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GUIDELINES

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

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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

Our recommendations regarding utilization of RAI and goals of therapy are adapted from the Martinique guidelines[760] and are summarized in Table 10. Important definitions include the following:

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.

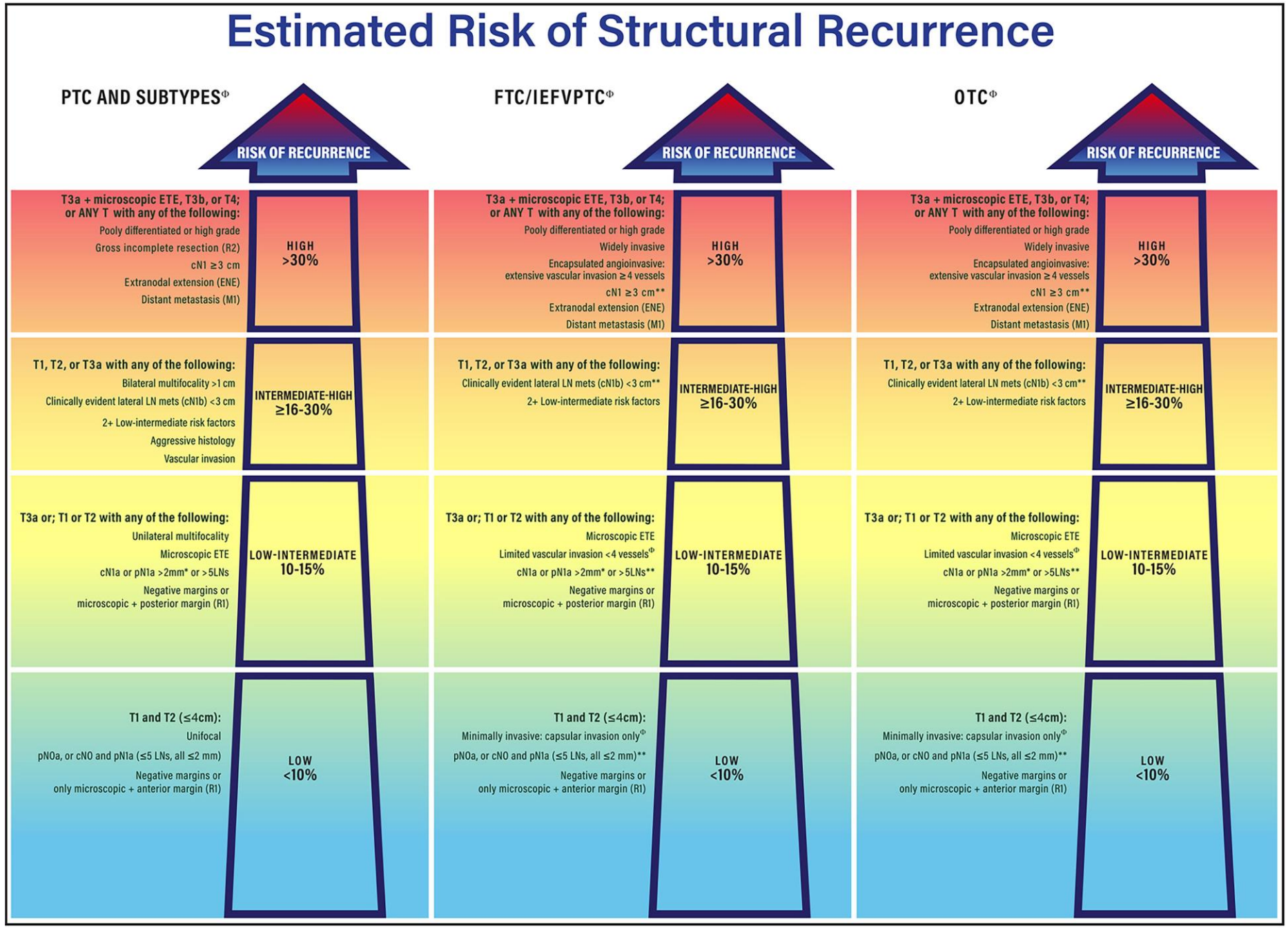
Table 10. Summary of Recommendations for Initial RAI Following Thyroidectomy[a]

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 these recommendations represent guidelines and that a variety of additional features including patient preference, comorbid conditions, access to care, pre-therapy imaging, and others may influence the decision to treat with RAI as well as the resulting activity level. Consistent with the Martinique documents, the final recommendation for administered activity should be based on multidisciplinary management recommendations.[760]

RAI, radioactive iodine.

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

	^{131}I Therapy		
Goal	Remnant Ablation	Adjuvant Treatment	Treatment of Known Disease
Initial staging	√	√	√
Facilitate follow-up	√	√	√
Improve disease-specific survival	-	√	√
Decrease recurrence	-	√	-
Improve progression-free survival	-	√	√
Curative intent	-	√	√
Palliative intent	-	-	√

FIG. 2. Terminology that should be used to communicate the goals of ^{131}I therapy.

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)***

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)***

tion. A low-iodine diet is generally defined as a restriction in iodine consumption to <50 mcg/day. Consultation prior to the administration of RAI should include a series of questions to confirm adherence to a low-iodine diet and exclude other known high-dose iodine sources (e.g., intravenous contrast within 3 months or amiodarone use) to prepare for the optimal timing of RAI imaging/therapy. Although urinary

Although low-iodine diets may be cumbersome or unpalatable, serious side effects are relatively infrequent,[803] with case reports of potentially life-threatening hyponatremia occurring most often in patients who (i) are elderly and subject to thyroid hormone withdrawal, (ii) have metastatic disease, (iii) are concurrently treated with thiazide diuretics, and (iv) are on a low-iodine diet for longer than a week.[812] It is important to avoid restriction of non-iodized salt during the low-iodine diet, since this may be associated with hyponatremia, especially in patients undergoing thyroid hormone withdrawal.

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)***

Overall, representative changes in management that can be obtained with use of pre-therapy WBS include (i) detection of very large thyroid remnants with greater than 15% uptake, which may be an indication for additional surgery; (ii) detection of an insignificant thyroid remnant, which, when combined with a Tg level of <1 ng/mL, may obviate the need for RAI therapy or lead to a dose reduction; and (iii) the detection of clinically unsuspected nodal or distant metastatic disease. These findings may alter the decision to pursue RAI treatment and could result in the modification of the selected activity.

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.[844] ***(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)***

Taken together, the evidence from studies with large number of patients suggests a small dose-related increase in SPM following RAI. Further studies to identify subgroups of patients at greatest versus lowest risk for SPM are needed to better individualize risk assessment for patients. The use of laxatives may decrease radiation exposure for the bowel, particularly in patients treated after prolonged thyroid hormone withdrawal; vigorous oral hydration reduces exposure of the bladder and gonads.[809,839,874]

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)***

therapies. Radiation to the bone marrow is impacted by several factors, including renal function. The kidneys are a major means of iodine excretion from the body, and physiological radioisotope study research in non-thyroidectomized individuals has shown that renal impairment significantly reduces RAI excretion.[871] In patients with significant renal failure, dosimetry-guided therapy should be considered. Females of

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)***

gestation. NIS is expressed in the placenta, and iodine is transported from the mother to the developing fetus; in addition to the direct effects of RAI in pregnancy from circulating ^{131}I on kidneys, bladder and bone marrow, there are recognized effects of radiation on the ovaries.[876–878] Tempo-

rical complications and pregnancy outcomes. Overall, there were no differences in the assessed outcomes if pregnancy occurred more than 6 months after RAI was administered. When pregnancy occurred less than 6 months after RAI, there was a small but significant increase in congenital malformations in the offspring (OR 1.74 [CI 1.01–2.97]).[885]

especially if more urgent treatment is desired.[823] Dopaminergic agents might be useful in decreasing breast exposure in recently lactating female patients, although caution should be exercised given the risk of serious, albeit rare, side effects, including cardiovascular, neurological, and psychiatric disorders associated with their routine use to suppress postpartum lactation.[891]

Although data are limited, it has been recommended that males who receive ^{131}I wait at least 120 days (the lifespan of sperm) after ^{131}I therapy before attempting conception or providing a sperm sample for assisted reproduction.[898]

It has been suggested that sperm banking be considered in males who receive cumulative RAI activities ≥14.8 GBq (400 mCi).[893] Gonadal radiation exposure is reduced with good hydration, frequent micturition to empty the bladder, and avoidance of constipation.[900]

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Review article

Effects of fetal involvement of inadvertent radioactive iodine therapy for the treatment of thyroid diseases during an unsuspected pregnancy

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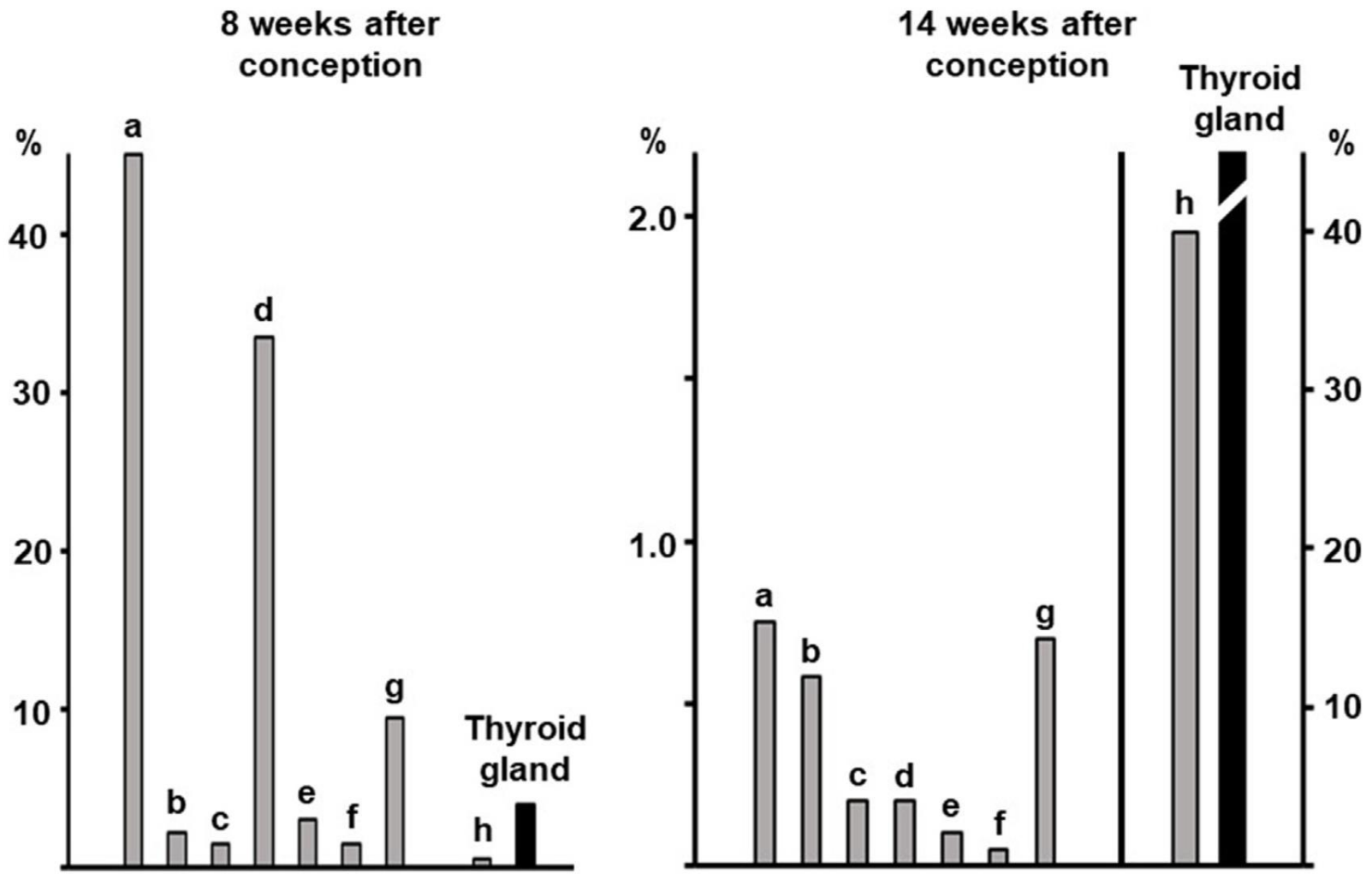


Fig. 1. Distribution of radioactive iodine (^{131}I) in fetal tissues at 8 and 14 weeks of gestation, according to Sternberg [31]: (a) liver; (b) lungs; (c) heart; (d) digestive tract; (e) kidney; (f) adrenal glands; (g) brain; (h) amniotic fluid.

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

▪ RECOMMENDATION 44

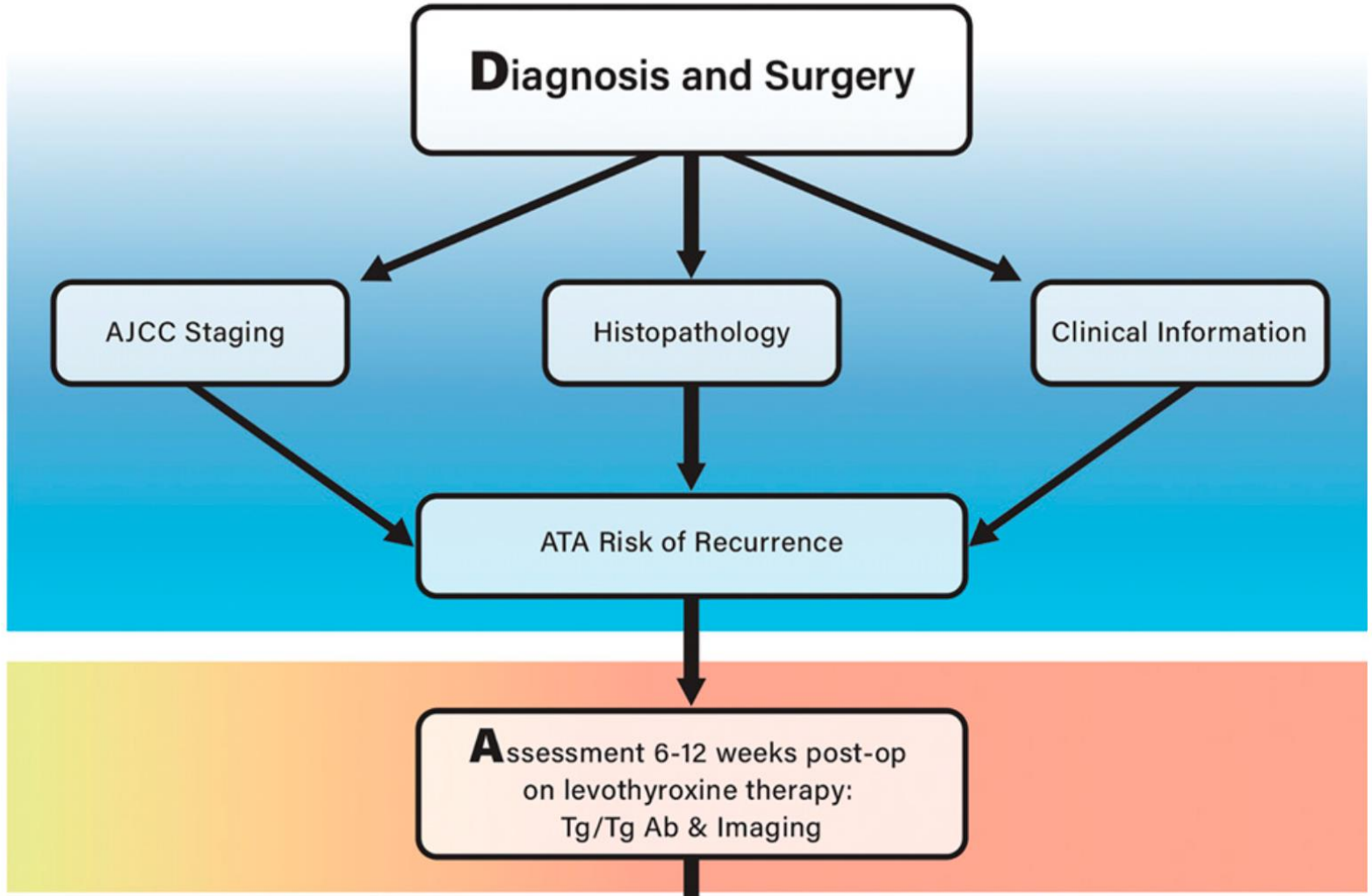
A. Adjuvant external beam radiotherapy (EBRT) for patients with DTC with high-risk features for locoregional disease progression (such as aggressive histologic subtype, gross extrathyroidal extension, positive margins, and visceral or soft tissue invasion) may be considered in select cases, especially if the expected disease progression would not be amenable to salvage surgery. The potential benefit of improving locoregional relapse-free survival must be weighed against the absence of data demonstrating improvement in overall survival and the known risks of clinically meaningful toxicity. (***Conditional recommendation, Low certainty evidence***)

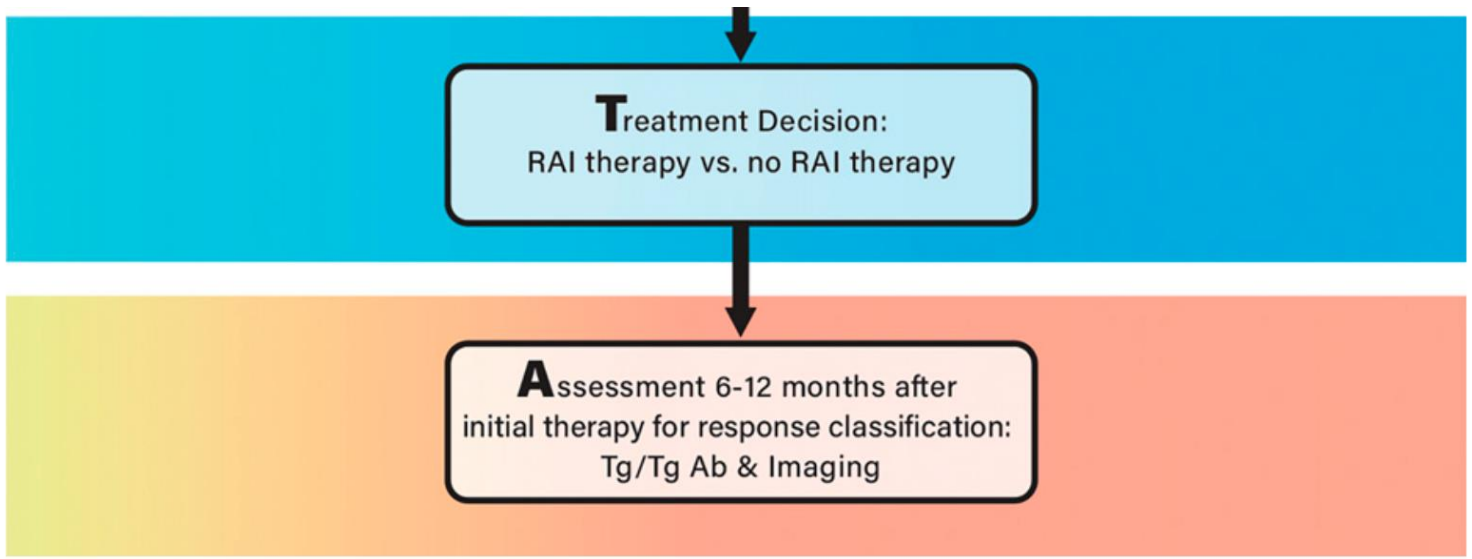
B. EBRT with or without concurrent chemotherapy in patients with DTC with gross residual disease in the postoperative setting or with locally advanced unresectable disease may be considered in select patients who may benefit from improved locoregional control. EBRT with or without concurrent chemotherapy 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




Treatment Decision:
RAI therapy vs. no RAI therapy
Assessment 6-12 months after
initial therapy for response classification:
Tg/Tg Ab & Imaging

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)***

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]

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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)***
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)***

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]

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)***

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

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 ^{123}I or low activity ^{131}I. ***(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)***

Hybrid cameras combine a dual-head SPECT gamma camera with a CT scanner in one gantry. This allows direct superimposition of functional and anatomical images. The radiation dose delivered to the patient by the low-dose CT scan is 2–5 mSv, which is much lower than the dose accompanied by the administration of 3.7 GBq (100 mCi) of ^{131}I (approximately 50 mSv). SPECT-CT performed after the administration of a diagnostic or a therapeutic dose (≥1.1 GBq, 30 mCi) of RAI is

isotope.[1012–1014] Additionally, a few small single-center studies have examined the role of other positron-emitting radiopharmaceuticals in detecting DTC, including [^{18}F]-tetralfuoroborate (TFB),[1015] [^{68}Ga]PSMA-11,[1016] and [^{68}Ga]DOTATATE/DOTANOC.[1017] The role of these novel agents in thyroid cancer remains undefined.

^{18}FDG-PET/CT scanning.

▪ RECOMMENDATION 50

A. Imaging using ^{18}FDG-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 ^{18}FDG-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)***

A meta-analysis from 2019 indicates that the sensitivity of TSH-stimulated ^{18}FDG-PET in detection of disease may not be superior to that of studies undertaken in an unstimulated setting.[1024] False positive results may be found with ^{18}FDG-PET imaging with TSH stimulation.[1031] The frequency of false positive lesions varies from 0% to 39% between series, even with TSH stimulation. These false positive rates justify a FNA biopsy with cytology and Tg measurement in the hub washout for cases where an accessible lymph node is identified by ^{18}FDG-PET/CT (to confirm the presence of thyroid cancer prior to initiating therapy). Detection of lesions in other locations should prompt dedicated cross-sectional imaging of those regions for confirmation and clinical decision-making. Finally, it is important to recognize that ^{18}FDG-PET is insensitive for detecting brain metastases and that standard imaging stops in the mid-thigh. Thus, if there is concern for metastases to brain or below the thighs, brain MRI and extension of images to the feet should be considered.

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)***

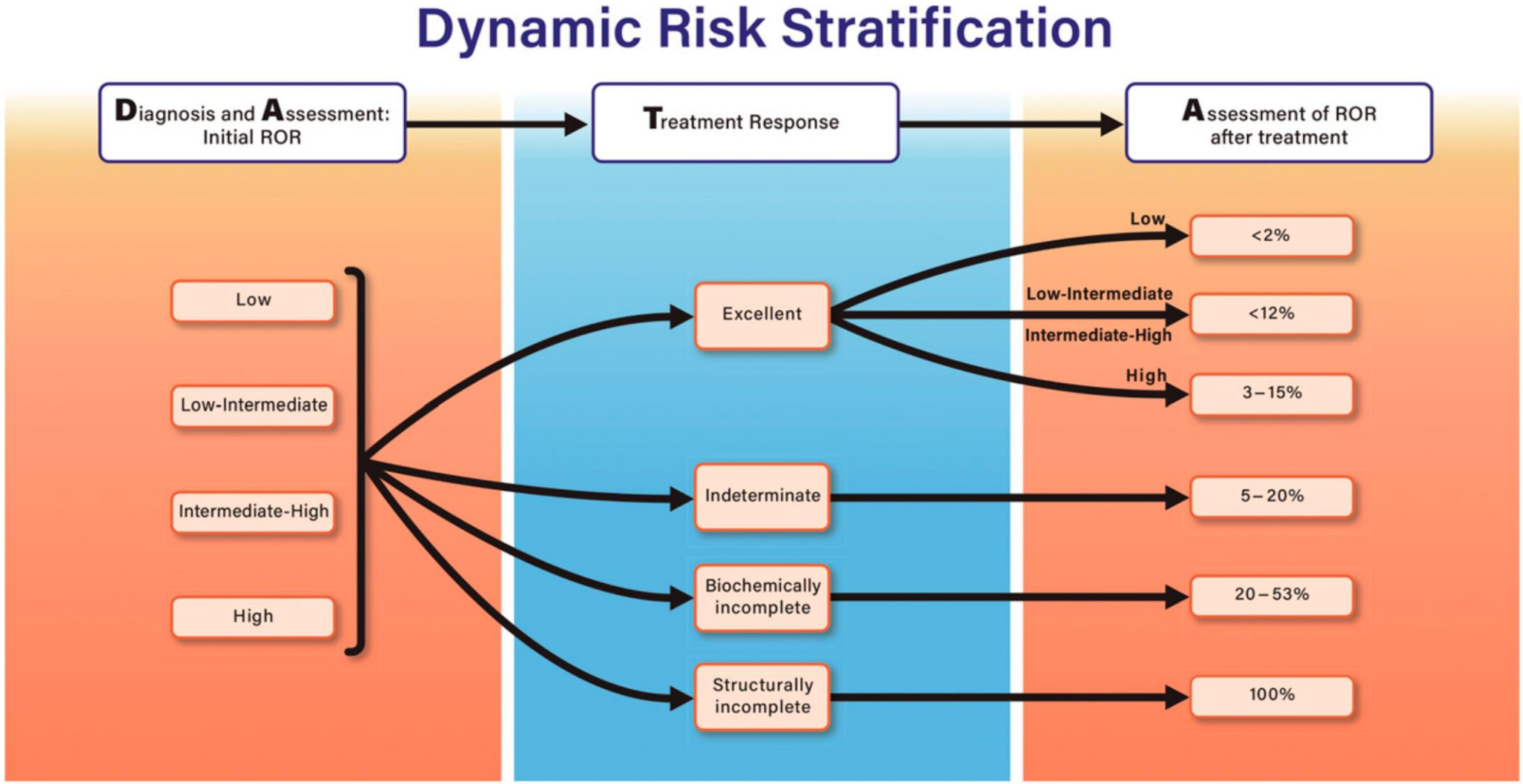
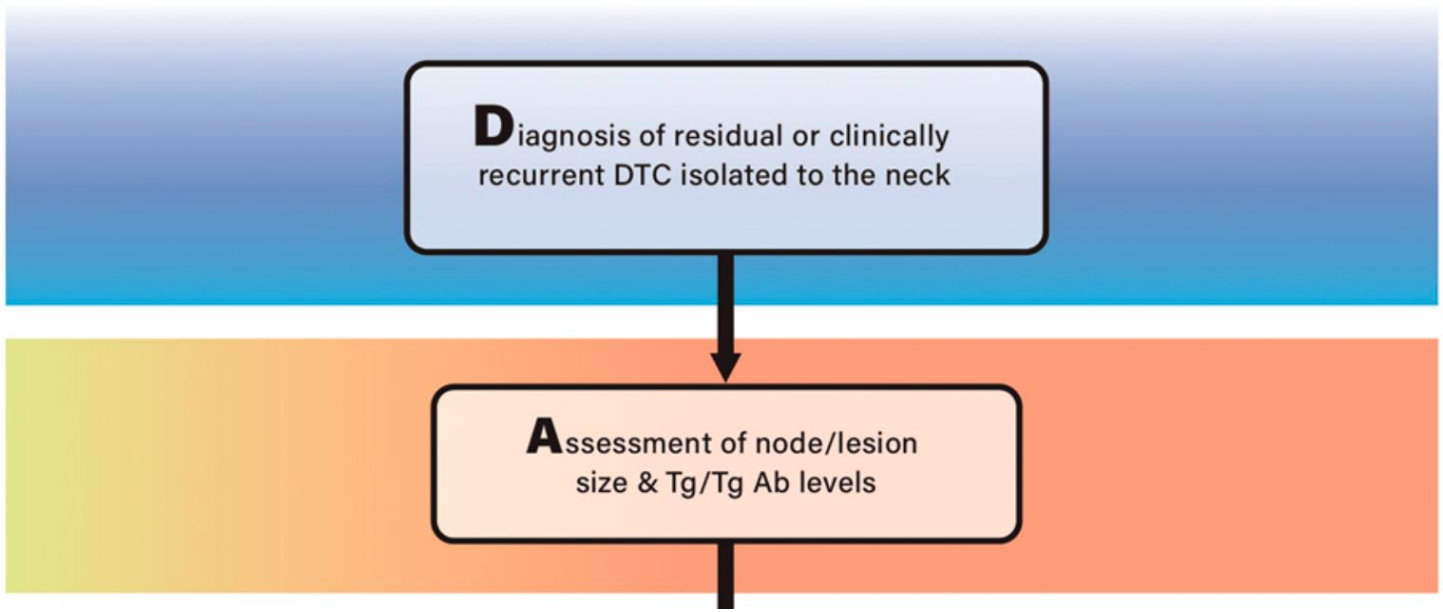


FIG. 6. Dynamic risk stratification and DATA after initial therapy. After initial pathology, imaging, and clinical evaluations are used to estimate risk of recurrence (ROR), a treatment decision is made followed by assessing response to therapy leading to a re-estimation of ROR to inform monitoring approaches.

DATA Framework for Persistent/Recurrent Disease



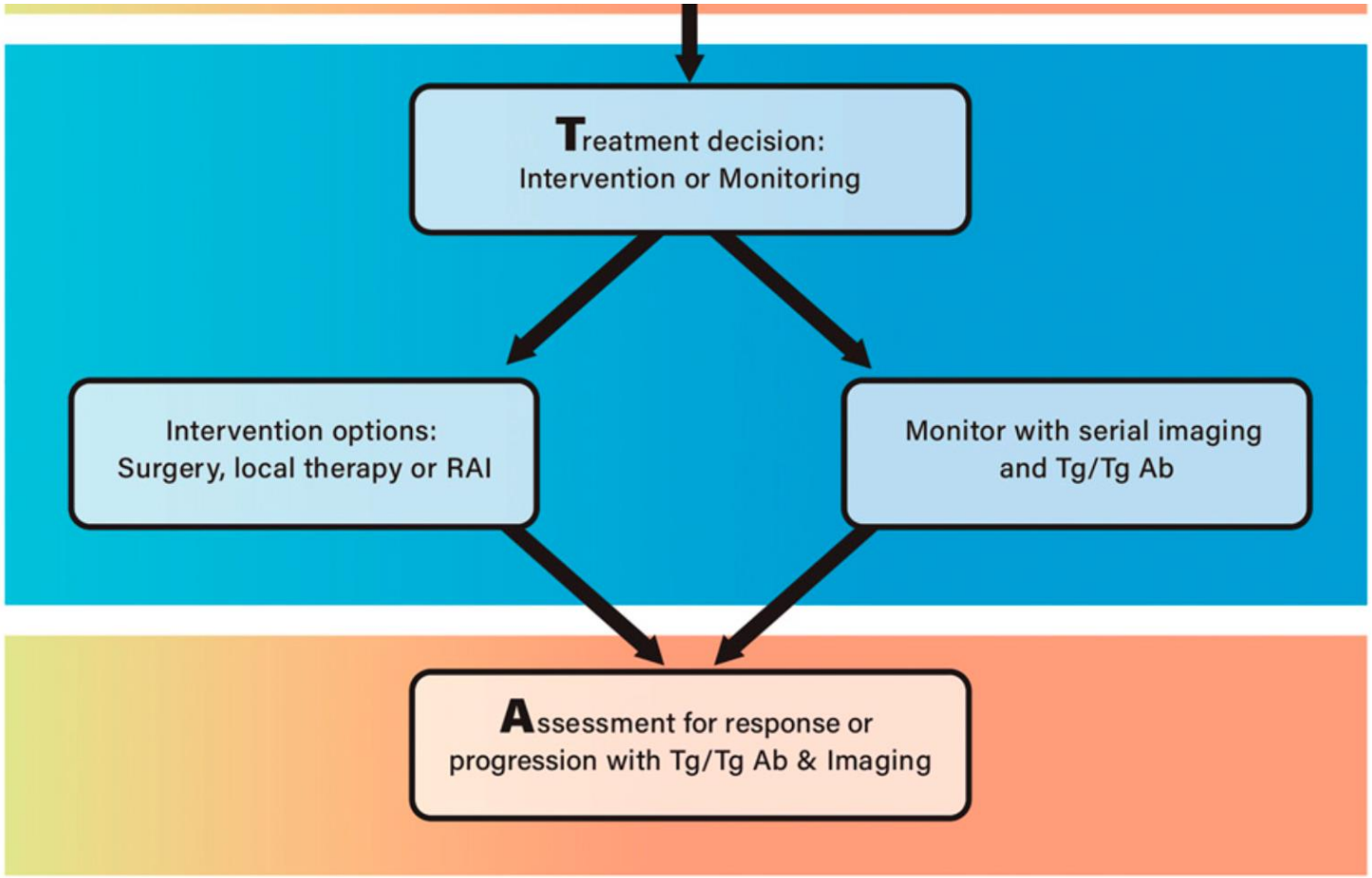


FIG. 7. DATA framework when a patient is diagnosed with residual or clinically recurrent localized DTC in the neck.

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)***

Hirsch et al. retrospectively studied the effect of a second RAI treatment in a cohort of patients with DTC with incomplete biochemical/structural response to initial treatment with surgery and RAI in the absence of distant metastases.[1088] For the incomplete biochemical response cohort, 44 of the 60 patients with evaluable data (73.3%) still had an elevated Tg level 1–2 years after the second RAI treatment. For the incomplete structural response cohort who underwent re-treatment with RAI alone (median lesion size 11.6 mm), no significant change in stimulated or unstimulated Tg levels ensued 1–2 years after the second RAI treat-

tural evidence of persistent locoregional disease. Hung et al. retrospectively evaluated use of RAI after reoperation for recurrent or persistent disease.[1089] Of 102 patients undergoing reoperation, 50 (49.0%) received additional RAI. Median Tg levels at all timepoints studied were similar between the reoperation with RAI group and the reoperation without RAI group (Tg before reoperation, 3.3 ng/mL vs. 2.4 ng/mL, respectively; Tg after reoperation, 0.6 ng/mL vs. 0.2 ng/mL; and Tg after RAI, 0.5 ng/mL vs. 0.2 ng/mL; all differences were nonsignificant). Structural recurrence after

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 ^{131}I >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)***

disease.[1122,1123] With brain metastases or metastases close to the spinal cord or superior vena cava, swelling can compromise neurological function or produce superior vena cava syndrome. If brain or spinal canal metastases are detected, EBRT prior to RAI and high-dose corticosteroid therapy are recommended to limit the risk of acute tumor swelling (see **Recommendation 79**). For the timing before and after RAI, dexamethasone 2–4 mg can be administered every 8 hours starting 6–12 hours prior to rhTSH and RAI administration or after 10–12 days of thyroid hormone withdrawal; the steroid dosages can be tapered (i) over 1 week post-therapy, or (ii) for 48–72 hours after rhTSH administration, or (iii) for 72 hours after re-institution of thyroxine therapy when thyroid hormone withdrawal was employed.[1119] In these challenging situations,

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 ^{18}FDG-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***)

Tg levels <10 ng/mL.[713,1094,1138,1141,1144,1149–1153] The most compelling evidence for benefit from empirical RAI therapy is for multiple pulmonary metastases, which are typically not amenable to surgical management or EBRT.[1138,1154]

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)***
B. Patients who have RAIR DTC should not receive additional empiric RAI therapy. Other treatments should be considered. ***(Good Practice Statement)***

Strong criteria suggesting iodine-refractory DTC include (i) absence of ^{131}I uptake on a post-therapy scan (**Recommendation 37**) in the setting of confirmed disease visible on structural or ^{18}FDG-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.

Supplemental criteria suggesting less RAI sensitivity.

A. No uptake present on a diagnostic ^{123}I or ^{131}I WBS in the presence of otherwise detectable disease. This criterion is known to predict less favorable response to RAI, but some fraction of patients in this category will have a positive post-therapy scan and may still derive some clinical benefit from RAI.
B. Uptake is present in some (but not all) tumor foci on post-therapy WBS. This criterion does not preclude use of RAI but instead suggests that a multimodal treatment approach could be appropriate depending on therapeutic response. RAI alone is not adequate treatment for this subgroup of patients.

Predictors for tumor response to RAI treatment are presence of ^{131}I uptake, younger patient age, well-differentiated histology, small metastases, and low ^{18}FDG uptake. These parameters are closely related[1154,1158,1159] and can predict response to treatment. About two-thirds of patients with metastases demonstrate ^{131}I uptake in them, and only half of such individuals will be cured with repeated courses of RAI.

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)***