COMMUNICATION

The American College of Surgeons Commission on Cancer and the American Cancer Society

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Initial Results from a Prospective Cohort Study of 5583 Cases of Thyroid Carcinoma Treated in the United States during 1996

An American College of Surgeons Commission on Cancer Patient Care Evaluation Study

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BACKGROUND. The American College of Surgeons Commission on Cancer (CoC) has conducted national Patient Care Evaluation (PCE) studies since 1976.

METHODS. Over 1500 hospitals with CoC-approved cancer programs were invited to participate in this prospective cohort study of U.S. thyroid carcinoma cases treated in 1996. Follow-up will be conducted through the National Cancer Data Base.

RESULTS. Of the 5584 cases of thyroid carcinoma, 81% were papillary, 10% follicular, 3.6% Hürthle cell, 0.5% familial medullary, 2.7% sporadic medullary, and 1.7% undifferentiated/anaplastic. Demographics and suspected risk factors were analyzed. Fine-needle aspiration of the thyroid gland (53%) or a neck lymph node (7%), thyroid nuclear scan (39%), and ultrasound (38%) constituted the most frequently utilized diagnostic modalities. The vast majority of patients with differentiated thyroid carcinoma presented with American Joint Committee on Cancer Stage I and II disease and relatively small tumors. For all histologies, near-total or total thyroidectomy constituted the dominant surgical treatment. No lymph nodes were examined in a substantial proportion of cases. Residual tumor after the

surgical event could be documented in 11% of cases, hypocalcemia in 10% of cases, and recurrent laryngeal nerve injury in 1.3% of cases. Complications were most frequently associated with total thyroidectomy combined with lymph node dissection. Thirty-day mortality was 0.3%; when undifferentiated/anaplastic cancer cases were eliminated, it decreased to 0.2%. Adjuvant treatment, probably underreported in this study, consisted of hormonal suppression (50% overall) and radioiodine (50% overall).

CONCLUSIONS. In addition to offering information concerning risk factors and symptoms, the current PCE study compliments the survival information from previous NCDB reports and offers a surveillance snapshot of current management of thyroid carcinoma in the U.S. Identified opportunities for improvement of care include 1) more frequent use of fine-needle aspiration cytology in making a diagnosis; 2) more frequent use of laryngoscopy in evaluating patients preoperatively, especially those with voice change; and 3) improved lymph node resection and analysis to improve staging and, in some situations, outcomes. [See commentary on pages 1–4, this issue and communication on pages 192–201, this issue.] ***Cancer*** **2000;89:202–17.**

KEYWORDS: thyroid carcinoma, papillary carcinoma, follicular carcinoma, Hürthle cell carcinoma, undifferentiated cancer, anaplastic cancer, surgery, iodine-131, hormonal therapy, adjuvant treatment, complications.

The relative infrequency of thyroid carcinoma, accounting for only 1% of all reportable malignancies,[1,2] and the relative indolence of its usual subtypes combine to render prospective, randomized clinical trials problematic. Of necessity, we base treatment recommendations on nonrandomized, retrospective analyses that often include patients treated in the distant past.[3–10] As diagnostic methods, treatments, and the delivery of medical care change, the need for updated, current information becomes obvious. In an effort to address this need, and building on a recent National Cancer Data Base (NCDB) review of 53,856 cases of thyroid carcinoma treated in the U.S. between 1985 and 1995,[11] the current prospective cohort study was initiated for cases treated in 1996. By including data elements not found in the NCDB data set, a more thorough characterization of both the disease and its treatment is possible.

The American College of Surgeons Commission on Cancer (CoC), a consortium of 36 professional organizations involved in cancer care in the U.S., has conducted national Patient Care Evaluation (PCE) studies since 1976. Through increasingly close linkage with the NCDB, which permits prospective, long term follow-up, these have been converted to prospective cohort studies.

The current study marks the first time international participation has been possible; results of a parallel German study are published in this issue. When approaches to a given disease differ between countries, such parallel, international studies should offer valuable insights with respect to health care systems, diagnostic strategies, and treatment.

METHODS

Since 1994, PCE studies have been merged with NCDB operations to an ever-increasing degree. Previously, in the late 1970s and 1980s, paper study forms were distributed to hospitals with CoC-approved cancer programs, completed by hand, and returned. With the

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cooperation and participation of vendors of registry software, ad hoc data elements used for PCE studies are now annually incorporated into the computerized abstract screens for given cancer sites, thus permitting electronic capture and transmission of data. The efficiency of such a system permits hospitals to report on all cases in a given year (with paper forms they were limited to the first 25 consecutive cases). With the increasing maturity of the NCDB,[12] obtaining follow-up and survival information through this system has proved to be advantageous, and retrospective retrieval of cases treated 5 years previously is no longer part of PCE studies. For PCE studies initiated in 1998, the first year all CoC-approved programs were required to participate with the NCDB, submissions became entirely electronic. The current study is among the last to merge electronic data with paper submissions.

The multidisciplinary U.S. Thyroid Cancer Study Group, formed in 1995, met that same year to design this study, which included establishing the case-capture criteria, the selection of data elements and their definitions, and the design and evaluation of the data form. All data elements that are currently part of the NCDB data set were automatically included. Methods of the CoC PCE studies prior to their linkage with the NCDB have been described previously.[13] Invitations to participate in the study and copies of the data collection form were mailed to the approximately 1500 U.S. hospitals with CoC-approved cancer programs and all U.S. vendors of registry software. Institutions submitting cases via paper forms were asked to submit their first 25 consecutive cases treated in 1996. Institutions submitting cases electronically were asked to submit all cases treated in 1996. Data was submitted from institutions in all 50 states, Puerto Rico, and the District of Columbia.

Commission on Cancer PCE studies are designed with local-level performance improvement in mind. Each participating hospital receives a detailed, customized report comparing its own data with that of the entire cohort in order to facilitate assessment of its own care patterns and outcomes. Such reports are reviewed, presented, and discussed at hospital Cancer Committees (in place at all institutions with CoC-approved cancer programs), which then initiate any warranted quality-improvement actions. Reports clearly comparing results for that hospital with national findings were mailed to all participating hospitals in December 1998.

Data are coded according to the schema published in the *Registry Operations and Data Standards (ROADS)* manual,[14] the third and fourth editions of the American Joint Committee for Cancer (AJCC) *Manual for Staging of Cancer,*[15,16] and the second edition of the *International Classification of Disease for Oncology* (ICD-O-2).[17] Formats for data reporting and electronic transmission are uniform, with such transmission occurring with diskettes or data tapes. Individual patient identifiers, such as social security numbers and names, are collected by individual hospital-based registries; but to ensure absolute confidentiality, they are neither transmitted to nor collected by the NCDB or CoC.

Institution numbers and individual case accession numbers are transmitted for every case reported, allowing the reporting of anonymous, individual cases that are uniquely identifiable only at the reporting

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hospital registry. Thus, further case specific studies using a pathfinder methodology are feasible.

Hospital Cancer Committees supervise the quality of institutional case finding, abstracting, internal reviews of abstracts by registry staff, and hospital-based computer data edits. Upon receipt of electronically submitted data, edit checks are performed to evaluate code validity and logic between data items. For this PCE study, hospitals were asked to submit only cases diagnosed and treated at the institution or cases that had the entire first course of treatment at the reporting institution but were diagnosed elsewhere.

Each patient was assigned the AJCC pathologic stage, if available. If a particular T, N, or M factor was not pathologically confirmed, then the patient was assigned the appropriate AJCC clinical factor and "combined stage" was reported. Presentation of "combined stage" minimized the number of patients with unknown stage entered into analysis. For this PCE study, because the vast majority of cases were treated surgically, and because central registries (which often do not code AJCC stage) did not participate, the proportion of cases pathologically staged was higher than in our previous NCDB report on thyroid carcinoma.[11]

This analysis covered primary carcinomas of the thyroid gland (ICD-O-2 site C73.9) coded as 1 of the 5 major histologies: papillary (8050/3, 8340/3), follicular (8330/3, 8332/3, and 8331/3), medullary (8510/3 and 8511/3), Hürthle cell (8290/3), and anaplastic/undifferentiated (8020/3 and 8021/3). Additional codes for papillary carcinoma, such as 8503/3 (coded to breast), 8504 (coded to ovary), and 8460 (coded to ovary), were not used, given their linkage to other sites. An additional code, 8260/3 (papillary adenocarcinoma, not otherwise specified), was not used because of lack of specificity. We subsequently discovered that, given current practice by pathologists in the U.S., registry practices, and practices by software vendors, approximately 15% of papillary carcinomas of the thyroid are indeed coded this way. This undoubtedly decreased our accrual of papillary carcinomas in this PCE study.

The data in this PCE study reflect information available in the hospital record or known to the treating physician. Patient questionnaires were not used for this PCE study.

SPSS software was used for the simple calculations found in this report.[18] Due to the methodology of the data collection, this report contains descriptive statistics to identify presenting characteristics of patients, insurance coverage, diagnostic methods, staging, treatment, and complications. The lack of a priori hypotheses and the very large sample size, which represents a substantial proportion of the population under study, contravene the assumptions necessary for inferential statistics and could confound results. We therefore advocate a straightforward interpretation of these data and do not offer detailed statistical comparisons. We do consider these data suitable for bench marking, for describing care patterns, for assessing national community-based outcomes, and for generating new hypotheses. Survival for the current PCE cohort will be described in future reports.

RESULTS

Patient Demographics and Medical History

Of the total of 5584 cases entered, 79.4% were both diagnosed and treated at the reporting institution, and 20.6% were treated at the reporting institution but diagnosed elsewhere. The ratio was the same for all histologies except two: anaplastic/undifferentiated cancer, where the ratio was 71.9% and 28.1%, respectively; and cases of medullary thyroid carcinoma associated with positive family history, where the ratio was 84.6% and 15.4%, respectively. Such ratios are consistent with greater referral of undifferentiated/anaplastic cancers and familial screening practices instituted when one member of a given family is identified as having medullary thyroid carcinoma.

Table 1 summarizes demographics by histology. Age distributions are very similar to those reported previously,[11] with median age at diagnosis increasing slightly from papillary (44 years) to follicular (47 years) to Hürthle cell carcinoma (61 years). It is noteworthy that cases of medullary carcinoma associated with positive family history were identified more commonly in the group ages 30–39 years rather than the group younger than 30 years. Anaplastic/undifferentiated carcinoma afflicts primarily the elderly.

Table 2 summarizes patients' family and personal histories of potential risk factors according to histology. On average, 11.7% of patients reported a family history of goiter or other thyroid disease and 4.9% reported a family history of thyroid carcinoma. Personal history of goiter (defined as enlargement of the thyroid gland for a period longer than 5 years prior to diagnosis) was the strongest risk factor for developing thyroid carcinoma; on average, 14.6% of patients gave such a history. By histology, this was 14.3% for papillary carcinoma and 15.9% for follicular carcinoma. Given the long natural history of thyroid carcinoma, goitrous enlargement of the gland, even if longer than 5 years' duration, may well have been due to cancer in some cases. The 25% personal history of goitrous enlargement reported by patients with undifferentiated/anaplastic cancer is noteworthy in this regard, because microscopically, papillary carcinomas are often found in association with these.

Prior personal exposure to radiation (excluding

TABLE 1
Percent Frequency Distribution of Patient Demographics by Histology

	Papillary	Follicular	Hürthle cell	Medullary, family history of thyroid CA	Medullary, no family history of thyroid CA	Undifferentiated/ anaplastic	Total
Age (yrs)							
<30	12.7	11.0	4.5	5.9	8.0	1.0	11.9
30–39	24.2	17.6	10.8	47.1	9.3	0.0	22.3
40–49	25.3	24.6	15.3	11.8	28.7	3.1	24.6
50–59	16.5	17.9	15.8	11.8	20.7	9.4	16.6
60–69	11.2	14.4	21.3	11.8	15.3	19.8	12.2
≥70	10.1	14.5	32.2	11.8	18.0	66.7	12.6
Ethnicity							
Non-Hispanic white	82.8	79.2	85.7	88.9	81.8	86.5	82.6
Hispanic	7.4	5.7	3.8	0.0	8.3	2.2	7
African American	4.7	10.8	8.2	5.6	8.3	9.0	5.7
Native American	0.2	0.2	0.0	0.0	0.8	0.0	0.2
Asian	4.8	4.2	2.2	5.6	0.8	2.2	4.5
Gender							
Male	23.2	28.8	36.6	46.2	44.4	29.2	25.1
Female	76.7	71.2	63.4	53.8	55.6	70.8	74.9
Cases	4522	583	205	27	150	96	5583

CA: carcinoma.

TABLE 2
Percent Frequency Distribution of Patients' Family and Personal Histories of Potential Risk Factors by Histology

	Papillary	Follicular	Hürthle cell	Medullary, family history of thyroid CA	Medullary, no family history of thyroid CA	Undifferentiated/ anaplastic	Total
Family history							
Goiter or other thyroid disease	11.9	12.2	7.8	19.2	8.6	10.4	11.7
Thyroid carcinoma	4.9	3.7	2.0	100.0	0.0	4.3	4.9
Personal history: nonneoplastic							
Graves disease	2.0	2.1	2.0	0.0	1.3	1.0	2.0
Thyroiditis	8.1	4.5	5.9	7.7	3.3	5.2	7.5
Prior exposure to radiation	4.8	4.1	3.4	0	1.3	9.4	4.7
Goiter	14.3	15.9	15.1	3.8	12.0	25.0	14.6
Personal history: neoplastic							
Lymphoma	0.7	0.7	1.0	0.0	0.0	1.0	0.7
Childhood malignancy	0.4	0.3	0.0	0.0	0.0	0.0	0.4
Other cancer	7.1	5.8	9.3	7.7	8.6	11.5	7.2
Cases	4522	583	205	27	150	96	5583

CA: carcinoma.

diagnostic chest or dental X-rays) was reported for 9.4% of patients with anaplastic/undifferentiated cancers, versus 4.7% overall. A personal history of prior thyroiditis was reported by 7.5% overall. Prior Graves disease was reported by 2% overall.

A surprising percentage of patients, 7.2% overall, reported a personal history of other, nonthyroid cancer. The incidence of prior lymphoma (sometimes treated with mantle irradiation) and the incidence of prior childhood malignancy were 0.7% and 0.4%, respectively.

Table 3 describes the frequency of local, regional, and distant symptoms by histology. Local symptoms most commonly began with a noticeable central neck mass (75.5%, no variation by histology), followed by noticeable dysphagia (11.7% overall and 40% for undifferentiated/anaplastic), followed by voice change (8.2% overall and 40% for undifferentiated/anaplas-

TABLE 3
Percent Frequency Distribution of Local, Regional, and Distant Symptoms by Histology

	Papillary	Follicular	Hürthle cell	Medullary	Undifferentiated/ anaplastic	Total
Local symptoms						
Dysphagia	10.4	14.9	16.6	11.9	40.0	11.7
Hoarseness/voice change	7.2	9.3	9.3	12.5	40.6	8.2
Stridor	3.5	6.2	3.4	6.2	24.0	4.2
Thyroid mass	74.9	78.1	81.5	73.3	77.1	75.5
Regional symptoms						
Lymph node mass	26.6	21.5	22.9	37.5	54.2	26.8
Neck pain	5.7	8.1	5.4	6.8	26.0	6.3
Systemic or distant symptoms						
Pathologic fracture	0.2	1.2	0.0	0.6	1.0	0.3
Bone pain	0.8	4.5	2.0	3.4	6.3	1.4
Weight loss	3.8	4.1	5.4	5.1	20.8	4.2
Other	11.8	10.3	7.4	11.9	23.2	11.7
Cases	4522	583	205	177	96	5583

TABLE 4
Percent Frequency Distribution of Diagnostic Exams and Procedures as Well as Imaging Procedures Directed at the Neck and Distant Sites

	Papillary	Follicular	Hürthle cell	Medullary	Undifferentiated/ anaplastic	Total
Surgical procedures						
Laryngoscopy	5.9	5.8	4.4	6.8	22.9	6.1
Needle aspiration of neck lymph node	7.4	5.1	6.8	9.6	14.6	7.3
Needle aspiration of thyroid	53.1	52.7	58.5	47.5	39.6	52.9
Incisional biopsy of thyroid or neck lymph node	13.1	10.8	13.2	16.9	34.4	13.3
Imaging procedures: neck						
Neck X-ray (AP & lateral)	2.7	4.8	3.9	7.3	10.4	3.3
CT scan of neck	15.3	15.8	12.7	32.2	66.7	16.7
MRI of neck	2.6	2.4	2.0	4.5	12.5	2.8
Thyroid scan	39.0	41.9	39.0	32.8	20.8	38.8
Ultrasound of thyroid	38.3	41.2	35.1	32.2	27.1	38.1
Imaging procedures: distant						
Chest X-ray	50.2	53.5	60.0	62.1	75.0	51.7
CT scan of chest	6.2	9.4	14.1	22.6	53.1	8.2
Bone scan	4.1	8.9	9.3	9.6	22.8	5.3
Cases	4522	583	205	177	96	5583

AP: anteroposterior; CT: computed tomography; MRI: magnetic resonance imaging.

tic), followed by stridor (4.2% overall and 24% for undifferentiated/anaplastic). Regional symptoms included a noticeable lymph node mass (26.8% overall and higher for medullary and undifferentiated/anaplastic at 37.5% and 54.2%, respectively) and neck pain (6.3% overall and 26% for undifferentiated/anaplastic). Distant/systemic symptoms were relatively less common, and only weight loss was reported with any frequency (4.2%).

Diagnostic Evaluation

Table 4 describes the frequency of diagnostic examinations and procedures as well as imaging procedures directed at the neck and distant sites. For diagnostic examinations and procedures, fine-needle aspiration cytology of the thyroid or a neck lymph node were most commonly employed (in 52.9% and 7.3% of cases, respectively). Incisional biopsy was surprisingly common at 13.3%. Overall, laryngoscopy was performed only 6.1% of the time, an unexpectedly low frequency. For neck imaging, thyroid scan was performed 38.8% of the time and ultrasound 38.1% of the time. Neck computed tomography (CT) and magnetic resonance imaging (MRI) were performed in 16.7% and 2.8% of cases, respectively. Imaging of distant sites was mostly (in 51.7% of cases) restricted to chest

TABLE 5
Percent Frequency Distribution of Pathologic Findings by Histology

	Papillary	Follicular	Hürthle cell	Medullary, family history of thyroid CA	Medullary, no family history of thyroid CA	Undifferentiated, anaplastic	Total
Tumor grade							
Well differentiated	14.7	23.9	12.2	0.0	2.0	0.0	14.9
Moderately differentiated	4.8	6.7	5.9	3.8	2.6	0.0	4.9
Poorly differentiated	1.4	6.0	3.9	0.0	5.3	9.4	2.2
Undifferentiated	0.4	1.5	0.5	0.0	4.0	82.3	2.1
Grade not determined	78.7	61.9	77.6	96.2	86.1	8.3	76.0
Blood vessel invasion							
Yes	4.8	29.7	25.4	7.7	14.0	20.8	8.7
No	80.4	56.1	59.0	73.1	69.3	30.2	75.9
Not applicable	0.5	1.0	1.0	0.0	0.0	17.7	0.9
Unknown	14.3	13.1	14.6	19.2	16.7	31.3	14.6
Diagnostic confirmation							
Positive histology	99.0	98.3	100.0	100.0	99.3	91.6	98.9
Positive cytology	0.9	1.5	0.0	0.0	0.7	7.4	1.0
Positive microscopic, method NOS	0.1	0.2	0.0	0.0	0.0	1.1	0.1
Tumor size (mm)							
1–5	14.3	1.5	1.5	26.9	6.0	1.1	12.1
6–10	13.0	4.0	1.5	11.5	4.6	2.1	11.2
11–15	13.4	7.9	6.8	15.4	6.6	0.0	12.2
16–20	13.2	10.3	9.3	7.7	13.9	2.1	12.5
21–25	10.0	12.4	8.3	3.8	7.9	2.1	9.9
26–30	7.6	11.5	12.2	0.0	10.6	4.2	8.1
31–40	7.8	14.1	14.6	0.0	12.6	7.4	8.8
> 40	7.9	24.6	29.3	11.5	19.9	35.8	11.2
Unknown	12.9	13.7	16.6	23.1	17.9	45.3	13.8
Multifocal							
No	61.6	73.1	73.2	46.2	68.7	46.9	63.1
Microscopic	17.2	9.5	7.8	34.6	9.3	6.3	15.8
Gross	4.4	2.4	2.9	11.5	6.0	5.2	4.2
Multifocal, NOS	7.2	3.6	3.4	3.8	5.3	5.2	6.6
Unknown	9.5	11.4	21.7	3.8	10.7	36.5	10.3
Regional lymph nodes examined							
No lymph nodes examined	54.3	77.0	70.7	23.1	39.7	63.5	56.9
1	11.9	6.7	10.2	3.8	7.9	12.5	11.2
2	5.8	2.9	3.9	3.8	2.6	2.1	5.3
3	3.3	0.9	1.0	3.8	2.6	1.0	2.9
4	2.3	0.9	0.5	3.8	1.3	1.0	2.0
5	1.7	0.7	0.0	7.7	4.0	0.0	1.6
> 5	10.9	2.6	3.4	46.2	32.5	8.3	10.5
Lymph nodes examined, no. not specified	7.3	4.8	5.9	7.7	6.0	10.4	7.0
Unknown if lymph nodes examined	2.3	3.6	4.4	0.0	3.3	1.0	2.5
Cases	4522	583	205	27	150	96	5583

CA: carcinoma; NOS: not otherwise specified.

X-ray. Chest CT (8.2%) and bone scan (5.3%) were performed relatively infrequently.

Disease Pathology

Table 5 describes pathologic findings. Grading of thyroid neoplasms was not commonly performed. Blood vessel invasion was infrequent in papillary neoplasms (4.8%) and more commonly found in follicular (29.7%), Hürthle cell (25.4%), and undifferentiated/anaplastic (20.8%) neoplasms. A greater proportion of papillary cases and familial medullary cases presented with small tumors. Conversely, 35.8% of anaplastic/undifferentiated cancers were 41 mm or larger at the time of diagnosis. Median tumor size by histology was 17 mm for papillary, 30 mm for follicular, 35 mm for Hürthle cell, 28 mm for familial medullary, 8 mm for

TABLE 6
Percent Frequency Distribution of AJCC Pathologic Stage and Combined Stage by Histology[a]

	Papillary	Follicular	Hürthle cell	Medullary, family history of thyroid CA	Medullary, no family history of thyroid CA	Undifferentiated/ anaplastic
Pathologic stage						
I	56.3	38.8	15.6	46.2	9.9	0.0
II	16.2	31.9	36.1	11.5	37.7	0.0
III	12.5	7.4	6.3	30.8	32.5	3.1
IV	1.7	6.0	3.9	7.7	5.3	57.3
Unknown	13.3	16.0	38.1	3.8	14.5	39.6
Combined stage[b]						
I	64.7	44.3	28.1	50.0	8.6	0.0
II	14.9	31.1	42.9	7.7	40.4	0.0
III	12.3	7.0	6.9	30.8	35.8	0.0
IV	1.6	9.1	6.4	7.7	8.6	100.0
Unknown	6.5	8.4	15.8	3.8	6.6	0.0
Cases	4522	583	205	27	150	96

AJCC: American Joint Committee on Cancer; CA: carcinoma.
[a] AJCC *Manual for Staging of Cancer*, 4th edition.
[b] Pathologic stage, supplemented by clinical stage when not available.

sporadic medullary, and 50 mm for undifferentiated/anaplastic neoplasms. Multifocality was more common for medullary carcinomas associated with positive family history (49.9% of cases when one sums microscopic, gross, and NOS multifocality) and for papillary carcinomas (28.8% of cases when microscopic, gross, and NOS multifocality were summed). For papillary carcinomas associated with positive family history, multifocality was 38.6%. Multifocality for follicular and Hürthle cell carcinomas was less common. No lymph nodes were examined microscopically in a substantial proportion of cases for all histologies, particularly for follicular (77.0%) and Hürthle cell (70.7%). Even in cases of medullary carcinoma, the proportion of cases with no lymph nodes examined was noticeably high (23.1% for familial cases and 39.7% for sporadic cases). When examined lymph nodes were positive, they were most commonly found in multiple sites, the lateral neck, and/or adjacent to the thyroid gland itself (data not shown).

Table 6 describes stage distribution by histology. Other than for undifferentiated/anaplastic cancer, for which all cases are Stage IV by definition, patients presented with predominately Stage I or II disease.

Over 75% of cases for all histologies were staged by the managing physician, the registrar, or a combination of physician and registrar (data not shown). Managing physicians at CoC-approved facilities are required to stage reported cases. In 5.5% of cases it could not be determined from the hospital record whether a specific AJCC stage was assigned.

Treatment

Approximately 95% of patients with papillary, follicular, or Hürthle cell neoplasms, the so-called "differentiated" histologies, received surgical treatment with or without hormonal or radioiodine therapy (Table 7). Participating registries could confirm that adjuvant hormonal therapy was used in approximately 50% of such cases. Unfortunately, the degree of suppression of thyroid-stimulating hormone as a result of such hormonal therapy could not be reliably captured, and we suspect that hormone use was underreported. For papillary and follicular carcinoma, adjuvant radiotherapy (radioiodine versus external beam in a ratio of over 20:1) was used in 17.3% and 19.6% of cases, respectively. For Hürthle cell carcinomas (which concentrate radioiodine poorly), 15.6% received radioiodine. We suspect that radioiodine treatment may also have been underreported in this study. Table 8 summarizes the doses of radioiodine used for initial and subsequent treatments. The median initial dose for the differentiated histologies was slightly over 100 mCi. The median subsequent dose was also over 100 mCi, but few patients required subsequent treatments, presumably because of failure to detect areas of uptake outside the thyroid bed when a scan was performed at the time of initial dose. External beam radiation was occasionally used to address unresected primary disease, but numbers were too small for meaningful dose distributions (data not shown).

Near-total or total thyroidectomy with or without

TABLE 7
Percent Frequency Distribution of Treatment, Type of Cancer-Directed Surgery, and Residual Disease following Cancer-Directed Surgery by Histology

	Papillary	Follicular	Hürthle cell	Medullary, family history of thyroid CA	Medullary, no family history of thyroid CA	Undifferentiated/ anaplastic	Total
Treatment modality							
Surgery alone	28.5	27.4	28.3	30.8	45.7	9.4	28.5
Surgery and hormones	17.7	10.5	17.6	46.2	26.5	2.1	17.0
Surgery, radiation, and hormones	33.3	36.5	34.1	11.5	9.3	7.3	32.5
Surgery and radiation	17.3	19.6	15.6	11.5	10.6	8.3	17.1
Other modalities	2.1	3.6	2.9	0.0	5.3	67.7	3.5
No treatment	0.5	1.2	0.5	0.0	1.3	4.2	0.6
Not indicated	0.6	1.2	1.0	0.0	1.3	1.0	0.7
Type of cancer-directed surgery							
No surgical procedure	2.4	5.3	2.4	0.0	6.0	40.6	3.4
Local surgical excision, partial removal of lobe	1.7	1.5	2.4	0.0	2.6	5.2	1.8
Lobectomy w/ or w/o isthmectomy w/o LND	16.1	20.9	14.6	0.0	7.3	11.5	16.2
Near-total thyroidectomy	15.5	14.9	14.1	0.0	13.9	8.3	15.2
Total thyroidectomy w/o LND	34.1	41.5	35.1	42.3	31.1	14.6	34.5
Total thyroidectomy w/ limited LND	21.4	10.1	24.4	23.1	20.5	12.5	20.1
Total thyroidectomy w/ radical LND	6.4	1.7	2.0	34.6	16.6	2.1	6.1
Thyroidectomy, NOS	1.3	2.2	2.4	0.0	0.7	0.0	1.4
Surgery of regional/distant sites/lymph nodes	0.3	1.2	0.0	0.0	0.7	1.0	0.4
Surgery, NOS	0.2	0.3	0.5	0.0	0.7	4.2	0.3
Residual primary tumor following cancer-directed surgery							
No residual tumor	74.2	72.0	74.6	88.5	68.0	8.7	72.8
Microscopic residual tumor	8.6	6.4	7.0	3.8	12.2	12.0	8.5
Macroscopic residual tumor	2.1	1.6	3.5	3.8	3.4	23.9	2.5
Not applicable, no surgery	1.6	5.4	2.0	0.0	5.4	37.0	2.7
Unknown	13.4	14.7	12.9	3.8	10.9	18.5	13.5
Cases	4522	583	205	27	150	96	5583

CA: carcinoma; LND: lymph node dissection; NOS: not otherwise specified.

lymph node dissection was performed in 77.4% of papillary, 68.2% of follicular, and 75.0% of Hürthle cell carcinomas (Table 7). The surgical treatment rendered to patients with differentiated thyroid carcinoma consisted of lobectomy in 16.1% of papillary, 20.9% of follicular, and 14.6%, of Hürthle cell carcinoma patients. The majority of these lobectomy patients had Stage I or II disease; only 4.9% and 6.0% had Stage III and IV disease treated by lobectomy (data not shown).

The treatment of medullary carcinoma was primarily surgical and predominately near-total or total thyroidectomy. However, 23.0% of familial cases and 19.9% of sporadic cases of medullary thyroid carcinoma received adjuvant radiotherapy, and for this histology external beam radiation was used more frequently than radioiodine in a ratio of 2:1.

Residual primary tumor following cancer-directed surgery could be documented in 10.7% of papillary, 8.0% of follicular, and 10.5% of Hürthle cell carcinoma patients. Residual primary tumor following cancer-directed surgery could be documented in 7.6% of cases of familial medullary carcinoma and 15.6% of sporadic cases of medullary carcinoma. When surgery was performed for undifferentiated/anaplastic carcinoma, residual tumor remained in 35.9% of cases.

As seen in Table 8, for undifferentiated/anaplastic carcinomas, external beam radiation represented the dominant treatment (66.7% of cases); two-thirds of the time, such treatment was concomitant with chemotherapy (41.7% of cases). Single-agent chemotherapy was employed more frequently than multiple agents in such cases, in a ratio of 2:1 (31.3% of cases vs. 15.6% of cases). Surgical therapy was used in 27.1% of cases, usually in combination with other treatments (see Tables 7 and 8).

Surgical Complications

Table 9 summarizes surgical complications by type of surgical procedure. Hypocalcemia (to be distinguished from permanent hypoparathyroidism) oc-

TABLE 8
Percent Frequency Distribution of Nonsurgical Treatments by Histology

	Papillary	Follicular	Hürthle cell	Medullary, family history of thyroid CA	Medullary, no family history of thyroid CA	Undifferentiated/ anaplastic	Total
Radiation therapy							
No radiation therapy	46.8	40.1	45.9	76.9	76.8	27.1	46.7
Beam radiation	2.2	4.3	2.0	15.4	13.9	66.7	3.9
Radioactive implants	1.0	1.2	2.4	0.0	0.7	0.0	1.1
Radioisotopes	47.8	51.3	47.3	7.7	7.3	3.1	46.1
Combination of beam w/ implants or isotopes	0.8	2.4	1.0	0.0	0.0	2.1	0.9
Radiation therapy, NOS	0.4	0.3	0.0	0.0	0.0	0.0	0.3
Unknown if recommended or performed	1.0	0.3	1.5	0.0	1.3	1.0	1.0
Total millicuries of radioiodine, initial dose (mCi)							
1–50	7.2	6.7	5.6	3.8	0.7	1.1	6.8
51–100	11.2	12.8	12.1	3.8	0.7	1.1	10.9
101–150	17.0	19.5	19.2	0.0	4.3	1.1	16.6
151–200	7.7	9.4	9.1	0.0	0.7	1.1	7.6
> 200	4.5	6.0	3.5	0.0	2.1	2.2	4.5
Unknown	15.4	13.2	16.7	3.8	26.2	23.7	15.6
Not applicable	37.0	32.5	33.8	88.5	65.2	69.9	38.0
Total millicuries of radioiodine, subsequent dose (mCi)							
1–100	1.7	1.7	0.5	0.0	0.0	0.0	1.5
101–200	2.1	2.1	1.1	0.0	0.0	0.0	1.9
> 200	0.6	0.9	0.0	0.0	1.4	1.1	0.7
Unknown	20.9	18.8	25.1	7.7	28.1	22.6	21.0
Not applicable	74.7	76.5	73.3	92.3	70.5	76.3	74.9
Chemotherapy							
No chemotherapy	98.6	98.6	99.0	100.0	94.0	46.9	97.6
Chemotherapy, NOS	0.0	0.2	0.0	0.0	0.7	5.2	0.1
Single agent	0.2	0.5	0.0	0.0	0.7	31.3	0.8
Multiple agents	0.2	0.2	0.0	0.0	4.0	15.6	0.5
Unknown if recommended or administered	1.0	0.5	1.0	0.0	0.7	1.0	0.9
Adjuvant chemotherapy with concomitant external beam radiation							
No concomitant treatment	91.9	92.6	92.4	96.0	84.9	46.9	91.0
Radiation & concomitant adjuvant chemotherapy	0.3	0.9	0.5	0.0	0.7	41.7	1.1
Unknown if therapy concomitant	7.7	6.5	7.1	4.0	14.4	11.5	7.8
Thyroid hormone therapy							
Yes	52.7	48.9	55.8	57.7	36.7	25.0	51.5
No	31.9	37.8	28.1	30.8	42.0	57.3	33.1
Unknown	15.4	13.3	16.1	11.5	21.3	17.7	15.4
Cases	4522	583	205	27	150	96	5583

CA: carcinoma; NOS: not otherwise specified.

curred in 6.2% of patients who underwent near-total thyroidectomy, 12.4% of patients who underwent total thyroidectomy without lymph node dissection, and 14.2% of patients who underwent total thyroidectomy with lymph node dissection. Hypocalcemia occurred in 3.3% of lobectomy patients, and it should be noted that we failed to obtain information related to any prior thyroid surgery in this study.

Recurrent laryngeal nerve injury occurred in 1.3% of cases overall and was highest for patients who underwent total thyroidectomy with lymph node dissection (2.7%). For patients who underwent total thyroidectomy without lymph node dissection it was 0.7%, and for patients who underwent lobectomy it was 0.9%. Significant postoperative voice change was coded as a recurrent nerve injury.

In order to eliminate disease specific variables, we analyzed complications for the subset of cases with T1N0M0 differentiated thyroid carcinoma (i.e., papillary, follicular, or Hürthle cell). For this subgroup analysis, the overall complication rate increases with magnitude of the surgical procedure, from a low of 4.8% for lobectomy to a high of 21.5% for total thyroidectomy with lymph node dissection (Table 10). Airway

TABLE 9
Percent Frequency Distribution of Surgical Complications and Deaths by Type of Surgical Procedure[a]

	Lobectomy	Near-total thyroidectomy	Total thyroidectomy without LND	Total thyroidectomy with limited or radical LND	Other/NOS	Total
Airway problem	0.6	0.6	0.6	1.3	1.9	0.8
Bleeding	1.0	0.5	0.6	0.8	0.9	0.7
Hypocalcemia	3.3	6.2	12.4	14.2	1.9	10.0
Recurrent nerve injury	0.9	1.2	0.7	2.7	0.5	1.3
Wound infection	0.2	0.1	0.2	0.3	0.0	0.2
Postoperative death within 30 days	0.3	0.2	0.2	0.2	1.4	0.3
Cases	903	840	1928	1464	219	5354

LND: lymph node dissection; NOS: not otherwise specified.
[a] Surgically treated cases only.

TABLE 10
Percent Frequency Distribution of Surgical Complications by Type of Surgical Procedure for T1N0M0 Papillary, Follicular, or Hürthle Cell Carcinomas

	Lobectomy	Near-total thyroidectomy	Total thyroidectomy without LND	Total thyroidectomy with limited or radical LND	Other/NOS	Total
Airway problem	0.0	0.5	0.3	2.5	0.0	0.5
Bleeding	1.1	0.5	0.9	2.5	0.0	1.0
Hypocalcemia	3.4	4.7	12.8	14.0	0.0	7.7
Recurrent nerve injury	0.3	0.0	0.3	1.7	0.0	0.4
Wound infection	0.0	0.5	0.0	0.8	0.0	0.2
Cases	352	214	343	122	48	1079

LND: lymph node dissection; NOS: not otherwise specified.

problems, bleeding, hypocalcemia, and recurrent nerve injury were all more common for total thyroidectomy with lymph node dissection.

Surgical mortality (defined as death within 30 days of the procedure) was 0.3% overall and, although the numbers were low, did not seem to vary significantly by type of surgical procedure (Table 9). An analysis of the 15 patients who expired within 30 days of a surgical procedure revealed that 5 were patients with undifferentiated/anaplastic carcinoma. We suspect that these patients died of disease progression rather than the surgical procedure. Surgical mortality exclusive of undifferentiated/anaplastic cancer was thus 0.2%. All of the remaining 10 patients who died had differentiated thyroid carcinoma, and 4 patients (all with Stage I disease) were age 40 years or younger. Of the 10 patients, 3 underwent lobectomy, 1 had total thyroidectomy without lymph node dissection, 3 had total thyroidectomy with lymph node dissection, and 3 underwent other variations of surgery. Unfortunately, we have no data on the specific causes of death for these patients.

Insurance Coverage

Table 11 summarizes insurance coverage by stage at presentation. The fact that the vast majority of patients with Medicare coverage are older than 65 years precludes comparisons for this subgroup, because age impacts on stage for thyroid carcinoma. Similarly, the military category includes those insured under the Veterans Administration, most of whom are older than the cutoff of age 45 years used in the staging system. For the other insurance subgroups, Stage IV presentations were lowest for private insurance and Health Maintenance Organizations (HMOs) at 1.6% and 1.6%, respectively. Government insurance, other government insurance (including unspecified state and federally funded programs, Medicaid, welfare, Indian Health Service, and Public Health Service), and uninsured categories were associated with Stage IV presen-

TABLE 11
Percent Frequency Distribution of Insurance Coverage by AJCC Stage of Disease at Presentation

	AJCC stage					
	I	II	III	IV	Unknown	Cases
Private	65.6	16.6	10.2	1.4	6.3	1981
HMO	66.4	16.8	10.0	1.6	5.2	1774
Medicare	19.5	29.3	21.5	16.6	13.1	856
Government[a]	68.3	7.3	9.8	4.9	9.8	41
Military	58.4	14.9	12.9	6.9	6.9	101
Other government[b]	65.9	9.5	12.7	6.3	5.6	255
Not insured	61.5	15.6	12.0	5.1	5.8	467
Unknown	75.7	11.2	6.5	2.8	3.7	108

AJCC: American Joint Committee on Cancer; HMO: Health Maintenance Organization.
[a] Government: state or federally funded, not otherwise specified.
[b] Other government: Medicaid, Welfare, Indian Health Service, Public Health Service.

tations between 4.9% and 6.3% of the time, but numbers were small. Early stage presentations, Stages I and II, were reciprocal. The highest percentages of early stage presentations were associated with private insurance (82.2%) and HMOs (83.2%).

DISCUSSION

As diagnostic methods, imaging techniques, and treatment paradigms shift over time, stage distribution, patterns of care, and outcomes can be expected to shift. Our findings for this PCE cohort represent the most current national assessment of presenting symptoms, diagnostic tests, treatment, and complications of treatment for thyroid carcinoma. Although accession of thyroid carcinomas to this PCE study was less than half the current annual accession to the NCDB, this PCE cohort nonetheless represented a very large sample, approximately 30% of incident thyroid carcinomas for the year.[19]

In general, for those data items common to both this PCE study and the NCDB, this study largely paralleled demographic findings from our previous 1985–1995 NCDB study.[11] Gender distribution, ethnic distribution, and income-level distribution also matched those from a 1992 NCDB report.[20] Briefly, females predominated for all histologies, especially for papillary, follicular, and undifferentiated/anaplastic. Ethnic distribution of papillary and follicular cases roughly paralleled that for the NCDB as a whole; however, case ratios for Asian Americans appeared slightly higher than expected both in this PCE and in the previous NCDB report.[11,20]

Overall, 4.9% of patients in this study reported a family history of thyroid carcinoma; 4.9% reported papillary, 3.7% reported follicular, and 2% reported Hürthle cell. Given the low incidence of thyroid carcinoma (less than 2 per 100,000),[1,2] this supports the concept of a genetic component of risk. Our data further support the concept that prior exposure to radiation, thyroiditis, prior Graves disease, and preexisting goiter are risk factors.[21] We have no way of evaluating the possibility that radioiodine treatment for Graves disease, rather than Graves disease pre se, confers risk. A notably high percentage reported a personal history of nonthyroid cancer (7.2% overall); only a small proportion of these cases were lymphoma or childhood malignancy. Unfortunately, we have no data regarding the nature of or treatment for such malignancies. Undoubtedly, some of these prior nonthyroid malignancies may have been skin cancers, but the incidence still seems high. We will try to establish comparison data for other malignancies by building this question into future nonthyroid PCE studies. Obviously, we lack an age-, gender-, and location-matched control group with which to compare.

Traditionally, symptoms of disease are described subjectively. This study has generated quantitative rates for common local, regional, and distant symptoms. As computing technology continues to develop and we try new ways of delivering medical care to the public, we envision a need for such quantitative symptom information in the design of patient-focused diagnostic software. Such quantitative data are available for the vast majority of cancers addressed in CoC PCE studies. In the current study, 75% of patients complained of a central neck mass, and the frequency of dysphagia (11.7%), voice change (8.2%), and frank stridor (4.2%) were common.

Overall, fine-needle aspiration (FNA) cytology was used in 52.9% of cases, making this the most common means of establishing diagnosis, a practice consistent with current recommendations.[22,33] Diagnostic ultrasound was used in 38.1% of cases. Worrisome practice patterns included a remarkably high incidence of open incisional biopsy (13.3%), which virtually all experts decry, and a remarkably low incidence of diagnostic laryngoscopy (6.1%) despite the fact that a substantial proportion of patients complained of voice change (8.2%), and despite the fact that some experts recommend it as a routine practice.[23] In addition, the use of CT scanning as an initial diagnostic test seems higher than one would expect; CT scans were more likely performed on patients with a lymph node mass.

Pathologists do not routinely grade thyroid neoplasms; no grade was assigned in 76% of these PCE cases. Multicentric disease in the thyroid was pathologically identified in 28.8% of papillary carcinomas, 15.5% of follicular carcinomas, and 14.1% of Hürthle cell carcinomas in this series, a finding which has

impacted on the treatment of such differentiated cancers (see below). A high percentage of patients in all histologic categories had no lymph nodes examined (e.g., 54.3% of papillary cases, 77.0% of follicular cases, 23.1% of familial medullary cases, and 39.7% of sporadic medullary cases). Particularly for medullary carcinoma, this runs contrary to expert recommendations.[23]

The vast majority of patients with differentiated thyroid carcinoma presented with AJCC Stage I or II disease. For familial medullary carcinoma cases, 57.7% presented with Stage I or II disease, and this declined to 49% for those with sporadic disease. As genetic diagnosis of familial cases gains popularity, we anticipate a shift to earlier stage and will track this through the NCDB.

The surgical treatment of papillary and follicular ("differentiated") thyroid carcinoma remains controversial.[23,24] Initial autopsy studies suggesting a very high degree of pathologically confirmed contralateral disease supported the routine performance of total thyroidectomy.[25] The significance of this finding became suspect, however, when U.S. autopsy studies showed a high incidence (3–6%) of asymptomatic, occult, intraglandular foci of this clinically rare cancer—with usual world standard reported incidence rates of 2–5 per 100,000—in patients dying of other causes,[26] and a very high autopsy incidence (14–24%) when glands were analyzed using fine step-sectioning techniques.[27,28] A large clinical series from the Memorial Sloan-Kettering Cancer Center with 20-year follow-up revealed excellent results (99% 20-year survival and only 4% local recurrence) associated with the treatment of patients with favorable prognostic factors, i.e., defined as "low risk" according to the Memorial Sloan-Kettering Cancer Center GAMES (grade, age, metastasis, extrathyroidal extension, and size) classification, by complete ipsilateral lobectomy and isthmusectomy and long term hormonal suppression.[29] Other series with long follow-up, using different risk group definitions, have also supported the selective use of complete lobectomy rather than routine total thyroidectomy.[7] These findings echo those of smaller, earlier studies.[30–32] Other major studies, however, have documented that recurrences and mortality were lower for unselected patients treated with total or near-total thyroidectomy and iodine-131.[4,9,10] A recent reanalysis of a very large series of low risk patients treated at the Mayo Clinic documented higher recurrences among patients treated by lobectomy-isthmusectomy regardless of radioiodine treatment, even though they presented with low risk disease.[33] The multiplicity of risk stratification schemes (with varying definitions of "low risk" or "favorable prognosis"), the variable use of iodine-131, and variable practice with respect to long term hormonal suppression complicate a stratified analysis of treatment-related outcomes. At this point, experts continue to disagree concerning the optimal treatment of the "low risk" patient with differentiated thyroid carcinoma. The current study does confirm the findings of earlier studies indicating that, in community practice, complications with lobectomy are lower than with total thyroidectomy with or without lymph node dissection.[34] Because effective salvage therapy in the presence of recurrence in the opposite lobe is possible, and because disease specific mortality has been shown by multiple studies to be low for the subgroup of patients deemed "low risk," several experts recommend that patients at low risk for recurrence be initially treated with simple lobectomy-isthmusectomy and long term hormonal suppression.[3,7,8,10,29]

These data provide a snapshot of current surgical opinion concerning the "lobectomy versus total" controversy. Overall, only 16% of patients with papillary carcinoma and 20% of patients with follicular carcinoma are treated by ipsilateral lobectomy. Our data show that, of patients with Stage I differentiated thyroid carcinoma (64.7% of papillary cases, 44.3% of follicular cases, and 28.1% of Hürthle cell cases), 30.4% have T1N0M0 disease. This suggests that U.S. surgeons apply selection criteria for ipsilateral lobectomy conservatively; however, we have no data concerning the frequency of the more aggressive columnar or tall cell variants of papillary carcinoma (usually rare), which would preclude this option.[26] Conversely, we noted that 4.9% and 6.0% of patients with Stage III and IV disease, respectively, underwent lobectomy despite the more advanced stage. Our previous 1985–1995 NCDB experience (with 18% of papillary carcinoma patients and 25% of follicular carcinoma patients undergoing lobectomy) showed that, with 5 years of follow-up, more extensive surgical resection failed to generate convincingly superior survival for any subgroup.[11] Given the indolence of this disease, prolonged follow-up is required for a true assessment of the survival impact of variation in surgical and adjuvant treatment. Stage-stratified survival rates and assessment of thyroid carcinoma risk models for differentiated carcinoma were addressed in the previous 1985–1995 NCDB study[11] and will be addressed in future articles about this PCE cohort.

When we attempted to control for extent of disease by analyzing T1N0M0 differentiated cases, complication rates for thyroid procedures increased with increasing extent of surgical treatment (see Table 10 for T1N0M0 differentiated cases; data for other subgroups are not shown). Hypocalcemia accounts for

the majority of complications. We recognize that postoperative hypocalcemia is not the same as permanent hypoparathyroidism, but applying strict diagnostic criteria for the latter diagnosis was not feasible in the context of this PCE study; thus, hypocalcemia was used as a surrogate. Techniques for management of the parathyroid glands during thyroidectomy for cancer, including autotransplantation techniques and the routine use of optical magnification,[35,36] are probably decreasing the rate of permanent hypoparathyroidism, but the current study shows an overall rate of 10% (Table 9), which is higher than the 8% rate of hypoparathyroidism in malignant goiter reported by Foster in a 1978 American College of Surgeons study.[34] The rate of recurrent laryngeal nerve injury in the current study, liberally coded as any significant postoperative voice change, is 1.3% overall and 0.4% for T1N0M0 cases of differentiated thyroid carcinoma. Cases in which the recurrent laryngeal nerve was sacrificed for direct tumor invasion were coded as nerve injury. Also, some cases of external laryngeal nerve injury may have caused noticeable voice change. The rates, according to procedure, are similar to those reported in the 1978 American College of Surgeons study; however, the definitions used in this PCE were more liberal.[34] Taking into account the problem of hypocalcemia versus permanent hypoparathyroidism described above, the rates appear comparable to those described in a recent review of other studies.[37]

Residual primary tumor following cancer-directed surgery could be documented in 10.7% of papillary cancers, 8.0% of follicular cancers, and 10.5% of Hürthle cell cancers. For familial medullary carcinoma the rate was 7.6%. For sporadic medullary carcinoma it was 15.6%. This suggests that, even for medullary carcinoma, surgeons are reluctant to perform more radical procedures, such as tracheal resection, in order to clear an involved margin. Such disease was usually managed with radiotherapy.

This study relies on events and treatments recorded in hospital records. Through active follow-up, hospital-based registries obtain information on treatments initiated after discharge. The accuracy of this postdischarge information depends on the meticulousness with which busy physicians review communications and inquiries from their hospital tumor registrars. We suspect some underreporting for both the postoperative administration of hormones and the use of radioiodine. Hormonal therapy, in either replacement doses or suppressive doses, was documented in only 49.5% of cases. Because even the proportion of total thyroidectomies exceeds this, underreporting is obvious. Fortunately, because patients are tracked longitudinally and clinicians have additional opportunities to correct any underreporting of treatment, the accuracy of such outpatient information improves.

When radioiodine treatment is documented, the median initial dose is slightly over 100 mCi. Studies of radioiodine ablation have shown no advantage for doses beyond the 100–149 mCi range.[38] One large randomized, prospective study documented that approximately 50 mCi of iodine-131 successfully ablated remnant thyroid tissue in 80% of patients and that larger doses (up to 150 mCi) did not appear more successful.[39] Another study, employing a disimetric approach to the calculation of ablative dose, documented similar results provided the mass of residual thyroid tissue to be ablated was less than 2 grams.[40]

Approximately 10% of medullary carcinoma cases in this PCE study were familial. Forty-seven percent of the familial cases were diagnosed in the group ages 30–39 years and only 5.9% in the group age < 30 years. This may stem from less frequent participation in CoC programs by pediatric hospitals, where the children of some kin groups are undoubtedly treated. Given the availability of genetic diagnosis and the recommendation that most familial and all MEN 2 cases be treated at age 5 years or earlier,[41,42] we anticipate ever-earlier age of diagnosis in the future. Most authorities recommend total thyroidectomy for patients with medullary carcinoma of the thyroid.[43,44] The vast majority of patients in this cohort were indeed treated by total thyroidectomy (100% of the familial group and 90% of the sporadic group).

Previous series of patients with undifferentiated/anaplastic carcinoma of the thyroid have documented occasional long term survivors, but the overall prognosis remains dismal. The previous 1985–1995 NCDB series indicated 14% 10-year relative survival.[11] In the current PCE study, 67.7% were treated nonsurgically, generally with radiotherapy or chemoradiation. This indicates shifting patterns of care that favor the multimodal techniques experts currently recommend.[45]

Analyzing stage distribution according to the type of primary insurance was confounded in the case of Medicare and for the military category (which includes mostly older Veterans Administration patients) because age is such an important staging and prognostic variable for patients with this disease. Using stage distribution as a measure of quality, performance for private insurance and HMO appeared slightly superior to that for other categories. Though interesting, without controlling for other potentially confounding variables (e.g., ages and educational levels of enrollees), one cannot simplistically ascribe the distributional differences to insufficient access to health care.

CONCLUSIONS

In addition to offering information concerning risk factors and symptoms, this compliments the survival information in previous NCDB reports and offers a surveillance snapshot of the current management of thyroid carcinoma in the U.S. Identified areas for improvement of care include 1) more frequent use of fine-needle aspiration cytology in making diagnosis; 2) more frequent use of laryngoscopy in evaluating patients preoperatively, especially those with voice change; and 3) improved lymph node resection and analysis to improve the staging of patients with differentiated carcinoma and to improve both the staging and outcomes for patients with medullary carcinoma.

In addition, particularly when PCE studies focus on treatments administered outside of a hospital setting (e.g., adjuvant hormonal suppression of thyroid-stimulating hormone), the timely updating of registry records appears problematic. Methodologies to address this are currently being explored, but it is unlikely that the problem will ever be entirely solved. Also, given current methodology, the capture of certain outpatient data elements may be beyond the scope of a PCE study such as this.

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