American Association of Clinical Endocrinology And Associazione Medici Endocrinologi Thyroid Nodule Algorithmic Tool

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Objective: The first edition of the American Association of Clinical Endocrinology/American College of Endocrinology/Associazione Medici Endocrinologi Guidelines for the Diagnosis and Management of Thyroid Nodules was published in 2006 and updated in 2010 and 2016. The American Association of Clinical Endocrinology/American College of Endocrinology/Associazione Medici Endocrinologi multi-disciplinary thyroid nodules task force was charged with developing a novel interactive electronic algorithmic tool to evaluate thyroid nodules.
**Key words:** algorithms
diagnostic techniques
fine-needle aspiration
internet
practice guidelines

**Methods:** The Thyroid Nodule App (termed TNAPP) was based on the updated 2016 clinical practice guideline recommendations while incorporating recent scientific evidence and avoiding unnecessary diagnostic procedures and surgical overtreatment. This manuscript describes the algorithmic tool development, its data requirements, and its basis for decision making. It provides links to the web-based algorithmic tool and a tutorial.

**Results:** TNAPP and TI-RADS were cross-checked on 95 thyroid nodules with histology-proven diagnoses. Conclusion: TNAPP is a novel interactive web-based tool that uses clinical, imaging, cytologic, and molecular marker data to guide clinical decision making to evaluate and manage thyroid nodules. It may be used as a heuristic tool for evaluating and managing patients with thyroid nodules. It can be adapted to create registries for solo practices, large multispecialty delivery systems, regional and national databases, and research consortiums. Prospective studies are underway to validate TNAPP to determine how it compares with other ultrasound-based classification systems and whether it can improve the care of patients with clinically significant thyroid nodules while reducing the substantial burden incurred by those who do not benefit from further evaluation and treatment.

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**Introduction**

Thyroid nodules are common. They are predominantly benign and asymptomatic and do not require evaluation, treatment, or monitoring, while the majority of thyroid malignancies are low-risk neoplasms that do not have an impact on survival. Diagnosis and treatment are costly and often have a detrimental impact on a patient’s physical, emotional, and financial status. In the United States, well over 500,000 fine-needle aspirations (FNAs) of thyroid nodules are performed per year, with as many as 200,000 of them being unnecessary. Similarly, in European countries, such as Germany and France, with well-functioning National Health Services, the vast majority of thyroidectomies performed for nodular thyroid disease have benign histopathology, while the minority that proves to be malignant is predominantly composed of low-risk thyroid cancers. Guidelines from the American Association of Clinical Endocrinology (AACE), Associazione Medici Endocrinologi (AME), American Thyroid Association (ATA), and American College of Radiology provide recommendations for reducing the collective burden of evaluating and treating thyroid nodules and low-risk thyroid cancers. However, their impact has been limited.

The variation in ultrasound (US) risk classification systems and interobserver assessments of thyroid nodule features contribute to this.

We designed a novel electronic algorithmic tool, termed TNAPP (Thyroid Nodule App, pronounced “tee nap”). It is largely based on the 2017 European Union Thyroid Imaging Reporting and Data System lexicon for categorizing US features, along with corresponding US images and cartoons as heuristic tools. It also incorporates nomenclature that is being developed by the International Thyroid Nodule Ultrasound Working Group (ITNUWG). One of our goals was to create an easy-to-apply tool and to ultimately compare its effectiveness with other society guidelines and published calculators. This will be accomplished by demonstrating a comparable or greater reduction in the number of clinically insignificant nodules undergoing FNA, surgery, or surveillance in a variety of clinical settings and populations.

**Educational Tools**

Over the past 3 decades, clinical practice guidelines have emerged as an increasingly important tool to aid clinicians in managing a host of medical conditions. Guidelines are regularly cited in publications and medical education forums, and they are used as a basis for medical decision making in both clinical and administrative settings. Yet, despite their widespread clinical use, there is substantial room for improvement. This includes establishing the cost effectiveness and validity of recommendations, which are often based on expert opinion, retrospective studies, and study populations that are not generalizable.

Implementing guidelines requires:

- Creating mechanisms for vetting guideline recommendations in various clinical situations and across different populations and cultures
- Gauging their implementation by tracking their use and applicability
- Addressing their often formidable length and the wealth of information they contain, which makes them hard to navigate as well as absorb and retain
- Providing timely updates of narrative multi-authored, highly validated documents
- Disseminating and distributing them
- Clinicians routinely using and assessing their effectiveness in real-world settings

**Novel Approach**

A computer-interpretable guideline (CIG) and narrative guideline provide recommendations that may require a sequence of logical steps. When clinical decision making requires multiple steps, narrative guidelines employ a series of recommendations and may illustrate them with flowcharts. CIG decision support systems employ execution engines (programs) to electronically provide, document, and track these recommendations. CIG offers a novel approach to address some of these challenges. CIGs have been shown to be effective in additional clinical domains, such as chronic diseases, diabetes, cancer, stroke, HIV, genetic counseling, and hypertension. They facilitate testing and validating recommendations prospectively and retrospectively. Cross-checking histology-proven cases served as a means of testing TNAPP’s logic and disambiguation by detecting contradictory or ambiguous guidance. Examples include the sequence and timing of when to implement recommendations.

**Other Uses**

The use of a computer-based tool can be tracked, used as a stand-alone tool for medical education, and integrated into an electronic health record. It can be used as a decision tool for single-use anonymized patient data entry that is not retained (akin to a...
mortgage calculator). It also may serve as a platform for different types of registries that store data for analysis and be used to study the impact of algorithms and recommendations on clinical outcomes. Registries could be created for solo practices, large multispecialty delivery systems, regional and national databases, and research consortiums. Hence, a computer-based tool has the potential to be a powerful instrument in a wide range of settings for studying health outcomes as well as their costs.

**Methods**

The AACE/AME Thyroid Nodule Task Force was formed in 2017 to update the 2016 clinical practice guideline for the diagnosis and management of thyroid nodules. The charge of the task force was to provide an updated approach to managing thyroid nodules. Rather than beginning with a narrative guideline as it had done in 2006, 2010, and 2016, the task force was asked to create an algorithmic tool based on prior recommendations, an updated literature review, and an expert opinion. Unlike what had been done in 2014, it did not create different pathways and recommendations for Europe and the United States, areas of iodine sufficiency and insufficiency, and whether or not calcitonin determinations were routinely done during the initial evaluation of a thyroid nodule. Areas of expertise were expanded. Previously, the task force was entirely composed of European and American endocrinologists. The task force now included endocrine surgeons, general surgeons and otolaryngologists, pathologists, an informatician, and a health economist.

The task force met regularly over 3 years during international meetings, including the AME annual congress, AACE annual meeting, ATA annual meeting, and the World Thyroid Congress, or by teleconference. Comprehensive minutes were taken by task force members and subsequently reviewed by all task force members. Revisions to the algorithmic tool were continually posted on the web for further review. This manuscript, written by the task force members and subsequently reviewed by all task force members, describes the development and contents of the algorithmic tool. It was reviewed by the Chairs of the AACE Thyroid Disease State Network and the AACE Executive Committee.

TNAPP is web-based (https://aace-thyroid.deontics.com) and features a tutorial on how to use it (https://deontics-external-publication.s3-eu-west-1.amazonaws.com/aace/Thyroid-nodule-App-videos.pptx).

**Factors Serving as the Basis for TNAPP’s Decision Algorithmic Tool**

**Exclusion Factors**

The impetus of the algorithmic tool was to provide guidance in the initial evaluation of ambulatory patients with thyroid nodules that were not extremely likely to be malignant. Thus, nodules in those who presented with elevated calcitonin levels, multiple endocrine neoplasia type 2 syndromes, previously documented thyroid cancer, and suspicious lymphadenopathy were excluded (Table 1).

**Clinical Factors**

Clinical factors were composed of features in favor of performing FNA, termed Clinical 2, and those with features against performing FNA, termed Clinical 1 (Table 2). These factors were not given relative weights. When factors for and against doing an FNA are present, clinical judgment becomes the default decision-making factor (ie, other medical conditions that take precedence at the time).

**Table 1**

<table>
<thead>
<tr>
<th>Exclusion Criteria</th>
</tr>
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<tbody>
<tr>
<td>Clinical criteria</td>
</tr>
<tr>
<td>Family history of thyroid cancer: familial DTC or MTC or other syndromes</td>
</tr>
<tr>
<td>PET-positive or sestamibi-positive nodule</td>
</tr>
<tr>
<td>Elevated calcitonin</td>
</tr>
<tr>
<td>Clinical or imaging finding of regional adenopathy suspicious of malignancy</td>
</tr>
<tr>
<td>Known diagnosis of thyroid cancer</td>
</tr>
<tr>
<td>Either a hard consistency or a fixed nodule</td>
</tr>
<tr>
<td>Ultrasound criteria</td>
</tr>
<tr>
<td>Obvious extrathyroidal extension or invasion</td>
</tr>
</tbody>
</table>

Abbreviations: DTC = differentiated thyroid cancer; MTC = medullary thyroid cancer; PET = positron emission tomography.

**US Characteristics**

A numeric scoring system based on the risk of malignancy associated with each US feature was created to categorize each nodule as US 1, 2, or 3 (low, intermediate, or high risk, respectively) (Table 3). In lieu of our prior descriptive (A, B, and C) classification, in the algorithmic tool, American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) scores are simultaneously displayed if a sufficient number of criteria to generate a score are entered (Fig. 1). ACR TI-RADS was chosen because its scoring system is based on the same discrete US criteria as TNAPP. The ATA classification system, for example, was not used because it employs pattern recognition.

**US Images and Cartoons**

While the TNAPP was being created, the multisociety ITNUWG was working to create a universal terminology for US descriptors. Three members of the task force, representing 2 societies (AACE and ATA) and who were also members of the ITNUWG, periodically updated the task force on its progress. The lexicon (Table 4) incorporates some of the ITNUWG terminology in effect at the time of publication. A subgroup of the TNAPP task force was charged with submitting US images that featured all the lexicon’s terms at the time that this manuscript was written. Corresponding cartoons with explanatory captions were then created to illustrate key US characteristics.

**Table 2**

<table>
<thead>
<tr>
<th>Clinical Criteria for (Clinical 2) and against (Clinical 1) FNA of Thyroid Nodules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical 1: One or more of the following clinical factors are against performing FNA:</td>
</tr>
<tr>
<td>Low thyrotropin&lt;sup&gt;a&lt;/sup&gt; and not on thyroid hormone</td>
</tr>
<tr>
<td>Autonomous nodule on imaging</td>
</tr>
<tr>
<td>Prior benign FNA of the same nodule</td>
</tr>
<tr>
<td>Other medical conditions that take precedence at the time</td>
</tr>
<tr>
<td>History of prior lobectomy with vocal cord paralysis</td>
</tr>
<tr>
<td>Significant comorbidity making thyroid surgery high risk at the time</td>
</tr>
<tr>
<td>Limited life expectancy (&lt;1 year)</td>
</tr>
<tr>
<td>Clinical 2: One or more of the following clinical factors favors FNA:</td>
</tr>
<tr>
<td>Head and neck radiation in the past</td>
</tr>
<tr>
<td>Compressive symptoms: dysphonia, dysphagia, or dyspnea without another cause</td>
</tr>
<tr>
<td>Nodule position either posterior or adjacent to thyroid capsule or trachea</td>
</tr>
<tr>
<td>History of documented growth</td>
</tr>
<tr>
<td>History of progressive growth ie, ≥50% increase in volume in ≤1 year, especially of the solid component, or 20% increase in 1 dimension</td>
</tr>
<tr>
<td>History of sudden enlargement</td>
</tr>
<tr>
<td>Planned thyroid or parathyroid surgery</td>
</tr>
<tr>
<td>Cosmetic concerns</td>
</tr>
<tr>
<td>Patient preference or anxiety</td>
</tr>
<tr>
<td>Protocol requiring documentation of cancer</td>
</tr>
</tbody>
</table>

Abbreviation: FNA = fine-needle aspiration.

<sup>a</sup> Below normal range for assay being used or default to <0.5 mU/L; up to 1.0 mU/L for multinodular goiter.2,3
The sum of points does not denote absolute risk. The categorization of characteristics and all of the
unambiguously establish whether a nodule falls within the low, intermediate or high risk for being malignant.

Abbreviation: US – ultrasound.
The sum of points does not denote absolute risk. The categorization of characteristics and all of the possible combinations of these characteristics under US 1, 2, and 3, unambiguously establish whether a nodule falls within the low, intermediate or high risk for being malignant.

features. The US images and corresponding cartoons comprise an imaging library (Fig. 2).

Cytology
Bethesda cytology categories I-VI were used to classify findings.34 Categories as well as descriptions of the findings in each class or subcategory are listed in Table 5.

Summary of Inputs (Entered by the User) and Outputs (Guidance Produced by TNAPP) (Fig. 3)

Inputs

1. Clinical features (Table 2): There are 26 clinical features in total. Although clinical factors are key determinants of the risk of malignancy, none are required for running the TNAPP.
2. US features (Tables 3 and 4): There are 36 US features in total. Size, composition, and echogenicity are the only data that have to be provided for TNAPP to categorize the US as US 1 (low risk), US 2 (intermediate risk), or US 3 (high risk).
3. Cytology features (Table 5): There are a combined total of 45 options from which to select. These are comprised of main categories (6), subcategories (33), or a combination of a main category and subcategory (6). All are optional inputs.

Outputs

1. Checks eligibility for using the TNAPP (Table 1): Yes/no
2. Calculates AACE US category of the nodule as low, intermediate, or high risk (Table 3): US 1/US 2/US 3
3. Calculates AACE clinical category for factors arguing against and for performing an FNA (Table 2): Clinical 1/Clinical 2
4. Provides guidance about whether to perform an FNA and advice about follow-up
5. Uses results of FNA when available to serve as the basis for recommending surgery, considering the use of molecular markers, repeating FNA, and duration of follow-up, if any
6. Simultaneously calculates ACR TI-RADS risk category: TR1/TR2/TR3/TR4/TR5 when a sufficient number of US features are provided
7. Simultaneously displays TI-RADS biopsy advice regarding FNA/follow-up whenever TI-RADS can be calculated
8. Calculates malignancy probability ranges based on published risk for malignancy—some prior to the introduction of noninvasive follicular thyroid neoplasm with papillary-like nuclear
features (NIFTP)—for each Bethesda category (Table 5). Because NIFTP is a surgical diagnosis of an indolent or premalignant lesion, it was considered malignant 9. Provides alerts whenever inconsistent data are entered (eg, spongiform and high-risk features, such as microcalcifications, etc)

Grids

Grids or tables, based on US classification (US 1, 2, or 3), clinical categorization (Clinical 1 or Clinical 2), size (<5, 5-10, >10-20, >20-40, or >40 mm), and Bethesda classification (I-VI), were created (Table 6, prior to FNA, and Table 7, after FNA). Each cell in each grid, totaling 30 for Table 6 and 180 for Table 7, was internally reviewed multiple times and ultimately populated with a consensus recommendation based on the 2016 Clinical Practice Guideline,8 updated literature review, and expert opinion.
Collectively, the recommendations found in each cell, which are not displayed to the user, serve as the basis for the recommendation provided by TNAPP.

Cross-checking TNAPP

Cases were submitted (Fig. 4) to test the user interface and detect any flaws in the logic used to make recommendations as well as the guidance itself. The authors were asked to submit 10 or more cases with surgical outcomes whose personal or familial history of thyroid cancer, serum thyrotropin level, diagnostic US, indication for FNA, and cytologic report were known. Six task force members from 3 U.S. and 2 European thyroid referral centers provided 10 or more cases, giving a total of 108 cases. Thirteen cases had the following exclusion criteria (Table 1): 5 elevated calcitonin levels, 4 familial thyroid cancer syndromes, 2 diagnoses of thyroid cancer, 1 suspicious cervical adenopathy, and 1 nodule that was positron emission tomography-positive. All 95 remaining cases (100%) had sufficient data to employ the TNAPP, but only 78 (82%) had sufficient US data to make a TI-RADS determination and guidance based on it. There was 79% concordance between TI-RADS and the TNAPP recommendation for whether to perform an FNA. Of the 95 cases that met inclusion criteria, there was insufficient information in 17 cases (18%) to use TI-RADS to provide a recommendation.

Future Studies

We are presently embarking on a prospective multicenter TNAPP validation trial. It will include establishing the impact of NIFTP on the classification of thyroid nodules and surgical recommendations for all noninvasive follicular variants of papillary thyroid cancer.

Limitations

There are several limitations to TNAPP:

- The subjective nature of weighting factors for and against a clinical intervention
- US interpretation, such as hypoechoogenicity and calcification, for nodules with predominantly follicular architecture
- Bethesda cytology categorization, particularly Bethesda category III
Using a small sample size of cancer-enriched, nonrandomly selected cases to crosscheck TNAPP

- Paucity of randomized controlled trials to support recommendations regarding thyroid nodule management

- The cost effectiveness of determining molecular markers is yet to be established

Conclusion

The AACE/AME TNAPP is an innovative approach to providing updated recommendations for managing thyroid nodules. It is an electronic tool that is an easily revised “living document.” As opposed to a single-document narrative clinical practice guideline, TNAPP is composed of modular knowledge components that can be readily expanded compared with other guidelines and speedily modified by continuously evaluating its usage and efficacy.

Once it is prospectively validated, we foresee employing this tool in a variety of settings. We trust that it will facilitate the care of patients with clinically significant thyroid nodules while reducing the substantial burden incurred by those who would not benefit from further evaluation and treatment.

Acknowledgment

We thank Franklin N. Tessler, MD, CM, and the International Thyroid Nodule Ultrasound Working Group (ITNUWG) for allowing us to use their terminology that was in effect at the time of publication and Stephanie Adams, PhD, Director, AACE Clinical Practice Guidelines Development, for her invaluable assistance.

Disclosure

- Cochairs: J.R.G. and E.P. have no multiplicity of interest to declare.
- Task Force Members: C.C.L. is the primary author for the 2020 American Association of Endocrine Surgeons Thyroidectomy Guidelines. A.F. is the
<table>
<thead>
<tr>
<th>Bethesda category</th>
<th>Bethesda subcategory</th>
</tr>
</thead>
</table>
| **I. Nondiagnostic or unsatisfactory** | Virtually acellular specimen  
Cyst fluid only  
Other (obscuring blood, clotting artifact, drying artifact, etc) |
| **II. Benign** | Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc)  
Consistent with chronic lymphocytic (Hashimoto) thyroiditis in the proper clinical context  
Consistent with granulomatous (subacute) thyroiditis  
Other |
| **III. Atypia of undetermined significance or follicular lesion of undetermined significance** | Focal cytologic (nuclear) atypia  
Extensive but mild cytologic (nuclear) atypia  
Atypical cyst-lining cells  
A scanty cellular specimen with architectural atypia  
Cytologic (nuclear) and architectural atypia (NIFTP may be present)  
Hürthle cell aspirates with low-risk pattern  
Atypia, not otherwise specified, not papillary type  
Psammomatous calcifications in the absence of cellular atypia  
Atypical lymphoid cells; rule out lymphoma |
| **IV. Follicular neoplasm or suspicious of a follicular neoplasm** | Cellular aspirate composed of follicular cells with altered architectural pattern  
and microfollicle formation  
Cellular aspirate composed of follicular cells with almost exclusively Hürthle cell features  
Follicular-patterned aspirates with mild nuclear changes (NIFTP may be present) |
| **V. Suspicious for malignancy** | Suspicious for papillary thyroid carcinoma  
Suspicious for medullary thyroid carcinoma  
Suspicious for metastatic carcinoma  
Suspicious for lymphoma  
Other |
| **VI. Malignant** | Papillary thyroid carcinoma  
Poorly-differentiated carcinoma  
Medullary thyroid carcinoma  
Undifferentiated (anaplastic) carcinoma  
Squamous cell carcinoma  
Carcinoma with mixed features (specify)  
Metastatic malignancy  
Non-Hodgkin lymphoma  
Other |

Abbreviation: NIFTP = noninvasive follicular thyroid neoplasm with papillary-like nuclear features.

**Fig. 3.** Summary of Thyroid Nodule App inputs (entered by the user) and outputs (guidance produced by the Thyroid Nodule App). AACE = American Association of Clinical Endocrinology; ACR TI-RADS = American College of Radiology Thyroid Imaging Reporting and Data System; FNA = fine-needle aspiration; FU = follow up; US = ultrasound.
### Table 6
**Grid Based on Ultrasound Classification Prior to FNA**

<table>
<thead>
<tr>
<th>Nodule size</th>
<th>Clinical 1</th>
<th>Clinical 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultrasound 1</td>
<td>No follow-up</td>
<td>No follow-up</td>
</tr>
<tr>
<td>Ultrasound 2</td>
<td>No follow-up</td>
<td>No follow-up</td>
</tr>
<tr>
<td>Ultrasound 3</td>
<td>Monitor at 18-24 mo then stop</td>
<td>Monitor at 18-24 mo then stop</td>
</tr>
<tr>
<td>5-10 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultrasound 1</td>
<td>No follow-up</td>
<td>No follow-up</td>
</tr>
<tr>
<td>Ultrasound 2</td>
<td>Monitor at 18-24 mo</td>
<td>No follow-up</td>
</tr>
<tr>
<td>Ultrasound 3</td>
<td>Either</td>
<td>Either</td>
</tr>
<tr>
<td></td>
<td>• Consider FNA</td>
<td>• Consider FNA</td>
</tr>
<tr>
<td></td>
<td>• If no FNA, then monitor at 18-24 mo</td>
<td>• If no FNA, then monitor at 12-24 mo</td>
</tr>
<tr>
<td>&gt;10-20 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultrasound 1</td>
<td>Monitor at 12-24 mo</td>
<td>Monitor at 12 mo</td>
</tr>
<tr>
<td>Ultrasound 2</td>
<td>Either</td>
<td>Recommend FNA</td>
</tr>
<tr>
<td>Ultrasound 3</td>
<td>• Consider FNA</td>
<td>Recommendation</td>
</tr>
<tr>
<td></td>
<td>• If no FNA, then monitor at 12 mo</td>
<td>Consider molecular testingb</td>
</tr>
<tr>
<td>&gt;20-40 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultrasound 1</td>
<td>Either</td>
<td>Either</td>
</tr>
<tr>
<td></td>
<td>• Consider FNA</td>
<td>• Consider FNA</td>
</tr>
<tr>
<td></td>
<td>• If no FNA, then monitor at 12 mo</td>
<td>• If no FNA, then monitor at 12 mo</td>
</tr>
<tr>
<td>Ultrasound 2</td>
<td>Recommendation</td>
<td>Recommendation</td>
</tr>
<tr>
<td>Ultrasound 3</td>
<td>Recommendation</td>
<td>Recommendation</td>
</tr>
</tbody>
</table>

### Table 7
**Grid Based on Ultrasound Classification Post FNA**

**Abbreviation:** FNA = fine-needle aspiration.

<table>
<thead>
<tr>
<th>US Classification</th>
<th>Bethesda I</th>
<th>Bethesda II</th>
<th>Bethesda III</th>
<th>Bethesda IV</th>
<th>Bethesda V</th>
<th>Bethesda VI</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5 mm</td>
<td>No recommendation</td>
<td>No recommendation</td>
<td>No recommendation</td>
<td>No recommendation</td>
<td>No recommendation</td>
<td>No recommendation</td>
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<tr>
<td>5-10 mm</td>
<td>No recommendation</td>
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<td>No recommendation</td>
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<tr>
<td>US 1 Clinical 1</td>
<td>No recommendation</td>
<td>No recommendation</td>
<td>No recommendation</td>
<td>No recommendation</td>
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<td>No recommendation</td>
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<tr>
<td>US 1 Clinical 2</td>
<td>No recommendation</td>
<td>No recommendation</td>
<td>No recommendation</td>
<td>No recommendation</td>
<td>No recommendation</td>
<td>No recommendation</td>
</tr>
<tr>
<td>US 2 Clinical 1</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
</tr>
<tr>
<td>US 2 Clinical 2</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
</tr>
<tr>
<td>&gt;10-20 mm</td>
<td>No recommendation</td>
<td>No recommendation</td>
<td>No recommendation</td>
<td>No recommendation</td>
<td>No recommendation</td>
<td>No recommendation</td>
</tr>
<tr>
<td>US 1 Clinical 1</td>
<td>Discharge</td>
<td>Discharge</td>
<td>Discharge</td>
<td>Discharge</td>
<td>Discharge</td>
<td>Discharge</td>
</tr>
<tr>
<td>US 1 Clinical 2</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
</tr>
<tr>
<td>US 2 Clinical 1</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
<td>Repeat FNA</td>
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<td>US Classification</td>
<td>Bethesda I</td>
<td>Bethesda II</td>
<td>Bethesda III</td>
<td>Bethesda IV</td>
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<td>US 2 Clinical 2</td>
<td>Repeat FNA</td>
<td>Repeat US at 12-18 mo and repeat FNA</td>
<td>Offer surgery - Consider molecular testing - Consider surgery - Consider active surveillance in select cases</td>
<td>Offer surgery - Consider molecular testing - Consider surgery - Consider active surveillance in select cases</td>
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<tr>
<td>US 3 Clinical 1</td>
<td>Repeat FNA</td>
<td>Repeat FNA within 12 mo</td>
<td>Offer surgery - Consider molecular testing - Consider surgery - Consider active surveillance in select cases</td>
<td>Offer surgery - Consider molecular testing - Consider surgery - Consider active surveillance in select cases</td>
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<td>Offer surgery - Consider molecular testing - Consider surgery - Consider active surveillance in select cases</td>
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<tr>
<td>US 3 Clinical 2</td>
<td>Repeat FNA</td>
<td>Repeat FNA within 6-12 mo</td>
<td>Offer surgery - Consider molecular testing - Consider surgery - Consider active surveillance in select cases</td>
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<td>&gt;20-40 mm</td>
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<td>US follow-up at 12-24 mo - Consider surgery or US-guided minimally invasive procedures based on size or symptoms after confirmatory FNA in select cases</td>
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<td>Repeat FNA</td>
<td>US follow-up at 12 mo</td>
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<td>US follow-up at 12 mo</td>
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<td>US follow-up at 6 mo and repeat FNA</td>
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<td>&gt;40 mm</td>
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<td>Offer US-guided minimally invasive procedures based on size or symptoms after confirmatory FNA</td>
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<td>Offer surgery - Consider molecular testing</td>
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European Thyroid Association writing committee member for guidelines on interventional techniques for begin thyroid nodules. M.L. is a consultant for Horizon, speaker for Eisai, and has received research grant support from Interpace, Quidel, Roche, and Takeda. V.P. is the founder and Chief Marketing Officer of Deontics Ltd. All other task force members have no multiplicity of interest to declare.

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