Total Thyroidectomy *Versus* Lobectomy for the Treatment of Follicular Thyroid Microcarcinoma

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Abstract. *Aim: To compare the effectiveness of total thyroidectomy versus thyroid lobectomy for the treatment of follicular thyroid microcarcinoma. Patients and Methods: Data were extracted from the Surveillance, Epidemiology, and End Results 18 Database. The study cohort included patients diagnosed with follicular thyroid microcarcinoma between 1988 and 2009, treated with either total thyroidectomy or thyroid lobectomy. Propensity-score analysis using inverse probability weighting was used to control for allocation bias. Results: A total of 203 patients were identified. The 5-year overall survival was 98% for patients treated with lobectomy and 99% for those treated with total thyroidectomy; this difference was not statistically significant (p=0.13). Unadjusted analysis and propensity-score analysis revealed no difference in overall survival between the two treatment groups (p=0.15 and p=0.49, respectively). Conclusion: Total thyroidectomy does not appear to offer any survival advantage over thyroid lobectomy for patients with follicular thyroid microcarcinoma.*

The incidence of thyroid microcarcinoma is rising (1). The management of thyroid microcarcinoma detected on thyroid lobectomy is controversial. Some surgeons advocate total thyroidectomy, while others prefer observation of the contralateral lobe. The most recent American Thyroid Association guidelines recognize thyroid lobectomy as sufficient treatment for thyroid microcarcinoma. However, their recommendations are mostly based on studies of papillary thyroid cancer (2).

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Several studies have shown no difference in survival outcome for the two treatment approaches for papillary microcarcinoma (PTMC). Lin and Bhattacharyya found no difference in overall survival between patients treated with total thyroidectomy, near-total/subtotal thyroidectomy, or lobectomy in their analysis of 7,818 patients with PTMC from the Surveillance, Epidemiology, and End Results (SEER) database (3). Another SEER database analysis also found no difference in disease-specific survival between patients undergoing total thyroidectomy and thyroid lobectomy (4). These findings are also supported by retrospective studies from other countries (5, 6).

Kuo *et al*. performed a limited analysis of total thyroidectomy *versus* lobectomy for patients with follicular or hurthle cell microcarcinoma, in their study comparing the characteristics and outcomes of PTMC *versus* follicular or hurthle cell microcarcinoma (7). They found no difference in disease-specific survival between the two treatment groups. However, their study had several limitations and did not specifically compare the effectiveness of total thyroidectomy *versus* lobectomy for the management of follicular thyroid microcarcinoma (FTMC). The goal of this study was to evaluate survival outcomes of total thyroidectomy *versus* thyroid lobectomy in the treatment of FTMC using a large population-based cancer database.

Patients and Methods

This was a non-concurrent cohort study. Data were extracted from the Surveillance, Epidemiology, and End Results (SEER) 18 Database of the National Cancer Institute, which includes data obtained from 18 population-based registries (8). The SEER program collects information on all new cases of cancer from 18 population-based cancer registries covering approximately 28% of the US population (9).

The study cohort included patients diagnosed with follicular thyroid carcinoma between 1988 and 2009 with tumor size of 1 cm or less. The following International Classification of Diseases for Oncology (ICD-O) code was used: C73.9 for thyroid gland (10).

Table I. *Patients' characteristics*.

Variable	Overall (N=203)	Procedure		*p*-Value
		Total thyroidectomy (N=145)	Lobectomy (N=58)	
Multifocal tumor	9 (4.4%)	6 (4.1%)	3 (5.2%)	0.72
Female gender	165 (81.3%)	119 (82.1%)	46 (79.3%)	0.65
Mean age, years	48.7	47.8	51	0.17
Race				0.39
Black	14 (6.9%)	9 (6.2%)	5 (8.6%)	
Other	16 (7.9%)	12 (8.3%)	4 (6.9%)	

Exclusion criteria included regional or distant metastasis, and multiple primary tumors.

The SEER computer software (SEER*Stat 8.1.5) was used to extract data from the SEER database. SAS University Edition version 9.4 (SAS Institute, Cary, NC, USA) was used for statistical analysis. Pearson Chi square test was used to evaluate the proportion of patients treated with total thyroidectomy. Unadjusted survival analysis was performed using Cox proportional-hazards regression model. The primary outcome measure was overall survival. The primary independent variable was the mode of therapy (total thyroidectomy *versus* thyroid lobectomy). Propensity-score analysis was performed to control for allocation bias. Propensity-score methods allow control of systematic differences in the distribution of measured baseline characteristics of study patients (11, 12). Logistic regression was used to build a model predicting total thyroidectomy (*vs*. hemithyroidectomy), including information on patient's age, sex, race, marital status, cancer characteristics (multifocal *vs*. unifocal), and the US state associated with the cancer registry from which patient data were extracted. Interactions between predictor variables were also included in the model. The discrimination of the model was assessed using the c-statistic (goal: c-statistic >0.75-0.90). Once the final model was developed, the overlap in propensity scores was assessed among patients treated with total thyroidectomy *versus* hemithyroidectomy to ensure that the distribution of covariates was similar across groups once adjusting for propensity scores. The comparative efficacy of total thyroidectomy *versus* hemithyroidectomy was assessed by Cox regression using inverse-probability weighting (by the inverse of the probability of treatment received). *p*-Values of less than 0.05 were considered statistically significant. This study was exempt from the Icahn School of Medicine at Mount Sinai Institutional Review Board review because it was conducted using de-identified public data.

Results

From 1988 to 2009, the SEER database identified a total of 203 patients meeting the inclusion criteria. The patient characteristics compared between the two treatment groups are displayed in Table I. Patient ages ranged from 14 to 84 years. Nine patients had multifocal disease. None of the patients had extrathyroidal extension. Seventy-one percent of patients were treated with total thyroidectomy.

Kaplan–Meier survival curves are displayed in Figure 1. The 5-year overall survival rates were 98% for patients treated with lobectomy and 99% for those treated with total thyroidectomy; this difference was not statistically significant (p=0.13). The results of the survival analysis are shown in Table II. Three patients were excluded from the propensity-score analysis due to missing data. Unadjusted analysis revealed no difference in overall survival between patients treated with total thyroidectomy and those treated with thyroid lobectomy alone (p=0.15). Propensity-score analysis also revealed no difference in overall survival between the two groups (p=0.49).

Discussion

The results of our study showed that total thyroidectomy does not confer additional survival advantage over thyroid lobectomy in the treatment of follicular microcarcinoma of the thyroid. This finding remains true even after adjusting for allocation bias. The management of FTMC remains controversial. There is a lack of studies adequately comparing the effectiveness of thyroid lobectomy compared to total thyroidectomy for FTMC. Therefore, the need for completion thyroidectomy in patients discovered to have FTMC after lobectomy is unclear. Several studies have shown no difference in survival outcomes for the two treatment approaches for PTMC (3-6). However, FTMC appears to behave differently from PTMC. Kuo *et al*. compared the characteristics and outcomes of PTMC *versus* follicular or hurthle cell microcarcinoma (7). They found that patients with follicular or hurthle cell microcarcinoma were more likely to have distant metastasis. Moreover, patients with follicular or hurthle cell microcarcinoma had poorer disease-specific survival compared to patients with PTMC. No difference in disease-specific survival was observed between patients with hurthle cell microcarcinoma and those with follicular microcarcinoma. Similar to our study, a subset analysis of patients with follicular or hurthle cell microcarcinoma revealed no difference in disease-specific survival between patients treated with thyroid lobectomy and those treated with total thyroidectomy. However, it is unclear if this analysis

Table II. *Overall survival of patients treated with total thyroidectomy vs. patients treated with lobectomy.*

Method	Coefficient (SE)	Wald χ^2	Hazard ratio	95% CI	*p*-Value
Unadjusted analysis: Lobectomy	0.98 (0.67)	2.12	2.66	0.71-9.93	0.15
Propensity-score analysis: Lobectomy	0.40 (0.59)	0.47	1.5	0.47-4.75	0.49

SE: Standard error; CI: confidence interval.

excluded patients with nodal or distant metastasis, and no separate analysis was performed for FTMC. Furthermore, allocation bias was not controlled for using multivariable or propensity-score methods for this subset analysis.

The findings of this study are similar to studies on PTMC. Lin and Bhattacharyya examined the effect of extent of thyroidectomy on survival in 7,818 patients with PTMC, using the SEER database (3). They found no difference in overall survival between patients treated with total thyroidectomy, near-total/subtotal thyroidectomy, or lobectomy. Similarly, Wang *et al*. found no difference in disease-specific survival between patients undergoing total thyroidectomy and thyroid lobectomy in their SEER cohort. However, patients who did not undergo any surgery had worse disease-specific survival (4).

A recent retrospective study reported on the outcomes of 2,014 patients treated for PTMC between March 1986 and December 2006 at a hospital in Korea (5). Patients were either treated with total thyroidectomy with central neck dissection, or thyroid lobectomy with central neck dissection. Propensity-score matching was used to control for allocation bias. There was no difference in the risk of death and locoregional recurrence between those treated with thyroid lobectomy and those treated with total thyroidectomy. Another retrospective study compared outcomes in patients undergoing hemithyroidectomy *versus* lobectomy for treatment of PTMC (6). The study included 293 patients from two medical centers in Israel with a mean follow-up of 7.2 years. Patients with lymph node metastasis and extraglandular extension were more likely to undergo total thyroidectomy. The incidence of recurrence was nearly identical in the two groups, 13.2% in the total thyroidectomy group and 14.3% in the lobectomy group.

Patients with regional and distant metastasis were excluded from our study. One potential disadvantage of thyroid lobectomy is the impaired ability to detect distant metastasis. Follicular thyroid carcinoma carries a significant risk of distant metastasis. Moreover, patients with FTMC are more likely to have distant metastasis than their counterparts with PTMC papillary (7). Distant metastasis is usually identified based on persistently elevated serum thyroglobulin levels and positive findings on whole-body thyroid scan. The

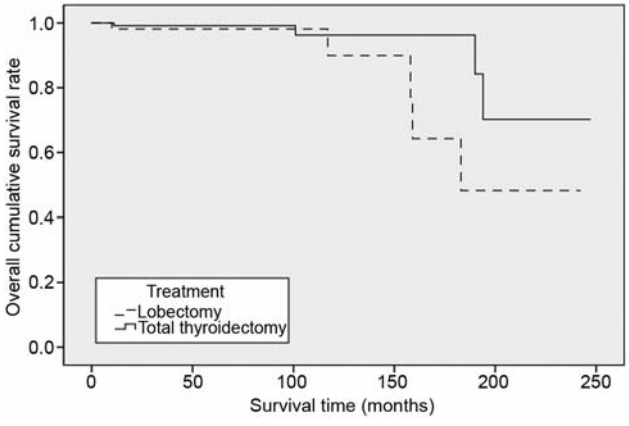

Figure 1. *Overall survival for patients based on therapy.*

presence of a functioning thyroid lobe would preclude the use of these surveillance tools. Therefore it may be prudent to rule out distant metastasis with other imaging modalities in patients who choose to undergo only thyroid lobectomy for the treatment of FTMC.

The main strength of this study lies in the quality of data in the SEER database. Utilizing the SEER database allows analysis of a large and diverse population with outstanding quality control. The catchment areas used in the SEER database were selected for their ability to maintain a high-quality cancer reporting system and for demographic characteristics that are representative of the US population as a whole. In this study, patients with regional and distant metastasis were excluded because these patients usually require radioactive iodine therapy, which would necessitate total thyroidectomy. This study has several limitations. The SEER database does not include information on disease recurrence, therefore, differences in recurrence rates cannot be examined. This study is also limited by the retrospective nature of the analysis, although the data were collected prospectively using high-quality cancer registries. However, allocation bias was controlled for using propensity-score analysis with inverse-probability weighting. Propensity-score methods allow control of systematic differences in the

distribution of measured baseline characteristics of study patients (11-12). Furthermore, propensity score analysis using inverse-probability weighting allows effective control of allocation bias without sacrificing statistical power.

This study may lack the statistical power to detect small differences in survival. Power in survival analysis is a function of the actual number of deaths observed in the treatment arms. Given that the mortality rate was extremely low in both treatment groups, this could have led to low statistical power. However, any difference in survival is unlikely to be clinically significant given the very high survival rates in both groups.

In conclusion, total thyroidectomy does not appear to offer any survival advantage over thyroid lobectomy for patients with FTMC. However, caution should be exercised in treating patients solely with lobectomy, given the increased risk of distant metastasis in follicular thyroid cancer. Serum thyroglobulin levels and whole-body thyroid scan cannot be used for surveillance in these patients, therefore other imaging studies should be used to evaluate for distant metastasis.

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