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American Thyroid Association Management Guidelines 2025 for Adult Patients with Differentiated Thyroid Cancer

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Introduction

- Differentiated thyroid cancer (DTC) is the most prevalent cancer of thyroid and is among the most frequently diagnosed cancers in the United States. The practice guidelines of the American Thyroid Association (ATA) for DTC management in adult patients (previously combined with thyroid nodules) were published initially in 1996, with subsequent revisions based on advances in the field. The goal of this update is to provide clinicians, patients, researchers, and those involved in health policy with rigorous, comprehensive, and contemporary guidelines to assist in the management of adult patients with DTC, emphasizing the patient journey beginning with a thyroid cancer diagnosis.

Introduction

- These revised guidelines begin with the initial cancer diagnosis and continue with recommendations for staging and risk assessment, initial treatment decisions, assessment of treatment responses, monitoring approaches, diagnostic testing, and subsequent therapies based on the strength of evidence for response and consideration of side effects and outcomes. Patient-reported outcomes and identified areas of need for additional high-quality research are highlighted.
- These revised evidence-based recommendations inform clinical decision-making in the management of DTC that reflect the changing science and optimize the evidence-based clinical care of patients throughout their journey with DTC. Critical areas of need for additional research are highlighted.

Dictionary and Definitions

Active surveillance

- The ongoing observation or active monitoring of a known or suspected primary, intrathyroidal, low-risk DTC with serial imaging as an alternative to upfront surgical intervention.

Disease monitoring

- Monitoring for biochemical (elevated level of serum Tg) and/or structural persistence or recurrence of disease (as confirmed by imaging and/or biopsy) following the diagnosis and initial treatment (surgery ± RAI) of thyroid cancer. It is deployed to evaluate patients for disease progression and inform the type and timing of interventions deemed appropriate.

Dictionary and Definitions

Response to therapy

- Response assessment is performed after intervention, either for initial or clinically persistent/recurrent disease

Excellent response

- No biochemical or structural evidence of persistent thyroid cancer (i.e., remission).

Dictionary and Definitions

Indeterminate response

- The presence of nonspecific findings on imaging; mildly elevated serum Tg levels; or positive, but stable or declining, anti-Tg antibody (TgAb) levels in persons who have undergone total thyroidectomy with or without RAI.

Biochemically incomplete response

- Elevated serum Tg concentrations or rising TgAb levels without radiological evidence of structural recurrence in persons who have undergone total thyroidectomy with or without RAI.

Dictionary and Definitions

Structurally incomplete response

- Structural evidence of disease recurrence (by imaging or biopsy), usually in conjunction with elevated Tg and/or TgAb levels.

Clinically persistent disease

- Biochemical or structural evidence of disease within 90 days of initial therapy (or intervention for persistent disease).

Clinically recurrent disease

- Biochemical or structural disease subsequently identified in patients previously deemed to have an excellent response following therapy.
- Clinically recurrent disease likely represents progression of residual disease that is below the lower limits of detection.

Dictionary and Definitions

Risk of recurrence

- We use the term “recurrence” to mean clinical recurrence, recognizing that most recurrences reflect growth of residual disease to clinically detectable levels

- **An overall assessment of risk of biochemical or structural recurrence is determined by incorporating a combination of factors: histopathologic characteristics of the resected tumor, American Joint Committee on Cancer (AJCC) staging, imaging, molecular analysis of tumor, and response to therapy at subsequent evaluation.**
- **For the purpose of these guidelines, categories are designated as low (<10%), low-intermediate (10–15%), intermediate-high (≥16–30%), and high (>30%) risk of recurrence.**

Dictionary and Definitions

Extent of surgery definitions (ATA website definitions)

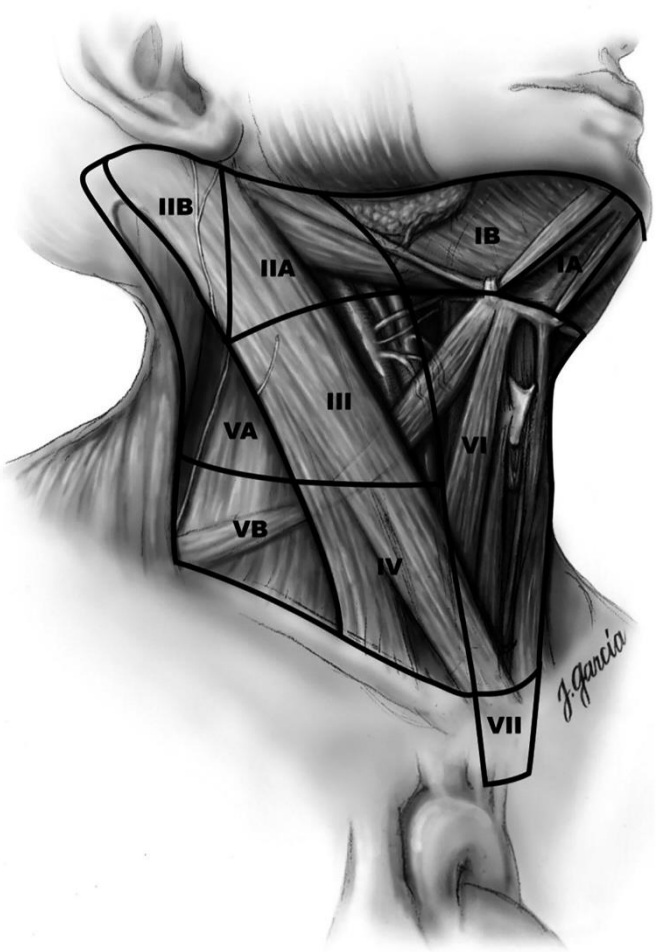
- **Total thyroidectomy:** Surgical removal of the entire thyroid gland.
- **Near-total thyroidectomy:** Intended extent of resection for thyroid cancer is total thyroidectomy, but a small remnant may be left for a specific reason (usually confidence in nerve preservation).
- **Lobectomy or hemithyroidectomy with or without isthmusectomy:** Surgical removal of one lobe (half) of the thyroid with or without the isthmus.
- **Subtotal thyroidectomy:** Surgical removal of almost all of the thyroid gland, leaving 3–5 g of thyroid tissue with the intent of maintaining adequate thyroid hormone production. This operation is not recommended if the diagnosis of thyroid cancer is known preoperatively.
- **Completion thyroidectomy:** Surgical removal of the remnant thyroid tissue following procedures of less than total or near-total thyroidectomy.

Dictionary and Definitions

Extent of lymphadenectomy definitions

- **Central neck dissection**

- Central neck lymph nodes include Levels VI and VII.
- Central neck dissection is a comprehensive removal of pretracheal and prelaryngeal lymph nodes, along with at least one paratracheal nodal basin.
- It can be unilateral or bilateral; the laterality and extent of dissection should be documented at the time of operation in addition to surgical intent (therapeutic vs. prophylactic).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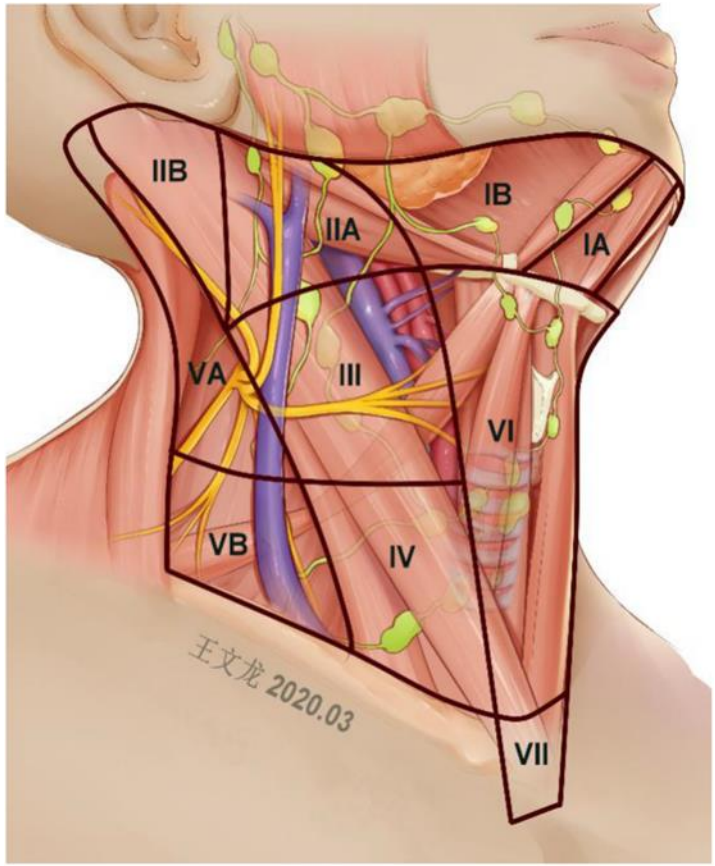
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Dictionary and Definitions

Extent of lymphadenectomy definitions

- **Therapeutic**
- It implies that metastatic nodal disease is apparent clinically preoperatively or intraoperatively by examination and/or imaging, cN1a.

- **Prophylactic**
- It implies that no metastatic nodes are detected by examination or imaging preoperatively or intraoperatively, cN0.

Dictionary and Definitions

Extent of lymphadenectomy definitions

- **Lateral neck dissection**

- Full compartment dissection of the lateral cervical neck lymph nodes in Levels IIA, III, IV, and VB ipsilateral to the tumor and performed for clinical evidence of metastatic involvement.
- Dissection of Levels I, IIB, and VA are not regularly performed but can be considered based on findings suggestive of metastatic disease in these compartments

Dictionary and Definitions

Completeness of surgical resection

- The goal of surgery is to remove safely as much thyroid cancer as possible.
- To define the completeness of resection, the AJCC created definitions that are used in these guidelines to facilitate communications.
- An R0 resection means that the surgical margin is microscopically negative for residual tumor.
- An R1 resection means that there is no residual macroscopic tumor but that microscopically positive margins still demonstrate the presence of tumor.
- R2 resection means that gross (macroscopic) disease remains post-surgery.

Dictionary and Definitions

^{131}I, RAI administration

- **Remnant ablation**
- RAI administration to destroy benign remnant thyroid tissue following total or near-total thyroidectomy.
- **Adjuvant therapy**
- RAI administration to destroy suspected (but not identified) remaining thyroid cancer following total or near-total thyroidectomy.
- **Therapeutic treatment**
- RAI administration to treat known residual or recurrent thyroid cancer, either initially or with subsequent progression of thyroid cancer after total or near-total thyroidectomy.
- **Thyrotropin suppression therapy**
- Use of thyroid hormone to suppress serum thyrotropin (TSH) concentrations below the normal range based on the risk of recurrence and/or response to therapy.

Initial DTC Management

Is NIFTP considered thyroid cancer?

RECOMMENDATION 1

- NIFTP and other tumors of uncertain malignant potential (Follicular Tumor of Uncertain Malignant Potential and Hyalinizing Trabecular Tumor) are diagnosed pathologically and have a very low malignant potential (lower than the lowest-risk DTC). Further treatment with completion thyroidectomy/lymphadenectomy and/or RAI is not advised routinely. The optimal approach to postoperative monitoring of these tumors is uncertain.

Which patients with DTC should be offered germline genetic testing?

RECOMMENDATION 2

- Germline genetic testing may be offered in the following scenarios:
- A. Clinical suspicion for Cowden/PTEN hamartoma tumor syndrome (PHTS) due to a combination of DTC and non-thyroid malignancy/tumors/features (Conditional recommendation, Moderate certainty evidence)
- B. In patients who were diagnosed with FNMTC as children, clinical and family history should be evaluated for features of DICER1 tumor predisposition. Consideration may be given to germline DICER1 testing in patients from families with pediatric patients with DTC. (Conditional recommendation, Very low certainty evidence)
- C. Pathologic diagnosis of cribriform morular thyroid carcinoma (APC gene) (Conditional recommendation, Moderate certainty evidence)
- D. Other combinations of tumors and/or cancers in a patient and/or their family members may raise concern for a hereditary predisposition condition, including rare conditions such as Carney complex or Werner syndrome. In these patients, genetic counseling and testing may be offered. (Conditional recommendation, Moderate certainty evidence).

Should patients with non-syndromic FNMTC receive genetic testing?

RECOMMENDATION 3

- There is a lack of evidence to suggest the utility of clinical germline genetic testing in non-syndromic FNMTC. In non-syndromic FNMTC, the non-thyroid malignancies in the family may drive decision-making regarding genetic testing. (Conditional recommendation, Moderate certainty evidence).

Should family members of patients with FNMTC be screened for thyroid cancer?

RECOMMENDATION 4

- Individuals with a family history of FNMTC should have a careful history and directed neck examination as a part of regular health maintenance. Ultrasound screening may be considered in first-degree family members of individuals who meet criteria for a clinical diagnosis of FNMTC due to the presence of three or more (first or second degree) related individuals with diagnoses of NMTC. Ultrasound screening may also be considered in families with only two affected individuals showing other concerning features (such as particularly young ages of diagnosis) or with limited family structure. The age for initiation of such screening requires further study and should be carefully weighed against the risk of overtreatment. (Conditional recommendation, Very low certainty evidence).

Syndromes Associated with DTC

TABLE 4. SYNDROMES ASSOCIATED WITH DTC

Syndrome (gene)	*Histology*	*Lifetime risk*	*Other features*	*Screening guidance*
Cowden syndrome/PHTS (*PTEN*)	FTC,[a] PTC	3–10%	Breast cancer, endometrial cancer, goiter, macrocephaly	NCCN—Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic
Familial adenomatous polyposis (*APC*)	CMTC, PTC	Up to 12%	Colon polyposis, CHRPE, desmoids	NCCN—Genetic/Familial High-Risk Assessment: Colorectal
DICER1 tumor predisposition (*DICER1*)	PTC, FTC,[a] PDTC	OR, 9.2 [CI 2.1–34.7]	Pleuropulmonary blastoma, cystic nephroma, ovarian sex cord stromal tumors	Schultz et al.[124]
Carney complex (*PRKAR1A*)	FTC,[a] PTC	Unknown	Pigmented abnormalities of the skin, myxomas, schwannomas, and endocrine tumors	Correa et al.[125]
Werner syndrome (*WRN*)	FTC,[a] PTC	Unknown	Premature aging, cataracts, DM, other cancers	Takemoto et al.[126]

[a]OTC was previously included as a subtype of FTC and is likely also associated with these hereditary predispositions.

CHRPE, congenital hypertrophy of the retinal pigment epithelium; CI, confidence interval; CMTC, cribriform-morular thyroid carcinoma; DM, diabetes mellitus; DTC, differentiated thyroid cancer; FTC, follicular thyroid carcinoma; NCCN, National Comprehensive Cancer Network; OR, odds ratio; OTC, oncocytic thyroid carcinoma; PDTC, poorly differentiated thyroid carcinoma; PHTS, PTEN hamartoma tumor syndrome.

When should germline genetic testing be offered to patients with DTC with alterations detected on tumor samples (somatic testing)?

RECOMMENDATION 5

- When genomic testing is performed on tumor samples for clinical purposes, both somatic and germline genetic alterations can be detected. If a potentially clinically relevant germline cancer-predisposing variant is detected, evaluate patients and their family histories for clinical correlation, and consider referral for genetic counseling for possible germline testing. (Conditional recommendation, Moderate certainty evidence).

Does surgical experience influence complication rates for thyroidectomy?

RECOMMENDATION 6

- Due to lower complication rates and improved outcomes on average associated with high volume thyroid surgeons (>25–50 thyroidectomies/year), patients with thyroid cancer should be offered referral to a high-volume surgeon, particularly for tumors requiring more extensive surgery. (Strong recommendation, Moderate certainty evidence).

What is the role of preoperative staging with diagnostic imaging and laboratory tests?

RECOMMENDATION 7

- A. Preoperative neck ultrasound to evaluate cervical lymph nodes in the central and lateral neck compartments as well as for gross extrathyroidal extension is recommended for all patients undergoing surgery for malignant cytologic or molecular findings. (Strong recommendation, Moderate certainty evidence)
- B. Ultrasound-guided FNA of sonographically suspicious lymph nodes greater than 8–10 mm in the smallest diameter should be performed to confirm malignancy if this would change management. (Strong recommendation, Moderate certainty evidence)
- C. The addition of FNA-Tg washout in the evaluation of suspicious cervical lymph nodes may be performed in select preoperative patients, but interpretation may be difficult in patients with an intact thyroid gland. (Conditional recommendation, Low certainty evidence).

When should preoperative cross-sectional or 18F-fluorodeoxyglucose-PET imaging be performed?

RECOMMENDATION 8

- Preoperative use of cross-sectional imaging studies (CT, magnetic resonance imaging [MRI]) of the neck and mediastinum with intravenous contrast is recommended as an adjunct to physical examination and ultrasound for patients with clinical suspicion for advanced or invasive disease, including primary tumors with gross extrathyroidal extension, extensive (e.g. bulky or invasive) adenopathy, or disease concerning for aerodigestive tract and/or thoracic involvement (Strong recommendation, Moderate certainty evidence)
- Performing preoperative cross-sectional imaging of the chest, abdomen, and pelvis in search for distant metastases is recommended in situations when results will influence extent of surgery. (Good Practice Statement)
- Routine preoperative 18F-fluorodeoxyglucose (FDG)-PET/CT is not recommended prior to surgery. (Strong recommendation, Moderate certainty evidence).

Should a serum Tg level be measured prior to surgery?

RECOMMENDATION 9

- Routine preoperative measurement of serum Tg or TgAb levels is not recommended. (Conditional recommendation, Low certainty evidence).

Should preoperative somatic genomic testing be performed to inform the extent of surgery?

RECOMMENDATION 10

- Genomic evaluation of confirmed DTC prior to surgery is not recommended routinely. However, if the genomic profile is known or performed, the presence or absence of specific combinations of abnormalities may be considered in the context of clinical, radiographical, and cytopathologic data to inform extent of surgery. (Conditional recommendation, Low certainty evidence)

Are there patients in whom active surveillance and percutaneous ablation are appropriate management options?

RECOMMENDATION 11

- A. Active surveillance may be offered as an appropriate management option for some patients with cT1aN0M0 PTCs. Shared clinical decision-making between the patient and clinical team regarding risks and benefits of this approach is essential. (Conditional recommendation, Low certainty evidence)
- B. Ultrasound-guided percutaneous ablation may be considered as an alternative to active surveillance or resection for cT1aN0M0 PTC in selected patients. Shared clinical decision-making between the patient and clinical team regarding risks and benefits of this approach is essential. (Conditional recommendation, Low certainty evidence)

What is the optimal approach for patients undergoing active surveillance?

RECOMMENDATION 12

- For patients undergoing active surveillance, neck ultrasound should be used to monitor disease progression. (Good Practice Statement)

Should serum Tg and TgAb levels be measured during active surveillance?

RECOMMENDATION 13

- For patients undergoing active surveillance, routine measurement of serum Tg and/or TgAb levels is not recommended. (Good Practice Statement)

Are there clear indications for when patients undergoing active surveillance should pursue resection?

RECOMMENDATION 14

- In patients undergoing active surveillance, surgical resection is indicated if there is evidence of new biopsy-proven lymph node metastases, growth of the primary tumor by ≥3 mm, distant metastases, evidence of extrathyroidal extension, posterior growth, when there is patient anxiety, inability to follow-up, and/or expressed preference for surgery. (Good Practice Statement)

Indication for Surgical Resection	Description / Criteria
New biopsy-proven lymph node metastases	Appearance of lymph node metastases confirmed by biopsy
Growth of the primary tumor by ≥3 mm	Increase in primary tumor size by 3 millimeters or more
Distant metastases	Evidence of metastasis outside the neck region
Evidence of extrathyroidal extension	Tumor extending beyond the thyroid capsule
Posterior growth	Tumor growth directed posteriorly (towards critical structures)
Patient anxiety	Significant psychological distress affecting patient's well-being
Inability to follow-up	Patient unable or unwilling to attend regular surveillance visits
Expressed preference for surgery	Patient requests surgery despite other criteria

What is the optimal operative approach for DTC?

RECOMMENDATION 15

- A. When resection is performed for patients with thyroid cancer ≤2 cm without gross extra-thyroidal extension (cT1) and without metastases (cN0M0), the initial surgical procedure should be a thyroid lobectomy unless there are bilateral cancers or other indications to remove the contralateral lobe. (Strong recommendation, Moderate certainty evidence)

What is the optimal operative approach for DTC?

RECOMMENDATION 15

- B. For patients with low risk, unilateral thyroid cancer >2 and ≤4 cm (cT2N0M0), thyroid lobectomy may be the preferred initial surgical treatment due to significantly lower risk and side effects.
- However, the patient and treatment team may adopt total thyroidectomy to enable RAI administration and/or enhance follow-up based on disease features, suspicious contralateral nodularity, and/or patient preferences.
- When thyroid lobectomy is offered as initial treatment, counsel the patient about the possibility of conversion to total thyroidectomy or need for subsequent completion thyroidectomy if higher-risk factors emerge intraoperatively or postoperatively. (Conditional recommendation, Low-moderate certainty evidence)

What is the optimal operative approach for DTC?

RECOMMENDATION 15

- C. For patients with thyroid cancer >4 cm (cT3a), cancer of any size with gross extra-thyroidal extension (cT3b or cT4), or clinically apparent metastatic disease to lymph nodes (cN1) or distant sites (cM1), the initial surgical procedure should include a total thyroidectomy with gross removal of all primary tumor and node dissection unless there are contraindications to this procedure. (Strong recommendation, Moderate certainty evidence)

What is the optimal operative approach for DTC?

TABLE 5. EXTENT OF INITIAL THYROID SURGERY FOR DTC

Clinical stage	*Extent of thyroidectomy*[a]
cT1N0M0 (Unilateral)	Lobectomy
cT1 (m) N0M0 (Bilateral)	Total thyroidectomy
cT2N0M0 (Unilateral)	Lobectomy or Total thyroidectomy
cT2 (m) N0M0 (Bilateral)	Total Thyroidectomy
cT3-4 or cN1 or cM1	Total thyroidectomy

Clinical stage based upon AJCC 8th edition.
[a]If surgery chosen for initial therapy.
AJCC, American Joint Committee on Cancer.

When should completion thyroidectomy be performed?

RECOMMENDATION 16

- A. Completion thyroidectomy for cancer following initial lobectomy may be considered to address persistent primary malignancy, facilitate RAI administration, and/or enhance follow-up based upon higher estimated risk of recurrence identified postoperatively, accounting for recurrent laryngeal nerve function. (Conditional recommendation, Low-moderate certainty evidence)
- B. Completion thyroidectomy for OTC may be considered based on indications like other histological types of DTC. (Conditional recommendation, Very low certainty evidence)

What is the surgical approach to thyroglossal duct carcinoma?

RECOMMENDATION 17

- A. Initial surgical therapy for thyroid carcinoma arising within a thyroglossal duct (TGDCa) should include complete tumor/cyst excision along with the central portion of the hyoid bone (Sistrunk procedure). (Conditional recommendation, Low certainty evidence)
- B. A Sistrunk procedure and thyroidectomy may be considered for TGDCa with significant/suspicious thyroid nodularity to ensure complete resection of possible multicentric disease and/or for larger tumors, particularly in older patients, to facilitate RAI and/or enhance follow-up. (Conditional recommendation, Low certainty evidence)
- C. A Sistrunk procedure and total thyroidectomy should be performed for TGDCa with evidence of more advanced disease (e.g., gross extension of tumor into surrounding tissues, nodal or distant metastasis). (Strong recommendation, Moderate certainty evidence)

When should completion thyroidectomy following Sistrunk procedure be performed?

RECOMMENDATION 18

- A. Completion (total) thyroidectomy may be considered following resection of TGDCa with higher-risk factors (similar to completion thyroidectomy after lobectomy) or that proves to be a metastasis to the Delphian/prelaryngeal lymph node(s). (Conditional recommendation, Moderate certainty evidence)
- B. Completion thyroidectomy may be considered following resection of lower-risk TGDCa associated with significant/suspicious thyroid nodularity to ensure complete resection of possible multicentric disease, or for larger tumors, particularly in older patients, to facilitate RAI and/or enhance follow-up. (Conditional recommendation, Low certainty evidence)

When should prophylactic central-compartment lymph node resection be performed?

RECOMMENDATION 19

- A. Prophylactic central-compartment lymph node dissection should not be performed for most small, noninvasive, clinically node-negative PTC (cT1-T2, cN0) and for most FTCs. (Strong recommendation, Moderate certainty evidence)
- B. Prophylactic central-compartment neck dissection may be considered in patients with PTC and clinically uninvolved lymph nodes (cN0) who have advanced primary tumors (T3 or T4) or for whom the information will be used to plan further steps in therapy, but this approach should be weighed against the risks as they evolve during thyroidectomy. (Conditional recommendation, Low certainty evidence)

What is the best approach for therapeutic central and lateral compartment node resections?

RECOMMENDATION 20

- A. Therapeutic central-compartment (Level VI and upper Level VII) neck dissection for patients with clinically involved central nodes (cN1a) should accompany thyroidectomy to clear disease from the central neck. (Strong recommendation, Moderate certainty evidence)
- B. Therapeutic CLND with dissection of the ipsilateral central compartment lymph nodes is recommended to accompany lateral-compartment neck dissection and thyroidectomy for patients with clinically involved lateral neck lymph nodes (cN1b). (Conditional recommendation, Low certainty evidence)
- C. Therapeutic lateral neck compartmental lymph node dissection, typically including Levels IIa, III, IV and Vb, should be performed as part of initial surgical therapy for patients with biopsy-proven or clinically obvious metastatic lateral compartment cervical lymphadenopathy. (Strong recommendation, Moderate certainty evidence)

What is the appropriate perioperative approach to voice and parathyroid issues?

RECOMMENDATION 21

- Prior to surgery, the surgeon should review surgical risks with the patient, including potential for nerve and parathyroid injury, through the informed consent process and communicate with associated physicians, including anesthesia colleagues, important findings elicited during the preoperative evaluation. (Good Practice Statement)

Should the patient undergo voice or laryngeal examination prior to surgery?

RECOMMENDATION 22

- A. All patients undergoing thyroid surgery should undergo voice assessment as part of their preoperative physical examination. This should include the patient's description of vocal changes and the physician's assessment of voice. (Strong recommendation, Moderate certainty evidence)
- B. Preoperative laryngeal exam should be performed in all patients with:
  - **a. Preoperative dysphonia (Strong recommendation, Moderate certainty evidence)**
  - **b. History of cervical or upper chest surgery, which places the recurrent laryngeal nerve or vagus nerve at risk (Strong recommendation, Moderate certainty evidence)**
  - **c. Known thyroid cancer with posterior extrathyroidal extension or extensive central compartment or jugular chain nodal metastases (Strong recommendation, Low certainty evidence)**

How should the recurrent laryngeal nerves be assessed intraoperatively?

RECOMMENDATION 23

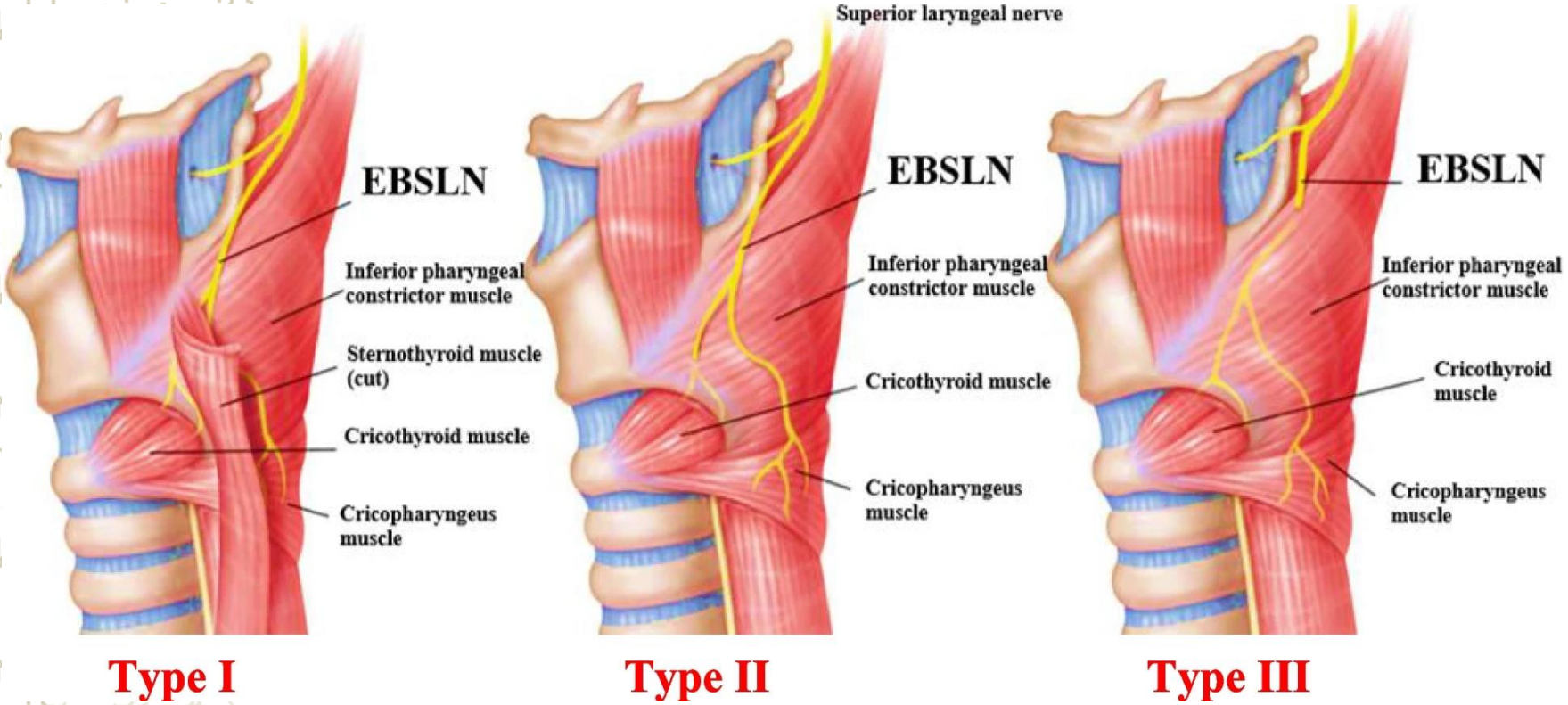
- A. Visual identification of the recurrent laryngeal nerve(s) (RLN) should be performed during thyroidectomy and/or para-tracheal node dissection, to preserve nerve integrity and function. (Good Practice Statement)
- B. Intraoperative neurophysiological monitoring of the RLN may be performed during thyroidectomy for malignancy in an effort to reduce the risk of RLN injury, particularly during total or re-operative thyroidectomy. (Conditional recommendation, Low-moderate certainty evidence)

How should the recurrent laryngeal nerves be assessed intraoperatively?

RECOMMENDATION 23

- C. Intraoperative identification and neurophysiological monitoring of the external branch of the superior laryngeal nerve (EBSLN) may be performed during thyroidectomy for malignancy in an effort to improve accurate nerve identification and improve voice outcomes. (Conditional recommendation, Moderate-high certainty evidence)
- D. Intraoperative vagal nerve or proximal RLN stimulation (with monitoring or laryngeal palpation) should be performed after initial lobectomy to assess RLN integrity and function prior to removing the contralateral lobe in an effort to avoid possible bilateral nerve injury. (Good Practice Statement)

Anatomy of the external branch of the superior laryngeal nerve (EBSLN)



Friedman classification. Type I: The EBSLN runs its whole course superficially or laterally to the IPC, descending with the superior thyroid vessels until it terminates in the CTM. Type II: the EBSLN penetrates the IPC about 1 cm proximal of the CTM. Type III: The EBSLN dives under the superior fibers of the IPC, remaining covered by this muscle throughout its course to the CTM

How should the parathyroid glands be managed intraoperatively and perioperatively?

RECOMMENDATION 24

- A. The parathyroid glands and their blood supply should be preserved during thyroid surgery to reduce the risk of hypoparathyroidism. Parathyroid glands, if devascularized or removed, should be auto-transplanted into nearby muscle after frozen section (of a portion) confirms benign parathyroid tissue. (Good Practice Statement)
- B. After total thyroidectomy and/or central lymph node dissection, or after unilateral operations that follow prior contralateral thyroid resections, parathyroid hormone-directed calcium and vitamin D supplementation (regular or selective) should be provided to reduce rates of hypocalcemia and shorten hospital stays compared with observation with serial calcium measurement alone. (Strong recommendation, Moderate certainty evidence)

Should drainage of the thyroidectomy bed be performed?

RECOMMENDATION 25

- Under most circumstances, drainage of the thyroidectomy bed is not recommended; it is associated with increased length of stay, may increase infections, and does not reduce the incidence of hematoma. (Conditional recommendation, High certainty evidence)

Selective use may be reasonable with very large (chiefly retrosternal) glands, excessive intraoperative bleeding, and/or bleeding disorders.

How should the surgeon manage postoperative voice changes and symptoms after surgery if they occur?

RECOMMENDATION 26

- A. Patients should have their voice assessed in the postoperative period. Formal laryngeal exam should be performed if the voice is abnormal. (Good Practice Statement)
- B. Important intraoperative findings and details of postoperative care should be communicated by the surgeon to the patient and other physicians who are important in the patient's post-operative care. (Good Practice Statement)
- C. If there is known recurrent laryngeal nerve injury from surgery, timely referral to a speech language pathologist and physician specializing in voice is recommended. (Good Practice Statement)

What are the basic principles of histopathologic evaluation of thyroidectomy samples?

RECOMMENDATION 27

- 1. In addition to the essential histopathologic features of the tumor required for the latest AJCC thyroid cancer staging (including status of resection margins), pathology reports should include additional information helpful for risk assessment, including: *
  - **the presence of vascular invasion and**
  - **the number of invaded vessels,**
  - **number of lymph nodes examined and involved with tumor,**
  - **size of the largest metastatic focus to the lymph nodes, and**
  - **presence or absence of extranodal extension of the metastatic tumor.**
- *(Good Practice Statement)

What are the basic principles of histopathologic evaluation of thyroidectomy samples?

RECOMMENDATION 27

- 2. Histopathologic subtypes of DTC associated with unfavorable (e.g., tall cell, columnar cell, and hobnail subtypes of PTC; widely invasive FTC and OTC; high-grade follicular cell-derived non-ATC) or favorable (e.g., IEFVPTC with minimal invasion, minimally invasive FTC) outcomes should be identified during histopathologic examination and reported. (Good Practice Statement)
- 3. Histopathologic subtypes associated with familial syndromes (cribriform-morular carcinoma can be associated with familial adenomatous polyposis, PHTS associated FTC or PTC) should be identified during histopathologic examination and reported. (Good Practice Statement)

Major histological subtypes of differentiated thyroid carcinomas. FA, follicular adenoma; FTC, follicular thyroid carcinoma; PTC, papillary thyroid carcinoma; NIFTP, noninvasive follicular thyroid neoplasm with papillary-like nuclear features; IEFVPTC, invasive encapsulated follicular variant of papillary thyroid carcinoma.

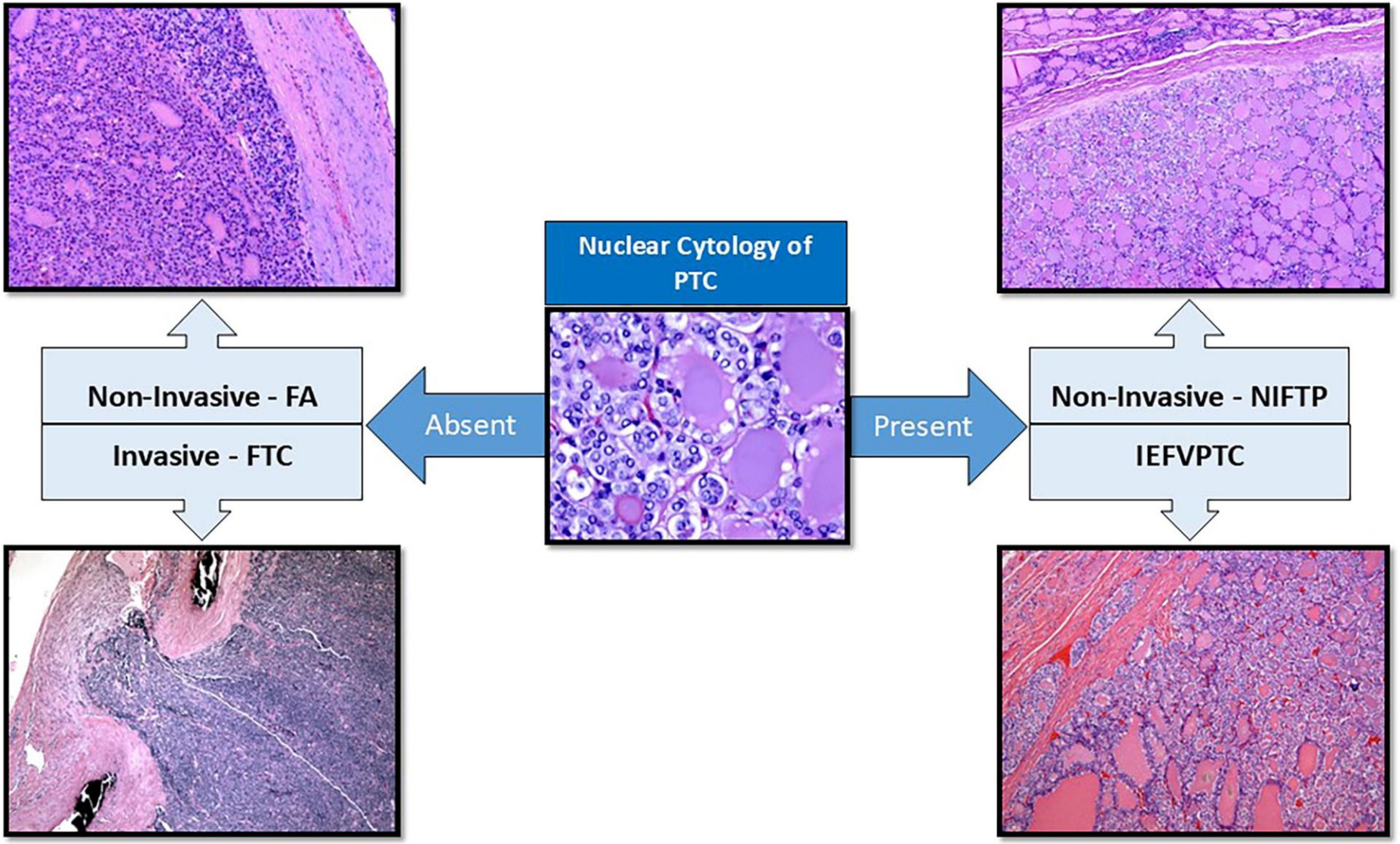


TABLE 3. WHO PATHOLOGICAL CLASSIFICATION OF DIFFERENTIATED THYROID CARCINOMA (WHO, 5TH EDITION)[24]

Follicular cell-derived neoplasms	*Subtypes*
Low-risk neoplasms	1. NIFTP[a,b] 2. Follicular tumor of uncertain malignant potential 3. Hyalinizing trabecular tumor
Malignant neoplasms	1. Follicular thyroid carcinoma a. Minimally invasive b. Encapsulated angioinvasive c. Widely invasive 2. Invasive encapsulated follicular variant papillary carcinoma 3. Papillary thyroid carcinoma-subtypes a. Classical b. Encapsulated classical c. Infiltrative follicular d. Tall cell e. Columnar cell f. Hobnail g. Diffuse sclerosing h. Solid / trabecular i. Warthin-like j. Oncocytic k. Others[c] 4. Oncocytic carcinoma a. Minimally invasive b. Encapsulated angioinvasive c. Widely invasive

	e. Widely invasive
Malignant neoplasms—high-grade follicular-cell derived non-anaplastic carcinoma	1. Poorly differentiated carcinoma (Turin-criteria): a. Solid/trabecular architecture b. Absence of nuclear features of papillary thyroid carcinoma c. Tumor necrosis d. Mitotic index ≥3/10 high power fields (HPFs) e. And/or convoluted tumor nuclei 2. Differentiated high-grade thyroid carcinoma a. Differentiated cytological and architectural features b. At least one the following two histomorphologic features c. Mitotic count ≥5/2 mm^2 and/or tumor necrosis
Other rare neoplasms	1. Salivary gland-type carcinomas a. Mucoepidermoid carcinoma of the thyroid b. Secretory carcinoma of salivary gland type 2. Thyroid tumors of uncertain histogenesis a. Sclerosing mucoepidermoid carcinoma with eosinophilia b. Cribriform morular thyroid carcinoma 3. Thymic tumors within the thyroid

[a]Formerly classified as noninvasive and encapsulated follicular variant of papillary thyroid carcinoma.
[b]See Table 2.
[c]Includes rare subtypes such as PTC with fibromatosis/fasciitis-like stroma, clear cell subtype, spindle cell subtype, and so forth.
PTC, papillary thyroid carcinoma; WHO, World Health Organization.

How should risk of recurrence and initial assessment be performed after surgery?

RECOMMENDATION 28

- A. The 2025 ATA Risk Stratification System, which evaluates the histopathologic features of the tumor and number of cervical lymph nodes in combination with the AJCC staging system, postoperative imaging, and serum Tg and TgAb testing (if appropriate), is recommended to determine the risk of structural disease persistence/recurrence (locoregionally and/or distantly) and/or survival in patients with DTC. (Strong Recommendation, Moderate certainty evidence)
- B. Molecular profiling of histologic specimens postoperatively is not recommended routinely. However, if such data have been obtained, they can be used to further estimate risks of recurrence derived from the 2025 ATA Risk Stratification System. (Conditional recommendation, Low certainty evidence)

TABLE 6. AJCC/UICC TNM STAGING: THE 8TH EDITION TNM[27,595]

	TNM	
CATEGORY[a]	*Code*	*Description*
Primary tumor (pT)	TX	Primary tumor cannot be assessed
	T0	No evidence of primary tumor
	T1	Tumor ≤2 cm limited to thyroid
	• T1a	Tumor ≤1 cm limited to thyroid
	• T1b	Tumor >1 cm but ≤2 cm limited to thyroid
	T2	Tumor >2 cm but ≤4 cm limited to thyroid
	T3	Tumor >4 cm or minimal extrathyroidal extension
	• T3a	Tumor >4 cm limited to thyroid
	• T3b	Gross extrathyroidal extension to strap muscles
	T4	Gross extrathyroidal extension to major neck structures
	• T4a	Invading soft tissue, larynx, trachea, esophagus, or recurrent laryngeal nerve
	• T4b	Invading prevertebral fascia or encasing carotid/mediastinal vessels
Regional lymph node (pN)	NX	Regional lymph nodes cannot be assessed
	N0	No evidence of regional lymph node metastasis
	• N0a	One or more cytological or histologically confirmed benign lymph nodes
	• N0b	No radiological/clinical evidence of metastasis
	N1	Metastasis to regional nodes
	• N1a	Metastasis to level VI or VII (pretracheal, paratracheal, prelaryngeal / Delphian or upper mediastinal) lymph nodes; this can be unilateral or bilateral disease
	• N1b	Metastasis to unilateral, bilateral or contralateral lateral neck lymph nodes (levels I, II, III, IV or V) or retropharyngeal lymph nodes
Distant metastasis (M)	M0	No distant metastasis
	M1	Distant metastasis present
STAGING		
1. <55 YEARS	Stage I	Any T, Any N, M0
	Stage II	Any T, Any N, M1
2. ≥55 YEARS	Stage I	T1–T2, N0/NX, M0
	Stage II	T1–T2, N1, M0 or T3a/T3b, Any N, M0
	Stage III	T4a, Any N, M0
	Stage IVA	T4b, Any N, M0
	Stage IVB	Any T, Any N, M1

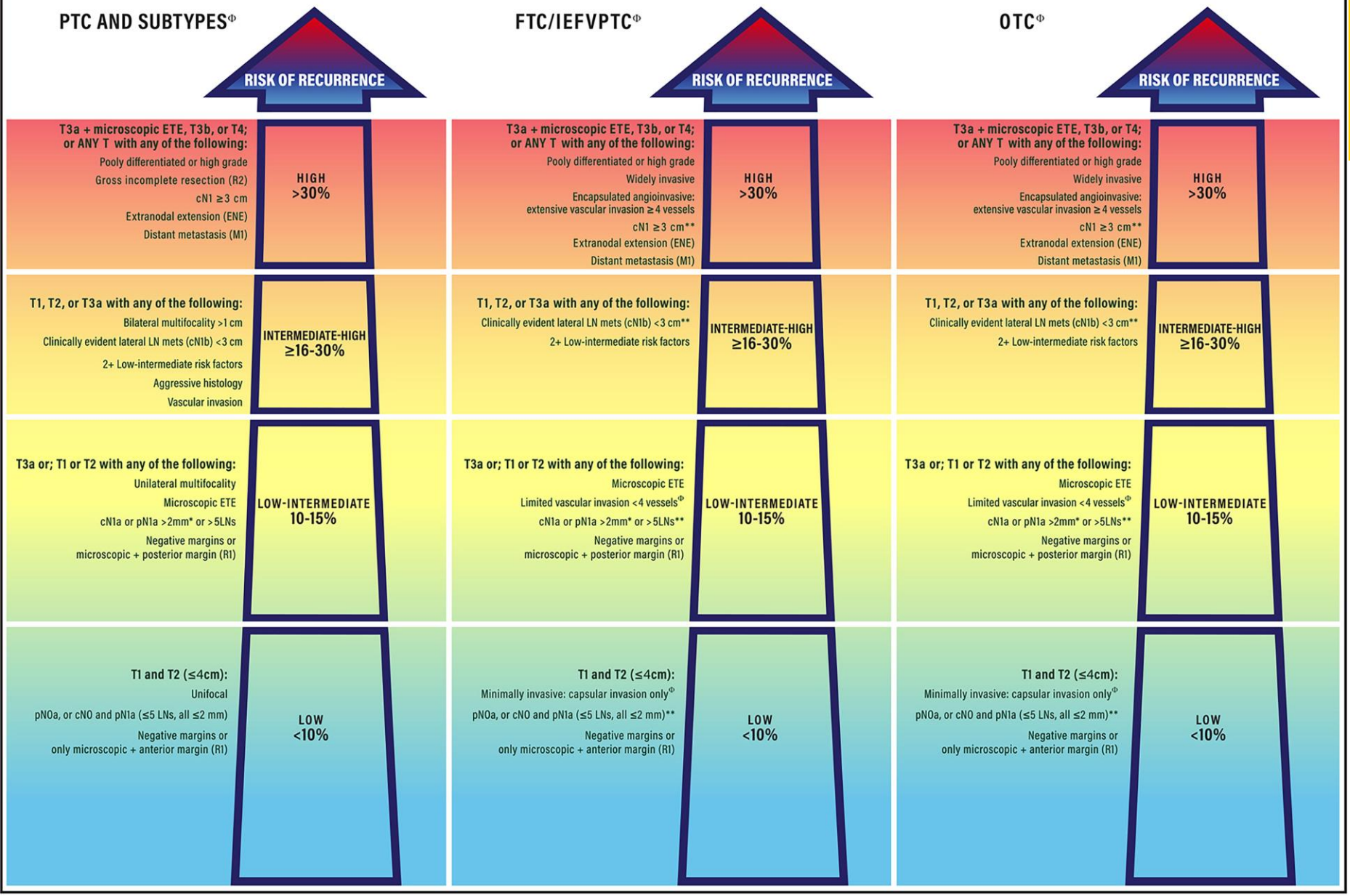
[a]Categories may be subdivided: (s) solitary tumor and (m) multifocal tumor (the largest tumor determines the classification).
UICC, Union for International Cancer Control.

Major Changes in AJCC/UICC TNM 8th Edition—Differentiated Thyroid Carcinoma, Compared with the 7th Edition

TABLE 7. MAJOR CHANGES IN AJCC/UICC TNM 8TH EDITION—DIFFERENTIATED THYROID CARCINOMA, COMPARED WITH THE 7TH EDITION[595,596]

A. Age cutoff used for staging was increased from 45 to 55 years at diagnosis.
B. Minimal extrathyroidal extension detected only on histological examination was removed from the definition of T3 disease and therefore has no impact on either T category or overall stage.
C. N1 disease no longer upstages a patient to stage III; if the patient's age is <55 years at diagnosis, N1 disease is stage I; if age is ≥55 years, N1 disease is stage II.
D. T3a is a new category for tumors >4 cm confined to the thyroid gland.
E. T3b is a new category for tumors of any size demonstrating gross extrathyroidal extension into strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles).
F. Level VII lymph nodes, previously classified as lateral neck lymph nodes (N1b), were reclassified as Central neck lymph nodes (N1a).
G. In DTC, the presence of distant metastases in older patients is classified as stage IVB disease rather than stage IVC disease; distant metastasis in anaplastic thyroid cancer continues to be classified as stage IVC disease.

Estimated Risk of Structural Recurrence



LEGEND: PTC: Papillary Thyroid Carcinoma FTC/IEFVPTC: Follicular Thyroid Carcinoma/Invasive Encapsulated Follicular Variant of Papillary Thyroid Carcinoma OTC: Oncocytic Thyroid Carcinoma [Φ]: WHO 2022 definition

*: No clear cutoffs for LNs between low-intermediate and high-intermediate risk groups. In general, smaller size and fewer lymph node metastases are associated with lower risk of recurrence.

**: LN mets are uncommon in OTC and FTC/IEFVPTC

How should clinical response to surgery be assessed?

RECOMMENDATION 29

- The ATA Response Criteria should be used to categorize response to surgery prior to determining intensity of additional therapy or monitoring in combination with the ATA Risk of Recurrence Estimates. (Strong Recommendation, Moderate certainty evidence)

Response Criteria After Initial Therapy Based on Type of Intervention

TABLE 9. RESPONSE CRITERIA AFTER INITIAL THERAPY BASED ON TYPE OF INTERVENTION

Response to therapy	*Post total thyroidectomy and/or neck dissection with RAI ablation or therapy*	*Post total thyroidectomy and/or neck dissection without RAI ablation*	*Post hemithyroidectomy*	*TSH goal*
Excellent	Nonstimulated Tg <0.2 or stimulated Tg <1 and negative imaging	Nonstimulated Tg <2.5	Normal or low-risk nodules in the contralateral lobe, or contralateral lobe nodules with benign biopsy AND no abnormal lymph nodes on imaging	TSH within normal reference range
Indeterminate	Nonspecific findings on imaging studies or nonstimulated Tg 0.2–1 or stimulated Tg 1–10 or stable/ declining TgAb levels	Nonspecific findings on imaging studies or nonstimulated Tg 2.5–5, or stable/ declining TgAb levels	N/A[a]	TSH within normal reference range[b]
Biochemically incomplete	Non-stimulated Tg >1 or stimulated Tg >10 or increasing TgAb levels and negative imaging	Nonstimulated Tg >5 or increasing TgAb levels and negative imaging	N/A[a]	TSH below normal reference range[c]
Structurally incomplete	Structural evidence of disease (suspicious imaging or biopsy proven local or distant metastatic disease)	Structural evidence of disease (suspicious imaging or biopsy proven local or distant metastatic disease)	Structural evidence of disease (suspicious imaging or biopsy proven local or distant metastatic disease)	TSH below normal reference range[c]

[a]See Recommendation 48 for specific comments regarding Tg levels (ng/mL) in patients treated with hemithyroidectomy.
[b]Data on optimal TSH target range are inconclusive.
[c]Data on optimal TSH target range are inconclusive and/or conflicting. If there is progression of residual disease or development of new recurrence, targeting a TSH below normal reference range may be reasonable. However, comorbidities such as atrial fibrillation and osteoporosis should be factored into the decision making process.
RAI, radioactive iodine; Tg, thyroglobulin; TgAb, anti-thyroglobulin antibody; TSH, thyrotropin.

When should Tg levels be measured after surgery?

RECOMMENDATION 30

- A. Measuring a postoperative serum Tg level 6–12 weeks after total thyroidectomy while on thyroid hormone therapy or after TSH stimulation is recommended. Such measurements may guide additional decision-making regarding clinical management. (Strong recommendation, Low certainty evidence)
- B. Measurement of serum Tg on one occasion 6–12 weeks after thyroid lobectomy with a normal TSH may be helpful to ensure that it is not unexpectedly elevated; however, a specific cutoff value is uncertain. (Good Practice Statement)

What is the role of ultrasound and other imaging techniques (CT, MRI, 18FDG-PET-CT) after primary resection?

RECOMMENDATION 31

- A. Ultrasound to evaluate the thyroid bed and central and lateral cervical lymph node compartments is the preferred method of imaging surveillance for most DTC. (Strong recommendation, Moderate certainty evidence)
- B. If the serum Tg level after surgery is above the excellent response range (see Table 9), and/or there are Tg Ab, cervical ultrasound and/or cross-sectional imaging should be performed prior to administering RAI. (Good Practice Statement)
- C. Six to 12 months following completion of initial therapy, cervical ultrasound to evaluate the thyroid bed and central and lateral cervical lymph node compartments should be performed. Timing and frequency thereafter are informed by the patient's risk for residual or recurrent disease and response to therapy. (Good Practice Statement)

What is the role of ultrasound and other imaging techniques (CT, MRI, 18FDG-PET-CT) after primary resection?

RECOMMENDATION 31

- D. Suspi…n may be followed wit…as the recurrent la…ional recommend…
- E. If cyto…nce treatment d…ous lymph nodes or les…d with FNA for cyt…ood Practice Sta…

For lymph nodes ≥8–10 mm in shortest diameter, a cystic appearance or hyperechoic foci in patients with a history of DTC should be considered malignant.

In addition, peripheral vascularity is worrisome, with a high sensitivity/specificity for malignancy.
With such findings, FNA biopsy is justified.

A hyperechoic hilum and central vascularity are reassuring.
A round shape, hypoechoic appearance, or the loss of the hyperechoic hilum does not, as isolated findings, justify FNA biopsy.

What is the role of ultrasound and other imaging techniques (CT, MRI, 18FDG-PET-CT) after primary resection?

RECOMMENDATION 31

- F. When Tg (or TgAb) levels rise following total thyroidectomy for DTC, and cervical ultrasound demonstrates no structural disease or only minimal tumor burden, additional cross-sectional imaging to evaluate common metastatic sites (e.g. lungs and bone) should be performed. (Good Practice Statement)
- G. When Tg (or TgAb) levels rise following total thyroidectomy for OTC and PDTC, and cervical ultrasound demonstrates no structural disease or shows only minimal tumor burden, 18FDG-PET/CT may be considered. (Conditional recommendation, Low certainty of evidence)

What is the role of RAI after thyroidectomy in the primary management of DTC?

RECOMMENDATION 32

- A. Remnant ablation is not recommended routinely after total thyroidectomy for patients with ATA low-risk DTC. (Strong recommendation, High certainty evidence)
- B. RAI adjuvant therapy may be considered after total thyroidectomy in patients with ATA low-intermediate and intermediate-high risk of recurrent DTC. (Conditional recommendation, Low certainty evidence)
- C. RAI adjuvant therapy is recommended routinely after total thyroidectomy for patients with ATA high-risk DTC. (Strong recommendation, Moderate certainty evidence)
- D. In patients with an initial diagnosis of DTC with distant metastases, RAI therapy is recommended routinely after total thyroidectomy. (Strong recommendation, Moderate certainty evidence)

Summary of Recommendations for Initial RAI Following Thyroidectomy

TABLE 10. SUMMARY OF RECOMMENDATIONS FOR INITIAL RAI FOLLOWING THYROIDECTOMY[a]

Risk category	*Typical RAI recommendation*	*Recommended ^{131}I activity level*	*Goals of therapy*
Low	No	1.1–1.85 GBq (30–50 mCi)	None or remnant ablation
Intermediate-low and intermediate-high	Consider	1.1–3.7 GBq (30–100 mCi)	Remnant ablation +/– adjuvant therapy
High	Yes	3.7–5.55 GBq (100–150 mCi)	Remnant ablation and adjuvant therapy
Distant metastases	Yes	3.7–7.4 GBq (100–200 mCi) or consider dosimetry	Treatment of known disease, remnant ablation

[a]Note that th… comorbid conditions, acc… g activity level. Consiste… sciplinary management re…
RAI, radioac…

Remnant ablation

Eliminate residual benign thyroid tissue in the thyroid bed to facilitate treatment monitoring.

Adjuvant therapy

Additional RAI administered to reduce the risk of recurrence.

Treatment of known disease

Treatment of known areas of residual/metastatic disease.

Should radioiodine be administered for OTC treatment?

RECOMMENDATION 33

- Outcome data are limited in OTC; thus, specific recommendations regarding use of RAI are not certain. If RAI is not administered empirically, evaluation of iodine avidity with a diagnostic whole-body scan (WBS) may be considered. (Conditional recommendation, Very low certainty evidence)

How should patients be prepared for RAI administration?

RECOMMENDATION 34

- A. In patients with DTC in whom RAI remnant ablation or adjuvant therapy is planned, preparation with rhTSH stimulation is preferred over thyroid hormone withdrawal. (Strong recommendation, High certainty evidence)
- B. In patients with DTC of any risk level with significant comorbidity that may preclude thyroid hormone withdrawal prior to RAI administration, rhTSH preparation should be considered. (Good Practice Statement)

How should patients be prepared for RAI administration?

RECOMMENDATION 34

- C. If thyroid hormone withdrawal is planned prior to RAI therapy or diagnostic testing, LT4 should be withdrawn for 3–4 weeks. If LT4 is withdrawn for ≥4 weeks, substitution of LT4 with liothyronine (LT3) in the initial weeks should be considered. In such circumstances LT3 should be withdrawn for at least 2 weeks. Serum TSH should be measured prior to radioisotope administration to evaluate the degree of TSH elevation. (Good Practice Statement)
- D. A goal of TSH >30 mIU/L should be employed in preparation for RAI therapy or diagnostic testing. (Good Practice Statement)
- E. In patients with known distant metastases, either LT4 withdrawal or rhTSH can be used for preparation. (Conditional recommendation, Low certainty evidence)

Should a low-iodine diet be prescribed prior to RAI administration?

RECOMMENDATION 35

- A low-iodine diet for approximately 1–2 weeks should be used for patients undergoing RAI remnant ablation or treatment. (Good Practice Statement)

When and how should diagnostic radioiodine WBS be performed?

RECOMMENDATION 36

- Postoperative diagnostic ^{123}I or low-dose ^{131}I WBS may be considered for patients undergoing RAI treatment prior to their therapeutic (ablative, adjuvant, or treatment) administration to help guide treatment planning. (Conditional recommendation, Low certainty evidence)

Should post-therapy WBS be performed?

RECOMMENDATION 37

- Post-RAI therapy scans should be performed after RAI treatment. (Strong recommendation, Moderate certainty evidence)

Should single photon emission computed tomography with computed tomography be performed with the WBS?

RECOMMENDATION 38

- Single photon emission computed tomography with computed tomography (SPECT/CT) may be performed when available with diagnostic or post-treatment WBS. (Conditional recommendation, Low certainty evidence)

How should patients be educated regarding radiation safety?

RECOMMENDATION 39

- Patients should be provided oral and written instructions before preparation for RAI begins to minimize exposure to their families and members of the public, consistent with guidelines in the country where therapy is performed (e.g., in the United States, those of the Nuclear Regulatory Commission). (Good Practice Statement)

How do you counsel and minimize risks of RAI side effects to the salivary glands and lacrimal ducts?

RECOMMENDATION 40

- A. Patients should be counseled that RAI treatment may be associated with (acute and chronic) salivary gland morbidity, lacrimal duct stenosis, and potential risk of secondary malignancies. (Good Practice Statement)
- B. For prevention of salivary gland side effects after RAI, general measures including hydration are recommended. (Good Practice Statement)
- C. Patients with xerostomia are at increased risk of dental caries and should discuss preventive strategies with their dental health professional. (Good Practice Statement)
- D. Surgical correction should be considered for nasolacrimal outflow obstruction, which often presents with excessive tearing (epiphora) but also predisposes to infection. (Good Practice Statement)

How should patients be counseled regarding the risk of second primary malignancy after receiving RAI therapy?

RECOMMENDATION 41

- Patients should be counseled about the risks of second primary malignancy (SPM) after RAI treatment for DTC. The absolute increase in risk attributable to RAI appears to be small and does not warrant additional screening for SPM. (Good Practice Statement)

What other testing should patients receiving RAI therapy undergo?

RECOMMENDATION 42

- Patients receiving therapeutic administration of RAI should have a baseline complete blood count and assessment of renal function. (Good Practice Statement)

How should patients be counseled about RAI therapy and pregnancy, nursing, and gonadal function?

RECOMMENDATION 43

- A. Female patients of reproductive age receiving RAI therapy should have a negative screening evaluation for pregnancy prior to RAI administration and avoid pregnancy for at least 6 months after receiving RAI. (Good Practice Statement)
- B. RAI should not be given to nursing female patients. Depending on the clinical situation, RAI therapy should be deferred until lactating women have stopped breast-feeding or pumping for at least 3 months. A diagnostic ^{123}I scan may be performed in recently lactating women to detect breast uptake that may warrant deferral of therapy. (Good Practice Statement)
- C. Male patients receiving cumulative radioiodine activities >14.8 GBq (400 mCi) should be counseled regarding potential risks of infertility. (Good Practice Statement)
- D. Female patients receiving RAI should be counseled that such therapy has not been shown to impact future fertility. (Good Practice Statement)

What is the role of radiotherapy, with or without chemotherapy, in patients with DTC?

RECOMMENDATION 44

- A. Adjuvant external beam radiotherapy (EBRT) for patients with DTC with high-risk features for locoregional disease progression (such as aggressive histologic subtype, gross extrathyroidal extension, positive margins, and visceral or soft tissue invasion) may be considered in select cases, especially if the expected disease progression would not be amenable to salvage surgery. The potential benefit of improving locoregio[illegible]e absence of data demonstratin[illegible]sks of clinically meaningful[illegible]y evidence)

Aggressive histologic subtype,
Gross extrathyroidal extension,
Positive margins, and
Visceral or soft tissue invasion

If the expected disease progression would not be amenable to salvage surgery.

What is the role of radiotherapy, with or without chemotherapy, in patients with DTC?

RECOMMENDATION 44

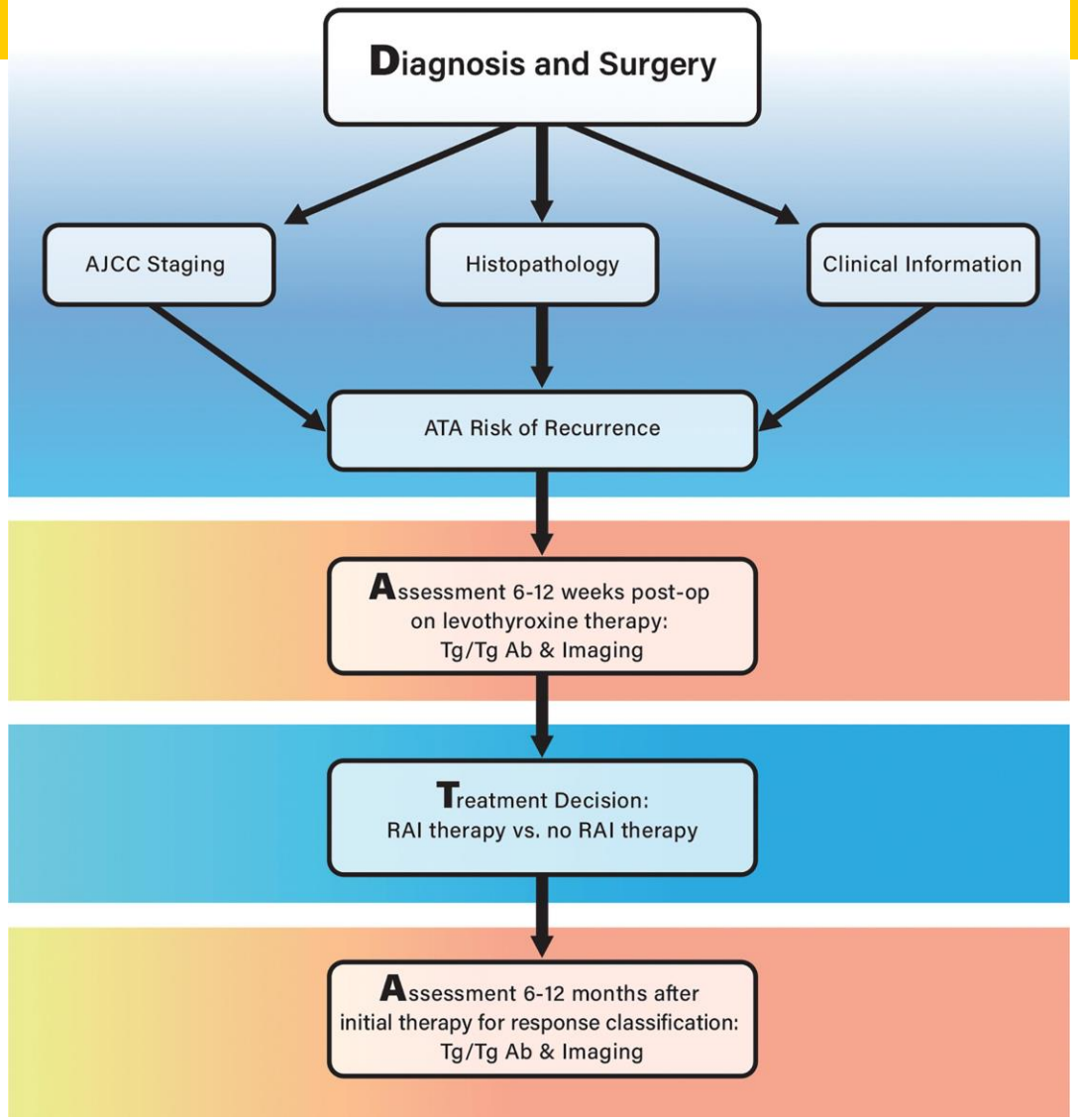
- B. EBRT with or without concurrent chemotherapy in patients with DTC with gross residual disease in the postoperative setting or with locally advanced unresectable disease may be considered in select patients who may benefit from improved locoregional control. EBRT with or without concurrent chemotherapy may increase locoregional control but also causes acute- and long-term treatment-related toxicity. (Conditional recommendation, Low certainty evidence)

Long-Term Management and Advanced DTC Management

What are the appropriate features of long-term management of patients with DTC?

DATA Framework for Initial Therapy

- DATA framework applied to the first 12 months after DTC diagnosis. Imaging timing and type depend on risk of recurrence, Tg levels, and pathology/clinical factors. DTC, differentiated thyroid cancer; Tg, thyroglobulin.



What is the appropriate degree of TSH suppression in patients treated for DTC?

RECOMMENDATION 45

- Individualization of decisions to initiate TSH suppression to below the reference range is recommended based on potential benefits and risks; recognizing that patients with high-risk disease may be more likely to benefit from a TSH in the subnormal range than those with low-risk disease (see Table 9). (Conditional recommendation, Low certainty evidence)

How long should TSH suppression to below the reference range be maintained?

RECOMMENDATION 46

- A. Long-term TSH suppression is not suggested for patients with low- or intermediate-risk disease who have no evidence of biochemical or structural recurrence. (Conditional recommendation, Low certainty evidence)
- B. Risks versus benefits of TSH suppression and TSH goals should be re-evaluated over time. (Good Practice Statement)

What is the role of serum Tg measurement in the follow-up of DTC?

RECOMMENDATION 47

- A. Serum Tg should be measured by an assay that is calibrated against the BCR457 standard. Tg antibodies should be quantitatively assessed with every measurement of serum Tg. (Good Practice Statement)
- B. Measure serum Tg (on thyroid hormone therapy) after total thyroidectomy, with or without RAI, to monitor for response to therapy and to determine recurrence (although the predictive value is greater after RAI). (Strong recommendation, Moderate certainty of evidence)
- C. Measurement of serum Tg during initial follow-up while receiving thyroxine therapy should be undertaken every 6–12 months. More frequent serum Tg measurements may be appropriate for ATA intermediate-high or high-risk patients. (Good Practice Statement)

What is the role of serum Tg measurement in the follow-up of DTC?

RECOMMENDATION 47

- D. Measurement of serum Tg on thyroid hormone in patients after lobectomy during initial follow-up is not recommended routinely (see Recommendation 30). (Conditional recommendation, Very low certainty evidence)
- E. In patients with circulating anti-Tg antibodies, trends of serial TgAb levels using the same assay may be useful to monitor disease. Current Tg immunometric assays (IMA) and radioimmunoassays (RIA) are often affected by TgAb, and Tg liquid chromatography-tandem mass spectrometry (LC-MS/MS) has low sensitivity. These should not be solely relied upon to monitor patients with circulating TgAb levels. Imaging is the primary modality for monitoring in this population. (Conditional recommendation, Low certainty evidence)

Can monitoring be de-escalated or discontinued in patients with low-risk DTC?

RECOMMENDATION 48

- 1. For patients with low-risk DTC treated with total thyroidectomy and RAI and a sustained excellent response 5–8 years after initial therapy, routine ultrasound can be discontinued, and patients can be followed subsequently with biochemical markers alone every 1–2 years. (Conditional recommendation, Low certainty of evidence)
- 2. Patients with low-risk DTC treated with total thyroidectomy and RAI and sustained excellent response for 10–15 years do not require continued routine biochemical monitoring for thyroid cancer and should be considered to have achieved a complete remission. (Good Practice Statement)
- 3. For patients with low-risk DTC treated with a total thyroidectomy alone and a sustained excellent response 5–8 years after initial therapy, routine ultrasound can be discontinued, and patients can be followed subsequently with biochemical markers alone every 1–2 years. (Conditional recommendation, Low certainty of evidence)

Can monitoring be de-escalated or discontinued in patients with low-risk DTC?

RECOMMENDATION 48

- 4. Patients with low-risk DTC treated with total thyroidectomy alone and sustained excellent response for 10–15 years do not require continued routine biochemical monitoring for thyroid cancer and have achieved a complete remission. (Good Practice Statement)
- 5. For patients with low-risk DTC treated with lobectomy, if initial ultrasound is negative, subsequent ultrasounds should be performed every 1–3 years for 5–8 years after initial therapy. Nodules in the residual lobe should be monitored as per ATA thyroid nodule guidelines. (Good Practice Statement)
- 6. For patients with low-risk DTC treated with lobectomy, if postoperative Tg is not markedly elevated (see Recommendation 30), additional Tg testing is not recommended routinely. (Good Practice Statement)

TABLE 11. LOW-RISK DTC WITH EXCELLENT RESPONSE TO THERAPY DE-ESCALATION RECOMMENDATIONS

Treatment and response to therapy	*Unstimulated thyroglobulin*	*TSH*	*Suggested frequency of neck ultrasound*
Hemithyroidectomy	Once postoperatively (see **Recommendation 48**)	Normal	[a]Every 1–3 years for 5–8 years
Total thyroidectomy, no RAI Excellent response	<2.5 ng/mL with undetectable TgAb	Normal	Every 1–3 years for 5–8 years, then discontinue unless Tg level rises or TgAb becomes newly detectable
Total thyroidectomy + RAI Excellent response	<0.2 ng/mL with undetectable TgAb	Normal	Every 1–3 years for 5–8 years and then discontinue unless Tg level rises or TgAb becomes newly detectable

Recommendations on ultrasound monitoring in low-risk patients after total thyroidectomy with excellent biochemical response and no suspicious features on imaging. Imaging is indicated in patients with rising thyroglobulin (Tg), new development of anti-thyroglobulin antibodies (TgAb), concerning physical exam, or symptoms. Type and location of imaging depends on the histological type of thyroid cancer and other pathology features. Use of Tg levels following hemithyroidectomy, and use of neck ultrasound in patients with FTC and OTC require further study.

[a]Assuming no nodules in residual lobe requiring monitoring as per ATA thyroid nodule guidelines.

ATA, American Thyroid Association.

Table 11. Low-Risk DTC with Excellent Response to Therapy De-escalation Recommendations

When should neck ultrasound and other imaging techniques (WBS, SPECT-CT, and 18FDG-PET-CT) be performed during follow-up?

Neck ultrasound

- Considerations regarding neck ultrasound after surgery are reviewed in Recommendation 31.

What is the role of ultrasound and other imaging techniques (CT, MRI, 18FDG-PET-CT) after primary resection?

RECOMMENDATION 31

- *A. Ultrasound to evaluate the thyroid bed and central and lateral cervical lymph node compartments is the preferred method of imaging surveillance for most DTC. (Strong recommendation, Moderate certainty evidence)*
- *B. If the serum Tg level after surgery is above the excellent response range (see Table 9), and/or there are Tg Ab, cervical ultrasound and/or cross-sectional imaging should be performed prior to administering RAI. (Good Practice Statement)*
- *C. Six to 12 months following completion of initial therapy, cervical ultrasound to evaluate the thyroid bed and central and lateral cervical lymph node compartments should be performed. Timing and frequency thereafter are informed by the patient's risk for residual or recurrent disease and response to therapy. (Good Practice Statement)*

What is the role of ultrasound and other imaging techniques (CT, MRI, 18FDG-PET-CT) after primary resection?

RECOMMENDATION 31

- *D. Suspicious lymph nodes or lesions <8–10 mm in shortest dimension may be followed without FNA unless they grow or threaten vital structures (such as the recurrent laryngeal nerve, trachea, esophagus, or great vessels). (Conditional recommendation, Low certainty evidence)*
- *E. If cytological diagnosis of recurrent or metastatic DTC would influence treatment decisions or change management, ultrasonographically suspicious lymph nodes or lesions ≥8–10 mm in the shortest dimension should be assessed with FNA for cytology and measurement of Tg in the needle washout fluid. (Good Practice Statement)*

When should neck ultrasound and other imaging techniques (WBS, SPECT-CT, and 18FDG-PET-CT) be performed during follow-up?

Diagnostic RAI WBS

RECOMMENDATION 49

- A. Patients who have undergone lobectomy or total thyroidectomy without RAI should not undergo surveillance radioiodine WBS. (Good Practice Statement)
- B. Patients with DTC who are at low- and low-intermediate risk of recurrence and who have excellent response to therapy do not require routine diagnostic radioiodine WBS during follow-up. (Conditional recommendation, Low certainty evidence)
- C. Patients with DTC who are at intermediate-high and high risk of recurrence can be evaluated with diagnostic radioiodine WBS to evaluate for iodine-avid disease if there is clinical suspicion for recurrence. WBS, if undertaken, can be performed with 123I or low activity 131I. (Conditional recommendation, Low certainty evidence)
- D. SPECT-CT radioiodine imaging may be performed in addition to planar imaging to anatomically localize the radioiodine uptake and distinguish between likely cancer and nonspecific uptake. (Conditional recommendation, Low certainty evidence)

When should neck ultrasound and other imaging techniques (WBS, SPECT-CT, and 18FDG-PET-CT) be performed during follow-up?

^{18}FDG-PET/CT scanning

RECOMMENDATION 50

- A. Imaging using 18FDG-PET/CT scanning may be performed in patients with DTC at high risk of recurrence with elevated serum Tg levels, particularly in patients with OTC or aggressive histologies and in patients who have a history of negative RAI imaging. (Conditional recommendation, Moderate certainty evidence)
- B. Imaging with 18FDG-PET/CT scanning may also be employed: (i) as a prognostic tool in patients at highest risk for rapid disease progression and disease-specific mortality and (ii) as an evaluation of post-treatment response following systemic or local therapy of invasive disease. (Conditional recommendation, Low certainty evidence)

Is ongoing risk stratification (response to therapy) useful in guiding long-term disease surveillance and therapeutic management decisions?

RECOMMENDATION 51

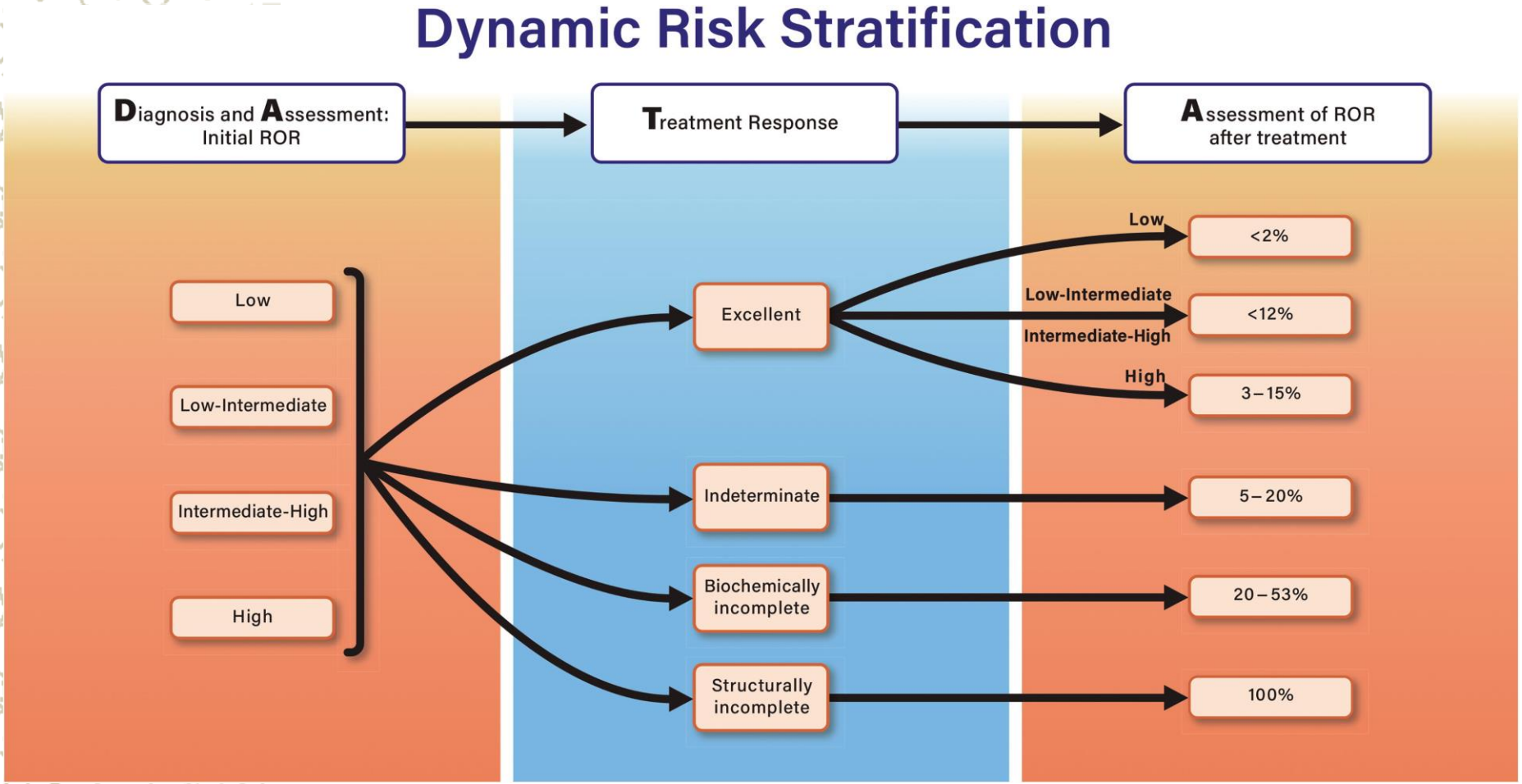
- Ongoing risk stratification (dynamic risk assessment), when used in combination with the initial risk of recurrence, allows the clinician to provide individualized management recommendations while risk estimates evolve over time and should be used to inform timing and type of imaging. (Good Practice Statement)

Is ongoing risk stratification (response to therapy) useful in guiding long-term disease surveillance and therapeutic management decisions?

RECOMMENDATION 51

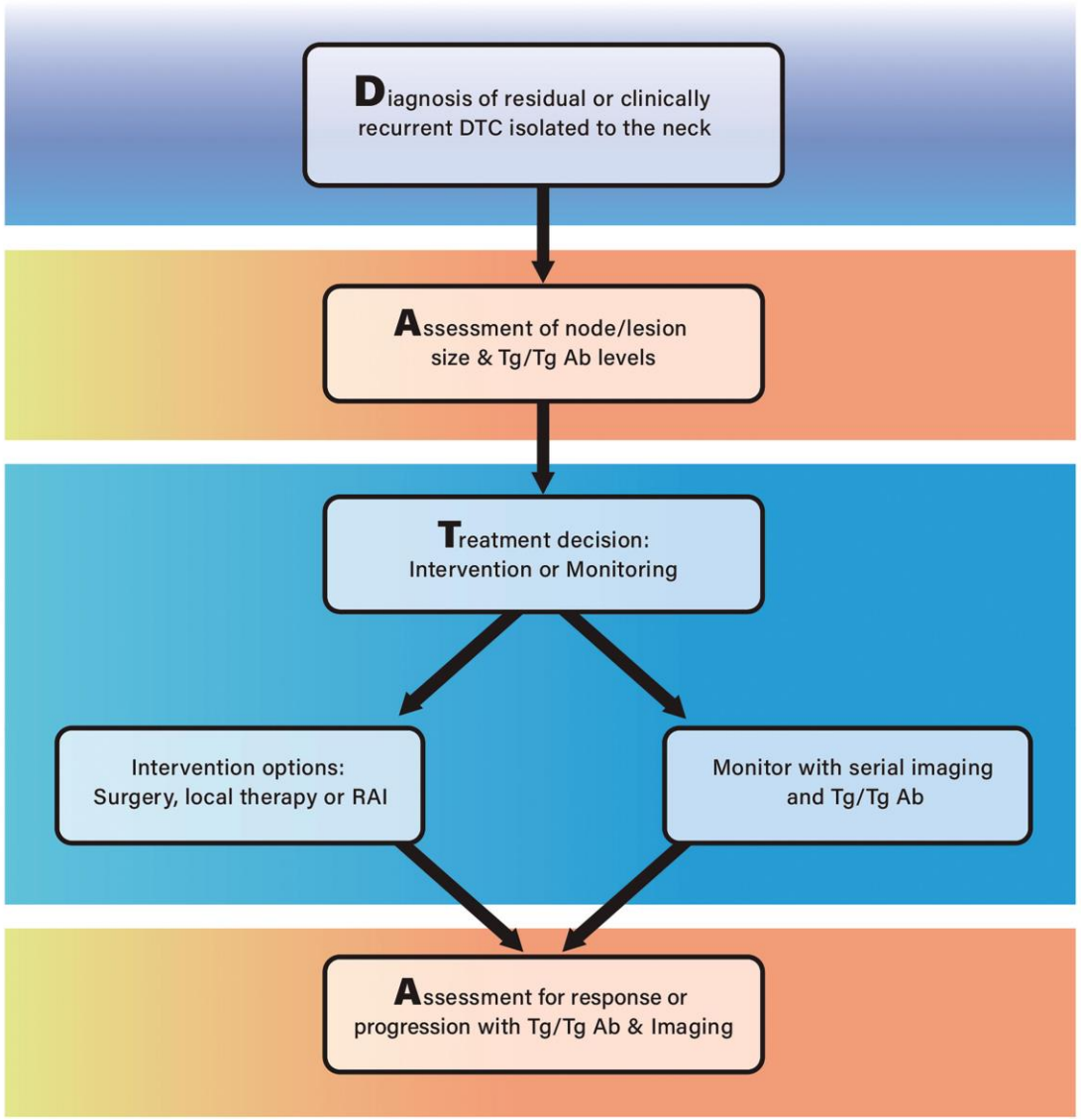
- Ongoing risk stratification (dynamic risk assessment), when used in combination with the initial risk of recurrence, allows the clinician to provide individualized management recommendations while risk estimates evolve over time and should be used to inform timing and type of imaging. (Good Practice Statement)

Dynamic risk assessment



DATA Framework for Persistent/Recurrent Disease

- DATA framework when a patient is diagnosed with residual or clinically recurrent localized DTC in the neck.



When and what type of treatment should be performed when there is evidence for locoregional residual, clinically recurrent, or progressive DTC?

RECOMMENDATION 52

- 1. A decision to perform a therapeutic compartmental or focused central and/or lateral neck operation in the re-operative setting should be based on a combination of factors. These include extent of prior operation(s), size and anatomic location of new disease, pace of growth, patient factors and preference, and context to overall disease management. (Good Practice Statement)
- 2. Percutaneous ethanol ablation may be considered an alternative therapy for recurrent or residual thyroid cancer, with greatest use in patients at high risk for complications from reoperation. (Conditional recommendation, Low certainty evidence)
- 3. RFA may be considered an alternative therapy in recurrent or residual thyroid cancer, with greatest use in patients at high risk for complications from reoperation. (Conditional recommendation, Low certainty evidence)

Should RAI therapy be used for the treatment of isolated cervical lymph node metastases?

RECOMMENDATION 53

- Additional RAI therapy for identified isolated cervical lymph node metastases may be considered after local therapy has been performed or if local therapy is not feasible. (Conditional recommendation, Low certainty evidence)

Should external beam radiation therapy be used in isolated cervical node metastases?

RECOMMENDATION 54

- EBRT using modern techniques such as IMRT and stereotactic radiation may be considered for locoregional recurrences that are not surgically resectable or when there is extranodal extension or involvement of soft tissues. (Conditional recommendation, Low certainty evidence)

What preparation and dosing strategies should be used for RAI therapy for locoregional and/or distant metastases?

RECOMMENDATION 55

- A. Empirically administered amounts of 131I >5.5 GBq (150 mCi) that have high potential to exceed toxicity parameters should be avoided in patients >70 years or with renal failure. Such patients should be evaluated with dosimetry to confirm safety prior to RAI administration if doses >5.5 GBq (150 mCi) are being considered. (Strong recommendation, Moderate certainty evidence)
- B. Dosimetry-guided RAI (either lesional or maximum tolerated activity) may be considered in patients with locoregional or metastatic disease when administered activities >5.5 GBq (150 mCi) are considered. (Conditional recommendation, Moderate certainty evidence)
- C. rhTSH-mediated elevation or LT4 withdrawal may be utilized to prepare patients with distant metastatic disease who are being treated with RAI. (Conditional recommendation, Low certainty evidence)

What RAI dosing strategies should be used for patients with pulmonary metastases?

RECOMMENDATION 56

- A. Pulmonary micrometastases can be treated with RAI therapy, and this may be repeated if the disease continues to concentrate RAI and clinically respond. (Conditional recommendation, Low certainty evidence)
- B. RAI dosing for pulmonary micrometastases should either be empiric (3.7–7.4 GBq, 100–200 mCi, or 3.7–5.55 GBq, 100–150 mCi for patients >70 years) or estimated by dosimetry to limit whole-body retention to 2.96 GBq (80 mCi) at 48 hours with 200 cGy to the bone marrow. (Good Practice Statement)
- C. Radioiodine-avid macronodular metastases can be treated with RAI, and treatment can be repeated when objective benefit is demonstrated. RAI dosing either may be empiric (3.7–7.4 GBq, 100–200 mCi, or 3.7–5.55 GBq, 100-150 mCi for patients >70 years) or informed by whole-body dosimetry to limit whole-body retention to 2.96 GBq (80 mCi) at 48 hours with 200 cGy to the bone marrow. (Conditional recommendation, Low certainty evidence)

What RAI dosing strategies should be used for patients with bony metastases?

RECOMMENDATION 57

- A. RAI for iodine-avid bone metastases has been associated with improved survival and should be employed. (Strong recommendation, Low certainty evidence)
- B. The activity administered could be given either empirically (3.7–7.4 GBq, 100–200 mCi) or as determined by dosimetry. (Conditional recommendation, Very low certainty evidence)

When should empirical RAI be considered for Tg-positive, RAI diagnostic scan-negative patients?

RECOMMENDATION 58

- A. In the absence of structurally demonstrable disease, patients with stimulated serum Tg <10 ng/mL after thyroid hormone withdrawal or <5 ng/mL with rhTSH (indeterminate response) can be followed with thyroid hormone therapy alone, reserving additional treatment for emergence of rising serum Tg levels over time or other evidence of structural disease progression. (Conditional recommendation, Low certainty evidence)
- B. Empiric (3.7–7.4 GBq, 100–200 mCi) or dosimetrically determined RAI therapy may be considered in patients with more significantly elevated or rapidly rising serum Tg levels where imaging (e.g., cross sectional imaging and/or 18FDG-PET/CT) has failed to reveal tumor amenable to directed therapy. (Conditional recommendation, Low certainty evidence)
- C. If persistent nonresectable disease is localized after empiric administration of RAI, and there is objective evidence of significant tumor reduction, then repeated RAI therapy can be considered until the tumor has been eradicated or the tumor no longer responds to treatment. (Conditional recommendation, Low certainty evidence)

How is radioiodine-refractory DTC classified?

RECOMMENDATION 59

- A. RAIR DTC (including OTC) cannot be diagnosed in patients who have not received an ablative or treatment dose of RAI. Patients who meet criteria for RAI should receive ablative or treatment administrations of RAI to determine status. (Good Practice Statement)
- Strong criteria suggesting iodine-refractory DTC include (i) absence of 131I uptake on a post-therapy scan (Recommendation 37) in the setting of confirmed disease visible on structural or 18FDG-PET imaging. This may occur at the time of initial treatment of metastatic DTC or at the time of a subsequent RAI, and/or (ii) progression of disease less than 6 months after a treatment appropriate administration of therapeutic RAI demonstrated uptake on post-therapy scans.

Which patients with metastatic DTC can be followed without additional therapy?

RECOMMENDATION 60

- A. Patients with RAIR metastatic DTC that is asymptomatic, stable, or minimally progressive, or who have clinically significant comorbidities, can be monitored on TSH-suppressive thyroid hormone therapy with serial radiographic imaging every 3–12 months. (Conditional recommendation, Low certainty evidence)
- B. In the absence of planned systemic treatment or redifferentiation therapy, molecular testing is not routinely recommended in patients with RAIR residual DTC. (Conditional recommendation, Moderate certainty evidence)

For patients with RAIR DTC deemed appropriate for systemic treatment, what is the optimal approach to choosing the best therapy?

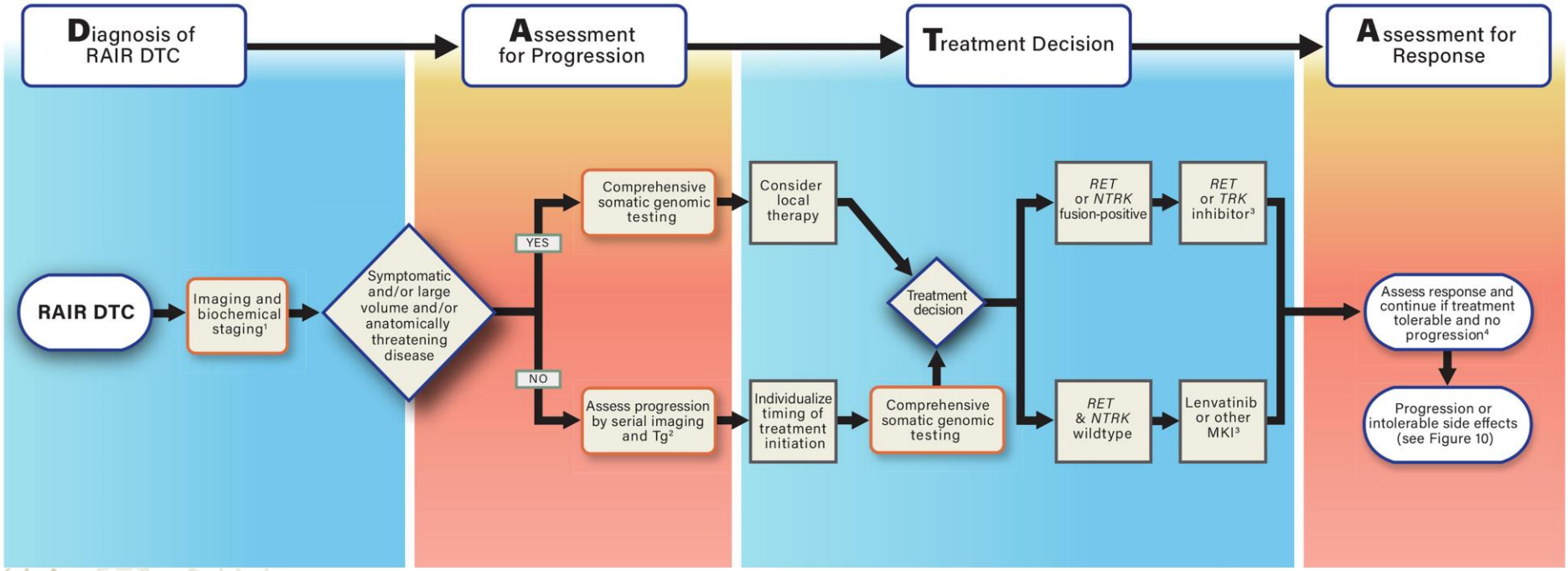
RECOMMENDATION 61

- Tissue-based biomarker testing to identify actionable oncogenic driver alterations in RAIR DTC should be performed prior to initiating systemic therapy for progressive disease. (Strong recommendation, Moderate certainty evidence)

What is the general approach for first-line therapy for patients with progressive RAIR DTC?

- While response rates to first-line therapies can be high, and medications can be well-tolerated, no current therapies are curative.
- The ability of patients to tolerate effective doses of therapies due to side-effects and/or toxicities varies without clear pre-treatment predictors other than known comorbidities.
- Thus, determination of the best treatment approach for each person with progressive RAI-refractory DTC should be individualized and determined in a shared decision-making model with the patient.
- Figure 8 outlines the general approach to assist in clinical decision-making as an application of the DATA framework.

DATA Framework for Therapy of Radioactive Iodine Resistant (RAIR) DTC



DATA framework for systemic treatment of patients with RAIR unresectable/metastatic DTC. 1) Initial staging may involve CT, MRI, and/or PET/CT. Consider brain MRI to rule out brain metastases. 2) First imaging and Tg monitoring after 2–6 months; timing thereafter is based on rate of progression and/or development of symptoms. 3) First-line gene-specific therapy in most patients with RET or NTRK fusion-positive disease is preferable. Multikinase inhibitors (MKIs) are recommended in general in patients with BRAFV600E or RAS-mutated DTC unless based on comorbidities/side effect concerns, patient preference, or clinical trial options. 4) When treatment is discontinued due to treatment related adverse events (TRAE), consider second-line therapy only after disease progression.

When patients with RAIR DTC without an actionable driver alteration need systemic therapy, what is the best initial treatment?

RECOMMENDATION 62

- For patients with progressive RAIR DTC without an actionable biomarker-linked FDA-approved first-line therapy, MKI therapy with either lenvatinib or sorafenib is recommended. In most cases, lenvatinib is the preferred first-line MKI. (Strong recommendation, High certainty evidence)

What is the best timing for the initiation of MKIs in patients with RAIR DTC?

RECOMMENDATION 63

- A. Lenvatinib or other therapy should be initiated without delay in patients with symptomatic RAIR DTC for whom local therapy, such as radiation or surgery, is not appropriate. (Strong recommendation, Moderate certainty evidence)
- B. For patients with asymptomatic RAIR DTC that has progressed over the prior 12–14 months and local therapy is not appropriate, if efficacy outcomes are the most important goal of treatment, earlier initiation of lenvatinib may be considered. For patients with asymptomatic progressive RAIR DTC for whom QoL is a major priority, delaying the initiation of lenvatinib and continuing disease monitoring may be most appropriate. (Good Practice Statement)

When initiating lenvatinib treatment for RAIR DTC, what is the best starting dose?

RECOMMENDATION 64

- A. For most patients with progressive RAI-refractory DTC initiating lenvatinib, 24 mg once daily is the recommended starting dose; a lower starting dose may be indicated in selected patients. (Strong recommendation, High certainty evidence)
- B. Dose holds and dose reductions are important strategies for managing adverse events related to lenvatinib. (Good Practice Statement)

How should adverse events in patients receiving VEGFR MKI therapy be managed?

RECOMMENDATION 65

- Prevention, amelioration, and timely management of adverse events are required for patients treated with MKIs. Patients initiating MKI therapy should be evaluated at baseline and no less often than every 2 weeks for the first 2 months of treatment to manage adverse events and then generally at 1- or 2-month intervals thereafter. (Good Practice Statement)

What is the preferred approach to second-line therapy for patients with RAIR DTC?

RECOMMENDATION 66

- Cabozantinib should be offered as second-line therapy for patients with RAIR DTC without an actionable oncogenic driver alteration who have progressed on or did not tolerate, prior MKI therapy, if they desire ongoing treatment, and do not have a contraindication to therapy. (Strong recommendation, High certainty evidence)

For patients with NTRK fusion-positive RAIR DTC, what is the optimal first-line therapy?

RECOMMENDATION 67

- In patients with progressive RAIR DTC harboring an oncogenic NTRK fusion, NTRK-targeted therapy is recommended in the first line. (Strong recommendation, Moderate certainty evidence)

For patients with RET fusion-positive RAIR DTC, what is the optimal first-line therapy?

RECOMMENDATION 68

- In patients with progressive RAIR DTC harboring an oncogenic RET fusion, RET-targeted therapy is recommended in the first line. (Strong recommendation, Moderate certainty evidence)

For patients with ALK fusion-positive RAIR DTC, what is the optimal first-line therapy?

RECOMMENDATION 69

- In patients with progressive RAIR DTC harboring an oncogenic ALK fusion, anaplastic lymphoma kinase (ALK)-targeted therapy is recommended in the first line. (Strong recommendation, Low certainty evidence)

For patients with BRAFV600E mutation-positive RAIR DTC, what is the optimal first-line therapy?

RECOMMENDATION 70

- a. In patients with progressive RAIR DTC harboring an oncogenic BRAFV600E mutation, BRAFV600E-directed therapy may be considered in the first line for patients who are poor candidates for lenvatinib. (Conditional recommendation, Moderate certainty evidence)
- b. BRAF-directed treatment is recommended in patients with BRAFV600E mutation-positive RAIR DTC who have progressed on or did not tolerate one or more prior MKI therapies. (Strong recommendation, Moderate certainty evidence)
- c. Currently approved BRAF-directed therapies are not recommended in DTCs harboring non-V600 BRAF alterations. (Strong recommendation, Moderate certainty evidence)

For patients with RAIR DTC harboring other potentially actionable targets, what is the optimal first-line therapy?

RECOMMENDATION 71

- In patients with progressive RAIR DTC harboring other potentially actionable non-NTRK/RET/ALK/BRAFV600E targets, enrollment in a clinical trial or first-line lenvatinib is suggested. (Conditional recommendation, Low certainty evidence)

Current prices of molecular testing in Rials

BRAF 21.280.000 R

MET 52.190.000 R

RET 36.590.000 R

NTRK 1 87.500.000 R

NTRK 2 87.500.000 R

NTRK 3 87.500.000 R

NTRK Fusion 262.500.000R

Alk4 32.450.000 R

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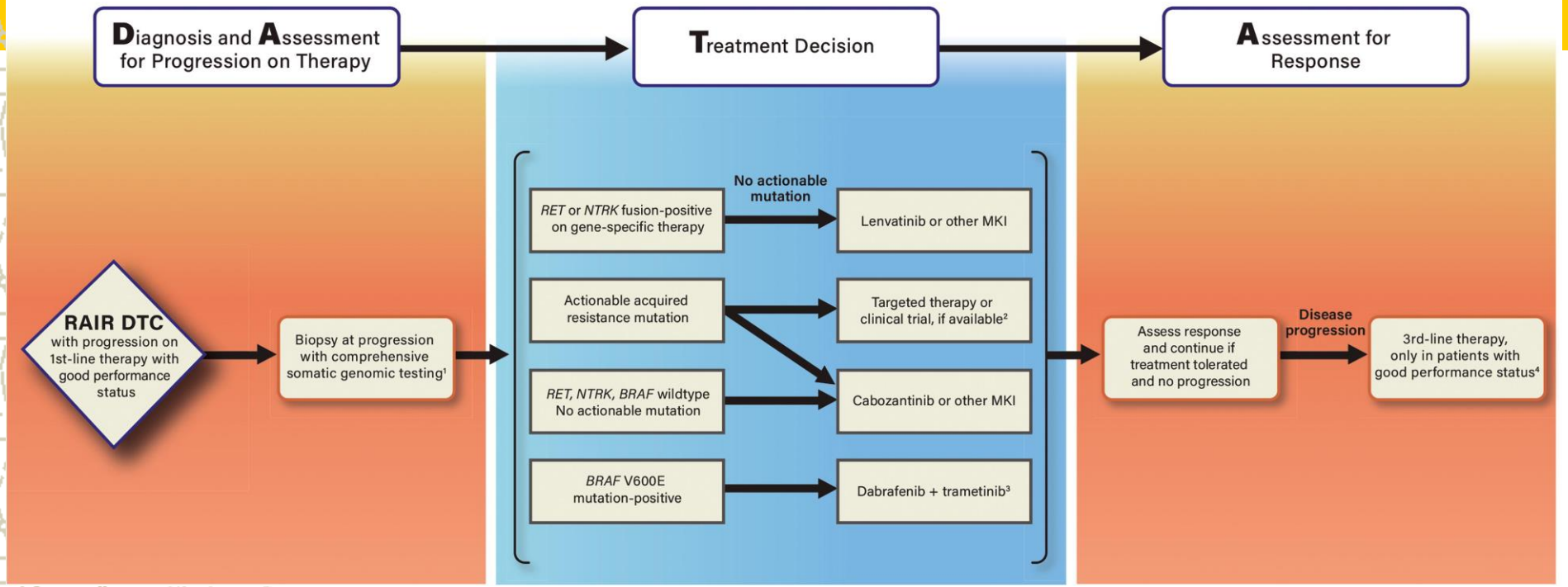
DATA Framework for Second-line Therapy of RAIR DTC



DATA framework for treatment of patients with progression on (or intolerance to) first-line therapy for RAIR metastatic DTC. 1) Biopsy of progressive disease when acquired resistance emerges is advised to evaluate for potentially actionable resistant mechanisms. 2) If targeted therapy or clinical trial is not available, cabozantinib or another MKI may be considered in patients treated with lenvatinib first-line. 3) Dabrafenib plus trametinib is FDA-approved for solid tumors with BRAFV600E mutation who have progressed on prior treatment. Dabrafenib plus trametinib was not superior to dabrafenib alone in progressive DTC; thus, dabrafenib monotherapy may be considered. 4) Enrollment in a treatment clinical trial when available is encouraged. Other third-line options may include lenvatinib, cabozantinib, or sorafenib if not already received.

What is the optimal approach to address disease progression in RAIR DTC on gene-specific therapy?

RECOMMENDATION 72

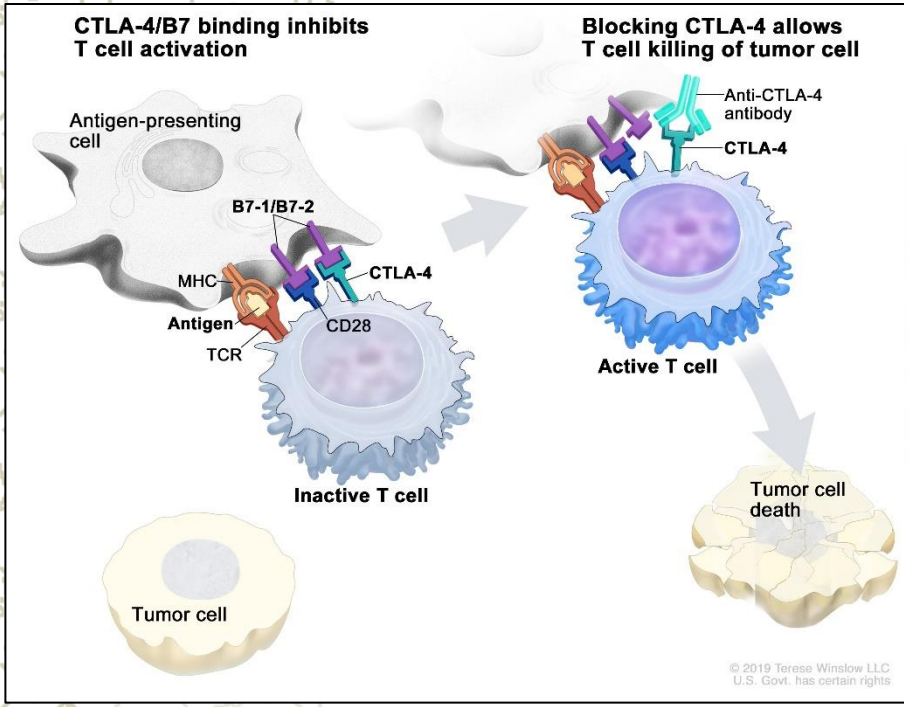
- A. Whenever feasible, surgical or core tumor biopsy to allow for NGS testing to identify potential molecular mechanisms of acquired resistance should be performed. (Good Practice Statement)
- B. Surgical or core biopsy is preferred over ctDNA(circulating tumor DNA) analysis, which may be considered for patients in whom tumor biopsy is not possible. (Conditional recommendation, Low certainty evidence)

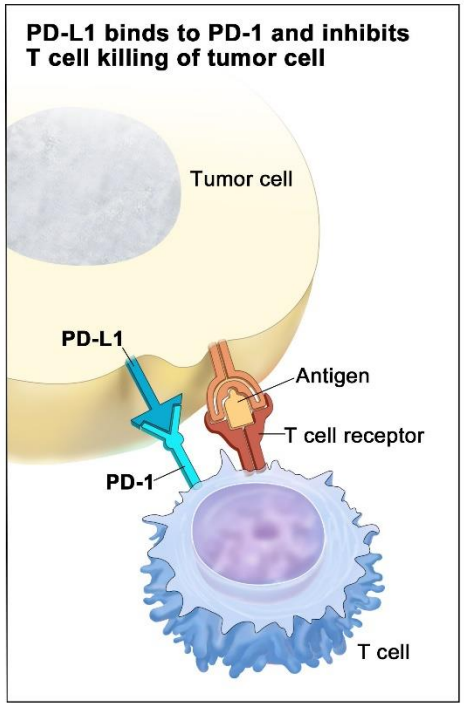
What is the role of immunotherapy in RAIR DTC?

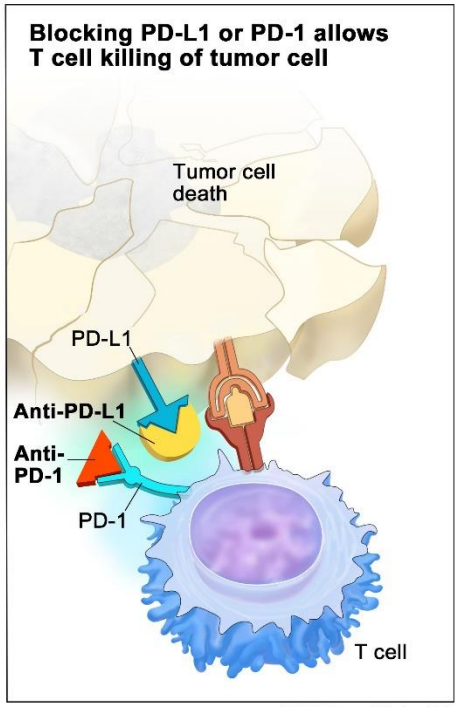
RECOMMENDATION 73

- Immune checkpoint inhibitors or other forms of immunotherapy may be offered in selected cases, such as when tumors harbor a high tumor mutational burden or are mismatch repair deficient. (Conditional recommendation, Low certainty evidence)

Immune checkpoint inhibitors







A type of drug that blocks proteins called checkpoints that are made by some types of immune system cells, such as T cells, and some cancer cells. These checkpoints help keep immune responses from being too strong and sometimes can keep T cells from killing cancer cells. When these checkpoints are blocked, T cells can kill cancer cells better. Examples of checkpoint proteins found on T cells or cancer cells include PD-1/PD-L1 and CTLA-4/B7-1/B7-2. Some immune checkpoint inhibitors are used to treat cancer.

For patients with RAIR DTC, what is the role for kinase inhibitor redifferentiation therapy?

RECOMMENDATION 74

- A. Redifferentiation by MAPK pathway blockade in patients with progressive RAIR DTC harboring targetable mutations may be considered in selected patients. Clinical trial participation is encouraged. (Conditional recommendation, Low certainty evidence)
- B. Redifferentiation approaches in adjuvant RAI treatment for patients with high-risk, non-gene selected DTC are not recommended. (Strong recommendation, Moderate certainty evidence)

What is the role of cytotoxic chemotherapy in RAIR DTC?

RECOMMENDATION 75

- Cytotoxic chemotherapy can be considered in patients with RAIR DTC with metastatic, rapidly progressive, symptomatic, and/or imminently threatening disease not amenable to control through other approaches. Use within the context of a therapeutic clinical trial is preferred. (Conditional recommendation, Low certainty evidence)

What is the optimal approach for patients with oligometastatic RAIR DTC?

RECOMMENDATION 76

- For patients with RAIR DTC with solitary or oligometastases (two to five lesions), focal ablative treatment may be considered. Optimal treatment approaches may be best addressed in a multidisciplinary setting. (Conditional recommendation, Low certainty evidence)

What is the optimal treatment approach for patients with site-specific symptomatic RAIR DTC?

RECOMMENDATION 77

- For patients with symptomatic RAIR DTC, local treatment is suggested. Surgery, radiotherapy, and percutaneous thermo-ablative approaches are available to treat individual symptomatic sites of disease. (Conditional recommendation, Moderate certainty evidence)

When should bone-directed agents be considered for patients with DTC?

RECOMMENDATION 78

- A. In patients with RAIR DTC with symptomatic and/or multiple bone metastases, treatment with a bone modifying agent is recommended to decrease the risk of skeletal-related events. (Strong recommendation, Low certainty evidence)
- B. A bone-modifying agent dosing schedule of every 3 months may be considered due to a reduction in the risk of adverse events, especially osteonecrosis of the jaw, compared with monthly dosing, but may increase the risk of symptomatic skeletal events. (Conditional recommendation, low certainty

Cost-effectiveness of denosumab compared with zoledronic acid has been studied. While the direct cost of denosumab is higher than that of zoledronic acid, this was offset by reduced costs related to bone complications. Quality-adjusted life-year and net monetary benefit analyses favored denosumab from the perspectives of society and payers.

What is the best treatment for patients with brain metastases?

RECOMMENDATION 79

- A. Resection and/or SBRT are the mainstays of therapy for central nervous system metastases. (Conditional recommendation, Low-certainty evidence)
- B. RAI can be considered if central nervous system metastases concentrate RAI. If RAI is planned, SBRT and concomitant glucocorticoid therapy are recommended prior to RAI therapy to minimize the effects of a potential TSH induced increase in tumor size and RAI induced inflammatory response. (Good Practice Statement)

Who should be considered for clinical trials?

RECOMMENDATION 80

- Patients should be counseled to consider enrolling in prospective clinical trials based upon specific eligibility requirements for given studies and the likelihood that the patient will benefit from participation. Clinicians considering referral of patients for trials should review available treatment options and eligibility criteria, preferably through discussions with personnel at the trial center and review of materials at the website www.clinicaltrials.gov. (Good Practice Statement)

Considerations managing pregnant patients with DTC

RECOMMENDATION 81

- A. In most pregnant patients, surgery can be safely delayed until after delivery. Exceptions include rare patients for whom there is concern for significant disease progression. If necessary, surgery may be performed in the second trimester of pregnancy. (Conditional recommendation, Low certainty evidence)
- B. For pregnant patients diagnosed with DTC during pregnancy, monitoring with neck ultrasound at least once in early second trimester and more often if clinically indicated is appropriate. Cross-sectional imaging using MRI may be performed in selected cases. Imaging modalities that require ionizing radiation should not be performed other than in exceptional circumstances. (Conditional recommendation, Low certainty evidence)

Considerations managing pregnant patients with DTC

RECOMMENDATION 81

- C. TSH goals for pregnant patients, in general, are the same TSH as determined preconception. Thyroxine dose may be adjusted toward less TSH suppression if there are concerns that excess thyroxine may have an adverse impact on the pregnancy. TSH should be monitored approximately every 4 weeks until 16–20 weeks of gestation and at least once between 26 and 32 weeks of gestation. (Good Practice Statement)
- D. Monitoring using neck ultrasound and Tg is appropriate for pregnant patients who have an incomplete response to therapy. If cross-sectional imaging is needed, MRI should be performed. Pregnant patients in excellent or indeterminate response categories should be monitored as for nonpregnant patients. (Conditional recommendation, Low certainty evidence)

What are long-term survivorship concerns related to initial thyroid cancer therapy?

RECOMMENDATION 82

- Patients should be made aware of potential long-term side effects of treatments and monitored with appropriate intervention and/or referrals during follow-up. (Good Practice Statement)
  - Hoarseness/voice change

- Postsurgical voice change is very common even when the recurrent laryngeal nerve and external branch of the superior laryngeal nerve are preserved and functional.
- Voice change has been reported in over 30% of patients long term, even without nerve injury.
- The incidence of vocal fold paralysis after thyroid surgery varies and is related to surgeon experience.
- Voice changes impacting quality of life should prompt referral to a laryngologist and speech language pathologist for optimal voice rehabilitation.
- Some patients may experience aspiration, which can also be managed by this team.
- Bilateral injury to the recurrent laryngeal nerves can cause dyspnea and necessitate tracheostomy.
- Every effort should be made to avoid total thyroidectomy after known recurrent laryngeal nerve injury to prevent this serious complication.

What are long-term survivorship concerns related to initial thyroid cancer therapy?

RECOMMENDATION 82

- Patients should be made aware of potential long-term side effects of treatments and monitored with appropriate intervention and/or referrals during follow-up. (Good Practice Statement)
  - Hypoparathyroidism

- The parathyroid glands may be injured or inadvertently removed during thyroid surgery.
- The risk of hypoparathyroidism varies with surgeon experience.
- The rate of temporary hypoparathyroidism ranges from 14% to 43%, and permanent hypoparathyroidism from 1% to 25%.
- Patients not adequately supported with calcium and vitamin D supplements may experience paresthesias, tetany, or cardiac arrhythmias.
- Permanent hypoparathyroidism after total thyroidectomy increases the risk for renal insufficiency and cardiovascular events in patients with pre-existing cardiovascular disease.
- The risk of death is significantly higher among patients with permanent hypoparathyroidism compared to those without it.
- Preservation of viable parathyroid glands during thyroid surgery is critically important.

What are long-term survivorship concerns related to initial thyroid cancer therapy?

RECOMMENDATION 82

- Patients should be made aware of potential long-term side effects of treatments and monitored with appropriate intervention and/or referrals during follow-up. (Good Practice Statement)
  - Scar/cosmesis

❖ Management of the scar and lessening its impact should be a focus for the thyroid surgeon.
❖ There are also remote access surgical options available for carefully selected patients that will avoid a neck scar.

What are long-term survivorship concerns related to initial thyroid cancer therapy?

RECOMMENDATION 82

- Patients should be made aware of potential long-term side effects of treatments and monitored with appropriate intervention and/or referrals during follow-up. (Good Practice Statement)
  - Neck tightness and dysphagia

- Many patients experience a "tight neck" from scarring and fibrosis after thyroid surgery, termed "post-thyroidectomy central compartment syndrome."
- This tightness is most noticeable in the first 3 months after surgery but may persist longer.
- The tightness may cause a globus sensation or dysphagia, which generally returns to preoperative baseline by 2–3 months.
- Massage and neck range of motion exercises in the immediate postoperative period may help minimize this effect.

How should financial hardship caused by thyroid cancer be addressed?

RECOMMENDATION 83

- A. Patients should be informed that resources exist for patients and families impacted by financial burden due to a diagnosis of thyroid cancer. (Good Practice Statement)
- B. Clinicians should know that many patients diagnosed with thyroid cancer experience financial burden engendered by the costs of cancer diagnosis, treatment, and monitoring. Clinicians should discuss these topics with patients and their families. (Good Practice Statement)

What are the critical psychosocial concerns of thyroid cancer survivors?

RECOMMENDATION 84

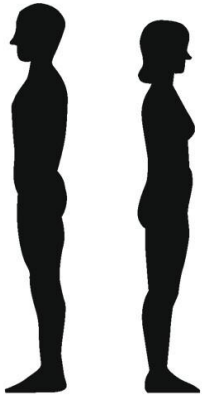
- A. Thyroid cancer survivors should be informed that services are available to support psychosocial needs related to having a cancer diagnosis. (Good Practice Statement)
- B. Clinicians treating patients diagnosed with thyroid cancer should be prepared to help patients manage the psychosocial implications of thyroid cancer diagnosis and management. (Good Practice Statement)

Disclaimer

- It is our goal in formulating these guidelines, and the ATA's goal in providing support for the development of these guidelines, that they assist in the clinical care of patients and share what we believe is current, rational, and optimal medical practice. In some circumstances, it may be apparent that the level of care recommended may be best provided in limited centers with specific expertise. Finally, it is not the intent of these guidelines to replace individual decision-making, the wishes of the patient or family, or clinical judgment.

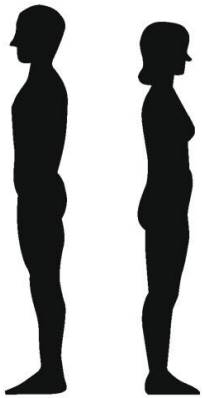
Estimated New Cases

Male			Female		
Prostate	299,010	29%	Breast	310,720	32%
Lung & bronchus	116,310	11%	Lung & bronchus	118,270	12%
Colon & rectum	81,540	8%	Colon & rectum	71,270	7%
Urinary bladder	63,070	6%	Uterine corpus	67,880	7%
Melanoma of the skin	59,170	6%	Melanoma of the skin	41,470	4%
Kidney & renal pelvis	52,380	5%	Non-Hodgkin lymphoma	36,030	4%
Non-Hodgkin lymphoma	44,590	4%	Pancreas	31,910	3%
Oral cavity & pharynx	41,510	4%	Thyroid	31,520	3%
Leukemia	36,450	4%	Kidney & renal pelvis	29,230	3%
Pancreas	34,530	3%	Leukemia	26,320	3%
All sites	**1,029,080**		**All sites**	**972,060**	

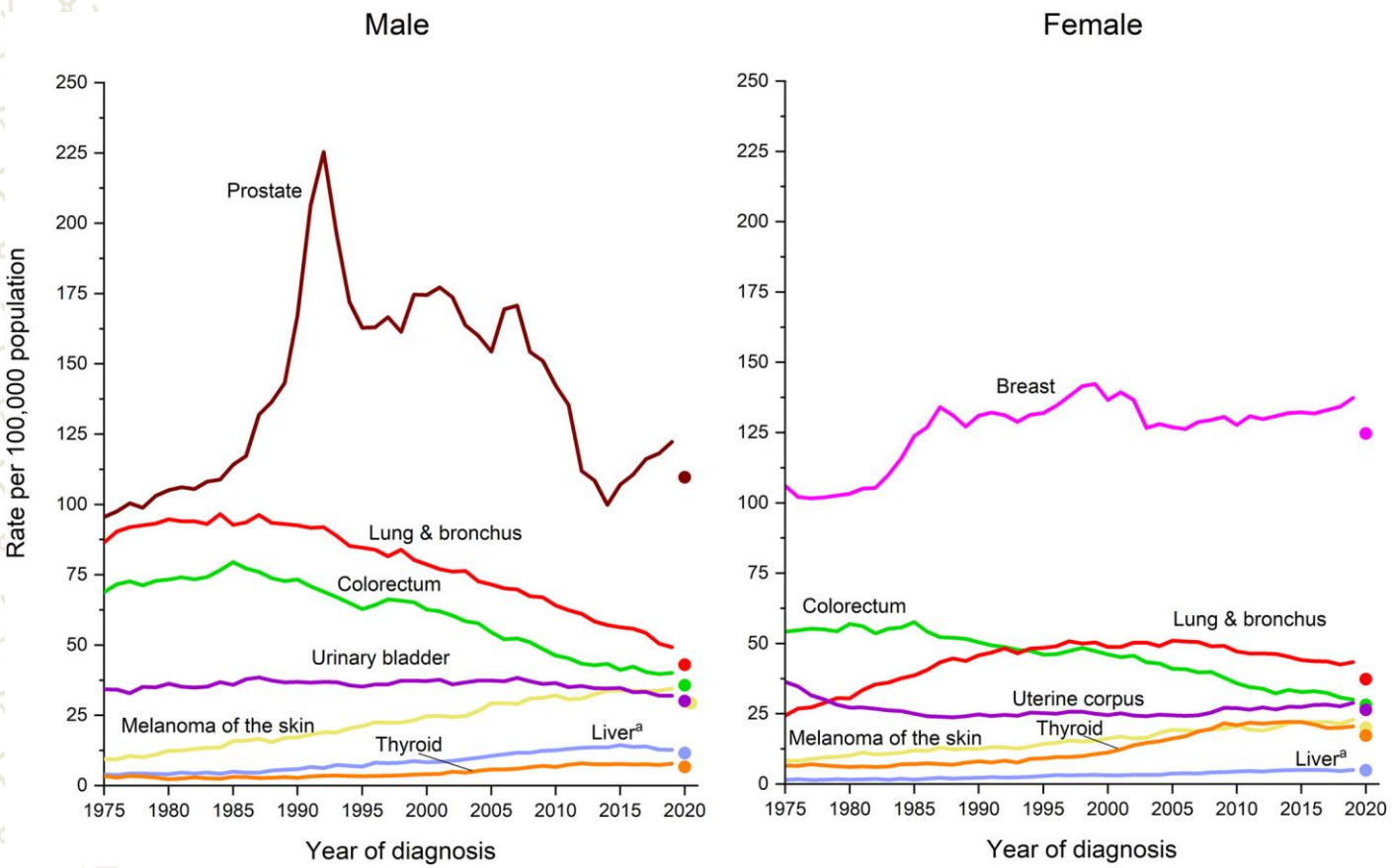


Estimated Deaths

Male			Female		
Lung & bronchus	65,790	20%	Lung & bronchus	59,280	21%
Prostate	35,250	11%	Breast	42,250	15%
Colon & rectum	28,700	9%	Pancreas	24,480	8%
Pancreas	27,270	8%	Colon & rectum	24,310	8%
Liver & intrahepatic bile duct	19,120	6%	Uterine corpus	13,250	5%
Leukemia	13,640	4%	Ovary	12,740	4%
Esophagus	12,880	4%	Liver & intrahepatic bile duct	10,720	4%
Urinary bladder	12,290	4%	Leukemia	10,030	3%
Non-Hodgkin lymphoma	11,780	4%	Non-Hodgkin lymphoma	8,360	3%
Brain & other nervous system	10,690	3%	Brain & other nervous system	8,070	3%
All sites	**322,800**		**All sites**	**288,920**	



Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.


Male
Female
Rate per 100,000 population
Year of diagnosis
Year of diagnosis
Prostate
Lung & bronchus
Colorectum
Urinary bladder
Melanoma of the skin
Thyroid
Liver[a]
Breast
Colorectum
Lung & bronchus
Uterine corpus
Melanoma of the skin
Thyroid
Liver[a]
0
25
50
75
100
125
150
175
200
225
250
1975
1980
1985
1990
1995
2000
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2010
2015
2020

Thank you and hope for a good rain