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Treatment of Toxic Multinodular Goiter (Plummer's Disease): Surgery or Radioiodine?

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The records of patients treated at the Mayo Clinic for toxic multinodular goiter during 1950–1954, 1960–1964, and 1970–1974 were reviewed to compare results of surgical and ^{131}I therapy, to define trends in treatment policy and outcome, and to attempt to elucidate factors associated with posttreatment hypothyroidism. The series involved 446 patients who underwent thyroidectomy as initial treatment and 89 who initially received ^{131}I. The time to success was significantly shorter ($p = 0.001$) in surgically treated patients than in patients initially receiving ^{131}I. Compared with patients treated medically, patients treated initially with surgery were much less likely to require a second treatment (0% versus 24%) during the first year after initial treatment. The probability of postthyroidectomy hypothyroidism increased from approximately 12% in the 1950s to more than 70% in the 1970s at 2 years after surgery. Neither more aggressive surgery nor use of more sensitive tests to diagnose hypothyroidism accounted for the increased probability in recent years.

Since the initial description by Plummer in 1913 [1], toxic multinodular goiter has been regarded as an important cause of hyperthyroidism and currently is estimated to account for 5–30% of patients with thyrotoxicosis [2]. Despite this frequency, proper management remains controversial. Whereas most patients with diffuse toxic goiter (Graves' disease) are treated nonsurgically, it is not clear whether subtotal thyroidectomy or radioiodine constitutes the proper treatment for toxic multinodular goiter [3–7].

Proponents of surgical therapy cite a low recurrence rate as the major advantage of this treatment modality. They also believe that radioiodine therapy is less effective, requires large doses, and is associated with minimal reduction in goiter size [6]. However, subtotal thyroidectomy is not without morbidity or mortality.

We reviewed 3 decades of our experience with the treatment of toxic multinodular goiter, comparing results of both surgical and ^{131}I therapies, defining trends in treatment policy and outcome, and attempting to elucidate factors associated with posttreatment hypothyroidism.

Materials and Methods

The medical records of all patients treated at the Mayo Clinic for toxic multinodular goiter during the time intervals 1950–1954, 1960–1964, and 1970–1974 were reviewed. Laboratory evidence supporting the diagnosis of hyperthyroidism was obtained in the vast majority of cases (89% of patients in the first study period, 93% in the second, and 86% in the third). Failure to obtain laboratory support for the clinical diagnosis of thyrotoxicosis was most commonly due to patients having already received antithyroid drugs or therapeutic iodine. The basal metabolic rate was the test most frequently used in the 1950s, the basal metabolic rate and the protein-bound iodine level in the 1960s, and the serum concentration of total thyroxine (T_4) in the 1970s.

Patients were excluded if they had endocrine ophthalmopathy (suggesting Graves' disease occur-

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ring in a multinodular goiter), if internodular thyroid hyperplasia was observed during histologic examination of surgical specimens from patients not receiving antithyroid drugs, or if evidence was insufficient to support the diagnosis of thyrotoxicosis.

In comparing patient characteristics and pretreatment laboratory test results between treatment groups, chi-squared tests and analysis of variance tests were performed on categorical and continuous variables, respectively. The comparison between actual and estimated gland weights is based on the paired *t*-test. The assessment of treatment "success" and the development of posttreatment complications (for example, hypothyroidism) are described by use of Kaplan-Meier methods [8], which appropriately use information from observations with incomplete follow-up (censored data). Statistical assessments of differences between treatment groups on posttreatment measures are based on the log-rank test [9] for censored data. The associations between ^{131}I success and the continuous variables (estimated gland weight, ^{131}I uptake, and ^{131}I dose) were assessed by the Cox regression model [10].

A treatment has been defined as being a "success" if, after treatment, the patient is no longer hyperthyroid. Since our follow-up assessments are episodic (based on physician visits or patient interview) rather than continuous, the date of treatment success has been reported in 2 ways: (a) first date when patient was found to be euthyroid or hypothyroid (conservative estimate) and (b) last date when patient was found to be hyperthyroid (liberal estimate). For purposes of analysis of the initial treatment, we have used the conservative estimate of success. A patient was considered censored when he or she had unknown thyroid status or had died. Patients receiving a second treatment for hyperthyroidism were considered unresolved with regard to their initial treatment for their entire follow-up, although they may have become euthyroid or hypothyroid after the second treatment.

Results

From 1950 to 1974, the number of patients seen at the Mayo Clinic with toxic multinodular goiter decreased dramatically (Table 1). As expected, women outnumbered men by approximately 4:1. The mean patient age increased from 61 to 71 years. The mean 24-hour thyroidal uptake of radioiodine in patients with toxic multinodular goiter was lower in patients seen in the 1970s than in the 2 previous study periods. From the earliest study period to the most recent, there was a decline in the number of patients undergoing thyroidectomy (90% to 63%).

Table 1. Characteristics of patients treated initially by radioiodine or surgery during 3 treatment periods.

	Treatment period		
	1950–1954	1960–1964	1970–1974
No. of patients	334	142	59
Females (% of patients)	257 (77%)	114 (80%)	46 (78%)
Mean age (yr)	61	64	71
Mean ^{131}I uptake (%)[a]	32.8	36.3	26.2
Initial treatment			
Surgery	302 (90%)	107 (75%)	37 (63%)
^{131}I	32 (10%)	35 (25%)	22 (37%)

[a]24-hr diagnostic ^{131}I uptake.

Follow-Up

Of the 89 patients initially treated with radioiodine, 69 were alive and had information about thyroid status available 1 year after treatment. This number decreased to 39 at 5 years and to 20 at 10 years. During the first year, 10 patients had died and an equal number either were lost to follow-up or had unknown thyroid status. At 5 years after treatment, 21 patients had died and 29 were lost to follow-up; at 10 years, these numbers were 34 and 35, respectively.

Of the 446 patients initially treated surgically, 363, 276, and 204 were still being followed at 1, 5, and 10 years, respectively. At these same time points, 10, 38, and 82 had died, and 73, 132, and 160 had been lost to follow-up.

Treatment Data

Patients selected for treatment with ^{131}I were older, more likely to have heart disease, and more likely to be hospitalized at the time of diagnosis than patients undergoing surgery (Table 2). There were no significant differences in the frequency of other medical illnesses between the 2 groups.

Patients treated with ^{131}I received a mean dose of 37 millicurie (mCi) (range 6.3 to 150 mCi). The breakdown by initial ^{131}I dose was 4, 23, 32, 16, and 14 patients with dose of 6.3–10, 11–20, 21–30, 31–50, and 51–150 mCi, respectively. Of the patients treated surgically, 95.5% underwent subtotal thyroidectomy, 4.2% underwent lobectomy, and 0.3% had total thyroidectomy.

Among all patients, the time to success was significantly shorter ($p = 0.001$) for surgical patients than for ^{131}I-treated patients. The hyperthyroidism in 50% of patients treated surgically was judged to be resolved within 45 days, whereas it took more than 4 months for the same proportion of

Table 2. Patient characteristics and outcomes according to initial therapy.

	Radioiodine	Surgery
Mean age (yr)	70	61[a]
Cardiovascular disorder (%)	57	27[a]
Hospitalized at diagnosis (%)	28	13[a]
Probability[b] of success by 1 yr (%)	57–64	74–95[a]
Probability[b] of success by 5 yr (%)	64–70	89–97[a]
Probability[b] of requiring 2nd treatment by 1 yr (%)	24	0[a]
Probability[b] of hypothyroidism by 1 yr (%)	16	16

[a]Significantly different from radioiodine treatment value (2-tailed t-test, $p < 0.001$).

[b]Determined actuarially; range for success based on conservative and liberal estimates; p value holds for both estimates.

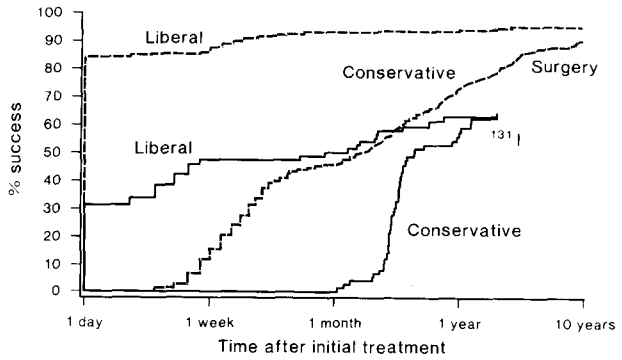

Fig. 1. Range of probability of becoming hypothyroid or euthyroid for patients with toxic multinodular goiter who were initially treated with radioiodine (between solid lines) or surgery (between dotted lines).

^{131}I-treated patients to become euthyroid or hypothyroid. However, at 1 year after treatment, the probability of success estimated actuarially was closer (57 ± 6% for ^{131}I; 74 ± 2% for surgery). Since use of the date that the patient was first known to be euthyroid or hypothyroid may overestimate the time required for treatment to be successful (that is, the hyperthyroidism resolves before the patient is seen in follow-up), a graph was constructed (Fig. 1) using the date when the patient was last known to be hyperthyroid and separately using the time first known to be euthyroid or hypothyroid. This was done for both forms of initial treatment. This graph provides a range of probability of success and acknowledges some of the limitations in defining exactly when hyperthyroidism resolves. A graph describing the actual duration of posttreatment hyperthyroidism would probably show the duration to be midway between the liberal and conservative estimates on Figure 1, but this is speculation. The graph describing probability of treatment success for ^{131}I-treated patients stops at 1 year because of the small number of patients.

There was no statistically significant association between probability of successful ^{131}I treatment and decade of treatment, estimated gland size, ^{131}I uptake, or dose of ^{131}I given, when each was considered separately.

Twenty-two of the patients initially treated with ^{131}I required a second treatment. Twenty of these were retreated within 1 year (persistent hyperthyroidism): 15 underwent surgery and 5 received a second ^{131}I dose. The other 2 patients received a second ^{131}I dose more than 2 years after the initial treatment (recurrent hyperthyroidism). In 5 of the 7 patients receiving a second dose, ^{131}I treatment was successful within 1 year of retreatment (1 patient died within 30 days, and the other was still hyperthyroid at 90 days and lost to follow-up). In 13 of the 15 patients who underwent surgery as the second treatment, success was achieved within 1 year of the surgery (1 died after 3 days, and the other died at 8 months). A few patients were given ^{131}I as the initial treatment because they were too ill to undergo thyroidectomy. It was only after considerable improvement of the hyperthyroidism resulting from ^{131}I treatment that the patients underwent surgery. In the few patients initially treated with thyroidectomy who required a second treatment, recurrences were noted more than 6 years after initial surgery, and all of these patients were treated with ^{131}I.

Complications of Treatment

Considering the initial treatment only, the actuarial probability of developing hypothyroidism at 1 year was 16% after ^{131}I therapy and 16% after thyroidectomy. Among patients requiring a second treatment after initially failing to respond to ^{131}I, hypothyroidism developed in 10 patients within 1 year after surgery and in 2 within 1 year of a second dose of radioiodine. Among patients in whom hypothyroidism developed after initial ^{131}I therapy, the diagnosis had been made within 6 months of being classified as euthyroid. In contrast, patients treated surgically continued to have slight increases in the probability of being discovered to be hypothyroid with continued follow-up (26% at 10 years).

Complications developing only in patients treated surgically were permanent vocal cord paralysis in 2.3%, permanent hypoparathyroidism in 0.5% (temporary hypoparathyroidism in another 2.5%), and significant postoperative bleeding in 1.4%. Other complications occurred in an additional 4.3% of this

group, including the need for postoperative tracheostomy (6 patients), postoperative stroke, wound infection, and wound hematoma (2 patients each), and postoperative myocardial infarction, death, atrial fibrillation, and confusion (1 patient each). No differences in the frequency of surgical complications were observed among the treatment intervals.

Gland Size and Histologic Findings

The weight of thyroid tissue removed during surgery was considered to be very close to the actual weight of the thyroid because the vast majority of patients underwent subtotal thyroidectomy, and only a few grams of tissue on either side of the neck were left behind. The average weight of the thyroid removed at initial surgery (n = 442) was 113 g, with a range of 5 to 639 g. An unexpectedly large number of glands (124 specimens) weighed less than 50 g, and 51 glands weighed less than 30 g. Although all specimens were initially interpreted as adenomatous goiter (3 had incidental thyroid carcinomas), the number of smaller-than-expected weights raised the possibility that some specimens of Graves' thyroid could have been classified as multinodular goiter. However, a review of 58 randomly selected pathologic specimens from glands weighing less than 50 g uncovered no instances of hyperplastic goiter being misclassified as adenomatous goiter.

An analysis of predicted gland weight, actual gland weight, and difference between predicted and actual weights (when available) was performed. There was a tendency to underestimate gland weight, which was statistically significant ($p < 0.001$, paired t-test). Seventy-five percent of the preoperative estimates of gland weights were less than the actual weight, and over 50% of the estimates were more than 25 g below the actual weight. The average estimated gland weight of patients initially treated with ^{131}I was 61.4 g, compared with 88.3 g for glands of patients treated surgically. The actual average gland weight of patients initially undergoing thyroidectomy was 113 g. Of the 223 patients whose initial treatment was surgery and whose preoperative estimates of thyroid weight were recorded, the average underestimation of gland weight was 39 g. For the 8 patients who underwent thyroidectomy after ^{131}I treatment failure and whose preoperative thyroid weights were estimated, the average underestimation was 70 g.

Discussion

Despite the decreasing number of patients currently being seen at the Mayo Clinic for the treatment of toxic multinodular goiter, it remains a not uncommon cause of thyrotoxicosis. Toxic multinodular goiter is a more frequent cause of hyperthyroidism in certain geographic areas. This is presumed to be related to the lower intake of iodine [2]. Selection of the most appropriate therapy for an individual patient may be facilitated by knowledge of the probable outcomes of the treatment options. Antithyroid drugs are generally not used for the long-term treatment of toxic multinodular goiter. Information is available in the literature describing the results of surgical [3, 11, 12] or radioiodine [4, 13, 14] treatment of toxic multinodular goiter. The study [5] comparing the results of both types of treatments for thyrotoxicosis included patients with both Graves' disease and toxic multinodular goiter, without identifying the 2 groups.

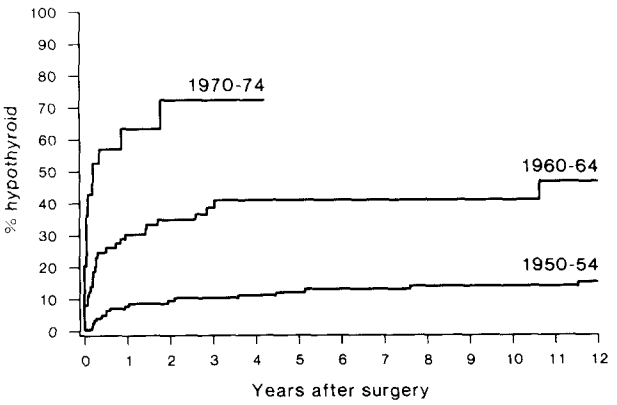

Fig. 2. Probability of developing postoperative hypothyroidism (by decade) in patients with toxic multinodular goiter.

Rapid control of thyrotoxicosis is considered to be a major advantage of thyroidectomy, but few studies report the actual time interval to success. The study by Green and Wilson [5] reported that 68% and 78% of patients treated surgically were euthyroid 6 months and 1 year after surgery, respectively. This is almost identical to the probability of success of initial thyroidectomy at 1 year in our series, but patients with Graves' disease were included in the Green and Wilson study [5]. At least half of the patients treated surgically at our institution were no longer thyrotoxic 6 weeks after surgery, and the probability of success at 1 year was between 74% and 95% (Fig. 1). The complication rates from surgery in our series are comparable to those reported from other institutions with large series [3, 11, 12]. Recurrence of thyrotoxicosis after thyroidectomy was rare in our patients.

In our study, the occurrence of postoperative hypothyroidism during long-term follow-up appears to be increasing in recent years (Fig. 2). The low probability of hypothyroidism after thyroidectomy

at our institution in the early 1950s is similar to that reported in some series [5, 15], while the increasing probabilities occurring in the 1960s and 1970s are similar to or higher than rates reported by other authors [3, 16]. Although an increasing frequency of posttreatment hypothyroidism in recent decades has been reported with ^{131}I therapy of toxic multinodular goiter [17], we are not aware that a similar finding has been reported after thyroidectomy. It is interesting to note that the frequency of hypothyroidism after surgery [18, 19] or radioiodine therapy [20] for Graves' disease also has increased during the decades at our institution, despite little apparent change in technique. If more aggressive surgical technique were responsible for this increase, we might see an increased frequency of complications, such as permanent vocal cord paralysis or hypoparathyroidism. This was not the case. Review of the laboratory measures used to confirm the diagnosis of hypothyroidism did not reveal an increasing tendency to diagnose subclinical hypothyroidism (that is, asymptomatic patients with mildly elevated levels of thyroid-stimulating hormone) in the 1960s or 1970s. This is evidence against more sensitive measurements being a primary explanation for the increasing rate of postoperative hypothyroidism in more recent years. Increases in the iodine intake may be partially responsible for the increased frequency incidence of posttherapeutic hypothyroidism [17, 20].

The use of ^{131}I for toxic multinodular goiter has never been the preferred therapy at our institution. Its increasing use in recent decades likely reflects hesitancy to recommend surgery to the older patients being treated at that time (Table 1). Concern that larger doses and multiple treatments may be necessary are borne out in the literature [4, 13, 14]. Compared with ^{131}I therapy for Graves' disease, ^{131}I therapy for toxic multinodular goiter had a longer duration of hyperthyroidism in some studies [14] but not in others [13]. The duration of hyperthyroidism after ^{131}I treatment in our series was similar to that observed by Holm et al. [13], but less than that in another series [14]. Patients receiving ^{131}I as initial treatment were hyperthyroid for a slightly longer time than those undergoing thyroidectomy (Fig. 1).

Retreatment with ^{131}I cures virtually all patients of hyperthyroidism [4, 13, 14], although as many as 5 or 6 doses may be required. In our series, the actuarial probability of requiring additional treatment within 1 year was 24%. Eller et al. [4] and Bliddal et al. [14] reported only 39% and 38%, respectively, of patients cured with a single ^{131}I dose. The higher average dose given to our patients (37 mCi) may partially account for the larger probability of success after a single treatment. When a second treatment was required, success was very likely. Outcomes of patients who received an additional dose of ^{131}I were favorable.

The probability of developing hypothyroidism within 1 year after initial ^{131}I therapy was 16% in our patients, with no apparent difference among the 3 time periods. This is in contrast to the observations of Holm and associates [13], which showed an increasing incidence of hypothyroidism during the same time periods, although it was less striking in patients with toxic multinodular goiter than in those with Graves' disease. In our series the small number of patients who actually became hypothyroid after ^{131}I therapy does not allow for a reliable statistical comparison among decades, as opposed to the large numbers of patients in the series of Holm and co-workers. A second treatment, whether surgical or ^{131}I, was very likely to result in permanent hypothyroidism.

It is generally believed that hyperthyroidism in multinodular goiter is uncommon in glands weighing less than 100 g [6]. While the actual weight of thyroids in our study averaged more than 100 g, 28% of the glands weighed less than 50 g. The absence of histologic evidence of Graves' disease, as well as a lower uptake of ^{131}I in our series (Table 1), compared with that of patients with Graves' disease treated at our institution from the same periods (approximately 62% during each decade) [20], is consistent with a diagnosis of toxic multinodular goiter and makes it unlikely that a significant proportion of our patients could have had Graves' disease in a previous multinodular goiter. Eller et al. [4] reported that the average estimated weight of the thyroid glands of their patients with toxic multinodular goiter was 53 g.

Our experience with estimating thyroid weight would prompt us not to rely too heavily on estimated weights. The large discrepancy (70 g) between the predicted and the actual weight in patients undergoing thyroidectomy after ^{131}I treatment failure may demonstrate a consequence of this error. Since ^{131}I dose is usually based on estimated gland size and thyroidal ^{131}I uptake, a gross underestimation would result in an insufficient ^{131}I dose, thereby predisposing to treatment failure. The inability to estimate thyroid size accurately in all patients may explain the lack of association between ^{131}I treatment outcome and ^{131}I dose, ^{131}I uptake, and gland size.

Despite the apparent selection of patients for ^{131}I treatment who were at increased surgical risk (Table 2), these patients fared reasonably well. This group was significantly older, with a higher frequency of heart disease, allowing a shorter average follow-up than for patients treated surgically. It is unlikely that these confounding influences would

make the probability of successful ^{131}I therapy of toxic multinodular goiter worse than our analysis indicates.

In summary, our retrospective study showed that, by 1 year, the probability of alleviating hyperthyroidism in toxic multinodular goiter in patients initially treated with ^{131}I is similar to that of patients initially treated surgically. Surgery is more likely to be successful sooner, and patients initially treated with ^{131}I are much more likely to require a second treatment, although other patient characteristics may influence this. When necessary, retreatment with either ^{131}I or surgery is almost always curative. Postoperative complications were experienced by 8.5% of the surgical patients, and the probability of developing postoperative hypothyroidism within 2 years was more than 70% in the most recent time period. By contrast, the probability of developing hypothyroidism after ^{131}I was 16%, although other studies have suggested that this incidence also may be increasing [17].

Based on our findings, it would seem that the patients who are in most need of surgical treatment with Plummer's disease are those in whom rapid resolution of hyperthyroidism is most critical. The patient who is ill from thyrotoxicosis is most likely to obtain the greatest benefit relative to the small risk of thyroidectomy. Patients with relatively mild hyperthyroidism seem to be more suitable candidates for radioiodine (and beta-blocking agent) therapy. Because of the dramatic increase in the frequency of postoperative hypothyroidism in recent years, our policy is to begin thyroid hormone replacement therapy sooner. It would be of interest if the phenomenon of increased postoperative hypothyroidism is observed in other institutions.

Résumé

Les dossiers de malades traités par les auteurs pour goître multinodulaire toxique de 1950 à 1954, de 1960 à 1964, et de 1970 à 1974 ont été revus pour comparer les résultats respectifs du traitement chirurgical et du traitement par l'I^{131}, pour définir les tendances de l'attitude thérapeutique et de l'évolution, pour tenter d'élucider les facteurs associés à l'hypothyroïdisme secondaire au traitement. Les 3 séries concernent 446 malades qui ont été traités par l'I^{131}. La période de temps nécessaire pour obtenir un bon résultat fut plus courte ($p = 0.001$) chez les sujets traités chirurgicalement que chez ceux traités médicalement. Par comparaison avec ces derniers les premiers furent moins nombreux à recevoir un traitement secondaire de nécessité (0% contre 24%) au cours de la première année qui suivit le traitement initial. Le risque d'hypothyroïdie secondaire à la thyroïdectomie, 2 ans après l'intervention, s'est élevé de 12% dans la première série à 70% dans la troisième. L'augmentation du risque au cours des années les plus récentes dépend ni d'une attitude chirurgicale plus agressive ni de l'emploi de tests plus sensibles pour dépister l'hypothyroïdie.

Resumen

Se revisaron las historias clínicas de los pacientes con bocio tóxico multinodular tratados en el Mayo Clinic en los períodos 1950–1954, 1960–1964 y 1970–1974 con el objeto de comparar los resultados de la cirugía y de la terapia con ^{131}I, de definir las tendencias en las políticas terapéuticas y sus resultados, y de tratar de identificar factores asociados con el desarrollo de hipotiroidismo post tratamiento. La serie incluye 446 pacientes que fueron sometidos a tiroidectomía como tratamiento inicial y 89 que inicialmente recibieron ^{131}I. El intervalo entre el tratamiento y el efecto deseado fue significativamente más corto ($p = 0.001$) en los pacientes tratados quirúrgicamente que en los pacientes que recibieron ^{131}I. Al compararlos con los pacientes de tratamiento médico, los pacientes inicialmente tratados con cirugía demostraron considerable menor necesidad de un segundo tratamiento (0% versus 24%) en el curso del primer año después del tratamiento inicial. La probabilidad de hipotiroidismo postirodectomía a los 2 años después de la cirugía aumentó de aproximadamente 12% en los años 1950's a más de 70% en los años 1970's. Ni la cirugía más agresiva ni el uso de métodos de diagnóstico del hipotiroidismo de mayor sensibilidad aparecen como factores de esta incrementada probabilidad observada en los años más recientes.

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References

1. Plummer, H.S.: The clinical and pathologic relationships of hyperplastic and nonhyperplastic goiter. J.A.M.A. *61*:650, 1913
2. Williams, I., Ankrett, V.O., Lazarus, J.H., Volpe, R.: Aetiology of hyperthyroidism in Canada and Wales. J. Epidemiol. Community Health *37*:245, 1983
3. Heimann, P., Martinson, J.: Surgical treatment of thyrotoxicosis: Results of 272 operations with special reference to preoperative treatment with antithyroid drugs and L-thyroxine. Br. J. Surg. *62*:683, 1975

4. Eller, M., Silver, S., Yohalem, S.B., Segal, R.L.: The treatment of toxic nodular goiter with radioactive iodine: 10 years' experience with 436 cases. Ann. Intern. Med. *52*:976, 1960
5. Green, M., Wilson, G.M.: Thyrotoxicosis treated by surgery of iodine-131: With special reference to development of hypothyroidism. Br. Med. J. *1*:1005, 1964
6. Miller, J.M.: Plummer's disease. Med. Clin. North Am. *59*:1203, 1975
7. Wiener, J.D.: Is partial thyroidectomy definitive treatment for Plummer's disease (autonomous goiter)? Clin. Nucl. Med. *8*:78, 1983
8. Kaplan, E.L., Meier, P.: Nonparametric estimation from incomplete observations. J. Am. Stat. Assoc. *53*:457, 1958
9. Mantel, N.: Ranking procedures for arbitrarily restricted observations. Biometrics *23*:65, 1967
10. Cox, D.R.: Regression models and life-tables. J. R. Stat. Soc. (Series B) *34*:187, 1972
11. Michie, W., Beck, J.S., Pollet, J.E.: Prevention and management of hypothyroidism after thyroidectomy for thyrotoxicosis. World J. Surg. *2*:307, 1978
12. Blichert-Toft, M., Jørgensen, S.J., Hansen, J.B., Watt-Boolsen, S., Christiansen, C., Ibsen, J.: Long-term observation of thyroid function after surgical treatment of thyrotoxicosis. Acta Chir. Scand. *143*:221, 1977
13. Holm, L.-E., Lundell, G., Israelsson, A., Dahlqvist, I.: Incidence of hypothyroidism occurring long after iodine-131 therapy for hyperthyroidism. J. Nucl. Med. *23*:103, 1982
14. Bliddal, H., Hansen, J.M., Rogowski, P., Johansen, K., Friis, T., Siersbaek-Nielsen, K.: ^{131}I treatment of diffuse and nodular toxic goitre with or without antithyroid agents. Acta Endocrinol. (Copenhagen) *99*:517, 1982
15. Lundström, B., Norrby, K.: Thyroid morphology and function after subtotal resection for hyperthyroidism. Br. J. Surg. *67*:357, 1980
16. Block, M.A.: Invited commentary to "Prevention and management of hypothyroidism after thyroidectomy for thyrotoxicosis." World J. Surg. *2*:315, 1978
17. Holm, L.-E.: Changing annual incidence of hypothyroidism after iodine-131 therapy for hyperthyroidism, 1951–1975. J. Nucl. Med. *23*:108, 1982
18. Beahrs, O.H., Sakulsky, S.B.: Surgical thyroidectomy in the management of exophthalmic goiter. Arch. Surg. *96*:512, 1968
19. Farnell, M.B., van Heerden, J.A., McConahey, W.M., Carpenter, H.A., Wolff, L.H., Jr.: Hypothyroidism after thyroidectomy for Graves' disease. Am. J. Surg. *142*:535, 1981
20. Cunnien, A.J., Hay, I.D., Gorman, C.A., Offord, K.P., Scanlon, P.W.: Radioiodine-induced hypothyroidism in Graves' disease: Factors associated with the increasing incidence. J. Nucl. Med. *23*:978, 1982

Invited Commentary

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The plummeting incidence of toxic nodular goiter parallels the subsidence of endemic goiter. In this study, Jensen and colleagues document a 5-fold reduction in its occurrence over a span of 3 decades at the institution in which the disease was first described. Plummer's disease now accounts for less than 15% of hyperthyroid cases in nonendemic goiter regions. Increased dietary iodine has fostered this declining trend along with lower iodine uptake levels.

The main therapeutic aim is to relieve hyperthyroidism safely. Whenever possible, one should reduce the bulk of these large glands and also minimize the risk of subsequent hypothyroidism. Selection of treatment is best individualized according to the patient's age and general health, severity of thyrotoxicosis, gland size, and the availability of a skilled thyroid surgeon.

In spite of the retrospective and uncontrolled nature of this study in which one-third of the patients were lost to follow-up after 5 years, the results may be regarded as representative of each treatment modality. Neither surgery nor radioiodine is uniformly satisfactory. The findings, however, tend to endorse our preference for surgical resection in healthy patients. Surgical treatment in the study was biased against by a preponderance of patients who had large glands or marked illness due to severe thyrotoxicosis. Still, it alleviated hyperthyroidism sooner and in more patients than single dose ^{131}I therapy. This was accomplished with acceptable morbidity and low mortality. Subtotal thyroidectomy is indicated in patients whose glands are large (> 100 g) since there are usually concomitant obstructive symptoms, or if there is a nodule suspicious of malignancy.

As shown in this study, radioiodine is more appropriate in elderly, frail patients who have concurrent illnesses but comparatively mild hyperthyroidism and smaller glands. Even though thyrotoxicosis did not resolve immediately in one-quarter of this group, most of the patients either improved sufficiently to undergo subsequent thyroidectomy or else responded satisfactorily to a second dose. The calculated ^{131}I dose, although quite large, often proved inadequate because the gland size tended to be underestimated. A supplementary dose for patients whose thyrotoxicosis persisted beyond 6 months would have improved their success rate at 1 year. Radioiodine is also indicated in the few in-