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Comparative analysis of radioactive iodine versus thyroidectomy for definitive treatment of Graves disease

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Abstract

Background—Management of Graves disease includes antithyroid drugs, ^{131}I therapy, or thyroidectomy. Our aim was to review our institutional experience with definitive treatments for Graves disease.

Methods—This was a retrospective review of patients undergoing ^{131}I therapy ($n = 295$) or thyroidectomy ($n = 103$) for Graves disease (2003–2015). Demographic, clinical, pathology, and outcome data were collected from institutional databases.

Results— ^{131}I therapy patients were older (39.1 years vs 33.4 years, $P = .001$). There was no difference in the presence of ophthalmopathy between groups. A larger proportion of children received thyroidectomy than ^{131}I therapy (17.1% vs 9.2%, $P = .026$). The success rate of the first ^{131}I therapy dose was 81.4%. Overall success rate, including additional doses, was 90.1%. Rapid turnover of iodine correlated with ^{131}I therapy failure (58.3% rapid turnover failure vs 14.9% non-rapid turnover failure, $P < .05$). All surgical patients underwent total or near-total thyroidectomy. ^{131}I therapy complications included worsening thyrotoxicosis (1%) and deteriorating orbitopathy (0.7%). Operative complications were higher than ^{131}I therapy complications ($P < .05$) but were transient. There was no worsening orbitopathy or recurrent Graves disease among surgical patients.

Conclusion—A higher proportion of pediatric Graves disease patients underwent thyroidectomy than ^{131}I therapy. Rapid turnover suggested more effective initial management with operation than ^{131}I therapy. Although transient operative complications were high, ^{131}I therapy complications included worsening of Graves orbitopathy among those with pre-existing orbitopathy.

Graves disease (GD) is the most common cause of hyperthyroidism in the United States. It occurs secondary to the effects of thyroid-stimulating immunoglobulins (TSI) on thyrotropin receptors of thyroid follicular cells. There are an estimated 20–30 cases of GD per 100,000 individuals per year with roughly 3% of women and 0.5% of men developing the disease.^{1–3}

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The peak incidence of GD is between 30–60 years of age, though it can affect all ages.³ In children, the incidence peaks during adolescence, and GD accounts for 2.5% of childhood goiters.⁴ Binding of TSI to thyrotropin receptors in retro-orbital tissues can lead to Graves orbitopathy (GO).^{3,5} The course of GO appears to be dependent on smoking, the level of thyroid dysfunction, presence of persistently elevated TSI levels, and the type of treatment pursued.^{6,7}

Management modalities for GD include antithyroid drugs (ATD) with definitive treatment by ¹³¹I radioactive iodine (RAI) or thyroidectomy. While ATD or operation is preferred over RAI in Europe and Japan, RAI has been the preferred therapy in the United States (US).^{1,2,8–10} However, recent guidelines have considered thyroidectomy as a comparable treatment option to RAI with an equivalent, long-term quality of life.^{2,8,11} In addition, recent publications show that the trend in definitive treatment of GD has become primarily operative in some US institutions serving patients with low socioeconomic status.^{3,12,13}

Controversy has existed in regard to the extent of thyroidectomy that should be performed. Subtotal thyroidectomy had been traditionally preferred over total or near-total thyroidectomy due to concerns of permanent hypothyroidism and possible higher complication rates.^{1,5,14} Over the past decade, however, total or near-total thyroidectomy gained favor after multiple studies showing no difference between complications and highlighting the recurrence risks and occurrence of hypothyroidism associated with subtotal resections.^{1,8,14,15}

Many factors are considered by both health care providers and patients in providing recommendations and choosing treatment modality. Factors favoring pursuit of RAI over operation include patients with a previously operated neck and those with comorbidities increasing operative risks. Contraindications to RAI are pregnancy, lactation, and presence of thyroid cancer.^{2,8} In the United States, operation is recommended in those with symptomatic compression, large goiters (>80 g), concern for malignancy, the presence of a large nonfunctioning or hypofunctioning nodule, hyperparathyroidism, women desiring pregnancy within 4–6 months, and moderate to severe, active GO.⁸

Given the gradual changes in the national trends of GD management in the last few decades, the purpose of this study was to review and compare the definitive treatments (RAI and thyroidectomy) for GD at the University of Iowa Hospitals and Clinics. We hypothesized that operation is a better definitive treatment over RAI for Graves disease when assessing complications and remission rates.

METHODS

After Institutional Review Board approval, a retrospective chart review was conducted encompassing both pediatric (<18) and adult patients undergoing radioactive iodine ($n = 295$) and/or thyroidectomy ($n = 103$) for GD between 2003 through 2015. A surgical database was compiled from endocrine surgeons at 5 University of Iowa Hospitals and Clinics (UIHC), and an RAI database was provided by the Department of Nuclear Medicine

at UIHC. Both databases were used to collect demographic, clinical, pathologic, and outcome data.

Limited information regarding ophthalmologic disease (eg, proptosis, exophthalmos) and goiter (eg, “enlarged”) was gathered based on providers’ physical exam documentation. Verification of GO or goiter with an ophthalmologist or ultrasonography, respectively, could be found in only a small number of patients. Patient symptoms were recorded, and primary indication for operative treatment was gathered from providers’ assessment portion of notes. Complications were found through review of operative notes, progress notes, follow-up notes, discharge summaries, and medication review during admission.

In the RAI group, pretreatment and treatment nuclear medicine reports were reviewed, which included 4- and 24-hour % uptake of iodine, imaging interpretation, and RAI administered activities. Rapid turnover (RT) was defined as % uptake of iodine that was higher at 4 hours than at 24 hours. RAI was considered successful if no additional RAI doses, thyroidectomy, or ATD was required at 6 months or longer. RAI was administered via a calculation-based approach incorporating 24-hour % uptake, estimated gland weight (palpation, ultrasonography when available), and target activity/g of thyroid tissue of 100–200 μCi .

In the operative group, patients were included if undergoing thyroidectomy and were excluded if no follow-up information was available. One patient with GD underwent lobectomy alone for a cold nodule and was excluded. Patients referred to UIHC solely for RAI and followed at other institutions were excluded. The operative group included 10 patients from the UIHC RAI group who failed treatment and 5 patients who failed RAI at outside institutions. Statistical calculations were performed using the SPSS software package (SPSS Inc, Chicago, IL).

RESULTS

A final cohort of 103 surgical patients and 295 RAI patients were identified and included for analysis (Table I). Overall, RAI patients were significantly older than those undergoing thyroidectomy (mean age 39.1 vs 33.14, respectively, $P < .001$). Adults constituted 82.5% of the operative group, while 17.5% were pediatric patients; in contrast, 90.8% were adults and 9.2% were pediatric patients in the RAI group. A higher proportion of pediatric patients were in the operative group than the RAI group (17.5% vs 9.2%, $P = .02$). Both operative and RAI groups were predominantly women (83.5% and 72.5%, respectively) and Caucasian (82.5% and 78%). GO was present at time of treatment in 29.7% of surgical patients and 29.6% of RAI patients. The operative group had more women ($P = .03$) and higher mean body mass index (BMI) than the RAI group (30.1 kg/m^2 vs 27.6 kg/m^2 , $P = .01$), but there was no significant difference in the presence of GO between the 2 groups. Of those undergoing thyroidectomy, 15 (14.8%) patients had previous RAI. Ten of the 15 were from the UIHC definitive RAI group, while the remaining 5 had previous RAI at other institutions.

The RAI group included 295 patients (268 adults and 27 pediatric patients mean age of 41.7 and 13.4, respectively, Table I). The RAI group had the presence of goiter in 73% of patients (size not accurately determinable); 48 of these patients (41 adults, 7 pediatric) underwent neck ultrasonography. A higher proportion of GO was present in children than adults though not statistically different (44.4% vs 28.1%, $P = .07$). The first RAI mean dose was 12.9 (± 4.2) mCi in adults and 11.2 (± 3.2) mCi in children. The second RAI mean dose was 16.1 (± 4.0) mCi. Average cumulative dose for patients undergoing 2 RAI therapies was 30.3 (± 10.8) mCi. The first RAI mean dose of adults failing therapy was 14.5 (± 7.3) mCi.

Radioactive iodine uptake values were observed at 4 and 24 hours (Table II) in all patients; the 4-hour uptake value was not available for one patient. Mean 4-hour values were 45.2% (± 22.7) in adults and 56% (± 20.8) in children (combined mean 46.2% ± 22.7), and mean 24-hour values in adults and children were 63.4% (± 17.4) and 64.7% (± 18.2), respectively (combined 63.6% ± 17.4). RT was determined to occur in 8.8% (26/294) with a trend for it being more common in children ($n = 21$ [8%] in adults and $n = 5$ [18.5%] in children, $P = .07$; Table II).

After the first RAI ablation, follow-up was available for 97% of patients ($n = 285/295$; Fig). Remission after the first RAI dose occurred in 81.4% ($n = 232/285$; 78.6% of those lost to follow-up are assumed to have failed treatment, worst-case scenario [wcs]). Of patients failing RAI who proceeded to a second RAI therapy ($n = 29$; 23 adults, 6 children), remission occurred in 75.8% (22/29; 68.7% wcs). Persistent failure occurred in 13.8% (4/29; 24.1% wcs). When including all patients undergoing a second RAI therapy, overall remission rate for RAI was 90.1% (254/282; 86.1% wcs). Of patients who failed the first RAI, the proportion of children who failed compared to adults was not different ($n = 7$, 26.9% vs $n = 46$, 17.8% respectively, $P = 0.25$).

The pediatric remission rate for the first RAI dose was 73.1% (70.4% wcs); however, overall remission including a second dose was 100% (92.6 wcs). The adult RAI remission rate after the first dose was 82.2% (79.5% wcs). Of adults failing RAI, half went on to a second RAI therapy. In this subgroup, remission occurred in 80% (69.6% wcs). Remission rate for adults including a second RAI therapy was 89.5% (85.4% wcs). Patients with RT rates were more likely to fail the first RAI treatment compared to patients without RT (58.3% vs 14.9%, $P < .05$, excluding those lost to follow-up).

A total of 103 (85 adults, 18 children) patients were evaluated in the operative group. The majority of patients underwent total thyroidectomy with a few undergoing near-total thyroidectomy. Common presenting symptoms included palpitations or tachycardia, mood changes (anxiety, irritability, mood swings), ophthalmopathy, weight loss, and tremors (Table III). For those with previous RAI therapy, the average time from RAI to operation was 3.8 (± 6.2) years. Compressive symptoms included dyspnea, dysphagia, and hoarseness. Common indications for operation included failure of antithyroid medication ($n = 21$), patient preference ($n = 19$), poor compliance ($n = 12$), failure of RAI ($n = 11$), GO ($n = 10$), and compressive symptoms ($n = 8$, Table III). Perioperative cold iodine (predominantly Lugols) was used in 75 patients. Of the 103 cases, nerve monitoring was used intraoperatively in 77 (75%).

Complications were higher in the operative group compared to the RAI group ($P < .05$). All surgical complications, however, were transient (Table IV). Surgical complications occurred in 30 adults and 8 children ($n = 38$, 36.9%). Temporary postoperative hypocalcemia (calcium < 8.0 mg/dL) occurred in 34 individuals, and there were no cases of permanent hypocalcemia. Ten hypocalcemic patients required IV calcium, while the remaining 24 patients were asymptomatic or only required oral calcium. Four of the 8 children required IV calcium.

Other operative complications included transient recurrent laryngeal paresis ($n = 3$), neck hematoma ($n = 1$) requiring reoperation, postoperative thyrotoxicosis ($n = 1$), and transient compression neuropathy of the right arm ($n = 1$). All cases of transient laryngeal nerve paresis occurred in patients with nerve monitoring. There was no worsening GO or recurrent GD in the operative patients in contrast to the RAI group. The patient with postoperative thyrotoxicosis was febrile and tachycardic in the recovery room despite being on beta-blockers. IV Decadron was administered followed by a dexamethasone taper on discharge. The patient otherwise recovered well.

Eight complications were present in the RAI group (all adults) and included 3 cases of thyrotoxicosis, 2 cases of transient dysphagia, 2 cases of progressive eye disease requiring escalation of therapy (both smokers), and 1 case of tachycardia immediately after treatment (Table IV). Based on chart review, a total of 87 patients undergoing RAI were deemed to have thyroid-related eye disease (with severity unknown and disease status often not confirmed by an ophthalmologist). Fourteen patients had disease advanced enough to warrant concurrent steroids. After RAI, 2 patients (2.2%) developed GO progression; 1 of the 2 was not on concurrent steroids at the time of therapy.

Of the 4 patients experiencing thyrotoxicosis or tachycardia, 2 (including the patient with tachycardia) were on a beta-blocker. Of these 4 patients, one had been treated for < 3 months with ATD with free T4 of 1.24 ng/dL (0.92–1.57 ng/dL) one week prior to RAI; one had been treated for 6 months with ATD with discontinuation one month prior to RAI due to development of severe hypothyroidism (but with no laboratory data available from the time of RAI therapy); one had been treated for 3–6 months with ATD with free T4 3.26 ng/dL one week prior to therapy; one had not received ATD treatment and had a free T4 of 4.03 ng/dL on record several months prior to receiving RAI.

Pathology in those with cold nodules diagnosed preoperatively revealed a 1.2 cm papillary carcinoma ($n = 1$), 3.9 cm Hurthle cell adenoma ($n = 1$), 0.6 cm papillary microcarcinoma and multiple Hurthle cell nodules ($n = 1$), 0.3 cm papillary microcarcinoma and multiple adenomatoid nodules ($n = 1$), and benign hyperplasia ($n = 1$). In the remaining 98 patients with other indications for thyroidectomy, 8 had papillary microcarcinoma ranging from 0.1 to 1.1 cm on final pathology. The mean specimen thyroid weight was 59.73 g. Mean weight for those with compressive symptoms was 135.1 g vs 53 g in those with other symptoms only ($P = .001$).

DISCUSSION

Few studies directly compare the definitive treatments for GD, and agreement regarding the best approach for management continues to be developing. In European countries, ATDs tend to be the primary treatment. Surgery or RAI is reserved for cases of recurrence, adverse effects of ATDs, or failure of ATDs^{6,9,10,14}; however, in the United States, RAI tends to be the preferred treatment with operation referral in the presence of potential or confirmed malignancy, in cases of large goiters causing symptomatic compression, with patient preference, or with RAI failure.^{1,8} Previous studies have shown evidence for progression of GO after RAI, and current ATA guidelines recommend operation or ATD over RAI in moderate or severe cases.^{6,8,16,17} This is the first study to evaluate operative and RAI management of GD in both adults and children at a tertiary care institution, and this study is unique compared to other series in its inclusion of RT of iodine data.

Pediatric patients constituted a higher proportion of surgical referrals compared to RAI referrals indicating a potential preference for this modality at our institution. Studies of RAI versus thyroidectomy in pediatric populations have both shown low complication rates and acceptable outcomes for either treatment modalities, though the indications for choosing a modality are not standardized.^{18–20} The low complication rate of the pediatric RAI group in our study supports a study by Rivkees and Dinauer¹⁸ who advocated the use of RAI in pediatric GD patients given its safety and efficacy.¹⁸

Chiapponi et al¹⁹ performed a retrospective, matched case-control study evaluating outcomes of total thyroidectomy between pediatric and adult patients for GD finding comparable complication rates. In their study, the rates of postoperative bleeding were the same between both groups (4.8%), transient laryngeal nerve palsy occurred in 4.8% of children compared to 0% in their adult group (not statistically significant), and a higher occurrence of postoperative, transient hypocalcemia was observed in the pediatric group (29.6% vs 4.8%, $P = .093$). Similar to the Chiapponi findings, we found a higher proportion of children with transient postoperative hypocalcemia compared to adults, but this did not reach statistical significance (44% vs 30.6%, $P = .256$). In regard to other complications, the only other pediatric complications that occurred were transient dyspnea due to pain ($n = 1$) and transient laryngeal nerve paresis ($n = 1$). Remission was 100% in the thyroidectomy group.

For RAI, Rivkees and Dinauer¹⁸ reported a >95% remission rate in the pediatric population. In comparison, the pediatric RAI remission rate in our study after the first dose was 73.1% ($n = 19$); however, overall remission after a second dose was 100% in whom follow-up was available. Overall, both treatments have similar outcomes in pediatric patients. Those managed by total thyroidectomy tended to have more transient complications but with greater remission rates. The remission rate for adults was comparable to a recent study by Schneider et al² and other studies.^{21–23} Of those failing initial RAI who opted for operative treatment, all were successfully treated.

Our analysis found that the presence of RT was associated with RAI failure, similar to findings by Aktay et al.²⁴ RT is a markedly hyperthyroid state with extreme rapid production

and release of thyroid hormone. This shortens the residency time for RAI in the thyroid, which results in a higher likelihood of failure after a single administration of RAI. This presents as a clinical challenge, as increasing RAI doses would not improve residency time and would contribute to increased whole body radiation dose in the form of circulating radioactive thyroid hormone. As a result, the finding of RT on an initial iodine uptake scan may indicate better resolution of this condition with primary definitive treatment by thyroidectomy rather than RAI.

The complication rate of operation was higher compared to the RAI group (36.9% vs 2.7%). However, all complications were transient, and the majority of complications were due to hypocalcemia with a small number of patients requiring IV calcium. Sundaresht et al²¹ performed a systematic review and meta-analysis of therapies for GD and reported complications of total thyroidectomy to include hypocalcemia (32.5% temporary, 2.6% permanent), recurrent laryngeal nerve injury (3.43% temporary, 1.46% permanent), and immediate postoperative bleeding (<1%) among 8 studies. In addition, common RAI complications identified by their analysis included new or worsened GO (15–33%) especially in smokers and radiation thyroiditis (1%).²¹

Although limited by the number of patients and nonmatched study design, both the operation and RAI groups in our study had a similar number of patients with GO, and only those undergoing RAI experienced long-term worsening eye disease among those with pre-existing GO. Known risk factors for adverse GO outcome after RAI include smokers, high pretreatment T3 values, active and progressive GO over the preceding 3 months, high pretreatment thyrotropin antibody levels, and hypothyroidism.⁸

This study is limited by its retrospective, single institution design with relatively small cohort numbers, especially in the pediatric groups for both operation and RAI data sets thus limiting extensive statistical analysis. In addition, the validation and quantification of either goiter or GO by ultrasonography or ophthalmologist were not often available.

In conclusion, this study provides a broad overview of the experience of a single institution with thyroidectomy and RAI as definitive treatments for GD in both pediatric and adult populations. Primary thyroidectomy was universally successful in achieving prompt and complete remission. Rates of remission for RAI were high in adults and children. Transient complications were greater after thyroidectomy. Only RAI patients with pre-existing GO had progressive eye disease requiring escalation of care (0.7%, less than in previous studies²⁵). Additionally, those with RT may be more effectively managed initially with thyroidectomy, as the failure rate of RAI in this group is higher necessitating additional RAI therapy.

Further investigation into the basis for referral patterns selecting for RAI over operation in those with GD and RT (eg, potential cost differences, convenience, and perceived risks among patients and providers) could help improve guidelines for definitive therapy in this subset of patients. Finally, consistent implementation of classification systems (eg, NOSPECS, VISA, or CAS) for Graves eye disease and thyroid ultrasonography for quantification of gland size could aid in completing future, prospective studies.

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References

1. Lal G, Ituarte P, Kebebew E, Siperstein A, Duh QY, Clark OH. Should total thyroidectomy become the preferred procedure for surgical management of Graves' disease? *Thyroid*. 2005; 15:569–74. [PubMed: 16029123]
2. Schneider DF, Sonderman PE, Jones MF, Ojomo KA, Chen H, Jaume JC, et al. Failure of radioactive iodine in the treatment of hyperthyroidism. *Ann Surg Oncol*. 2014; 21:4174–80. [PubMed: 25001092]
3. Burch HB, Cooper DS. Management of Graves disease: a review. *JAMA*. 2015; 314:2544–54. [PubMed: 26670972]
4. Dieson, DL., Skinner, MA. Endocrine disorders and tumors. In: Holcomb, GW.Murphy, JP., Ostlie, DJ., editors. *Ashcraft's pediatric surgery*. 6. London: Elsevier Saunders; 2014. p. xxiv
5. DeGroot, LJ. Diagnosis and treatment of Graves' disease. In: De Groot, LJ.Beck-Peccoz, P.Chrousos, G.Dungan, K.Grossman, A.Hershman, JM., et al., editors. *Endotext*. South Dart-mouth (MA): MDText.com, Inc; 2000.
6. Kautbally S, Alexopoulou O, Daumerie C, Jamar F, Mourad M, Maiter D. Greater efficacy of total thyroidectomy versus radioiodine therapy on hyperthyroidism and thyroid-stimulating immunoglobulin levels in patients with Graves' disease previously treated with antithyroid drugs. *Eur Thyroid J*. 2012; 1:122–8. [PubMed: 24783007]
7. De Bellis A, Conzo G, Cennamo G, Pane E, Bellastella G, Colella C, et al. Time course of Graves' ophthalmopathy after total thyroidectomy alone or followed by radioiodine therapy: a 2-year longitudinal study. *Endocrine*. 2012; 41:320–6. [PubMed: 22169963]
8. Bahn RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, Klein I, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. *Endocr Pract*. 2011; 17:1–65.
9. Wartofsky L, Glinioer D, Solomon B, Nagataki S, Lagasse R, Nagayama Y, et al. Differences and similarities in the diagnosis and treatment of Graves' disease in Europe, Japan, and the United States. *Thyroid*. 1991; 1:129–35. [PubMed: 1688014]
10. Werga-Kjellman P, Zedenius J, Tallstedt L, Traisk F, Lundell G, Wallin G. Surgical treatment of hyperthyroidism: a ten-year experience. *Thyroid*. 2001; 11:187–92. [PubMed: 11288990]
11. Abraham-Nordling M, Torring O, Hamberger B, Lundell G, Tallstedt L, Calissendorff J, et al. Graves' disease: a long-term quality-of-life follow up of patients randomized to treatment with antithyroid drugs, radioiodine, or surgery. *Thyroid*. 2005; 15:1279–86. [PubMed: 16356093]
12. Elfenbein DM, Schneider DF, Havlena J, Chen H, Sippel RS. Clinical and socioeconomic factors influence treatment decisions in Graves' disease. *Ann Surg Oncol*. 2015; 22:1196–9. [PubMed: 25245130]
13. Jin J, Sandoval V, Lawless ME, Sehgal AR, McHenry CR. Disparity in the management of Graves' disease observed at an urban county hospital: a decade-long experience. *Am J Surg*. 2012; 204:199–202. [PubMed: 22317948]
14. Bojic T, Paunovic I, Diklic A, Zivaljevic V, Zoric G, Kalezic N, et al. Total thyroidectomy as a method of choice in the treatment of Graves' disease - analysis of 1432 patients. *BMC Surg*. 2015; 15:39. [PubMed: 25888210]
15. Liu ZW, Masterson L, Fish B, Jani P, Chatterjee K. Thyroid surgery for Graves' disease and Graves' ophthalmopathy. *Cochrane Database Syst Rev*. 2015; 11:CD010576.
16. Acharya SH, Avenell A, Philip S, Burr J, Bevan JS, Abraham P. Radioiodine therapy (RAI) for Graves' disease (GD) and the effect on ophthalmopathy: a systematic review. *Clin Endocrinol*. 2008; 69:943–50.

17. Tallstedt L, Lundell G, Törring O, Wallin G, Ljunggren JG, Blomgren H, et al. Occurrence of ophthalmopathy after treatment for Graves' hyperthyroidism. The Thyroid Study Group. *N Engl J Med*. 1992; 326:1733–8. [PubMed: 1489388]
18. Rivkees SA, Dinan C. An optimal treatment for pediatric Graves' disease is radioiodine. *J Clin Endocrinol Metab*. 2007; 92:797–800. [PubMed: 17341574]
19. Chiapponi C, Stocker U, Mussack T, Gallwas J, Hallfeldt K, Ladurner R. The surgical treatment of Graves' disease in children and adolescents. *World J Surg*. 2011; 35:2428–31. [PubMed: 21879423]
20. Cappa M, Bizzarri C, Crea F. Autoimmune thyroid diseases in children. *J Thyroid Res*. 2010; 2011:675703. [PubMed: 21209713]
21. Sundaresh V, Brito JP, Wang Z, Prokop LJ, Stan MN, Murad MH, et al. Comparative effectiveness of therapies for Graves' hyperthyroidism: a systematic review and network meta-analysis. *J Clin Endocrinol Metab*. 2013; 98:3671–7. [PubMed: 23824415]
22. Menconi F, Leo M, Vitti P, Marcocci C, Marino M. Total thyroid ablation in Graves' orbitopathy. *J Endocrinol Invest*. 2015; 38:809–15. [PubMed: 25740065]
23. Sztal-Mazer S, Nakatani VY, Bortolini LG, Boguszewski CL, Graf H, de Carvalho GA. Evidence for higher success rates and successful treatment earlier in Graves' disease with higher radioactive iodine doses. *Thyroid*. 2012; 22:991–5. [PubMed: 22953990]
24. Aktay R, Rezai K, Seabold JE, Bar RS, Kirchner PT. Four- to twenty-four-hour uptake ratio: an index of rapid iodine-131 turnover in hyperthyroidism. *J Nucl Med*. 1996; 37:1815–9. [PubMed: 8917181]
25. Ponto KA, Zang S, Kahaly GJ. The tale of radioiodine and Graves' orbitopathy. *Thyroid*. 2010; 20:785–93. [PubMed: 20578895]

Fig.
Overview and outcome of patients undergoing RAI in adults and children.

Table I

Patient characteristics of the operation and radioactive iodine (RAI) groups

	Operation group (<i>n</i> = 103)	RAI group (<i>n</i> = 295)	<i>P</i> value
All patients			
Adults (18)	85 (82.5%)	268 (90.8%)	
Pediatric (<18)	18 (17.5%)	27 (9.2%)	.02 *
Procedure			
Total thyroidectomy	103	0	
Age (mean y)			
All patients	33.1 (±15.3)	39.1 (±15.3)	.001 *
Adults	37.5 (±13.2)	41.7 (±13.6)	.03 *
Pediatric	12.6 (±2.3)	13.4 (±3.7)	.15
Sex			
Male	17 (16.5%)	81 (27.5%)	
Female	86 (83.5%)	214 (72.5%)	.03 *
Race			
Caucasian	85 (82.5%)	230 (78%)	
African American/black	5 (4.9%)	15 (5.1%)	
Asian	2 (1.9%)	10 (3.4%)	
Hispanic	2 (1.9%)	17 (5.8%)	
Native American	0	2 (0.7%)	
Pacific Islander	0	1 (0.3%)	
Multiracial	0	2 (0.7%)	
Unspecified	9 (8.8%)	18 (6.1%)	
BMI (mean kg/m ²)			
Adults	30.1 (±9.3)	27.6 (±6.9)	.01 *
Graves' orbitopathy	30 (29.7%)	87 (29.6%)	.93
RAI prior thyroidectomy [†]	15	0	
Post-RAI thyroidectomy	0	10	

* Indicates a significant result.

[†]The operation group included 10 RAI patients from the UIHC RAI group and 5 patients with previous RAI from other institutions.

Table II

Measured 4- and 24-hour % uptake in patients treated with radioactive iodine (RAI) with all patients, first RAI dose success and failure subsets, and RT subsets

All patients treated with RAI (<i>n</i> = 295)		
	Adult (<i>n</i> = 268)	Pediatric (<i>n</i> = 27)
4-h uptake (mean %)	45.2	56.0
24-h uptake (mean %)	63.4	64.7
All patients successfully treated with RAI (<i>n</i> = 232, 81.4%)		
	Adults (<i>n</i> = 213)	Pediatric (<i>n</i> = 19)
4-h uptake (mean %)	41.8	53.6
24-h uptake (mean %)	62.1	64.4
All patients failing first RAI dose (<i>n</i> = 53, 18.6%)		
	Adult (<i>n</i> = 46)	Pediatric (<i>n</i> = 7)
4-h uptake (mean %)	59.5	61.6
24-h uptake (mean %)	68.9	65.4
Patients with RT (<i>n</i> = 26, 8.9%)		
	Adult (<i>n</i> = 21)	Pediatric (<i>n</i> = 5)
4-h uptake (mean %)	77.9	70.0
24-h uptake (mean %)	70.0	56.4
Rapid turnover patients failing first RAI (<i>n</i> = 14)		
	Adult (<i>n</i> = 12)	Pediatric (<i>n</i> = 2)
4-h uptake (mean %)	81.0	77.5
24-h uptake (mean %)	71.4	62.5

Table III

Common symptoms at the time of operative presentation, and indications for surgical intervention in patients undergoing thyroidectomy

Symptoms at presentation	<i>n</i>	Indications for thyroidectomy	<i>n</i>
Palpitations/tachycardia	52	Failure of ATD	21
Weight loss	31	Patient preference	19
Ophthalmopathy	30	Poor patient compliance	12
Tremors	20	Failed RAI	11
Mood changes	19	Graves' orbitopathy	10
Heat intolerance	12	Compressive symptoms	8
Fatigue	12	Adverse reaction to ATD	8
Compressive symptoms	12	Desire for pregnancy	5
Hair loss	6	Cold nodule	5
Hypertension	5	Multiple thyroid nodule	1
Goiter	4	Impending thyroid storm	1
GI symptoms	4	Large goiter	1
Thyroiditis	1	NA	1
Pretibial myxedema	1		
Syncope	1	Total	103

GI, Gastrointestinal.

Table IVComplication types in the operation ($n = 38$) and RAI ($n = 8$) groups (individuals may have >1 complication)

	<i>n</i> (%)
Operative complications ($n = 44$)	
Transient hypocalcemia (Ca < 8.0 mg/dL)	34 (79.1)
Asymptomatic or oral Supplementation	24
Requiring IV calcium	10
Transient recurrent laryngeal nerve paresis	3 (7)
Flap hematoma	1 (2.3)
Postoperative thyrotoxicosis	1 (2.3)
Seroma	1 (2.3)
Compression neuropathy (right arm)	1 (2.3)
Ecchymosis	1 (2.3)
Dyspnea	1 (2.3)
RAI complications ($n = 8$)	
Thyrotoxicosis	3 (37.5)
Dysphagia	2 (25)
Dysthyroid orbitopathy	2 (25)
Tachycardia	1 (12.5)