Original Article

Impact of Post-Thyroidectomy I-123 Versus I-131 Whole Body Scan on the Outcome of Radioactive Iodine (I-131) Ablation for Differentiated Thyroid Carcinoma

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ABSTRACT:

Objectives: I-131 is a widely used radiopharmaceutical for the management of patients with differentiated thyroid carcinoma (DTC). It is the main agent for the ablation of residual thyroid tissue and the treatment of recurrent or metastatic DTC. However, diagnostic doses of I-131 may cause some form of cell damage "stunning" which reduce subsequent uptake of the therapeutic dose of I-131. In contrast, I-123 is considered an ideal isotope for diagnostic studies; it emits only gamma radiation and thus lacks the stunning effect. The aim of the current study was to assess the impact of post-thyroidectomy I-123 versus I-131 Whole Body Scan (WBS) on the outcome of I-131 ablation for DTC. **Methods:** 70 consecutive DTC patients (60 papillary thyroid Ca., and 10 Follicular thyroid Ca.), underwent total thyroidectomy, followed by WBS, neck ultrasound (US), and subsequent I-131 ablation after 40 days without thyroid hormone replacement (TSH > 30 µIU/ml) were retrospectively enrolled in current study. Scans were acquired using the Forte dual head gamma camera (Phillips medical systems) equipped with a low energy parallel hole collimator, 24 hours after an oral administration of 37-111 MBq (1-3 mCi) of I-123, in 41 patients (Group 1), and equipped with a high energy parallel hole collimator, 48 hours after an oral administration of 74-185 MBq (2-5mCi) of I-131 in 29 patients (Group 2). 6 months later follow up I-131 WBS, neck US, serum thyroglobulin (Tg) and Tg antibodies (TgAb) were performed following suspension of L-thyroxin for one month (TSH > 30 µIU/ml) in 61 patients and following rhTSH stimulation in 9 patients. **Results:** No significant difference regarding age, gender and histopathology between both groups. 32/41, (78%) patients of group (1) and 16/29 (55%) of group (2) had negative follow up WBS, however, 5 patients of group (1), and 4 of group (2) with negative follow up WBS, had Tg > 5 ng/ml, with US findings suggestive of residual disease in the neck. The overall successful ablation rate were 27/41, 66% in group (1) versus 12/29, 41.4% in group (2) (P = 0.042). **Conclusions:** We found a significantly higher successful I-131 ablation rate among patients studied with I-123 WBS compared to those studied with I-131 WBS before radioiodine ablation, and recommend the use of I-123 instead of I-131 for WBS before radioiodine ablation.

Key words: Differentiated thyroid carcinoma – I-123 WBS - ablation.

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INTRODUCTION:

Differentiated thyroid carcinoma (DTC) is the most common endocrine malignancy [(1)]. Its incidence has even increased worldwide during the past decades [(1–5)]. Primary treatment of DTC consists of total or near-total thyroidectomy followed by ablation of thyroid tissue remnants and possible metastases by means of radioactive iodine-131 (I-131). The goals of initial therapy for DTC are to remove the primary tumor and thyroid tissue to permit accurate staging of the disease, and facilitate post-operative remnant ablation with I-131. Radioactive iodine-131 ablation has two-targets; firstly to ablate the residual normal thyroid remaining after total or near-total thyroidectomy, thus facilitating the early detection of recurrence based on serum thyroglobulin (Tg) measurement, and secondly it is to destroy persistent thyroid cancer cells after appropriate surgery as an adjuvant therapy employing the potential tumoricidal effect of I-131[(6,7)].Accurate post-operative staging is a crucial element in the management of patients with DTC, as disease staging can assist with initial prognostication, disease management, and follow-up strategies[(6,8,9)]. Several studies demonstrated that post-thyroidectomy whole body scans (WBS) affect the staging of patients with thyroid cancer and that the information obtained with post-thyroidectomy WBS changes management decisions (such as whether to proceed with or to omit therapeutic I-131 administration, refer the patient for surgical debulking before I-131 therapy, or perform additional imaging studies when non–iodine-avid disease is demonstrated by negative WBS but elevated Tg levels). The findings on post-thyroidectomy WBS may also change the prescribed I-131 activity for thyroid cancer patients, either by adjusting I-131 doses or performing dosimetry calculations for maximizing therapeutic I-131 activity for treatment of distant metastatic disease [(10 – 13)].Radioactive iodine-131 is a widely used radio-pharmaceutical for imaging patients with DTC. However, diagnostic doses of I-131 may cause some form of cell damage “stunning”, which reduce subsequent uptake of the therapeutic dose of I-131[(14, 15)]. In contrast, I-123 is considered an ideal isotope for diagnostic studies; it results in a significantly lower radiation absorbed dose to thyroid tissue [16], thereby making stunning highly unlikely [(15)]. The aim of the current study was to assess the impact of post-thyroidectomy I-123 versus I-131 Whole Body Scan (WBS) on the outcome of I-131 ablation for DTC.

MATERIALS AND METHODS:

Following approval by the institutional ethics committee, 70 consecutive patients with DTC, who underwent post-thyroidectomy WBS, subsequent I-131 ablation, and follow-up WBS at our institution from January 2010 to December 2013, were retrospectively enrolled in this study. An informed consent was waived for this retrospective study. Initial treatment was total or near total thyroidectomy. Post-operatively, all patients underwent

WBS, neck ultrasound (US), serum thyroglobulin (Tg) and Tg anti-bodies (TgAb) assay after 40 days without thyroid hormone replacement to induce a hypothyroid state (TSH > 30 µIU/ml). The patients followed a low-iodine diet for 10–15 days before the WBS. Subsequently, I-131 ablation dose was administered to all patients to ablate normal thyroid and residual disease and to treat metastatic lesions, followed by a post-ablationWBS.A postthyroidectomy WBS, and static views of the head and neck were acquired using the Forte dual head gamma camera (Phillips medical systems) set at 159 keV with a 20% energy window, and equipped with a low energy parallel hole collimator, 24 hours after an oral administration of 37-111 MBq (1-3 mCi) of I-123, in 41 patients (Group 1). In the other 29 patients, scans were acquired using a high energy parallel hole collimator, fitted to the Forte dual head gamma camera set at 364 keV with a 20% energy window, 48 hours after an oral administration of 74-185 MBq (2-5mCi) of I-131 (Group 2). Ultrasound evaluation of the thyroid bed and both central and lateral neck compartments was performed on the day of administration of the diagnostic dose of radioiodine using a 7.5 MHz linear-array transducer (Accuvix A30 US System; Samsung Medison Healthcare). Suspicion of malignant lymph node was based on the following criteria: Hyperechoic punctuations, cystic appearance, hyper vascularization, round shape node without hyperechoic hilum, and a short axis >7 mm. Patients received ablation I-131 doses in the range of 1.11–6.4 GBq (30–173 mCi) depending on the results of post-thyroidectomy WBS, Neck US and histopathology findings, followed by thyrotropin-suppressive doses of L-thyroxin. Post-ablation WBS and static views of the anterior neck were acquired within 5 days after the I-131 ablation. Six months after I-131 ablation, follow-up including clinical assessment, I-131 WBS, neck U/S, Tg and TgAb assay were performed following suspension of L-thyroxin for 1-month (TSH >30 µIU/ml) in 61 patients and following recombinant human TSH (rhTSH) stimulation in nine patients. Stimulated Tg <1 ng/mL, negative WBS, and normal US were considered as the criteria for successful ablation.

Statistical analysis: Quantitative data were expressed as mean ± standard deviation, and qualitative data were expressed in percentage. Statistical analysis of the categorical variables was conducted using a Chi-square test or Fisher's exact test. Comparisons between continuous variables were performed with an independent t-test. A $P < 0.05$ was considered as statistically significant. All the analyses were performed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA).

RESULTS:

A total of 70 consecutive patients (age 37.33 ± 8.74 years, female: male = 48:22) with DTC, were retrospectively enrolled in current study. Sixty patients were diagnosed with papillary thyroid cancer, and ten with follicular thyroid cancer. The TSH levels of the whole group were over 30 µIU/mL (94.24 ±

58.86 µIU/mL) before post-thyroidectomy WBS, and the average Tg levels were (6.62±7.39 ng/mL). Demographic, histopathology, and laboratory findings of prognostic relevance are summarized in Table 1. There was no significant difference regarding age, gender, histopathology, pre-WBS TSH and serum Tg levels between DTC patients who underwent post-thyroidectomy WBS using I-123 and those who underwent WBS using I-131.The ultrasonographic findings of DTC patients studied with I-123 were as follow: unremarkable in 14/41(34.1%), residual tissues at the thyroid bed in 20/41patients (48.8%), enlarged ipsi-lateral cervical LN with preserved fatty hilum in 1/41 (2.4%), enlarged ipsi-lateral cervical LN with loss of fatty hilum in 2/41 (4.9%), and both residual tissues at the thyroid bed and enlarged cervical LN with loss of fatty hilum in 4/41 (9.8%); while in DTC patients studied with I-131, the ultrasonographic findings were as follow: unremarkable in 6/29 (20.7%), residual tissues at the thyroid bed in 20/29 (69%), enlarged cervical LN with loss of fatty hilum in 1/29 (3.4%), and both residual tissues at the thyroid bed and ipsilateral enlarged cervical LN with preserved fatty hilum in 2/29 (6.9%).Post-thyroidectomy WBS showed uptake in the neck which considered positive for functioning thyroid tissue in all patients. The average ablation dose of radioiodine was 4.335 ± 1.228 GBq (117.16 ± 33. 2 mCi) in the patients studied with I-123 and 3.962 ± 1.116 GBq (107.07 ± 30.16 mCi) in the patients studied with I-131 (P = 0.203). Six months after I-131 ablation, follow-up I-131 WBS was negative in 32/41, (78%) patients of group (1) (figure 1), compared to 16/29 (55%) of group (2) (P = 0.042), however, 5 patients of group (1), and 4 of group (2) with negative follow-up WBS, had Tg > 5 ng/ml, with ultrasonographic findings suggestive of residual disease in the neck. Thus the overall successful remnant ablation rate was significantly higher among patients studied with I-123 (27/41, 66%) compared to patients studied with I-131 prior to I-131 ablation (12/29, 41.4%) (P = 0.042).

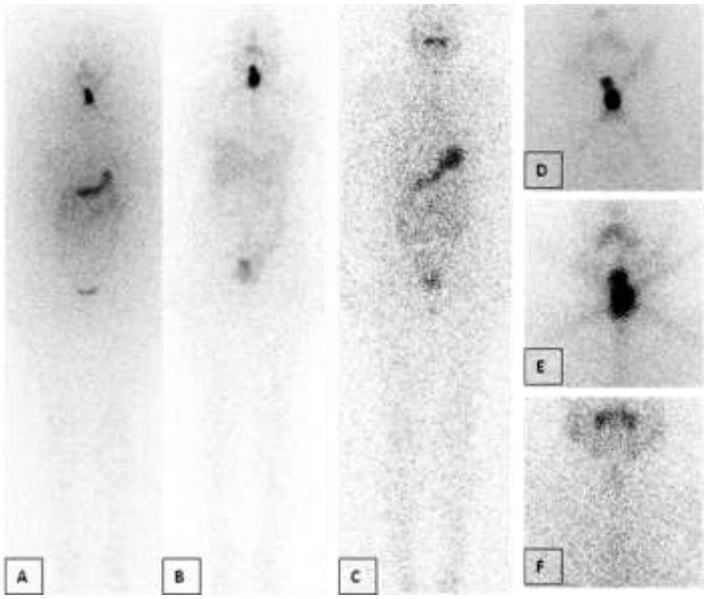

Figure (1): Anterior (A) and anterior neck images (D) of 1-123 post-thyroidectomy whole body scan (WBS) showed abnormal radiotracer uptake at the bed of the thyroid gland. A post-therapy I-131 WBS (B & E) showed good tracer localization in residual thyroid tissue in the neck and no distant metastasis. Follow-up I-131 WBS after 6 months (C & F) showed unremarkable radiotracer localization and serum Tg was less than 0.8 ng/ml, suggest successful ablation.

Table (1): Comparison of demographic, histopathology and laboratory findings among DTC patients studied with I-123 and those studied with I-131 priot to I-131 ablation

	I-123 WBS group	*I-131 WBS group*	*P- value*
Number	41 (58.6%)	29 (41.4%)	
Age	39 ±8.95	35 ± 8	NS
Gender			
Female	27(56.2%)	21 (43.8%)	NS
Male	14 (63.6%)	8 (36.4%)	
Histopathology			
Papillary	37 (61.7%)	23 (38.3%)	NS
Follicular	4 (40%)	6 (60%)	
Maximum tumor size	1.98 ± 1.24 cm	2.48 ±1.3 cm	NS
Thyroiditis on pathology	14/41 (34%)	7/29 (24%)	NS
Multiplicity	17/41 (41.5%)	12/29 (41.4%)	NS
Bilaterality	13/41 (31.7%)	7/29 (24%)	NS
Extrathyroidal extension	5/41(12.2%)	6/29 (20.7%)	NS
Lymphatic invasion	2/41 (4.9%)	3/29 (10.3%)	NS
Lymph node metastasis	10/41(24.4%)	6/29 (20.7%)	NS
TSH before ablation	93.58±60.39	96.15±56.63	NS
Serum Tg before ablation	5.89±6.38	7.97±8.99	NS
Follow-up TSH	105.75±53.64	117.06±64.95	NS

DTC, differentiated thyroid carcinoma; WBS, whole body scan; Tg, thyroglobulin; NS, non significant

DISCUSSION:

The current American Thyroid Association and European Thyroid Association guidelines recommend total or near-total thyroidectomy for DTC of >1 cm [6, 7]. The amount of thyroid remnant is influenced by many factors, depending on the peri-operative findings related to tumor extent, surgical experience and training [17].A post-thyroidectomy radioiodine scan or measurement of I-131 thyroid bed uptake is useful when the extent of the thyroid remnant cannot be accurately ascertained from the surgical report, or when the results would alter subsequent management [6, 7]. The primary goal of I-131 therapy should be determined before I-131 dose administration and must take into account clinical and histopathology information and the findings on post-thyroidectomy WBS for each individual patient [10].The information obtained with diagnostic post-thyroidectomy WBS has the potential to alter staging and risk stratification, the decision to proceed with, or to omit I-131 therapy, the activity of I-131 to be administered, and the long-term follow-up strategy (10-13). The standard and widely used method for imaging patients with DTC is to perform whole body imaging with I-131(18). I-131 properties make it a unique radiopharmaceutical for the management of patients with DTC. It emits both gamma rays and B-particles, is readily available, and has a low cost and a long half-life (8.02 days). However, its principal gamma-ray of 364 keV and principal β-particle with a maximum energy of 0.606 MeV, result in a significantly high radiation absorbed dose to thyroid tissue(19). I-131 irradiation triggers cellular changes, and reduces expression of sodium iodide symporter (NIS) at the transcriptional level in still-viable thyrocytes, leading to marked reduction of thyrotropin-stimulated iodide transport mediated by the NIS(20). This results in a reduction or absence of I-131 uptake by the thyroid remnant observed on post-therapy WBS performed after a diagnostic I-131WBS, referred to as "stunning"(21). This phenomenon may occur even with small I-131 activities as low as 40 MBq, and would impair the uptake of a subsequent therapeutic dose, leading to ineffective treatment [14]. In contrast, I-123 is a pure gamma-emitter with a gamma-energy of 159 keV, lacks B-particle emission, has a relatively short half-life (13.3 h), and delivers lower radiation dose to patients (22-25). It is considered an optimal agent for diagnostic purposes before therapy with I-131, and several studies indicate that I-123 is comparable to high-dose I-131 post-treatment imaging in the detection of thyroid remnants after thyroidectomy (22,23,26). In addition, it is becoming more available worldwide and is now widely available throughout the United States(15). In spite of these advantages, I-123 is more expensive than I-131 and limited availability is another concern in some areas of the world (13). In current study we assessed the impact of post-thyroidectomy I-123 versus I-131 WBS on the outcome of I-131 ablation for DTC. We found a statistically significant higher successful I-131 ablation rate among patients studied with I-123 WBS compared to those studied with I-131 WBS before radioiodine ablation. Our results were

consistent with those reported by Park et al, 1997[27] who compared the successful ablation rate of functioning thyroid tissue, one year following I-131 therapy administered after diagnostic I-123 WBS in 47 patients and after I-131 WBS in 43 patients. Using the one-year follow-up WBS, without a Tg level, they reported that total ablation was obtained in 72% of patients who received (300 μCi) 11.1 MBq of I-123 as diagnostic dosages before ablation and in 56% of those who received (3-10 mCi) 111–370 MBq of I-131 as diagnostic dosages. Our results are also in line with those reported by Verburg et al, 2009 [14] who evaluated the impact of pre-therapeutic I-131 uptake measurement with 40 MBq I-131 on the success rate of I -131 ablation in DTC patients. They retrospectively studied ninety nine patients with non-metastatic DTC who underwent total thyroidectomy; followed by thyroid remnant ablation. No diagnostic I-131 was applied before ablation in 48 DTC patients, whereas in the other 51 DTC patients, a 24-h uptake-measurement with 40 MBq I-131 was performed. They defined successful ablation as absence of pathological I-131 uptake on follow up diagnostic WBS and undetectable TSH- stimulated Tg levels. Ablation was successful in 65% of patients who had no diagnostic I-131 before ablation, compared to 33% of patients who underwent a 24-h uptake-measurement with 40 MBq I-131 before ablation. They concluded that the success rate of ablation is severely reduced, after applying a diagnostic activity of 40 MBq I-131 before ablation. Chen et al, 2012[13] retrospectively reviewed 122 DTC patients who underwent total thyroidectomy followed by I-123 pre-therapy scan and I-131 ablation. They have not observed any stunning effect from I-123 pre-therapy scans, and they found that the pre-therapy scans provided additional critical information in 25% of the cases. For cases demonstrating >3% uptake with midline lymph nodes, the pre-therapy scan provided additional information in 50% of the cases. They concluded that I-123 pre-therapy scans provide valuable information with regard to unsuspected lymph nodes or distant metastases, indicating the requirement for a significantly higher I-131 dose, and unexpected large thyroid remnants, suggesting the need for two-step ablation. They recommend stimulated pre-therapy scans and adjustment of the treatment dosing accordingly. On the other hand, Silberstein 2007[28] who examined the outcomes of I-131 therapy after diagnostic studies with either I-123 or I-131 to determine if the diagnostic dosages of these radionuclides used in DTC patients reduce the efficacy of I-131 for remnant ablation. He studied fifty patients with non-metastatic DTC underwent total thyroidectomy; followed by thyroid hormone withdrawal to achieve a serum TSH level more than 30 μIU/mL. Patients were divided prospectively into 2 groups. First group had diagnostic imaging with (400 μCi) 14.8 MBq of I-123 and in the second group diagnostic scan was performed with (2 mCi) 74 MBq of I-131. This is followed by empirical ablation with (100 mCi) 3.7-GBq I-131 dosage in both groups. There was no significant difference between both groups demographically, in tumor burden or stage, or in the post-

thyroidectomy ablation rate (group 1, 81%; group 2, 74%; P > 0.05). They concluded that I-131 ablation has the same outcome whether (2 mCi) 74 MBq of I-131 used as a diagnostic agent or (400 µCi) 14.8 MBq of I-123 used for imaging prior to I-131 ablation. Although these conflicting results could be attributed to the fact that iodide transport and NIS messenger RNA (NIS mRNA) expression were reduced by both I-131 and I-123[29], the stunning observed following I-123 could not be explained by errors in the estimation of relative uptake due to different tissue absorption of the I-131 and I-123 photons, nor by the radiation dose delivered by the I-123 [30]. The resultant radiation dose to the thyroid remnant, as the therapeutic radioiodine is being taken up, may be sufficient to inhibit the uptake process, thus leading to a reduction in maximum uptake when compared with that of a diagnostic activity of radioiodine [30].A unique advantage of this study is that it is one of a few studies that compared outcome of I-131 ablation in age-, gender-, histopathology-matched patient groups following either post-thyroidectomy I-123 or I-131WBS.

CONCLUSIONS:

We found a significantly higher successful I-131 ablation rate among patients studied with I-123 WBS compared to those studied with I-131 WBS before radioiodine ablation, and recommend the use of I-123 instead of I-131 for WBS before radioiodine ablation.

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