Extent of Initial Surgery for Differentiated Thyroid Cancer (DTC)

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Introduction

It is essential to understand the biology of differentiated thyroid cancer (DTC) to make decisions based on prognostic factors and risk-group analysis. Various clinical and pathological prognostic factors for thyroid cancer have been reported around the world which includes age, grade of tumor, extrathyroid extension, size of tumor histological features, and distant metastasis. Based on prognostic factors, patients can be divided into low-risk (i.e., young patients with favorable prognostic factors) or high-risk (older patients with unfavorable prognostic factors). Another category of intermediate risk is added which includes patients less than 45 years but with unfavorable prognostic factors and patients more than 45 years with favorable prognostic factors [1]. On the basis of these risk-group analysis, survival in patients with DTC is 99% in low risk groups, 87% in intermediate groups and 57% in high-risk groups [2].

The ideal extent of surgery for DTC remains controversial despite numerous retrospective studies. The main reason for ongoing controversy is the fact that a randomized, prospective trial comparing extent of surgery is almost impossible to perform, given the low mortality rate in thyroid cancer. Optimal thyroidectomy is one of the four cornerstones of thyroid cancer management, others being remnant radio-iodine ablation (RAI), thyroxine suppression and surveillance. Optimal thyroidectomy could be either total thyroidectomy or various hemithyroidectomies. The evidence in favor of either of these procedures will be based on the risk of complications, rate of loco-regional recurrence and cause specific mortality.

Evidence in Favour of Hemithyroidectomy

a) Proponents of lesser procedures put forth the argument that most low risk cancers have an excellent prognosis irrespective of the extent of primary operation. Several studies have shown no difference in survival or recurrence in papillary thyroid cancer (PTC) based on the extent of resection. Shaha and colleagues [3] performed a retrospective survival analysis on 1,038 low-risk patients with low-risk differentiated thyroid cancers, defined by age less than 45, tumors less than 4 cm in diameter, low-grade histology, and absence of extrathyroidal extension or distant metastasis. Recurrence and survival rates were compared among groups who underwent partial lobectomy, total lobectomy and total thyroidectomy with a median follow-up of 20 years. Although a statistically significant increase in local recurrence was seen in the partial lobectomy group compared with the total lobectomy and total thyroidectomy groups, no statistical difference in recurrence or survival was found between the total lobectomy and total thyroidectomy groups.

b) Another important issue in considering the extent of surgical resection is the rate of complications associated with thyroid surgery. Proponents of thyroid surgery feel that complications increase with the extent of surgery. Permanent hypocalcemia is

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more likely after more extensive bilateral thyroid resection [10]. The fact that complication rate is inversely proportion to the experience of the operating surgeon is countered by the fact that most thyroid operations worldwide are likely to be performed by non-experts. Another common argument for total thyroidectomy that is put forth is to remove any microscopic multicentric PTC in contralateral lobe. However, it is not clear if multicentric sub-centimeter cancers are clinically relevant [12]. Less than 5% of patients develop a recurrent disease in contralateral lobe and these could be treated [3,13].

Evidence in Favour of Total Thyroidectomy

There is little debate that all patients belonging to high-risk category should undergo an initial total thyroidectomy. This should also include these patients with bilateral clinically important disease, those with nodal metastasis and those who had irradiation to head and neck in childhood. However, there are compelling reasons for doing total thyroidectomy even in patients belonging to low-risk category:

(a) Complete thyroid resection facilitates the use of RAI for remnant ablation to both the residual normal and microscopic cancerous tissue. Removal of all thyroid tissue lowers the dose of RAI needed for ablation, raising the likelihood of successful ablation.

Extent of Resection Impacts Recurrence / Survival

A considerable number of large series suggest that more extensive thyroid resection for PTC is associated with decreased recurrence or improved survival. The impact of extent of surgery on outcomes in a study group of nearly 2500 PTC patients treated at the Mayo Clinic during approximately the last 60 years has been reported via several retrospective reviews. [10,12,14,15] A total of 1,656 of these patients were treated with primary surgical therapy within 60 days of the initial diagnosis from the years 1940 through 1991 and identified as low risk by AMES criteria [12]. At 20 years, the rate of recurrence at any site for patients undergoing unilateral lobectomy was 22.2%, which was significantly greater than the 8.3% recurrence rate after bilateral lobar resection. When patients with PTC who underwent postoperative radiodine remnant ablation were excluded from this analysis, the recurrence rate remained significantly higher in the unilateral group at 22.3% compared with 7.5% in the bilateral group.

Although 30-year disease specific mortality was higher in the unilateral lobectomy group at 2.6% compared with 2.4% in the bilateral lobar resection group, this result did not achieve statistical significance. Data from PTC patients followed up at the Mayo Clinic also showed that incomplete resection was significantly associated with death from PTC. A variable for incomplete resection was included in the M.A.G.I.S prognostic scoring model developed using regression analysis of multiple candidate predictors of survival after surgery for PTC. Mazzaferri and colleagues [16-18] examined outcomes in PTC patients treated at the Ohio State University hospitals and the United States Air Force between the years 1962 and 1994. A total of 571 United States Air Force patients receiving initial surgical therapy were classified into either subtotal thyroidectomy or total thyroidectomy groups and followed up for a median of 10.3 years [18]. The 310 patients who underwent total thyroidectomy had significantly fewer recurrences than those treated by subtotal thyroidectomy. A lower frequency of death from cancer was also observed in this group (0.6% after total thyroidectomy and 1.5% after subtotal thyroidectomy); however, this result was not statistically significant.

In patients with cervical lymph node metastases, no significant differences in outcome were observed after simple excision compared with more extensive neck dissection. In an analysis by DeGroot and colleagues [19], bilateral lobar resection for PTC larger than 1 cm showed a better long-term survival rate in a series of 269 patients followed up for a mean of 12 years at the University Chicago. Patients undergoing less extensive initial surgery (i.e., lobectomy or bilateral subtotal thyroidectomy) were compared with those undergoing more extensive initial therapy (i.e., lobectomy plus contralateral subtotal lobectomy, near total thyroidectomy, or total thyroidectomy), using multivariate survival analyses adjusting for confounding factors. A statistically significant higher recurrence rate was observed with the less extensive initial surgery group when all patients were included in the analysis. Survival was better in patients who underwent more extensive initial surgery for PTC tumors larger than 1 cm; however, a trend in improved survival after more extensive surgery for tumors smaller than 1 cm did not achieve significance. Improved survival and decreased recurrence rates were also found in a series of 103 patients with PTC treated at the M.D. Anderson Cancer Center from 1951 to 1975 by total thyroidectomy compared with less extensive procedures [20].

(a) Bilaterality in DTC may be present to the extent of 30-80% which is likely to result in persistent disease if less than total thyroidectomy is done [21-23].

(b) The detrimental effects of recurrent disease in the contralateral lobe should be kept to a minimum since central recurrence in the thyroid bed, the contralateral lobe or both are substantial, associated with increased morbidity and mortality, and always requires re-operative surgery which is associated with more complications compared with initial surgery.

c) Thyroidectomy in the hands of experienced surgeons has a <2% rate of permanent recurrent laryngeal nerve injury [10,24,25] or hypocalcemia [24,25]. We feel that total thyroidectomy is actually lobectomy performed twice. Hence, if a non-expert thyroid surgeon can perform a lobectomy well, he should be able to do a good total thyroidectomy!!

d) Further, total thyroidectomy permits recurrence monitoring by the use of serial RAI scans and thyroglobulin measurements [16,23].
Concluding Remarks

Total thyroidectomy for PTCs greater than 1 cm in size yields the best outcome in terms of risk of recurrence and death and maintains quality of life. However, the surgical treatment of DTC needs to be individualized based on the patient, biological characteristics of tumor and the experience of the surgeon. Decisions about management should be made in joint consultation between the thyroid surgeon, endocrinologist and nuclear physician so that the patients are not confused by conflicting recommendations.

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