

JAMA Clinical Guidelines Synopsis

Management of Adult Patients With Thyroid Nodules and Differentiated Thyroid Cancer

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GUIDELINE TITLE 2015 American Thyroid Association Management Guidelines for Adult Patients With Thyroid Nodules and Differentiated Thyroid Cancer

DEVELOPER American Thyroid Association (ATA)

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PRIOR VERSION November 4, 2009

TARGET POPULATION Adults aged 18 years or older with thyroid nodules, thyroid cancer, or both

MAJOR RECOMMENDATIONS (1) Decisions regarding fine-needle aspiration biopsy (FNAB) should be based on ultrasound characteristics, not merely the size of the nodule; (2) lobectomy is now considered an appropriate surgical choice in certain lower-risk patients; (3) radioactive iodine should be administered postoperatively to patients with high-risk differentiated thyroid cancer (DTC) and some with intermediate-risk DTC but not to low-risk patients; and (4) ongoing risk stratification is proposed to select the degree of optimal thyrotropin suppression.

Summary of the Clinical Problem

Thyroid nodules are typically asymptomatic, and 33% to 68% of adults have thyroid nodules when evaluated by ultrasound.¹ Most thyroid nodules are benign, but about 7% to 15% of individuals with thyroid nodules harbor thyroid cancer.² Thyroid nodules may also cause morbidity due to hyperthyroidism or local compression. Population-based studies suggest a doubling in thyroid cancer incidence in recent decades, but nearly all of this increase is attributable to clinically occult cancers detected incidentally on imaging or pathology.

Although thyroid cancer is generally associated with a good prognosis, some thyroid cancers exhibit a more aggressive course. Differentiated thyroid cancers including papillary thyroid cancers, follicular thyroid cancers, and Hurthle cell thyroid cancers are derived from thyroid follicular cells. Other important types of thyroid cancer include medullary thyroid cancer and anaplastic thyroid cancer and are addressed in other ATA guidelines.

Characteristics of the Guideline Source

The ATA developed these guidelines³ through a task force of experts in various specialties, including endocrinology, surgery, nuclear medicine, radiology, pathology, oncology, molecular diagnostics, and epidemiology. The ATA's policy replaces one-third of the task force for each iteration of these guidelines and establishes editorial independence from the ATA. Individual committee members were not paid by the ATA or industry.

Evidence Base

The guidelines were developed in a stepwise fashion for each question. The primary reviewer performed a literature review and generated recommendations, discussion, and references. The secondary reviewer revised the section and presented it for review by the entire panel followed by an online survey of ATA members. The guidelines were reviewed and approved by the ATA Board of Directors, then submitted for peer review. Overall, 101 recommendations were developed, and the reference list included 1078 articles. The American College of

Physicians (ACP) grading system⁴ for therapeutic interventions was adapted for the recommendations. Recommendations are associated with strength of the recommendation (strong, weak, or no recommendation) and quality of evidence (high, moderate, or low). These guidelines apply to individuals aged 18 years or older, with earlier ATA guidelines addressing pediatric thyroid nodules and thyroid cancer.

A significant change in the new guideline is the addition of guidance on which thyroid nodules are most appropriate for FNAB. The recommendations are based on 3 particularly pertinent studies. Tae et al⁵ identified sonographic patterns suggestive of malignancy in 580 patients; these patterns included presence of microcalcifications, irregular or microlobulated borders, marked hypoechogenicity, and a shape taller than wide. Ito et al⁶ evaluated 1145 nodules from 900 patients and divided risk into 5 main categories ranging from cystic lesion (least suspicious) to solid, irregular nodules with extrathyroidal extension (most suspicious). And in 2009, the Thyroid Imaging Reporting and Data System (TIRADS)⁷ evaluated FNAB results from 1959 thyroid lesions to develop criteria for concerning ultrasound patterns. The current guidelines used this evidence base to divide thyroid nodules into degrees of suspicion: high, intermediate, low, very low, and benign.³ These categories of nodule risk can inform biopsy decisions and are summarized in the **Table**. Revised TIRAD criteria have also been proposed, and a committee has been convened by the American College of Radiology to harmonize these approaches.⁸

Benefits and Harms

Most thyroid nodules are benign and most cases of DTC are not aggressive, challenging clinicians seeking to diagnose and treat the clinically important ones. There are risks associated with treatments such as surgery and radioactive iodine (RAI). Surgery may lead to long-term hypothyroidism and carries some risk of hypoparathyroidism and laryngeal nerve damage, with the extent of surgery influencing the degree of risk. Radioactive iodine decreases the risk of cancer recurrence in certain patients with DTC but increases risk of salivary gland dysfunction, dental caries, taste changes, and nasolacrimal

Table. Sonographic Patterns, Malignancy Risk, and Fine Needle Aspiration Biopsy Guidance for Thyroid Nodules^a

Risk Group	Ultrasound Features	Risk of Malignancy, %	Consider Biopsy
High	Irregular margins, microcalcifications, taller than wide, extrathyroidal extension, extrusion of soft tissue into calcified rim	>70-90	Size ≥1 cm
Intermediate	Hypoechoic solid (no high-risk features)	10-20	Size ≥1 cm
Low	Isoechoic or hyperechoic solid nodule, partially cystic nodule with eccentric solid areas (no high-risk features)	5-10	Size ≥1.5 cm
Very low	Spongiform nodule (no high-risk features)	<3	Consider if size ≥2 cm, but observation also an option
Benign	Simple cysts	<1	No biopsy

^a Adapted from Haugen et al.³

tear duct dysfunction. Moreover, a number of studies suggest a small increased risk of secondary malignancies after RAI, especially leukemia and salivary gland cancers. Such issues emphasize the need for better ways to manage patients with thyroid nodules and more selectively diagnose and treat clinically important cancer.

Discussion

These guidelines provide recommendations on a variety of topics, including which thyroid nodules to biopsy, when to proceed to surgery, the extent of such surgery, and when patients with DTC should be treated with additional treatments such as RAI. Major changes from prior guidelines also include (1) consideration of molecular markers in the evaluation of thyroid nodules; (2) use of cross-sectional imaging for patients with thyroid cancer undergoing surgery; (3) voice evaluation prior to surgery; (4) thyroid lobectomy as a potential option for certain patients with thyroid nodules; (5) noting the benefits of ongoing risk assessment; and (6) a discussion of novel approaches to RAI-resistant DTC, such as tyrosine kinase inhibitors. Use of molecular markers in stratification of nodule risk is discussed, but it is unclear when they should be used. In a change from prior guidelines, use of lobectomy for certain low-risk DTC can be considered, for example, if the lesion is smaller than 4 cm. The guidelines state that RAI is routinely recommended for high-risk disease and can be considered for patients with intermediate-risk DTC.

Overall, the recommendations are often limited by areas of low- or medium-quality evidence because there are few randomized clinical trials in this patient population. However, these limitations are clearly stated in the guidelines.

Areas in Need of Future Study or Ongoing Research

The guidelines discuss areas in need of future research, including (1) use of molecular markers; (2) when active surveillance of DTC primary tumors might be indicated; (3) how risk stratification can be improved; (4) risks and benefits of DTC treatments and their optimal implementation; (5) difficulties with thyroglobulin and antithyroglobulin antibody measurement and use of thyroglobulin measurements by tandem mass spectrometry and new ultrasensitive assays; (6) optimal management of metastatic cervical adenopathy; (7) use of novel therapies for RAI-refractory disease; and (8) survivorship care. Recent nomenclature revisions should reduce pressure to treat highly indolent encapsulated papillary neoplasms.⁹ Recent work has applied quality management principles to FNAB follow-up¹⁰; extending such efforts to support appropriate primary care management of thyroid nodules would be welcome.

Related Guidelines and Other Resources

2010 American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association Medical Guidelines for Clinical Practice for the Diagnosis and Management of Thyroid Nodules

2012 Society for Nuclear Medicine and Molecular Imaging Practice Guideline for Therapy of Thyroid Disease With ¹³¹I 3.0

2014 British Thyroid Association Guidelines for the Management of Thyroid Cancer

ARTICLE INFORMATION

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