## THYROID CANCER

# CLINICAL THYROIDOLOGY

# Surgery for thyroid cancer increases the survival rate and enhances the quality of life of elderly patients providing they are well enough to tolerate surgery

Matsuyama H, Sugitani I, Fujimoto Y, Kawabata K. Indications for thyroid cancer surgery in elderly patients. Surg Today 2009;39:652-7.

### **SUMMARY**

**BACKGROUND** Thyroid cancer is typically more aggressive in elderly patients than in younger patients. Elderly individuals with thyroid cancer may have other chronic diseases that make thyroid surgery difficult. As a result, they may experience increased morbidity from thyroid cancer therapy and may not be able to tolerate extensive surgery and postoperative radioiodine or external-beam radiation therapy. This is a retrospective study aimed at comparing the clinical characteristics of thyroid cancer therapy in elderly and younger patients to assess how the elderly fare with surgery as compared with younger patients.

**METHODS** This is a retrospective study of patients treated for thyroid cancer from 1994 through 2004 in the Department of Otolaryngology in Chuo, Japan, and at the Department of Head and Neck, Cancer Institute Hospital (CIH) in Tokyo. Study patients were divided into two groups: an "elderly group" who were age 75 years or older, and a "young group" age 30 years or younger. Patients were further divided into "primary patients" who had initial surgery at CIH, and "secondary patients" who were first treated elsewhere and were referred to CIH for treatment of a recurrence. The characteristics of thyroid cancer were studied in older and younger patients to further understand the specific characteristics of thyroid cancer therapy in these two groups. Patients were classified as high or low risk according to the authors' papillary thyroid cancer risk-group classification. The study also assessed the quality of life in patients with local tumor recurrence and in those who had invasive cancer. Here and elsewhere, percentages are rounded to an integer.

### **RESULTS PRIMARY PATIENTS:** Comparison of the Elderly and Young

Groups Of the 685 primary patients treated at CIH during the 11-year period under study, 42 (6%) were in the elderly group, 13 of whom were men (31%) and 29 women (69%), with a mean age of 78 years (range, 75 to 89). The mean follow-up in this group was 41 months (range, 2 to 123). The young group comprised 37 patients (5%) of whom 9 (24%) were men and 28 (76%) were women, with a mean age of 25 years (range, 16 to 29). The cancer histology was papillary thyroid cancer (PTC) in 32 of 42 elderly patients (76%), follicular thyroid cancer (FTC) in 2 of 42 elderly patients (5%) and 0% in the younger group of patients, and was medullary thyroid cancer (MTC) in 7 of 42 elderly patients (2%) and 3 of 37 younger patients (8%) One or more of the following systemic disorders were present in the elderly: hypertension (n = 1), cardiopulmonary disease (n = 14), tuberculosis (n = 7), other malignant tumors (n = 13), diabetes mellitus (n=5), cerebral infarction (n=3), asthma (n= 2), hepatitis (n = 1), chronic respiratory failure (n = 1), and dementia (n = 1). Of the younger patients, two of the three with MTC had pheochromocytoma and one had tuberculosis. None of the elderly patients had a family history of thyroid cancer, but two of the younger group had a family history of PTC. There was no significant difference in the clinical characteristics of patients with PTC; there was no significant difference in the proportion of patients with tumor  $\geq 4$  cm between the older and younger groups. However, obvious extrathyroidal invasion of adjacent tissues, including the recurrent laryngeal nerve and the trachea, with or without esophageal invasion, was found in the



**Figure 1.** This figure shows the clinicopathological characteristics of the elderly patient group categorized as "primary patients" (initially treated at CIH) as compared with outcomes in the young group with papillary thyroid cancer. \*P = 0.01 and †P = 0.0001, comparing the elderly group with the young group. The figure is derived from Table 1 of Matsuyama et al.



**Figure 2.** This figure shows the putative prognostic factors affecting cumulative 2-year survival rates after surgery. The only variable reaching statistical significance was the number of recurrences (\*P = 0.1). This figure is derived from Table 2 of Matsuyama et al.

## THYROID CANCER

elderly patient group. As a consequence, combined resection of the thyroid tumor that involved adjacent organs was necessary significantly more often in the elderly than in the younger group and hospitalization was significantly longer in the elderly as compared with the younger patients (Figure 1).

Recurrence of PTC was found in 7 of 32 patients in the elderly group (17%), all of whom had lymph-node metastases (Figure 2). Three patients also had lung metastases and two died of other diseases. In the 34 young patients with PTC, only one had a recurrence, which was in lymph nodes (3%), and none died of thyroid cancer. In the elderly group, the 5-year disease-specific survival rate (DSS) was 100% and the cumulative survival rate (CS) was 92%, as compared with 100% DSS and 100% CS in the young group. The CS was significantly higher in the young group as compared with the older group (P = 0.03), but DSS was not significantly different in the two groups (Figure 3).

According to the authors' stage classification, tumors were categorized as high-risk in patients <50 years of age with distant metastases, and in those  $\geq$ 50 years with distant metastases, extrathyroidal invasion, or lymph-node metastases  $\geq$ 3 cm. In elderly patients, tumors were classified as high-risk in 16 of 32 with PTC (50%) and as low-risk in 16 of 34 (50%). In the young age group, tumors were classified as high-risk in 2 of 37 patients (5%) and as low-risk in 35 of 37 (95%) patients. The quality of life deteriorated in 2 of 32 (6%) elderly patients with extremely aggressive, advanced tumor; it was affected in none of the young patients (Figure 3)

# **OUTCOMES** of the Elderly Patients with Recurrent Thyroid Cancer

Of the 30 elderly patients who had surgery for recurrent thyroid cancer, 18 (60%) were primary patients who had initial surgery at CIH and 12 (40%) were secondary patients who were referred to CIH for treatment of a recurrence. Their mean age was 81 years (range, 75 to 88); 4 were men (20%) and 24 were women (80%). Of this group, 26 had PTC (87%) and 4 had FTC (13%).



**Figure 3.** This figure shows the rate of high-and low-risk tumors in elderly and young patients. CS = cumulative survival; DSS = disease-specific survival; PTC = papillary thyroid carcinoma. The only significant difference between the elderly and young patients is cumulative survival ( $\uparrow$ P = 0.03). This figure is derived from data of Matsuyama et al.

After a mean follow-up of 26 months (range, 0.5 to 63 months), lymph-node recurrences were found in the lateral lymph-node compartments in 18 of the 26 patients with PTC (69%) and in the central compartment lymph-node metastases in 12 of 26 (46%), including the overlap of metastases in both neck compartments. (Figure 4). Thirteen of 26 patients (50%) required combined resection of the recurrence and adjacent tissues, which included the recurrent laryngeal nerve (n = 4), muscle layer of the esophagus (n = 3), the trachea (n = 3), neck skin (n =3), accessory nerve (n =2), larynx (n =1), and the posterior cervical muscles (n = 1), including the overlap of tumor sites. The mean number of recurrences was 1.3 (range, 1 to 4). Nine of the 26 patients (35%) died of primary cancer. After surgery, the 2-year DSS was 84% and the CS was 81% (Figure 4).

Although survival tended to be worse for secondary patients than for primary patients initially treated at CIH, the difference did not differ significantly (P = 0.08). Likewise, survival also tended to be worse for patients who had single-lymph-node resection ("berry picking") rather than a modified neck dissection but did not differ significantly (P = 0.07). Likewise, age, sex, number of tumor recurrences, extent of surgery, and duration of hospitalization did not differ significantly. Outcome also did not differ significantly after resection of adjacent tissues and patients who had simple tumor resection or between patients who had palliative versus radical surgery, although the 2-year CS after radical surgery was 91%, as compared with 65% after palliative resection (Figure 2).

### OUTCOMES of Elderly Patients Treated Nonoperatively

Among a total of 85 elderly patients with thyroid cancer, 13 (15%) were treated nonoperatively. Of 13 such patients, 12 had PTC and 1 had FTC; 4 were men (31%) and 9 were women (69%); their mean age was 81 years (range, 75 to 88). Seven had primary thyroid cancer (54%) and 6 had recurrent thyroid cancer (46%). Nonoperative management was done because general anesthesia was contraindicated because of poor general



**Figure 4.** This figure shows the location of and outcomes with recurrent papillary thyroid cancer. CS = cumulative survival; DSS = disease-specific survival. Combined resection is surgical excision of lymph-node metastases and surrounding neck tissues involved with invasive tumor. Radical resection is surgical removal of invasive tumor. Palliative resection is removal only of lymph-node metastases.

## THYROID CANCER



Figure 5. This figure shows the outcomes of elderly patients treated nonoperatively and 2-year cumulative survival with and without surgery. P < 0.03.

### COMMENTARY

There is little question that advanced patient age is associated with advanced tumor stage. Thyroid carcinoma in elderly patients behaves more aggressively and these patients have a less favorable prognosis as compared with younger adults. Advanced age is associated with an increased risk for locoregional and a higher incidence of distant metastases (1-3). In the study by Matsuyama et al., patients with low-risk PTC had a prognosis that was not worse in elderly patients than that in young patients. Still, many of the elderly with PTC required resection of lymphnode metastases and locoregional metastases outside the thyroid bed, which resulted in longer than usual hospitalization. Likewise, the quality of life was severely impaired by various conditions, such as dyspnea and dysphagia produced by invasive tumors. Elderly patients with recurrent PTC had no significant differences in survival, including those who had recurrences prior to a second operation, as compared with patients who had metastases at the time of initial surgery. In addition, elderly patients had one or more serious medical conditions such as hypertension, cardiopulmonary disease, tuberculosis, other malignant tumors, diabetes mellitus and stroke.

Comorbidity is known to be an important contributory factor to poor outcomes with thyroid cancer, especially in elderly patients. For example, a population-based observational study from the Netherlands (3) found that hypertension was the most frequent comorbidity with thyroid cancer (18%), followed by other serious conditions such as cardiovascular diseases (6%) and diabetes mellitus (6%). In fact, the prevalence of hypertension was twice as high as expected in all age groups, yet comorbidity was not independently associated with overall survival up to 5 years (3). health, such as lung lobectomy or dementia, or because of heart failure, advanced cancer, or a patient's refusal of surgery or small tumors causing few physical complaints. Three of these patients died of primary cancer, 8 were alive with persistent tumor, and 1 was lost to follow-up. Three patients died, one was in poor general health, one had advanced tumor, and one who refused surgery died of primary cancer.

The 2-year DSS and CS were both 100% for the 16 patients treated surgically, and were both 80% for the 5 patients not treated surgically. CS was significantly higher in the patients treated surgically (P = 0.02). During follow-up, the quality of life was severely impaired in of 8 of 12 patients not treated surgically (67%) and in 2 of 32 treated surgically (6%). The latter two patients with PTC deteriorated during follow-up as a result of extremely aggressive and advanced tumors (Figure 4).

**CONCLUSIONS** Surgery for thyroid cancer increases the survival rate and enhances the quality of life of elderly patients providing they are well enough to tolerate the procedure.

These observations are similar to those made by Matsuyama et al. in elderly patients. In their study of elderly patients with recurrent PTC, there were no statistically significant differences in survival among patients with locoregional metastases when patients had metastases found on the initial surgery or were secondarily identified as locoregional recurrences later in the course of follow-up. Although outcome tended to be worse in patients undergoing a second surgery for recurrent metastases, the difference was not statistically significant as compared with patients who had metastases at the time of initial surgery.

An interesting observation was that half of the elderly patients had tumors classified as high-risk and half had low-risk tumors and 5% of the younger patients had low-risk tumors. The 2-year survival rate in elderly patients with a high-risk tumor was significantly lower in patients treated surgically than in those not treated surgically. The authors suggest that surgery for thyroid cancer increases the survival rate and promotes the quality of life in elderly patients with persistent or recurrent thyroid cancer, providing they are well enough to tolerate surgery.

Although there are a few problems with the study, including its retrospective design and the relatively small number of patients and lack of rigorous statistical analysis, this study underscores the fact that advanced age alone is not a sound reason to forgo surgery—or any other treatment for that matter. This decision must be based on the patient's health status and willingness to undergo surgery that may be riskier than usual because of comorbidities. As usual, the patient must be the final arbiter.

#### Ernest L. Mazzaferri, MD, MACP

### References

1. Mazzaferri EL, Jhiang SM. Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. Am J Med 1994;97:418-28.

2. Vini L, Hyer SL, Marshall J, et al. Long-term results in

elderly patients with differentiated thyroid carcinoma. Cancer 2003;97:2736-42.

3. Kuijpens JL, Janssen-Heijnen ML, Lemmens VE, et al. Comorbidity in newly diagnosed thyroid cancer patients: a population-based study on prevalence and the impact on treatment and survival. Clin Endocrinol (Oxf) 2006;64:450-5.