



American Head and Neck Society - Journal Club

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For this Journal Club issue, we chose to highlight portions of the new 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer. Since there is so much material in the guidelines, we selected several topics that we felt were both more clinically relevant for surgeons and significant changes from the previous guidelines. Obviously, we were unable to cover all of the important material, but we attempted to at least distill some of it down to highlight certain key aspects. We hope that you find these summaries useful and informative.

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Recommendation 8

Thyroid nodule diagnostic FNA is recommended for:

- A. Nodules > 1cm in greatest dimension with high suspicion sonographic pattern (Strong recommendation, Moderate-quality evidence)
- B. Nodules > 1 cm in greatest dimension with intermediate suspicion sonographic (Strong recommendation, Low-quality evidence)
- C. Nodules > 1.5cm in greatest dimension with low suspicion sonographic pattern (Weak recommendation, Low-quality evidence)

Thyroid nodule diagnostic FNA may be considered for (Figure 2, Table 6):

- A. Nodules > 2cm in greatest dimension with very low suspicion sonographic pattern (e.g. – spongiform). Observation without FNA is also a reasonable option (Weak recommendation, Moderate-quality evidence)

Thyroid nodule diagnostic FNA is not required for (Figure 2, Table 6):

- A. Nodules that do not meet the above criteria. (Strong recommendation, Moderate quality evidence)
- B. Nodules that are purely cystic (Strong recommendation, Moderate-quality)

From the report:

Studies consistently report that several US gray scale features in multivariate analyses are associated with thyroid cancer, which include microcalcifications, nodule hypoechoogenicity compared with the surrounding thyroid, irregular margins, and a shape taller than wide measured on a transverse view.



Features with the highest specificities (median >90%) for thyroid cancer are microcalcifications, irregular margins, and tall shape, although the sensitivities are significantly lower for any single feature.

High suspicion [malignancy risk >70-90%: Solid hypoechoic nodule or a solid hypoechoic component in a partially cystic nodule with one or more of the following features: irregular margins (specifically defined as infiltrative, microlobulated, or spiculated), microcalcifications, taller than wide shape, disrupted rim calcifications with small extrusive hypoechoic soft tissue component, or evidence of extrathyroidal extension. Nodules with the high suspicion pattern and > 1cm should undergo diagnostic fine needle biopsy to refute or confirm malignancy.

Intermediate suspicion [malignancy risk 10-20%: Hypoechoic solid nodule with a smooth regular margin, without microcalcifications, extrathyroidal extension, or taller than wide shape. This appearance has the highest sensitivity (60-80%) for PTC, but a lower specificity than the above high suspicion pattern, and fine needle biopsy should be considered for these nodules > 1cm to refute malignancy.

Low suspicion [malignancy risk 5-10%]: Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric uniformly solid areas without microcalcifications, irregular margin or extrathyroidal extension, or taller than wide shape. Only about 15% -20% of thyroid cancers are iso- or hyperechoic on ultrasound, and these are generally the follicular variant of papillary thyroid cancer or follicular thyroid cancers. Fewer than 20% of these nodules are partially cystic. Therefore, these appearances are associated with a lower probability of malignancy and observation may be warranted until the size is > 1.5cm.

Very low suspicion (<3%): Spongiform or partially cystic nodules without any of the sonographic features described in the low, intermediate or high suspicion patterns have a low risk of malignancy (<3%). If FNA is performed, the nodule should be at least 2 cm. Observation without FNA may also be considered for nodules > 2 cm.

Benign [<1%]: Purely cystic nodules are very unlikely to be malignant and FNA is not indicated for diagnostic purposes.

These results are largely based on well conducted observational studies and mostly denote a strong recommendation where the benefit clearly outweighs the harm.

TABLE 6. SONOGRAPHIC PATTERNS, ESTIMATED RISK OF MALIGNANCY, AND FINE-NEEDLE ASPIRATION GUIDANCE FOR THYROID NODULES

| Sonographic pattern | US features | Estimated risk of malignancy, % | FNA size cutoff (largest dimension) |
|----------------------------|---|--|--|
| High suspicion | Solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule with one or more of the following features: irregular margins (infiltrative, microlobulated), microcalcifications, taller than wide shape, rim calcifications with small extrusive soft tissue component, evidence of ETE | >70–90 [±] | Recommend FNA at ≥1 cm |
| Intermediate suspicion | Hypoechoic solid nodule with smooth margins without microcalcifications, ETE, or taller than wide shape | 10–20 | Recommend FNA at ≥1 cm |
| Low suspicion | Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric solid areas, without microcalcification, irregular margin or ETE, or taller than wide shape. | 5–10 | Recommend FNA at ≥1.5 cm |
| Very low suspicion | Spongiform or partially cystic nodules without any of the sonographic features described in low, intermediate, or high suspicion patterns | <3 | Consider FNA at ≥2 cm Observation without FNA is also a reasonable option |
| Benign | Purely cystic nodules (no solid component) | <1 | No biopsy [±] |

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Recommendation 13

If molecular testing is being considered, patients should be counseled regarding the potential benefits and limitations of testing and about the possible uncertainties in the therapeutic and long-term clinical implications of results. (Strong recommendation, Low-quality evidence)

The largest studies of preoperative molecular markers in patients with indeterminate FNA cytology have evaluated:

1. a seven-gene panel of genetic mutations and rearrangements (BRAF, RAS, RET/PTC, PAX8/PPARc)
 - Rule-in (“If the test result for a highly specific test is positive you can be nearly certain that they actually have the disease.” www.med.emory.edu)
 - High specificity (86-100%), high PPV (84-100%)
 - BRAF^{V600E} single mutation has a specificity of approximately 99% but sensitivity too low to be used for rule-out cancer (Therefore, mutational panels have been expanded to include multiple mutations/translocations including BRAF, NRAS, HRAS, and KRAS point mutations, as well as RET/PTC1 and RET/PTC3, with or without PAX8/PPARc rearrangements).
 - In indeterminate cytology thyroid nodules, the sensitivity of the seven gene mutational panel testing is variable, with reports ranging from 44% to 100%. Therefore, it cannot be used to reliably rule out malignancy with a negative test in this population.
 - Next-generation sequencing of an expanded panel of point mutations, single base insertions/deletions (indels), and gene rearrangements has been reported to have a sensitivity of 90% for FN/SFN FNA cytology specimens from a single-center study.
 - This test is most useful when surgery is favored. However, this is based on the assumption that the surgical approach would be altered with a positive test, and long-term outcome data proving the overall benefit of this therapeutic strategy are needed. Furthermore, long-term outcome data from a strategy of using molecular markers in indeterminate FNA specimens to stratify surgical approach are currently lacking.
2. a gene expression classifier (167 GEC; mRNA expression of 167 genes)
 - Rule-out (“If the test is highly sensitive and the test result is negative you can be nearly certain that they don’t have disease” www.med.emory.edu)
 - High sensitivity (92%) and NPV (93%)
 - low specificity of the 167 GEC test (mean values 48%–53% in indeterminate nodules subject to histopathologic confirmation) suggests that the test cannot definitively rule-in malignancy in indeterminate nodules
 - Data demonstrates:
 - The prevalence of malignancy confirmed by histopathology in 167 GEC “suspicious” nodules ranged from
 - 33% to 80% in the 48 nodules in the AUS/FLUS group across institutions
 - 33% to 67% in the 65 nodules in the FN (follicular neoplasm) group
 - For the 174 patients with 167 GEC “benign” readings, 6% of patients in this group (11/174) had surgery, with one histopathologically confirmed malignancy.
 - Reproducibility of results has been questioned. It is not known to what extent differences in techniques used to perform mutational testing by various groups may affect test performance, and direct, head-to-head comparisons of these tests within the same population are lacking.
3. Other tests

- Immunohistochemical stains galectin-3 and HBME-1 (requires cell blocks)
 - high rates of specificity, but low sensitivity, for cancer detection
- mRNA markers and miRNA markers
 - Combination seven-gene mutational testing with expression of a set of 10 miRNA genes on preoperative FNA in patient with AUS/ FLUS or FN
 - 89% sensitivity, 85% specificity, with a 73% PPV and 94% NPV on this group with a 32% prevalence of malignancy
- Peripheral blood TSH receptor mRNA assay
 - 90% PPV and 39% NPV in FNA-based assessment of thyroid nodules with atypical or suspicious cytology in a single-center, prospective validation study

In summary, there is currently no single optimal molecular test that can definitively rule in or rule out malignancy in all cases of indeterminate cytology, and long-term outcome data proving clinical utility are needed.

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Recommendation 14

If intended for clinical use, molecular testing should be performed in Clinical Laboratory Improvement Amendments/ College of American Pathologists (CLIA/CAP)-certified molecular laboratories, or the international equivalent, because reported quality assurance practices may be superior compared to other settings. (Strong recommendation, Low-quality evidence)

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Recommendation 15

Thyroid nodules with atypia of undetermined significance/follicular lesion of indeterminate significance (AUS/FLUS) have a reported risk of cancer between 6-48% with a mean risk of 16% (191). These lesions present a clinical dilemma and are discussed in this recommendation. After considering worrisome clinical and sonographic features repeat FNA or molecular testing can be considered to stratify the risk of malignancy (weak recommendation, moderate-quality evidence) prior to making a decision to observe or proceed with surgery (strong recommendation, low quality evidence).

The rate of malignancy on surgical follow up after a single FNA demonstrating AUS/FLUS is 41%, after two successive AUS/FLUS diagnosis is 43%, and a benign interpretation following an initial AUS/FLUS diagnosis is 29%, thus a repeat FNA can be helpful in the evaluation of AUS/FLUS lesions (196).

Molecular testing can also be of assistance in evaluation of AUS/FLUS lesions with sensitivities ranging from 63-90%. Interpretation of this data can be complex but in summary, BRAF has a high specificity and a low sensitivity (198,199). Testing with panels of molecular markers including BRAF, NRAS, KRAS, RET/PTC1, RET/PTC3, PAX8/PPAR γ has improved sensitivities to up to 80%. (162, 165). Ongoing analysis and long term follow ups may eventually lead to a stronger recommendation.

Depending on clinical risk factors, sonographic pattern, molecular markers, and patient preference an observational or surgical approach is decided in patients with thyroid nodules with atypia of undetermined significance/follicular lesion of indeterminate significance.

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Recommendations 19 & 20

What is the appropriate operation for cytologically indeterminate thyroid nodules? (A21)

Recommendation 19:

When surgery is considered for patients with a solitary, cytologically indeterminate nodule, thyroid lobectomy is the recommended initial surgical approach. This approach may be modified based on clinical or sonographic characteristics, patient preference, and/or molecular testing when performed (see Recommendations 13–16). (Strong recommendation, Moderate-quality evidence)

Recommendation 20:

- A. Because of increased risk for malignancy, total thyroidectomy may be preferred in patients with indeterminate nodules that are cytologically suspicious for malignancy, positive for known mutations specific for carcinoma, sonographically suspicious, or large (>4 cm), or in patients with familial thyroid carcinoma or history of radiation exposure, if completion thyroidectomy would be recommended based on the indeterminate nodule being malignant following lobectomy. (Strong recommendation, Moderate-quality evidence)
- B. Patients with indeterminate nodules who have bilateral nodular disease, those with significant medical co-morbidities, or those who prefer to undergo bilateral thyroidectomy to avoid the possibility of requiring a future surgery on the contralateral lobe, may undergo total or near-total thyroidectomy, assuming completion thyroidectomy would be recommended if the indeterminate nodule proved malignant following lobectomy. (Weak recommendation, Low-quality evidence)



Comments:

These recommendations address all the key points in relation to the management of indeterminate and follicular lesion results via FNA of a nodule. The decision for extent of surgery is multifactorial but one should note the strong recommendation to perform a hemithyroidectomy as a initial surgical approach. When the risk of malignancy significantly increases there is also a strong recommendations to consider a total thyroidectomy. Patient preferences and health factors as well as surgeon factors should considered when working with patient to find the proper surgical plan.

Key Points from Commentary in Guidelines:

The primary goal of thyroid surgery for a thyroid nodule that is cytologically indeterminate (AUS/FLUS or FN or SUSP) is to establish a histological diagnosis and definitive removal, while reducing the risks associated with remedial surgery in the previously operated field if the nodule proves to be malignant.

Surgical options to address the nodule should be limited to lobectomy (hemithyroidectomy) with or without isthmusectomy, near-total thyroidectomy (removal of all grossly visible thyroid tissue, leaving only a small amount [<1 g] of tissue adjacent to the recurrent laryngeal nerve near the ligament of Berry), or total thyroidectomy (removal of all grossly visible thyroid tissue). Decisions regarding the extent of surgery for indeterminate thyroid nodules are influenced by several factors including the estimated presurgical likelihood of malignancy based upon clinical risk factors (>4 cm, family history, and/or history of radiation) These risk factors, as well as patient preference, presence of contralateral nodularity or coexistent hyperthyroidism, and medical comorbidities, impact decisions regarding thyroid lobectomy with the possible need for subsequent completion thyroidectomy versus total thyroidectomy up front.

The risks of total thyroidectomy are significantly greater than that for thyroid lobectomy, with a recent meta-analysis suggesting a pooled relative risk (RR) significantly greater for all complications, including recurrent laryngeal nerve injury (transient RR = 1.7, permanent RR = 1.9), hypocalcemia (transient RR = 10.7, permanent RR = 3.2), and hemorrhage/hematoma (RR = 2.6) (231). Further, total thyroidectomy is associated with the rare but potential risk of bilateral recurrent laryngeal nerve injury necessitating tracheostomy. Surgeon experience likely influences the risks of thyroidectomy, with higher volume surgeons having lower complication rates. Hypothyroidism is not an indication for thyroidectomy, and its use as justification for total thyroidectomy over lobectomy should be weighed against the higher risks associated with total thyroidectomy. In contrast, coexistent hyperthyroidism may be an indication for total thyroidectomy depending upon the etiology. Thyroid lobectomy (hemithyroidectomy) provides definitive histological diagnosis and complete tumor removal for cytologically indeterminate nodules with a lower risk of complications compared to total thyroidectomy and may be sufficient for smaller, solitary intra-thyroidal nodules that ultimately prove malignant. As the likelihood of malignancy increases, the potential need for a second operation also increases, if the cytologically indeterminate nodule ultimately proves malignant and if completion thyroidectomy would be recommended. Intraoperative evaluation, with or without frozen section, can occasionally confirm malignancy at the time of lobectomy allowing for conversion to total thyroidectomy if indicated. Frozen section is most helpful if the histopathologic diagnosis is classic PTC, whereas its impact is low in follicular variant of PTC and FTC. **The individual patient must weigh the relative advantages and disadvantages of thyroid lobectomy with possible total thyroidectomy or subsequent completion thyroidectomy versus initial total thyroidectomy.**

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Recommendation 33

Locally invasive disease constitutes about 10% to 15% of most reported well-differentiated thyroid carcinoma series. It is associated with a worse prognosis and increased risk of mortality if the surgical resection is incomplete. Local invasion may manifest through vocal cord palsy (with or without hoarseness), hemoptysis, laryngeal stridor or dysphagia. However, it is usually asymptomatic and clinical examination can also be negative. Preoperative laryngoscopy is mandatory in all cases, and impairment of vocal cord mobility is the most frequent finding suggesting extrathyroid invasion. Bronchoscopy and esophagoscopy are indicated only in selected patients. A cross-sectional imaging preoperative study is considered useful supplement for surgical planning because it can accurately delineate the extent of laryngotracheal, esophageal or vascular involvement.

ATA Recommendation number 33 refers to preoperative indication of imaging studies (CT, MRI and PET) as an adjunct to US for patients with clinical suspicion for advanced locoregional disease. US evaluation is the standard method used for initial evaluation, however it is operator dependent and not adequately image trachea, esophagus, prevertebral fascia and other deeper anatomical structures. Furthermore, patients with bulky and widely distributed metastatic lymph nodes can present involvement of additional lymph node regions such as retropharyngeal, infraclavicular and mediastinal. Although supported by low-quality evidence, preoperative MRI or CT (with contrast) was strongly recommended, and PET was not recommended. The rationale for these recommendations are the following studies. Ahn et al (World J Surg, 32:1552-8, 2008) reported a series of patients who had preoperative CT and US prior to total thyroidectomy and neck dissection. The sensitivity of CT (77%) was significantly better than US (62%) for the evaluation central and lateral compartment lymph nodes. Choi et al (AJR Am J Roentgenol 193:871-8, 2009) reported a series of 299 patients with papillary thyroid carcinoma who underwent preoperative CT and US. US was more accurate than CT in predicting extrathyroidal tumor extension and lateral compartment lymph node metastases. Lesnik et al (Head Neck 36:191-202, 2014) showed that combined preoperative US and CT was superior to US alone in the detection of level VI neck disease. On the other side, Jeong et al. (Clin Endocrinol, 65:402-7, 2006) reported a lower sensitivity (30%-40%) of MRI and PET for the detection of neck lymph node metastases. According to Kaplan et al (AJNR Am J Neuroradiol 30:608-12, 2009), MRI can be affected by respiratory movement artifacts and may be more difficult to interpret than CT scanning. The specificity of PET is reduced because it can detect a large number of inflammatory lymph nodes (Jeong et al, 2006). However, according to Yeh et al (Thyroid, 25:3-14, 2015) ¹⁸F-DG-PET scanning may be sensitive in some patients for neck or mediastinal lymph node involvement and also may show distant metastases. These preoperative features can influence the surgical plan.

Recommendation 33 also emphasizes that chest CT is useful in defining the inferior limit of the disease and diagnose the involvement of mediastinal structures. CT findings are also crucial on planning surgical management (the need of sternotomy, laryngotracheal and or esophageal resection and vascular approach) that do require assembling additional resources and personnel in preparation for a complex comprehensive radical resection (extended thyroidectomy with appropriate selective or extended neck/mediastinum lymph node dissection and reconstruction).

Finally, when CT is performed, use of IV iodine contrast is an important adjunct that improves delineation between the primary tumor or lymph node metastases and the normal structures. Preoperative contrast enhanced CT does not significantly delay postoperative whole-body scan nor preclude RAI treatment because iodine is usually cleared from 4 to 8 weeks. If there is a concern, urinary iodine can be measured (Padovani et al, Thyroid, 22:926-30, 2012).

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Recommendation 35

- A) For patients with thyroid cancer >4 cm, or with gross extrathyroidal extension (clinical T4), or clinically apparent metastatic disease to nodes (clinical N1) or distant sites (clinical M1), the initial surgical procedure should include a near-total or total thyroidectomy and gross removal of all primary tumor unless there are contraindications to this procedure. (Strong recommendation, Moderate-quality evidence)

- B) For patients with thyroid cancer >1 cm and <4 cm without extrathyroidal extension, and without clinical evidence of any lymph node metastases (cN0), the initial surgical procedure can be either a bilateral procedure (near total or total thyroidectomy) or a unilateral procedure (lobectomy). Thyroid lobectomy alone may be sufficient initial treatment for low-risk papillary and follicular carcinomas; however, the treatment team may choose total thyroidectomy to enable RAI therapy or to enhance followup based upon disease features and/or patient preferences. (Strong recommendation, Moderate-quality evidence)

- C) If surgery is chosen for patients with thyroid cancer <1 cm without extrathyroidal extension and cN0, the initial surgical procedure should be a thyroid lobectomy unless there are clear indications to remove the contralateral lobe. Thyroid lobectomy alone is sufficient treatment for small, unifocal, intrathyroidal carcinomas in the absence of prior head and neck radiation, familial thyroid carcinoma, or clinically detectable cervical nodal metastases. (Strong recommendation, Moderate-quality evidence)

Previous guidelines have endorsed total thyroidectomy as a primary initial surgical treatment option for nearly all patients with differentiated thyroid cancers that are greater than 1 cm including those without evidence of local regional or distant metastases. Recent data have demonstrated that in properly selected patients clinical outcomes are similar following unilateral or bilateral thyroid surgery. In addition given the recommendation for more selective use of radioactive in low to intermediate risk patients than previously recommended and that the reason for total thyroidectomy was to facilitate iodine ablation, the need for total thyroidectomy is less. In addition, single-sided surgery may obviate the need for lifelong exogenous thyroid hormone and given that the follow-up management is now more heavily weighted towards neck ultrasound and serial thyroglobulin measurements rather than whole-body radioactive iodine scanning, unilateral surgery is compatible with this approach.

Analysis of over 52,000 patients from the National Cancer Database evaluating overall survival and recurrence rates between unilateral and bilateral surgery revealed small differences in both. When analyzed by the size of the primary tumor, statistically significant differences in survival and recurrence were seen for all sizes greater than 1 cm based on the extent of initial surgery. However data on extrathyroidal extension, completeness of resection and other comorbid conditions which would have a major impact on survival recurrence were not available.

Other studies reviewing the SEER database have indicated that there is no difference in 10 year survival between total thyroidectomy and thyroid lobectomy when risk stratified by the AMES classification system. 2 additional studies using the SEER database and evaluating over 300,000 patients also failed to demonstrate significant difference in survival when comparing total thyroidectomy with thyroid lobectomy.

Conclusion: In properly selected low to intermediate risk patients, the extent of initial thyroid surgery probably has little impact the disease specific survival. In the few patients that may recur, salvage surgery is quite effective following thyroid lobectomy. Near-total or total thyroidectomy is necessary if the

overall strategy is to include radioactive iodine therapy postoperatively and thus is recommended if the primary thyroid carcinoma is greater than 4 cm, if there is gross extrathyroidal extension or if regional or distant metastases are clinically present. For tumors that are between 1 and 4 cm in size, either a bilateral thyroidectomy or unilateral procedure may be suitable as a treatment plan. Older age, contralateral thyroid nodules and a personal history radiation to the head and neck and familial differential thyroid cancer may be criteria for recommending a bilateral procedure because of plans for radioactive iodine therapy or to facilitate follow up strategies or address suspicions of bilateral disease.

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Recommendation 36

- A. Therapeutic central-compartment (level VI) neck dissection for patients with clinically involved central nodes should accompany total thyroidectomy to provide clearance of disease from the central neck. (Strong Recommendation, Moderate-quality evidence)
- B. Prophylactic central-compartment neck dissection (ipsilateral or bilateral) should be considered in patients with papillary thyroid carcinoma with clinically uninvolved central neck lymph nodes (cN0) who have advanced primary tumors (T3 or T4), clinically involved lateral neck nodes (cN1b), or if the information will be used to plan further steps in therapy. (Weak Recommendation, Low-quality evidence)
- C. Thyroidectomy without prophylactic central neck dissection may be appropriate for small (T1 or T2), noninvasive, clinically node-negative PTC (cN0) and for most follicular cancers. (Strong Recommendation, Moderate-quality evidence)

Lymph node metastases are present at the time of diagnosis in a majority of patients with papillary carcinomas. The role of therapeutic lymph node dissection for treatment of thyroid cancer node metastases is well accepted for cN1 disease. However, the value of routine prophylactic level VI (central) neck dissection for cN0 disease remains unclear. PTC lymph node metastases are reported by some to have no clinically important effect on outcome in low risk patients, while other SEER and NCDB studies show that lymph node involvement confers prognostic information. Common to all of these studies is the conclusion that the effect of the presence or absence of lymph node metastases on overall survival, if present, is small and probably most significant in older patients.

The cervical node sites are well-defined, and the most common site of nodal metastases is in the central neck (level VI). Central compartment dissection (therapeutic or prophylactic) can be achieved with low morbidity by experienced thyroid surgeons. Value for an individual patient depends upon the utility of the staging information to the treatment team in specific patient circumstances. Based on limited and imperfect data, prophylactic dissection has been suggested to improve disease-specific survival, local recurrence and post-treatment thyroglobulin levels. It has also been used to inform the use of adjuvant RAI and improve the accuracy of the estimates of risk of recurrence. However, in several studies, prophylactic dissection has shown no improvement in long-term patient outcome, while increasing the likelihood of temporary morbidity, including hypocalcemia. For these reasons, groups may elect to include prophylactic dissection for patients with some prognostic features associated with an increased risk of metastasis and recurrence (older or very young age, larger tumor size, multifocal disease, extrathyroidal extension, known lateral node metastases) to contribute to decision-making and disease control. For some groups it appears reasonable to use a selective approach that applies level VI lymph node dissection at the time of initial operation only to patients with clinically evident disease based on preoperative physical exam, preoperative radiographic evaluation or intraoperative demonstration of



detectable disease.

The information from prophylactic central neck dissection must be used cautiously for staging information. Since microscopic nodal positivity occurs frequently, prophylactic dissection often converts patients from clinical N0 to pathologic N1a, upstaging many patients over age 45 from American Joint Committee on Cancer (AJCC) stage I to stage III. However, microscopic nodal positivity does not carry the recurrence risk of macroscopic clinically detectable disease.

The above recommendations should be interpreted in light of available surgical expertise. For patients with small, noninvasive, cN0 tumors, the balance of risk and benefit may favor thyroid lobectomy and close intraoperative inspection of the central compartment, with the plan adjusted to total thyroidectomy with compartmental dissection only in the presence of involved lymph nodes.

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