or more suspicious characteristics), and 76 (20.3%) were classified as #THY4 (a lesion for which endocrinologist or head and neck surgeon input was requested).

The remaining 110 (22.7%) biopsies were performed on patients who previously had a thyroid ultrasound that was classified as #THY1 (11 patients) or #THY2 (99 patients). Of the 483 thyroid biopsies conducted from 2017 through 2019, 106 were found to be cancer, follicular neoplasm, or suspicious for follicular neoplasm on biopsy. Twenty-three lesions reported as follicular neoplasm or suspicious for follicular neoplasm on biopsy did not undergo surgical excision for definitive confirmation but were included in the total number of cancers. Eighty-three were confirmed papillary thyroid carcinoma or other cancer confirmed by biopsy or surgical excision. Other cancers included 1 anaplastic thyroid cancer, 4 cases of lymphoma, and 3 metastases from a different primary malignancy. Collectively, the malignancy rate for this 3-year period was 21.9%, with a surgically confirmed malignancy rate of 17.1%. There was a significant increase in the rate of cancers reported between 2010–2012 and 2017–2019 (\( \chi^2 \) for trends, \( P < 0.00001 \)).

For both time periods, we did not include FLUS because it is unknown whether these lesions have oncological significance. However, there were 53 cases of FLUS in 2010–2012 and 17 cases of FLUS in 2017–2019. There was no significant difference in the number of FLUS cases between the 2 time periods (\( \chi^2 \) for trends, \( P = 0.056 \)). None of FLUS samples from 2017–2019 underwent additional molecular testing. Three of the 17 underwent repeat biopsy and were
reported as benign. One patient had open surgery with benign pathology. The remaining 13 patients elected to have clinical and imaging follow-up.

Compared to the historical volume of 332 thyroid biopsies per year in 2010–2012, the implementation of the new classification system resulted in 161 thyroid biopsies per year in 2017–2019. This represents an approximate 50% reduction in number of biopsies and also achieved a target prevalence of malignancy similar to that of the ACR-TIRADS recommendations. There was no significant difference for gender (χ2 for trends, P = 0.28) or age (t-test, P = 0.90) between the 2 time periods.

Despite having the classification of THY#1, when no further follow-up is recommended, there were 11 patients who underwent biopsy. On chart review, common reasons for biopsy were patient preference or head and neck surgery/endocrinology recommendation based on clinical history. One patient had a biopsy that reported a lesion suspicious for follicular neoplasm. Because of the family history of thyroid neoplasia and its large size, the patient elected to have the lesion excised surgically. It proved to be a papillary thyroid cancer. Another patient also had a biopsy report suspicious for follicular neoplasm, but elected to have clinical and imaging follow-up.

Similarly, there were 99 thyroid biopsies performed on patients with THY#2 classification, which recommends ultrasound follow-up in 12 months. Again, the decision to perform a biopsy was usually made by the clinician based on the patient’s clinical history and patient preference. Of these 99 patients, biopsy revealed papillary thyroid cancer in 3, other malignancy in 1, follicular neoplasm in 7, and suspicious for neoplasm in 5. Of the 12 patients with follicular neoplasm or lesion suspicious for neoplasm, 7 underwent surgical excision. One patient with a suspicious lesion was found to have a papillary thyroid cancer. Another patient with a follicular lesion was found to have a 0.1-cm micropapillary thyroid cancer separate from the follicular lesion.

**DISCUSSION**

The 2015 ATA guidelines recommend conducting a biopsy of any solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule ≥ 1 cm with 1 or more suspicious characteristics due to an estimated > 70% risk of malignancy. These characteristics include irregular margins (infiltrative, microlobulated); microcalcifications; taller than wide shape; rim calcifications with a small, extrusive soft tissue component; or evidence of extrathyroidal extension. In addition, they cite a 10% to 20% estimated risk of malignancy for hypoechoic solid nodule ≥ 1 cm with smooth margins without any other suspicious characteristics. However, as noted in a footnote within the guidelines, these estimates are derived from high-volume centers; the overall risk of malignancy may be lower given the inter-observer variability in sonography. From 2010–2012 we recommended thyroid biopsies for lesions > 1 cm with at least 1 suspicious characteristic. This resulted in a malignancy rate of 12.8%, which is very much lower than the 70% to 90% chance of malignancy that the ATA cites.

Although our thyroid classification system is similar to ACR-TIRADS, we do not use a point system to determine into which category the lesion falls. Instead, we base our recommendations on the size of the lesion and the number of suspicious characteristics. With ACR-TIRADS, TR5 (score ≥ 7), which is assigned to highly suspicious lesions, has an estimated malignancy rate of > 20%. Similarly, in our classification system, we achieved a malignancy rate of 17.1% for surgically documented cancer.

Despite having a higher threshold to conduct a biopsy, we were not able to reproduce the > 70% positivity rate cited by the ATA guidelines for lesions ≥ 1 cm with at least 1 suspicious characteristic. Therefore, we recommend other centers that are not high-volume centers for thyroid biopsy to review their malignancy rates among their thyroid biopsies to ensure they are achieving the expected prevalence of malignancy in their biopsy specimens.

Molecular tests such as the Afirma Gene Expression Classifier (Veracyte Inc, South San Francisco, California) on FNA specimens reported as FLUS are available to our clinicians. According to our institutional policy, a molecular test on thyroid FNA samples is generally reserved for patients who have FLUS on 2 consecutive FNA specimens. However, for patients with a diagnosis of FLUS on FNA, our endocrinologists generally prefer to monitor these patients or obtain a core biopsy. Therefore, none of the patients with FLUS in our study underwent molecular testing.

Last, it is important to note that in our patient population, approximately 20% of biopsies was performed on patients in whom a biopsy was not recommended by the radiologist. In most cases, the biopsy was performed on the recommendation of the endocrinologist or head and neck surgeon, who based their decision on additional information obtained from the patient’s medical history and clinical presentation. There were also a few biopsies performed at the patient’s insistence. Based on our 3-year experience with our new classification system, approximately 20% of biopsies may be requested based on clinical factors rather than on imaging features alone.

**Limitations**

There is operator variability associated with the devices used to obtain images of the thyroid, the sonographers’ experience with thyroid imaging, and the radiologists’ interpretation of the images. However, we did not review any
images as part of our study, nor did we record which sonographer or radiologist was involved in the cases that led to the decision for biopsy, because the purpose of our study was to assess overall rates of malignancy in patients undergoing thyroid biopsy.

We did not look at the specific features of lesions that determined the need for a biopsy in each time period. Therefore, no regression analysis was performed on which factors among the generally accepted suspicious features were most associated with the likelihood of malignancy. There have been numerous published studies that have tried to address this issue, including a meta-analysis that favored using a combination of features rather than a single feature.4

Last, we assume there was no change in the underlying prevalence of thyroid cancer in our patients between the 2 study periods. A recent meta-analysis by Furuya-Kanamori et al5 reports that the baseline prevalence of incidental differentiated thyroid cancer in autopsy specimens has remained stable at about 11% since 1970.

CONCLUSION

Using a 1-cm cutoff with 2 suspicious characteristics as the threshold for thyroid biopsy resulted in a 25% prevalence of malignancy in our biopsy specimens more than halved the volume of yearly biopsies compared to historical numbers. 

Disclosure Statement
The authors have no conflicts of interest to disclose.

Authors’ Contributions
Kori Higashya, BS, participated in the acquisition and analysis of data, and drafting, review, and submission of the final manuscript. Liam Delgesso, BS, participated in the acquisition and analysis of data. Hyo-Chun Yoon, MD, PhD, participated in the study design, acquisition of data, and drafting and review of the final manuscript.

Funding
The authors did not receive funding for this study.

References