

Complication of Thyroidectomy in Patients With Radiation-Induced Thyroid Neoplasms

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Hypothesis: The complication rate for thyroidectomy is the same in patients with and without a history of radiation exposure.

Design: Retrospective medical record review of 171 consecutive patients who had a previous history of radiation treatment and had undergone a thyroid operation from 1961 to 1999.

Setting: University of California, San Francisco, Medical Center and affiliated hospitals.

Patients: We selected 107 patients with a history of radiation exposure who had undergone thyroid operations (81 total thyroidectomies) and 107 control patients who underwent comparable operations but had no history of radiation exposure.

Results: Among patients with a history of radiation exposure (mean age, 47.2 years), there was 1 recurrent nerve injury, 1 external nerve injury, 20 patients with tran-

sient hypocalcemia, and 1 patient with a hematoma. Among patients without a history of radiation exposure (mean age, 47.5 years), there were 2 recurrent nerve injuries, 18 patients with transient hypocalcemia, and 1 patient with a hematoma. All cases of hypocalcemia and recurrent nerve injury in both groups were transient. One patient had a permanent superior laryngeal nerve injury. In patients who underwent operations since January 1, 1990, duration of hospitalization was 1.2 days in patients with a history of radiation exposure (65 patients) and 1.1 days in patients without (101 patients).

Conclusions: Our data document that the risk of transient and permanent complications after total thyroidectomy is similar in patients with and without a history of radiation exposure. The relatively low long-term complication rate supports prophylactic total thyroidectomy for patients with thyroid nodules and a history of radiation exposure.

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IT IS WELL KNOWN THAT A HISTORY of exposure to low-dose therapeutic head and neck radiation increases the risk of developing both benign and malignant thyroid neoplasms in both animals and man.¹ Animals and humans also have an increased risk of developing thyroid nodules and thyroid cancer after exposure to iodine I 131. The risk of developing thyroid cancer after therapeutic iodine I 131 administration for Graves disease is very low. It is apparent from review of the literature that patients who develop 1 or more thyroid nodules after exposure to external low-dose radiation have a higher chance of thyroid cancer than do patients with thyroid nodules and no known history of radiation exposure.^{2,3}

Total thyroidectomy is frequently recommended for patients with a history of radiation and 1 or more thyroid nodules because (1) thyroid cancer is present in

40% of these patients, (2) all multifocal tumors are removed, (3) it eliminates the possible subsequent transformation of a well-differentiated thyroid cancer to an undifferentiated thyroid cancer, (4) it lowers the overall recurrence rate in patients with thyroid cancer, (5) it enables one to scan with radioiodine and to ablate persistent disease or metastasis, and (6) blood thyroglobulin levels become more sensitive markers of persistent disease.⁴ We recommend total thyroidectomy for these reasons. Prognosis-predicting classifications, such as TNM, age/metastasis/extent/size, and age/grade/extent/size, are determined postoperatively, and the natural history of patients with thyroid cancer with or without previous radiation exposure is unknown. We and others also believe that total thyroidectomy can be done with a relatively low complication rate.^{5,6} The risk of developing benign and malignant thyroid neoplasms after radiation expo-

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Table 1. Procedures in Patients With and Without a History of Radiation Exposure

| | No. of Patients With History of Radiation Exposure | No. of Patients Without History of Radiation Exposure |
|-------------------------------|--|---|
| Sample size | 107 | 107 |
| Total thyroidectomy | 81 | 71 |
| With modified neck dissection | 4 | 12 |
| Less than total thyroidectomy | 26 | 36 |
| Near total | 1 | 5 |
| Then completion thyroidectomy | 0 | 0 |
| Subtotal | 6 | 14 |
| Then completion thyroidectomy | 3 | 1 |
| Lobectomy | 19 | 17 |
| Then completion thyroidectomy | 7 | 4 |

sure is closely related and increases between 0.07 and 20.00 Gy.⁷ Children and young adults are most prone to develop thyroid cancer after radiation exposure including either a low or intermediate dose of external radiation and radioiodine exposure.^{1,5,8}

Although, to our knowledge, there are no prospective studies regarding the management of patients with thyroid nodules and a history of radiation, most surgeons recommend total thyroidectomy as the treatment of choice for these patients. It has theoretical and practical advantages but presumably is associated with a slightly higher complication rate than less extensive operative procedures. The incidence of transient hypocalcemia after total thyroidectomy is reported to be 2.9% to 8.5%⁹ and permanent hypocalcemia, 0.6% to 5.0%.¹⁰ The incidence of permanent recurrent laryngeal nerve injury is reported to be 0% to 5%.^{9,11-13}

The purpose of this investigation was to document the transient and permanent complication rates after thyroidectomy in patients with and without a history of radiation. One hundred seven patients who underwent thyroid operations after radiation exposure were compared with 107 control patients matched for age, sex, diagnosis year, and histologic diagnosis who underwent the same operations to determine whether the risk of complications differed in these 2 groups.

METHODS

A retrospective medical record review was performed. Of the 171 consecutive patients who had a history of radiation treatment and a thyroid operation, we selected 107 patients in whom age, sex, histologic diagnosis, diagnosis year, and procedure performed could be determined. We then selected 107 matched control patients who underwent the same thyroid operation but had no known history of radiation exposure. For the purpose of matching patients for control, total thyroidectomy, near total thyroidectomy, and subtotal thyroidectomy were considered equivalent. Operations were performed between 1980 and 1999 at University of California, San Francisco, Medical Center, University of California, San Francisco/Mt Zion Medical Cen-

ter, and Veterans Affairs Medical Center, San Francisco. Transient hypocalcemia was defined as a serum calcium level of less than 8.0 mg/dL (<2 mmol/L), and the patients received calcium supplementation with or without vitamin D. All patients who received calcium and vitamin D and were hypocalcemic for more than 6 months were considered to have permanent hypocalcemia. Direct laryngoscopy was performed preoperatively in all patients who had previous neck surgery or a history of hoarseness or change in voice. It was also performed postoperatively in all patients who had a change in voice or hoarseness.

We used the *t* test for continuous variables, and the Fisher exact test for categorical data.

RESULTS

DEMOGRAPHICS FOR PATIENTS WITH AND WITHOUT A HISTORY OF RADIATION EXPOSURE

One hundred seven patients (32 male and 75 female; mean age, 47.2 years) had a history of radiation exposure. Eighty-one were treated by total thyroidectomy and 26 by less than total thyroidectomy (10 followed by completion thyroidectomy) (**Table 1**). Pathological findings included 48 thyroid cancers (43 papillary cancers, 3 follicular cancers, 1 medullary cancer, and 1 carcinosarcoma) and 59 benign thyroid tumors (13 follicular adenomas, 2 Hurthle cell adenomas, 43 multinodular goiters, and 1 other).

Among the 107 control patients with no history of radiation exposure, there were 32 male and 75 female patients (mean age, 47.5 years). Seventy-one were treated by total thyroidectomy and 36 by less than total thyroidectomy (19 followed by completion thyroidectomy) (Table 1). Pathological findings included 48 thyroid cancers (45 papillary cancers, 2 follicular cancers, and 1 medullary cancer) and 59 benign thyroid tumors (11 follicular adenomas, 2 Hurthle cell adenomas, 45 multinodular goiters, and 1 benign histiocytoma).

THYROIDECTOMY COMPLICATIONS IN PATIENTS WITH AND WITHOUT A HISTORY OF RADIATION EXPOSURE

Among patients with a history of radiation exposure, 1 patient with stage I papillary carcinoma developed a transient recurrent nerve injury, 1 patient with a multinodular goiter developed an external laryngeal nerve injury, 20 patients had transient hypocalcemia, and 1 patient developed a postoperative neck hematoma (**Table 2**). Among patients without a history of radiation exposure, 1 patient with stage III papillary carcinoma and 1 with Graves disease developed transient recurrent nerve injuries, 18 patients had transient hypocalcemia, and 1 patient had a postoperative hematoma. All recurrent laryngeal nerve and hypocalcemic complications were transient, but the 1 external laryngeal nerve injury was permanent. The complication rate in patients who underwent reoperations was not different from those who underwent initial operations. There was no statistical significance between transient or permanent complications in either group of patients.

**DURATION OF HOSPITAL STAY
IN PATIENTS WITH AND WITHOUT
A HISTORY OF RADIATION EXPOSURE**

The overall duration of hospitalization in patients treated since January 1, 1990, was 1.2 days in patients with a history of radiation exposure and 1.1 days in patients without a history of radiation exposure. Patients hospitalized for 23 hours were considered as staying 1 hospital day. The duration of hospitalization prior to 1990 was considerably longer in both groups based on tradition. The duration of hospitalization was similar in the 2 groups.

COMMENT

Our retrospective study documents that total thyroidectomy and completion total thyroidectomy can be done safely in patients with or without a history of exposure to low-dose therapeutic radiation by experienced surgeons. Benign and malignant thyroid neoplasms as well as Hashimoto thyroiditis all occur more often in individuals with a history of radiation exposure.¹ One might question whether complications occur more often after thyroidectomy in patients exposed to low-dose radiation because of multifocality of the tumors or less often because patients might be diagnosed and treated at an earlier stage of disease. Our study documents that the complication rate in patients with a history of radiation exposure undergoing thyroid operations is relatively low and comparable with that in a control group.

Recurrent nerve injury and hypoparathyroidism are the most serious long-term complications that occur after thyroid operation, whereas postoperative neck hematomas may be immediately life threatening. During a hemithyroidectomy, only 2 parathyroid glands and 1 recurrent laryngeal nerve are at risk. Thus, permanent hypoparathyroidism or bilateral vocal cord paralysis should virtually never occur. These complications are also uncommon after total thyroidectomy when the operation is done by an experienced surgeon.¹⁴ The latter operation has, however, both theoretical and practical advantages for patients with differentiated thyroid cancers, especially in patients with a history of radiation exposure and those with familial disease, because thyroid cancer in these 2 groups of patients is more common and the cancers are often multifocal.

Recurrent laryngeal nerve dysfunction (temporary or permanent hoarseness) has been reported to occur in 0% to 5% of the patients.¹⁵⁻²¹ Postoperative hoarseness with recurrent laryngeal nerve dysfunction, for up to 6 months, may occur in patients with an intact recurrent laryngeal nerve that has been stretched or partially devascularized or for other reasons. Patients with bilateral recurrent laryngeal nerve paralysis usually have profound dyspnea, difficulty breathing, and usually require reintubation. Surprisingly, such patients can usually talk, which often confuses health care professionals who therefore believe that both recurrent nerves are intact. When vocal cord dysfunction continues for more than 6 months, it is usually permanent.²² To avoid injury to the recurrent laryngeal nerves, surgeons must be aware of the

Table 2. Thyroidectomy Complications in Patients With and Without a History of Radiation Exposure

| | No. of Patients With History of Radiation Exposure | No. of Patients Without History of Radiation Exposure |
|---------------------------------|--|---|
| Sample size | 107 | 107 |
| Recurrent nerve injury | 1 | 2 |
| Transient | 1 | 2 |
| Permanent | 0 | 0 |
| External laryngeal nerve injury | 1* | 0 |
| Hypocalcemia | 20 | 18 |
| Transient | 20 | 18 |
| Permanent | 0 | 0 |
| Hematoma | 1 | 1 |

*This patient had a history of internal irradiation for a nodular goiter that caused a toxic reaction and underwent a left lobectomy.

course of the left and right recurrent laryngeal nerves and operate in a blood-free field. Nothing should be clamped or cut that might be the recurrent nerve until the nerve is identified.²³ Patients with larger and invasive thyroid cancers, those with extensive lymphnodectomy, and those requiring reoperation are more likely to develop complications.¹⁷

Permanent hypoparathyroidism has been reported to occur in 0.6% to 5.0% of patients, whereas transient postoperative hypocalcemia is much more common.^{15-18,20,24} When a parathyroid gland cannot be safely dissected from the thyroid gland on its vascular pedicle, it should be removed, a biopsy should be performed to confirm it is parathyroid, and it should be autotransplanted into the contralateral sternocleidomastoid muscle. The thyroid gland should also be examined on removal, and if a suspected parathyroid gland is identified, another biopsy should be performed and the gland should be autotransplanted. Using operating magnifying glasses is recommended during thyroid operation, because it helps the surgeon identify and preserve vital structures. Some studies suggest that one should not ligate the trunk of the inferior thyroid artery during thyroidectomy because it increases the risk of hypoparathyroidism.²⁵

The external laryngeal nerve is a branch of the superior laryngeal nerve. Because the course of this nerve varies more than that of the recurrent nerve and it is smaller than the recurrent laryngeal nerve, knowledge of its anatomy is important. Injury to the external laryngeal nerve often results in loss of voice range and projection, inability to sing high notes or scream, and voice fatigue. Lennquist et al²⁶ reported that inappropriate use of coagulator close to the cricothyroid muscle and external laryngeal nerve could cause damage and therefore should be avoided.

One of our patients had persistent dysfunction of her external laryngeal nerve. She had a history of iodine I 131 therapy for a nodular goiter that caused a toxic reaction and had undergone a left lobectomy. Postoperatively, she complained of hoarseness and difficulty projecting her voice. Direct laryngoscopy and videoscopes revealed a left external laryngeal nerve injury.

Hemorrhage can be a life-threatening complication of thyroid surgery, so patients must be closely observed post-thyroidectomy.^{27,28} Antiemetics should be given for nausea and vomiting. Some surgeons recommend same-day hospital discharge after 6 hours of observation. We are reluctant to accept this recommendation because postoperative hemorrhage can result in dyspnea and death.²⁷ Virtually all of our patients since 1990 have been discharged from the hospital within 23 or 24 hours whether having total or less than total thyroidectomy.

CONCLUSION

Our investigation documents that the risk of complications after total thyroidectomy is similar in patients with and without a history of radiation exposure. It also documents that total thyroidectomy can be done safely with a relatively low complication rate by experienced surgeons.

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