Cost Savings of Patients With a MACIS Score Lower Than 6 When Radioactive Iodine Is Not Given

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Objective: To assess the cost savings if the current policy of treating patients with a MACIS (metastases, age, completeness of resection, invasion, and size) score lower than 6 using radioactive iodine (RAI) was changed to reflect the findings of recent studies.

Design: Retrospective medical record review.

Setting: Mount Sinai Hospital, Toronto, Ontario.

Patients: Between January 1, 2002, and July 1, 2005, 199 consecutive patients with a MACIS score lower than 6 who received RAI treatment after total thyroidectomy.

Main Outcome Measures: Patient demographics were analyzed. Costs for the dose of RAI, hospital stay, and health insurance claims were included in the calculations.

Results: For 199 consecutive patients, the cost for sodium iodide 131 treatment totaled Can$161,588, and the required 2-day stay in isolation totaled Can$764,558. The overall cost to the health care system was Can$934,106, which translates into approximately Can$4,694 per patient.

Conclusions: By following the recommendations of recent evidence-based studies and by ceasing to treat patients with a MACIS score lower than 6 after total thyroidectomy using RAI, cost savings can be accrued for health care systems involved in the treatment of thyroid cancer. Alternate strategies, such as treating patients who need RAI therapy on an outpatient basis and reducing the dose of RAI, can lower costs as well.

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Previous studies have concluded that radioactive iodine (RAI) treatment in patients with well-differentiated thyroid carcinoma (WDTC) and a MACIS (metastases, age, completeness of resection, invasion, and size) score lower than 6 is unnecessary because it does not decrease the rate of recurrence or affect survival. Well-differentiated thyroid carcinoma accounts for approximately 90% of all thyroid malignant neoplasms. This type of thyroid cancer tends to grow slowly and takes a long time to become clinically significant. Papillary and follicular carcinoma fall under the umbrella of WDTC, which often manifests as asymptomatic nodules. The current accepted treatment of WDTC is surgery. Controversy arises about the necessity and extent of surgery, including central compartment and lateral neck dissections, and the indications for adjuvant RAI treatment.

There are several reasons for administering RAI treatment in the postoperative setting. First, it destroys residual thyroid tissue so that subsequent sodium iodide 131 (131I) scanning can detect persistent disease. Radioactive iodine treatment also destroys occult microscopic carcinoma, decreasing disease recurrence. Second, RAI therapy enables follow-up using the serum thyroglobulin level as a sensitive tool for detecting recurrent disease. Testing the serum thyroglobulin level in patients with residual thyroid tissue could be problematic. Third, RAI treatment in the postoperative setting facilitates the use of a high therapeutic dose of RAI that may be necessary for ablation of subsequent persistent carcinoma.

The effect on survival rates of the postsurgical management of WDTC using RAI treatment has been debated for decades. Recent studies demonstrate that postoperative 131I treatment should be reserved for high-risk patients to decrease recurrence and death rates. It has also been reported that the long-term prognosis in low-risk patients after total thyroidectomy alone is favorable and that RAI treatment does not confer an added benefit. Hay et al. showed that RAI treatment in low-risk patients with a MACIS score lower than 6 does not decrease the recurrence rate or improve survival.

Health care institutions are constantly dealing with the reality of resource accountability. Therefore, we sought to assess the financial burden of ablation therapy at our institution (Mount Sinai Hospital, Toronto, Ontario) in treating patients with a MACIS score lower than 6 after total thyroidec-
tomy using RAI. The objective of our study was to provide insight into the possible cost savings that could be realized by following the recommendations of current evidence-based studies and by ceasing postthyroidectomy RAI treatment in this patient group. In addition, by accounting for the costs involved in treating patients using RAI, we explored potential ways for institutions to save money when RAI treatment is indicated.

METHODS

A retrospective medical record review of the thyroid cancer database at Mount Sinai Hospital between January 1, 2002, and July 1, 2005, was performed. To be included in the study, patients with WDTC had to have a MACIS score lower than 6 and treatment with total thyroidectomy followed by RAI. Data from 241 consecutive patients with WDTC were collected, but only 199 patients were included in the study. Forty-two patients were excluded because they had MACIS scores of 6 or higher.

Relevant patient demographics (age, sex, and date of surgery), tumor data (type, size, histologic findings, multifocal tumors, and extrathyroidal spread), treatment modalities (total thyroidectomy, adjuvant 131I therapy, and dose in megacuries), and outcomes (survival) were collected primarily from the pathology and surgical reports. The MACIS score was calculated as follows: 3.1 (if age ≤ 39 years or 0.08 × age if age ≥ 40 years) + 0.3 × tumor size (in centimeters) + 1 (if completely resected) + 1 (if locally invasive) + 3 (if distant metastases present).1,2

The costs of each specific dose of RAI, as well as the Provincial Health Care system claims totals, were then calculated. The accounting department was consulted for the costs of a 2-day hospital stay, and the Department of Medical Imaging was consulted for the 2005 costs per dose of RAI treatment. The study was approved by the Mount Sinai Hospital research ethics board before collecting data from patient files.

RESULTS

Patients (n = 99) with a MACIS score lower than 6 following total thyroidectomy for WDTC were included in the study. There were 161 women and 38 men in the study. The mean age was 42 years (age range, 17-73 years). The mean MACIS score was 4.51 (range, 3.25-5.90).

The breakdown of costs for hospital stay and RAI treatment is given in Table 1. The mean length of stay in the hospital for patients receiving RAI treatment after total thyroidectomy was 2 days. The treatment required isolation plus registered nurse care for a minimum of 3 h/d. This resulted in a cost of Can$3842 per patient and Can$764 558 for 199 patients for hospital costs alone. Included in the costs are Ontario Health Insurance Plan billing 350 69 650 Registered nurse care, 6 h 300 59 700 Private room, 2 d 580 115 420 Hospital stay during treatment, 2 d 2612 519 788 RAI Treatment Cost

The breakdown of the costs of RAI treatment is given in Table 2. Overall, the mean RAI dose given was 100 mCi at a cost of Can$822 per patient. In total, the cost of RAI treatment per patient, including shipping costs of RAI (Can$30 per patient), amounted to Can$852 per patient and Can$169 548 for 199 patients. Table 3 gives the difference in cost of RAI treatment when a mean dose of RAI (100 mCi) is used vs the actual dose of RAI (Can$169 548 vs Can$167 558), a negligible difference. Therefore, the overall cost to our institution for the 43-month period amounted to Can$934 106, which translates into Can$4694 per patient.

Table 4 gives the cost per dose (in megacuries of 131I capsules (in 2005) and the number of patients with a MACIS score lower than 6 receiving 131I treatment. One hundred twenty-eight of 199 patients with a MACIS score lower than 6 received 3700 MBq, amounting to Can$105 280. Thirty-five patients received less than 3700 MBq, whereas 32 patients received greater than 3700 MBq. The total cost for 199 patients to receive RAI treatment amounted to Can$161 588. Furthermore, the mean dose of 131I was 3700 MBq (range, 3644-3755 MBq) among 199 patients with a MACIS score lower than 6 and 3885 MBq (range, 3777-3992 MBq) among 42 patients with a MACIS score of 6 or higher during 43 consecutive months.

COMMENT

Most patients with WDTC such as papillary thyroid cancer and follicular thyroid cancer have a good prognosis.1,5 Papillary thyroid carcinoma accounts for 80% of cases and spreads via the lymphatic system, whereas follicular carcinoma accounts for 11% of cases and tends to spread through the blood.4 According to the US National Cancer Database, the 10-year survival rates are 93% for patients with papillary thyroid carcinoma and 85% for patients with follicular thyroid carcinoma.5

The current accepted approach for treating most WDTC is surgery, with the possibility of adjuvant RAI therapy. Following surgery, the MACIS score allows one to identify whether patients are at high risk or low risk for recurrent disease.1,2,13 Other scoring systems exist as guides to help clinicians establish prognosis,5,14 including the EORTC (the earliest classification, developed by
the European Organization for Research and Treatment of Cancer center), TNM stage (updated in 2003), AGES (age, grade, extension, and size, developed in 1987 by the Mayo Clinic), AMES (age, metastases, extent, and size, developed in 1988 by Cady and Rossi15), and the system by Mazzaferri and Jhiang.7 Although all of the schemes have been reported to be effective at identifying patients at low risk of death, the EORTC and MACIS systems identify a broader spectrum of risk groups.2 Furthermore, the MACIS system is considered an accurate prognosis scoring system because it accounts for surgical removal of all tumor tissue, which seems most important for a favorable outcome.16

At our institution, RAI treatment is indicated for papillary carcinoma greater than 1.5 cm or for multifocal disease regardless of the size. Radioactive iodine treatment is usually given 6 to 8 weeks after surgery to ablate any persistent thyroid tissue to facilitate long-term monitoring for recurrence.5,7-10 These reasons for administering RAI treatment are important for treating and then monitoring patients who are at high risk for disease recurrence. However, for low-risk disease, it has been shown that RAI treatment is less likely to confer notable advantage and that the risks of the RAI therapy may outweigh the perceived benefits.2,11

In support of recent evidence-based medicine, an approach for reducing the economic burden to our health care system is to discontinue administering RAI treatment after total thyroidectomy in patients with a MACIS score lower than 6. In the United States, the incidences of death due to thyroid cancer in men and women are 0.17% and 0.26%, respectively.17 Hay et al2 found at 10 years after surgery that the cause-specific survival in the low-risk group is 100% whether or not ablation is performed. Furthermore, they reported that 84% (1917 of 2286) of patients analyzed during 5 decades (1950-1999) had a MACIS score lower than 6 and a 10-year rate of cause-specific survival approaching 100% whether or not RAI treatment was given.2 Tumor recurrence was estimated at 7% to 8%.2 Similarly, in a retrospective study5 of the French population, an overall survival rate among middle-aged adults with thyroid carcinomas was reported to be 80% to 95%. With this in mind, the evidence suggests that patients with a MACIS score lower than 6 do not reap added benefits from a more aggressive treatment approach using adjuvant RAI therapy.

An additional strategy to minimize the costs is the administration of RAI treatment as an outpatient procedure. Outpatient therapies using high doses of131I have been shown to be safe provided that patients comply with precautions, understand the risks involved, and have a suitable home environment.18 As of May 1997, the US Nuclear Regulatory Commission amended its regulations so that patients could receive RAI therapy on an outpatient basis provided that the total effective dose equivalent to any other individual resulting from exposure to the treated individual does not exceed the 5.0-mSv (to convert millicurie equivalents to millicurie, multiply by 100) limit.19,20

Minimizing the dose of RAI given to patients with low-risk disease is another strategy to reduce the financial burden to the health care system.21 Although the dose of RAI used at our institution is similar to doses reported in the

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<tr>
<th>Variable</th>
<th>Mean Dose (3700 MBq)</th>
<th>Actual Dose</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Per Patient, Can$</td>
<td>For 199 Patients, Can$</td>
</tr>
<tr>
<td>Cost of RAI plus shipping</td>
<td>852 &amp;</td>
<td>169 548</td>
</tr>
<tr>
<td>Hospital cost</td>
<td>3842</td>
<td>764 558</td>
</tr>
<tr>
<td>Total</td>
<td>4694</td>
<td>934 106</td>
</tr>
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</table>

Table 3. Total Hospital and Radioactive Iodine (RAI) Treatment Costs for 199 Patients

a Cost of the mean dose (3700 MBq) of RAI.

<table>
<thead>
<tr>
<th>Dose, MBq</th>
<th>Cost per Dose, Can$</th>
<th>No. of Patients Receiving Dose</th>
<th>Patients per RAI Dose, %</th>
<th>Total Costs, Can$</th>
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<td>1110</td>
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<tr>
<td>Total</td>
<td>...</td>
<td>199</td>
<td>...</td>
<td>161 587 70</td>
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</table>

Table 4. Cost Per Dose of Sodium Iodide 131 (131I) Capsules (in 2005) and Number of Patients Receiving 131I With a MACIS (Metastases, Age, Completeness of Resection, Invasion, and Size) Score Less Than 6

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literature, there is little evidence to demonstrate that 3700 MBq has superior benefit over lower doses of RAI in patients with a MACIS score lower than 6. However, Mazzaferri and Jhiang found that low doses of 131I (29-50 mCi [to convert to mega becquerels multiply by 37]) were as effective as high doses (51-200 mCi) in controlling tumor recurrence (7% vs 9%) in patients with stage 2 or stage 3 tumors.

In addition to the monetary costs associated with postsurgical RAI treatment, the cost to the patient includes the adverse effects of the treatment. The concern is that patients may be unnecessarily exposed to irradiation and to its inherent complications. A portion of patients experience adverse effects from RAI treatment. The incidence of local adverse effects increases as the dose of RAI increases. These adverse effects include nausea (67% of patients), taste dysfunction (approximately 50%), radiation thyroiditis and neck pain (≈ 20%), saliadenitis that may produce chronic xerostomia (12%), and skin changes. Less common adverse effects include leukemia and decreased sperm count due to testicular damage after RAI therapy.

Rubino et al found a statistically significant relationship between the long-term effects of 131I administration and colorectal cancer, salivary gland cancer, and second primary malignancy of bone and soft tissue. In a European cohort of 6841 patients with thyroid cancer, they concluded that absolute risks of 14.4 for solid cancer and 0.8 for leukemia exist per gigabecquerel of 131I and 10^6 person-years of follow-up. These results demonstrate the need for careful evaluation of the extent of thyroid disease when deciding the dose of 131I treatment after surgery.

As previously suggested by others, the management of WDTC should be based on risk group analysis rather than on individual physician or institutional protocols. Based on the surrounding evidence, we are of the opinion that patients with a MACIS score lower than 6 should not receive postsurgical RAI treatment because the prognosis after surgery is close to 100%. Moreover, if RAI therapy is warranted, then treating patients on an outpatient basis would lower the costs, and so would reducing the dose of RAI administered. At our institution, we accrued close to Can$1 million in health care costs associated with hospitalization and RAI treatment during 43 months. By adopting evidence-based practices, a substantial amount of resources could be saved by health care systems on a national level.

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Author Contributions: Drs Pace-Asciak and Payne had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Pace-Asciak, Payne, Walfish, and Freeman. Acquisition of data: Pace-Asciak, Payne, Eski, Walfish, Damani, and Freeman. Analysis and interpretation of data: Pace-Asciak, Payne, Eski, and Freeman. Drafting of the manuscript: Pace-Asciak, Payne, Walfish, and Freeman.

Critical revision of the manuscript for important intellectual content: Pace-Asciak, Payne, Walfish, Damani, and Freeman. Statistical analysis: Payne.

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REFERENCES