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Thyroid nodule evaluation and management in older adults: A review of practical considerations for clinical endocrinologists

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Abstract

Objective: Contextualizing the evaluation of older adults with thyroid nodules is necessary in order to fully understand which management strategy is the most appropriate. Our goal was to summarize available clinical evidence to provide guidance in the care of older adults with thyroid nodules, and highlight special considerations for thyroid nodule evaluation and management in this population.

Methods: We conducted a literature search of PubMed and Ovid MEDLINE from January 2000 to November 2020 to identify relevant peer-reviewed articles in English. The references from the included articles, as well as articles identified by the authors were also reviewed.

Results: The prevalence of thyroid nodules increases with age. Even though thyroid nodules in older adults have a lower risk of malignancy, identified cancers are more likely to be of high-risk histology. The goals of thyroid nodule evaluation and the tools used for diagnosis are similar for older and younger patients with thyroid nodules. However, limited evidence exists regarding thyroid nodule evaluation and management to guide personalized decision making in the geriatric population.

Conclusion: Considering patient context is important in the diagnosis and management of thyroid nodules in older adults. When making management decisions in this population, it is essential to carefully weigh risks and benefits of thyroid nodule diagnosis and treatment, in view of older adults' higher prevalence of high-risk thyroid cancer, as well as increased risk for multimorbidity, functional and cognitive decline, and treatment complications.

Keywords

thyroid nodules; older adults; decision making

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INTRODUCTION

Almost 50 million Americans are aged ≥65 years and it is projected that the United States (U.S.) older population will grow by almost 50% from 2016 to 2030.[1,2] Thyroid nodules are prevalent in older adults and their incidence increases with age.[3] It is estimated that approximately half of adults aged ≥60 years in the U.S. have thyroid nodules.[4,5] The increased detection of thyroid nodules on imaging studies has been implicated in the recent exponential increase in thyroid cancer diagnosis, especially low-risk differentiated thyroid cancer.[6–9] Evidence suggests that although older adults have a higher prevalence of thyroid nodules, they have an overall lower prevalence of thyroid cancer. However, if thyroid cancer is diagnosed, there is a higher likelihood of it being high-risk thyroid cancer based on histological findings.[10–12] Moreover, older individuals have higher risks of treatment complications and worse clinical outcomes after thyroid cancer treatment. [12–15] Thus, the evaluation and management of thyroid nodules as the population ages emerges as a challenging but common clinical scenario.

Clinicians evaluating older adults with thyroid nodules need to weigh the potential harms of thyroid cancer overdiagnosis against the risks of a delayed thyroid cancer diagnosis when deciding the next step in management (e.g., follow up with neck ultrasound, thyroid nodule fine needle aspiration [FNA] biopsy, etc.).[16] Adding to the complexity of decision making for older adults are special considerations commonly addressed in a comprehensive geriatric assessment, such as multimorbidity leading to competing causes of death, frailty, functional and cognitive status, and social support systems.[17,18] Overall, the assessment of risks and benefits, while taking into account patient context, preferences and goals of care, is critical when navigating decisions for older patients with thyroid nodules. We provide an evidence-based review to guide the evaluation and management of older adults with thyroid nodules, while highlighting practical considerations to aid in contextualizing the care of each patient.

METHODS

The PubMed and Ovid MEDLINE databases were searched from January 2000 to November 2020 to identify pertinent articles published in English for inclusion in the literature review. The following search terms were used: “thyroid nodule”, “elderly”, “aging”, “older adults”, “epidemiology”, “decision making”, “guidelines”, “patient preferences”, “comorbidities”, “harms”, “life expectancy”, “malignancy risks”, “surveillance”, “follow up”, “thyroid ultrasound” and “genetic testing”. Additional salient studies were selected after reviewing relevant references of identified articles. There were no exclusions based on article type. We prioritized clinical practice guidelines, systematic reviews and randomized controlled trials and observational studies over case series and case reports. Some studies that were of higher interest to the readership were also prioritized. For the purposes of this review, older adults were considered those aged ≥65 years. However, in view of the paucity of literature regarding some aspects of thyroid nodule assessment and management in adults aged ≥65 years, some studies focusing on the general population that addressed patient age as a variable have also been included.

RESULTS

Thyroid Nodule Prevalence and Age

Advancing age correlates with increased thyroid nodule discovery but the reasons for this relationship are not entirely clear. It has been shown that the prevalence of thyroid nodules varies according to the method of detection in addition to patient age and iodine status.[5,16,19] For example, autopsy data have shown a 30–50% prevalence of thyroid nodules ≥1 cm in patients without previously known thyroid disease.[20,21] As expected, detection rates are higher with ultrasound when compared to palpation, and can be as high as ~67% compared to ~4–7% by physical examination.[5,19] Partly owing to the more frequent use of imaging studies in recent decades, such as ultrasound, thyroid nodule and cancer detection have considerably increased, including in older adults.[8,22] This is despite the U.S. Preventive Services Task Force recommending against screening for thyroid cancer in asymptomatic adults, given a negative net benefit, with harms outweighing the benefits.[23] On the contrary, government-funded national cancer screening programs in other countries, such as in South Korea, have been clearly associated with the global thyroid cancer epidemic.[24]

Several studies have evaluated the association between thyroid nodule prevalence and age. A large multicenter study from Korea (N=72,319) found that the prevalence of thyroid nodules detected by ultrasound during health check-ups was 34%, increasing to 55% for patients aged ≥70 years. Although the proportion of nodules ≥1cm increased with age, the majority of detected nodules in patients ≥70 years were <1 cm (70%).[25] Similarly, a cohort study of 874 centenarians found that 74% had a thyroid nodule on ultrasound exam, ranging from 58.0% of men to 77.6% of women. The presence of comorbidities was associated with the likelihood of a thyroid nodule detection.[26]

A large prospective cohort study in the U.S. evaluated the impact of patient age on nodule formation, multinodularity and risk of thyroid malignancy in patients who presented at an academic center between 1995 and 2011. A total of 6,391 patients underwent neck ultrasound and FNA biopsy for nodules ≥1 cm that were mostly solid (total number of nodules: 12,115; average nodule size: 2.1 cm). The study found that the prevalence of thyroid nodules significantly increased with advancing age, with the mean number of nodules ≥1cm at presentation increasing from 1.55 in the youngest cohort (age 20–29 years) to 2.21 in the oldest cohort (age ≥70 years) ($p<0.001$).[10]

Thyroid Nodule Evaluation

Overall approach to initial evaluation: Clinical, laboratory and ultrasound assessment—The goals and diagnostic tools used for the evaluation of thyroid nodules do not significantly differ between younger and older patients; however, certain considerations might be more salient in the decision making for older adults[3,12] (Figure 1). Clinicians can inform the estimated risk for thyroid cancer by assessing the clinical risk factors and presentation, thyroid hormone levels and neck ultrasound findings.[12,16]

Initially, clinical risk factors (including family history of thyroid cancer, history of neck radiation, age and sex) and the presence and evolution of symptoms related to thyroid nodule enlargement (e.g., neck pressure, dysphagia, positional dyspnea) should be identified.

[3,12,16,27,28] The mode of detection can also provide diagnostic clues in terms of thyroid cancer risk, as thyroid nodules associated with rapid enlargement and symptoms require prompt evaluation to rule out more aggressive disease. Additionally, thyroid nodules incidentally found on PET/CT (^{18}F-Fluorodeoxyglucose [FDG]-avid) have a higher baseline risk for malignancy, with up to one-third found to be cancerous.[12,29–31]

Evaluation of thyroid function is necessary to rule out hyperthyroidism, given that toxic nodules have a very low risk of malignancy and their management mostly focuses on control of hyperthyroidism.[12] There is, however, controversy regarding the value of routinely measuring serum calcitonin during the evaluation of thyroid nodules.[12,32] A recent meta-analysis of 16 studies with 72,368 participants with thyroid nodules in whom calcitonin was measured routinely, aimed to determine the diagnostic accuracy of serum calcitonin for the detection of medullary thyroid cancer in individuals with nodular thyroid disease.[33] The median prevalence of medullary thyroid cancer was 0.23%, while the sensitivity and specificity of basal calcitonin were high (83%–100%, 94%–100%, respectively).[33] The authors concluded that due to the low prevalence of medullary thyroid cancer, the routine use of serum calcitonin remains questionable; however, in cases of high clinical suspicion and/or inconclusive results, consideration of calcitonin measurement is reasonable.[33] Lastly, the routine use of thyroglobulin in the evaluation of patients with thyroid nodules is not recommended.[12]

In regards to imaging, if the serum TSH indicates euthyroidism or hypothyroidism in patients with suspected thyroid nodules, the next step is a neck ultrasound in order to: 1) confirm the presence and size of thyroid nodules, 2) evaluate ultrasound risk features and estimate the risk for thyroid cancer, and 3) assess for suspicious lymphadenopathy.[12,34]

Thyroid cancer risk assessment – Ultrasound findings—Similar to younger patients with thyroid nodules, one of the pivotal goals of thyroid nodule evaluation in older patients is to assess for thyroid cancer.[12,16] This is challenging, as evidence suggests that although thyroid cancer is less common in older patients with thyroid nodules than younger patients, the prevalence of clinically significant thyroid cancer based on histological features is higher.[10,11] In a cohort of 1,018 patients diagnosed with thyroid nodules, each advancing year was associated with a 2.2% reduction in the relative risk for thyroid malignancy in patients between ages 20 and 60 years, with the risk subsequently stabilizing. Thyroid cancer incidence was 22.9% in patients aged 20–29 years compared to 12.6% in those ≥70 years ($p<0.001$).[10] Moreover, the proportion of high-risk thyroid malignancy, defined as anaplastic, medullary, poorly differentiated carcinoma or distant metastatic carcinoma, was higher in patients aged ≥60 years (range, 13–16%) compared to patients aged 20–59 years (range, 0–4%) ($p<0.001$).[10]

Thyroid ultrasound is the most important imaging modality in the assessment of thyroid nodules and sonographic findings are crucial for stratifying thyroid nodules according to their estimated malignancy risk and to support personalized care.[12,34] Although computed tomography (CT) has a role in evaluating patients with goiter and possible substernal extension, delineating the presence of tracheal compression in patients with positional dyspnea, and assessing select patients with thyroid cancer, it is not currently recommended

for the routine assessment of thyroid nodules.[12,35,36] Multiple ultrasound-based risk stratification systems are available to clinicians and provide recommendations for FNA biopsy according to specific thyroid nodule sonographic characteristics that have been shown to be associated with higher risk of thyroid cancer.[12,16,34,37,38] These are summarized in Table 1. Although there is debate about which system is associated with the best diagnostic properties and reproducibility, their integration in clinical practice represents a significant step towards individualized patient care and reduction of unnecessary FNA biopsies and subsequent surgery.[39] A systematic review and meta-analysis of eight studies including 13,092 thyroid nodules compared unnecessary biopsy rates and diagnostic performance of four representative ultrasound-based risk stratification systems: the American College of Radiology Thyroid Imaging and Reporting System (ACR-TIRADS), the American Thyroid Association (ATA), the Korean Thyroid Imaging and Reporting System (K-TIRADS) and European Thyroid Imaging and Reporting System (EU-TIRADS).[12,34,37,40] The pooled rate of unnecessary FNA biopsies was significantly lower with ACR-TIRADS (25%) when compared to ATA (51%, $p<0.001$) and K-TIRADS (55%, $p<0.001$), and also lower but not statistically different than EU-TIRADS (38%, $p=0.087$).[39] The diagnostic odds ratios were comparable between the four systems.[39] However, ACR-TIRADS had a lower sensitivity, highlighting the need to further clarify: 1) the definition of unnecessary FNA biopsy, 2) the balance between excessive/too stringent guidelines for thyroid biopsy and risk of missed malignancy and 3) the importance of focusing not on thyroid cancer diagnosis in general, but identifying clinically relevant thyroid cancer, as new versions of these ultrasound-based risk stratification systems become available.[16,39] A notable limitation in the implementation of the current ultrasound risk stratifications systems is their reproducibility.[41,42] Variable levels of reproducibility have been reported and can be impacted by the interpreter's experience and the characteristics of image acquisition.[41,42] The application of artificial intelligence emerges as a possible solution to enhance reproducibility and significantly improve our current risk stratification systems.[16,42]

A few studies have evaluated the validity of using the aforementioned ultrasound-based risk stratification systems specifically in older patients.[43,44] Grani et al, evaluated the diagnostic properties of five ultrasound stratification systems, including the ACR-TIRADS, ATA, K-TIRADS, EU-TIRADS and the American Association of Clinical Endocrinologists/ American College of Endocrinology/Associazione Medici Endocrinologi (AACE/ACE/ AME) guidelines.[12,34,36,37,40,44] Of 818 thyroid nodules evaluated by ultrasound (median size, 2.1 cm) and referred for FNA biopsy, 57 were found to be malignant. The malignancy rate was higher in patients aged ≤65 years (8.1%) compared to patients older than 65 years (3.8%; $p=0.02$). The proportion of high-risk thyroid cancers was not reported.[44] Evaluation of ultrasound features showed a higher proportion of cystic nodules in the younger group (3.8% vs 0.5%, $p=0.006$) and a higher proportion of calcifications in the older group (12.2% vs 19.8% macrocalcifications and 7.6% vs 10.8% microcalcifications; $p=0.005$).[44] Use of ACR-TIRADS as a rule-out test resulted in the highest avoidance of biopsies in both age groups and had the highest specificity.[16,44] The proportion of patients who eventually underwent surgery was similar in both groups (6.1% in those >65 years versus 10.2% in those ≤65 years; $p=0.096$).[44]

Another cross-sectional study of 1,867 patients with thyroid nodules referred to an academic center for an FNA biopsy (median age, 71 years) comparatively assessed the performance of the ACR-TIRADS, ATA and AACE/ACE/AME classification systems in an older adult population.[43] Overall, the majority of patients had benign cytology (83%) and only 3% had cytology consistent with malignancy.[43] Of 50 malignant nodules, 31 (62%) underwent surgical resection. The reasons for deferred surgery were not reported.[43] The ACR-TIRADS and AACE/ACE/AME systems were able to predict thyroid cancer more accurately than the ATA when unclassifiable malignant nodules were considered, with the use of ACR-TIRADS leading to higher avoidance of invasive procedures in this older population.[43] Similar results were demonstrated by Pantano et al, in a study which confirmed that ACR-TIRADS, ATA and AACE/ACE/AME correctly identified nodules that were high-risk on cytology, with ACR-TIRADS and AACE/ACE/AME performing better than the ATA due to fewer non-classifiable nodules (N=1,077 total nodules).[45] The diagnostic performance of ACR-TIRADS and AACE/ACE/AME was significantly improved when incorporating sex and age as covariates in the regression model (male sex and younger age were associated with increased risk of malignancy, $p<0.001$ for both).[45]

Thyroid nodule FNA biopsy and cytological evaluation—Cytological evaluation using FNA biopsy is the cornerstone diagnostic tool for thyroid nodules.[12,46,47] FNA biopsy is safe in older adults.[3] Benign and malignant cytology results, when evaluated in the setting of other clinical variables, are extremely helpful when deciding next steps in management. Indeterminate results can pose a more challenging scenario and are one of the limitations of thyroid biopsy.[12,48,49]

A study of 1,129 patients aged ≥70 years with thyroid nodules ≥1 cm (median size, 1.7 cm) evaluated ultrasound use and thyroid biopsy findings to guide management in older adults.[11] Majority of thyroid nodules were benign (67%), with suspicious for malignancy (6%) and malignant (4%) results occurring less frequently.[11] Atypia of undetermined significance (8%) and suspicious for follicular neoplasm (8%) accounted for the remaining cases. As expected in this cohort of older patients, not all patients with suspicious or malignant cytology underwent surgery due to presence of serious comorbidities, presence of another active malignancy, extent of current disease or advanced age.[11] Indications for surgery in patients with benign disease included symptoms from nodule enlargement, nodules >4 cm without symptoms and presence of hyperparathyroidism.[11] Thyroid biopsy was safe, with only one reported complication (symptomatic hematoma).[11] Fourteen percent (n=17) of the diagnosed malignancies were considered high-risk, including nine cases of anaplastic thyroid cancer. The ultrasound findings in these high-risk cases included evidence of local invasion (n=7) and other high-risk features such as solid, hypoechoic nodules and microcalcifications.[11]

Molecular testing—Identifying patients with asymptomatic benign thyroid nodules or small and low-risk thyroid cancer, in whom thyroid surgery is likely not beneficial, is critical.[12,16] Indeterminate cytology is usually evident in approximately 15–30% of thyroid nodules.[50–52] Further evaluation with molecular testing can help refine thyroid cancer risk in these nodules and provide additional guidance in personalizing management in some

instances.[12,16,47] An extensive review of the available molecular tests for the diagnosis of indeterminate thyroid nodules is outside the scope of this review and has been reported elsewhere.[53–55] A recent multicenter, parallel randomized clinical trial compared the diagnostic performance between the current versions of two of the most commonly used molecular tests (Afirma genomic sequencing classifier, an RNA test, and ThyroSeq v3 multigene genomic classifier, a DNA-RNA test) in 346 patients with 427 cytologically indeterminate nodules (median age, 55 years).[56] They found that both molecular tests showed high specificity with no significant differences in diagnostic performance, leading to 49% of patients avoiding diagnostic surgery. The diagnostic performance of molecular tests has been reported as highly variable, but we are not aware of studies associating patient age to this variability.[57,58] Moreover, their use is not currently routinely recommended, and cost and availability emerge as important implementation barriers for some settings.[12,16,47] Nonetheless, our increasing understanding of the genomic landscape of thyroid cancer has the potential to improve our diagnostic, prognostic and treatment approach, including in the older adult population.[59]

Thyroid Nodule Management: Practical Considerations and Decision Making

Multiple factors need to be considered when making decisions regarding thyroid nodule management in older adults (Figure 2). In addition to thyroid nodule risk stratification and consideration of thyroid cancer biology, the evaluation of patients' overall health, comorbidities, preferences and goals of care should guide steps for individualized management.[12,60,61] Shared decision making, an approach based on active collaboration between patients and clinicians when choosing among management options, can be useful when caring for older adults with thyroid nodules.[16,60] The ATA guidelines currently advocate that a conservative approach may be reasonable in older adults with very low-risk tumors, those at high surgical risk and those with a relatively short lifespan expectancy in whom the benefits of intervention, be it FNA biopsy or surgery, may be unrealized.[12] Table 2 shows examples of clinical scenarios of older adults (age ≥65) with thyroid nodules that highlight the complexity of decision making and important management considerations.

Data to date suggest that it is reasonable to utilize high-quality ultrasound, with or without FNA biopsy in older adults for initial evaluation of thyroid nodules ≥1cm, with access to an experienced radiologist and a multidisciplinary care team.[11] This strategy has been shown to safely and accurately identify benign cytology in two-thirds of patients, subsequently allowing for conservative management unless there are compressive symptoms.[11] Although contextualizing the need to perform an FNA biopsy upon thyroid nodule detection is important for older patients, studies suggest there is variation in clinical practice. In a study of 129 patients with suspicious subcentimeter nodules (mean age, 58 years), the rate of FNA biopsy was 39%. Even though this study did not specifically focus on older adults, patient age and comorbidities were not associated with biopsy rates.[61] A population-based study showed that 35% of thyroid cancers diagnosed by ultrasound in patients ≥65 years between 2003 and 2013 were <1 cm.[8] Additionally, a prospective, multicenter, observational study involving 992 patients with up to four asymptomatic nodules that were benign by sonographic or cytologic criteria who were followed for 5 years, showed that age ≥60 years was associated with a lower risk of growth than age <45 years (OR 0.5, 95% CI 0.3–0.9).[21]

Only five patients were diagnosed with thyroid cancer during follow-up of original nodules, and one patient had thyroid cancer detected in a new nodule.[21] These results highlight the importance of risk-stratifying thyroid nodules based on ultrasound features to guide the selection of thyroid nodules for biopsy, while ensuring patient context and preferences are incorporated in decision making.[8,61]

In the event of biopsy-proven thyroid cancer, the decision to proceed with surgical or minimally invasive intervention versus active surveillance is more complex. As older patients are at higher risk for aggressive thyroid cancers and death from thyroid cancer, careful consideration should be undertaken for prompt recognition of high-risk thyroid cancer that would impact survival. Advancing age at the time of thyroid cancer diagnosis has been identified as a risk factor for disease-specific mortality.[62,63] An analysis of 53,581 patients with papillary thyroid cancer from the Surveillance, Epidemiology and End Results (SEER) database, found that the 5-year survival rate decreased by each increasing category of age when patients were stratified in 5-year categories by age at diagnosis from 20–84 years-old, with patients ≥85 years categorized together.[63] Furthermore, several studies have shown that older adults, especially those with comorbidities, are more vulnerable to complications from thyroid cancer treatment, including surgical complications, as well as cardiovascular and skeletal adverse effects from subsequent TSH suppression therapy.[14,64–69] These studies collectively provide further guidance in carefully balancing benefits and risks to tailor treatment to the patient. Even though it is generally acknowledged that the potential benefits outweigh the risks for surgery for clinically relevant thyroid cancers that are >1 cm with better outcomes if referred to high-volume surgeons,[12,70–75] recent evidence supports that surveillance may be a safe alternative in those with small nodules resulting in indeterminate cytology, papillary microcarcinomas or patients with limited lifespan.[12,76–78]

An additional consideration in older adults with either suspected or biopsy-proven thyroid cancer is the presence of comorbidities and/or competing causes of death. Although this topic has been studied in other cancer types, it remains underexplored in older adults with thyroid cancer.[79–82] Attempting to incorporate competing risks of death in the management of thyroid cancer, Yang et al used data from 29,225 patients with thyroid cancer (tumor size ≤2 cm) from SEER.[83] The authors developed a nomogram based on a competing risks model to predict the probability of death for thyroid cancer patients. Patients aged ≥75 years had a nearly two-fold higher 10-year incidence of death from non-cancer causes compared to death from thyroid cancer (29.9% versus 16.0%, $p<0.001$).[83] A single-center study evaluated the relationship between comorbidities, overall mortality and cause of death in 2,070 patients who underwent surgery for differentiated thyroid cancer.[82] This study showed that a higher number of comorbidities was associated with a higher probability of death from other causes and a lower probability of death from thyroid cancer.[82] In another single institution study of patients aged ≥70 years with thyroid nodules (N=1,129), 14% had coronary artery disease and 25% had a non-thyroidal malignancy (25%), and the presence of these comorbidities was associated with increased overall mortality.[11] If life expectancy is limited due to comorbidities, then harms associated with treatments should be balanced with the prospect of improved survival. Therefore, it should be considered that older adults with high risk of dying from comorbid conditions may not benefit from work-up and/or treatment of thyroid nodules.

Finally, understanding the health status of older adults through a comprehensive geriatric assessment which provides a detailed evaluation of overall well-being, frailty, functional, cognitive and psychosocial status to identify areas of vulnerability, can provide equally important information as understanding the underlying tumor biology, and guide individualized treatment decisions.[84,85] However, no studies to date evaluating the impact of geriatric assessments on cancer outcomes have focused on older adults with thyroid cancer.

CONCLUSION

In an aging population with prevalent multimorbidity leading to increased healthcare utilization and subsequent thyroid nodule detection, physicians should take multiple factors into consideration when deciding which patients to refer for further evaluation and management. Potential harms from thyroid cancer overdiagnosis should be balanced against prompt recognition of potentially aggressive thyroid cancers, which are more likely to occur in older adults. Efforts should focus towards evidence-based personalized management to reduce patient harm, improve health-related quality of life and lower costs.

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HIGHLIGHTS

- Older patients with thyroid nodules have an overall lower risk of thyroid cancer.
- Thyroid cancer with high-risk histology is more common in older adults.
- Thyroid nodule ultrasound risk stratification can help guide management.
- Patient context is important when caring for older adults with thyroid nodules.
- Individualized, evidence-based approaches to care in older adults can reduce harm.

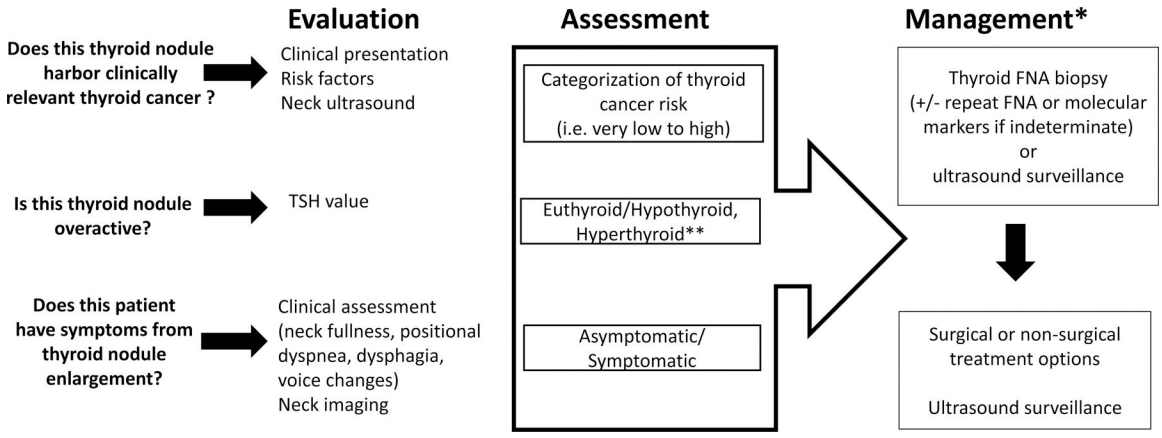

Figure 1.

Overall approach to thyroid nodule evaluation and management.

*To be contextualized by individual patient factors.

**Work-up for hyperthyroid patients may include nuclear medicine imaging and/or measurement of TRAb to delineate etiology.

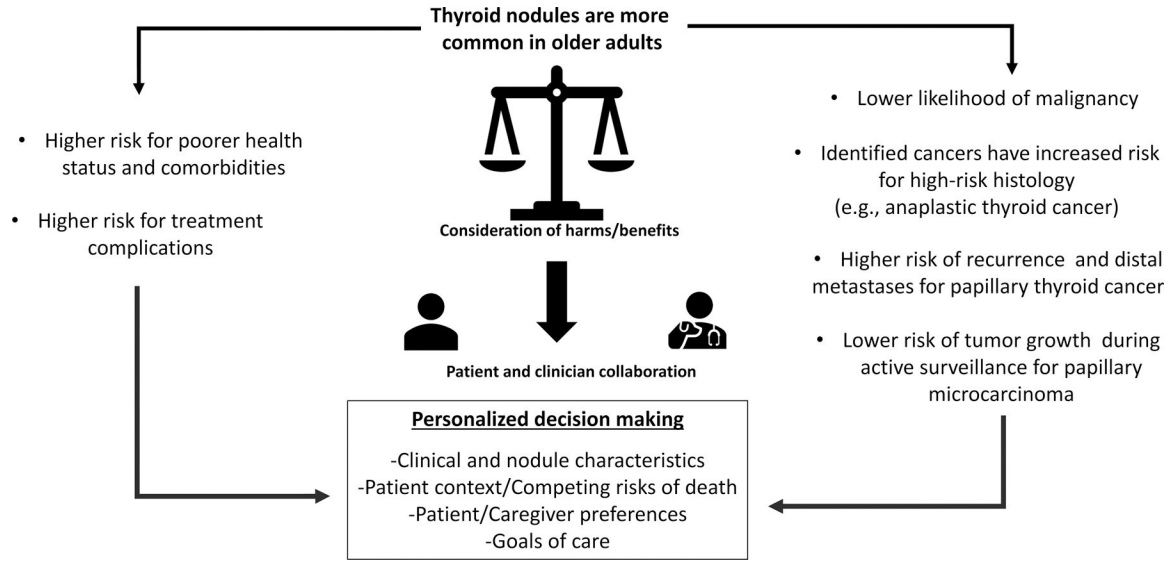

Figure 2.

Special considerations in the care of older patients with thyroid nodules. Patient context should be incorporated into decision making to personalize management of thyroid nodules in older adults.

Table 1.

Commonly Used Thyroid Nodule Ultrasound Risk Stratification Systems

System	General Description	Risk Categories (Expected Risk of Malignancy)	Recommendation for Thyroid FNA or Follow Up	Comments
ACR-TIRADS	Point-based risk stratification based on evaluation of: • Composition • Echogenicity • Shape • Margin • Echogenic foci	TR1 – benign (<2%) TR2- not suspicious (<2%) TR3- mildly suspicious (<5%) TR4- moderately suspicious (5–20%) TR5- highly suspicious (≥20%)	No FNA No FNA FNA if ≥ 2.5 cm; Follow if ≥ 1.5 cm FNA if ≥ 1.5 cm; Follow if ≥ 1 cm FNA if ≥ 1 cm; Follow if ≥ 0.5 cm	All nodules can be assigned a category In general, there is a higher threshold for biopsy and explicit follow up recommendations
ATA	Pattern-based risk stratification based on the evaluation of: • Composition • Echogenicity • Shape • Margins • Echogenic foci • Abnormal cervical lymph nodes, explicitly considered in the high-risk category	Benign (<1%) Very low suspicion (<3%) Low suspicion (5–10%) Intermediate suspicion (10–20%) High suspicion (>70–90%)	No FNA Consider FNA at ≥2 cm Recommend FNA if ≥1.5 cm Recommend FNA if ≥1 cm Recommend FNA if ≥1 cm	Some nodules might not fit the pattern-based categories
AACE/ACE/AME	Pattern-based risk stratification based on the evaluation of: • Composition • Echogenicity • Shape • Margins • Echogenic foci • Vascularization • Abnormal cervical lymph nodes, explicitly considered in the high risk category • Elastography	Low risk lesion (~1%) Intermediate-risk thyroid lesion (5–15%) High-risk thyroid lesion (50–90%)	FNA recommended if >2.0 cm and increasing in size or associated with a high-risk history, and before thyroid surgery or minimally invasive ablation therapy. FNA recommended if ≥ 2 cm Consider FNA if 0.5–1 cm FNA recommended if ≥ 1 cm	Additional recommendations according to clinical and ultrasound risk features Some nodules might not fit the pattern-based categories

Abbreviations: ACR TIRADS, American College of Radiology Thyroid Imaging Reporting and Data System; ATA, American Thyroid Association; AACE/ACE/AME, American Association of Clinical Endocrinologists, American College of Endocrinology and Associazione Medici Endocrinologi; FNA, fine needle aspiration biopsy.

Table 2.

Examples of clinical scenarios of older adults with thyroid nodules *

Patient aged ≥65 years	Clinical Presentation	Neck Ultrasound Features	Patient Preferences	Clinical Context	Management Considerations
Relatively healthy, robust functional status	Incidental 1.2 cm thyroid nodule on CT scan	Thyroid nodule 1.3 cm, TIRADS 4 (risk of malignancy 5–20%), no suspicious lymph nodes	Minimal, non-invasive management unless absolutely necessary	Reliable and expert multidisciplinary team, patient with access to care for follow up, strong social support system **	According to TIRADS criteria, FNA biopsy recommended when nodule size ≥ 1.5 cm. It is reasonable to consider observation with repeat neck ultrasound in 6–12 months given patient preferences, availability of clinical expertise and social support. However, if the patient has low tolerance for uncertainty and/or their ability to follow up is limited, pursuing FNA biopsy at this point may be appropriate.
History of metastatic lung cancer with lack of response to treatment, frail	Incidental FDG-avid 1.5 cm thyroid nodule on PET/CT	Thyroid nodule 1.5 cm, TIRADS 5 (risk of malignancy >20%), no suspicious lymph nodes	Aggressive management	Reliable and expert multidisciplinary team, patient with access to care for follow up, strong social support system	According to TIRADS criteria, FNA biopsy recommended when nodule size ≥ 1 cm. FDG-avid thyroid nodules have higher malignancy risk. However, patient's prognosis / life expectancy more likely affected by progressive lung cancer, poor functional status. Reasonable to consider observation and including the oncology team when considering management options.
Relatively healthy, good functional status, independent on activities of daily living	Acute onset of neck pressure and dyspnea, rapidly enlarging neck mass	Thyroid nodule 6 cm, evidence of extra-thyroidal extension and local invasion, TIRADS 5 (risk of malignancy >20%)	Aggressive management	Lack of expert multidisciplinary team, patient with access to care for follow up, strong social support system	Presentation concerning for anaplastic thyroid cancer, given acute onset of symptoms and rapid progression, in addition to ultrasound findings. Prompt diagnosis followed by thorough consideration of treatment options, with immediate referral to a high-volume institution with a multidisciplinary team.
Advanced dementia, frail	Incidental 0.8 cm thyroid nodule on CT scan	No suspicious lymph nodes, 1 cm TIRADS 5 (risk of malignancy >20%)	Unknown	Reliable and expert multidisciplinary team, patient with access to care for follow up, strong social support system	According to TIRADS criteria, thyroid biopsy recommended when nodule size ≥ 1 cm. However, given advanced dementia and frailty, aggressive management of micro-papillary thyroid cancer is unlikely to be beneficial.

* Assume lack of thyroid cancer risk factors, euthyroid and asymptomatic patients unless specifically noted.

** Multidisciplinary expert care team includes clinicians (primary care, geriatrician, endocrinologist), radiologists, surgeons with expertise in thyroid nodule/cancer care; access to care and social support constitute multiple factors that can affect the ability to complete follow-up care (e.g.., insurance status, family/friends to coordinate and drive to appointments).

Abbreviations: CT, computed tomography; FDG/PET, 18-fluorodeoxyglucose-positron emission tomography; TIRADS, Thyroid Imaging Reporting and Data System.