Pre-ablative Diagnostic Whole-body Scan Following Total Thyroidectomy for Well-differentiated Thyroid Cancer: Is It Necessary?

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OBJECTIVE: This study reviewed the incidence of positive pre-ablative diagnostic scan after total thyroidectomy and the efficacy of the current ablative dose. The predictive factors for outcome using a standard ablative dose and postoperative complications of total thyroidectomy were also examined.

METHODS: This was a retrospective review of patients referred for radioiodine ablation after total thyroidectomy between September 1997 and September 2001.

RESULTS: Forty patients were included in this study, of whom 95% had a positive scan after total thyroidectomy. Of the 30 patients who underwent standard 80-mCi radioiodine ablation, 21 (70%) had successful single ablation while the remaining nine patients needed a higher ablative dose. There were no significant differences between patients who had successful ablation with the standard dose and those who did not in terms of tumour size, patient age, lymph node status and extra-thyroidal extension. Fifteen percent suffered from permanent hypoparathyroidism requiring calcium supplementation. Three patients had documented recurrent laryngeal nerve paralysis.

CONCLUSION: Bypassing the pre-ablative diagnostic scan is feasible. The present ablation dose of 80 mCi of radioiodine is effective. The relatively high postoperative morbidity after difficult total thyroidectomy suggests less aggressive excision and postoperative radioiodine ablation of the remnant tissue. [Asian J Surg 2005;28(2):90–6]

Key Words: radioiodine ablation, recurrent laryngeal nerve, thyroid carcinoma, total thyroidectomy

Introduction

Thyroid cancer is rare (3.7–4.7/100,000 population), accounting for less than 1% of all malignancies and 0.5% of all cancer deaths.1–3 Of thyroid cancers, 90% are well-differentiated, arising from follicular cells, and have an excellent prognosis irrespective of treatment.4 Papillary thyroid cancer is the commonest form and accounts for at least 50% of all thyroid malignancies. This figure is even higher in children and in post-irradiation cases. Follicular carcinoma accounts for 15–25% of thyroid cancers. The peak incidence of papillary cancer is in patients aged 30–40 years, while follicular carcinoma occurs in a slightly older age group (35–45 years). Both carcinomas are three times more common in females than males.5

The objectives of treatment for thyroid cancers are to eradicate the primary tumour, reduce the incidence of local or distant recurrence, facilitate treatment of metastasis and cure the maximum number of patients with minimal morbidity. There is general agreement that surgery is the treatment of choice, but the extent of the procedure remains

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controversial.6–9 The extent of thyroid resection for carcinoma has generated a considerable amount of literature and discussion. There are two schools of thought, one proposing total thyroidectomy (total macroscopic excision of thyroidal tissue) and the other advocating near-total thyroidectomy, in which the surgeon deliberately leaves some remnant of thyroid tissue in order to avoid operative morbidity. Unfortunately, most reports are retrospective, making it difficult to interpret which procedure is better. A prospective randomized trial to look into the survival difference with these two surgical approaches is almost impossible because the excellent prognosis of the disease requires a very long follow-up and a large number of patients would be needed to show any meaningful statistical differences in outcomes. For patients with low-risk disease such as young patients with a small lesion, near-total thyroidectomy may be adequate. For high-risk patients, those with large, multifocal and extensive tumours, total thyroidectomy followed by radioiodine ablation is recommended. Total thyroidectomy is advocated at our centre for all patients with well-differentiated thyroid cancer, except for those with small lesions and at low risk. The major arguments for total thyroidectomy include the possible presence of microscopic disease in the opposite lobe, the reduced need for adjuvant radioiodine therapy and the ability to use thyroglobulin as a postoperative tumour marker. However, the more extensive surgery involved in total thyroidectomy carries some extra morbidity. In patients with gross disease in both lobes of the thyroid, total thyroidectomy is the best surgical procedure. However, in a young individual with a small primary carcinoma, the question will arise of whether near-total thyroidectomy is sufficient. Surgeons need to consider potential complications when formulating the surgical plan for such patients, weighing the benefits of the aggressive approach against the potential complications of radical surgery.

Most of our patients who undergo total thyroidectomy have unseen thyroid remnants that are identifiable with postoperative radioiodine scanning. This remaining thyroid tissue should then be destroyed with radioiodine.10 If most patients require radioiodine ablation after macroscopic total thyroidectomy, then perhaps such extensive dissection is not necessary and surgery-related morbidity can be reduced. This would also indicate that routine postoperative scanning is unnecessary and all patients should undergo immediate ablation.

Radioiodine scan to localize uptake before ablation is usually performed using an oral radioiodine dose of 2–5 mCi. The uptake of radioiodine is dependent on adequate stimulation by thyroid-stimulating hormone (TSH), so thyroxine replacement should be withdrawn at least a few weeks before the scan. Between 24 and 96 hours after administration of the diagnostic dose, whole-body scan is performed using a large-field-of-view gamma scintillation camera fitted with a high-energy parallel-hole collimator to give spot images of the neck and other areas of uptake. Nevertheless, there is debate as to whether a postoperative, pre-ablation scintigram is necessary.11–13 Relatively low diagnostic doses of radioiodine may impair the ability of the remnant tissue to take up the subsequent therapeutic dose of radioiodine due to sublethal radiation delivered in the diagnostic dose, the so-called “stunning” effect.14–16 There is considerable controversy concerning the dose of radioiodine needed to achieve complete remnant ablation in thyroid cancer patients.17–20

The aim of this study was to look at the completeness of our macroscopic total thyroidectomy based on the incidence of positive diagnostic radioiodine whole-body scan, which is routine in our hospital after total thyroidectomy for thyroid cancer, to determine whether bypassing the diagnostic whole-body scan would reduce time and cost and prevent the stunning effect before patients undergo radio-ablation. We also reviewed the ablative dose of radioiodine in our local practice and examined the complications of our thyroid cancer surgery to date.

Patients and methods

This study was a retrospective analysis of all post-total thyroidectomy patients with well-differentiated thyroid cancers referred for radioiodine ablation between September 1997 and December 2001. Most of these patients had undergone surgery at this institution and the rest were referred from other government and private hospitals. Demographic data were collected and operative notes and histopathological reports were reviewed to confirm tumour size, histological type, regional lymph node metastasis and extra-thyroidal extension. Patients were assessed during the follow-up for any surgical complications. Patients who had incomplete surgery or did not have a well-differentiated tumour were excluded. Of 56 patients for whom records were traced and reviewed, 40 patients were recruited.

Qualitative reports of diagnostic radioiodine whole-body scans were reviewed. The scans were reported as either tracer accumulation in the thyroid bed or in a regional area other than the thyroid bed or distant accumulation. Thyroid hormone replacement therapy was withdrawn for at least 4 weeks...
before the scan to allow the TSH level to rise before scanning. The incidence of residual uptake after total thyroidectomy was determined. Patients with positive scans subsequently received a standard ablative dose of radioiodine (80 mCi $^{131}$I). Ablation success was determined by radioiodine whole-body scan 6–9 months after ablation. A successful ablation was defined as no detectable uptake in the thyroid bed or elsewhere. Patients with successful ablation were compared with those without successful ablation in terms of possible predictive factors such as primary tumour size, age, lymph node status and evidence of extra-thyroidal extension using Fisher’s exact test. A $p$ value of less than 0.05 was considered significant.

**Results**

Of the 40 patients, 34 had undergone surgery at this institution and the remaining six were referred from other hospitals nationwide. There were seven male and 33 female patients, with 19 Malays (47.5%), 14 Chinese (35%), three Indian (7.5%) and four others (10%), including Indonesian, Seranian and other foreigners. The mean age was 38.6 years (range, 14–76 years). Most patients (37, 92.5%) had papillary thyroid carcinoma while the remaining three (7.5%) had follicular carcinoma.

The mean size of the primary tumour was 3.62 cm (range, 0.5–6 cm); 82% of tumours larger than 4 cm had extra-thyroidal extension. Tumour size and patient gender and age were not correlated with the presence of cervical lymph node metastases. Based on the American Joint Committee on Cancer (AJCC) classification, 25 patients had stage 1 disease, 10 had stage 2, four had stage 3 and one had stage 4 disease. Seven patients underwent completion of previous hemithyroidectomy, 23 underwent primary total thyroidectomy and 10 underwent total thyroidectomy with neck dissection.

All patients except one underwent pre-ablative whole-body scan, which was positive in 37 (94.9%). The two patients with negative scans both had small tumours (< 3 cm), no neck node metastases and no extra-thyroidal extension. Both were females with papillary carcinoma; one had undergone completion of thyroidectomy while the other had undergone total thyroidectomy.

The 30 patients who agreed to ablation received the standard dose of 80 mCi radioiodine. Reasons for not undergoing radio-ablation were defaulting follow-up, refusing further intervention and receiving radiotherapy instead. Radioablation was successful in 21 patients (70%). The nine patients who failed primary ablation were subjected to repeat ablation at higher doses until their follow-up scans were negative. They needed up to three ablations. Total ablative doses ranged between 80 and 380 mCi. When patients were compared based on the success or otherwise of initial ablation, there were no significant differences in terms of tumour size ($p = 0.69$), age ($p = 1.0$), lymph node status ($p = 0.23$) and extra-thyroidal extension ($p = 0.64$) (Table).

Two post-total thyroidectomy complications were noted: permanent hypocalcaemia and recurrent laryngeal nerve injury. Permanent hypocalcaemia was found in 15% ($n = 6$) of patients, four after total thyroidectomy and two after total thyroidec
tomy with neck dissection. Three patients (7.5%) had hoarseness of voice during follow-up. Laryngoscopy showed evidence

<table>
<thead>
<tr>
<th>Predictive factors</th>
<th>Standard 80 mCi radioiodine ablation</th>
<th>Total</th>
<th>$p$</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Successful ($n = 21$)</td>
<td>Not successful and &gt; 80 mCi required ($n = 9$)</td>
<td></td>
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<tr>
<td><strong>Tumour size</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt; 4 cm</td>
<td>11 (65%)</td>
<td>6 (35%)</td>
<td>17</td>
</tr>
<tr>
<td>$\geq$ 4 cm</td>
<td>10 (77%)</td>
<td>3 (23%)</td>
<td>13</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 45 years</td>
<td>17 (71%)</td>
<td>7 (29%)</td>
<td>24</td>
</tr>
<tr>
<td>$\geq$ 45 years</td>
<td>4 (67%)</td>
<td>2 (33%)</td>
<td>6</td>
</tr>
<tr>
<td><strong>Lymph node metastasis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nil</td>
<td>11 (85%)</td>
<td>2 (15%)</td>
<td>13</td>
</tr>
<tr>
<td>Present</td>
<td>10 (59%)</td>
<td>7 (41%)</td>
<td>17</td>
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<tr>
<td><strong>Extra-thyroidal extension</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nil</td>
<td>17 (74%)</td>
<td>6 (26%)</td>
<td>23</td>
</tr>
<tr>
<td>Present</td>
<td>4 (57%)</td>
<td>3 (43%)</td>
<td>7</td>
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of vocal cord palsy in keeping with recurrent laryngeal nerve injury. All three patients had large primary tumours with intraoperative evidence of extensive local infiltration to muscles, jugular veins and encasing the recurrent laryngeal nerve.

Discussion

This retrospective study allows the reviewer to look into the local data in Malaysia that were not previously available. There are limited data from similar studies in other Asian countries. The results of this study are helpful in better understanding thyroid cancer in Malaysia and in reaching a common protocol for the management of all thyroid cancers.

Although the number of patients in this study was small, it was sufficient to achieve the study objectives. The sample size was about the same as in most other studies. Our institution has an endocrine unit that takes thyroid cancer patients from all over Malaysia, so 15% of the study sample was referred from other hospitals.

The male-to-female ratio was 1.5, which is comparable to other studies of thyroid cancer, which report ratios of 1.3 and 1:9. There is a higher incidence of thyroid cancer in females than males. However, gender is not a prognostic indicator. Wanebo et al found that mortality from thyroid cancer was significantly lower in female patients who had undergone more extensive surgery than females who had undergone lobectomy. Most of the study population was Malay (47.5%), followed by Chinese (35%), foreigners (10%), and Indians (7.5%). This reflects the population in Malaysia, which consists mainly of Malays followed by Chinese.

The largest age group in this study was 20–30 years old, and the mean age was 38.6 years, which is comparable to that in other studies. In Chao et al’s study, ages ranged from 20 to 60 years with a mean of 39 years. In Grigsby et al’s study, the range was 9–76 years and the mean was 42 years. An age of more than 40 years increases the likelihood of cancer death and recurrence. Hence, age is considered in the prognostic scoring systems AGES, AMES and MACIS. In TNM staging, patients with T4 disease (extending beyond the thyroid capsule) belong to a high-risk group with a long-term (20-year) survival rate of only 57%. This group of patients needs total thyroidectomy and radioiodine therapy. If unilateral lobectomy is performed for papillary thyroid cancer, the incidence of contralateral recurrence is less than 5%, even though the incidence of microscopic multicentric disease can be as high as 40–70%.

More than half of patients (55%) had evidence of neck lymph node metastasis. No relationship was found between tumour size and the incidence of lymph node metastasis. Tumour size was not a predictor of neck lymph node metastasis. Regional lymph node metastasis is one of the factors in the prognostic scoring systems AMES and MACIS. In the TNM staging classification, N1 represents lymph node metastasis. The risk of recurrence is higher in this group of patients. Beasley et al showed that patients with neck node metastasis outside the central compartment of the neck have an approximately six-fold risk of developing recurrence, mostly in the neck. They reported no significant differences in nodal metastasis when gender, family history of thyroid disease and history of radiation exposure were considered.

Most patients (63%) had stage 1 disease, 25% had stage 2, 10% had stage 3 and 2% had stage 4 disease. One patient had a large papillary thyroid carcinoma with distant metastasis in the lung. Patients older than 45 years with nodal metastasis are considered to have stage 3 disease, and those with distant metastasis are considered to have stage 4 disease. These older patients have a poorer prognosis than those younger than 45 years.
Surgeries performed were total thyroidectomy (57%), total thyroidectomy with neck dissection (25%) and completion thyroidectomy (18%). Wanebo et al had 35% total thyroidectomies, 30% near- or subtotal thyroidectomies and 35% lobectomies in their thyroid cancer series. After postoperative 131I ablation, they report 10-year survival rates of 82% in patients who had undergone total thyroidectomy, 78% in those who had undergone subtotal thyroidectomy and 89% in lobectomy patients. The authors concluded that total thyroidectomy did not significantly alter the outcome in patients with thyroid cancer compared with the lesser procedures of subtotal thyroidectomy or lobectomy.

Of patients who underwent pre-ablation whole-body scan, 94.9% had tracer detected in the thyroid bed or at an extra-thyroidal site. Only 5.1% of patients had a negative scan, all of whom had a preoperative tumour size of less than 3 cm, no extra-thyroidal involvement and no lymph node metastasis. Utiger suggests routine pre-ablation 131I scanning to detect any remaining thyroid tissue so that it can be destroyed by radioiodine ablation. However, Kim et al report a false-positive 131I whole-body scan in chronic parotitis and Coover reports that a false-negative total-body scan can be caused by benign thyroid tissue after 131I ablation. Hypofunctioning of residual tissue may be suppressed under euthyroid conditions, protecting it from ablation. This tissue may be stimulated by high TSH levels and begin accumulating 131I, which can produce a false-positive result. We did not detect any false-positive scans in our study population. The stunning effect of preablative 131I can decrease the therapeutic effect of subsequent ablation. Gerard and Cavalieri demonstrated that the effectiveness of ablation is affected by stunning. The absorbed radiation dose depends on the scanning dose administered, the volume of target tissue and the kinetics of radioiodine in the tissue. Gerard and Cavalieri suggested using 123I, which carries less risk of stunning. The importance of and requirement for pre-ablation scanning need to be reviewed in future because 95% of patients have positive scans despite extensive surgery. The advantages of bypassing pre-ablation scan should be considered: avoiding the stunning effect of pre-ablation scanning and reducing the cost of investigation, number of patient visits and time to radioablation. Klerk et al concluded that high-dose radioiodine ablation without a prior diagnostic scintigram results in a high rate of successful ablation. This prevents repeat treatment with 131I and reduces the cost of the procedure and the hypothyroidism burden to patients. Utiger explained the reasons for postoperative ablation: microscopic carcinoma foci in the thyroid remnant can be destroyed because they receive radiation from adjacent normal thyroid tissue; if carcinoma recurs, it is likely to be detectable by radioiodine scanning because there is no more normal thyroid tissue; some carcinoma outside the thyroid bed may be detectable and treated; and, after all normal thyroid tissue has been destroyed, serum thyroglobulin becomes a better marker of recurrent carcinoma.

In our institution, a standard dose of 80 mCi is used for primary radioiodine ablation. This dose was sufficient in 70% of patients, but 30% of patients required repeated ablation at higher doses. Some patients needed up to three ablative doses, and maximum total dose was 390 mCi. Hence, in our institution, the effective dose is between 80 and 390 mCi. In the USA, 29 mCi is the maximum dose that can be given to a patient without admission. In Stael et al’s study, 12 patients needed 25–150 mCi (mean, 44 mCi). Two patients with lung metastasis were treated with up to five doses at a total of 300 mCi. In Taube and Lundell’s study of radioiodine dosage, 63% of patients had successful ablation with 30 mCi, 77% with 50 mCi, 73.7% with 90 mCi and 76.7% with 155 mCi. They concluded that the optimum dose to the thyroid remnant is about 50 mCi (about 30,000 cGy), as higher doses do not appear to yield a higher ablation rate. Johansen et al did not find any difference between low- and high-dose 131I administration in the number of doses needed for complete ablation of residual functioning thyroid tissue. However, Arslan et al used 170 mCi of radioiodine in 242 patients; a single treatment was successful in 74.3% and a second treatment was successful in 17%, giving a success rate of 91.3% with two treatments. They did not use pre-ablative 131I diagnostic scintigraphy, but used ultrasound to measure the thyroid remnant volume, which was significantly different (higher doses were required in larger remnants) (p = 0.04) in those who had successful ablation compared with those who did not. They concluded that fixed high-dose 131I treatment is clinically feasible with an acceptable dose underestimation rate, and ultrasound-determined thyroid remnant volume provides a more accurate and reproducible result.

We did not look into the side effects of radioiodine ablation, which may be dose dependent and may also be found at low doses. Lin et al reported that the side effects of low-dose (40 mCi) oral radioiodine ablation included xerostomia, nausea (5.35%), gastralgia (3.57%), pain in the thyroid bed, tenderness over the parotid gland and submandibular gland, change in taste, and vomiting (1.78%). These effects occur because high concentrations of iodine in the salivary gland can cause sialadenitis after treatment. The maximum reactions occur...
between 24 and 48 hours after therapy and resolve completely within 1 week. The authors suggest that for patients with large remnants, low-dose rather than high-dose $^{131}$I ablation should be chosen to avoid frequent or severe local side effects.

This study also looked into the relationship of tumour size, age, lymph node status and extra-thyroidal extension with successful radioiodine ablation. The total $^{131}$I dose needed for successful ablation is significantly higher in males than females. Patients with higher postoperative thyroglobulin levels and those with a higher stage of disease also require higher doses. There are no correlations between remnant thyroid volume, regional or distant metastases, histopathology and the total $^{131}$I dose needed. In this study, we did not determine the postoperative thyroglobulin level, which may be useful to predict the required dose.

Successful ablation was achieved with standard-dose radioiodine (80 mCi) in 64% of patients with tumours of less than 4 cm and in 77% of those with tumours of more than 4 cm. This difference was not significant. We did not use the ultrasound-determined thyroid remnant volume to predict the required radioiodine dose, as in Arslan et al’s study. The success rate with 80 mCi $^{131}$I was higher in patients aged less than 45 years (71%) than in those aged more than 45 years (67%). This may be due to better responsiveness to treatment and prognosis in those less than 45 years old. The difference was not statistically significant, which may be due to the small sample size.

Patients without evidence of lymph node metastasis had a higher success rate with 80 mCi radioiodine ablation (85%) than those with lymph node metastasis (58%). This may suggest that patients with lymph node metastasis are more resistant to radioiodine ablation and may need a higher dose. However, this difference was not significant.

Patients without extra-thyroidal extension had a higher success rate with the 80-mCi ablative dose (74%) than those with extra-thyroidal extension (57%). This may mean that patients with extra-thyroidal extension need a higher dose. The difference was not significant.

This study also looked into the complications of surgery for thyroid cancer. Permanent hypoparathyroidism was slightly higher than in other studies, which reported rates of 6.6%, 4%, 2.9%, 1% and 1%. These patients had larger tumours with extensive local infiltration to the surrounding structures. In this situation, injury to the nerve is inevitable to achieve good surgical clearance. Less aggressive surgery and radioiodine ablation of the remnant may offer a feasible alternative. Bergamaschi et al found a higher incidence of recurrent laryngeal nerve injury after total thyroidectomy with node dissection than without node dissection. Lo et al reported that only 1% of patients who had postoperative unilateral cord paralysis were recognizable during operations, indicating the difficulty of preventing nerve injury in the enthusiasm of performing aggressive surgery. Other complications such as wound infection, haematoma, bleeding and airway obstruction were not seen in this study.

Conclusion

Almost all patients have positive residual scintigraphy scan of the thyroid bed after total thyroidectomy. Bypassing this pre-ablative scan can avoid the stunning effect, resulting in better radio-ablation and reducing investigation cost and patient time. The present ablative dose of 80 mCi is effective. The patients referred to this tertiary institution usually have large tumours with local infiltration. Hence, aggressive surgery to achieve a clearer surgical margin should be replaced by postoperative radioiodine ablation to avoid unwanted postoperative complications.

References

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Our rate of postoperative recurrent laryngeal palsy (7%) was slightly higher than that in other studies, which reported rates of 6.6%, 4%, 2.9%, 1% and 1%. These patients had larger tumours with extensive local infiltration to the surrounding structures. In this situation, injury to the nerve is inevitable to achieve good surgical clearance. Less aggressive surgery and radioiodine ablation of the remnant may offer a feasible alternative. Bergamaschi et al found a higher incidence of recurrent laryngeal nerve injury after total thyroidectomy with node dissection than without node dissection. Lo et al reported that only 1% of patients who had postoperative unilateral cord paralysis were recognizable during operations, indicating the difficulty of preventing nerve injury in the enthusiasm of performing aggressive surgery. Other complications such as wound infection, haematoma, bleeding and airway obstruction were not seen in this study.