ORIGINAL ARTICLE

Cost-effective Management of Low-Risk Papillary Thyroid Carcinoma

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Objective: To compare the 20-year cost-effectiveness of initial hemithyroidectomy vs total thyroidectomy in the management of small papillary thyroid cancer in the low-risk patient.

Design: Pooled data from the published literature were used to determine key statistics for decision analysis such as rates of recurrence, rates of complications for all interventions undertaken, and rates of death. The 2005 costs were obtained from the US Department of Health and Human Services, as well as from Medicare reimbursement schedules. Future costs were discounted at 6%.

Setting: Decision analysis study.

Patients: Data from the published literature.

Main Outcome Measures: A state-transition (Markov) decision model was constructed based on the most recent American Thyroid Association recommendations. A cost-effectiveness analysis was performed using fixed probability estimates and Monte Carlo microsimulation, with effectiveness defined as cause-specific mortality or recurrence-free survival. After identifying initial results, sensitivity and threshold analyses were performed to assess the strength of the recommendations.

Results: Initial probability estimates were determined from a review of 940 abstracts and 31 relevant studies examining outcomes in patients with low-risk thyroid cancer undergoing thyroidectomy or neck dissection. During 20 years, cost estimates (including initial surgery, follow-up, and treatment of recurrence) were between \$13 896.81 and \$14 241.24 for total thyroidectomy and between \$15 037.58 and \$15 063.75 for hemithyroidectomy. Cause-specific mortality was similar for both treatment strategies, but recurrence-free survival was higher in the total thyroidectomy group. Sensitivity and threshold analyses demonstrated that these results were sensitive to rates of recurrence and cost of follow-up but remained robust when compared with willingness to pay.

Conclusions: Total thyroidectomy dominates over hemithyroidectomy as initial treatment for low-risk papillary thyroid cancer. However, in sensitivity analyses, these results varied by institution because of heterogeneity in long-term treatment outcomes. With changing protocols of management, it is possible that hemithyroidectomy will emerge as being more cost-effective. Long-term prospective trials are necessary to validate our findings.

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TREATMENT OF LOW-RISK, well-differentiated, papillary thyroid carcinoma is controversial. Because of favorable long-term survival, treatment strategies for this disease have become increasingly conservative during the past half century. However, initial surgical management is a subject of debate: some authors recommend hemithyroidectomy with or without isthmusectomy as treatment, while others recommend initial total thyroidectomy. Long-term prospective randomized surgical trials are lacking because of the protracted nature of follow-up. Moreover, existing observational data are subject to design limitations and potential bias.

As a result of the rising cost of health care, there is a commensurate rising interest in cost-containment and cost-effectiveness. Studies[1-6] of the cost-effective management of various surgical and nonsurgical entities have been published with increasing frequency in the past 2 decades. A search for the most appropriate modality in the management of low-risk papillary thyroid carcinoma is ideal for such an analysis. The rates of complications from each operative procedure are readily available in the literature, as are the rates of recurrence, progression, and death. Cost may easily be estimated from a standardized reimbursement schedule.

Treatment of papillary thyroid carcinoma does not end after surgery; follow-up extends for years, and cost-effectiveness analyses must reflect this reality. Therefore, this study was per-

Table 1. Initial Cost Estimates[a]

Variable	Value (Range), $
Total thyroidectomy	
Operative procedure	6436.61 (4054-6660)
First-year follow-up	307.57 (100-608)
Yearly follow-up	201.56 (62.50-380)
Hemithyroidectomy	
Operative procedure	5684.52 (3535-5982)
First-year follow-up	208.22 (62.50-304)
Yearly follow-up	61.91 (20-133)
Complications	
Allergic reaction	2258.19 (147.50-3800)
Chylous leak	15 404.21 (3750-30 480)
Hematoma	5754.24 (1250-11 430)
Medialization laryngoplasty	4511.80 (2618-5021)
Sialadenitis	5047.87 (1500-5700)
Thyroiditis	7781.16 (3750-9500)
Tracheotomy	22 049.61 (12 500-24 320)
Hypocalcemia yearly cost	101.26 (37.50-190)
Tracheotomy yearly cost	596.46 (250-1140)
Death	1 130 000 (0-3 000 000)[10]
Recurrence	
Radioactive iodine, 30-100 mCi	643.67 (200-1216)
High-dose radioactive iodine, >100 mCi	1059.65 (250-1520)
Neck dissection	6482.33 (3636-7403)
Yearly follow-up	201.56 (62.50-380)

SI conversion factor: To convert millicuries to megabecquerels, multiply by 37.

[a] Unless otherwise indicated, all costs are estimated from the Healthcare Cost and Utilization Project,[7] Medicare Provider Analysis and Review,[8] public use files of the Centers for Medicare and Medicaid Services,[9] or American Medical Association *Current Procedural Terminology* code/relative value search.[11]

formed to compare the long-term costs and benefits of an initial strategy comprising hemithyroidectomy with one comprising total thyroidectomy in the treatment of low-risk papillary thyroid cancer.

METHODS

LITERATURE REVIEW AND INCLUSION CRITERIA

A PubMed search using the Medical Subject Headings *thyroid neoplasms* and *thyroidectomy* yielded 4523 citations published between January 1, 1966, and January 1, 2007. Limiting these citations to those written in English and to those examining adults with papillary adenocarcinomas pared the list to 940 citations. Each citation was evaluated and its bibliography searched for citations missed in the initial screen. We included data from observational studies reporting the type of surgical treatment undertaken, the rate or type of surgical complications, overall survival rates, or cause-specific survival rates, as well as local, regional, or distant recurrence rates after treatment. Case reports were excluded. Thirty-one studies were identified that met the inclusion criteria. We defined low-risk thyroid carcinoma as an AMES (age, metastasis, extent, and size of tumor) score of less than 6, an AGES (age, tumor grade, extent, and size) score of less than 4, or adherence to the Memorial Sloan-Kettering low-risk categories. As much as possible, data were abstracted only for individuals who did not undergo adjuvant radioactive iodine remnant ablation. Hemithyroidectomy included lobectomy, total lobectomy with isthmusectomy, and, as much as possible, total lobectomy with isthmusectomy and partial resection of the contralateral lobe. Total thyroidectomy included complete and near-complete removal of the entire thyroid gland. We did not separate patients who had undergone level VI neck dissections from those who had not. Patients who had undergone less than total lobectomies (ie, lumpectomies and open biopsies) were excluded.

ESTIMATION OF RISKS OF INTERVENTIONS AND RECURRENCE RATES

Recurrence was defined as any second occurrence of papillary thyroid cancer, including occurrences within the undissected remnant lobe (discussed further herein). Yearly rates of recurrence were calculated from reported rates using the following conversion: $r = -(1/t) \times ln(1-P)$, where r represents the yearly rate; t, the length of time during which the probability is reported; ln, log normal, and P, the reported probability. Rates of recurrence and complication were determined by calculating a weighted mean of rates reported in the pooled sample.

COST ESTIMATION

Hospital charges for each inpatient operative procedure were calculated by data obtained from the Healthcare Cost and Utilization Project of the US Department of Health and Human Services[7] and were converted to costs based on a cost-to-charge conversion ratio obtained from the Medicare Provider Analysis and Review,[8] standardized by state (New York) and by diagnosis-related group (group 290 [thyroid procedures]) for 2005. The primary *International Classification of Diseases, Ninth Revision*, code used for these determinations was code 193 (thyroid carcinoma). Costs for nonoperative procedures were obtained from Medicare reimbursements, standardized for April 2007 in Manhattan, New York.[9]

Inpatient operative procedure costs included all costs incurred during the inpatient stay, including surgeon reimbursement, anesthesia reimbursement, and costs to the hospital. Costs for follow-up included, as needed, costs of clinic visits, fiberoptic endoscopies, thyroid and calcium replacement therapy, thyroglobulin, ultrasonography, and fine-needle aspiration biopsies. Radiographic and pathologic costs included radiologist and pathologist interpretations, respectively. All costs are summarized in **Table 1**.

To complete the analysis, it was necessary to assign a cost for death. This estimation can be problematic and varies across industries. The National Safety Council estimates death from unintentional injuries to be worth $1 130 000. This was adopted in our study. In addition, costs were discounted at a rate of 6% per year. All variables, including the discount rate and the ratio of cost-to-charge, were subjected to a sensitivity analysis (described herein).

DESIGN OF THE DECISION TREES

Treatment, follow-up, recurrence, complications, and death associated with low-risk papillary thyroid carcinoma were modeled using a 19-state state-transition (Markov) model (**Figure 1**). Protocols for follow-up were constructed in accord with the 2006 American Thyroid Association clinical practice guidelines for the management of well-differentiated thyroid carcinoma.[12] A deterministic decision tree was constructed around the Markov model. For each initial operative intervention, branches were constructed for uncomplicated treatment, temporary complications, permanent complications, death from

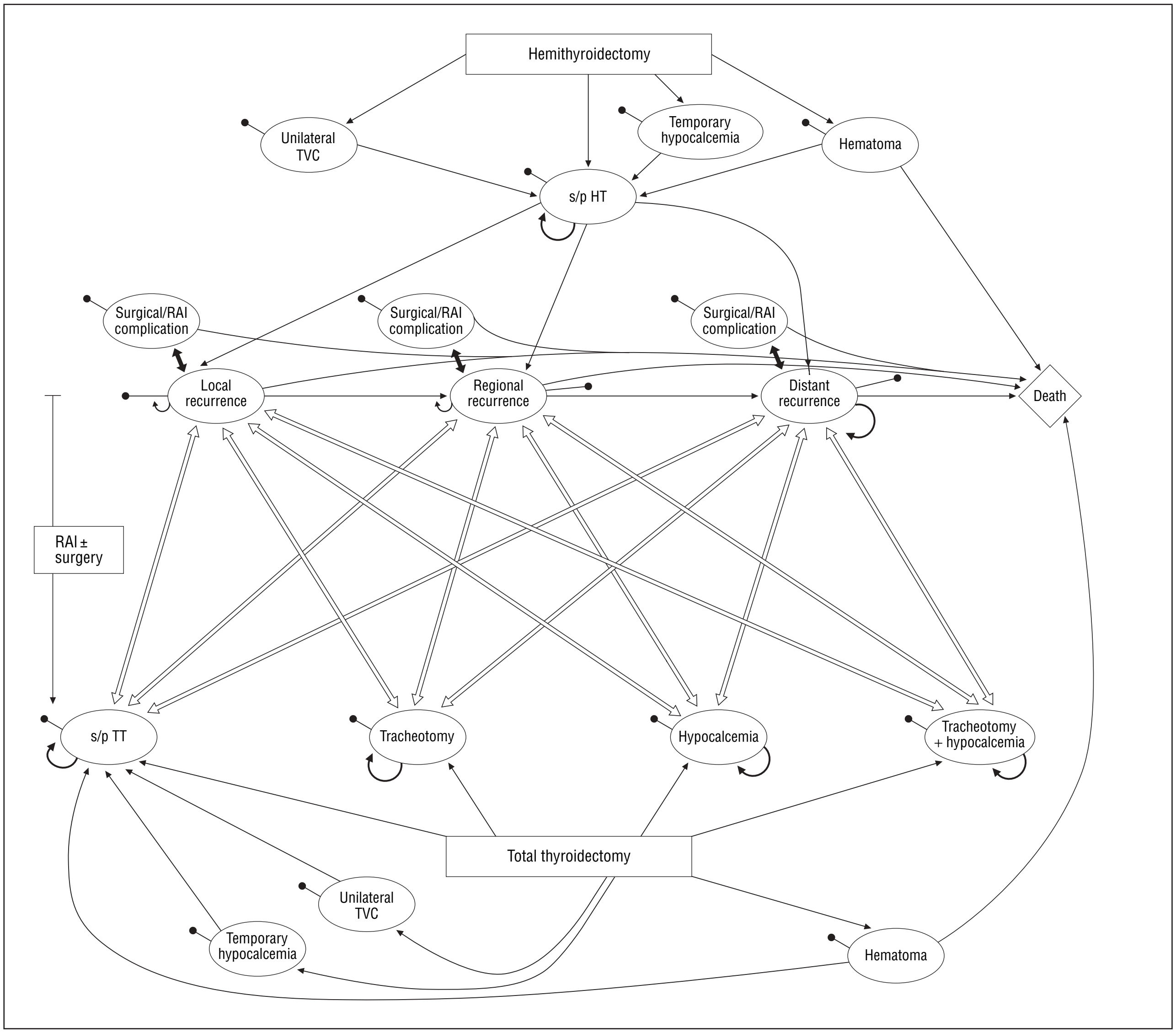

Figure 1. A 19-state Markov state-transition model representing the management and follow-up of patients with low-risk papillary thyroid carcinoma. RAI indicates radioactive iodine; s/p HT, status post hemithyroidectomy; s/p TT, status post total thyroidectomy; TVC, true vocal cord paresis or paralysis; ovals and diamond, health states; arrows, probability of transition between health states; boxes, therapeutic interventions; and solid circles, probability of dying of unrelated causes at each health state.

other causes, and death from disease, as well as local, regional, and distant recurrences.

COST-EFFECTIVENESS ANALYSIS

Effectiveness was defined first as cause-specific survival. After 21 iterations (representing 20 years of follow-up), patients who were classified to any state except dead of disease were assigned an effectiveness score of 1. Patients who died of their disease were assigned an effectiveness score of 0.

To model recurrence-free survival, the definition of effectiveness was changed, and patients in this decision tree who ended in any of the states of recurrence (local, regional, or distant, with or without permanent complications) or patients who died as a result of their disease or its treatment were assigned an effectiveness score of 0. Those who ended the 20 years in any of the other states of health were assigned an effectiveness score of 1.

The theoretical bases of cost-effectiveness calculations have been well explained elsewhere.[6] We ran our models using fixed probabilities and Monte Carlo simulations of 1 million patients each. Cost-effectiveness analysis was performed using decision analysis software (TreeAge Pro Healthcare Module 2007, DATA Version 4.0; TreeAge Software, Inc, Williamstown, Massachusetts).

SENSITIVITY ANALYSIS

One-way sensitivity analyses were performed on every base-case prevalence and cost value, within limits defined in Table 1 and **Table 2**. The results of the model were said to be sensitive to any particular variable if the recommendation changed at any point over that range.

ASSUMPTIONS

We assumed that patients did not receive radioactive iodine remnant ablation after total thyroidectomy or hemithyroidectomy. Recurrences were diagnosed on appropriate imaging and were confirmed using fine-needle aspiration. Unstimulated thy-

Table 2. Initial Treatment-Related Probability Estimates

Variable	Value (Range)[a]
Base variables	
Discount rate, convention	0.06 (0.03-0.06)
Cost-to-charge ratio	0.38 (0.258-0.5)[8]
Overall yearly mortality rate, all causes	0.001252 (0-0.01)[13]
Total thyroidectomy	
Unilateral true vocal cord paresis	0.0212 (0-0.1)[14-24]
Hematoma	0.0173 (0-0.1)[15,19,23,25,26]
Death after hematoma	0.002 (0-0.05)[7]
Permanent hypocalcemia	0.0187 (0-0.1)[14,15,17-23,27,28]
Temporary hypocalcemia	0.0781 (0-0.15)[14,19-21,23,28]
Tracheotomy	0.00127 (0-0.05)[16,19,20,29]
Tracheotomy plus hypocalcemia, estimate	0 (0-0.05)
Perioperative death	0.00121 (0-0.05)[4,16-20,27]
Hemithyroidectomy	
Unilateral true vocal cord paresis	0.00479 (0-0.1)[16-21,23,24,28,30]
Hematoma	0.0175 (0-0.1)[19,23,25,26,28]
Death after hematoma	0.002 (0-0.05)[7]
Permanent hypocalcemia	0.00685 (0-0.05)[14,15,17-19,21,23,27,28]
Temporary hypocalcemia	0.0482 (0-0.15)[15,19-21,23,28,30]
Tracheotomy	0 (0-0.05)[16,19,20,29]
Tracheotomy plus hypocalcemia, estimate	0 (0-0.05)
Perioperative death	0.00001 (0-0.05)[4,16-20,27]
Radioactive iodine therapy for recurrence	
Allergic reactions, estimate	0.001 (0-0.12)
Thyroiditis	0.0323 (0-0.1)[31]
Sialadenitis	0.065 (0-0.139)[32,33]
Neck dissection	
Chylous leak or fistula	0.0186 (0-0.2)[34-36]
Perioperative death	0 (0-0.05)[37]
Recurrence	
Local	0
After hemithyroidectomy	0.006476 (0-0.05)[17,18,38-41]
After total thyroidectomy	0.0009070 (0-0.05)[17,18,38-41]
Progression to regional recurrence, estimate	0.5 (0-0.5)
Progression to distant recurrence, estimate	0.05 (0-0.1)
Death	0.00256 (0-0.05)[1]
Successful treatment	0.25 (0-0.5)[12]
Regional	
After hemithyroidectomy	0.006561 (0-0.1)[17,18,38,39]
After total thyroidectomy	0.003242 (0-0.1)[17,18,38,39]
Progression to distant recurrence, estimate	0.25 (0-0.5)
Death	0.002 (0-0.05)[4]
Successful treatment	0.25 (0-0.33)[12]
Distant	
After hemithyroidectomy	0.001155 (0-0.05)[17,18,38,39]
After total thyroidectomy	0.000937 (0-0.05)[17,18,38,39]
Death	0.0288 (0-0.2)[4,42]
Successful treatment	0.25 (0-0.33)[12]

[a] Values are per-year rates. Ranges indicate those used in the sensitivity analysis.

roglobulin measurements were assumed to be performed during follow-up in the total thyroidectomy group.

We assumed that every patient had undergone a complete history and physical examination and adequate workup before each operation. We chose not to model the risks of late-onset radiation–induced second primary neoplasms after radioactive iodine treatment for recurrence because the numbers are too low and the types of cancers too heterogeneous to allow for accurate modeling.

RESULTS

LITERATURE REVIEW

We screened data from 940 abstracts and cited data from 31 relevant studies in our analyses (Table 2). The combined studies evaluated 14 920 patients. Of these, 8 studies (including 2795 patients) were evaluated for data on radioactive iodine treatment or neck dissections; the remainder were evaluated for data on thyroidectomy. Prevalence rates extracted from these studies are summarized in Table 2.

COST ESTIMATION

Costs were estimated based on Medicare reimbursement, calculated from data obtained from the Healthcare Cost and Utilization Project, and maintained by the US Department of Health and Human Services.[7] Hospital charges obtained from the Healthcare Cost and Utilization Project were converted to costs based on data obtained from the Medicare Provider Analysis and Review,[8] standardized by state (New York) and by diagnosis related group (group 290 [thyroid procedures]) for 2005, the last available year for which these data existed. Outpatient costs were determined based on Medicare reimbursement for each visit, test, or procedure obtained from public use files from the Centers for Medicare and Medicaid Services.[9] The estimated costs are summarized in Table 1.

DESIGN AND VALIDATION OF THE DECISION TREE

A 19-state state-transition (Markov) model was constructed comprehensively modeling surgical management outcomes of low-risk papillary thyroid carcinoma (Figure 1). Using follow-up protocols defined by the 2006 American Thyroid Association,[12] a deterministic decision tree was then constructed.

The published cause-specific mortality for patients with low-risk papillary thyroid carcinoma is approximately 1% to 2% at 20 years, regardless of initial operative intervention.[38,39,43] Our decision tree predicts a 20-year cause-specific survival of approximately 99% for patients undergoing hemithyroidectomy (99.5% in our model) and total thyroidectomy (99.2% in our model; published data, 98%-100%[38,39,43-45]).

COST-EFFECTIVENESS ANALYSIS

With 21 iterations of the Markov model (representing 20 years of follow-up), hemithyroidectomy yielded a cause-specific survival of 99.2%, and total thyroidectomy yielded a cause-specific survival of 99.5%. Attaining these survival rates required mean per-patient expenditures of $15 063.75 for hemithyroidectomy and

Table 3. Expected Costs, Effectiveness, and Incremental Cost-effectiveness Ratios (ICER) for 20-Year Overall Survival

Operative Procedure	Expected Cost, $	Incremental Cost, $	Expected Effect, %	Incremental Effect, %	Cost/Effect, $	ICER
Total thyroidectomy	13 910.00	NA	99.5	NA	13 979	NA
Hemithyroidectomy	15 063.75	1153.74	99.2	−0.296	15 184	Dominated[a]

Abbreviation: NA, not available.
[a]See the "Cost-effectiveness Analysis" subsection of the "Results" section.

Table 4. Expected Costs, Effectiveness, and Incremental Cost-effectiveness Ratios (ICER) for 20-Year Recurrence-Free Survival

Operative Procedure	Expected Cost, $	Incremental Cost, $	Expected Effect, %	Incremental Effect, %	Cost/Effect, $	ICER
Total thyroidectomy	13 910.00	NA	89.9	NA	15 464	NA
Hemithyroidectomy	15 063.75	1153.74	75.2	−14.7	20 005	Dominated[a]

Abbreviation: NA, not available.
[a]See the "Cost-effectiveness Analysis" subsection of the "Results" section.

Table 5. Results of a Monte Carlo Simulation of 100 000 Patients

Operative Procedure	Expected Cost, $	Incremental Cost, $	Expected Effect, %	Incremental Effect, %	Cost/Effect, $	ICER
Overall survival						
Total thyroidectomy	14 241.24	NA	99.5	NA	14 317	NA
Hemithyroidectomy	15 037.58	796.35	99.2	−0.249	15 155	Dominated[a]
Recurrence-free survival						
Total thyroidectomy	13 896.81	NA	90.0	NA	15 440	NA
Hemithyroidectomy	15 036.50	1139.69	75.5	−14.5	19 916	Dominated[a]

Abbreviations: ICER, incremental cost-effectiveness ratio; NA, not available.
[a]See the "Cost-effectiveness Analysis" subsection of the "Results" section.

$13 910.00 for total thyroidectomy (**Table 3**). For the same costs, hemithyroidectomy achieved a recurrence-free survival of 75.2% during 20 years, while total thyroidectomy achieved a recurrence-free survival of 89.9% (**Table 4**). In both instances, total thyroidectomy dominated over hemithyroidectomy as an initial treatment strategy for low-risk papillary thyroid carcinoma. Monte Carlo microsimulations were then performed, with 100 000 trials for each treatment strategy. The results were unchanged (**Table 5**).

WILLINGNESS TO PAY

Willingness-to-pay calculations were not explicitly performed in this cost-effectiveness analysis. However, a comparison of net monetary benefits obtained from total thyroidectomy and hemithyroidectomy using a variable range of willingness-to-pay values (**Figure 2**) reveals persistence of the dominance of total thyroidectomy over hemithyroidectomy.

SENSITIVITY ANALYSIS

To assess how dependent our results were on the value chosen for each variable, sensitivity and threshold analyses were performed on all variables in both decision trees within the limits summarized in Table 1 and Table 2. Both decision trees revealed identical threshold values for identical variables. These are given in **Table 6**. Our recommendation of total thyroidectomy as being most cost-effective is predominantly dependent on the rates of local, regional, and distant recurrences. Because of its substantial potential contribution to the overall cost, we varied the cost of death from $0 to $3 million. At no point in that range did hemithyroidectomy become more cost-effective.

Regarding the rates of recurrence, in most cases the rate of local, regional, or distant recurrence would have to increase or decrease drastically before hemithyroidectomy becomes the more cost-effective mode of treatment. However, there is notable variability in the literature regarding these particular values. As a result, the model was run using the data from each individual series alone. The most substantial differences in results were found in sensitivity analyses using outcome data from the Memorial Sloan-Kettering Cancer Center[39] and the Mayo Clinic.[38] The results of the model run using these institutional data are given in **Table 7**. For patients at the Mayo Clinic, total thyroidectomy was found to dominate the decision analysis. For patients at the Memorial

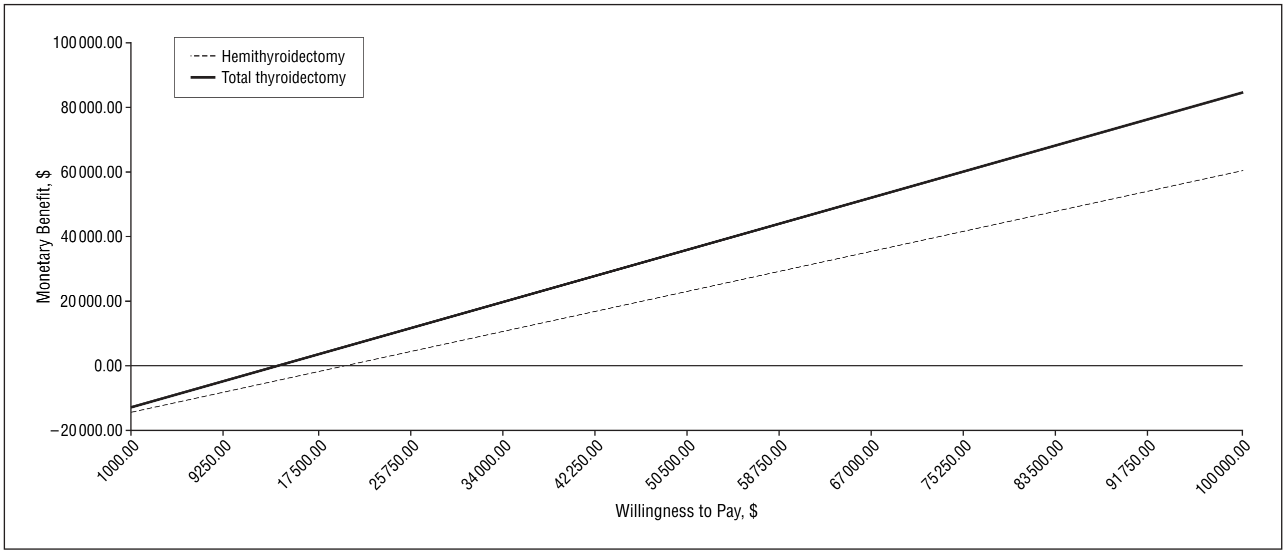

Figure 2. Net monetary benefits vs willingness to pay for the overall decision tree. Across all willingness-to-pay values, net monetary benefits are maximized by total thyroidectomy.

Table 6. Thresholds of Sensitivity[a]

Variable	Original Value, %	Threshold Value, %	% Difference
Death after total thyroidectomy	0.121	0.247	204
Death from DR	2.88	1.08	38
LR after total thyroidectomy	1.80	6.69	372
RR after total thyroidectomy	6.28	10.93	174
DR after total thyroidectomy	1.86	4.61	248
LR after hemithyroidectomy	12.15	8.16	67
RR after hemithyroidectomy	12.30	10.45	85
Cost of hemithyroidectomy, $	5685	4688	82
Cost of follow-up after total thyroidectomy, $	201.56	319.84	159
Tracheotomy after total thyroidectomy	0.127	4.1	3235
Tracheotomy plus hypocalcemia after total thyroidectomy	0	3.9	. . .

Abbreviations: DR, distant recurrence; LR, local recurrence; RR, regional recurrence; ellipsis, not applicable.

[a] See the "Cost-effectiveness Analysis" subsection of the "Results" section.

Sloan-Kettering Cancer Center, although total thyroidectomy was associated with better recurrence-free survival, it cost $3391 more during 20 years for each recurrence-free patient than hemithyroidectomy. Willingness to pay was analyzed against net monetary benefit for patients at the Memorial Sloan-Kettering Cancer Center. Total thyroidectomy was still found to deliver the greatest net monetary benefit over a range of willingness-to-pay values (data not shown).

COMMENT

Disagreement over the most appropriate initial surgical management for low-risk papillary thyroid carcinoma has persisted for decades. Initial radical surgical treatment (including, in rare cases, disfiguring total laryngectomies and radical external-beam radiation therapy[46]) has given way to increasingly conservative management. Controversies now focus on postoperative adjuvant radiotherapy, the necessity for routine dissection of the central neck, and the extent of initial surgical therapy. It is this latter controversy we sought to address in this study concerning the extent of initial surgical therapy.

In the current cost-saving milieu in which medicine is practiced, cost-effectiveness analyses are important, and the question of the most appropriate modality for the initial treatment of low-risk papillary thyroid carcinoma is ideal for this sort of analysis. Therefore, we set out to construct a mathematical model to determine, during 2 decades, whether total thyroidectomy represents the most cost-effective treatment modality for low-risk papillary thyroid carcinoma.

Initial comparisons of the 2 treatment modalities reveal that hemithyroidectomy is equivalent to total thyroidectomy in long-term cause-specific mortality, a fact that validates our model with respect to the published literature.[38,39,43-45] Because of the need for secondary operative procedures in these patients, the long-term cost of hemithyroidectomy is greater than that of total thyroidectomy. This is true despite the greater initial cost of total thyroidectomy and its subsequent follow-up. In addition, local and regional recurrence rates are lower in patients who undergo total thyroidectomy. As a result, total thyroidectomy dominates the calculations as a less costly and more effective initial surgical option and may be recommended as a first-line therapeutic procedure for low-risk papillary thyroid carcinoma. For each patient, there is a $300 to $3000 added cost associated with more conservative initial surgical management. Approximately 24 000 new cases of thyroid cancer were diagnosed in 2002, most of which were low-risk papillary carcinoma,[42] allowing almost $2 million annual cost savings for initial management of total thyroidectomy.

However, the definition of recurrence is important. Biologically, papillary thyroid carcinoma is a multifocal disease.[47] In terms of biologic outcome, recurrence in the

Table 7. Institution-Specific Recurrence-Free Survival Costs, Effectiveness, and Incremental Cost-effectiveness Ratios (ICER)

Operative Procedure	Expected Cost, $	Incremental Cost, $	Expected Effect, %	Incremental Effect, %	Cost/Effect, $	ICER
Mayo Clinic[38]						
Total thyroidectomy	13 951.75	NA	89.9	NA	15 521	NA
Hemithyroidectomy	17 653.90	3702.14	68.3	–21.6	25 854	Dominated[a]
Memorial Sloan-Kettering Cancer Center[39]						
Hemithyroidectomy	12 826.74	NA	82.3	NA	15 580	NA
Total thyroidectomy	13 155.78	329.04	92.0	9.7	14 259	3391

Abbreviation: NA, not available.
[a]See the "Cost-effectiveness Analysis" subsection of the "Results" section.

contralateral undissected lobe in a patient who has undergone hemithyroidectomy may not be of true significance. However, patients with local and regional recurrences, despite having no notable difference in their overall survival,[38,39,43,44] must undergo more operative procedures, thereby increasing their risk of complications and increasing the cost burden to the health care system. With reference to this burden, we compared the net monetary benefits obtained from total thyroidectomy vs hemithyroidectomy across a range of possible willingness-to-pay values. Across this range, as shown in Figure 2, total thyroidectomy continues to deliver more net monetary benefit than hemithyroidectomy.

In these calculations, we did not look specifically at satisfaction or quality-of-life considerations, which have been reported previously.[1,3] It deserves mention that patients judge a second operation as less desirable than living without a thyroid and recurrence as less desirable than most thyroidectomy complications (except tracheotomy).[3] In addition, patients treated with total thyroidectomy do not seem to have a notably different quality of life than patients treated with hemithyroidectomy.[48]

To perform this study, we were required to estimate costs and probabilities from the best available data in the literature. This introduces some heterogeneity into our model. For this reason, sensitivity and threshold analyses were performed on every variable. Although 11 variables seemed to affect our calculations, in most cases this effect occurs only at thresholds drastically different from values quoted in the literature. For example, although the initial cost of hemithyroidectomy influences our overall conclusions, the threshold cost at which hemithyroidectomy becomes more cost-effective falls outside the range of error reported for the cost incurred for thyroid procedures in the United States in 2004.[7]

The sensitivity of our results to recurrence rates deserves further exploration. The literature is replete with various estimates by retrospective analysis of recurrence rates for patients with low-risk papillary thyroid carcinoma. Many simply quote an overall recurrence rate.[49-51] We limited our model to the few studies that divide this into local, regional, and distant recurrences. Of those that do, there is substantial variability in conclusions. We observed important heterogeneity among institutions, particularly the Mayo Clinic and the Memorial Sloan-Kettering Cancer Center, in treatment outcomes comparing total thyroidectomy with hemithyroidectomy.

The dominance of total thyroidectomy over hemithyroidectomy persists in the published Mayo Clinic[38] data but does not when the published Memorial Sloan-Kettering Cancer Center[39] data are substituted into the model. In the Memorial Sloan-Kettering Cancer Center analysis, total thyroidectomy portends a greater chance of recurrence-free survival but does so at a greater cost. These institutional differences in treatment outcomes may reflect differences in the definition of recurrence or differences in populations, follow-up strategies, and local expertise.

Two other decision analyses have been conducted surrounding this question. Both attempted to answer the question from a quality-adjusted life-year or utility standpoint, and both came to the conclusion that total thyroidectomy represents the best treatment paradigm. The first analysis, by Kebebew et al,[3] is a single-iteration decision analysis without long-term modeling. In that study, patients are categorized as having a complicated or an uncomplicated operation, without reference to the type of complication or modeling of temporary complications. In the second analysis, by Esnaola et al,[1] a Markov model is constructed for low-risk and high-risk patients. Recurrences are categorized as local and distant, but sensitivity analysis is not performed on these recurrence variables. In addition, complications are not well examined. Therefore, the present model represents the first attempt to answer this question from a purely economic standpoint, iterated during 20 years, using a comprehensive mathematical model of medical and surgical complications, recurrence, and cause of death.

Two rates are assumed constant that likely are not. We assumed that the rates of recurrence and death from unrelated causes remained constant during 20 years. This is likely an oversimplification: most recurrences are known to occur within the first 5 years of treatment.[40] The economic effect of late recurrences is subject to decades of discounting. That said, because recurrence most likely occurs after hemithyroidectomy, front-loading the recurrences would likely further establish total thyroidectomy as dominant over hemithyroidectomy.

In our analysis, radioactive iodine was not originally included in the up-front costs of total thyroidectomy. This decision was made because the initial use of radioiodine ablation in low-risk papillary thyroid carcinoma is controversial and its effect on long-term outcome is uncertain.[12,52] In addition, the use of recombinant human thyrotropin is new, and its cost-effectiveness is still debated.[53,54] Therefore, it was left out of the model. The current Medicare reimbursement for a single 0.9-mg injection of thyrotropin is \$765.38.[9] It is possible that the routine administration of adjuvant radioactive iodine and the use of these sensitive follow-up strategies would cross the threshold of sensitivity, at which point hemithyroidectomy would become the preferred treatment modality.

In addition to these assumptions, there are weaknesses of this study that must be mentioned. Our probabilities are estimated from a review of the literature and a combined analysis of the data contained in 31 studies. These studies are heterogeneous and contribute substantial variability to our data. In addition, as much as possible, the type of operation performed was standardized. This was difficult given the lack of a consistent objective definition of the amount of remnant tissue left. Prospective studies evaluating recurrence rates against postoperative radioiodine uptake would obviate this difficulty. Finally, as is the case with any cost-effectiveness analysis, the costs assumed in our analysis can be expected to vary among institutions and regions.

CONCLUSIONS

For a patient with low-risk papillary thyroid carcinoma, total thyroidectomy likely represents the most cost-effective initial surgical management, although this may be institution dependent. This recommendation is sensitive to rates of recurrence but remains robust compared with willingness-to-pay calculations. The routine use of recombinant human thyrotropin may alter recommendations in favor of hemithyroidectomy. Prospective clinical studies are warranted to validate these findings.

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