Complete Summary

GUIDELINE TITLE

Management guidelines for patients with thyroid nodules and differentiated thyroid cancer.

BIBLIOGRAPHIC SOURCE(S)

Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B, Sherman SI, Tuttle RM, The American Thyroid Association Guidelines Taskforce. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 2006 Feb;16(2):109-42. [301 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse (NGC): This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- May 18, 2005, Aredia (pamidronate disodium) and Zometa (zoledronic acid): Dental healthcare professionals notified of revisions to the prescribing information to describe the occurrence of osteonecrosis of the jaw (ONJ) observed in cancer patients receiving treatment with intravenous bisphosphonates.
- March 25, 2005, Zometa (zoledronic acid): Revisions to the DOSAGE AND ADMINISTRATION and WARNINGS sections of the prescribing information for the drug, to reflect new safety information on management of patients with advanced cancer and renal impairment.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Thyroid nodules and differentiated thyroid cancer

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Endocrinology
Oncology
Radiation Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide recommendations for the management of patients with thyroid nodules and differentiated thyroid cancer

TARGET POPULATION

Patients with thyroid nodules and differentiated thyroid cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation

1. Serum thyrotropin (TSH)
2. Thyroid sonography
3. Serum thyroglobulin (Note: currently not recommended)
4. Serum calcitonin (Note: currently not recommended)
5. Fine needle aspiration (FNA), including close observation or surgical excision (cystic nodules)
6. Specific molecular markers (Note: currently not recommended)
7. Radioiodine thyroid scan

8. Routine suppression therapy of benign nodules (Note: currently not recommended)

Treatment/Management

1. Pre-operative ultrasound staging (Note: routine pre-operative use of other imaging studies, including computed tomography [CT], magnetic resonance imaging [MRI], positron emission tomography [PET] is not currently recommended)
2. Surgery
    - Lobectomy or total thyroidectomy
    - Completion thyroidectomy
    - Lymph node dissection
3. Ablation with radioactive iodine, including pre-therapy scans and/or measurement of thyroid bed uptake and post-therapy scan
4. Post-operative staging
5. Thyrotropin suppression
6. External beam irradiation
7. Chemotherapy (Note: currently not recommended)
8. Post-treatment whole body radioiodine scan (RxWBS) and diagnostic whole body radioiodine scan (DxWBS)
9. Recombinant human thyrotropin (rhTSH)-mediated therapy
10. Surgical resection of metastases
11. Periodic follow-up thyroglobulin levels
12. Referral to clinical trials

MAJOR OUTCOMES CONSIDERED

- Sensitivity and specificity of diagnostic tests
- Disease-related morbidity and mortality
- Disease recurrence/metastatic spread

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Relevant articles were identified by searching MEDLINE using the following search terms: {THRYOID NODULE/diagnosis, drug therapy, surgery, therapy, ultrasonography} or {CANCER} or {CARCINOMA} and {THYROID} and {FOLLICULAR CARCINOMA} or {PAPILLARY CACINOMA} and {FOLLOW-UP} and {TREATMENT} and {RECURRENCE}. All English language papers published between 1995 and December 2004 were reviewed and categorized in tabular form by date, author, subject, and whether it represented a randomized controlled trial, meta-analysis, or clinical case series. Relevant review articles, book chapters, and pre-1995 articles were also supplied by taskforce members.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The taskforce categorized the published data using modified criteria adopted from the U.S. Preventive Services Task Force (USPSTF). The taskforce then made specific recommendations, rated the strength of the recommendation using the schema proposed by the USPSTF (see Table 1 in the original guideline document and the "Rating Scheme for the Strength of the Recommendations" field below). Given the paucity of randomized controlled trials in the treatment of thyroid cancer, the panel relied on all the available published evidence. When evidence was judged to be insufficient, the taskforce members also relied on their experience and judgment to answer the questions that had been posed. The taskforce met again in April 2005 and in June 2005 to refine the document and include new references. Supplementing these meetings were multiple teleconferences and detailed e-mail communications that continued through July 2005.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of Recommendations*

A: Strongly recommends. The recommendation is based on good evidence that the service or intervention can improve important health outcomes. Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

B: Recommends. The recommendation is based on fair evidence that the service or intervention can improve important health outcomes. The evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes.

C: Recommends. The recommendation is based on expert opinion.

D: Recommends against. The recommendation is based on expert opinion.

E: Recommends against. The recommendation is based on fair evidence that the service or intervention does not improve important health outcomes or that harms outweigh benefits.

F: Strongly recommends against. The recommendation is based on good evidence that the service or intervention does not improve important health outcomes or that harms outweigh benefits.

I: Recommends neither for nor against. The panel concludes that the evidence is insufficient to recommend for or against providing the service or intervention because evidence is lacking that the service or intervention improves important health outcomes, the evidence is of poor quality, or the evidence is conflicting. As a result, the balance of benefits and harms cannot be determined.

*Adapted from the U.S. Preventive Services Task Force, Agency for Healthcare Research and Quality

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendations are followed by strength classifications (A-F, I) indicating the strength of the recommendation based on the available evidence. Definitions for the strength of the recommendations are presented at the end of the "Major Recommendations" field.

Thyroid Nodules

Evaluation

Laboratory Tests and Imaging Modalities

R1. Measure serum thyrotropin (TSH) in the initial evaluation of a patient with a thyroid nodule—Recommendation C

R2. Thyroid sonography should be performed in all patients with one or more suspected thyroid nodules—Recommendation B

R3. Routine measurement of serum thyroglobulin for initial evaluation of thyroid nodules is not recommended—Recommendation F

R4. The panel cannot recommend either for or against the routine measurement of serum calcitonin—Recommendation I

Fine Needle Aspiration (FNA) Biopsy

R5. Fine needle aspiration (FNA) is the procedure of choice in the evaluation of thyroid nodules—Recommendation A

R6. Cystic nodules that repeatedly yield nondiagnostic aspirates need close observation or surgical excision. Surgery should be more strongly considered if the cytologically nondiagnostic nodule is solid—Recommendation A

R7. If a cytology result is diagnostic of malignancy, surgery is recommended (Gharib, Goellner, & Johnson, 1993)—Recommendation A

R8. At the present time, the use of specific molecular markers to improve the diagnostic accuracy of indeterminate nodules is not recommended—Recommendation I

R9. If the cytology reading is indeterminate (often termed "suspicious," "follicular lesion," or "follicular neoplasm"), a radioiodine thyroid scan should be considered, if not already done. If a concordant autonomously functioning nodule is not seen, lobectomy or total thyroidectomy should be considered—Recommendation B

R10. If the reading is "suspicious for papillary carcinoma or Hürthle cell neoplasm," a radionuclide scan is not needed, and either lobectomy or total thyroidectomy is recommended (Tyler et al., 1994)—Recommendation A

R11. If the nodule is benign on cytology, further immediate diagnostic studies or treatment are not routinely required—Recommendation A

R12a. In the presence of two or more thyroid nodules larger than 1 to 1.5 cm, those with a suspicious sonographic appearance should be aspirated preferentially—Recommendation B

R12b. If none of the nodules has a suspicious sonographic appearance and multiple sonographically similar coalescent nodules are present, the likelihood of malignancy is low and it is reasonable to aspirate the largest nodules only—Recommendation C

R13. A low or low-normal serum TSH concentration may suggest the presence of autonomous nodule(s). A radioiodine scan should be performed and directly compared to the ultrasound images to determine functionality of each nodule larger than 1 to 1.5 cm. FNA should then be considered only for those isofunctioning or nonfunctioning nodules, among which those with suspicious sonographic features should be aspirated preferentially—Recommendation B

Follow-Up

Long-Term Follow-Up

R14. Easily palpable benign nodules do not require sonographic monitoring, but patients should be followed clinically at 6- to 18-month intervals. It is recommended that all other benign thyroid nodules be followed with serial ultrasound examinations 6 to 18 months after initial FNA. If nodule size is stable, the interval before the next follow-up clinical examination or ultrasound may be longer—Recommendation B

R15. If there is evidence for nodule growth either by palpation or sonographically, repeat FNA, preferably with ultrasound guidance—Recommendation B

Medical Therapy

R16. The panel does not recommend routine suppression therapy of benign thyroid nodules—Recommendation F

R17. Patients with growing nodules that are benign after repeat biopsy should be considered for continued monitoring or intervention with surgery based on symptoms and clinical concern—Recommendation C. There are no data on the use of levothyroxine in this subpopulation of patients—Recommendation I

Management in Children and Pregnant Women

R18. The diagnostic and therapeutic approach to one or more thyroid nodules in a child should be the same as it would be in an adult (clinical evaluation, serum TSH, ultrasound, FNA)—Recommendation A

R19. For euthyroid and hypothyroid pregnant women with thyroid nodules, FNA should be performed. For women with suppressed serum TSH levels that persist after the first trimester, FNA may be deferred until after pregnancy when a radionuclide scan can be performed to evaluate nodule function—Recommendation A

R20. A nodule with malignant cytology discovered early in pregnancy should be monitored sonographically and if it grows substantially (as defined above) by 24 weeks' gestation, surgery should be performed at that point. However, if it

remains stable by mid-gestation or if it is diagnosed in the second half of pregnancy, surgery may be performed after delivery—Recommendation C

Differentiated Thyroid Cancer--Initial Management

Preoperative Staging

R21. Preoperative neck ultrasound for the contralateral lobe and cervical (central and bilateral) lymph nodes is recommended for all patients undergoing thyroidectomy for malignant cytologic findings on biopsy—Recommendation B

R22. Routine preoperative use of other imaging studies (computed tomography [CT], magnetic resonance imaging [MRI], positron emission tomography [PET]) is not recommended—Recommendation E

R23. Routine preoperative measurement of serum thyroglobulin is not currently recommended—Recommendation E

Surgery

Initial Surgery

R24. For patients with an isolated indeterminate solitary nodule who prefer a more limited surgical procedure, thyroid lobectomy is the recommended initial surgical approach—Recommendation C

R25. Because of an increased risk for malignancy, total thyroidectomy is indicated in patients with large tumors (>4 cm) when marked atypia is seen on biopsy, when the biopsy reading is "suspicious for papillary carcinoma," in patients with a family history of thyroid carcinoma, and in patients with a history of radiation exposure (Tuttle, Lemar, & Burch, 1998; Goldstein et al., 2002; Schlinkert et al., 1997). Patients with bilateral nodular disease or those who prefer to undergo bilateral thyroidectomy to avoid the possibility of requiring a future surgery on the contralateral lobe should also undergo total thyroidectomy—Recommendation A

R26. For most patients with thyroid cancer, the initial surgical procedure should be a near-total or total thyroidectomy. Thyroid lobectomy alone may be sufficient treatment for small, low-risk, isolated, intrathyroidal papillary carcinomas in the absence of cervical nodal metastases—Recommendation A

R27. Routine central-compartment (level VI) neck dissection should be considered for patients with papillary thyroid carcinoma and suspected Hürthle carcinoma. Near-total or total thyroidectomy without central node dissection may be appropriate for follicular cancer, and when followed by radioactive iodine therapy, may provide an alternative approach for papillary and Hürthle cell cancers—Recommendation B

R28. Lateral neck compartmental lymph node dissection should be performed for patients with biopsy-proven metastatic cervical lymphadenopathy detected clinically or by imaging, especially when they are likely to fail radioactive iodine

treatment based on lymph node size, number, or other factors, such as aggressive histology of the primary tumor—Recommendation B

Completion Thyroidectomy

R29. Completion thyroidectomy should be offered to those patients for whom a near-total or total thyroidectomy would have been recommended had the diagnosis been available before the initial surgery. This includes all patients with thyroid cancer except those with small (<1 cm), intrathyroidal, node-negative, low-risk tumors—Recommendation B

R30. Ablation of the remaining lobe with radioactive iodine has been used as an alternative to completion thyroidectomy (Randolph & Daniels, 2002). It is unknown whether this approach results in similar long term outcomes. Consequently, radioactive iodine ablation in lieu of completion thyroidectomy is not recommended—Recommendation E

Postoperative Staging Systems

R31. Because of its utility in predicting disease mortality, and its requirement for cancer registries, American Joint Commission on Cancer/International Union Against Cancer (AJCC/UICC) staging is recommended for all patients with differentiated thyroid cancer. The use of postoperative clinicopathologic staging systems is also recommended to improve prognostication and to plan follow-up for patients with differentiated thyroid carcinoma—Recommendation B

Postoperative Radioiodine Remnant Ablation

R32. Radioiodine ablation is recommended for patients with stages III and IV disease (American Joint Commission on Cancer sixth edition; Table 2 in the original guideline document), all patients with stage II disease younger than age 45 years and most patients with stage II disease 45 years or older, and selected patients with stage I disease, especially those with multifocal disease, nodal metastases, extrathyroidal or vascular invasion, and/or more aggressive histologies—Recommendation B

R33. Patients undergoing radioiodine therapy or diagnostic testing can be prepared by LT_4 withdrawal for at least 3 weeks or T_3 treatment for 2 to 4 weeks and T_3 withdrawal for 2 weeks with measurement of serum TSH to determine timing of testing or therapy (TSH >30 mU/L)—Recommendation B

R34. Pretherapy scans and/or measurement of thyroid bed uptake may be useful when the extent of the thyroid remnant cannot be accurately ascertained from the surgical report or neck ultrasonography, or when the results would alter either the decision to treat or the activity of radioiodine that is administered. If performed, pretherapy scans should utilize low-dose ^{131}I (1 to 3 mCi) or ^{123}I—Recommendation C

R35. The minimum activity (30 to 100 mCi) necessary to achieve successful remnant ablation should be chosen, particularly for low-risk patients—Recommendation B

R36. If residual microscopic disease is suspected or documented, or if there is a more aggressive tumor histology (e.g. tall cell, insular, columnar cell carcinoma), then higher activities (100 to 200 mCi) may be appropriate—Recommendation C

R37. Remnant ablation can be performed following thyroxine withdrawal or recombinant human thyrotropin (rhTSH) stimulation—Recommendation B

R38. A low-iodine diet for 1 to 2 weeks is recommended for patients undergoing radioiodine remnant ablation, particularly for those patients with high iodine intake—Recommendation B

R39. A posttherapy scan is recommended after radioiodine remnant ablation. This is typically done 5 to 8 days after the therapeutic dose is administered, although published data supporting this time interval are lacking—Recommendation B

Thyroxine Suppression Therapy

R40. Initial thyrotropin suppression to below 0.1 mU/L is recommended for high-risk patients with thyroid cancer, while maintenance of the TSH at or slightly below the lower limit of normal (0.1 to 0.5 mU/L) is appropriate for low-risk patients—Recommendation B

External Beam Radiation and Chemotherapy

R41. The use of external beam irradiation should be considered in patients over age 45 with grossly visible extrathyroidal extension at the time of surgery and a high likelihood of microscopic residual disease, and for those patients with gross residual tumor in whom further surgery or radioactive iodine would likely be ineffective—Recommendation B

R42. There is no role for the routine adjunctive use of chemotherapy in patients with differentiated thyroid cancer—Recommendation F

Differentiated Thyroid Cancer: Long-Term Management

Serum Thyroglobulin Measurements

R43. Serum thyroglobulin should be measured every 6 to 12 months by an immunometric assay, ideally in the same laboratory and using the same assay, during follow-up of patients with differentiated thyroid carcinoma who have undergone total or near-total thyroidectomy and thyroid remnant ablation. Thyroglobulin antibodies should be quantitatively assessed with every measurement of serum thyroglobulin—Recommendation A

R44. Periodic serum thyroglobulin measurements should be considered during follow-up of patients with differentiated thyroid carcinoma who have undergone less than total thyroidectomy, and in patients who have had a total thyroidectomy but not radioiodine ablation. The cutoff levels to detect tumor during TSH suppression or stimulation are not known, but unstimulated or stimulated levels greater than 2 ng/mL that increase over time may represent recurrent disease—Recommendation C

R45. In low risk patients who have had remnant ablation and negative cervical ultrasound and TSH-suppressed thyroglobulin 6 months after treatment, serum thyroglobulin should be measured after thyroxine withdrawal or rhTSH stimulation approximately 12 months after the ablation to verify absence of disease. The timing or necessity of subsequent stimulated testing is uncertain for those found to be free of disease—Recommendation A

Diagnostic Radioiodine Scans, Ultrasound, and other Imaging Techniques

R46. After the first posttreatment wholebody radioiodine scan (RxWBS) performed after radioiodine remnant ablation, low-risk patients with negative TSH-stimulated thyroglobulin and cervical ultrasound do not require routine diagnostic whole body radioiodine scans (DxWBS) during follow-up—Recommendation A

R47. DxWBS 6 to 12 months after remnant ablation may be of value in the follow-up of patients with high or intermediate risk of persistent disease, but should be done with low dose ^{131}I or ^{123}I—Recommendation C

R48. After surgery, cervical ultrasound to evaluate the thyroid bed and central and lateral cervical nodal compartments should be performed at 6 and 12 months and then annually for at least 3 to 5 years, depending on the patients' risk for recurrent disease and thyroglobulin status—Recommendation B

Long-Term Thyroxine Suppression Therapy

R49. In patients with persistent disease, the serum TSH should be maintained below 0.1 mU/L indefinitely in the absence of specific contraindications—Recommendation B

R50. In patients who are clinically free of disease but who presented with high risk disease, consideration should be given to maintaining TSH suppressive therapy to achieve serum TSH levels of 0.1 to 0.5 mU/L for 5 to 10 years—Recommendation C

R51. In patients free of disease, especially those at low risk for recurrence, the TSH may be kept within the low normal range (0.3 to 2 mU/L)—Recommendation C

Management of Patients with Metastatic Disease

Locoregional Recurrence

R52. Patients with persistent/recurrent disease confined to the neck should undergo complete ipsilateral or central compartmental dissection of involved compartments while sparing vital structures—Recommendation B

R53. When technically feasible, surgery for aero-digestive disease is recommended in combination with radioiodine and/or external beam radiotherapy—Recommendation B

R54. In the treatment of locoregional or metastatic disease, no recommendation can be made about the superiority of one method of radioiodine administration over another (empiric high dose versus blood or body dosimetry)—Recommendation I

R55. There are currently insufficient outcome data to recommend rhTSH-mediated therapy for all patients with metastatic disease being treated with ^{131}I—Recommendation D

R56. rhTSH-mediated therapy may be indicated in selected patients with underlying comorbidities making iatrogenic hypothyroidism potentially risky, in patients with pituitary disease who are unable to raise their serum TSH, or in patients in whom a delay in therapy might be deleterious—Recommendation C

R57. Because there are no outcome data that demonstrate a better outcome of patients treated with ^{131}I in the setting of lithium therapy, the committee cannot recommend for or against its use—Recommendation I

Distant Metastatic Disease

Pulmonary Metastases

R58. Pulmonary micrometastases should be treated with radioiodine therapy, repeated every 6 to 12 months as long as disease continues to respond, as the highest rates of complete remission are reported in these subgroups (Ronga et al., 2004; Schlumberger et al., 1996; Ilgan et al., 2004)—Recommendation A

R59. The selection of radioiodine activity to administer for pulmonary micrometastases can be empiric (100 to 300 mCi) or estimated by dosimetry to limit whole body retention to 80 mCi at 48 hours and 200 cGy to the red bone marrow—Recommendation C

R60. Radioiodine-avid macronodular metastases should be treated with radioiodine, and treatment repeated when objective benefit is demonstrated (decrease in the size of the lesions, decreasing thyroglobulin), but complete remission is not common and survival remains poor. The selection of radioiodine activity to administer can be made empirically (100 to 300 mCi) or estimated by dosimetry to limit whole body retention to 80 mCi at 48 hours and 200 cGy to the red bone marrow—Recommendation B

R61. Evidence of benefit of routine treatment of nonradioiodine avid pulmonary metastases is insufficient to recommend any specific systemic therapy—Recommendation I

R62. For many patients, metastatic disease is slowly progressive and patients can often be followed conservatively on TSH-suppressive therapy with minimal evidence of radiographic or symptomatic progression. For selected patients, however, other treatment options need to be considered, such as metastasectomy, endobronchial laser ablation, or external beam radiation for palliation of symptomatic intrathoracic lesions (e.g., obstructing or bleeding endobronchial masses), and pleural or pericardial drainage for symptomatic

effusions. Referral for participation in clinical trials should be considered—Recommendation C

Bone Metastases

R63. Complete surgical resection of isolated symptomatic metastases has been associated with improved survival and should be considered, especially in patients less than 45 years old (Bernier et al., 2001; Zettinig et al., 2002)—Recommendation B

R64. Radioiodine therapy of iodine-avid bone metastases has been associated with improved survival and should be used (Bernier et al., 2001; Schlumberger et al., 1996). The radioiodine activity administered can be given empirically (150 to 300 mCi) or estimated by dosimetry (Maxon et al., 1983)—Recommendation B

R65. When skeletal metastatic lesions arise in locations where acute swelling may produce severe pain, fracture, or neurologic complications, external radiation and the concomitant use of glucocorticoids to minimize potential TSH-induced and/or radiation related tumor expansion should be strongly considered (Luster et al., 2005)—Recommendation C

R66. Painful lesions that cannot be resected can also be treated by several options individually or in combination, including: radioiodine, external beam radiotherapy; intra-arterial embolization (Eustatia-Rutten et al., 2003; Van Tol et al., 2000), radiofrequency ablation (Posteraro, Dupuy, & Mayo-Smith, 2004), periodic pamidronate or zoledronate infusions (with monitoring for development of possible osteonecrosis) (Vitale et al., 2001), or bone-seeking radiopharmaceuticals such as strontium-89 or samarium-153 (Hellman & Krasnow, 1998). While many of these modalities have been shown to relieve bone pain in cancer, they have not necessarily been reported to have been used in patients with thyroid cancer—Recommendation C

R67. Evidence is insufficient to recommend treatment of asymptomatic, non-radioiodine responsive, stable lesions that do not threaten nearby critical structures—Recommendation I

Brain Metastases

R68. Complete surgical resection of central nervous system (CNS) metastases should be considered regardless of radioiodine avidity, as it is associated with significantly longer survival—Recommendation B

R69. CNS lesions that are not amenable to surgery should be considered for external beam irradiation. Often very targeted approaches (such as radiosurgery) are employed to limit the radiation exposure of the surrounding brain tissue. Wholebrain and spine irradiation could be considered if multiple metastases are present—Recommendation C

R70. If CNS metastases do concentrate radioiodine, then radioiodine could be considered. If radioiodine is being considered, prior external beam radiotherapy and concomitant glucocorticoid therapy are strongly recommended to minimize

the effects of a potential TSH-induced increase in tumor size and the subsequent inflammatory effects of the radioiodine (Luster et al., 2005)—Recommendation C

Complications of Radioiodine Therapy

R71. For acute transient loss of taste or change in taste and sialadenitis, some have recommended measures to prevent damage to the salivary glands including amifostine, hydration, sour candies, and cholinergic agents (Mandel & Mandel, 2003), but evidence is insufficient to recommend for or against these modalities. One recent study suggested sour candy may actually increase salivary gland damage when given within 1 hour of radioiodine therapy, compared to its use until 24 hours posttherapy (Nakada et al., 2005). For chronic salivary gland complications, such as dry mouth and dental caries, cholinergic agents may increase salivary flow (Mandel & Mandel, 2005)—Recommendation I

R72. Patients with xerostomia are at increased risk of dental caries and should discuss preventative strategies with their dentists—Recommendation C

R73. Surgical correction should be considered for nasolacrimal outflow obstruction, which often presents as excessive tearing (epiphora) but also predisposes to infection—Recommendation B

R74. Because there is no evidence demonstrating a benefit of more intensive screening, all patients with thyroid cancer should be encouraged to seek age-appropriate screenings for cancer according to routine health maintenance recommendations—Recommendation C

R75. Patients receiving therapeutic doses of radioiodine should have baseline complete blood cell (CBC), platelet count, and assessment of renal function—Recommendation C

R76. Women receiving radioactive iodine therapy should avoid pregnancy for 6 to 12 months—Recommendation B

R77. Radioactive iodine should not be given to breast-feeding women. Depending on the clinical situation, radioiodine therapy could be deferred until a time when lactating women have stopped breast-feeding for at least 6 to 8 weeks. Dopaminergic agents might be useful in decreasing breast exposure, although caution should be exercised given the risk of serious side-effects associated with their routine use to suppress postpartum lactation—Recommendation B

Thyroglobulin-Positive Patients

R78. Empiric radioactive iodine therapy (100–200 mCi) might be considered in patients with elevated or rising serum thyroglobulin levels in whom imaging has failed to reveal a potential tumor source—Recommendation C

R79. If persistent nonresectable disease is localized after an empiric dose of radioiodine, and there is objective evidence of significant tumor reduction, then radioiodine therapy should be repeated until the tumor has been eradicated or the tumor no longer responds to treatment. The risk of repeated therapeutic does of

radioiodine must be balanced against uncertain long-term benefits—Recommendation C

R80. If an empiric dose (100 to 200 mCi) of radioiodine fails to localize the persistent disease, 18-fluorodeoxyglucose positron emission tomography (FDG-PET) scanning should be considered, especially in patients with unstimulated serum thyroglobulin levels more than 10 to 20 ng/mL, in order to localize metastatic lesions that may require treatment or continued close observation (Wang et al., 1999; Helal et al., 2001)—Recommendation B

R81. Thyroglobulin positive, RxWBS-negative patients with disease that is incurable with surgery and is structurally evident or visualized on FDG-PET scan can be managed with thyroid hormone suppression therapy, external beam radiotherapy, chemotherapy, radiofrequency ablation, chemoembolization, or monitoring without additional therapy if stable. Clinical trials should also be considered—Recommendation C

R82. Thyroglobulin-positive, RxWBS-negative patients with no structural evidence of disease can be followed with serial structural imaging studies and serial thyroglobulin measurements, with both performed more frequently if the thyroglobulin level is rising. When and how often to repeat FDG-PET imaging in this setting is less certain—Recommendation C

External Beam Radiotherapy and Chemotherapy

R83. External beam radiation should be used in the management of unresectable gross residual cervical disease, painful bone metastases, metastatic lesions in critical locations likely to result in fracture, neurological, or compressive symptoms that are not amenable to surgery (e.g., vertebral metastases, CNS metastases, selected mediastinal or subcarinal lymph nodes, pelvic metastases) (Tsang et al., 1998; Brierley & Tsang, 1999)—Recommendation B

R84. Chemotherapy has modest benefit in patients with advanced, radioiodine-resistant thyroid cancer. Patients with progressive disease should first be considered for clinical trials. If clinical trials are unavailable or the patient prefers standard cytotoxic chemotherapy, doxorubicin used as a single agent or in combination with other agents may be considered—Recommendation C

R85. Patients with advanced, progressive, unresectable radioiodine non-responsive thyroid cancer who are being considered for chemotherapy should be considered for entry into clinical trials—Recommendation C

Definitions:

Strength of Recommendations

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CLINICAL ALGORITHM(S)

Clinical algorithms are provided in the original guideline document for the following:

- Evaluation of patients with one or more thyroid nodules
- Initial follow-up of patients with differentiated thyroid carcinoma
- Longer term follow-up of patients with differentiated thyroid carcinoma
- Considerations for empiric treatment with radioiodine

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Given the paucity of randomized controlled trials in the treatment of thyroid cancer, the panel relied on all the available published evidence. When evidence was judged to be insufficient, the taskforce members also relied on their experience and judgment to answer the questions that had been posed.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of patients with thyroid nodules and differentiated thyroid cancer

POTENTIAL HARMS

- Adverse effects of serum thyrotropin (TSH) suppression may include the known consequences of subclinical thyrotoxicosis, including exacerbation of angina in patients with ischemic heart disease, increased risk for atrial fibrillation, and increased risk of osteoporosis in postmenopausal women.
- While radioiodine appears to be a reasonably safe therapy, it is associated with a cumulative dose-related low risk of early and late onset complications such as salivary gland damage, nasolacrimal duct obstruction, and secondary malignancies.
- Published data indicate that when administered activities are selected to remain below 200 cGy to the bone marrow, minimal transient effects are noted in white blood cell (WBC) and platelet counts. However, persistent mild decrements in white blood count and/or platelets are not uncommon in patients who have received multiple radioiodine therapies. Furthermore, radiation to the bone marrow is impacted by several factors, including renal function.
- Ovarian damage from radioiodine therapy may result in menopause occurring approximately 1 year earlier than the general population, but this result was not associated with cumulative dose administered or the age at which the therapy was given. In men, radioiodine therapy may be associated with a temporary reduction in sperm counts and elevated serum follicle-stimulating hormone (FSH) levels. Higher cumulative doses (500 to 800 mCi) in men are associated with an increased risk of persistent elevation of serum follicle-stimulating hormone levels, but fertility and risks of miscarriage or congenital abnormalities in subsequent pregnancies are not changed with moderate radioiodine doses (approximately 200 mCi).

CONTRAINDICATIONS

CONTRAINDICATIONS

Radionuclide scan is contraindicated in pregnant women.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B, Sherman SI, Tuttle RM, The American Thyroid Association Guidelines Taskforce. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 2006 Feb;16(2):109-42. [301 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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American Thyroid Association - Professional Association

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GUIDELINE COMMITTEE

American Thyroid Association Guidelines Taskforce

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

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GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from American Thyroid Association Web site.

Print copies: Available from American Thyroid Association, 6066 Leesburg Pike, Suite 550, Falls Church, VA 22041.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

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