Role of preoperative ultrasonography in the surgical management of patients with thyroid cancer

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Background. *Cervical recurrence occurs in up to 30% of patients with differentiated thyroid carcinoma. We retrospectively compared preoperative transcutaneous ultrasonography and physical examination (PE) results in the detection of local-regional metastases (lymph node and soft tissue) in patients with thyroid cancer.*

Methods. *Data were collected retrospectively from the medical records of patients with thyroid carcinoma who underwent preoperative ultrasonography. Patients were divided into 3 groups: group 1, those undergoing primary thyroid/neck surgery; group 2, those undergoing reoperation for persistent disease; and group 3, those undergoing reoperation for recurrent thyroid carcinoma. For each group, we recorded the frequencies with which ultrasonography detected disease in a neck compartment (central or lateral) that was normal on PE.*

Results. *Two hundred twelve patients underwent operation for primary, persistent, or recurrent papillary (n = 130), medullary (n = 61), or follicular/Hürthle cell (n = 21) carcinoma. Ultrasonography detected additional sites of metastatic disease not appreciated on PE in 21 (20%) of 107 group 1 patients, 9 (32%) of 28 group 2 patients, and 52 (68%) of 77 group 3 patients. The surgical procedure performed was altered by the information obtained from preoperative ultrasonography in 82 (39%) of the 212 patients. Of the 107 group 1 patients, cervical recurrence has been detected in only 6 (6%) at a median follow-up of 36 months, in spite of 67 (63%) having tumors larger than 2 cm or lymph node metastases.*

Conclusions. *Preoperative high-quality ultrasonography detected lymph node or soft-tissue metastases in neck compartments believed to be uninvolved by PE in 39% of patients. Ultrasound findings altered the operative procedure in these patients, facilitating complete resection of disease and potentially minimizing local-regional recurrence. (Surgery 2003;134:946-55.)*

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THYROID CANCER HAS A UNIQUE and largely unexplained tumor biology, characterized by early spread to regional lymph nodes and occasional extrathyroidal soft tissue extension, but a low incidence of distant metastases and infrequent death.[1-3] For example, the incidence of thyroid cancer has been increasing over the past 3 decades, with 22,000 new cases expected in the United States in 2003; however, thyroid cancer-related deaths will number only 1400 (6%) in 2003.[2] The modest death rate and the visible nature of surgical complications such as injury to the recurrent laryngeal nerve and hypoparathyroidism may result in a conservative surgical approach to local-regional disease. To what degree this contributes to the high rates of cervical recurrence is not known. However, cervical recurrences, mostly regional lymph node metastases, have been reported in up to 31% of patients with differentiated thyroid carcinoma (DTC)[4-6] and up to 65% of patients with medullary thyroid carcinoma (MTC).[7] Such high rates of cervical recurrence suggest that many patients have macroscopic lymph node metastases at the time of initial surgery and, if detected and removed, may prevent subsequent reoperation for recurrence in the neck.

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The realization that preoperative physical examination (PE) is inadequate for the detection of extrathyroidal cervical metastases has caused many clinicians to consider transcutaneous ultrasonography for preoperative staging and follow-up in patients with thyroid cancer.[8-12] High-quality ultrasonography is an established diagnostic tool for detecting local-regional metastatic disease as small as 2 to 3 mm in patients with thyroid cancer.[9-11] Although there is little support for prophylactic neck dissection to remove microscopic disease in patients with DTC, compartment-oriented surgery (COS) for macroscopic disease detected by ultrasonography may minimize future neck recurrence and patient morbidity.[13] The purpose of this study was to examine the sensitivity of preoperative ultrasonography in detecting local-regional metastases and the impact of preoperative ultrasonography on surgical management in patients with DTC and MTC.

METHODS

We retrospectively reviewed the medical records of all patients with DTC (papillary thyroid carcinoma [PTC] or follicular/Hürthle cell carcinoma) or MTC who underwent preoperative cervical ultrasonography followed by cervical operation in the Department of Surgical Oncology at The University of Texas M.D. Anderson Cancer Center from 1991 to 2003. Study patients were divided into 3 groups on the basis of whether their operation was for primary, persistent, or recurrent disease: group 1 patients underwent thyroidectomy with or without neck dissection as their primary surgical procedure; group 2 patients underwent reoperation for persistent disease, which was defined as occurring within 6 months of a prereferral thyroid cancer operation; and group 3 patients underwent reoperation for recurrent disease, which was defined as occurring greater than 6 months following a prereferral thyroid cancer operation.

Initial pathologic TNM stage (American Joint Committee on Cancer staging system, 6th edition[14]) was determined by the histopathologic results from all operations performed within 6 months of the patient's initial operation.[14] If lymph node status was not mentioned on the histopathologic report, N status was considered N0. The presence or absence of lymph node metastasis on PE was recorded as negative or positive. The presence or absence of lymph node metastasis on ultrasonography was recorded as negative (benign), positive (malignant), indeterminate, or suspicious.

Ultrasound scanning of the soft tissues of the neck was performed with a high-resolution ultrasound scanner (Sequoia, Acuson, Mountain View, California; Elegra, Siemens, Issaquah, Washington; HDI 5000, Philips-ATL, Bothell, Washington; or Powervision 7000, Toshiba, Tokyo, Japan) equipped with a high-frequency linear-array transducer of at least 7 MHz and up to 13 MHz. The ultrasound examination included evaluation of the lymph nodes in the lateral neck compartments and of the thyroid (when present) and associated soft tissues in the central neck compartment. The location of cervical lymph nodes on ultrasonography was considered central (level VI) or lateral (levels IIA, III, IV, or V).[15] Small volume disease was localized in the operating room with transcutaneous ultrasonography (before the skin incision was made) at the discretion of the operating surgeon. If additional disease was detected at the time of intraoperative ultrasonography, it was added to the ultrasound findings for all analyses. Some patients with positive ultrasound findings underwent ultrasound-guided fine-needle aspiration (FNA), which was performed with a 20-gauge needle inserted obliquely along the scan plane. The needle tip was under constant ultrasound observation during the entire biopsy procedure.

A lymph node was considered benign on ultrasound evaluation when the appearance was oval and flattened, with a smooth cortex, and the central fatty hilum paralleled the smooth cortex. A lymph node was considered malignant when it was rounded or had an absence or truncation of the central fatty hilum. The spectrum of indeterminate to suspicious was subjective and based on the individual ultrasonographers' assessments of the lymph nodes including characteristics such as the size and position of the central fatty hilum, the presence or absence of eccentric cortical widening, rounded versus elongated shape, markedly decreased echogenicity, alteration in intranodal vascularity, and calcifications.[16] Lymph node size was not a diagnostic criterion for metastasis. Lymph nodes that were suspicious for metastasis were considered positive for purposes of analysis. Lymph nodes that were indeterminate for metastasis were considered negative except in one patient in whom FNA biopsy of an indeterminate lymph node confirmed cancer; therefore this ultrasound scanning result was considered positive.

Our surgical management of patients with MTC has been previously published.[15] Our surgical approach to patients with DTC and suspected or

proven central or lateral compartment lymph node metastases also emphasized COS; "node plucking" was not performed except in patients with recurrent disease in a previously dissected compartment. When performed, central compartment dissection involved removal of all lymph nodes and soft tissues in level VI usually with the overlying sternothyroid muscle. In patients with DTC (in contrast to MTC) the level VI dissection was largely limited to the ipsilateral tracheoesophageal groove, unless preoperative ultrasonography suggested metastatic disease in the contralateral paratracheal region. Lateral compartment dissection (modified radical neck dissection) involved removal of all lymph nodes and soft tissues in levels IIA, III, IV, and V with preservation of the jugular vein, carotid artery, vagus nerve, phrenic nerve, and spinal accessory nerve when possible. In patients with papillary or Hürthle cell carcinoma and no evidence of regional lymph node metastases, we routinely removed the ipsilateral paratracheal lymph nodes; however, the lateral compartment was not dissected in the absence of clinical or ultrasound evidence of lymph node metastases. In contrast to selected patients with MTC, we did not consider elective reoperation in patients with DTC for an elevation in thyroglobulin in the absence of clinical or ultrasound evidence of lymph node metastases.

Postoperative 5-mCi radioiodine scanning was performed after surgery in patients with DTC in preparation for adjuvant radioiodine therapy. The percent uptake of the ingested dose of radioiodine was used to measure the adequacy of surgical resection.

Cervical recurrence was defined as metastatic involvement of any cervical lymph node or soft tissue and was considered local when the central compartment was involved and regional when either lateral compartment was involved. Cervical recurrences were considered local-regional when both the central and lateral compartments were involved.

Disease status at last follow-up was categorized as no evidence of disease (NED; no evidence of disease by physical examination and radiographic imaging), alive with disease (AWD; biopsy confirmation of distant metastases was not routinely performed), dead of disease (DOD), or dead of other causes.

The statistical correlations between categorical variables were assessed by χ^2 and Fisher's exact tests. Associations of continuous variables with different groups were evaluated using the nonparametric Mann-Whitney or Kruscal-Wallis tests. All analyses were performed using the Stat View (version 5.01) statistical software package (Abacus Concepts Inc.; Berkeley, CA). Differences were considered statistically significant when the P value was $< .05$.

RESULTS

From 1991 to 2003, 216 consecutive patients underwent preoperative ultrasonography and surgery for primary, persistent, or recurrent thyroid carcinoma. Four patients had incidentally discovered papillary carcinomas (index nodule was benign) and were excluded from further analysis, leaving a study population of 212 patients. There were 67 male patients (32%) and 145 female patients (68%); the median age at diagnosis was 43 years (range, 5 to 86 years). Histopathologic diagnoses included 130 PTC, 61 MTC, and 21 follicular/Hürthle cell carcinomas. Three patients who underwent reoperative completion thyroidectomy for PTC in the absence of other sites of cervical disease were included in group 2. Twenty-two (36%) of 61 MTC patients had hereditary forms of MTC (multiple endocrine neoplasia type 2 [MEN 2] or familial MTC). Five of these patients underwent prophylactic surgery for MEN 2 or familial MTC and had histologic evidence of invasive MTC.

Pathologic tumor stages by group and histopathologic tumor type are shown in Table I. Patients with MTC presented with more advanced disease than did those with DTC ($P < .0001$). The primary tumor was unilateral in 152 patients, bilateral in 55, and isthmic in 5.

Ultrasound examination detected lymph node metastases or soft tissue recurrence in 113 (53%) of 212 patients. Sixty-nine (61%) of the 113 patients with positive findings on ultrasonography underwent FNA biopsy. Cytologic results confirmed the presence of metastatic or recurrent disease in 64 (93%) of 69 patients. Ultrasound-positive disease not detected on PE was found in 105 neck compartments of 82 patients (39%): 52 (34%) of 151 with DTC and 30 (49%) of 61 with MTC. These 82 patients included 21 patients (20%) in group 1, 9 (32%) in group 2, and 52 (68%) in group 3. The difference between groups (PE missed more group 3 cases) was significant ($P < .0001$). The location of ultrasound-positive disease not appreciated on PE for each patient group and histopathologic type are shown in Table II. Ultrasound-positive disease not appreciated on PE was found in the central neck compartment in 58 (27%) of the 212 patients, in the ipsilateral neck compartment in 32 (15%),

and in the contralateral neck compartment in 14 (7%).

One hundred eighty-three of 212 patients had histopathologic analysis of regional lymph nodes or soft tissues. Twenty-nine patients did not undergo compartment dissection because of negative findings on both PE and ultrasonography. Histopathologic study confirmed local-regional metastatic disease in 150 (82%) of 183 patients: in 50 (60%) of the 83 patients from group 1 and in all 24 (100%) and 76 (100%) patients in group 2 and group 3, respectively. The relationship between preoperative ultrasound findings and histopathologic findings by compartment is shown in Table III. The sensitivity and specificity of ultrasonography within each compartment was as follows: central compartment 52% and 95%, respectively; ipsilateral compartment 77% and 93%, respectively; and the contralateral compartment 79% and 96%, respectively. We interpreted ultrasound results as false-positive on the basis of final histopathologic findings in 4 compartments of 4 patients. One patient had sporadic MTC and underwent reoperation for recurrent disease. Bulky disease was present in the central and ipsilateral neck compartments. In the contralateral compartment, an 8 mm lymph node posterior to the internal jugular vein was interpreted as suspicious because of the absence of a fatty hilum; histopathologic study demonstrated no evidence of metastatic disease in 21 lymph nodes within this compartment. Another patient underwent thyroidectomy along with central and bilateral neck dissection for biopsy-proven familial MTC (codon 804 *RET* mutation). Preoperative ultrasonography demonstrated an abnormal-appearing 1.6-cm lymph node containing fine calcifications, interpreted as metastatic lymphadenopathy; histopathologic study demonstrated no evidence of metastatic disease in 60 cervical lymph nodes. A third patient had sporadic MTC and underwent reoperation for persistent disease within both lateral neck compartments. There were also 2 lymph nodes within the central neck compartment that were 1 cm in diameter and interpreted as suspicious for metastatic disease on ultrasonography; histopathologic study of the central neck dissection specimen demonstrated no evidence of recurrent MTC. The fourth patient had sporadic MTC and underwent reoperation for persistent disease. A 9-mm nodule in the central neck compartment was interpreted as suspicious for metastatic disease on ultrasonography; histopathologic study demonstrated suture material and foreign body giant cell reaction with no evidence of MTC.

Table I. Pathologic tumor staging in 212 patients with thyroid carcinoma*

Tumor type and stage	*No. patients*			
	Group 1	*Group 2*	*Group 3*	*Total (%)*
DTC				
All patients	85	18	48	151
Stage I	55	13	31	99 (66)
Stage II	9	0	2	11 (7)
Stage III	13	2	2	17 (11)
Stage IVA	3	2	6	11 (7)
Stage IVC	4	1	2	7 (5)
Stage not assessed	1†	0	5‡	6 (4)
MTC				
All patients	22	10	29	61
Stage I	10	0	4	14 (23)
Stage II	0	0	3	3 (5)
Stage III	1	1	6	8 (13)
Stage IVA	7	9	15	31 (51)
Stage IVC	4	0	1	5 (8)

*AJCC Cancer Staging Manual (6th ed).[14]
DTC, Differentiated thyroid carcinoma; *MTC*, medullary thyroid carcinoma.
†Stage could not be assessed from the incomplete information on tumor size from the initial operation at M.D. Anderson.
‡Stage could not be assessed from the incomplete reoperation at M.D. Anderson.

Histopathologic study demonstrated metastatic disease in 1 or more neck compartments of 74 patients (35%) with no evidence of metastatic disease by ultrasonography (false-negative ultrasonography result): 47 patients with DTC (all had PTC) and 27 with MTC (Table IV). The rate of false-negative results is influenced by the extent of surgery; a false-negative result is not possible if lymph nodes are not removed and pathologically analyzed. In group 1 patients with PTC or Hürthle cell carcinoma, it was standard practice to remove the ipsilateral paratracheal lymph nodes (central compartment, level VI) at the time of thyroidectomy regardless of the findings on preoperative ultrasonography. Among patients with DTC, false-negative ultrasound results in the lateral compartments occurred in patients with indeterminate ultrasound findings in the setting of advanced disease in one or more other neck compartments. Surgeon preference in these cases was to extend the dissection to the compartment with indeterminate findings. In group 1 patients with invasive MTC, we performed central neck dissection in all cases, dissection of the ipsilateral lateral compartment in cases of sporadic MTC, and frequently, bilateral neck dissection in cases with familial MTC.[15]

The surgical procedure was altered by the information obtained from preoperative ultra-

Table II. Recurrent or metastatic disease detected by ultrasonography but not physical examination in 212 patients with thyroid carcinoma

	No. Patients (%)			
	Group 1	*Group 2*	*Group 3*	*Total*
DTC				
All patients	85	18	48	151
Patients with positive US and negative PE	15 (18)	2 (11)	35 (73)	52 (34)
Cervical compartments with positive US and negative PE*				
Central	6 (7)	1 (6)	26 (54)	33 (22)
Ipsilateral	4 (5)	1 (6)	16 (33)	21 (14)
Contralateral	8 (9)	0	3 (6)	11 (7)
MTC				
All patients	22	10	29	61
Patients with positive US and negative PE	6 (27)	7 (70)	17 (59)	30 (49)
Cervical compartments with positive US and negative PE*				
Central	4 (18)	7 (70)	14 (48)	25 (41)
Ipsiltateral	2 (9)	2 (20)	7 (24)	11 (18)
Contralateral	0	3 (30)	1 (3)	4 (7)

DTC, Differentiated thyroid carcinoma; *MTC*, medullary thyroid carcinoma; *PE*, physical examination; *US*, ultrasonography.
*If the index tumor was bilateral, then lymph node and soft tissue in either lateral compartment was considered ipsilateral. Some patients had metastatic-appearing lymph nodes in more than one neck compartment.

sonography in 82 (39%) of 212 patients. All ultrasound-positive disease was surgically excised except in 1 patient, in whom neck dissection was limited to the one compartment with large-volume disease because of the presence of extensive extracervical metastases. Of the 151 patients with DTC, unsuspected disease was found by ultrasonography in 52 (34%) and altered the operation to include a more extensive dissection of the central compartment in 32, the ipsilateral compartment in 21, and the contralateral compartment in 9 patients. In group 1 patients with DTC, preoperative ultrasonography changed the primary thyroid cancer operation to include 6 central compartment lymphadenectomies and 4 ipsilateral and 8 contralateral functional neck dissections. Of the 61 patients with MTC, unsuspected disease was found by ultrasonography in 26 patients (43%) (excluding the 4 false-positive results) and alerted the surgeon to the need for a detailed dissection of the central neck compartment in 22 patients and for inclusion of the ipsilateral neck compartment in 8 and the contralateral neck compartment in 2.

Results of postoperative radioiodine scans in patients with DTC are summarized in Table V. The number of patients with cervical uptake of 1% or less of the total ingested dose is provided as a surrogate marker of the adequacy of surgical therapy. In group 1 patients, 77% had cervical uptake of 1% or less of the ingested dose.

The median follow-up was 36 months (range, 1 to 140 months). Cervical recurrence following primary or reoperative surgery at M. D. Anderson Cancer Center developed in 16 (8%) of 207 patients with follow up: 6 (6%) in group 1, 3 (12%) in group 2, and 7 (9%) in group 3 (Table VI). Of note, 67 (65%) of 103 group 1 patients had primary tumors larger than 2 cm in size or lymph node metastases. Cervical recurrences were local in 8 patients (50%), regional in 5 (31%), and local-regional in 3 (19%). Cervical recurrences involved lymph nodes in 11 patients, soft tissue in 1, and both lymph nodes and soft tissue in 4. The median size of recurrent lesions was 1.0 cm (range, 0.5 to 2.4 cm).

Thyroglobulin levels were reviewed for the 124 patients with DTC who were NED at last follow-up and were available for 114. Of these 114 patients, anti-thyroglobulin antibodies were present in 27 and not measured in 6. Of the 81 patients without detectable antibodies, the most recently available thyroglobulin level was undetectable in 62 (76.5%). The median thyroglobulin level in the remaining 19 patients with detectable thyroglobulin levels was 3.0 with a median TSH level of 0.68 mcU/mL.

DISCUSSION

This study reports the impact of preoperative ultrasonography on the operative management of a consecutive series of 212 patients with thyroid

Table III. Ultrasonography versus histopathologic findings in all dissected cervical compartments

Histopathologic findings by compartment	No. patients by ultrasound findings		
	Negative	Positive	Total
Central cervical compartment			
Negative	41	2†	43
Positive	57‡	61	118
Total	98	63	161
Ipsilateral cervical compartment*			
Negative	13	1†	14
Positive	22‡	75	97
Total	35	76	111
Contralateral cervical compartment			
Negative	27	1†	28
Positive	5‡	19	24
Total	32	20	52

*If the index tumor was bilateral, then lymph node or soft tissue disease in either lateral compartment was considered ipsilateral.
†False-positive US results.
‡False-negative US results.

Table IV. False-negative ultrasound results by compartment for patients with DTC and MTC

Site of false-negative ultrasound findings	No. patients		
	Group I	Groups II and III	Total
DTC			
All patients	85	66	151
Patients with false-negative US†‡	31	16	47
Central	31	12	43
Ipsilateral*	1	4	5
Contralateral	0	3	3
MTC			
All patients	22	39	61
Patients with false-negative US†‡	8	19	27
Central	7	7	14
Ipsilateral*	3	14	17
Contralateral	0	2	2

DTC, Differentiated thyroid carcinoma; *MTC*, medullary thyroid carcinoma.
*If the index tumor was bilateral, then lymph node or soft tissue disease in either lateral compartment was considered ipsilateral.
†Some patients had metastatic-appearing lymph nodes in more than one neck compartment.
‡False-negative US: lymph nodes within a compartment appeared negative on preoperative US but were found to be positive for metastasis on histopathologic study.

cancer. Unsuspected soft tissue or lymph node metastases were found by ultrasonography in 52 (34%) of 151 patients with DTC and in 26 (43%) of 61 patients with MTC and resulted in the performance of more extensive surgery. These patients were treated with a COS approach using standard techniques of neck dissection in an effort to prevent subsequent recurrence. At a median follow-up of 36 months, cervical recurrences developed in only 16 (8%) of 207 evaluable patients. An additional measure of the adequacy of surgical resection, in patients with DTC, were the results of the postoperative radioiodine scans.[17,18] In evaluable group 1 patients with DTC, 77% had cervical uptake of 1% or less of the ingested dose, excluding those 7 patients with no uptake. This compares favorably with the 46% of patients reported to have cervical uptake of 2% or less by Hudgson et al.[19]

As suggested by previous investigators, ultrasonography was both sensitive and specific for the diagnosis of soft tissue or lymph node metastases.[20-24] The specificities of ultrasonography in the central, ipsilateral, and contralateral compartments were 95%, 93%, and 96%, respectively. All 4 of the patients with false-positive ultrasound results had MTC, and 3 of them underwent ultrasonography before reoperation for persistent or recurrent MTC. Because we performed COS, we cannot verify that the metastatic disease found histologically within a specific compartment was the exact lymph node or soft tissue metastasis seen on preoperative ultrasonography. However, our experience with ultrasound-guided FNA biopsy indicates the high specificity of ultrasonography; cytologic study results of ultrasound-guided FNA confirmed the presence of carcinoma in 64 (93%) of 69 patients. Our current practice is to limit the use of FNA biopsy to patients with suspected recurrent thyroid cancer, especially those with recurrent disease in a previously dissected compartment. We do not perform reoperative cervical surgery in a previously dissected neck compartment without a cytologic diagnosis of cancer. For patients undergoing ultrasonography before their first thyroid cancer operation (group 1), we do not believe it is necessary to confirm cytologically a positive or suspicious ultrasound finding in the central or lateral neck compartments. However, we are more liberal in the application of ultrasound-guided FNA in patients with indeterminate ultrasound findings and those without a definitive cytologic diagnosis of cancer.

Pathologic evaluation of the surgical specimen demonstrated metastatic disease in one or more neck compartments of 74 patients (35%) with no evidence of metastatic disease by ultrasonography. The sensitivities of ultrasonography in the central, ipsilateral, and contralateral compartments were

Table V. Results of postoperative radioiodine scans in patients with DTC*

	No. patients			
	Group 1	*Group 2*	*Group 3*	*Total*
Patients with DTC	85	17	49	151
Patients with DTC who had WBS	77	14	28	119
No uptake	7	0	15	22
Cervical uptake only	63	13	12	88
Extracervical uptake only	1	0	0	1
Cervical & extracervical uptake	6	1	1	8
All patients with cervical uptake $\leq 1\%$†	46/60 (77%)	7/13 (54%)	4/7 (57%)	57/80 (71%)

WBS, Whole body scan; *DTC*, differentiated thyroid carcinoma.
*Postoperative scans were performed with 5 mCi of ^{131}I before ^{131}I ablation treatment.
†Not all patients had specific uptake values reported.

Table VI. Recurrence and outcome in patients with thyroid carcinoma

	No. patients			
Outcome	*Group 1*	*Group 2*	*Group 3*	*Total*
DTC				
All patients	84	16	49	149
Median follow-up (range)*	40 mo (1-132)	47 mo (7-110)	29 mo (1-105)	36 mo (1-132)
Patients with follow-up < 1 yr	20	1	12	33
Patients with cervical recurrence	5 (6%)	0	4 (8%)	9 (6%)
Median time to first cervical recurrence (range)	22 mo (11-49)	NA	21 mo (14-29)	22 mo (11-49)
Patients Alive, NED	71	14	39	124
Patients AWD	7	1	6	14
Patients DOD	3	1	2	6
Patients Dead of Other Causes	3	0	2	5
MTC				
All patients	19	10	29	58
Median follow-up (range)*	35 mo (3-140)	58 mo (24-82)	32 mo (1-95)	40 mo (1-140)
Patients with Follow-up < 1 yr	4	0	6	10
Patients with cervical recurrence	1 (5%)	3 (30%)	3 (10%)	7 (12%)
Median time to first cervical recurrence (range)	125 mo	22 mo (20-26)	25 mo (9-34)	25 mo (9-125)
Patients Alive, NED	14	8	19	41
Patients AWD	3	1	9	13
Patients DOD	2	1	1	4

AWD, Alive with disease; *DOD*, dead of disease; NA, not applicable; DTC, differentiated thyroid carcinoma; MTC, medullary thyroid carcinoma; NED, no existing disease.
*Time zero = Date of first MDACC operation. Five patients who were immediately lost to follow-up after surgery were excluded from analysis.

52%, 77%, and 79%, respectively. Most false-negative ultrasound results occurred in the central neck compartment, and more than half were in patients whose thyroid gland was still in situ (group 1). With the thyroid gland in situ, ultrasonography cannot assess the central compartment with the sensitivity possible after the thyroid is removed. Therefore we have adopted the practice of removing the ipsilateral paratracheal lymph nodes in patients with PTC or Hürthle cell carcinoma. Central compartment dissection is already an accepted surgical procedure in any patient with invasive MTC. Most false-negative ultrasound results in the lateral compartments occurred in patients with indeterminate ultrasound results, often in the setting of more advanced disease in another compartment of the neck.

The impact of the extent of thyroidectomy and regional lymph node dissection on the survival of patients with DTC and MTC remains a subject of controversy. Because of the indolent nature of these malignancies, the extent of surgery will likely never be the subject of a prospective, phase III, randomized trial. Although more extensive cervical surgery may have only a limited impact on survival duration, it may significantly impact the quality of

survival by minimizing cervical recurrence.[13] The known high rates of cervical recurrence in patients with DTC and MTC have alerted physicians, especially endocrinologists, to the importance of long-term follow-up. The common use of serum marker (thyroglobulin and calcitonin) measurements, radioiodine scanning (with thyrogen stimulation), and ultrasonography in follow-up will likely result in the diagnosis of even more recurrences. Therefore, if ultrasonography is to be performed in the postoperative follow-up period, it seems only logical to perform ultrasonography before the first surgical procedure in an effort to remove all gross metastatic disease, which is frequently not palpable. This strategy may minimize patient confusion and physician indecision during the postoperative follow-up period, prevent the indiscriminate and, sometimes, unnecessary use of radioiodine therapy, and minimize cervical recurrence with its negative impact on the physical and emotional state of the patient.[13,25] This manuscript provides preliminary evidence to support such a strategy.

Further follow-up will be necessary to determine the true impact of high-quality preoperative ultrasonography and standardized COS on rates of cervical recurrence in patients with DTC and MTC, but our preliminary findings appear promising. Although one can argue that patients with invasive MTC should undergo a routine dissection of at least level VI, and therefore preoperative ultrasound findings may not alter the planned surgical procedure, the extent and location of regional metastases will alert the surgeon to the need for a more detailed dissection, and those surgeons less experienced with neck dissection may wish to refer such patients to a center more experienced with the operative management of locally advanced thyroid cancer.

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DISCUSSION

Dr Keith S. Heller (New Hyde Park, NY). Very nice presentation. I have trouble with your conclusions. Many years ago a former vice president of this Society, Joseph Attie, performed hundreds of elective neck dissections for well-differentiated thyroid cancer. As you have demonstrated, he found the incidence of occult positive nodes to be about 40%. Yet, he and virtually everybody else abandoned that approach because nobody was able to show any benefit from operating on these people with clinically insignificant metastatic nodes. Do you have any data whatsoever to suggest that the patients benefit from your aggressive surgical approach toward nonpalpable, occult disease?

Dr Kouvaraki. We do not perform elective neck dissection in patients with well-differentiated carcinoma of the thyroid. In contrast, we do perform therapeutic dissection when gross disease is seen on preoperative ultrasonography. When cervical lymph node metastases are large enough to be detected by ultrasonography, they are not considered microscopic. Thus the incidence of positive lymph nodes we report in this study corresponds to gross disease.

Dr Allan Siperstein (Cleveland, Ohio). I very much enjoyed this study, especially as an advocate of doing preoperative ultrasound examination in all of these patients where we found sizable disease that was nonpalpable. In terms of comparing palpation with ultrasonography, when was the ultrasound scanning performed, before or after the physical examination, or was the surgeon aware of the ultrasound findings before the examination? Second, who performed the ultrasound scan? Was it surgically performed, as is my preference, or is it done in the radiology department?

Dr Kouvaraki. In all cases the physical examination was done before the ultrasound scan, and thus the surgeon was not aware of the ultrasound results. All neck ultrasound scans at M.D. Anderson are performed in the Radiology Department by radiologists specializing in cervical ultrasonography.

Dr Ian D. Hay (Rochester, Minn). I stand before this august audience to comment on this study as a nonaggressive nonsurgical clinician who sees about 400 patients with differentiated thyroid cancer annually. Rather like the well-documented role of ultrasonography in permitting the differentiation between solitary and multinodular goiters, the preoperative use of high-resolution ultrasonography in differentiated thyroid cancer has left a simple neck palpator a humbled and more honest individual.

Since 1985 at Mayo, we not only regularly use a preoperative ultrasonography map to aid in determining the extent of thyroid cancer operation but also as the most cost-effective imaging method for delineating the presence after operation of persistent or recurrent neck disease. It is our hope and expectation that neck reexploration numbers for recurrence will be minimized by regular use of this powerful imaging modality. Particularly this weekend when, for the first time in my experience, we had a concomitant ultrasound workshop for endocrine surgeons in North America, I think it would be important for many centers to follow the lead of M.D. Anderson, Mayo, and others in using this exciting modality to improve the lot of our patients; and second, to reduce recurrence rates in the future.

Dr Irving B. Rosen (Toronto, Ontario, Canada). I concur with the notion of ultrasonography and ultrasound needle biopsy as being well established, and I have done a node sampling approach for a lengthy period of time. Did these modalities really influence the extent or the nature of the central neck dissection that you carried out? In the contralateral positive nodes in group I, did you have multicentric or bilateral disease?

Dr Kouvaraki. In all patients with invasive MTC we routinely perform central neck dissection, and therefore preoperative ultrasound findings may not alter the planned surgical procedure. However, the extent and location of regional metastases may alert the surgeon to the need for a more detailed dissection, especially those surgeons who are less experienced in neck dissection. In addition, the extent of cervical disease, if known before operation, may cause some surgeons to consider the referral of such patients to a center more experienced with the operative management of locally advanced thyroid cancer. Second, cervical metastatic disease was considered as ipsilateral in patients with bilateral or multicentric primaries in the thyroid.

Dr Scott Wilhelm (Chicago, Ill). In terms of the criteria used for determining your abnormal lymph nodes, the ultrasound scan you showed revealed an 8-mm, smooth-appearing node. I know you said that one node in particular came back as metastatic. What criteria does your group use to define a "malignant-appearing" node?

Your FNA results of the nodes were impressive. You had 64 of 69 patients with a 93% positive cytologic study result. Are you doing hematoxylin & eosin staining and immunohistochemistry on the FNAs?

Last, you had 4 false-positive ultrasound scan results in your MTCs. Did those patients have FNAs or was it false-positive on the basis of your diagnostic criteria for what you found was an abnormal node prompting your dissection?

Dr Kouvaraki. Lymph node assessment on ultrasonography was somewhat subjective. However, a lymph node was considered malignant when it was rounded or had an absence or truncation of the central fatty hilum. The spectrum of indeterminate to suspicious was subjective and based on characteristics such as the size and position of the central fatty hilum, the presence or