Thyroid Nodules and Cancer

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Introduction and Clinical Importance

Thyroid nodules are very common in clinical practice with a prevalence ranging from 2% to 6% by palpation [1] and up to 19–68% by ultrasound [2–4]. Most patients with a palpable thyroid nodule on physical examination have additional nodules on US investigation [5, 6]. The main clinical importance of these nodules is to rule out malignancy.

The majority of nodules are benign; approximately 6% are malignant [1, 3]. The incidence of thyroid cancer has been increasing due to the use of neck ultrasonography and other imaging leading to early diagnosis of occult and incidental cancer with unclear clinical significance [7]. The incidence of thyroid cancer has tripled from 4.9 per 100,000 in 1975 to 14.3 per 100,000 in 2009 [8, 9]. The estimated annual incidence of thyroid nodules is 0.1% per year, suggesting that approximately 350,000 new nodules will be detected this year, conferring a 10% lifetime probability for developing a thyroid nodule [3, 10]. Thyroid nodules are more common in elderly persons, in women, and in areas with iodine deficiency and with a history of childhood radiation exposure [6, 11]. The prevalence of nodular thyroid disease is high so the main purpose of thyroid nodule evaluation is to determine which nodules are malignant or require surgical intervention.

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History and Physical Examination

Clinical evaluation begins with a complete medical history and thyroid palpation. Both benign and malignant disorders can cause thyroid nodules (Table 3.1). Attention should be directed to information on prior history of radiation treatment of the head and neck, rate of growth of the mass (location, size, and consistency), associated cervical lymphadenopathy, local symptoms (pain, dysphonia, dyspnea, or dysphagia), and other associated symptoms of hypothyroidism or hyperthyroidism. Most patients will have no symptoms during evaluation as the majority of thyroid nodules will be discovered incidentally. Malignancy rate in younger and older patients is increased three- to four-fold when compared to adults [12, 13].

Family history should be obtained, paying special attention to a history of medullary thyroid carcinoma (MTC), papillary thyroid carcinoma, multiple endocrine neoplasia types 2A and 2B, familial polyposis disease, Cowden disease, Carney complex, Gardner syndrome, and other rare diseases [14–17]. Table 3.2 shows findings suggestive of increased risk of malignancy potential.

Table 3.1 Common causes of thyroid nodules

Common causes of thyroid nodules
Benign nodular goiter
Thyroiditis
Cysts
Primary thyroid cancer
Papillary carcinoma
Follicular carcinoma
Hurtle cell carcinoma
C cell-derived carcinoma, medullary carcinoma
Anaplastic carcinoma
Metastatic cancer
Lymphoma

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Table 3.2 Findings of increased malignancy potential

Findings of increased malignancy potential
Prior history of head and neck irradiation
Family history of MTC, MEN type 2, PTC, or other syndromes
Age <14 or >70 years
Male sex
Growing nodule, firm or hard consistency, fixed
Cervical adenopathy
Persistent dysphonia, dysphagia, dyspnea, or vocal cord paralysis

Diagnostic Evaluation

Serum Markers

Besides a complete history and physical exam, all patients should have a serum TSH measurement [8, 18]. If the TSH is low, a thyroid scintigraphy should be performed to determine the functional status of the nodule as low TSH suggests overt or subclinical hyperthyroidism, hyperfunctioning ("hot"), and autonomous functioning adenoma. If indeed the nodule is found to be "hot," it is unlikely to be malignant, and FNA should be deferred [19].

TSH levels are independent predictors of malignancy in patients with thyroid nodules: the risk of malignancy increases as the TSH levels also increase [20, 21]. Routine measurement of serum thyroglobulin (Tg) for initial evaluation of thyroid nodules is not recommended [8].

Calcitonin is a marker for detection of C-cell hyperplasia and MTC, and levels >10 pg/mL have high sensitivity for the detection of MTC. Calcitonin should be measured in high-risk patients, such as in those with a family history of MTC, with high clinical suspicion of MTC by US or cytology, or with MEN 2 syndromes. Overall, the prevalence of MTC is low enough in the United States that both the recent ATA and AACE Guidelines recommend "neither for or against routine calcitonin measurement" [8, 22].

Thyroid Ultrasound and Indication for Fine-Needle Aspiration (FNA)

Ultrasonography, more sensitive than palpation, is the imaging of choice to detect a thyroid nodule. Thyroid ultrasound (US) with survey of the cervical lymph nodes should be performed in all patients with a suspected thyroid nodule, a goiter, or after an incidentally found nodule by other imaging modalities [8]. Thyroid US is noninvasive and inexpensive, has a sensitivity of 95%, and can identify nodules usually not palpated on the physical exam. Ultrasound provides a very good evaluation of nodule size, dimensions, structure, and any possible suspicious features. It can also differentiate solid from cystic nodules [8, 22, 23].

Ultrasound-guided fine-needle aspiration (FNA) is the procedure of choice (gold standard) in the evaluation of thyroid nodules and is the most accurate test for determining malignancy [8, 22]. It is safe, cost-effective, and preferred over palpation-guided leading to much lower rates of non-diagnostic and false-negative cytology results [24]. When performed by experienced physicians, adequate sample can be obtained from solid nodules in 90–97% of aspirations [24]. There is no single ultrasound characteristic of malignancy but instead a combination of features that need to be evaluated as predictors of malignancy [10].

The most recent American Thyroid Association guidelines classify nodules into five risk groups based on a constellation of sonographic pattern [8], while the current AACE guidelines offer a more practical, three-tier risk analysis, including low (<1%), intermediate (5–15%), and high risk (50–90%) [22]. Per ATA guidelines, the recommendations for diagnostic FNA are the following:

- Nodules ≥1 cm in greatest dimension with high suspicious sonographic pattern.
- Nodules ≥1 cm in greatest dimension with intermediate suspicion sonographic pattern.
- Nodules ≥1.5 cm in greatest dimension with low suspicion sonographic pattern.
- FNA may be considered in nodules ≥2 cm in greatest dimension with very low suspicion sonographic pattern (spongiform). Observation is an option.
- Cystic nodules are considered to have very low suspicion sonographic pattern and don't require FNA.

The nodular characteristics mostly associated with being predictive of malignancy include shape that is taller than wide in the transverse dimension, hypoechogenicity, irregular margins, microcalcifications, and absent halo. These characteristics have high specificity, but the positive predictive value is lowered by their relatively low sensitivity. None of these features alone is enough to differentiate a benign from malignant lesion [25–28]. Findings such as isoechogenicity and spongiform appearance are features of benignity [29]. Complex nodules with solid and cystic components often with a dominant cystic part are frequently benign.

Numbers of nodules and size are not predictive of malignancy. In a gland with multiple nodules, the selection for FNA should be based on the US features rather than size alone. Cancer is not less frequent in small nodules so diameter cutoff alone to evaluate cancer risk is not recommended [30, 31]. Ultrasound should only be performed in patients with known or suspected thyroid nodules or the presence of risk factors [8]. Advances in diagnostic imaging have improved the management of thyroid nodules, but it also increased the discovery of incidentalomas (small thyroid nodules with <1 cm in diameter).

Other Imaging

Other techniques like MRI and CT scan are not recommended as routine tests as they are expensive and rarely diagnostic. CT scan and MRI have more value to assess goiter size, substernal extension, or extension to surround structures. Iodine contrast should be avoided as it decreases subsequent iodine 131 uptake [22]. Thyroid scintigraphy should be performed when there is suspicion of autonomy of the nodule (low TSH) suggesting overt subclinical hyperthyroidism.

Cytology

Thyroid FNA slides should be reviewed by a cytopathologist with experience in thyroid. FNA has reduced the number of surgical procedures in patients with nodules by more than 50% and substantially increased the malignancy yield at thyroidectomy [32]. An adequate sample is highly accurate for diagnosing thyroid cancer. Biopsy results may be classified as satisfactory or unsatisfactory (non-diagnostic). To be considered diagnostic or satisfactory, the aspirate needs to contain no less than six groups of well-preserved thyroid epithelial cells consisting of at least ten cells in each group [33].

The *Bethesda System for Reporting Thyroid Cytopathology* is the most commonly used. Currently there are six diagnostic categories: benign; malignant; suspicious for malignancy; follicular neoplasm or suspicious for a follicular neoplasm (FN/SFN); follicular lesion or atypia of undetermined significance (FLUS or AUS); non-diagnostic (Table 3.3) [33] [34]. The expertise of the cytopathologist is crucial in correct and clear interpretation of FNA slides and classification of the cytology [35].

Overall, 6–11% of the FNAs will be unsatisfactory (non-diagnostic), usually because of sampling error, bloody smears, or poor technique [36–38]. Biopsy should be repeated, but ultimately, about 5% of nodules will still be unsatisfactory [8, 39–42]. The false-negative rates range from 1 to 11% but usually will be less than 5% in most clinics with enough FNA experience [41, 43].

Management, Therapy, and Follow-Up

Benign Thyroid Nodule

The most common benign lesions include colloid nodule, macrofollicular adenoma, benign cyst, and lymphocytic thyroiditis. The majority of these nodules do not need specific treatment once malignancy and abnormal thyroid function are excluded [1, 8, 22]. If patient reports local symptoms including dysphagia, choking, dysphonia, dyspnea, or pain, surgical treatment may be warranted. The clinician should make sure that the symptoms are caused by the thyroid mass or enlargement, and not due to other processes such as pulmonary, cardiac, or esophageal disorders [10]. Patients with a single toxic nodule or a toxic multinodular goiter may be treated with surgery or radioiodine. Treatment with 131 I for large toxic nodules is not preferred as these nodules usually require high doses and are associated with more side effects [18].

Routine use of T4 suppressive therapy has no role in the management of benign thyroid nodules [8, 22]. Therapy with levothyroxine may be associated with increased risk of atrial fibrillation, other cardiac abnormalities, and reduced bone density, so therapy should be avoided in patients with large nodules, long-standing goiters, low TSH levels, postmenopausal women, and men older than 60 years [44–46].

The chance of a false-negative FNA (malignancy rate) is reported around 1–2% only [47, 48], and an initial benign FNA has negligible mortality risk in long-term follow-up [49]. Some studies report an increased risk of malignancy in nodules greater than 4 cm due to decreased FNA accuracy and recommend surgery [50–52], but based on current evi-

Table 3.3 Bethesda system; data compiled from Baloch et al. [33]

The Bethesda system for reporting thyroid cytopathology: implied risk of malignancy and recommended clinical management			
Diagnostic category	Risk of malignancy (%)	Actual risk of malignancy	Management
Non-diagnostic	1–4	20 (9–32)	Repeat FNA with ultrasound guidance
Benign	0–3	2.5 (1–10)	Clinical follow-up
Atypia of undetermined significance/follicular lesion of undetermined significance	5–15	14 (6–48)	Repeat FNA
Follicular neoplasm/ suspicious for a follicular neoplasm	15–30	25 (14–34)	Surgical lobectomy
Suspicious for malignancy	60–75	70 (53–97)	Near-total thyroidectomy or surgical lobectomy
Malignancy	97–99	99 (94–100)	Near-total thyroidectomy

dence, it is still unclear if patients with nodules with greater than 4 cm and benign cytology carry higher risk of malignancy [8].

The follow-up of thyroid nodules with benign cytology should be determined by risk stratification according to ultrasonography pattern [8]. The current guidelines of the American Thyroid Association published recommend that nodules with high suspicion US pattern should undergo repeat US and US-guided FNA within 12 months. Nodules with low to intermediate suspicion US pattern should have repeat US at 12–24 months; in nodules with very low suspicion US pattern, the utility of surveillance US and assessment of nodule growth as an indication to consider repetition of FNA are limited. If US is considered, it should be done at >24 months. If the nodule has undergone repeat US-guided FNA with a second benign cytology results, US surveillance for evaluation of malignancy is no longer warranted [8].

Malignant Thyroid Nodule

If cytologic results are positive for thyroid malignancy, surgery is almost always indicated [8] [22]. Consultation with an experienced endocrine surgeon is preferred and should be done as soon as possible. This category includes papillary cancer, follicular carcinoma, Hurthle cell (oncocytic) carcinoma, medullary cancer, thyroid lymphoma, anaplastic cancer, and metastatic cancer to the thyroid. Metastatic disease to the thyroid is rare [53] and usually precludes immediate surgery until further investigation for the primary site is completed. Full workup should also be performed for anaplastic carcinoma and lymphoma [18].

An active surveillance approach may be considered in a small subgroup of patients including those with a very low-risk tumors (papillary thyroid microcarcinoma without evident metastasis or local invasion), high surgical risk patients due to comorbid conditions, and patients with short remaining life spans [8]. Most patients with papillary thyroid carcinoma have an indolent course, and a few prospective studies have reported very good outcomes with very low rate of loco-regional recurrence and distant metastasis, and this approach may be considered in thyroid micro-carcinoma (tumors <1 cm in diameter) [54].

Suspicious for Malignancy

This category represents the cytologic results with strong suspicious for malignancy but lacking clear diagnostic criteria, with an estimated cancer risk of 60–75% [34]. Usually surgical management is similar to a malignant cytology, depending on clinical risk factors, sonographic features, patient preference, and possible mutation testing. As more data become available from the molecular testing field, management of this category may change in the future. Mutation testing could improve risk stratification prior to surgery, including possibly BRAF mutations and seven-gene panel of mutations (including BRAF, RAS< RET/PTC, with or without PAX9/PPARy) [55, 56].

Indeterminate Thyroid Nodule (AUS/FLUS and FN/SFN)

This group carries the most challenging diagnostic dilemma. In this category a clear cytologic diagnosis cannot be made, and examples include follicular neoplasms, Hurthle cell neoplasm, atypical PTC, or lymphoma. Indeterminate cytology also includes AUS/FLUS (atypia of undetermined significance/follicular lesion of undetermined significance) and FN/SFN (follicular neoplasm/suspicious for follicular neoplasm).

According to the Bethesda system, AUS/FLUS compromises specimens that contain cells with architectural and/or nuclear atypia that is more pronounced than expected for benign changes but not sufficient to be placed on the higher-risk categories [57]. Frequency range is around 7% of reports, and the risk of cancer is between 6 and 48%, with a mean risk of 16% [58].

Treatment options for AUS/FLUS include a repeat FNA, molecular testing, observation, and surgical intervention. Providers should take into consideration clinical and ultrasound risk factors and patient preferences when making management decisions. Of repeated FNAs 10–30% yield again AUS/FLUS [59–61]. Thyroid core needle biopsy could also be considered [62]. Molecular testing is another option commonly used in this subset of patients. Mutation testing for BRAF has a high specificity but low sensitivity [63, 64], while a panel of mutations (BRAF, NRAS, HRAS, KRAS, RET/PTC1, RET/PTC3, PAX8/PPARy) has a higher sensitivity [55] [65]. Recent studies are also using sonographic features to estimate risk of malignancy [66].

FN/SFN cytology compromises follicular cells arranged in an altered architectural pattern characterized by cell crowding and/or microfollicle formation and lacking nuclear features of papillary carcinoma or compromised almost exclusively of oncocytic (Hurthle) cells [33]. This category carries a 14–33% risk of malignancy (mean 26%), with a frequency of 1–25% (mean 10%) of all thyroid FNA samples [58].

For this category usually surgical excision for diagnosis had been an established practice. Again, with the introduction and availability of molecular testing, this can be used to supplement malignancy risk assessment after considering

the clinical and ultrasound risk factors and patient preferences [8]. Risk stratification with molecular testing including seven-gene panel shows a sensitivity of 57–75% and specificity of 97–100%, PPV of 87–100%, and NMPV of 79–86% [55, 65].

Non-diagnostic

Patients with non-diagnostic biopsies are those that do not meet specified criteria (the presence of at least six follicular cell groups, each containing 10–15 cells derived from at least two aspirates of a nodule) [33]. If initial FNA biopsy is non-diagnostic, it should be repeated with possible onsite cytological assessment [8, 22, 67]. If the results are again non-diagnostic, core needle biopsy, close observation, or surgery should be considered, the latter especially if there are suspicious pattern on ultrasound, clinical risk factors, and growth of the nodule. A repeat FNA after initial non-diagnostic cytology may yield a 75% diagnostic cytology in solid nodules and 50% in cystic nodules [68].

Figure 3.1 shows an algorithm with a summary for the diagnosis and management of palpable thyroid nodules.

Special Situations

Thyroid Nodule During Pregnancy

The majority of the thyroid nodules during pregnancy are pre-existing, but in some cases they can be initially diagnosed. Overall they should be managed exactly the same way in non-pregnant women except that radioactive agents should be avoided [22] [69]. If the clinical and imaging features are suspicious for malignancy, patient will require a FNA biopsy, regardless of the gestational age [70]. Some studies showed that the cancer behavior during pregnancy is the same when compared to the general population, without any differences in survival rates or recurrence. Suppressive therapy with levothyroxine for thyroid nodules is not recommended.

Patient's preferences should always be considered, and a multi-disciplinary approach including an endocrinologist, pathologist, obstetrician, surgeon, and anesthesiologist is recommended. Women with no evidence of aggressive thyroid cancer may be reassured, and surgical treatment can be

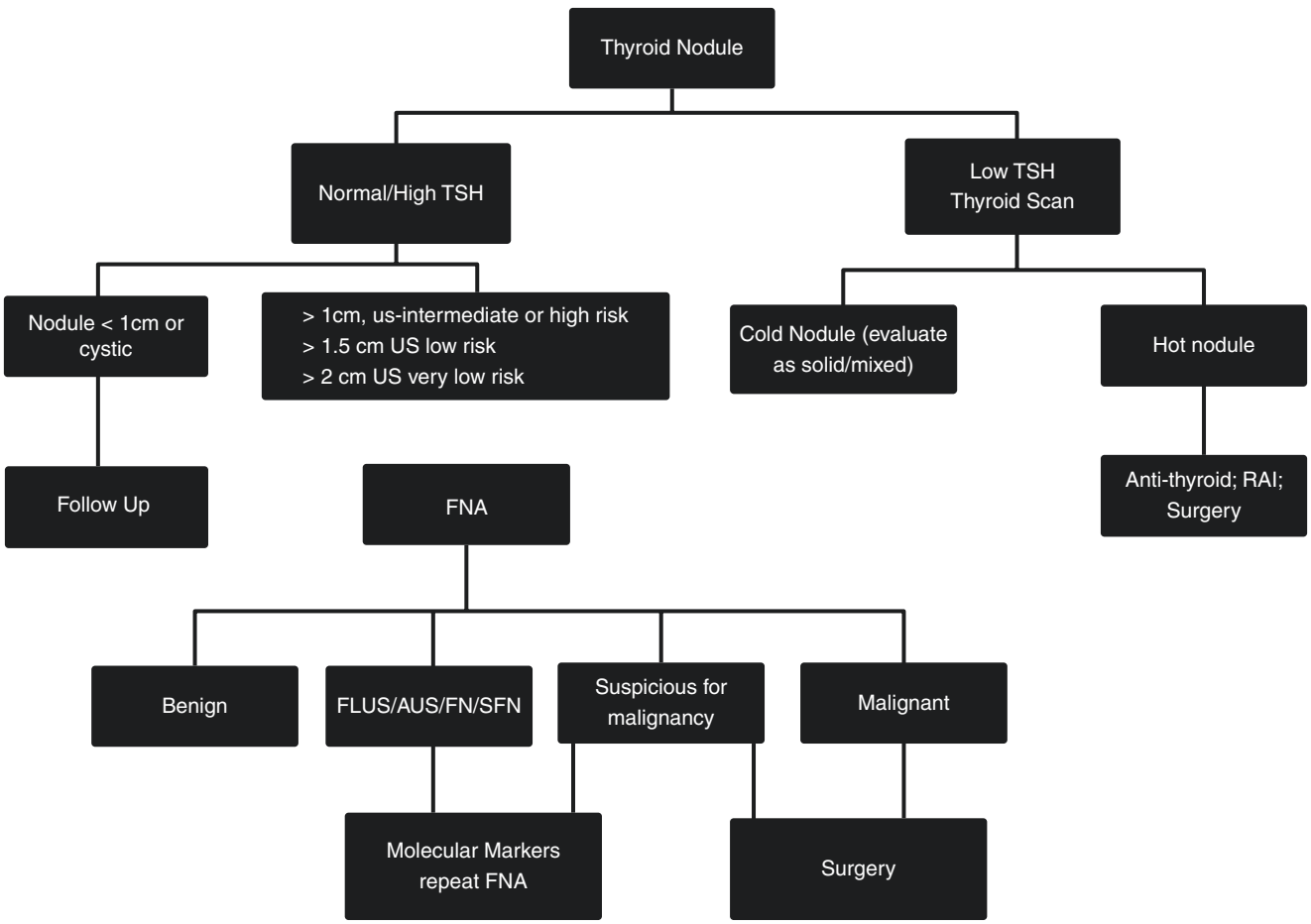

Fig. 3.1 Algorithm for the diagnosis and management of palpable thyroid nodules

performed after delivery [71]. The cytologic suspicious nodule is the most challenging situation during pregnancy. The malignancy rate is similar between pregnant women and non-pregnant women, so deferring surgical treatment to the postpartum is reasonable [72]. Some may recommend postponing FNA until delivery unless worrisome features are seen in the ultrasound as this may lead to possible thyroidectomy during pregnancy depending of the FNA results. If the outcome of the results will be unchanged, meaning that surgical treatment will be postponed, this will just expose the patient to anxiety regarding diagnosis and except management [73].

Thyroid Nodules in Children

The prevalence of thyroid nodules in children is up to 1.8%, and some cohort studies showed higher malignancy rates [74, 75]. These findings suggest that the surgical approach for thyroid nodules in children is more common than that in adults. The evaluation of nodular disease in children is similar to adults. Overall the prognosis of thyroid cancer in children remains good despite the increase prevalence of local metastatic disease [76]. As in adults, the most common thyroid cancer is the papillary.

Thyroid Cancer

The most common histologic types of thyroid cancers are follicular cell-derived and medullary thyroid cancers. *Follicular cell-derived cancer* includes all variants of papillary thyroid carcinoma (85% of all thyroid cancers) and follicular thyroid carcinoma (10–15% lesions, including Hürthle cell cancer). The other follicular cell-derived cancer is anaplastic carcinoma that accounts for less than 5% of thyroid tumors [77].

Medullary thyroid cancer originates in C cells and accounts for less than 5% of thyroid malignancies. While the majority has sporadic MTC, around 25% of patients may have a hereditary form as part of the multiple endocrine neoplasia type 2 syndromes (MEN 2). They will also require thyroidectomy and are followed with tumor markers like calcitonin. Even though the majority of medullary thyroid cancer is sporadic, genetic testing is recommended to all patients for evaluation including RET proto-oncogene mutation. If a mutation is found, all family members should undergo screening for the same mutation as early as possible.

The recently published recommendations of the American Thyroid Association (ATA) for differentiated thyroid cancer will be reviewed briefly in the following [8].

Goals of thyroidectomy include removing the tumor, improving overall disease-specific survival, and decreasing the rate of recurrence and morbidity. All patients should undergo pre-operative neck ultrasound for evaluation of lymphadenopathy. *Risk stratification* after surgery is paramount to outline a strategy for radioiodine treatment, follow-up plan, and TSH suppression.

For tumors <1 cm, without extra-thyroidal extension or regional lymph node metastasis, a thyroid lobectomy may be sufficient. For tumors 1–4 cm, without extra-thyroidal extension or lymph nodes, total thyroidectomy or, in selected patients, a lobectomy may be considered. Tumors greater or equal to 4 cm, with extra-thyroidal extension or metastases, should always undergo total thyroidectomy.

American Thyroid Association Risk Stratification System

ATA Low Risk

Patients with *papillary thyroid cancer* with no local or distant metastasis; all macroscopic tumor has been resected, no tumor invasion of loco-regional tissues or structures, no aggressive histology (tall cell, hobnail variant, columnar cell carcinoma); if I131 is given, no RAI avid metastatic foci outside the thyroid bed on the first post-treatment whole body RAI scan, no vascular invasion, clinical N0 or <5 pathologic N1 micro metastases (<0.2 cm in the largest dimension); *intrathyroidal, encapsulated follicular variant of papillary thyroid cancer*; *intrathyroidal, well-differentiated follicular thyroid cancer* with capsular invasion and no or minimal (<4 foci) vascular invasion; *intrathyroidal, papillary microcarcinoma, unifocal or multifocal, including V600E BRAF mutated.*

For this group of patients, especially in tumors <1 cm (unifocal or multifocal), there is no evidence suggesting that radioactive iodine (RAI) improves disease-specific and disease-free survival. Overall post-surgical RAI is not indicated. In patients with tumor size 1–4 cm, there are conflicting data that RAI improves disease-free survival and post-surgical RAI is not routinely indicated.

In patients that undergo total thyroidectomy, initial TSH goal is 0.5–2 mU/L if non-stimulated TG <0.2 ng/mL, and TSH goal is 0.1–0.5 mU/L if non-stimulated Tg >0.2 ng/mL. Evaluation of response to therapy includes at least annual thyroglobulin testing and neck ultrasound. Diagnostic whole body scan is not routinely recommended. Follow-up is usually annually for the first 5 years. If serum TG level is rising or neck ultrasound is abnormal, patient may require further diagnostic tests.

In patients undergoing lobectomy, post-op serum TG may be considered as well as neck ultrasound. Although after partial thyroidectomy serum TG will be undetectable, an increase in stable TG levels should give rise to suspicion of recurrent disease warranting further evaluation. RAI remnant

ablation is not recommended and initial TSH goal should be 0.5–2 mU/L. Evaluation for response to therapy includes annual ultrasound and consideration for thyroglobulin testing.

ATA Intermediate Risk

Patients with microscopic invasion of tumor into the peri-thyroidal soft tissues, RAI avid metastatic foci in the neck on the first post-treatment whole body RAI scan, aggressive histology, papillary thyroid cancer with vascular invasion, clinical N1 or ≥5 pathologic N1 with all involved lymph nodes <3 cm in largest dimension, intrathyroid, papillary thyroid cancer, primary tumor 1–4 cm, V600E BRAF mutated, multifocal papillary micro-carcinoma with extra-thyroidal extension and V600E BRAF mutated.

In patients with tumor size >4 cm, post-surgical RAI may be considered, especially in patients with adverse features. In patients with microscopic extra-thyroidal extension (any size tumors), post-surgical RAI is usually favored based on risk of recurrence of disease.

In patients with central compartment neck lymph node metastasis, post-surgical RAI is usually favored, mainly due to higher risk of persistent and recurrent disease, especially in larger tumors (>2 cm) or clinical evidence of lymph nodes or extra-nodal extension.

Initial therapy for these patients includes total thyroidectomy, neck dissection for clinical N1 disease, and possible prophylactic central neck dissection. Diagnostic RAI scanning may be considered. Surveillance includes serum thyroglobulin and ultrasound of the neck.

RAI scanning should be considered in patients with intermediate risk. For remnant ablation 30 mCI may be considered. For adjuvant therapy, usually up to 150 mCi is given. Initial TSH goal is 0.1–0.5 mU/L, and evaluation for response to therapy includes thyroglobulin testing, neck ultrasound, and consideration for diagnostic whole body scan. Again, periodic (annual) evaluation with thyroglobulin (non-stimulated) and ultrasound of the neck are recommended.

ATA High Risk

This group of patients includes macroscopic invasion of tumor into the peri-thyroidal soft tissues (gross extra-thyroidal extension), incomplete tumor resection, distant metastases, and post-operative serum thyroglobulin suggestive of distant metastases.

In patients with ATA high risk, the body of evidence suggests that RAI improves disease-specific survival and disease-free survival; therefore routine RAI use is recommended. Initial therapy includes total thyroidectomy, therapeutic neck dissection, and possible prophylactic central neck dissection. Post-operatively, monitoring with thyroglobulin, ultrasound, and RAI scanning are recommended.

RAI therapy is routinely recommended with up to 150 mCI as adjuvant therapy. For known structural disease, empiric 100–200 mCI or dosimetry-guided dosing is recommended. Initial TSH goal is <0.1 mU/L. This group of patients is at increased risk for recurrence, and follow-up should include thyroglobulin testing, neck ultrasound, whole body scan, and CT/MRI or FDG/PET scanning.

Summary

Thyroid nodules are very common and are usually benign; only around 5% carry the risk of malignancy. The challenge in the management of thyroid nodules is to reliably identify benign nodules and diagnose malignant thyroid disease as early as possible. Thyroid evaluation starts with a careful history and physical exam followed by thyroid function tests and ultrasound exam. An initial low TSH requires additional tests for evaluation of hyperthyroidism. When TSH is normal and US shows an indeterminate or suspicious nodule, an US-FNA should follow as it remains the single most important procedure for differentiating benign from malignant thyroid nodules. When cytology is suspicious for malignancy, surgery is usually recommended. Benign thyroid nodules can be followed clinically and with serial ultrasound images. An indeterminate nodule poses a clinical challenge; treatment may include observation, molecular markers, or surgery. The most common type of thyroid cancer is papillary thyroid cancer. Treatment usually entails total thyroidectomy with or without lymph node dissection. Depending on risk stratification, some patients may benefit from radioactive iodine therapy. Long-term follow-up includes ultrasound of the neck, TSH, and thyroglobulin. The overall prognosis of thyroid cancer remains good.

Appendix

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