Surgical Treatment of Cervical Nodal Metastases in Patients With Papillary Thyroid Carcinoma

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Objective: To determine if more extensive neck dissection in patients with papillary carcinoma of the thyroid affords a survival benefit vs limited lymphadenectomy of positive nodal disease.

Design: Survey analysis of a national cancer database.

Methods: Cases of papillary thyroid carcinoma were extracted from the Surveillance, Epidemiology, and End Results database for January 1, 1988, to December 31, 1999, along with demographic, staging, and treatment variables. Cases were limited to patients who underwent total thyroidectomy and postoperative radioactive iodine treatment along with excision of 1 or more positive cervical nodes. Patients were divided into 2 groups: those undergoing limited lymphadenectomy of only positive nodes and those undergoing more extensive neck dissection with removal of positive and negative nodes.

Results: Among 2097 patients with papillary carcinoma meeting treatment criteria, 880 underwent limited lymphadenectomy and 1217 underwent neck dissection. The mean age, sex distribution, primary tumor extent and size, and follow-up duration were not different between these 2 groups (\(P > .05\) for all). The mean survival for patients undergoing limited lymphadenectomy was 135 months, vs 136 months for patients undergoing neck dissection. Actuarial 5-year (10-year) survival rates were 94.4% (91.3%) and 95.9% (92.4%), respectively. Kaplan-Meier survival was not different between groups (\(P = .40\), log-rank test).

Conclusions: Limited lymphadenectomy of positive nodal disease in patients with papillary carcinoma affords survival similar to that of patients undergoing more extensive neck dissections. Therefore, a formal neck dissection may not be required for the effective treatment of cervical nodal metastases in patients with papillary carcinoma of the thyroid.

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Papillary carcinoma of the thyroid gland is one of the most commonly encountered endocrine malignancies. Among the different malignant tumor histological conditions encountered within the thyroid gland, papillary carcinoma is not only the most common but it is also the most likely tumor type to manifest cervical nodal metastasis. In general, survival for patients with papillary thyroid carcinoma is believed to be relatively good, especially when compared with that of patients with other thyroid and nonthyroid malignancies. However, not all patients with papillary carcinoma of the thyroid fare well, and one of the major challenges is to identify patients with poor prognoses to offer more aggressive and efficacious treatment.

One element of controversy in the treatment of papillary thyroid carcinoma concerns treatment of the pathologically positive neck. In the pathologically positive setting, there is general consensus that in experienced hands, total thyroidec- tomy followed by postoperative radioactive iodine is the treatment of choice for primary site disease. While most investigators would agree that formal neck dissection is unnecessary in the N0 neck, for pathologically positive disease, some researchers recommend formal neck dissection, while others recommend removal of gross positive disease without more extensive dissection of the neck. The present study was conducted to determine if simple removal of positive nodal disease from the neck offered the same survival as formal neck dissection in cases of node-positive papillary carcinoma of the thyroid.
Table 1. Classification of Primary Site Extent of Disease for Differentiated/Thyroid/Carcinoma

<table>
<thead>
<tr>
<th>Degree of Local Extension</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrathyroidal</td>
<td>Tumor does not extend outside the capsule of the thyroid gland and may be multifocal within the gland</td>
</tr>
<tr>
<td>Minor</td>
<td>Tumor invades the soft/connective tissue of the thyroid gland, parathyroid glands, strap musculature, or recurrent laryngeal nerve</td>
</tr>
<tr>
<td>Major</td>
<td>Tumor extends into the carotid sheath, sternocleidomastoid muscle, esophagus, or thyroid/cricoid cartilages</td>
</tr>
<tr>
<td>Extravisceral</td>
<td>Tumor invades the trachea, paraspinal musculature, or vertebral bone</td>
</tr>
</tbody>
</table>

*Data from Bhattacharyya.*

Table 2. Comparison of Clinical Variables Between the Limited Lymphadenectomy and the Neck Dissection Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Limited Lymphadenectomy Group</th>
<th>Neck Dissection Group</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean, y</td>
<td>41.5</td>
<td>40.7</td>
<td>.26†</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>68.0</td>
<td>70.5</td>
<td>.21‡</td>
</tr>
<tr>
<td>Male</td>
<td>32.0</td>
<td>29.5</td>
<td></td>
</tr>
<tr>
<td>Tumor size, mean, cm</td>
<td>2.3</td>
<td>2.3</td>
<td>.48†</td>
</tr>
<tr>
<td>Degree of local extension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrathyroidal</td>
<td>68.1</td>
<td>66.2</td>
<td></td>
</tr>
<tr>
<td>Minor</td>
<td>23.8</td>
<td>23.9</td>
<td>.60‡</td>
</tr>
<tr>
<td>Major</td>
<td>3.1</td>
<td>3.8</td>
<td></td>
</tr>
<tr>
<td>Extravisceral</td>
<td>5.1</td>
<td>6.1</td>
<td></td>
</tr>
<tr>
<td>Follow-up, mean, mo</td>
<td>53.6</td>
<td>52.4</td>
<td>.49†</td>
</tr>
</tbody>
</table>

*Data are given as percentage of patients in each group unless otherwise indicated. Percentages may not total 100 because of rounding.†T Test.‡χ² Test.

December 31, 1999, was examined. All cases of papillary carcinoma of the thyroid for January 1, 1988, to December 31, 1999, were extracted and imported into SPSS, version 10.0 (SPSS Inc., Chicago, Ill). From the extent of disease information, disease at the primary (thyroid) site was subclassified as previously reported (Table 1). Patients with distant metastatic disease or unknown local extension were excluded from subsequent analysis. Only patients for whom at least 1 pathologically positive node was identified were included in the subsequent analysis. To ensure homogeneity of treatment, the database was further restricted to patients who underwent total thyroidectomy as the primary surgical procedure along with postoperative radioactive iodine treatment.

Patients were then divided into 2 groups, based on treatment of the positive nodal disease in the neck. The first group consisted of patients who underwent removal of only pathologically positive nodes and in whom no benign nodes were excised (limited lymphadenectomy group). The second group consisted of those patients who underwent neck dissection (neck dissection group). Patients in whom more total nodes were harvested than were pathologically positive were considered to have undergone “neck dissection.” Kaplan-Meier survival analysis was then conducted to determine overall survival differences between these 2 groups based on treatment of the neck. Comparisons for age, sex, primary tumor size, and degree of local extension were also conducted to check for potential differences between these 2 groups that might affect treatment of the neck and overall survival.

A total of 2097 cases of papillary carcinoma with pathologically positive cervical node metastasis were identified for the period under consideration. The mean age at diagnosis was 41.0 years, with a female-male ratio of 2.3:1. Of these cases, 880 patients underwent limited lymphadenectomy of positive nodal disease and 1217 underwent more formal neck dissection. For patients undergoing limited lymphadenectomy, the average number of positive nodes was 2.6. For patients undergoing neck dissection, an average of 5.3 positive nodes were recovered from an average of 14.0 total nodes sampled.

There was no significant (P = .40) survival benefit for patients undergoing more formal neck dissection vs those undergoing limited lymphadenectomy, as indicated in the Figure. The 5- and 10-year actuarial survival rates were 94.4% and 91.3% for limited lymphadenectomy and 95.9% and 92.4% for neck dissection, respectively. The Kaplan-Meier survival was 135 months for the limited lymphadenectomy group vs 136 months for the neck dissection group (P = .40, log-rank test). The remaining results of the statistical analysis are displayed in Table 2. There was no difference between the 2 groups with respect to age at diagnosis, sex distribution, extent of disease at the thyroid primary site, or follow-up duration. As indicated by the selection criteria, both groups were equally treated with total thyroidectomy and postoperative radioactive iodine treatment. Because the 2 matched groups differed in the mean number of positive nodes recovered, a Cox proportional hazards regression analysis was conducted with type of lymphadenectomy and mean number of positive nodes as covariates to ensure that differences in the mean number of positive nodes did not affect survival. The results of the Cox proportional hazards regression analysis indicated that neither type of lymphadenectomy nor number of positive nodes statistically in-
fluenced survival (P = .41 and P = .93 for group and number of positive nodes, respectively).

**COMMENT**

Papillary carcinoma is the most common malignancy of the thyroid gland and is among the most common malignancies experienced in the middle decades of life.\(^1\) Although survival for papillary carcinoma is generally good, a small subset of patients will fare poorly.\(^8\) As a result, identifying individuals who possess a poor prognosis is a central problem with papillary carcinoma. To determine survival differences for various factors, large sample sizes with lengthy follow-up periods are required.\(^9\)

Among thyroid malignancies, papillary carcinoma easily carries the highest risk of cervical metastasis, ranging from 15% to 40% in the literature.\(^10\) Despite this tendency, it also carries the best individual prognosis among the various types of thyroid carcinomas. Overall survival rates for those with papillary carcinoma range from 92% to 95% at 5 years and from 89% to 90% at 10 years.\(^11-14\) With such excellent overall survival rates, determining the effect of cervical nodal metastasis on survival in patients with papillary carcinoma is naturally difficult.

Several studies\(^7\) have documented that cervical node metastasis in patients with papillary carcinoma does not necessarily adversely affect overall survival. However, many of the studies have been completely retrospective and have not stratified patients according to various risk groups. A handful of other studies\(^10\) have suggested that nodal metastases affect locoregional recurrence and may affect long-term overall survival. I recently showed in a large-scale multivariate analysis\(^8\) that nodal metastasis in patients with papillary carcinoma does not statistically significantly influence survival. Therefore, the absence of a survival influence for cervical nodal metastasis immediately questions the true therapeutic benefit of more extensive neck dissections in the treatment of a pathologically positive node in papillary carcinoma. In the pathologically positive neck setting, some researchers have advocated comprehensive or modified radical neck dissections, whereas others have advocated central compartment and lateral selective neck dissections; still others recommend simple removal of grossly positive node disease.\(^4\) An analysis of the literature is further hampered by the fact that in many of the series, inconsistencies are present with respect to completeness of thyroidectomy and the use of postoperative radioactive iodine.

The patient population for the present study was homogeneously treated with total thyroidectomy and postoperative radioactive iodine to eliminate potential variability among treatment groups. In addition, the 2 treatment groups were further examined to determine if other known prognostic factors, such as age, sex, degree of local extension, and tumor size, were different among them. Such differences would naturally affect overall survival, as indicated by previous risk stratification studies\(^5\) for thyroid carcinoma. We found no differences between groups for these risk stratification variables, reducing such potential biases on prognosis.

Several different types of neck dissection have been proposed for papillary thyroid carcinoma. Most commonly, central compartment neck dissection is performed with or without lateral compartment dissection.\(^1\) I previously showed that functional neck dissections recover approximately 16 nodes per side dissected and supraomohyoid neck dissections recover approximately 10 nodes per side dissected.\(^13\) In the current sample, the mean number of nodes recovered for the neck dissection group falls within this range, suggesting that these patients did undergo a true neck dissection. Other investigators\(^16\) have attempted to determine which patients will or will not benefit from cervical node dissection, making a cogent argument for modified neck dissections in patients with cervical node involvement and features such as female sex, age older than 60 years, and significant extrathyroidal extension. Neck dissection likely still has a role for selected patients with papillary thyroid carcinoma and cervical metastasis. Formal neck dissection should be considered in patients with extremely bulky disease and in patients with disease involving the carotid artery or jugular vein.\(^16\)

Limiting the extent of neck dissection in patients with papillary thyroid carcinoma will likely decrease morbidity. For example, the addition of a formal neck dissection to total thyroidectomy in patients with papillary carcinoma may increase the risk of postoperative hypocalcemia, although this has been debated.\(^17,18\) In addition, neck dissection also carries with it risks to the spinal accessory nerve, thoracic duct, and other vital cervical structures. Finally, formal neck dissection consumes additional operative time and medical resources. In the absence of a survival benefit, potential morbidities and medical economics argue against the relative value of the routine use of formal or comprehensive neck dissection in this setting.

The SEER database is a nationally maintained governmental database.\(^5\) This database is extraordinarily well maintained and has been used to study several different head and neck malignancies, such as salivary gland carcinoma, nasal cavity cancer, thyroid carcinoma, and squamous cell carcinoma of the upper aerodigestive tract.\(^14,19-21\) The SEER database overcomes many of the problems associated with performing a long-term study for a relatively indolent malignancy such as papillary thyroid carcinoma. One of the major advantages of the SEER database is that it includes a sampling from several different regions of the United States. Therefore, regional treatment biases tend to be minimized. Such biases have been implicated in the management of differentiated thyroid carcinoma and as such may affect the reporting of treatment results.\(^1\) However, an analysis of such a large independently maintained database also has its limitations. First, the SEER database only affords examination of overall survival, and local or regional control cannot be assessed. For thyroid carcinoma, locoregional control may not be as important, because previous studies\(^22\) have shown that mortality in patients with thyroid carcinoma is most commonly secondary to distant metastasis rather than locally advanced disease. Second, we cannot comment on the exact nature of the neck dissections performed in this population. Beginning with cases coded in 1998, the SEER database adopted more standard classification of neck dissections based on American Acad-
emy of Otolaryngology terminology; before 1998, more accurate classification of the type of neck dissection is problematic for the purpose of variable analysis.

In conclusion, the presence of cervical nodal metastasis in patients with papillary carcinoma likely has a limited effect on overall survival. When practical and feasible, simple removal of grossly positive nodal disease is likely to offer an equivalent survival vs more formal neck dissection and may spare patients unnecessary morbidity.

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REFERENCES