Thyroid Nodules

Geanina Popoveniuc, MD[a,b], Jacqueline Jonklaas, MD, PhD[a,*]

KEYWORDS

• Thyroid nodule • TSH • Ultrasonography • FNA biopsy
• Elastography • Molecular markers • Indeterminate cytology
• Malignancy

INTRODUCTION

Thyroid nodules are common entities, frequently discovered in clinical practice, either during physical examination, but also incidentally, during various imaging procedures. They are clinically important primarily due to their malignant potential. For this reason the initial evaluation should always include a history and physical examination focusing on features suggestive of malignancy. Serum thyrotropin (TSH) and thyroid ultrasonography (US) are pivotal in the evaluation of thyroid nodules, as they provide important information regarding thyroid nodule functionality and the presence of features suspicious for malignancy, respectively. Fine needle aspiration (FNA) biopsy is the most accurate and reliable tool for diagnosing thyroid malignancy and selecting candidates for surgery, particularly if performed under ultrasound guidance. The cytology findings from FNA biopsies will fall into an indeterminate category in approximately 25% of the cases, in which case malignancy cannot be safely excluded. The recent use of panels of gene mutations and molecular markers, when combined with the cytologic diagnosis, show promising results in improving the preoperative diagnosis of indeterminate thyroid nodules, thus reducing the number of unnecessary surgeries. Other tools for predicting the malignant potential of thyroid nodules still under investigation include elastography and 18F-fluorodeoxyglucose positron emission tomography (18FDG-PET) scanning. An approach to the initial evaluation and management of single nodules, functioning nodules, multinodular glands, incidental nodules, and cysts are discussed. Therapeutic interventions for benign nodules, when needed, may include surgery, radioiodine (131-I) therapy, or percutaneous

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[a] Division of Endocrinology, Georgetown University Medical Center, 4000 Reservoir Road, NW, Washington, DC 20007, USA
[b] Section of Endocrinology, Washington Hospital Center, 110 Irving Street, NW, Washington, DC 20010, USA
* Corresponding author. Division of Endocrinology, Georgetown University Medical Center, Suite 230, Building D, 4000 Reservoir Road, NW, Washington, DC 20007.
E-mail address: jonklaaj@georgetown.edu

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ethanol injection (PEI), as indicated. Levothyroxine (T4) suppressive therapy is currently controversial and usually not recommended. The evaluation of thyroid nodules discovered during pregnancy is generally the same as for non-pregnant patients, except for the contraindication to radionuclide scanning. Thyroid cancer discovered during pregnancy may be safely managed by thyroidectomy after delivery in most of the cases, but if aggressive features are present, surgery should be ideally performed during the second trimester.

DEFINITION, CLINICAL IMPORTANCE, EPIDEMIOLOGY

- *Thyroid nodules are most common in women and older populations*
- *The purpose of thyroid nodule evaluation is to determine which nodules are malignant or require surgical attention*

Thyroid nodules have been defined by the American Thyroid Association (ATA) as "discrete lesions within the thyroid gland, radiologically distinct from surrounding thyroid parenchyma."[1] They may be discovered by palpation during a general physical examination or with radiographic studies performed for medical evaluations, such as carotid duplex ultrasound (US), computed tomography (CT) scans, magnetic resonance imaging (MRI) studies, or 18FDG-PET scanning. The latter entities are called "thyroid incidentalomas" and they generally do not correspond to palpable thyroid lesions. Conversely, clinicians may identify palpable thyroid lesions that do not correspond to distinct radiological entities, and therefore would not be defined as thyroid nodules.[2]

Thyroid nodules are common, their prevalence being largely dependent on the identification method. The estimated prevalence by palpation alone ranges from 4% to 7%,[3,4] whereas US detects nodules in 20% to 76% of the adult population,[4–6] particularly with the current use of high-resolution US techniques.[7] The reported frequencies detected by US correlate with the prevalence reported at surgery and autopsy with ranges between 50% and 65%.[8]

The estimated annual incidence of thyroid nodules in the United States is approximately 0.1% per year, conferring a 10% lifetime probability for developing a thyroid nodule.[6] Thyroid nodules are 4 times more common in women than men and their frequency increases with age and low iodine intake.[4] The gender disparity is perhaps explained by the hormonal influences of both estrogen and progesterone, as increasing nodule size and new nodule development have been demonstrated to be related to pregnancy and multiparity.[9,10] Exposure to ionizing radiation, either during childhood, or as an occupational exposure, will cause a rate of development of thyroid nodules of 2% per year, reaching a peak incidence in 15 to 25 years.[11,12]

Thyroid nodules are clinically important for several reasons. They may cause thyroid dysfunction and, rarely, compressive symptoms, but they are primarily important because of the need to exclude thyroid cancer. The reported prevalence of malignancy in thyroid nodules evaluated by biopsy ranges from 4.0% to 6.5% and is largely independent of the nodule size.[13,14] Despite this, papillary microcarcinomas (smaller than 1 cm) incidentally found at the time of surgery are much more common (up to 36%),[15,16] but it is controversial whether or not a survival benefit exists with the diagnosis and treatment of such entities, given their generally benign course.[17,18] Importantly, the incidence of thyroid nodules discovered incidentally during 18FDG-PET imaging is small (1%–2%), but the risk of malignancy may be as high as 27%, thus such nodules require immediate evaluation.[19]