Large remnant $^{131}$I ablation as an alternative to completion/total thyroidectomy in the treatment of well-differentiated thyroid cancer

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**Background.** An alternative to completion thyroidectomy for well-differentiated thyroid carcinoma is to ablate the remnant lobe with $^{131}$I. The purpose of this study is to review our own experience with large remnant ablation.

**Methods.** A retrospective review of 169 patients with well-differentiated thyroid cancer treated at one institution over a 14-year period was undertaken. Seventy-one patients who underwent partial thyroidectomy (PT) followed by $^{131}$I ablation were identified. This group was compared to 98 patients treated with total thyroidectomy (TT).

**Results.** Mean follow-up was 6.2 years for the 71 PT + $^{131}$I versus 4.7 years for the 98 TT patients ($P = .184$). Recurrence occurred in 4 of 71 PT + $^{131}$I patients (5.6%) versus 9 of 98 TT patients (9.2%) ($P = .393$). Other than a tendency for the size of the primary to be slightly larger and for the histology to be follicular carcinoma in the PT + $^{131}$I patients, the 2 groups were nearly identical in age, gender, and other prognostic factors such as capsular invasion and metastases.

**Conclusions.** Large-dose ablation with $^{131}$I is a viable alternative to completion thyroidectomy. Recurrence rates over an average 6-year period are similar to TT. Long-term monitoring of these cohorts is required. (Surgery 2004;136:1275-80.)

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Because of the limitations of fine-needle aspiration cytology, it is not always possible to secure a definitive preoperative diagnosis of malignancy before thyroidectomy.1,3 Furthermore, the intraoperative, frozen-section diagnosis of malignancy can be challenging, thereby limiting the extent of surgery until a definitive diagnosis can be rendered upon review of the final pathology.4,5 In such instances, when a final diagnosis of well-differentiated thyroid cancer (WDTC) is confirmed on permanent section, completion thyroidectomy is often advocated, resulting in the equivalent of a total thyroidectomy.6 Unfortunately, completion thyroidectomy is associated with increased morbidity7,9 and, therefore, as an alternative to reoperation, radiiodine ablation ($^{131}$I) of the contralateral remnant could be considered in place of completion thyroidectomy. The feasibility of large remnant ablation has been shown in a few studies.10,12 Data on long-term follow-up, however, is not available. The purpose of this study is to compare recurrence rates in patients who had undergone partial thyroidectomy (PT) with ablation of the remnant lobe with $^{131}$I to patients who had total thyroidectomy (TT) for WDTC.

**Patients and Methods.**

After receiving approval from the McGill University Hospital Center ethical committee, the authors reviewed the records of the Montreal General Hospital from 1989 to 2003 for patients treated with WDTC who underwent “hemithyroidectomy” followed by $^{131}$I large remnant ablation. Although the extent of resection varied, all patients in this partial thyroidectomy group were left, at a minimum, with an anatomically normal contralateral lobe. Seventy-one patients were identified as having undergone Partial thyroidectomy followed by $^{131}$I ablation.
partial thyroidectomy plus radioiodine (PT +131I) and were compared to a second group of 98 patients who had undergone either total or completion thyroidectomy (the TT group) for WDTC. Patients with incidental, micropapillary cancers were excluded.

All patients were diagnosed, treated, and followed at the Montreal General Hospital. In the PT +131I group, patients at the very least were left with an anatomically normal contralateral lobe as determined intraoperatively through palpation and inspection. After the diagnosis of WDTC was rendered postoperatively, 131I was administered at a dose of 100mCi.

The TT group included 2 patients who had undergone completion thyroidectomy. In this group, central compartment lymph nodes dissection was done. Patients in the TT group received adjuvant 131I if either postoperative serum thyroglobulin concentration was >1.0 ng/mL or neck radioiodine uptake was >1 %. The dose of adjuvant 131I used was 100mCi.

Patients in both groups were followed every 4 to 6 months with physical examination along with serum thyroglobulin and thyroid-stimulating hormone (TSH) measurements. All patients received L-thyroxine suppressive therapy with the aim of achieving a TSH concentration of 0.1 mIU/L or less.

Statistical analysis was performed using SPSS version 12.0 for Windows (SPSS, Inc, Chicago, Ill). Between-group comparisons were assessed by using the chi-square statistic and t test for categorical and continuous variables, respectively. P values of less than .05 were considered to be statistically significant.

A logistic regression model was used to control for potential confounding in the assessment of the association between the primary outcome (recurrence of carcinoma) and potential confounders. A significance level of 5% was set as the maximum for statistical significance. The dependent variable for the model was recurrence of carcinoma (binary variable: recurrence = 1, lack of recurrence = 0). Independent variables included in the model were: patient age and size of the lesion (continuous variables), and surgical procedure, patient gender, presence of metastasis, and intra- versus extracapsular extent of the lesion (categorical variables).

RESULTS

The clinicopathologic profile of both groups are presented in Table I. As expected, women predominated (72.4%) in the TT group, and 81.7% of the PT +131I group were female. There was no statistically significant difference in gender, age, extent of disease, and the presence of metastases between the 2 groups. The mean size of lesions was slightly larger in the PT +131I group compared to the TT group (2.75 ± 1.82 cm vs 2.13 ± 1.09 cm; P = .012). Tumor pathology for each group is presented in Table II. Follicular carcinoma was more common in the PT group compared to the TT group (23.9% vs 3.1%; P < .001), reflecting the difficulty in the frozen-section diagnosis of follicular neoplasms. The follow-up was similar between both groups. Mean ± SD follow-up was 74.3 ± 11.72 months (6.2 years) for the PT +131I versus 56.8 ± 37.8 months (4.7 years) for the TT patients (P = .184).

Recurrence was found in 4 of the 71 patients who underwent PT +131I (5.6%): 3 were pulmonary and 1 was regional. All 4 patients were older than 65 years at diagnosis (range, 67-80), and 3 of the 4 recurrences occurred in patients with papillary cancer. In the TT group, recurrence was noted in 9 of the 98 patients (9.2%). Eight of the 9 patients received adjuvant 131I. There were 2 local recurrences, 5 regional recurrences, and 1 instance of osseous metastases. One recurrence was associated with a rising serum thyroglobulin alone (72.2 ng/mL) without evidence of a specific site of origin. There was no statistically significant difference in recurrence between the 2 groups.

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<th>Table I. Clinical and pathologic prognostic factors of 71 patients treated with PT + 131I and 98 patients treated with TT</th>
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TT, Total thyroidectomy; PT, partial thyroidectomy followed by 131I ablation.

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<th>Table II. Tumor pathology in 71 patients treated with PT + 131I and 98 patients treated with TT</th>
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TT, Total thyroidectomy; PT, partial thyroidectomy followed by 131I ablation.
(P = .393). One death from distant disease was documented in each group. Using a logistic regression model to control for potential confounding variables (age, gender, extent of disease, size and presence of metastases), we found no difference in recurrence between PT + 131I and TT (OR = 0.561; P = .397).

The median serum thyroglobulin concentration after large remnant ablation in the PT + 131I group was 0.2 ng/mL; 68 of 71 patients (95.7%) achieved a level <1 ng/mL after only 1 dose of 100 mCi 131I. In the TT group, 131I was given postoperatively to 65 patients (66%) either because neck radioiodine uptake was >1% or the serum thyroglobulin concentration was elevated.

In the PT + 131I group, adverse effects associated with high-dose radioiodine were noted in 7 patients (9.9%) and included painful thyroiditis in 5 patients, headache and nausea in 1 patient, and transient dysphagia in 1 patient. No instance of sialoadenitis was observed.

DISCUSSION

The extent of surgical resection needed for optimum surgical treatment of WDTC remains controversial. The current trend has been toward more extensive surgery.13 Both the American Thyroid Association and the American Association of Clinical Endocrinology advocate total or near-total thyroidectomy for WDTC.14,15 Thus, if less than a total thyroidectomy is performed (ie, partial thyroidectomy) and if the final pathology on permanent section reveals WDTC, it is advised to proceed to completion thyroidectomy.

Several reasons are cited in favor of completion thyroidectomy. First, residual cancer has been found in up to 45% in the contralateral lobe at completion thyroidectomy,16,17 especially in papillary cancer, which is often multicentric.18-20 Removal of all residual thyroid tissue has been shown to reduce the recurrence rate compared to more limited surgery.21-23 In one large series, local recurrence of low-risk papillary thyroid cancer was decreased from 14% to 2% with TT.22 Second, follow-up of patients with serum thyroglobulin and radioiodine scan requires minimal normal thyroid in situ to maximize sensitivity. Third, detection and treatment of nodal or distant disease are easier when the remaining lobe is removed because one can avoid the “sink” effect when 131I is required therapeutically.

Completion thyroidectomy is not without its costs and is associated with a higher incidence of complications, most notably permanent hypoparathyroidism and recurrent laryngeal nerve injury.7-9 An alternative to completion thyroidectomy is to ablate the anatomically normal, contralateral lobe with 131I. The ablation of a large remnant was heretofore avoided because of the high dose of 131I required and its potential for toxicity.24,25 More recently, however, the feasibility of large remnant ablation has been demonstrated. Randolph et al12 showed that lobar ablation was equivalent to TT in terms of residual radioiodine uptake and serum TSH. The 24-hour radioiodine uptake was less than 1% in 80% of patients undergoing large remnant ablation. Bal et al10 also reported their experience with large remnant ablation in 93 patients. A cumulative success rate of ablation was 100% after 3 doses of about 30 mCi 131I . In the present study, we relied on a single dose of 100 mCi 131I and achieved ablation in 96% of our patients, and rendered posttreatment serum thyroglobulin to a level comparable to that achieved after total thyroidectomy alone. Indeed, 66% of our TT patients required adjuvant postoperative 131I to treat an elevated thyroglobulin or a positive total body scan.

Although the feasibility of large remnant ablation has been demonstrated, no data exist as to its oncologic soundness. Total thyroidectomy is the procedure of choice when there is an unequivocal pre- or intraoperative diagnosis of WDTC. However, in patients in whom the diagnosis is deferred and because of limitations in critical resources at our institution, we pursued a policy of large remnant ablation instead of completion thyroidectomy. With a mean follow-up of 6.2 years, there was no difference in term of disease-free survival between patients who had PT + 131I versus patients who had TT. Both groups were similar in terms of important prognostic factors: age, extent of disease, and distant metastases. There was, however, a difference in the distribution of the histologic types between the 2 groups, namely a preponderance of follicular carcinoma in the PT + 131I group. This is not unexpected given the greater difficulties in securing a definitive pre- and intraoperative diagnosis of follicular carcinoma.

The dose of 131I used for large remnant ablation in this study was 100 mCi. When the volume of the remnant is large, smaller doses are less likely to result in successful ablation.24,25 In 2 series, large remnant ablation was successful in 56.9% and 36% after a single dose of about 30 mCi 131I .10,11

In our series, large remnant ablation was associated with minimal morbidity with less than 10% of patients reporting symptoms. The most common complication was pain and swelling representing
acute radiation thyroiditis originating from the lobe left in situ. This is comparable to that reported by others.\textsuperscript{10,12} Although it can be distressing, it rarely lasts more than a couple of days and is self-limiting.

The limitation of our study is the relatively short follow-up. The median follow-up was 4.3 years in the PT group and 4.2 years in the TT group. Only 49.3\% of the patients in the PT group were followed more than 5 years.

Provided the remnant is anatomically normal, large remnant thyroid ablation with \textsuperscript{131}I is a viable alternative to completion thyroidectomy in patients with WDTC. Recurrence rates over an average 6-year period are similar to TT \pm adjuvant \textsuperscript{131}I over an average 5-year period. Long-term monitoring of these cohorts is required to determine if these recurrence rates remain comparable over a longer period of follow-up because WDTC is notorious for recurring many years after apparently successful treatment.

REFERENCES


DISCUSSION

Dr Jack M. Monchik (Providence, RI). Was ultrasound used to determine a recurrence in the neck after large remnant \textsuperscript{131}I? Was ultrasound used to determine if nodules were present in the remnant before proceeding with \textsuperscript{131}I ablation?
**Dr Ashok R. Shaha** (New York, NY). I think the fact remains that you can ablate the remaining thyroid lobe, that is what used to be called medical thyroidectomy. The basic question is, do you need it or not? Just because you can achieve it does not mean it is necessary.

I am still unclear about your completion thyroidectomy or completion treatment for follicular carcinoma because you did not define whether it was minimally invasive, vascular invasive, or major capsular invasive. Jon van Heerden presented a paper in 1992 before this organization about minimally invasive thyroid cancer where he used the term “non-threatening malignancy with 100% survival.” So, I find it difficult to interpret your paper as to the recurrence, local recurrence and regional recurrence, based on RAI treatment for completion thyroidectomy.

The second question is, in your patients where you used radioactive iodine with extrathyroidal extension, I am a little surprised that at the time of initial surgery if you did notice extrathyroidal extension why you did not consider total thyroidectomy? That along with RAI would be the common procedures one would consider to avoid a high incidence of local recurrence.

The last issue is your numbers are so small in both the groups as far as local recurrence is concerned that it would be difficult to interpret. The regional recurrence that you have reported of 5 patients in 1 group and 2 in the other is affected little with RAI or completion thyroidectomy.

**Dr Quan-Yang Duh** (San Francisco, Calif). My comment relates to the selection of the control group. You have a group who had total thyroidectomy and another group who only had lobectomy. It does not appear that you control for the stage of disease. How was the control group selected?

One of the reasons we do total thyroidectomy is for the ease of follow-up with thyroglobulin. Did you measure thyroglobulin to see if there was any difference between the 2 groups?

**Dr Marco Raffaelli** (Rome, Italy). Some of the questions I have, have already been asked by Dr Shaha. I have 2 additional questions concerning the completeness of the large remnants ablation. You reported a mean serum thyroglobulin level of 0.2 ng/mL after radioactive iodine ablation. But, was this level off levothyroxine treatment? Serum thyroglobulin on levothyroxine is not as accurate as serum thyroglobulin measured in hypothyroid condition, after levothyroxine withdrawal. Moreover, did you perform any radioiodine scan, 6-12 months after large remnant ablation, to verify its completeness?

**Dr Lawrence A. Danto** (Truckee, Calif). I agree with your conclusion, and I understand your dilemma about the small lesion. But let me ask you, in the operating room, do you examine the specimen grossly with your pathologist? Have you learned to know what differentiated thyroid carcinoma looks like grossly so you can anticipate small malignancies?

Do you examine the contralateral lobe by elevating the strap muscles off it so you can see and feel it well? If you look for reasons to remove the contralateral lobe at the first operation, you will get yourself out of this problem most of the time.

**Dr Samuel K. Snyder** (Temple, Tex). It was a nice paper showing how thyroid remnant ablation could be achieved. I am a little concerned about looking at differentiated thyroid cancer recurrence rates in patients with only average follow-ups of 4.7 years and 6.2 years. I assume that there are a number of patients that are less than 5 years at follow-up. So looking at recurrence rates in those patients may not be valid. Can you tell me what percentage of your patients actually had a minimum of 5 years of follow up? That is one question.

My second question is, I am quite so sure that the 2 groups are comparable because 1 of them primarily had a percentage of papillary cancers. It appears like a big enough difference to be significant. I wondered if you had looked at that. And the treatment was a little bit different. All the patients got radioactive iodine in 1 group and in the other group only part of them did. Was the dose different in the total thyroidectomy group that got radioactive iodine, from the lobectomy group?

**Dr Thomas Smith Reeve** (Sydney, Australia). I would just like to ask you, as you have allowed, that you could easily remove the remnant surgically with little morbidity. Why load patients with a significant body burden of radiation that they don’t need?

**Dr LeBlanc.** Dr Monchik asked about the use of ultrasound. For the large remnant group, what was done during surgery was exploration of the contralateral lobe just to make sure that everything was normal, but, in fact, after that, there was no ultrasound to look at if there were any nodules found in the contralateral lobes. Every patient who had a diagnosis of well-differentiated thyroid cancer only received thyroxinomy when final diagnosis was confirmed at frozen section.

Dr Duh asked how we selected the control group and whether we measured thyroglobulin. In fact, we only looked at the data of thyroglobulin in the large remnant ablation group, and the way the control group was chosen is that they were patients who initially had total thyroidectomy.

Dr Shaha asked about our rationale for ablating the remaining intact thyroid lobe and about our small numbers for local recurrence. I agree that the numbers are small. It is true that just because it is feasible, why do it. The main reason we are doing it is because we like to follow patients after surgery with thyroglobulins and, with 1 complete lobe left intact, it is harder to follow patients.

Why are we using large remnant ablation instead of doing surgery? The reason is quite simple. We have, in Montreal, some resource problems, and we don’t have a lot of operating room time, so instead of going back to the operating room to do the completion thyroidectomy, we use this technique instead.

Dr Raffaelli asked how we measured serum thyroglobulin and whether we performed radioiodine scans. That is a good question. In fact, these were measured under suppressive therapy. What we are doing more and...
more is that we are starting to use scans for control, but the problem, at the beginning, is that we were not using scans. Therefore, only a few patients are scanned now. The patients who had large remnant ablation and who were scanned had no uptake.

Dr Danto asked how we examined the specimen and the contralateral lobe. At surgery we mobilize strap muscles to evaluate the contralateral lobe.

Dr Snyder asked about the radioactive iodine dose in both groups. The dose was the same. I didn’t mention it, but in the total thyroidectomy group, in fact, around 66% of the patients received adjuvant radioactive iodine.

Dr Reeve asked about the necessity of radiation therapy. The reason is that we only do this at initial surgery when we are not sure of the diagnosis, if the pathologist cannot tell us if it is a carcinoma. When you know it is a carcinoma, the initial surgery is always total thyroidectomy. It is what we do, but in cases where we are not sure, we do that instead of going back, just because we don’t have the resources to do it.