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Surgical treatment of thyroid cancer: the Singapore General Hospital experience

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Patients with differentiated thyroid cancers generally have a good prognosis. This should be considered when deciding the extent of surgical resection. Radical surgery, however, may be appropriate in the control of locally advanced disease. An audit of 149 cases of thyroid cancer treated in the Department of General Surgery, Singapore General Hospital between October 1988 and June 1994 is presented. Particular attention is drawn to eight patients who underwent radical surgery. There were 111 (74.5%) women and 38 (25.5%) men. The median age was 45 years (range 12 to 83 years) and 80.5% of the cancers were papillary carcinomas, 14.8% follicular, 2.7% medullary and 2.0% anaplastic. Total or near-total thyroidectomy was the most common procedure for primary disease in about 75% of patients. Eight patients (5.4%) underwent radical surgery—four laryngectomy, one partial pharyngectomy and three median sternotomy—for tumour clearance. Morbidity included: wound complications in 2%; hypocalcaemia, transient in 16.8% and permanent in 3.4%; and hoarseness of voice in 8.1%, with 4.7% having proved recurrent laryngeal nerve palsy. All three patients with anaplastic thyroid cancer died within 3 months. Of the eight who underwent radical surgery, three (37.5%) are alive and disease-free at median follow-up of 20 months. In a correctly selected group of patients with locally invasive differentiated thyroid cancer, aggressive surgery is appropriate, with acceptable morbidity and mortality.

Keywords: laryngectomy, pharyngectomy, radical surgery, thyroid cancer.

Well-differentiated thyroid carcinomas are tumours of low-grade malignancy; 80% of these patients do well regardless of the extent of operation.[1] However, a minority of these tumours have an aggressive biological behaviour. Laryngotracheal invasion by a well-differentiated thyroid carcinoma has been reported to vary from 1 to 13%.25 Although complete surgical resection of tumour tissue is thought to be the best way to cure the disease, the sequelae of aggressive surgery cannot be ignored.

We report in this paper our experience with the management of 149 cases of thyroid cancer. Morbidity and mortality are reviewed to address in particular whether radical surgery is the most appropriate treatment for patients with locally advanced disease.

PATIENTS AND METHODS

All patients with histologically confirmed thyroid cancer who were operated on in the Department of General Surgery, Singapore General Hospital between October 1988 and June 1994 were included in this study. The list was retrieved from the Department's dedicated database and case notes were retrospectively reviewed for all details presented in this paper. All patients were followed-up until death or the conclusion of the study period.

Serum calcium and phosphate were routinely measured after total and near-total thyroidectomy, and after hemithyroidectomy when indicated. Hypocalcaemia was considered to be permanent if calcium supplements were required more than 6 months postoperatively. Pre-operative laryngoscopy (direct and/or indirect) was performed in patients undergoing further surgery or when there was a hoarseness of voice. Post-operative laryngoscopy was performed when there was a hoarseness of voice.

RESULTS

One hundred and forty-nine patients were entered in this study. There were 111(74.5%) women and 38 (25.5%) men. The median age was 45 years, range 12 to 83 years. Papillary carcinoma was the most common histology, occurring in approximately 80% of patients; follicular carcinoma was encountered in approximately 15%, medullary carcinoma in 2.7% and anaplastic carcinoma in 2%. There was no case of lymphoma (Table 1).

Table 1 Histology

Type of carcinoma	No. (%) of patients
Papillary	120(80.5)
Follicular	22(14.8)
Medullary	4(2.7)
Anaplastic	3(2.0)
Total	149(100)

The most common operation performed for primary disease was total or near-total thyroidectomy, carried out in more than 75% of patients. Of these, about one-third had in addition a modified radical neck dissection (MRND). Hemithyroidectomy was performed in 12.5% of patients, of whom approximately one-third also had MRND. Radical surgery was performed for primary disease in 4.4%, while debulking surgery and subtotal thyroidectomy were infrequently performed (1.5%) (see Table 2).

Table 2 Surgery for primary disease

Type of surgery	No. of patients
Total/near-total/completion thyroidectomy	112(34 MRND*)
Hemithyroidectomy	17(5 MRND)
Radical surgery	6
Debulking	1
Subtotal thyroidectomy	1
Total	137

* MRND, Modified radical neck dissection.

Twelve patients with recurrent disease had a further operation, of whom 10 had papillary and two follicular carcinomas. Eleven were local neck recurrences and one was a solitary metastasis to the mandible (follicular carcinoma). The median time to recurrence after initial surgery was 25 months (range 12 to 89 months). The initial and subsequent surgery performed in these patients with recurrent disease are detailed in Tables 3 and 4, respectively. Of these 12 patients, seven had previous total thyroidectomy, of whom three had nodal clearance; three had previous subtotal thyroidectomy and two had previous hemithyroidectomy. Nodal recurrence in the neck accounted for two-thirds (eight patients) of recurrent disease and were managed with MRND, of whom two patients had completion thyroidectomy as well; two patients required radical surgery and one completion thyroidectomy. Segmental mandibulectomy was performed for the patient with solitary bony recurrence in the mandible.

Table 3 Recurrent disease: initial surgery

Type of surgery	No. of patients
Total thyroidectomy	7(3 with nodal dissection)
Subtotal thyroidectomy	3
Hemithyroidectomy	2
Total	12

Table 4 Surgery for recurrent disease

Type of surgery	No. of patients
Modified radical neck dissection (two with completion thyroidectomy)	8
Radical surgery	
Total laryngectomy	1
Median sternotomy for tumour clearance	1
Completion thyroidectomy	1
Segmental mandibulectomy	1

In the group having radical operations for locally invasive disease (all were papillary carcinomas), total laryngectomy was performed in four, partial pharyngectomy in one and median sternotomy for tumour clearance in three patients (Table 5). All received postoperative adjuvant radioactive iodine and thyroid hormone suppressive treatment with or without external beam radiotherapy.

Table 5 Radical surgery

Type of surgery	No. of patients
Total laryngectomy	4
Partial pharyngectomy (with primary repair)	1
Median sternotomy for tumour clearance	3

The overall morbidity is given in Table 6. Wound-related complications occurred in 2% of patients. The major complications were those of hypocalcaemia, transient in 16.8% and permanent in 3.4% of patients, and recurrent laryngeal nerve injury in 4.7% (half of the 8.1% who reported post-operative hoarseness of voice). This included three patients in whom the recurrent laryngeal nerve was intentionally removed because of disease and one patient in whom the damaged nerve was primarily repaired with a good result. Horner's syndrome and stiff shoulders were peculiar to the group who had MRND, occurring in 4 and 10%, respectively. Three patients required tracheostomy, all pre-operatively.

Table 6 Morbidity

Type of problem	Non-radical (n=141)	Type of surgery (No. (%) Radical n=8)	Total (n=149)
Wound complications	3(2.1)	—	3(2.0)
Hypocalcaemia			
Transient	21(14.9)	4(50.0)	5(16.8)
Permanent	4(2.8)	1(12.5)	5(3.4)
Hoarseness of voice	10(7.1)	2(25.0)	12(8.1)
Recurrent laryngeal nerve injury	5* (3.5)	2#(25.0)	7(4.7)
Horner's syndrome		2/47 with MRND§	
Stiff shoulders		5/47 with MRND	

* Includes one patient and # includes two patients in whom the recurrent laryngeal nerves were intentionally sacrificed because of disease.

§MRND, Modified radical neck dissection.

Mortality and survival

Anaplastic cancer. Two patients had total thyroidectomy, of whom one required tracheostomy; the third patient had debulking surgery after initial tracheostomy. All three patients died within 3 months.

Non-radical surgery. There were two deaths among the 141 patients who underwent non-radical surgery. One died of hypocalcaemic crisis due to non-compliance with long-term calcium supplements, the other from lung metastases. Two patients in this group are alive with known lung metastases, both from follicular carcinoma.

Radical surgery. There were three disease-related and two unrelated deaths among the eight patients who had radical surgery. Three are alive and disease-free at a median follow-up of 2O months (Table 7).

Table 7 Mortality and survival after radical surgery

Disease-related mortality
One from tracheoinnominate fistula at 4 months
One from local neck recurrence at 10 months
One from lung metastases at 3.5 years
Unrelated mortality
One from primary lung cancer at 4 months (with disease)
One from end-stage renal failure at 2 years (disease-free)
Survival
Three (37.5%) alive and disease-free at median follow-up of 20 months, range 9 to 48 months

DISCUSSION

Considerable controversy exists in published work as to whether total thyroidectomy or less than total thyroidectomy is the preferable operation for patients with well-differentiated thyroid carcinoma.[6-11] In our series, total or near-total or completion thyroidectomy was the most common procedure performed for primary thyroid carcinoma in more than 75% of patients.

The fact that local recurrence signifies a substantial risk of subsequent tumour-related mortality is emphasized by several workers.[7,12] Total thyroidectomy eliminates the multicentric microscopic foci present in up to 85% of papillary carcinomas[6,12] as potential sites of local recurrence, or the anaplastic transformation that occurs in 1%.[13] Patients undergoing lobectomy have a recurrence rate in the contralateral lobe of 5 to 25%, with a mean of 7%, and up to one- half of these patients eventually die of thyroid cancer, some of whom were initially considered low risk.[13] Tollefsen *et a!.*[14] reported a 5.7% local recurrence rate in the contralateral thyroid remnant, and 41% of these patients died. They highlighted, however, the marked discrepancy of clinical local recurrence of only 5.7% versus what might have been expected if all contralateral microscopic multicentric disease—38% in their study—had actually become manifest. This led them to 'interpret those laboratory evidences of cancer in the opposite lobe as being of little clinical importance'. Mazzaferri and Young[15] reported a recurrence rate of 11% after total thyroidectomy compared with 22% after subtotal thyroidectomy. The result of this retrospective study probably underestimates the benefits of these treatments because patients with more extensive disease were more likely to be included in the group receiving more extensive treatment. Shah *et a!.*[10] concluded that in low-risk patients (primary tumour of 4 cm or less, limited to

the thyroid gland, without gross contralateral disease, and no evidence of distant metastasis), total thyroidectomy provides no survival advantage over lobectomy. They could not, however,address the issue of local recurrence because of the analytical method used in their review. The Mayo Clinic experience[8,9] showed that in both low-risk (AGES score 3.99 or less) and high-risk (AGES score of 4 or more) groups there was a highly significant difference in the risk of local recurrence comparing unilateral and bilateral resections, but none between total thyroidectomy and bilateral subtotal/near-total thyroidectomy. Survival was not influenced by the extent of resection in the low-risk group, and only a trend towards improved survival was observed with bilateral compared with unilateral resection in the high-risk group. In neither group was survival improved by total thyroidectomy. We are in agreement with the Memorial and Mayo experiences and do not advocate total thyroidectomy for all patients, though it was the most common operation performed by us for differentiated thyroid carcinoma.

Damage to the recurrent laryngeal nerve can range from frank severance, to immediate but temporary paresis, to the delayed appearance of paralysis as a result of surrounding infection or scarring. The reported incidence of recurrent laryngeal nerve damage varies from 0 to 13%[16] with the higher range in bilateral exposures, such as in total thyroidectomy, and in unilateral thyroid lobectomy combined with neck dissection. The incidence of recurrent laryngeal nerve damage reported in most series, ours included, is probably an underestimate because of the lack of routine laryngoscopy, whether direct or indirect. Laryngoscopy is necessary to prove recurrent laryngeal nerve damage in patients whose voices are normal because of the compensatory movement of the contralateral cord across the midline. Conversely, post-operative hoarseness of voice is not always due to operative laryngeal nerve injury as 1—2% of patients have a paralysed vocal cord before thyroid surgery.[17]

Our recurrent laryngeal nerve injury rate of 4.7% is modest and, although an underestimate of the true rate, does emphasize the interesting fact that it accounts for just over half of our patients with post-operative hoarseness of voice. Oedema of the intrinsic larynx is the most common cause of post-thyroidectomy hoarseness.

With total thyroidectomy, hypocalcaemia will occur in 20—25% of patients. In most of these the decrease in calcium will be small and transitory. It will persist in 1-4%.[18] It is well documented that the risk of permanent vocal cord paralysis and hypoparathyroidism associated with total thyroidectomy performed by competent surgeons is fairly low.[11,16,19] However, we do not believe that the ability to carry out an operation with low morbidity can alone justify its routine performance. Although our rate of transient hypocalcaemia at 16.8% and permanent hypocalcaemia at 3.4% are within the reported range, we are reminded by the death of one patient from hypocalcaemic crisis due to non-compliance with calcium supplements that if there is no benefit with total thyroidectomy in appropriately selected patients, then even a small increased risk of morbidity cannot be justified. The reservation of only one parathyroid gland will avoid the problem of hypoparathyroidism. Auto-transplantation of the parathyroid glands is also useful to this end.[20,21]

In the Mayo series,[18] permanent unilateral vocal cord paralysis occurred in 2% and permanent hypocalcaemia in 5% of patients. The extent of resection was not apparently associated with vocal cord paralysis, but was highly associated with hypocalcaemia, being 32% after total thyroidectomy and 0.3% after less extensive surgical resection. Our numbers are too small, however, to attempt subgroup analysis.

Upper aerodigestive tract invasion by differentiated thyroid cancer is reported to occur in 1—13% of patients.[2-5] Surgical management of locally invasive well-differentiated thyroid cancer is controversial. Frazell and Foot[22] performed total laryngectomy in four of 393 (1.0%) of their patients with papillary thyroid cancer. Clark *eta!.*[23] performed laryngectomy in five of 2l 8(2.3%), whereas Schindel[24]

performed this in eight of 225 patients (3.6%). We have performed total laryngectomy and partial pharyngectomy in five of 149 (3.4%) patients, with no 30-day post-operative mortality, while achieving 37.5% disease-free survival at 20 months. However, we have little experience with laryngopharyngeal reconstruction in this group of patients. On the other hand, other surgeons prefer conservative procedures with partial preservation of the anatomical structures and laryngotracheal functions, stating that conservative surgery is possible in most patients with adequate local control.[4,25,26] Shvili *et al.*[26] believed that in patients with invasive, well-differentiated thyroid cancer, radical excision of the tumour, partial resection of the larynx and trachea, and reconstruction with the myoperichondrial flap in minimal resections, or with primary anastomosis in extensive resections, is the preferred method of treatment. In a Japanese series,[5] the survival rates when analysed showed no significant difference between patients aged 40 or older in the palliative group and those in the radical group with upper aerodigestive tract resection. The control of local disease, however, was much more difficult in the palliative group. In the palliative group, the survival rate of patients aged less than 40 was significantly better than that of patients aged 40 or older. Those workers hence considered that it may be better to avoid radical surgery in patients less than 40 if it would result in a severe deterioration in their quality of life. In a Korean study of tracheal cartilage invasion by thyroid carcinoma treated by cartilage shaving procedure,[27] only four of 16 patients remained disease-free; the disease was not controlled in the other 12, of whom seven eventually died of their disease. Those workers thus felt that a more extensive resection than cartilage shaving should be considered, even in patients with superficial tracheal invasion, to increase the disease-free survival.

We believe that whether resection can be performed with acceptable morbidity in cases of locally invasive disease is an important consideration which depends on the wishes of the patient, the presence of metastases and the availability of reconstructive options. In the presence of metastatic disease, resection of symptomatic local disease should still be considered. Patient selection, however, is of the utmost importance and we draw from the experience of two recent publications.[28,29] The Mayo Clinic experience[28] suggests that when a papillary thyroid carcinoma extends beyond the thyroid capsule and invades adjacent structures, the site invaded will influence survival. The factors that had a significant influence on survival were invasion of the trachea and oesophagus. Muscle, laryngeal and recurrent laryngeal nerve invasion had no significant independent influence on survival. Survival may be improved by complete surgical excision of the tumour. Shin *et al.*[29] proposed a pathological staging of papillary thyroid carcinoma with airway invasion. Patients with stages I, II and III disease (which included cases ranging from abutment of the external tracheal perichondrium through cases in which the tumour extended through cartilage but did not elevate the epithelium) had less frequent positive margins and no postoperative mortality. Stage IV carcinomas were those that extended through the entire thickness of the trachea and expanded the mucosa (which would be clinically seen by bronchoscopy). Because of the direct invasion of the trachea by papillary thyroid carcinoma, shaving the thyroid from the trachea or endotracheal laser resection would not be an adequate treatment for tracheal invasion. These workers predict that *en bloc* resection of the tumour and invaded trachea should produce a long-term cure in all but those patients with state 1V disease. It would seem then that in a correctly selected group of patients (stages I—III), functional aerodigestive structures can be sacrificed with acceptable morbidity and mortality in an attempt to achieve a better local control and survival, whereas in stage IV patients, there will be no advantage in sacrificing airway, voice and swallowing functions.

CONCLUSIONS

(1) The prognosis of anaplastic thyroid cancer is uniformly dismal.

(2) Thyroid surgery can be performed with low post-operative morbidity.

(3) In a correctly selected group of locally invasive differentiated thyroid carcinomas, aggressive

surgery is appropriate with acceptable morbidity and mortality.

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