

Evidence-Based Evaluation of the Thyroid Nodule



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KEYWORDS

• Thyroid • Thyroid nodule • Thyroid cancer • Evaluation • Thyroid neoplasm risk

KEY POINTS

- Thyroid nodules are extraordinarily common; by age 90, virtually everyone has nodules.
- Ultrasound is the most valuable imaging study for making decisions about which nodules to biopsy.
- Nodules that are greater than 2 cm in size, that are entirely solid in composition, and that have microcalcifications are most likely to harbor a cancer.
- Molecular markers can help predict the presence of malignancy in cytologically indeterminate nodules, but markers do not accurately predict aggressiveness of cancers.
- Small papillary thyroid cancers can be safely observed in selected patients; discussions with patients should incorporate this option.

THE THYROID NODULE—SCOPE OF THE PROBLEM

Thyroid nodules are extraordinarily common. A key challenge for clinicians is to decide which ones require evaluation and intervention. Half of people age 50 or over with clinically normal thyroid glands and thyroid function have thyroid nodules, and by age 90, virtually everyone has nodules.¹ Thyroid cancer is commonly found at autopsy in

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individuals who have died of other causes, never having been detected in that patient's life. Estimates of cancer prevalence at autopsy are quite variable and depend largely on the method used to detect the cancers and geographic location, but range from a low of about 4% to a high of 36%.¹⁻⁵ Thus, thyroid cancers can be clinically insignificant for many patients. The workup and treatment can potentially expose the patient to the risks of treatment without the likelihood of any benefit. This challenging aspect of thyroid nodules has been recognized for some time, but the problem has been compounded in recent years by advances in and proliferation of imaging technology.

Advanced radiologic imaging rates (computed tomography [CT], magnetic resonance imaging [MRI], nuclear medicine, and ultrasound) have increased 3-fold since 1996.⁶ These scans commonly reveal small, nonpalpable thyroid nodules, which in the past would never have been identified because they were too small to detect by palpation, and too small to cause symptoms to the patient. Because so many of these incidental thyroid findings are now being uncovered, a dramatic increase in the observed incidence of small thyroid cancers is being experienced.^{7,8}

The increase in thyroid cancer incidence caused by this phenomenon is a problem for several reasons. First, patients are exposed to harm from what is ultimately unnecessary treatment. Second, these incidental findings unnecessarily create "patients with cancer" with all the attendant anxiety, surveillance needs, and financial ramifications.⁹ Last, these patients affect the validity of studies designed to understand and mitigate the risks of death or recurrence from thyroid cancer by serving to falsely improve the results of clinical trials. With this in mind, the chief challenge to clinicians today is deciding which nodules require workup, and how aggressively to treat them. What follows is a review of the current evidence related to the approach to the patient with a nodule.

PATIENT PRESENTATION

When a patient comes to the office with a thyroid nodule, the mechanism of detection is of paramount importance and will determine what next steps should be taken (**Fig. 1**). A patient who presents with symptoms of tracheal or esophageal compression should raise concern for a malignancy, although large goiter and Hashimoto thyroiditis can also cause these types of symptoms. The clinician should inquire regarding symptoms related to change in ease of breathing, swallowing, and speech quality. In contrast, a mass that was first noticed by the patient but that is not otherwise causing symptoms will have a much broader differential diagnosis (**Table 1**). Although a rapid increase in size can signal malignancy, it can also signal hemorrhage into a benign neoplasm.

Today, many thyroid nodules come to attention through radiologic imaging studies. The nodules are subclinical—not causing any symptoms for the patient and generally not apparent on the physical examination. There are 2 main pathways of such radiologic detection—the first is through incidental detection on radiologic imaging studies done for other reasons, such as chest CT (obtained for cough, for example), neck MRI (performed after motor vehicle accident/suspected whiplash injury, for example), or carotid ultrasound. The second pathway is detection through a "diagnostic cascade" of nontargeted and sometimes inappropriate initial testing—for example, when a thyroid ultrasound is inappropriately ordered as part of a more general workup for weight gain, fatigue, or hair loss—and a thyroid nodule is found but is unrelated to the patient's presenting symptoms.⁸ There are emerging data suggesting that traditional thyroid cancer risk factors, such as age, may be different for subclinical nodules that turn out to be papillary thyroid cancer on evaluation than for clinically apparent cancers, so obtaining a complete history is of even greater importance than in the past.¹⁰

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