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Original Article

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Efficacy of I-131 Treatment Dosage for Hyperthyroidism With Current Institution Formula

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Abstract

Background: I-131 (radioactive iodine (RAI)) therapy effectively targets overactivity of the thyroid gland; however, the literature provides conflicting outcomes regarding dosage optimization of I-131 for patients with hyperthyroidism and associated clinical complications. This retrospective study aimed to validate the therapeutic efficacy of an empirically derived I-131 institution formula in resolving hyperthyroidism by establishing a euthyroid or hypothyroid state.

Methods: This retrospective chart review was undertaken for 89 adult patients (> 18 years) who received I-131 therapy from 2016 to 2020 at H&H/Queens, New York. The I-131 dose range was determined in accordance with their thyroid gland weight and thyroid uptake percentages; however, the follow-up assessment was performed for a duration of 6 - 12 months. IRB approval with reference HS-STUDY-21-01760 was obtained. All the subjects consented using a written consent document in a private room. All the patient's data are stored confidentially in a password-protected computer, which is accessible only to the study group. The primary endpoint (i.e., treatment success) was defined by the interim development of a euthyroid state, hypothyroidism, subclinical/questionable/suspected hypothyroidism, or a questionable euthyroid state. The secondary endpoints included the frequency of repeat RAI doses and post-ablation thyroid function tests (TFTs).

Results: The univariate and multivariate analysis of patient data indicated an 83% I-131 treatment success rate defined by the achievement of a euthyroid state and hypothyroidism in 6.7% and 70.8% of patients, along with the attainment of questionable euthyroid status, questionable hypothyroidism, subclinical hypothyroidism, and suspected hypothyroidism in 1.1%, 1.1%, 2.2%, and 1.1% of patients, respectively. In addition, a low number (i.e., 9%) of patients with hyperthyroidism required repeat I-131 treatment dosages to achieve a hypothyroid or euthyroid state. The results indicated a clinically significant impact of I-131 treatment dosages on post-ablation thyroid-stimulating hormone (TSH), triiodothyronine (T3), and free thyroxin (FT4) levels.

Conclusion: The results of this study testified to the therapeutic efficacy of the current institution's formula for I-131 treatment dosages in treating hyperthyroidism. In addition, 83% treatment success and a low retreatment requirement strengthened current evidence favoring the optimization of RAI therapy for hyperthyroidism.

Keywords: Radioactive iodine; Hypothyroidism; RAI therapy; Hyperthyroidism

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Introduction

The excessive production of thyroid hormone triggers the progression of hyperthyroidism that eventually results in thyrotoxicosis [1]. The predominant causes of hyperthyroidism include toxic multinodular goiter, Graves' disease, thyrotoxicosis factitial (or factitious thyroiditis), postpartum thyroiditis, subacute (or de Quervain) thyroiditis, and Jod-Basedow phenomenon (or iodine-induced hyperthyroidism) [2-7]. The excessive intake of pharmaceutical thyroid hormone or thyroxine abuse in weight loss candidates also triggers hyperthyroidism due to factitious thyroiditis [8, 9]. In addition, thyroxine-secreting tissue and its ectopic foci also add to the incidence of hyperthyroidism [10]. The Jod-Basedow phenomenon is the outcome of iodine-induced hyperthyroidism, which is predominantly triggered by iodine-containing medications, including amiodarone [11].

Radioactive iodine (I-131) or RAI therapy is the preferred approach for the routine medical management of hyperthyroidism; however, patients with recurrent Graves' disease or nodular goiter often require surgical treatment [12]. Approximately 20-25% of patients with Graves' disease experience remission within 3 - 6 months of treatment completion [13]. The potential adversities associated with antithyroid drugs include hepatotoxicity and agranulocytosis [14]. The outcome attainment depends on the I-131 dosage calculated by considering the iodine-trapping ability and weight of the thyroid gland [15]. The optimization of a fixed-dose range, however, aims to standardize I-131 treatment for hyperthyroidism [16].

The contemporary literature reveals the utilization of RAI for treating malignant and benign thyroid complications [17]. The establishment of a hypothyroid or euthyroid state via RAI depends on its ability to disrupt the thyroid tissue for minimizing its overactivity [16]. The selection of the beta-emitting radionuclide (I-131) for treating hyperthyroidism is based on its

long half-life (i.e., > 8 days), tissue range (i.e., 0.8 mm), average energy (i.e., 0.192 MeV), and maximum energy (i.e., 0.61 MeV) [18]. The iodide transporter in the thyroid gland takes up the thyroxine precursor (i.e., RAI) that eventually deteriorates follicular cells and minimizes thyrotoxicosis by reducing thyroid volume [19]. RAI therapy is, however, contraindicated in severe uncontrolled thyrotoxicosis, breastfeeding, and pregnancy [20].

The dosing approach of RAI therapy remains controversial and varies with treatment goals based on the avoidance of hypothyroidism or control of hyperthyroidism [16]. The dosage calculations rely on ultrasound-directed assessments of iodine uptake and volume of the thyroid gland [21, 22]. The administration of a high I-131 dosage aims to achieve a hypothyroid state; however, this treatment strategy adds to the incidence of pretreatment hospital visits and long-term follow-ups [23, 24]. Other potential RAI treatment strategies include the optimization of a fixed (safe) I-131 dosage, dose correction based on the thyroid gland's size or volume, and dose quantification or calibration for the controlled destruction of the thyroid tissue [25-28]. The appropriate RAI uptake requires restricting iodine in the diet and discontinuing the intake of iodine-based therapies or antithyroid medication, 10 - 14 days before treatment initiation [29]. In addition, RAI administration increases the risk of permanent hypothyroidism in 70% of the treated patients who transiently develop a hypothyroid state after therapy [16, 30]. Ultimately, patients who undergo RAI therapy require lifelong follow-up for hypothyroidism or experience a recurrence of the initial disease [31]. This study aimed to evaluate the efficacy of our empirically constituted I-131 institution formula in establishing a euthyroid or a hypothyroid state in patients with a definitive diagnosis of hyperthyroidism.

Materials and Methods

Patients and dosage

A retrospective chart review was conducted for 89 adult patients (> 18 years) who received RAI treatment from 2016 to 2020 for hyperthyroidism at NYC Health + Hospitals/Queens, New York. Post-ablation thyroid function test (TFT) findings were additionally retrieved from the electronic medical records. The I-131 dosage for RAI treatment was calculated with the following institution formula which was modified from DeGroot formula [32]:

$$\text{I-131 dose} = \frac{\text{Thyroid weight (g)} \times 5}{\text{Thyroid uptake percentage (\%)}}.$$

The I-131 dose range varied between 4 and 40 millicurie (mCi) across patients in accordance with their thyroid gland weight and thyroid uptake percentages [33].

Patient preparation

The precautions and procedures (including the restriction of iodine-based treatments and diets) were thoroughly explained to all participants. The pretreatment exclusion of water-soluble iodinated contrast medium-based screenings was also mandated for the patients. They were further required to discontinue their antithyroid prescriptions 1 week before RAI treatment.

TFTs were conducted to investigate the levels of thyroid-stimulating hormone (TSH) (reference range: 0.35 - 4.50 mIU/mL), triiodothyronine (T3) (reference range: 60 - 180 ng/dL), and free thyroxin (FT4) (reference range: 0.9 - 2.3 ng/dL) [34]. Informed consent was obtained from all patients before administering RAI therapy [35]. The patients were updated about radiation safeguards, treatment side-effects, and all other safety/efficacy-related concerns and possibilities [36, 37]. In addition, adult and elderly patients with comorbid conditions who were at a high risk of transient (post-treatment) hyperthyroidism exacerbation received antithyroid drugs after 1 week of RAI treatment [38].

RAI administration

RAI was administered to patients as I-131 (sodium iodide) in liquid or capsule form [39, 40]. The primary and secondary dosages varied between 10 - 15 mCi and 10 - 40 mCi, respectively. A 6-month follow-up was undertaken for evaluating the post-ablation status and TFTs. Treatment success was majorly defined as the establishment of hypothyroid (i.e., serum TSH > 4.0 mU/L) or euthyroid state (i.e., serum TSH: 0.45 - 4.49 mU/L) or the absence of hyperthyroidism [41, 42]. Other parameters that defined treatment success included subclinical or suspected or questionable hypothyroid and euthyroid states [42-44].

Inclusion and exclusion criteria

The adult patients (≥ 18 years) with hyperthyroidism received I-131 therapy and underwent post-treatment monitoring for 6 months. Patients who lost follow-up after RAI ablation or received I-131 doses for thyroid cancer were excluded from the final assessment. The female patients with breastfeeding and pregnancy statuses were also excluded from this study.

Primary and secondary endpoints

Treatment success was the primary endpoint for this study defined by the interim development of a euthyroid state, or hypothyroidism, or subclinical/questionable/suspected hypothyroidism, or questionable euthyroid state. The secondary endpoints included the frequency of repeat RAI doses and post-ablation TFTs. Treatment failure was affirmed by unresolved hyperthyroidism within the post-ablation tenure of 6 - 12 months.

Questionable hypothyroidism refers to cases where TFTs are inconclusive or borderline, making it difficult to determine whether a patient has hypothyroidism. In such cases, physicians may need to rely on clinical judgment, symptoms, and risk factors to guide their decision-making process. Questionable euthyroid state term refers to situations where it is unclear whether a patient has normal thyroid function (euthyroid state)

or not. It might be used in cases where TFTs return borderline or conflicting results. In such cases, a physician may need to consider additional testing or follow-up assessments to determine the patient's thyroid status. Suspected hypothyroidism refers to cases where a patient exhibits symptoms consistent with hypothyroidism, but the diagnosis has not yet been confirmed with laboratory tests. Physicians may suspect hypothyroidism based on clinical presentation and may order TFTs to confirm or rule out the diagnosis.

Statistical analysis

The univariate and multivariate analyses of patient data were undertaken by the SPSS-28 tool of IBM corporation, Armonk, New York [45, 46]. The quantitative and qualitative data were presented as means (with standard deviations (SDs)) and percentages/frequencies, respectively [47]. The outcomes indicating a statistical relationship between I-131 treatments and post-ablation status or resolution TFTs were defined within 95% confidence intervals (CIs) [47].

We utilized a multivariate regression model to assess I-131 dosages and their correlation with post-ablation diagnoses and TFTs. In addition, the univariate analysis was utilized to evaluate the baseline characteristics of patients with hyperthyroidism. The univariate logistic regression analysis was also used to compare baseline factors in patients with successful and unsuccessful I-131 treatment outcomes. The multivariate analysis further revealed the percentages of post-ablation diagnoses in the treated patients.

The model fitting criteria, likelihood ratio tests (including the Chi-square test), and the goodness-of-fit approach were utilized to assess the adequacy of the multivariate regression approach in evaluating the relationship between I-131 treatment dosages and respective (primary and secondary) outcomes [48]. The multivariate approach determined the relationship between I-131 treatment dosages and observed versus predicted frequencies of post-ablation outcomes, including euthyroid, hypothyroid, and hyperthyroid states. Similar relationships were assessed for post-treatment TFTs.

Institutional Review Board of the Mount Sinai School of Medicine, in accordance with Mount Sinai's Federal Wide Assurances (FWA#00005656, FWA#00005651) to the Department of Health and Human Services, approved the human subject research.

Results

Demographic information

Table 1 presents the demographic characteristics of the included patients. One hundred one patients were initially enrolled for this study, while complete data were available for 89 patients who received I-131 therapy for hyperthyroidism. The age range of patients varied between 18 and 82 years (mean 48.77 ± 13.26). Approximately 83.1% (n = 74) of them were females, while 16.9% (n = 15) were males. The majority of patients (i.e., 52.8%) had a non-Hispanic origin, while 1.1% were other Hispanic, 4.5% Mexican, 1.1% Guatemalan, 2.2% Filipino, 1.1% Ecuadorian, 1.1% Chinese, and 2.2% of unknown ethnicity. Their morbidities included Graves' disease/hyperthyroidism (67.4%) with or without thyrotoxicosis (1.1%), hyperthyroidism (without Graves' disease) (2.2%), multinodular goiter (1.1%), questionable thyroid nodule (1.1%), subclinical hyperthyroidism (1.1%), thyrotoxicosis (without Graves' disease) (2.2%), toxic multinodular goiter (10.1%), and toxic thyroid nodule (10.1%). The thyroid uptake percentages in patients varied within the range of 8-101% (mean 62.03 ± 23.89).

Table 1. Baseline Characteristics of Patients With Radioactive Iodine Therapy (n = 89)

Age (mean ± SD)	**48.7753 ± 13.26286**
Gender, n %	
Females	74 (83.1%)
Males	15 (16.9%)
Ethnicity, %	
Chinese	1.1%
Declined	2.2%
Ecuadorian	1.1%
Filipino	2.2%
Guatemalan	1.1%
Mexican/Mexican American	4.5%
Non-Hispanic	52.8%
Other Hispanic	1.1%
Salvadoran	2.2%
Unknown	31.5%
Preliminary diagnosis, %	
Graves with thyrotoxicosis	1.1%
Graves' disease	67.4%
Hyperthyroidism	2.2%
Multinodular goiter	3.4%
Multinodular goiter or thyroid adenoma	1.1%
Questionable toxic thyroid nodule	1.1%
Subclinical hyperthyroidism	1.1%
Thyrotoxicosis	2.2%
Toxic multinodular goitre	10.1%
Toxic thyroid nodule	10.1%
Thyroid uptake percentage (mean ± SD)	62.03 ± 23.89

SD: standard deviation.

Repeat I-131 or RAI dosages

The univariate (post-ablation) analysis segregated the frequency of repeat I-131 dosages administered to achieve euthyroid or hypothyroid state in eight (i.e., 9%) of the treated patients

Table 2. Univariate Post-Ablation Analysis

Dosage (I-131) in mCi	N	%
10.60	1	1.1%
15.00	2	2.2%
20.00	1	1.1%
25.00	1	1.1%
30.00	1	1.1%
31.00	1	1.1%
39.70	1	1.1%

(Table 2). The respective dosages were 10.6 mCi (n = 1), 15 mCi (n = 2), 20 mCi (n = 1), 25 mCi (n = 1), 30 mCi (n = 1), 31 mCi (n = 1), and 39.7 mCi (n = 1), respectively.

Failed versus successful I-131 treatments

The univariate logistic regression analysis further classified patients based on the failure and success of the I-131 treatment (Supplementary Material 1, www.jofem.org). Fifteen patients who received RAI therapy showed a poor response and could not achieve a euthyroid or hypothyroid status. The patients with treatment failure corresponded to the age range of 28 - 77 years (mean 48.46 ± 15.42); however, those with successful therapy were within the age group of 14 - 82 years (mean 48.84 ± 12.89). The mean thyroid uptake percentages in patients with unsuccessful versus successful treatments were recorded as 65.4 ± 19.77 and 61.32 ± 24.73, respectively. Similarly, mean I-131 dosages were found to be 19.02 ± 5.25 mCi and 10.6 ± 2.36 mCi in patients with failed and successful treatments. Treatment success was recorded in 62 (83.8%) females and 12 (16.2%) males as compared to 12 (80%) females and three (20%) males who could not get the therapeutic advantage from I-131 dosages. The majority of patients with treatment success were of non-Hispanic origin (n = 42, 56.8%). Filipino (2.7%), Guatemalan (1.4%), Mexican (4.1%), other Hispanic (1.4%), Chinese (1.4%), Salvadoran (2.7%), and unknown ethnicities (28.4%) included the remaining patients who developed euthyroid or hypothyroid status after receiving I-131 treatment. The ethnicities concerning failed treatment included non-Hispanic (33.3%), Mexican (6.7%), Ecuadorian (6.7%), and unknown (46.7%), respectively. Fifty-one (68.9%) patients with successful I-131 treatment had a primary diagnosis of Graves' disease compared to nine (60%) with failed therapy. The mean thyroid uptakes in patients with successful and unsuccessful treatments were recorded as 1.4% and 6.7%, respectively.

All (i.e., n = 15, 100%) patients with I-131 treatment failure were re-confirmed with hyperthyroidism; however, diagnostic assessment of successfully treated patients indicated euthyroid status (n = 6, 8.1%) and hypothyroidism (n = 63, 85.1%) (Supplementary Material 2, www.jofem.org). In addition, questionable euthyroid status, questionable hypothyroidism, subclinical hypothyroidism, and suspected hypothyroidism were recorded in four patients with successful therapy.

The multivariate regression reassessment of overall post-treatment outcomes revealed the following conditions: 1) euthyroid status (n = 6, 6.7%), 2) hyperthyroidism (n = 15, 16.9%), 3) hypothyroidism (n = 63, 70.8%), 4) questionable euthyroid status (n = 1, 1.1%), 5) questionable hypothyroidism (n = 1, 1.1%), 6) subclinical hypothyroidism (n = 2, 2.2%), and 7) suspected hypothyroidism (n = 1, 1.1%) (Supplementary Material 3, www.jofem.org). These findings confirmed an 83% success rate recorded within 6 months of administering I-131 therapy.

Post-treatment diagnosis

The multivariate regression assessment via model fitting criteria and likelihood ratio tests indicated the statistical significance of intercept ($P < 0.001$) compared to I-131 treatment dosage ($P = 0.321$) (Supplementary Material 4, www.jofem.org). The goodness-of-fit approach indicated statistically insignificant Chi-square outcomes and degrees of freedom for Pearson ($P = 0.994$) and deviance residuals ($P = 1.00$) (Supplementary Material 5, www.jofem.org). The parameter estimates categorized euthyroid state, hyperthyroidism, hypothyroidism, questionable euthyroid state, questionable hypothyroidism, and subclinical hypothyroidism within 95% CIs (Supplementary Materials 6, www.jofem.org). The majority of outcomes were statistically insignificant for I-131 treatment dosage versus intercept, thereby reaffirming the potential of RAI treatment to establish the post-ablation diagnoses. Supplementary Material 7 (www.jofem.org) presents observed versus predicted frequencies for I-131 treatment dosages and their individualized impact on the post-ablation status.

Post-treatment TFT

Supplementary Material 8 (www.jofem.org) presents the case processing summary indicating marginal percentages of post-ablation TSH levels in patients treated with I-131 dosage. The model fitting criteria (Supplementary Material 9, www.jofem.org), likelihood ratio tests (Supplementary Material 10, www.jofem.org), goodness-of-fit criteria (Supplementary Material 11, www.jofem.org), and parameter estimates (Supplementary Material 12, www.jofem.org) revealed the suitability of the multivariate regression approach to testify to the potential impact of I-131 treatment dosages on TSH levels of patients with hyperthyroidism. Supplementary Material 13 (www.jofem.org) presents the observed and predicted frequencies of I-131 treatment dosages and their impact on TSH levels.

Supplementary Material 14 (www.jofem.org) presents the case processing summary delineating marginal percentages of post-treatment T3 levels in patients who received RAI treatment. The goodness-of-fit approach produced insignificant results ($P > 0.05$) indicating the appropriateness of multivariate regression to investigate the impact of I-131 treatment dosage on post-ablation T3 levels (Supplementary Material 15, www.jofem.org). In addition, parameter estimates were statistically insignificant for the intercept ($P > 0.05$) and post-ablation T3 levels based on I-131 treatment dosages ($P > 0.05$) (Supplementary Material 16, www.jofem.org). The Supplementary

Material 17 (www.jofem.org) presents observed and predicted frequencies of I-131 treatment dose-based post-ablation T3 levels.

The case processing summary depicted in Supplementary Material 18 (www.jofem.org) segregates post-ablation FT4 percentages based on I-131 treatment dosages. In addition, the likelihood ratio tests and goodness-of-fit approach produced insignificant results for the intercept (P = 0.081), I-131 treatment dosages (P = 0.008), and the deviance residual (P = 1.00) (Supplementary Materials 19 and 20, www.jofem.org). These findings substantiated the therapeutic impact of the independent variable (i.e., I-131 treatment) on the dependent outcome (i.e., FT4). The parameter estimates categorized post-ablation FT4 levels based on intercept and I-131 treatment dosages (Supplementary Material 21, www.jofem.org). The statistically insignificant results were indicated by the corresponding P-value range (P = 0.06 - 0.9). These outcomes reaffirmed the impact of the I-131 institutional formula (i.e., the independent variable) on FT4 levels at various dose ranges. The Supplementary Material 22 (www.jofem.org) presents observed and predicted frequencies concerning post-ablation FT4 levels for each of the I-131 treatment dosages.

Discussion

The univariate and multivariate regression analysis confirmed the therapeutic efficacy of I-131 treatment dosages (between 4 and 40 mCi) (governed by the current institutional formula) for hyperthyroidism. The results also indicated the clinically significant impact of RAI therapy on post-ablation TSH, T3, and FT4 levels. The findings revealed an 83% success rate of RAI treatment defined by the achievement of euthyroid state and hypothyroidism. The absence of hyperthyroidism after I-131 treatment was further affirmed by questionable euthyroid state, subclinical hypothyroidism, questionable hypothyroidism, and suspected hypothyroidism. The treatment failure rate of 17% was, however, indicated by the reconfirmation of hyperthyroidism in 15 patients. In addition, a low number (i.e., 9%) of patients with hyperthyroidism required repeat I-131 treatment dosages to achieve a hypothyroid or euthyroid state. Inversely proportional to the 24-h radioactive iodine uptake (RAIU) is the I-131 dose. This indicates that as the RAIU increases, so does the I-131 dosage, and *vice versa*. Failure of treatment with a high RAIU may therefore be due to an insufficiently calculated I-131 dose. The results, therefore, strongly advocated the therapeutic efficacy of the empirically derived I-131 institution formula in patients with hyperthyroidism and related complications.

The results of this retrospective study strengthen the outcomes of a 10-year Australian cohort study by Fanning et al that indicated a 79.3% treatment success rate and requirement of repeat I-131 dosages in 13% of patients to achieve hypothyroidism [49]. Our findings also added value to the results of the retrospective study of Isah et al that confirmed a 68% success rate of I-131 therapy at 6 months and 89% at 12 months [50]. However, the results of this study contradicted the outcomes of Isah et al indicating the need for a repeat I-131 dose in 32% of patients. The current outcomes concorded with the retrospective single-center assessment by Mohamadien et al that indicated a 79.7% success rate of I-131 treatment at 3 months in patients with hyperthyroidism [12]. In addition, our secondary finding (i.e., a low percentage of repeat I-131 dosages) contradicted the findings of Mohamadien et al revealing 20.3% of cases with repeated RAI therapy. Our results further strengthened the outcome of retrospective analysis by Kuanrakcharoen that indicated a 66.3% success rate of I-131 treatment at 1 year [51]. However, the current findings contradicted the results of a recent retrospective study by Arora et al that indicated a variable (i.e., 31-60%) success rate of RAI treatment [52].

There are a few additional formulas. The first is the Marinelli formula, which is based on iodine uptake and targeted dose calculation, and demonstrated relatively low deviation [1]. ^{131}I (mCi) = estimated thyroid mass (g) × absorption dose (Gy/g) × 0.67/($T_{1/2eff}$ (days) × maximum ^{131}I thyroid uptake (%)). Amit Allahabadia et al utilized the 370 MBq single fixed dose. This cohort study was also contingent on the size of the thyroid gland and the severity of hyperthyroidism, and most patients required more than one dose of therapy [2]. Alexander et al described the dose formula: ^{131}I = (8 mCi × 100)/(% uptake at 24 h). This study utilized high doses of radioactive iodine; however, despite the use of high doses of radioactive iodine, some patients developed transient hypothyroidism followed by hyperthyroidism, and a small number required a second round of treatment [3]. Sahmaran et al studied the minimally significant changes and reproducibility of ^{131}I uptake. Gultekin utilized the following formula: Dose = k (MBq/g) × thyroid weight (g)/24-h RAIU; this study has statistically non-significant differences between RAIU measurements; this study has age and remeasurement-related geometric limitations [4]. After reviewing these calculations and formulas, we chose our institute's formula because we believe it is more precise, accurate, and yields better results than other studies.

The therapeutic efficacy of I-131 dosages depends on the iodine uptake capacity of thyroid cells in patients with hyperthyroidism [53]. The interaction of the intracellular water with I-131 beta particles triggers the production of cytotoxic free radicals capable of destroying the follicular cells [16]. American Thyroid Association (ATA) guidelines recommend single treatment doses of I-131 (i.e., 10 - 20 mCi and 10 - 15 mCi) for treating toxic multinodular goiter and Grave's disease, respectively [39, 54]. ATA further recommends the administration of methimazole or beta-adrenergic blockers to patients with hyperthyroidism before I-131 therapy to minimize the risk and incidence of transient thyrotoxicosis [55]. These treatment guidelines are highly recommended for at-risk patients (with hyperthyroidism and cardiovascular complications) and those above 65 years of age [39].

Limitations

This retrospective study has several limitations that restrict the generalization of its outcomes in a diverse patient population with hyperthyroidism and its associated complications. First, the small sample size limits the optimization of the empirically derived I-131 institution formula for hyperthyroidism treatment in other clinical settings. Second, 6-month follow-up compared to larger follow-up durations evaluated by contemporary

studies impacts the reliability of currently assessed treatment success rate and dose repetition frequency. Third, due to sample size and timeline restrictions, this study did not segregate RAI therapy's success and failure rates based on the individualized I-131 dosages. Fourth, due to data restrictions, this study did not perform I-131 dose-based comparisons between pretreatment and post-treatment TFT scores. Fifth, this study did not evaluate the adverse effects of I-131 therapy in patients with hyperthyroidism. Sixth, a few instances of missing patient data added to the risk of selection bias. Seventh, the financial burden and exposure to RAI for NM scans, which should be performed to calculate therapeutic dose rather than using a fixed dose.

Conclusion

The findings of this study indicated an 83% RAI treatment success rate and the requirement of a second treatment session in 9% of patients with hyperthyroidism. The results, however, did not support the need for a third I-131 treatment session. The outcomes indicated the impact of I-131 treatment on post-ablation TFT scores. The majority (i.e., 70.8%) of successfully treated patients were diagnosed with hypothyroidism followed by 6.7% who achieved a euthyroid status. The highest I-131 treatment dose based on the current institution formula did not exceed 40 mCi. In addition, I-131 dose assessments varied in accordance with thyroid gland weight and thyroid uptake percentages. Future randomized controlled trials should re-investigate the therapeutic efficacy and safety of RAI therapy for a large subset of patients with hyperthyroidism and associated morbidities and comorbidities.

Learning points

The I-131 treatment dosage calculation for hyperthyroidism management depends on the weight and uptake percentage of the thyroid gland. RAI therapy is associated with an 83% success rate based on establishing hypothyroidism and a euthyroid state in 70.8% and 6.7% of patients, initially with hyperthyroidism. A low percentage (i.e., 9%) of patients with hyperthyroidism require treatment with I-131 dosages. I-131 treatment dosages have clinically significant password-protected FT4 levels in patients treated for hyperthyroidism.

Supplementary Material

Suppl 1. Univariate Logistic Regression Analysis for the Failure and Success of I-131 Treatment.

Suppl 2. Univariate Logistic Regression Analysis for the Diagnostic Assessment of Patients With Failed Versus Successful Treatments.

Suppl 3. Multivariate Regression Reassessment of Overall Post-Treatment Outcome.

Suppl 4. Model Fitting Criteria for Post-Ablation Status.

Suppl 5. Goodness-of-Fit Model for Post-Ablation Status.

Suppl 6. Parameter Estimates for Post-Ablation Status.

Suppl 7. Observed and Predicted Frequencies of I-131 Treatment Dosages Based on Post-Ablation Status.

Suppl 8. Case Processing Summary of Post-Ablation TSH Levels.

Suppl 9. Model Fitting Criteria for Post-Ablation TSH Levels.

Suppl 10. Likelihood Ratio Tests for Post-Ablation TSH Levels.

Suppl 11. Goodness-of-Fit Criteria for Post-Ablation TSH Levels.

Suppl 12. Parameter Estimates for Post-Ablation TSH.

Suppl 13. Observed and Predicted Frequencies for Post-Ablation TSH Levels.

Suppl 14. Case Processing Summary for Post-Ablation T3 Levels.

Suppl 15. Goodness-of-Fit Criteria for Post-Ablation T3 Levels.

Suppl 16. Parameter Estimates for Post-Ablation T3 Levels.

Suppl 17. Observed and Predicted frequencies of Post-Ablation T3 Levels.

Suppl 18. Case Processing Summary for Post-Ablation FT4 Levels.

Suppl 19. Likelihood Ratio Tests for Post-Ablation T4 Levels.

Suppl 20. Goodness-of-Fit Criteria for Post-Ablation T4 Levels.

Suppl 21. Parameter Estimates for Post-Ablation T4 Levels.

Suppl 22. Observed and Predicted Frequencies for Post-Ablation FT4 Levels.

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None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Informed Consent

The request for a waiver of informed consent was approved.

Author Contributions

Sanna Salam is the first author and responsible for manuscript

writing and editing. Nso Nso is responsible for manuscript writing and data analysis. Ravali Konaveeti and Tsung Han Scottie Ching are responsible for data extraction. Mahmoud Nassar is responsible for literature review.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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