Review Article

Measures to Reduce Diagnostic Error and Improve Clinical Decision Making in Thyroid FNA Aspiration Cytology: A Proposed Framework

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Thyroid fine-needle aspiration cytology (FNA) and histopathology can be subjective areas of medical diagnosis and subject to different interpretations. On the basis of the authors' personal experience, 12 recommendations with potential to improve clinical decision making, ensure quality, and reduce diagnostic error in thyroid FNAC and histopathology are presented. 1) use a standardized reporting terminology for thyroid FNAC; 2) understand and explain to service users the limitations of cytology and the standardized thyroid FNAC reporting terminology used; 3) the cytopathologist should review all relevant clinical and ultrasound findings, if feasible; 4) include the risk of malignancy in all FNAC reports if feasible; 5) collect data to calculate the local institutional risk of malignancy for FNAC if feasible; 6) accept that nondiagnostic FNAC will include small numbers of carcinomas; 7) use rapid on-site evaluation and/or educational sessions for aspirators if the nondiagnostic aspiration rate is high; 8) know the diagnostic pitfalls of both cytology and histopathology; 9) use special immunohistochemical and molecular techniques that are evidence-based; 10) make use of second opinions, either in-house or interinstitutional; 11) multidisciplinary discussion of cases before surgery or therapy is invaluable; and, finally, 12) manage patient and clinician expectations of thyroid cytology and histopathology. These 12 recommendations may assist in quality-improvement initiatives and may reduce diagnostic errors in thyroid cytology and histopathology. Thyroid multidisciplinary case discussion remains the principal, overarching method for error reduction and for providing high-quality clinical decision making. ***Cancer Cytopathol* 2020;0:1-11**.

KEY WORDS: cytology; diagnostic error; pathology; thyroid.

INTRODUCTION

Medical diagnostic error is defined in a report from the US Institute of Medicine as failure to 1) establish an accurate and timely explanation of the patient's health problem(s) or 2) communicate that explanation to the patient.[1] Thyroid cytology and histopathology are to some extent subjective areas of medical diagnosis and thus are subject to differing interpretations and potential likelihood of diagnostic error. The diagnostic pitfalls are relatively well documented.[2,3] In histopathology, the pitfalls include papillary carcinoma (PTC) nuclei, a requirement to use strict criteria for the diagnosis of capsular or vascular invasion in follicular thyroid carcinoma,[4]

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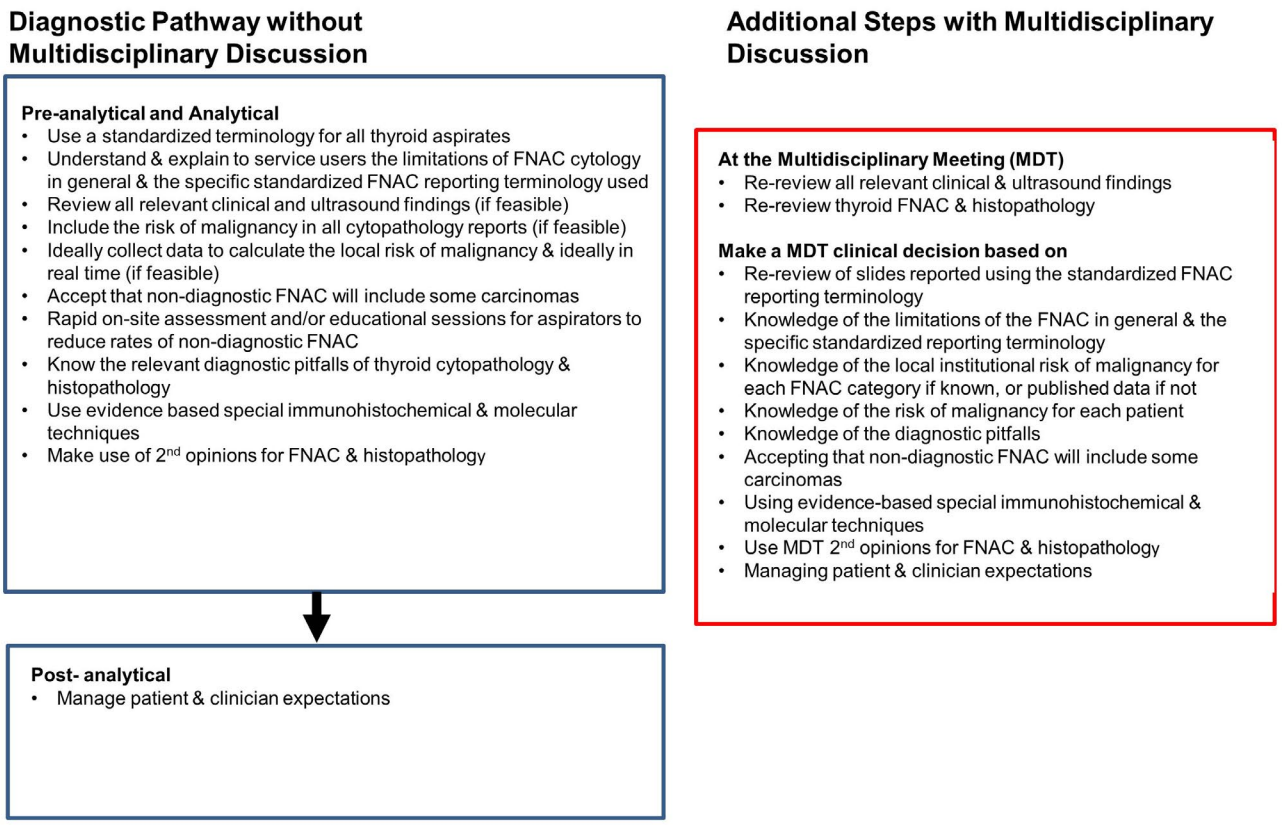

FIGURE 1. (*Left*) This flowchart illustrates preanalytical, analytical, and postanalytical aspects of the 12 suggested recommendations. (*Right*) The effect of multidisciplinary discussion enables review of 11 of the 12 suggested recommendations (excluding suggestion 7; rapid on-site evaluation/aspirator training). FNAC indicates fine-needle aspiration cytology.

benign nuclear bubbles (nuclear pseudo-pseudoinclusions) resembling those seen in papillary thyroid carcinoma,[5] psammoma body-like dystrophic calcifications resembling calcifications seen in PTC,[6] and benign parasitic nodules that can be mistaken for malignancy.[7] In thyroid cytology, cystic lesions, acute suppurative thyroiditis, granulomatous thyroiditis, lymphocytic thyroiditis, Graves disease, noninvasive follicular thyroid neoplasm with papillary-like nuclei (NIFTP), oncocytic lesions, follicular patterned lesions, papillary thyroid lesions, medullary thyroid carcinoma, and oncocytic lesions can all create diagnostic problems.[2] Diagnostic errors in thyroid cytology/histopathology may involve the preanalytical phase, which is the specimen collection and transmission process to the laboratory; the analytical phase, which is the diagnostic workup in the laboratory; or the postanalytical phase, which is the handling of the results outside the laboratory once the result is generated within the laboratory. In the postanalytical phase, the communication of results is aided by close liaison with clinical teams and the use of standardized reporting terminology nomenclature. Failsafe quality-management systems for tracking and follow-up of patients for a thyroid nodule clinic can be used to ensure quality of patient care and that results are acted upon.[8] We have reviewed our experience in relation to thyroid cytology/histopathology to provide a list of recommendations that could be used to potentially improve pathologic and clinical decision-making, ensure quality, and reduce diagnostic errors, especially for thyroid cytology. A list of 12 suggested recommendations is proposed from our personal experience and clinical practice in 3 different settings (Fig. 1). This suggested list of recommendations is developmental because, currently, it may not be possible to implement all of these in any given practice setting. This is not intended to be a comprehensive or prescriptive framework but, rather, a proposal for a series of quality measures that could be implemented, according to their clinical practice, by cytopathologists,

histopathologists, and clinicians, who are the intended audience for this article.

1. Use a Standardized Reporting Terminology for Thyroid Fine-Needle Aspiration Cytology and All Thyroid Aspirates

The use of reporting terminologies for thyroid fine-needle aspiration (FNA) cytology (FNAC) dates back to the Papanicolaou Society Classification in 2005.[9] After the Bethesda Thyroid Fine-Needle Aspiration State of the Science Conference in 2007 in Bethesda, Maryland, The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was published in 2008, and the second edition was published in 2017.[10] Other reporting terminologies exist. There is the British *Thy* terminology,[11] the Italian *TIR* terminology,[12] an Australian terminology, and a Japanese system.[13] All of these systems are broadly similar, although with slight differences. All seek to classify and codify thyroid FNACs according to the likely histopathologic diagnosis, to give some indication of the risk of malignancy (ROM), and to suggest clinical management of the patient (Table 1). Reports should include both descriptive text, describing the cytologic findings of the lesions(s) and suggesting a diagnosis or differential diagnosis, and then a code for the final diagnostic terminology category. For various reasons, some thyroid FNAs are still not always reported using a standardized terminology, either through omission or because, on occasion, for valid reasons if it is not clear that an FNAC is necessarily arising from the thyroid gland or from a structure surrounding the thyroid or lymph node. If a standardized FNAC terminology is not used, this can lead to ambiguity and uncertainty in the understanding and application of the report to patient management.

2. Understand and Explain to Service Users the Limitations of Cytology and the Standardized Thyroid FNAC Reporting Terminology Used

Although using a standardized terminology is important, it is equally important to understand the intrinsic limitations of thyroid FNAC in general and hence the reporting system used. Thyroid cytology requires both qualitative and quantitative interpretation of microscopic features. The interobserver reproducibility of the different subcategories of the various FNAC terminology systems is far from perfect.[14-19] Whereas training, experience, and

TABLE 1. Internationally Used Terminology Systems for Thyroid Fine-Needle Aspiration Cytology

RCPath	Bethesda	Italian	Australian	Japanese
Thy1: Nondiagnostic for cytologic diagnosis	I: Nondiagnostic or unsatisfactory	TIR 1: Nondiagnostic	1: Nondiagnostic	1: Inadequate
Thy1c: Nondiagnostic for cytologic diagnosis—cystic lesion		TIR 1c: Nondiagnostic cystic		
Thy2: Nonneoplastic	II: Benign	TIR 2: Nonmalignant	2: Benign	2: Normal or benign
Thy2c: Nonneoplastic—cystic lesion				
Thy3a: Neoplasm possible—atypia/nondiagnostic	III: Atypia of undetermined significance or follicular lesion of undetermined significance	TIR 3A: Low-risk indeterminate lesion	3: Indeterminate or follicular lesion of undetermined significance	3: Indeterminate (B, others)
Thy3f: Neoplasm possible, suggesting follicular neoplasm	IV: Follicular neoplasm or suspicious for a follicular neoplasm	TIR 3B: High-risk indeterminate lesion	4: Suggestive of a follicular neoplasm	3: Indeterminate (A, follicular neoplasms; A-1, favor benign; A-2, borderline; A-3, favor malignant)
Thy4: Suspicious of malignancy	V: Suspicious for malignancy	TIR 4: Suspicious of malignancy	5: Suspicious of malignancy	4: Malignancy suspected
Thy5: Malignant	VI: Malignant	TIR 5: Malignant	6: Malignant	5: Malignancy

Abbreviations: Bethesda, The Bethesda System for Reporting Thyroid Cytopathology; Italian, Italian Consensus for the Classification and Reporting of Thyroid Cytology (TIR); RCPath, UK Royal College of Pathologists.

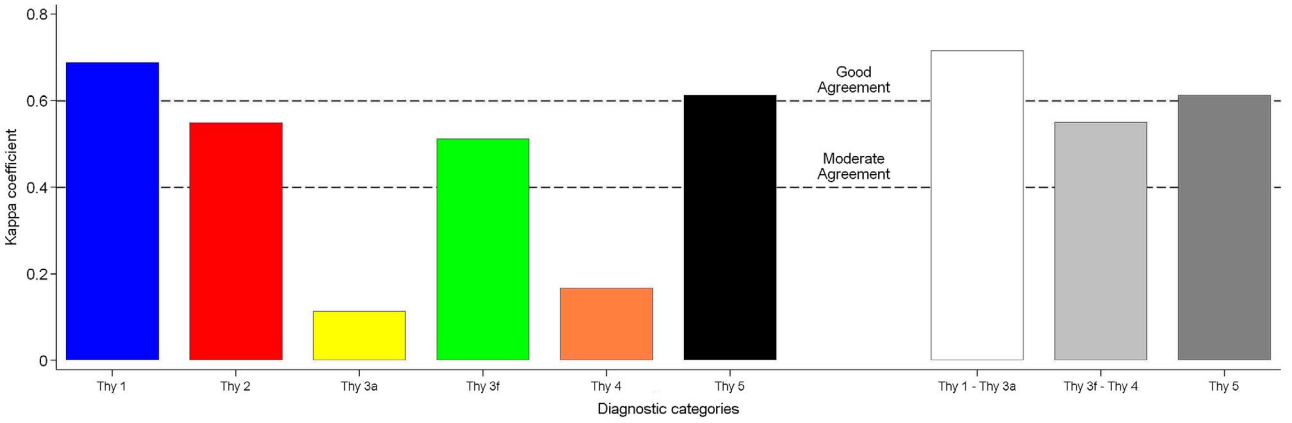

FIGURE 2. This diagram illustrates the interobserver reproducibility of the various categories within the UK Thy terminology system, indicating that interobserver reproducibility of the Thy 3a and Thy 4 categories is low. Thy 3a is equivalent to The Bethesda System for Reporting Thyroid Cytopathology category III (atypia of undetermined significance/follicular lesion of undetermined significance), and Thy 4 is equivalent to category V (suspicious of malignancy).

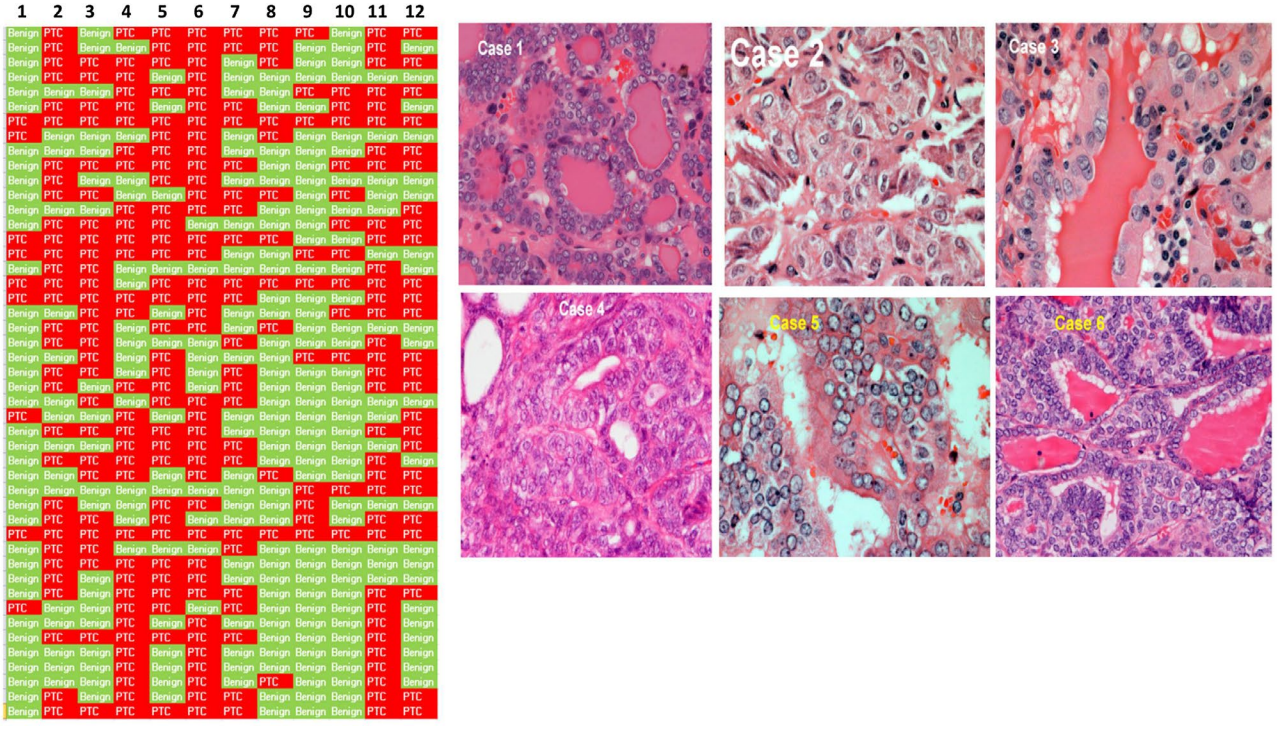

FIGURE 3. This is a heat-map of the responses of 47 participants to 12 static images of thyroid lesions showing wideinterobserver variation in the assessment of papillary carcinoma or benign nuclei. PTC indicates a participant diagnosis of papillary thyroid carcinoma based on assessment of the relevant static image. Only the first 6 cases are illustrated (Royal College of Pathologists Endocrine Pathology Update, 2018; see www.thyroid2018.com, accessed May 28, 2020). Reproduced with permission from NIFTP.org.

personal and institutional case volume are factors, at best, studies demonstrate moderate, and sometimes very poor, interobserver reproducibility for some of the FNAC sub-categories, particularly for Thy3a ($\kappa = 0.11$) (Fig. 2)[18] or atypia of undetermined significance/follicular lesion of undetermined significance (Bethesda category III). Cibas et al, using TBSRTC, demonstrated a 64% rate of concordance between local and central cytopathology review and 74.7% intraobserver concordance.[20] Clinical decision making and follow-up depend on assigning a

particular FNAC to a particular category with a suggested ROM. Because the interobserver reproducibility of the various reporting terminology subcategories in all terminology systems is not perfect, there is always some degree of uncertainty for the clinical management if this is based on the cytologic findings alone. For example, an FNA categorized as Thy 3a or Bethesda category III by an individual cytopathologist might be reasonably categorized as category II/Thy 2 (benign) or category IV/Thy 3f (follicular neoplasm or suspicious for a follicular neoplasm) by another equally skilled and competent cytologist.[18] Compounding the subjectivity of pathologic interpretation are the well known morphologic limitations of thyroid FNAC in the diagnosis of follicular-patterned lesions, with the cytologic appearances of follicular adenoma and well differentiated follicular carcinoma often being identical. Histology diagnoses affect the ROMs: according to TBSRTC, the positive predictive value for a malignant category VI thyroid FNAC is 97% to 99% if NIFTP lesions are included as malignant and 94% to 96% if NIFTP lesions are no longer regarded as malignant.[10] The degree of uncertainty in the subcategorization of thyroid FNAC can be expressed as confidence limits, at a significant level of 1 standard deviation or 2 standard deviations assuming a normal distribution of results around a mean value. However, in clinical practice, this is difficult to do given the subjectivity of cytologic diagnosis and the known interobserver degree of variation. Therefore, it is important that cytopathologists, histopathologists, and clinicians are aware of the limitations of thyroid cytology in general and the interobserver reproducibility of the various cytologic subcategories in the terminology system used and that they use this information in their clinical decision making with full knowledge of the degree of uncertainty.

3. Review All Relevant Clinical and Ultrasound Findings (if Feasible and/or Available)

Many cytopathologists and histopathologists still receive specimens in the pathology laboratory with a laboratory request form that states, "thyroid nodule, ultrasound-guided FNA." It is important that thyroid FNACs are appropriately labeled as to site(s) and side(s) (eg, left lobe, right lobe, or isthmus) to prevent inappropriate surgery. Thyroid FNAC slides can be viewed independent of the clinical history and ultrasound characteristics without the prior cognitive bias of the full details of the relevant clinical information, the medical history, and ultrasound findings; however, this ignores the wealth of clinical information available, which is not typically included on pathology laboratory request forms.[21] This clinical history includes hematology and biochemistry results, which may be relevant to inflammatory or autoimmune conditions of the thyroid (eg, granulomatous or Hashimoto thyroiditis, elevated serum calcitonin and CEA levels, details of previous thyroid or head and neck surgery, or hypercalcemia in parathyroid lesions). The ultrasound characteristics of the nodule(s) and a grading or scoring system based on the ultrasound findings, as now recommended in major international guidelines, are also important.[22,23] Hence a reduction in the potential for diagnostic error, if possible and if this information is available, requires knowledge of the clinical findings, clinical history, relevant laboratory investigations and ultrasound characteristics, or other imaging characteristics (eg, positron emission tomography/computed tomography) of the nodule or thyroid lesions aspirated. It may also be possible for the cytopathologist to review the ultrasound images and include this information in the cytopathologic assessment if the cytopathologist has training to do this.[24]

4. Include the Risk of Malignancy in All Cytopathology Reports (if Feasible)

The ROM is the probability that, if a thyroid nodule (or lesion) is excised, then the lesion will be malignant at histopathologic examination. The TBSRTC second edition suggests including the ROM in cytopathology reports,[10] which is useful because it helps to convey to clinicians and patients the likely ROM and hence the cytologic level of concern. However, this may create anxiety in the patient, particularly because lesions that are cytologically concerning or malignant may be clinically indolent or could be incidentally discovered nodules that are unlikely to progress: so-called thyroid *incidentalomas*.[25] Nevertheless, knowledge of the ROM is crucial in guiding clinical management, including discussions with patients about the level of risk. The ROM provided ideally should be locally derived[26]; however, if this is not possible, then, as an alternative, the ROM quoted in the published literature for the relevant reporting terminology could be included in the cytology report.[10]

It is important to consider carefully how the ROM is calculated. The TBSRTC ROM for each category is based

on the published literature, whereas the local institutional ROM for each category may vary quite widely from the published literature.[27] Patients with *unsatisfactory* or *benign* FNACs who undergo surgery are more likely to have clinicoradiologic features that are of concern than patients who do not. Hence using as a denominator the number of patients with subsequent histology is more relevant for higher risk categories, in which most patients will undergo surgery. In contrast, a denominator comprising all patients in the relevant cytology terminology category will be more relevant for the benign and unsatisfactory categories, in which most patients will not undergo surgery. As highlighted in recommendation 8, below, there is also considerable subjectivity in the benign or malignant diagnosis of follicular-patterned lesions of the thyroid, hence histopathologic assessment cannot always be regarded as a true benchmark gold standard.[4,20,28-30]

5. Collect Data to Calculate the Local ROM and Ideally in Real-Time (if Feasible)

TBSRTC[10] and the other international terminologies give a stated ROM for the various cytologic subcategories.[11-13] However, there is relatively wide interinstitutional variation in the ROM for the various categories, which is related to the subjectivity of thyroid cytology, the prevalence of thyroid cancer in the local population, and interindividual or interinstitutional factors, including patient management pathways.[27,31-33] Hence. if feasible. accurate data can be obtained from local institutional cytologic/histopathologic audit of the ROM for each of the cytologic subcategories for the reporting terminology used. The process of information collection ideally should be contemporary, but it is recognized that there may be a delay before the patient has proceeded to surgery and confirmatory histologic assessment. The confidence intervals or the degree of certainty of the ROM within any given thyroid FNA terminology subcategory is difficult to calculate; however, from a scientific perspective, the confidence limits of the ROM for each terminology subcategory are useful to know, hence we believe that, in the future, this will be something that service users will require.

6. Accept That Nondiagnostic FNAs Will Include Small Numbers of Carcinomas, Comprising Mainly Cystic PTC

The nondiagnostic category[11-13,34] inevitably includes a small number of missed carcinomas, usually because the aspirator has failed to adequately sample the lesion or target the relevant lesion(s) seen on ultrasound or because the lesion is cystic. Retrospective studies have reported lower rates of both nondiagnostic and false-negative cytology from FNAC procedures performed using ultrasound guidance compared with palpation.[22] The nondiagnostic rate depends on the nature of the lesion aspirated and the experience of the aspirator. Unilocular thyroid cysts without radiologically or ultrasound concerning features have a very low ROM, so, even if the aspirate contains only nonepithelial material consistent with the cyst content, the ROM is low. Cysts with solid areas should be sampled in the solid component to avoid misdiagnosis of a cystic PTC. Solid lesions and some mixed cystic/solid lesions should produce a qualitative and quantitative cellular yield.

7. Rapid On-Site Evaluation and/or Educational Sessions for Aspirators Will Almost Certainly Reduce the Rate of Nondiagnostic Aspirates if the Number of Nondiagnostic Aspirates Is High

Rapid on-site evaluation (ROSE) is an important measure that can be implemented if the nondiagnostic rate is high.[35] TBSRTC,[10] the UK terminology system,[11] and other terminologies suggest a minimum adequacy criterion consisting of 6 groups of 10 epithelial cells for a specimen to be considered adequate. Most published evidence shows that implementation of ROSE will reduce nondiagnostic rates for thyroid FNA if nondiagnostic rates are high.[35] Who should undertake ROSE? This can be performed by cytotechnologists and biomedical science staff or by pathologists and cytologists, depending on local institutional preference.[36] It is also well documented that higher yields of satisfactory FNAC are seen with increasing operator experience. Monitoring the rate of unsatisfactory specimens once aspirators are fully trained can identify underperformance, which can be addressed by additional specific training.

8. Know the Relevant Diagnostic Pitfalls of Both Cytopathology and Histopathology

There are multiple pitfalls in making diagnoses in thyroid cytology and pathology. These are dealt with elsewhere in several publications.[2,3] In thyroid cytology, the principal diagnostic risks are underdiagnosis of a malignant condition, overdiagnosis as malignant or suspicious of malignancy of a benign or very low ROM condition, or failure

to diagnose a benign inflammatory process as benign. In thyroid histopathology, many of the diagnostic pitfalls are very similar to those seen in cytology, particularly the diagnosis of papillary carcinoma-type nuclei and the minimum histopathologic thresholds for a diagnosis of PTC or NIFTP.[37-39]

Regarding papillary carcinoma-like nuclei, there is significant interobserver variation in the histopathologic thresholds for diagnosis of the nuclei for PTC.[29,30] This has been borne out by multiple articles in the literature. Another example of this is an exercise undertaken involving participants at a conference of the UK Endocrine Pathology Society and Royal College of Pathologists in 2018. Forty-seven conference participants, all of whom were either established consultants or senior trainees in pathology, undertook an assessment of 12 photomicrographic images from a sample of follicular-patterned thyroid tumors with the option to suggest a diagnosis of PTC or benign nuclei (the images of the 12 thyroid lesions can be viewed at www.thyroid2018.com, accessed May 28, 2020). The heat map of responses shown in Figure 3 indicates that, in difficult cases, there can be wide interobserver variation in the diagnosis of PTC or benign. With the use of NIFTP terminology, reference to the older literature from before 2016 becomes problematic because, in many series, approximately 20% to 25% of newly diagnosed thyroid carcinomas before 2016 were diagnosed as encapsulated follicular variant of PTC, many of which would now be diagnosed as NIFTP lesions.[37] The literature shows that up to 8% of FNAs classified as malignant and approximately 24% of those classified as suspicious of malignancy are NIFTP lesions.[40,41] When a NIFTP tumor is suspected, free text comments are suggested (eg, overall cytomorphologic features suggest a follicular variant of papillary carcinoma or its recently described indolent counterpart, NIFTP; definitive distinction between these is not possible on cytologic material[10]). The latest edition of TBSRTC has revised the cytologic criteria for diagnosis of PTC.[10] Lesions with follicular architecture that lack intranuclear cytoplasmic inclusions are now regarded as suspicious of malignancy rather than malignant. Conversely, the presence on FNAC of either ≥3 nuclear pseudoinclusions or true papillae and/or psammoma bodies is highly predictive of a diagnosis of PTC.[42]

There is very poor interobserver reproducibility, as evidenced by κ statistics for the diagnosis of capsular invasion and vascular invasion in follicular thyroid carcinoma,[28] further compounding difficulty in the histopathologic diagnosis of follicular-patterned lesions for benign versus malignant. Published evidence shows rates of interrater disagreement for histopathologic assessment of thyroid nodules for a benign diagnosis versus a malignant diagnosis of 9.7%, with concordance between 2 expert histopathologists in 691 of 765 nodules.[20] The level of agreement increased to 98.5% after the 2 experts conferred.

9. Use Special Immunohistochemical and Molecular Techniques That Are Evidence-Based Immunohistochemistry

Cytohistologic cell-block examination with immunohistochemistry is useful in thyroid FNAC.[43] Examples include confirmation of the diagnosis of medullary thyroid carcinoma, which is typically positive for calcitonin and mCEA; anaplastic thyroid carcinoma, which is typically negative for thyroglobulin and TTF1 and positive for PAX-8; parathyroid lesions which are usually negative for thyroglobulin and TTF1 and positive for parathormone, chromogranin A, and GATA 3. It is also useful for suspected metastatic tumors to the thyroid (eg, a carcinoma of unknown primary site panel or another tailored immunopanel for the suspected primary site). Immunohistochemical panels for the distinction of benign and malignant follicular lesions are not recommended because of problems standardizing the results obtained in differing laboratories.[43]

MOLECULAR TECHNIQUES

The use of molecular techniques for thyroid lesions is now common, particularly in North America, where various proprietary systems are marketed. The most specific single molecular diagnostic test is *BRAF* V600E mutation, which, if present, indicates with 99% certainty the presence of thyroid carcinoma.[44] However, as a screening test, the sensitivity of *BRAF* V600E mutation is too low to reliably rule out thyroid carcinoma.[45] Other gene mutations may be useful and suggest adverse prognosis (eg, *TERT* promoter mutation, *PIK3CA*, *TP53*, and *AKT1*). Gene mutations such as *RAS* have much less clinical value because these mutations are present at low frequency in both benign and malignant lesions.[46-48] Molecular tests for thyroid cytology can be used as *rule-in* or *rule-out* tests for thyroid carcinoma. Afirma, ThyGeNEXT/ThyraMIR (Interpace Diagnostics), or ThyroSeq 3 (University of

Pittsburgh Medical Center/CBLPath) are the 3 principal test methodologies available and are most useful for indeterminate thyroid nodules.[49] The limitations of molecular diagnosis are that its positive and negative predictive values are very much influenced by the prevalence of cancer in the relevant cytologic category, which may vary widely between institutions.[50] Comparison of validation studies in TBSRTC category III for ThyroSeq v3, ThyGenX/ThyraMIR, and Afirma show respective sensitivities of 94%, 89%, and 91%; specificities of 82%,85%, and 68%; negative predictive values for malignancy of 97%, 94%, and 96%; and positive predictive values for malignancy of 66%, 74%, and 47%.[49] Therefore, molecular testing has some limitations in clinical practice, and patients and clinicians need to be aware of them. Molecular clinical practice continues to evolve in response to new developments. For NIFTP genotyping, panels frequently show *NRAS/HRAS* mutations and *THADA* fusions and Afirma gene expression classifier *suspicious* results.[49] The Afirma test has a high negative predictive value for malignancy but a lower positive predictive value for malignancy, hence approximately one-half of patients with Afirma gene expression classifer *suspicious* calls do not have thyroid cancer.[51]

10. Second Opinions Are Very Valuable and May Be In-House or Interinstitutional

In-house second opinions are useful for reducing interpretation errors, which some centers achieve through in-house internal consensus conferences, with external second opinions being sought for the most challenging cases.[52-54] In-house second opinions in thyroid pathology, although useful and relatively easy to obtain, may be subject to so-called *leadership* bias[28] in contrast to externally obtained second opinions. The Association of Directors of Anatomic and Surgical Pathology many years ago recommended that, if a patient is transferred or referred to another institution, the pertinent pathology slides and reports should be reviewed at the second institution,[55] hence second-opinion pathology review is valuable.[56] There are multiple studies examining the usefulness of second opinions in thyroid FNAC. In a review by Gerhard and Boerner in 2014, of a total of 7154 thyroid FNAs reviewed, there was an overall discrepancy rate between the initial diagnosis and the second-opinion diagnosis of 28.6%.[57] In general, the second-opinion diagnosis was better supported by clinical follow-up than the histologic diagnosis. Almost one-third (30.4%) of discordant cases resulted in changes in the clinical management of patients with thyroid nodules. Those authors found that thyroid FNACs initially categorized as *indeterminate* could often be definitively classified as benign or malignant by a second-opinion diagnosis. This illustrates the value of seeking another pathologist's opinion on a case. If there is interobserver diagnostic discrepancy, then an overall consensus opinion or a third opinion can be sought.

11. Multidisciplinary Discussion of Cases Before Surgery or Therapy Is Invaluable

Most published reporting terminologies for cytopathology do not require multidisciplinary discussion as a mandatory core element, with the exception of the UK Thy terminology.[11] The advantage of multidisciplinary discussion is that it allows the diagnostic and therapeutic decisions to be revisited before the final decision for any individual patient is made by a team of multidisciplinary experts. Reviewing the current list of 12 recommendations, 11 of the 12 proposed recommendations could be addressed in the thyroid multidisciplinary meeting, (Fig. 1, right). The 2015 US National Institute of Medicine report on improving diagnosis in health care states that treatment planning conferences (also known as tumor boards) may help to identify and avoid potential diagnostic errors by bringing multiple perspectives to challenging diagnoses and comments that this approach could also be applied to diagnoses other than cancer, especially those with serious health consequences or complex symptom presentations.[1] Good clinical practice suggests that, in an *ideal* situation, all FNACs could be reviewed jointly with the cytopathologist, radiologist, and endocrinologist or surgeon. As a measure of good clinical practice, all patients for whom therapy or surgery is being considered or is required may be reviewed in the multidisciplinary setting with the radiologist, cytopathologist/histopathologist, surgeon, endocrinologist, nuclear medicine physician, and oncologist. However, this is difficult to achieve, and multidisciplinary working arrangements may vary, depending on the local practice setting. In the United Kingdom, The Royal College of Pathologists recommends that thyroid cytology cases categorized as Thy4 or Thy5 (equivalent to TBSRTC categories V and VI, respectively) will be reviewed by a cytologist/histopathologist member of the thyroid multidisciplinary team and discussed in the multidisciplinary setting.[11] Other cases,

such as Thy3a and Thy3f (equivalent to TBSRTC categories III and IV, respectively) and cases classed as Thy1 or Thy2 (equivalent to TBSRTC categories I and II, respectively), can benefit from multidisciplinary discussion, especially if there is any concern.[11]

In some parts of the world, multidisciplinary teams are well established, although local practice may vary.[58] The quality of cytopathologic assessment and reporting can be improved by local cytopathologists working with regional and national cytopathology experts.[59] The issues discussed above in relation to cytopathologic/histopathologic diagnosis suggest that multidisciplinary discussion will most likely be of value for most patients. The ultrasound characteristics of a given thyroid lesion or nodule(s), the cytopathologic interpretation of the nodule(s), including in-house or interinstitutional second opinions, and the histopathologic assessment of needle-core biopsy or of the excised thyroid specimen(s) are all potentially subjective, at least to some limited extent, with ultrasound imaging and cytology having the highest rates of interobserver variation. This suggests that at, every stage of the diagnostic process, there is potential for some diagnostic uncertainty; therefore, decision making in thyroid disease is not binary (yes or no) but requires the combined input of multiple specialties and expertise into decision making for patient management.

12. Manage Patient and Clinician Expectations of Thyroid Cytopathology and Histopathology

This is a difficult area for pathology and cytopathology but is essential in multidisciplinary patient management. Managing patient and clinician expectations requires multidisciplinary input, both when providing the cytology or histopathology reports and when explaining the limitations of cytologic and histopathologic assessment. The clinical history and presentation and the radiologic, cytologic, and pathologic findings must be reviewed carefully and considered together. Patient preference and the extent of surgery undertaken require shared multidisciplinary clinical decision making with patients. Although we would not necessarily advocate this for thyroid cytology, various initiatives have been proposed, including *pathology explanation clinics* for laboratory results, to try and help patients understand the meaning and relevance of their pathology results.[60] For examplean important issue would be to explain to patients before surgery that most of those with cytologically *indeterminate* thyroid nodules diagnosed as *follicular neoplasm/suspicious of follicular neoplasm* after undergoing surgery are unlikely to have carcinoma.

Conclusions

The objective of this brief review is to provide pathologists and clinicians with useful suggestions to reduce diagnostic errors, assist in quality-improvement initiatives for thyroid FNAC, and encourage and stimulate debate and discussion of error and decision making in thyroid cytology and histopathology. This list of recommendations is developmental but represents a framework that should be helpful to reduce diagnostic error and improve clinical decision making after thyroid FNA.

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Measures to Reduce Diagnostic Error and Improve Clinical Decision Making in Thyroid FNA Aspiration Cytology: A Proposed Framework

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This review discusses the reasons for diagnostic error in thyroid cytology and histopathology and provides 12 recommendations for cytology and histopathology to improve quality and reduce the likelihood of clinical diagnostic errors. For each of the 12 recommendations, the rationale is explained together with the overarching requirement for multidisciplinary case discussion if there is clinical or diagnostic uncertainty.