

Preventable reoperations for persistent and recurrent papillary thyroid carcinoma

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Background. Cervical recurrence occurs in up to 25% of patients with papillary thyroid carcinoma (PTC) due either to the aggressive biology of PTC or to inadequate treatment. This retrospective study was designed to determine the frequency of inadequate surgical or medical therapy as a cause of persistent or recurrent PTC.

Methods. We identified all patients who underwent reoperation for persistent (within 6 months of initial or prereferral operation) or recurrent (greater than 6 months after initial or prereferral operation) PTC from 1992 to 2003. Medical records including initial preoperative imaging, operative, and histopathology reports were reviewed. The initial surgical procedure was considered incomplete if all gross neoplasm was not removed or if "node plucking" was performed, and a subsequent recurrence occurred in the same cervical compartment.

Results. Seventy-two consecutive patients underwent reoperation for persistent (17) or recurrent (55) PTC. Of the 17 patients with persistent PTC, reoperation was judged to have been possibly preventable in 14 (82%) due to inadequate preoperative imaging or incomplete initial surgery. Of the 55 patients with recurrent PTC, reoperation was judged to have been possibly preventable due to incomplete initial surgery in 14 (25%). Based on the National Comprehensive Cancer Network guidelines, 33 (46%) of 72 patients with persistent or recurrent PTC received inadequate initial local treatment.

Conclusions. Reoperation in 28 (39%) of 72 patients with persistent or recurrent PTC was potentially preventable. Accurate preoperative staging and adherence to the suggested National Comprehensive Cancer Network treatment guidelines may minimize the need for cervical reoperation. (Surgery 2004;136:1183-91.)

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THE OPTIMAL TREATMENT strategy for patients with papillary thyroid cancer (PTC) involves complete surgical resection of clinically and radiographically evident disease within the neck, the selective use of adjuvant radioiodine therapy (RAI), and postoperative thyroid-stimulating hormone (TSH) suppression.¹⁻³ Multiple retrospective studies have validated the risk stratification of patients by low versus intermediate and high risk for recurrence and death based on prognostic factors including patient age,

the presence or absence of extracervical metastatic disease, tumor size, the presence or absence of extrathyroidal extension and regional lymph node metastases.^{1,2,4-7} Although 23,600 new cases of thyroid cancer are expected this year in the United States, death from PTC, the most common form of thyroid cancer, is very rare, occurring mostly in patients with extracervical distant metastases who are older than 45 years.^{8,9} This observation is appropriately reflected in the current American Joint Committee on Cancer (AJCC) TNM staging system, which classifies all patients under the age of 45 years as having either stage I (M0) or stage II (M1) disease.¹⁰ Therefore, death cannot be used as a valid endpoint for the assessment of treatment efficacy in the vast majority of patients with PTC. However, cervical recurrence, usually in the form of regional lymph node metastases, occurs in up to 20% of patients with low-risk PTC and 59% of patients with high-risk PTC.^{6,7,11} Although cervical recurrence necessitating reoperation does not

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predict the development of extracervical metastatic disease and may not significantly impact survival duration, especially in low- and intermediate-risk patients, reoperation is a traumatic event for patients and may be associated with complications such as injury to the recurrent laryngeal nerve, hypoparathyroidism, palsy of the spinal accessory nerve, and the cosmetic concerns of cervical incisions.^{7,12,13}

The incidence of cervical recurrence is not just a function of patient- and tumor-related prognostic factors but is also influenced by treatment-related factors. The extent of thyroidectomy and the performance of an R0 or R1 resection (resection of all gross disease) clearly influence the frequency of cervical recurrence.^{11,12} Additional treatment-related factors may also impact recurrence rates such as the use of compartment-oriented neck dissection rather than node-plucking procedures, postoperative TSH suppression, and possibly adjuvant RAI. The observation that cervical recurrence rates are unacceptably high, especially for a disease with such a low mortality, and may be impacted by the extent of surgical and postoperative therapy was concluded by multiple retrospective studies over the past 2 decades.^{1-5,11} This realization is reflected in the National Comprehensive Cancer Network (NCCN) practice guidelines for the treatment of thyroid carcinoma.^{7,14} These guidelines advocate the use of preoperative fine-needle aspiration (FNA) biopsy, the practice of total thyroidectomy in high-risk patients, complete extirpation (R0/R1 resection) of all disease evident on physical examination and preoperative imaging studies, and the use of postoperative TSH suppression.¹⁴ These guidelines represent a medical consensus strongly influenced by the published rates of cervical recurrence.^{1-5,11,12}

Therefore, we retrospectively examined all patients who underwent cervical reoperation for persistent or recurrent PTC during the past 11 years at our institution to determine to what extent the reoperation would have been preventable if standard surgical and medical management had been performed.

METHODS

Using the prospective database of the Department of Surgical Oncology at the University of Texas M. D. Anderson Cancer Center, we identified all patients with PTC who underwent reoperation from 1992 through 2003. Study patients were divided into 2 groups: group 1 patients underwent reoperation for persistent disease, which was defined as disease occurring within 6 months of initial or prereferral operation; group 2 patients

underwent reoperation for recurrent disease, which was defined as disease occurring more than 6 months after initial or prereferral operation.

To determine the adequacy of initial or prereferral operation, we reviewed all medical records, including reports of initial preoperative imaging, operative notes, and histopathology reports. For group 1 patients, we defined inadequate initial treatment as failure to perform preoperative imaging of the thyroid or lateral (levels II-V) neck compartments in patients found to have a positive imaging study before reoperation, and/or failure to remove all gross neoplasm during the initial surgical procedure. For group 2 patients, we defined inadequate initial treatment as performance of a "node-plucking" operation (rather than a compartment-oriented lymphadenectomy) with subsequent recurrence in the same cervical compartment; failure to perform a lymph node dissection during the initial operation despite preoperative knowledge of lymph node metastases; and/or failure to suppress TSH postoperatively. Inadequate TSH suppression was defined as a TSH level above the lower limit of normal (0.5 μ U/mL) at all recorded measurements done within 2 years of the diagnosis of cervical recurrence.

In addition, we evaluated the extent of initial surgery based on 2000 through 2003 NCCN guidelines (Table I).¹⁴ In accordance with these guidelines, we considered less than total or less than near-total thyroidectomy (thyroid lobectomy) as inadequate initial local surgical treatment for patients with PTC who were under age 15 or over age 45, had a history of radiation treatment to the head or neck, had a primary tumor size greater than 4 cm, or had bilateral or extrathyroidal disease, a family history of PTC, or lymph node metastases. If patients met 1 or more of the above criteria preoperatively or intraoperatively and underwent less than total or less than near-total thyroidectomy due to the failure to perform a preoperative FNA biopsy or an intraoperative frozen-section, they were also judged to have received inadequate initial surgery. A node-plucking operation was considered inadequate regional surgical treatment with respect to the NCCN guidelines.

TNM stage (AJCC staging system, 6th edition) was determined by a review of histopathology reports from all operations performed within 6 months of the patient's initial thyroidectomy.¹⁰

Pretreatment evaluation at our institution included physical examination, ultrasonography of the soft tissues of the neck, and, when indicated, ultrasonography-guided FNA of regional lymph nodes or soft tissue recurrence.¹⁵ Chest radiogra-

Table I. Selected summary of NCCN guidelines for PTC

Preoperative or intraoperative indications for total thyroidectomy (any of the following)
Age <15 y or >45 y
Radiation history
Known distant metastases
Bilateral disease
Extrathyroidal extension
Neoplasm >4 cm in diameter
Cervical lymph node metastases
Family history of PTC or follicular thyroid cancer
Indications for completion thyroidectomy (if not initially done)
Any of the above indications or any of the following:
Aggressive variant (tall cell, columnar cell, insular, or poorly differentiated features)
Positive margins
Multifocal disease
Indications for neck reoperation
Residual disease in neck
Clinically suspicious lymph nodes or contralateral lesion (based on physical examination and/or ultrasonography)
Postoperative TSH suppression (<0.5 μU/mL)
All patients

NCCN, National Comprehensive Cancer Network; PTC, papillary thyroid carcinoma; TSH, thyroid-stimulating hormone.

phy and computed tomography (CT) were performed selectively.

RESULTS

We identified 72 consecutive patients who underwent reoperation for persistent (group 1, n = 17) or recurrent (group 2, n = 55) PTC from 1992 to 2003. There were 53 women (74%) and 19 men (26%) with a median age at initial PTC diagnosis of 37 years (range, 16-80 years). In total, 65 patients (90%) had 1 or more adverse prognostic factors (Table II), and 49 patients (68%) had stage I disease (Table III). Before reoperation, thyroglobulin levels were available for 62 (84%) of 72 patients. The median nonstimulated serum thyroglobulin for all 62 patients was 14.5 ng/mL (range, 2-810 ng/mL), it was >1 ng/mL in 38 (61%) of 62 patients and was undetectable in 24 (39%). Antithyroglobulin antibodies were present in 14 (58%) of the 24 patients with undetectable thyroglobulin levels.

Of the 17 group 1 patients (those who underwent reoperation for persistent PTC), 16 underwent initial surgery before referral to our institution. Of these 16 patients, 12 were thought to have undergone complete cervical surgery and were referred to our institution for adjuvant RAI, 1

Table II. Patient- and tumor-related adverse prognostic factors in 72 patients who underwent reoperation*

	Group 1 (%)	Group 2 (%)	Total (%)
Total patients	17	55	72
Patient-related adverse prognostic factors			
Age <15 or >45 y	6 (35)	15 (27)	21 (29)
Family history of PTC	1 (6)	4 (7)	5 (7)
Radiation history	1 (6)	2 (4)	3 (4)
Tumor-related adverse prognostic variables			
Multifocal PTC	12 (71)	29 (53)	41 (57)
Bilateral PTC	11 (65)	16 (29)	27 (38)
Primary neoplasm >4 cm	1 (6)	2 (4)	3 (4)
Extrathyroidal extension	5 (29)	19 (35)	24 (33)
Total patients with 1 or more adverse prognostic factors	17 (100)	48 (87)	65 (90)

PTC, Papillary thyroid carcinoma.

*Some patients had more than 1 adverse prognostic factor.

was referred for management of possible pulmonary metastases, 2 were referred with known persistent disease in the neck, and 1 requested a second opinion after presumed complete initial therapy. The single group 1 patient who underwent initial surgical treatment at our institution and was found to have persistent disease postoperatively had large-volume disease in the neck treated with total thyroidectomy, and central and bilateral modified radical neck dissection. At the time of the first postoperative ultrasonography examination, a single level VB lymph node metastasis was found; this patient therefore underwent a second operation for excision of this disease before RAI.

Persistent disease was detected on physical examination and/or ultrasonography in 15 (88%) of the 17 group 1 patients; disease was palpable in 6 patients and visible on ultrasonography in 15. Two (12%) of 17 patients had no measurable disease before reoperation. Both patients had initially undergone thyroid lobectomy. Completion total thyroidectomy was recommended because of the presence of extrathyroidal extension in 1 patient and a strong family history of PTC in the other patient; both patients were found to have PTC in the remnant contralateral lobe after reoperation. Reoperations in these 17 patients included completion total thyroidectomy in 5, completion thyroidectomy with central and/

Table III. Pathologic tumor stage in 72 patients with PTC*

Tumor type/stage	No. of patients		
	Group 1 (%) (n = 17)	Group 2 (%) (n = 55)	Total (%) (n = 72)
Primary neoplasm (T)			
TX†	0	4 (7)	4 (6)
T1	7 (41)	20 (36)	27 (38)
T2	4 (24)	11 (20)	15 (21)
T3	5 (29)	19 (35)	24 (33)
T4a	1 (6)	1 (2)	2 (3)
Regional lymph nodes (N)			
NX	2 (12)	23 (42)	25 (35)
N0	2 (12)	2 (4)	4 (6)
N1a	3 (18)	11 (20)	14 (19)
N1b	10 (59)	19 (35)	29 (40)
Stage grouping			
Stage I	11 (65)	38 (69)	49 (68)
Stage II	0	1 (2)	1 (1)
Stage III	3 (18)	3 (5)	6 (8)
Stage IVA	2 (12)	7 (13)	9 (13)
Stage IVB	0	0	0
Stage IVC	0	0	0
Stage not assessed‡	1 (6)	6 (11)	7 (10)

PTC, Papillary thyroid carcinoma.

*AJCC Cancer Staging Manual (6th ed).¹⁰

†Primary tumor size was not recorded in the pathology report.

‡Stage could not be assessed from the incomplete pathology report.

or lateral neck dissection in 7, neck dissection alone in 3, and limited neck dissection in a previously dissected compartment in 2. PTC was found in the thyroid remnant in 7 of 12 patients who underwent completion thyroidectomy, and regional lymph node metastases were found in 11 of 12 patients who underwent some form of neck dissection. One patient with PTC in the thyroid remnant also underwent a level VI neck dissection; all lymph nodes examined were without evidence of metastatic PTC.

Among the 17 group 1 patients, reoperation was judged to have been possibly preventable in 14 (82%) due to inadequate preoperative imaging (3), incomplete initial surgery (2), or both (9). Among the 12 patients judged to have undergone inadequate preoperative imaging, ultrasonography examination at our institution demonstrated a suspicious neoplasm in the thyroid remnant in 5 and lymph node metastases in the central or lateral neck compartment in 9. By definition, disease seen on ultrasonography is grossly visible disease and in these patients, ranged in size from 0.5 cm to 2.2

cm. The 11 patients judged to have undergone incomplete surgery were 3 patients with known lateral neck disease who did not undergo neck dissection, 2 patients who underwent some form of node plucking (from the lateral neck compartment) and were found to have persistent nodal disease in the same neck compartment, 1 patient who underwent thyroid lobectomy despite preoperative imaging suggesting bilateral multifocal PTC, 1 patient who underwent open thyroid (excisional) biopsy without formal thyroidectomy, and 4 patients with bulky central compartment (level VI) disease that was not completely resected because of the surgeon's inexperience (Table IV).

Group 2 comprised 55 patients who underwent reoperation for recurrent PTC. The median time to first recurrence was 1.8 years with a mean time to recurrence of 4.6 years. Ten of the 55 patients underwent initial surgery at our institution and all received postoperative adjuvant RAI. The remaining 45 patients underwent initial surgery before referral, and 34 (76%) received postoperative adjuvant RAI. Among the latter 45 patients, 13 (29%) were referred to our institution for routine follow-up, 3 (7%) for adjuvant RAI therapy more than 6 months after thyroidectomy, and 29 (64%) for further evaluation of suspected recurrent or metastatic disease. In these 29 patients, recurrent PTC was suspected from physical examination in 8 (28%), imaging studies in 12 (41%; ultrasonography, 6; magnetic resonance imaging (MRI), 1; RAI 5), and an elevation in serum thyroglobulin levels in 9 (31%).

Evaluation at our institution of all 55 patients (group 2) demonstrated recurrent disease on physical examination in 21 (38%) and by ultrasonography in 52 (95%). The 3 patients who did not have disease on ultrasonography included 1 patient with a remnant recurrence and a normal preoperative ultrasonography (completion thyroidectomy done before RAI), 1 patient with indeterminate ultrasonography of the ipsilateral lateral neck compartment in whom subsequent neck dissection demonstrated metastatic PTC, and 1 patient who had bilateral bulky lymphadenopathy and in whom it was believed that preoperative ultrasonography would not alter the need for bilateral (and central compartment) neck dissection. Reoperations in these 55 patients consisted of completion total thyroidectomy in 1, completion thyroidectomy and central and/or lateral neck dissection in 6, neck dissection alone in 41, and limited neck dissection (in a previously dissected compartment) in 7. PTC was found in the remnant thyroid in 3 (43%) of 7 patients who underwent

Table IV. Preventability of reoperation in 72 patients with persistent or recurrent PTC

	<i>No. of Patients</i>
I. Group 1 (persistent PTC)	17
A. Reoperation preventable	14 (82%)
1. Inadequate preoperative imaging*	12 (71%)
a. Ultrasonography not performed before surgery	4
b. Ultrasonography of thyroid performed without assessment of levels II to V	8
2. Incomplete initial surgery	11 (65%)
a. Known lateral neck disease not dissected	3
b. Node plucking (from lateral neck) at initial surgery with persistent disease in the same compartment	2
c. Incomplete resection of the primary thyroid neoplasm	2
d. Bulky central compartment disease not completely resected	4
B. NCCN guidelines not followed	11 (65%)
1. Less than total or less than near-total thyroidectomy performed	8
2. Gross lymph node metastases but neck dissection not performed	6†
II. Group 2 (recurrent PTC)	55
A. Reoperation preventable	27 (49%)
1. Incomplete initial operation	14 (25%)
a. Node plucking at initial surgery with recurrence in the same compartment	9
b. Gross lymph node metastases not removed	5
2. Inadequate TSH suppression (>0.5 μU/mL)	17 (31%)
B. NCCN guidelines not followed	22 (40%)
1. Less than total or near-total thyroidectomy performed	4
2. Completion total thyroidectomy not performed	1‡
3. Gross lymph node metastases but neck dissection not performed	17

PTC, Papillary thyroid carcinoma; NCCN, National Comprehensive Cancer Network; TSH, thyroid-stimulating hormone.

*For 2 patients, whether they had ultrasonography before initial surgery was not recorded.

†Three of 6 also underwent thyroid lobectomy and are included in the row above.

‡In addition to 3 of the 4 patients in the row above.

completion thyroidectomy and in regional lymph nodes in 53 (98%) of 54 patients who underwent some form of neck dissection; soft tissue recurrence thought to be unrelated to a lymph node recurrence was found in 1 patient.

Among the 55 group 2 patients, reoperation was judged to have been possibly preventable in 27 (49%) due to incomplete initial surgery (10), ab-

sence of TSH suppression (13), or both (4) (Table IV). Of the 14 patients judged to have undergone incomplete initial surgery, 9 (64%) underwent lymph node plucking rather than standard neck dissection using a compartment-oriented approach (and recurred in the same neck compartment), and 5 (36%) did not undergo any form of lymph node dissection at initial surgery despite preoperative knowledge of lymph node metastases.

Based on the NCCN guidelines for extent of thyroidectomy and management of regional lymph node metastases, 11 (65%) of the 17 group 1 patients and 22 (40%) of the 55 group 2 patients received inadequate initial local treatment (Table IV). All 17 patients with persistent PTC had preoperative or intraoperative criteria for total thyroidectomy; however, 8 underwent thyroid lobectomy. Four of the 8 patients did not have a preoperative or intraoperative diagnosis of PTC due to the absence of both a preoperative FNA biopsy and intraoperative frozen-section. This likely contributed to the failure to perform a total or near-total thyroidectomy. Six of the 17 group 1 patients (including 3 of 8 who underwent thyroid lobectomy) had regional lymph node metastases treated with either no dissection or lymph node plucking. Of the 22 group 2 patients who received inadequate initial local treatment, 4 had preoperative or intraoperative criteria for total thyroidectomy but underwent thyroid lobectomy. One additional patient who underwent thyroid lobectomy had histologic evidence of a positive thyroid transection margin and did not undergo completion total thyroidectomy until referral for recurrence. The remaining 17 patients had regional lymph node metastases treated with either no dissection or lymph node plucking.

In addition, 10 of the 55 group 2 patients did not undergo preoperative FNA biopsy before initial surgery, and 6 of these 10 patients were treated with thyroid lobectomy. After initial thyroid lobectomy, 4 of these 6 patients had histologic findings (extrathyroidal extension [3] or positive margins [1]) to support reoperative completion total thyroidectomy; however, this was not performed until they presented to our institution with recurrent disease.

A complete R0/R1 resection was successfully performed in all 72 patients, and PTC was histologically confirmed in all surgical specimens.

DISCUSSION

Overall, reoperation in 41 (57%) of 72 patients with persistent or recurrent PTC was judged to have been possibly preventable. Among the 17

patients who required early reoperation for persistent or incompletely resected disease, reoperation was judged to have been preventable in 14 (82%). Four of these 14 patients had bulky central compartment disease that may not have been appreciated until surgery. The operative surgeon was uncomfortable proceeding with complete tumor extirpation and therefore appropriately referred these patients to our institution for reoperation. One could argue that the surgical management of these patients was appropriate and that occasionally the extent of disease cannot be appreciated until the neck is opened. With the benefit of more contemporary imaging including high-quality ultrasonography, CT, and/or MRI, this is now uncommon.¹⁵ Of the remaining 10 patients who were found to have persistent disease in the neck, the majority were referred for adjuvant RAI. It has been our general practice to utilize RAI in high-risk patients, but only after confirmation that, when technically possible, a complete gross resection (R0/R1) has been performed. RAI is not therapeutically equivalent to surgical resection for grossly visible disease seen on ultrasonography.¹⁶⁻¹⁸ Therefore, we routinely perform ultrasonography of the neck on patients who have undergone preoperative surgery before considering hormone withdrawal and adjuvant RAI. If the ultrasonography examination identifies grossly visible disease that appears surgically resectable, the patient undergoes cervical reoperation before RAI. Our experience demonstrates that patients thought to have undergone complete resection of all cervical disease may have persistent disease in the neck that requires reoperation. Importantly, in this report, adequate preoperative imaging combined with compartment-oriented surgery would have allowed a complete resection of all gross disease at the first operation and likely prevented 10 of 17 group 1 patients from requiring reoperation for persistent PTC. Our previous work is in agreement with the NCCN guidelines that advocate careful preoperative imaging using high-quality ultrasonography and standard techniques of neck dissection to facilitate complete tumor extirpation.^{15,19}

The need for reoperation was also judged to have been possibly preventable in 27 (49%) of 55 patients with recurrent PTC. Fourteen of 27 patients underwent an incomplete initial operation. These 14 patients included 5 patients in whom preoperative imaging or intraoperative findings suggested more extensive disease than was successfully removed by the operating surgeon. Clearly, surgeon experience may have been a factor that contributed to the need for reoperation in

these patients. In the other 9 patients, recurrent lymph node metastases occurred in the same cervical compartment in which a node-plucking procedure had previously been performed. It therefore is reasonable to conclude that if formal compartment-oriented dissection had been performed initially, these recurrences may not have occurred.¹⁵ Although we have seen isolated lymph node or soft tissue recurrences in previously dissected neck compartments, this is a rare event.^{15,19} There is emerging consensus that compartment-oriented neck dissection minimizes the incidence of subsequent neck recurrence and is far superior to a node-plucking procedure.¹⁴ Importantly, dissection of the lateral neck compartments (levels IIA through V) is associated with minimal morbidity in the absence of injury to the spinal accessory nerve.^{15,20,21}

We also found that 17 of 55 group 2 patients had evidence of inadequate TSH suppression. Although the failure of TSH suppression alone may not have been responsible for the development of recurrent disease, it is reasonable to assume that this had a significant impact on tumor growth.¹ Postoperative thyroid hormone therapy is recommended for all patients with PTC because it minimizes recurrence and improves survival.^{1,14,22} Careful monitoring of thyroid function in patients with PTC requires both attention to detail on the part of treating physicians and compliance and understanding on the part of the patients.²³

Although the patients in this report were treated between 1992 and 2003, we believed it is appropriate to compare their treatment with the 2000-2003 NCCN guidelines.¹⁴ These guidelines were based on multiple retrospective studies published over the prior 2 decades that provided support for the treatments recommended.^{1-7,12} The NCCN guidelines thus represent a consensus of previously published information rather than new information not previously available to clinicians. Eight of 17 group 1 patients underwent thyroid lobectomy despite having preoperative patient or neoplastic characteristics for which the NCCN guidelines recommend total or near-total thyroidectomy. In 4 of the 8 patients, a total or near-total thyroidectomy was not performed because of the absence of a preoperative diagnosis of PTC. These patients underwent neither preoperative FNA biopsy nor intraoperative frozen-section evaluation. The use of FNA biopsy in the preoperative evaluation of thyroid nodules can prevent intraoperative indecision and can facilitate accurate preoperative staging of the neck by ultrasonography if a diagnosis of carcinoma is

obtained.^{7,14} Similarly, 4 group 2 patients underwent thyroid lobectomy despite having preoperative patient or neoplastic characteristics supporting the performance of total or near-total thyroidectomy. The importance of total or near-total thyroidectomy for decreasing recurrence in high-risk patients is now well accepted.^{2,5,12,24,25}

CONCLUSION

Our critical review of the medical records of all patients who required reoperation for persistent or recurrent PTC demonstrated that approximately half of these operations might have been preventable. One can argue that we may have overestimated the importance of adequate TSH suppression. However, even if those patients are excluded from the analysis, reoperation may have been preventable in 28 (39%) of the 72 patients with persistent or recurrent PTC. The liberal use of FNA biopsy and the availability of accurate preoperative ultrasonography staging of the neck will enhance the ability of surgeons to completely remove all gross disease. Accurate staging of the extent of cervical disease will also allow, when appropriate, the referral of patients to surgeons more experienced with techniques of neck dissection, which is especially important for patients with bulky central or lateral compartment disease. Although the optimal operative and postoperative management of patients with low-risk PTC remains controversial, there is little argument that removal of all gross disease (as defined by physical examination and radiographic imaging) will maximize local-regional tumor control. Compartment-oriented surgery consisting of formal dissection of the central (level VI) and lateral (level IIA through V) neck compartments, when performed for gross disease (palpable or visible on ultrasonography), will minimize subsequent lymph node recurrences.¹⁵ For the vast majority of patients who have little or no risk of death from PTC, the endpoint for assessment of treatment algorithms including the extent of surgery, the use of adjuvant RAI, and TSH suppression should be the development of cervical recurrence. This report provides initial data suggesting that treatment factors may be as important as tumor biology in predicting the development of cervical recurrence after initial surgery for PTC.

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DISCUSSION

Dr Ashok R. Shaha (New York, NY). Do you really believe that the TSH suppression will minimize or decrease the incidence of reoperative surgery? NCCN guidelines do suggest TSH suppression, but I just wanted to get your feeling, does it really change the subsequent incidence of local or regional nodal metastasis?

The second question is, you talk about node plucking at the first operation, is that the node plucking in the jugular chain or in the central compartment? We all do node plucking in the central compartment near the recurrent laryngeal nerve, which is quite a different procedure from the node plucking for disease in the lateral compartment.

Dr Keith S. Heller (Lake Success, NY). This is a very interesting way to look at your data, which obviously is a very select subset of patients because of the referral pattern in your institution. I have a question, though, specifically concerning what you consider adequate therapy of the lateral cervical lymph nodes. Your implication is that adequate therapy mandates ultrasonography of the lateral neck and, I assume, ultrasound-guided needle biopsy in order to avoid missing those patients who have otherwise occult disease in the neck. Do you have data to suggest that by doing that, you cure more patients rather than simply finding more disease? We know that if you do neck dissections on everybody with papillary thyroid cancer, you will find positive nodes in 40% of patients. If your recommendation is that we do ultrasonography on everybody, we would do a lot of unnecessary neck dissections to avoid a small number of possibly insignificant recurrences.

Dr Blake Cady (Providence, RI). It is still discouraging to me not to find papers on thyroid cancer presented in

terms of risk group. Low-risk patients with thyroid cancer are marked by very common node metastases, up to 75% when routine neck dissections were done, yet there is no impact whatsoever in any of the staging systems of nodal metastases on outcome. Therefore, to say that we ought to do ultrasound follow-up on necks that are palpably negative, is just going to create a lot more disease that doesn't have any impact on outcome.

Do you have any separation of patients by risk group? Low-risk patients shouldn't be studied for nodes except by physical examination. You should leave them alone until nodes become palpable. Once they are palpable, do something about it. But looking for a node by ultrasound is a waste of time.

Dr Sally E. Carty (Pittsburgh, Pa). Madam Chairman, would you please poll the audience and ask something like: How many people believe then that routine imaging is obligatory before every thyroid lobectomy?

Dr Martha A. Zeiger (Baltimore, Md). For a patient who presents with papillary thyroid cancer, how many in the audience assess the lateral neck with ultrasound preoperatively? And, how many do not? How many proceed with thyroidectomy and radioactive iodine and no preoperative ultrasound? The audience is split 50-50. I sense that this will likely be one of many debates for the AAES in the 21st century.

Dr Kouvaraki. Dr Shaha asked if TSH really decreases the incidence of reoperation. Although TSH suppression alone may not be responsible for the prevention of recurrent disease, TSH has a significant clinical impact on tumor growth (Pujol et al. *JCEM* 1996;81:4318-4323) as emphasized in all published guidelines including those of the NCCN.

As for the site of node plucking, in prereferral operative notes, node plucking is most commonly reported as being done within the lateral neck compartments (levels III and IV), as in the case that I presented at the beginning of my talk. However, formal dissection of the right or left aspect of the central neck (level VI) involves removal of all lymph nodes and soft tissue in the tracheoesophageal groove and is a more extensive procedure than one would associate with the term node plucking, but your point is well taken.

Dr Heller asked if preoperative ultrasound increased the cure rate. Ultrasound (US) is a modality that detects gross disease and not microscopic disease. By the time disease is visible by ultrasound it is considered gross disease. Last year at this meeting we presented our work concerning the usefulness of preoperative US (Kouvaraki et al. *Surgery* 2003;134:946-954), and our results showed first, that physical examination can miss gross cervical lymph node metastases (visible on US) in up to 40% of patients, and second, that cervical recurrence rates can be minimized by removing US-detected disease (8% in our report). Therefore, we recommend ultrasound examination preoperatively in all patients with PTC. The wide spread adoption of this philosophy by the endocrinology community is in direct response to the high rates of cervical recurrence in patients with PTC. As

a practical reality, your postoperative patients will be followed with cervical US by their endocrinologist. Unless you plan to ignore the postoperative detection of cervical metastases, you may want to reconsider the routine use of preoperative US thereby allowing all gross disease to be resected in one rather than two operations.

Dr Cady asked about using only physical examination in low-risk patients. As I said previously, lymph node metastases in the neck are frequently difficult to palpate due to the large size of the sternocleidomastoid muscle. In contrast, US is used to accurately detect metastatic cervical lymph nodes (Pacini et al. *JCEM* 2003;88:3668-3673), which again, represent gross disease, in the same manner that MRI and CT are traditionally used to detect regional and distant metastases from all other solid tumors. By definition, again, microscopic disease is the disease that is not visible by any conventional imaging modality, thus neck dissection for US detectable cervical metastasis is considered therapeutic and not prophylactic.

Dr Carty asked if routine imaging is necessary before every thyroidectomy. We perform preoperative ultrasound of the neck in patients with suspected or biopsy-proven thyroid cancer, and not in all patients with thyroid disease.

Dr Evans. I would like to add a response to Dr Cady's comment. Very simply, your position against preoperative US can be supported only if you are going to follow patients (with PTC) after surgery with just physical examination. The reality of today's environment is that postoperative follow-up involves evaluation of serum levels of thyroglobulin (often thyrogen stimulated),

RAI scanning, cervical US, and occasionally PET scanning. Why is this you ask? This change in practice pattern is in direct response to the published rates of cervical recurrence (25%-30%) seen even in low- and intermediate-risk patients; such high rates of recurrence are felt to be unacceptable by most physicians. We presented a paper at this meeting 3 years ago (Esnaola et al. *Surgery* 2001;130:921-930) where we looked at the quality of life implications of cervical recurrence. While you can tell a patient who has 2 young children that she is not going to die of that cervical recurrence in her left lateral neck, conversation and the emotional and physical impact of recurrent cancer on such a patient is significant even if not associated with an increased risk of death. In low- and intermediate-risk patients, our endpoint for evaluation of treatment algorithms should not be survival, we know such patients rarely die of this disease, it should be trying to decrease the incidence of cervical recurrence, which is unacceptably high and certainly cannot be paralleled in any other solid tumor.

Dr Cady. Just keep in mind that 99% cure rate can't be improved on by any kind of techniques we are doing here. Therefore, one of the major goals is to reduce the morbidity of treatment.

In response to the speaker, the thing that is unique about this low-risk papillary cancer is it is a different disease. The implications of lymph node metastases are different than almost all other human cancers and that needs to be appreciated in order to put therapy of low-risk cancers on a rational basis.