CLINICAL SIGNIFICANCE OF DIFFUSE HEPATIC UPTAKE ON POST-ABLATIVE RADIO-IODINE SCAN IN DIFFERENTIATED THYROID CANCER

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Abstract

Background: Whole-body 131I scintigraphy and thyroglobulin have always been the mainstay of monitoring patients suffering from differentiated thyroid carcinoma (DTC) after ablation and thyroidectomy.

Objective: This study investigates any significant parameters and clinical outcomes of the diffuse thyroid bed and hepatic uptake of 131I on post-ablative whole-body iodine scans (PAWBIS) in DTC patients.

Research Design and Methods: About 195 patients with recently diagnosed pathologically proven DTC, aged more than 16 years old, underwent complete/nearly complete thyroidectomy regardless of neck dissection and pathologically confirmed to be DTC, with no signs of local residual or distant metastasis, and receiving their first dose of radioactive iodine ablation (RIA) were recruited for this prospective study and divided into three groups: Group 1 (Low-risk group with intra-thyroidal DTC), Group 2 (Intermediate risk group showing either metastasis of cervical lymph gland, microscopic extra-thyroidal extension, vascular invasion, virulent tumor histology, or RAI-avid disease in the neck surrounding the thyroid bed) and Group 3 (High-risk group demonstrating either partial tumor resection, gross extra-thyroidal extension, remote metastases, or unacceptable values of post-operative serum thyroglobulin (TG)).

Results: Primary tumor size, patient gender, age, cervical LN status, and degree of liver visualization were found to be the independent variables of prognosis in DCT in both low and high-dose groups. While in the high-dose group, Cox regression revealed that female patients, mono-focal tumors, and high levels of liver uptake were the only virtuous prognostic factors.

Conclusion: Good and clear hepatic visualization signifies effective ablation, and consequently, reliable prognosis. However, less hepatic visualization may be correlated to a lower chance of full response to 131I therapy.

Keywords: Diffuse hepatic uptake, Differentiated thyroid carcinoma, post-ablative radio-iodine scan

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Introduction:

Cancer of the thyroid gland is considered one of the leading causes of cancer all over the world and is believed to be the cause of about 1% of clinical malignancies, while well-differentiated follicular cell cancer is considered to be the prominent cause of 80% to 90% of all thyroid carcinoma[1].

Iodine 131 (131I) ablation therapy in addition to thyroid-stimulating hormone (TSH) suppressive medications showed to be significantly useful in reducing the relapse and mortalities from differentiated thyroid carcinoma (DTC) after complete or near-complete thyroidectomy[2].

Patients with DTC have been monitored using whole-body 131I scintigraphy and thyroglobulin post-ablation and thyroidectomy. Iodine builds up in some organs as remaining normal or malignant thyroid tissue, breast, liver, salivary glands, and stomach, which are all visible on radioiodine scans[3].

Cases who undergo diagnostic or therapeutic scans for DTC are also found to have diffuse liver absorption of 131I. Some claim that hepatic visualization on 131I whole-body scans in DTC patients reveals whether a functional residual normal thyroid tissue, repeated or persistent tumor, or both of them [4].

On the other hand, others suppose diffuse liver absorption is a physiological process and does not fairly reflect diffuse thyroid cancer or remaining normal thyroid tissue. This prospective study aimed to conclude the prevalence of diffuse hepatic uptake, the probability of its association with any remaining

normal thyroid tissue, and whether it may be utilized as a prognostic indicator.

The target of this work was to investigate any significant parameters and clinical outcomes of the diffuse thyroid bed and hepatic uptake of 131I on post-ablative whole body iodine scans (PAWBIS) of DTC patients.

Patients and Methods:

About 195 patients with recently diagnosed pathologically confirmed DTC, aged more than 16 years old, underwent complete/nearly complete thyroidectomy regardless neck dissection and pathologically defined to be DTC, with no signs of local residual or distant metastasis, and receiving their initial dose of radioactive iodine ablation (RIA) were recruited for this prospective study and divided into three groups: Kasr Al-Ainy Ethical Committee, Cairo University Hospitals, Egypt approved this study between January-2015 and December 2016. Patients themselves or their relatives signed a written informed consent before inclusion in the study.

Exclusion criteria were cases less than 16 years old, evidence of remote disease after surgery, already received previous ablative/therapeutic doses of RAI, or diagnostic post-operative whole-body scan, life-threatening impairment of organ function, serum (TSH) level < 30 IU/ml during RIA, pathology is proven to show anaplastic changes or poorly differentiated thyroid cancer, known already liver disease.

Following the revised American thyroid association (ATA) management guidelines' risk stratification criteria, Patients were allocated into three groups as follows:

Group 1: Low risk with intra-thyroidal DTC that shows no sign of extra-thyroidal extension, metastases or vascular invasion.

Group 2: Intermediate risk revealing either microscopic extension in the extra-thyroidal region, metastases of cervical lymph gland, RAI-avid disease in the neck out of the thyroid bed, virulent tumor histology, or vascular invasion.

Group 3: High-risk gross extension in the extra-thyroidal region, incomplete mass resection, remote metastases, or unacceptable values of serum thyroglobulin (TG) after the operation.

All patients underwent the following procedure: recording patient history, medical examination, Laboratory Investigations [Baseline TG, serum TSH following surgery and/or after discontinuation of L-troxen by at least one month, liver function tests: SGPT, SGOT, ALK.P, complete blood count (CBC), serum albumin and Kidney function tests (KFTs), pregnancy test (β-hCG)], Radiological Investigations (neck u/, chest X-ray (AP+LAT.) or chest CT without contrast).

Radioactive iodine Ablation (RIA):

Suitable amounts of radioactive iodine were calculated empirically between 1.1 and 5.55 GBq (30 -150 mCi), the corresponding calculated doses were delivered to the patients in the form of orally administered capsules at least four weeks after surgery or discontinuation of thyroid hormone therapy, with serum TSH > 30 IU/ml and patients were instructed to follow a low iodine diet strictly for at least two weeks prior to RIA administration.

Post-ablative whole body iodine (PAWBI) imaging and interpretation:

About 7 to 10 days after RIA, Patients underwent whole-body iodine scanning using a wide field-of-view gamma camera with computer acquisition, moreover, a high-energy parallel-hole collimator was applied, a 20% window was focused on the principle photopeak of I-131 (364 keV), Taking into account that the whole body imaging was performed at 5 cm/minute, and ten-minute spot views were done to show mediastinum, head and neck.

The intensity of diffuse hepatic uptake (DHU) visualization in PAWBIS was scored visually by three blinded nuclear physicians into 4 grades according to the activity of the background as following: Grade 0: zero uptake, Grade I: Barely uptake, Grade II: Fairly uptake, Grade III: Remarkable uptake.

Thyroid bed remnant uptake (TBU) intensity was relatedly scaled from 0 to 3.

Patients' monitoring was for at least 24 months or until they showed either histopathologic or radiologic proof of the disease's persistence or recurrence.

During periodical clinical follow-up visits, the patient's disease status was updated by detailed, diagnostic Whole-Body Scan (DWBS), clinical examination, stimulated serum TG, neck ultrasound, CT on abdomen /chest, Anti-TG-AB or FDG-PET/CT whenever needed.

Response criteria:

1) Successful ablation / no evidence of disease (NED) as the absence of serum TG, no indication of local or diffused disease on DWBS and in neck ultrasound
2) Persistence of disease was defined as the presence of any cytological/histological evidence of illness, elevated serum TG level during thyroid hormone substitution or following TSH stimulation, Iodine-131 avid lesions in the DWBIS, US of suspected neck LNs, an indication of metastatic deposits by MRI or CT and F-18 FDG avid lesions when needed.
3) Recurrence was defined as occurring of any of the previous events after a good follow-up interval (NED).

Statistical analysis

SPSS v22 (IBM Corp, Armonk, NY, USA) was used for the statistical analysis. Qualitative variables were described in terms of percentage (%) and frequency while Quantitative variables were described in terms of standard deviation (SD) and mean. Different numerical variables between the study groups were compared using Chi-square (X^2) test, and survival

analysis using Kaplan Maier statistics was done to analyze the different outcome measures to estimate both mean and median survival time for every group with their 95%CI and the corresponding survival graphs, then a comparison between various variables was done using the Log-rank approach using the Cox-Mantel equation. And finally, to determine the preferential effect of critical variables Cox multivariate regression was used. A two-tailed P value < 0.05 was regarded as significant.

Results:

1

A dramatically significant statistical variation was observed between the two groups regarding gender, age, and outcome as a relatively worse outcome was encountered with the male patients.

No significant statistical variation between the pathological types of DCT and the outcome. The tumor sizes were more than 1cm and multifocal tumors were associated with relatively worse outcomes with significant. There was a significant association between good outcomes and negative history of metastatic cervical LNs. Table

Table1: Demographic details of studied cases regarding the final outcome

		Outcome			Total (n =195)	*p* value
		NED (n = 172)	Persistent disease (n = 19)	Recurrence (n =4)		
Gender	Female	123(71.5%)	4(21.1%)	2(50%)	129(66.2%)	**0.004**
	Male	49(28.5%)	15(78.9%)	2(50%)	66(33.8%)	
Age	< 45 years	135(78.5%)	3(15.8%)	1(25%)	139(71.3%)	**<0.005**
	≥45	37(21.5%)	16(84.2%)	3(75%)	56 (28.7%)	
Pathology	Follicular	13(7.6%)	0	1(25%)	14(7.2%)	0.253
	Papillary	126(73.3%)	13(68.4%)	3(75%)	142(72.8%)	
	Papillary (Follicular variant)	33(19.2%)	6(31.6%)	0	39(20.0%)	
Tumor Size	<1cm	137(79.7%)	6(31.6%)	0	143(73.3%)	**0.005**
	>1cm	35(20.3%)	13(68.4%)	4(100%)	5226.7%)	
Tumor multiplicity	Unifocal	150(87.2%)	9(47.4%)	1(25%)	16082.1%)	**0.02**
	Multifocal	22(12.8%)	10(52.6%)	3(75%)	3517.9%)	
Stage	I	138(80.2%)	5(26.3%)	0	143(73.3%)	**0.03**
	II	23(13.4%)	7(36.8%)	1(25%)	31(15.9%)	
	III	11(6.4%)	5(26.3%)	3(75%)	19(9.7%)	
	IV	0	2	0	2	
LN status	Negative	159(92.4%)	12(63.2%)	0	171(87.7%)	**0.05**
	Positive	13(7.6%)	7(36.8%)	4(100%)	24(12.3%)	

Data are presented as frequency (%). LN: lymph node

Regarding high and low doses there was significant association with liver uptake grades and no association with thyroid uptake. Table 2

Table 2: Liver and Thyroid uptake grades versus low and high dose groups

		Group		Total (n = 195)	*p* value
		Low dose (n = 59)	**High dose (n = 136)**		
Liver grade	No uptake	14(23.7%)	11(8.1%)	25(12.8%)	**0.004**
	Mild	23(39.0%)	33(24.3%)	56(28.7%)	
	Moderate	22(37.3%)	67(49.3%)	89(45.6%)	
	Marked	0	25(18.4%)	2512.8%)	
Thyroid grade	No	0	2(1.5%)	21.0%)	0.471
	Mild	20(33.9%)	28(20.6%)	4824.6%0	
	Moderate	33(55.9%)	73(53.7%)	10654.4%)	
	Marked	6(10.2%)	33(24.3%)	39(20.0%)	

Data are presented as frequency (%).

Different grades of DHU analysis in both low and high-dose groups indicated a strong correlation between liver grade and the outcome, it also showed considerable variation between hepatic visualization and the uptake levels in the thyroid bed. Table 3

Table 3: Liver and Thyroid uptake grades versus the outcome

		Outcome			Total	*p* value
		NED **(n = 172)**	Evident disease **(n = 19)**	Recurrence **(n = 4)**	**(n = 195)**	
Liver grade	No	15(8.7%)	8(42.1%)	2(50.0%)	25(12.8%)	**0.001**
	Mild	43(25.0%)	11(57.9%)	2(50.0%)	56(28.7%)	
	Moderate	89(51.7%)	0	0	89(45.6%)	
	Marked	25(14.5%)	0	0	25(12.8%)	
Thyroid grade	No	2(1.2%)	0	0	2(1.0%)	0.404
	Mild	38(22.1%)	8(42.1%)	2(50.0%)	48(24.6%)	
	Moderate	95(55.2%)	9(47.4%)	2(50.0%)	106(54.4%)	
	Marked	37(21.5%)	2(10.5%)	0	39(20.0%)	

Data are presented in the term of frequency (%).
There was a considerable and significant association between liver and thyroid uptake grades in both high and low-dose groups. Table 4

Table 4: Thyroid and liver uptake grades in high and low-dose group

		Liver uptake grade				Total	p value	r factor
		No	**Mild**	**Moderate**	**Marked**			
Thyroid uptake grade								
low dose group	Mild	10	10	0	-	20	**0.005**	**0.552**
	Moderate	4	12	17	-	33		
	Marked	0	1	5	-	6		
Total		14	23	22	-	59		
high dose group	No	0	0	1	1	2	**0.002**	**0.239**
	Mild	4	12	11	1	28		
	Moderate	7	16	30	20	73		
	Marked	0	5	25	3	33		
Total		11	33	67	25	136		

The univariate analysis of recurrence-free survival among the low and high dose groups showed that primary tumor size, patient gender, age, cervical LN status and degree of liver visualization can be identified as

independent predictor of prognosis in DCT with noted worse prognosis in the lower liver uptake scores (grade 0 and 1), while the high grades (2 and 3) were the best prognostic groups. Table 5

Table 5: Univariate analysis of recurrence-free survival

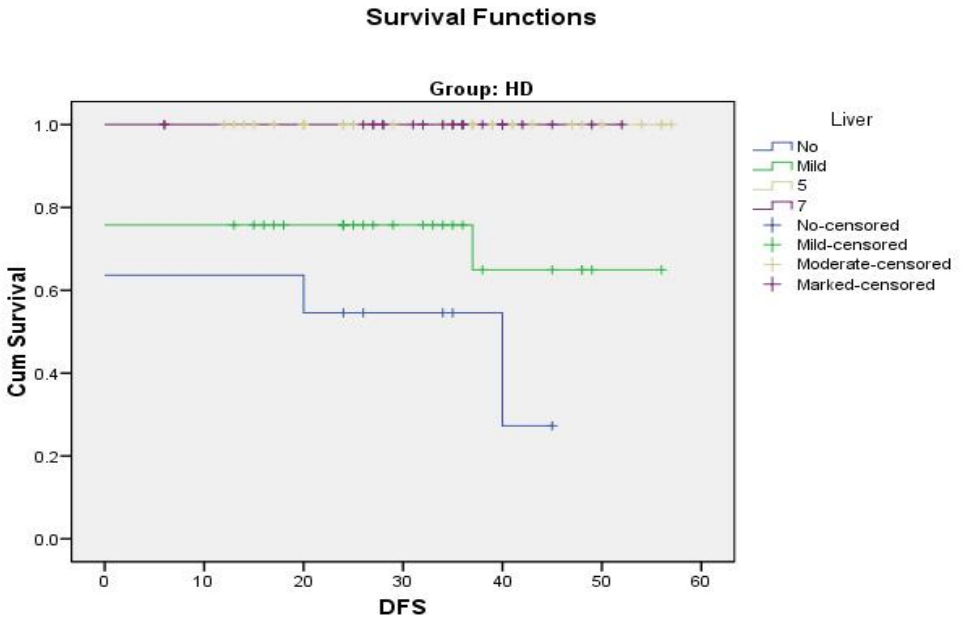
Group		**Low dose**		**High dose**	
Variable		Mean	p value	Mean	p value
Sex	Male	37.540	**0.002**	39.072	
	Female	44.762		54.679	**0.005**
Age	<45	55.705	**0.001**	55.280	
	45 or more	30.867		29.684	**0.05**
Pathology	Papillary	50.491	0.668	51.891	
	Follicular	48.330		49.750	0.361
Multiplicity	Uni-focal	50.145	0.597	54.964	
	Multifocal	42.545		24.786	**0.005**
Tumor size	>1cm	24.764	**<0.005**	30.436	
	<1cm	54.625		54.600	**0.001**
LN metastasis	Positive	31.000	0.333	28.153	
	Negative	49.875		54.522	**0.005**
TBU	Global	-	0.312	-	0.685
DHU	Global	-	**0.043**	-	**0.005**

On multivariate analysis, Cox regression revealed that female patients, mono-focal tumors, and high levels of liver uptake are solely good prognostic factors regarding the **high-dose group**. Table 6

Table 6: Multivariate analysis of recurrence-free survival

	Low-dose group		**High-dose group**	
	B factor	p value	B factor	p value
Gender	9.642	0.334	1.612	0.048
Age	2.974	0.400	0.938	0.288
Pathology	19.238	0.335	-0.726	0.250
Multiplicity	10.169	0.325	1.597	0.042
Size	10.700	0.287	-1.080	0.358
LN	-1.820	0.251	1.250	0.175
BLTg	0.046	0.385	-0.004	0.477
Thyroid	-0.260	0.835	0.116	0.830
Liver	-9.161	0.350	-1.333	0.009

None of the variables is considered a significant predictor for disease-free survival regarding the low-dose group and this may be due to the limited sample size of the low-dose group compared to the high-dose ones. Figure 1



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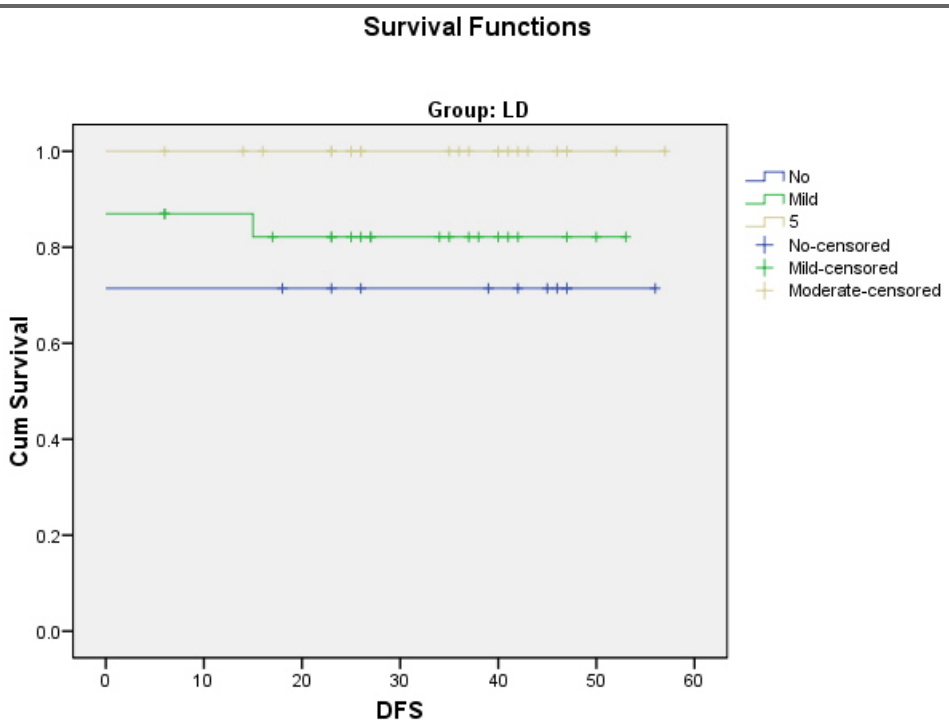

B

Figure 1: Recurrence-free survival curve of patients received (A) high doses regarding groups divided by liver uptake scores (B) low dose regarding groups divided by thyroid uptake scores.

Discussion:

Diffuse hepatic uptake (DHU) of RAI is considered a frequently encountered outcome in the whole-body iodine scan (WBIS) performed for DTC patients. This pattern of uptake is physiological, and it does not represent a metastatic disease of the liver which appears as focal affection113[5].

In the current study. A comparison regarding the different levels of DHU intensity was done between both study groups and there was a statistically significant variation between both high and low-dose groups, also found that the percentages of DHU among PA-WBSs were 76% and 92% in low and high doses groups respectively. While those patients

getting higher ablative doses of RAI were noticed to have more hepatic grades. Likewise, many other authors exhibited that DHU was frequently noticed on post-ablative/therapeutic RAI scans instead of diagnostic RAI scans. DHU fluctuated between 39% - 71% of the therapeutic scans and between 8.5% - 13% in the diagnostic WBISs in their findings[6, 7].

Further authors such as Tatar et al. [8] found zero DHU with all diagnostic scans (2-5 mCi) of the enrolled 118 patients in his clinical study, however, After receiving the conventional ablative doses of RAI-131, DHU was detected in about 95.8% of them.

The published literature shows conflicting results on the clinical significance of DHU, particularly concerning its prognosis. In this clinical study, it was discovered that the patient's outcome and recurrence-free survival in both univariate and multivariate analysis could be successfully predicted using the grade of DHU. moreover, it was observed that the greater the grade of uptake the better the prognosis. i.e., a higher incidence of disease remission was encountered in patients with moderate and intense DHU (grades 2 and 3) in their PA-WBIS.

This shows and agreement with the findings of Kim et al. [9] who reported that faint hepatic visualization combined with intense TBU predicts a relatively poor prognosis, they thought that this may indicate inadequate thyroid tissue damage.

Relatedly, Jun et al. [10] noticed that patients with significant iodine avid disease had greater DHU intensity on 131I post-therapy whole-body scans, which is concomitant with a higher percentage of serum TG reduction and ensures improved prognosis.

Serum TG is a protein that is naturally produced from thyroid follicular cells into the thyroid follicle and then iodinated to synthesize thyroid hormones. Serum TG may be released in both DTC and normal thyroid tissue. It is thought to be a tumor burden marker, and its levels have been frequently used for post-surgical surveillance after DTC[11]. Several investigations have indicated that a temporary increase in serum TG following 131I delivery was associated to the ablative treatment effectiveness. This transient TG increase might be due to thyroid tissue injury. Some of the 131I-labeled TG aggregates in the liver during excretion and leads to DHU [12, 13].

DHU has been observed in more than 90% of post-ablative and post-therapeutic whole-body scans, while rarely seen in DWBS. These findings harmonize with our current hypothesis that DHU indicates functioning thyroid tissue damage after 131I- treatment, while a greater DHU may basically reflect a higher dose of administered radioactivity, it is possible to hypothesize that more functioning thyroid tissue damage may result from a greater dose of 131I.

In the present study, the PA-WBSs of all patients without any disease evidence during their follow-up period demonstrate high scores of hepatic uptakes signifying more tissue destruction and subsequently more in vivo labeling of the produced TG from that ablation. The patients with no or low hepatic visualization on PA-WBSs were associated with bad outcomes despite the degree of the thyroid bed uptake. So, we assumed that DHU might be used to reflect the level of tissue destruction rather than the amount of functioning thyroid tissue. This was in agreement with Jun et al.[10] who also reported that an intense DHU was a reliable predictor of remission.

In contrast, Ferris et al. [14] stated that more intense hepatic uptake is related to a reduced chance of a complete response to I-131 therapy for DHU patients and otherwise negative whole-body scans after 131I treatment.

Chung et al.[6] hypothesized that hidden metastases may be considered if there is hepatic uptake but no thyroid uptake or other indicators of metastasis, Contrary, Tatar et al. [8] observed that 13 of the patients in their study had no evidence of 131I-uptake in the liver or thyroid bed of all patients were diffusely visualized, nevertheless, these patients have no indication of local or remote metastasis. They also document that hepatic uptake in patients following complete thyroidectomy for patients with DTC is unrelated to the existence of remaining normal thyroid tissue or it's recurring or persistent thyroid carcinoma. This was also consistent with the findings of Lee et al. [15].

Jun et al. [10] suggested that DHU additional 131I-positive lesions may imply inefficient 131I-therapy, owing to variable degrees of tumor tissue dedifferentiation.

Regarding the present study, all patients were of normal liver enzymes except for those six patients who have relatively elevated enzymes likely for non-specific causes. However, Omur et al. [16] mentioned that intensities of DHU were shown to be relatively linked with the amount of both hepatic enzymes (ALT, AST), and both were more in fatty liver patients detected by ultrasonography. Lee et al. [15] Accordingly stated related outcomes as in patients with a higher DHU, ALT levels seem to be significantly increased. On the other hand, Jun et al. [10] found no significant relationship between DHU and hepatic enzymes.

Conclusions:

Good and clear hepatic visualization reflects effective ablation, and consequently, enhanced prognosis. However, less hepatic visualization may be correlated to lower chance of full response to 131I therapy.

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References:

1. Nosé V. Thyroid cancer of follicular cell origin in inherited tumor syndromes. Adv Anat Pathol. 2010;17:428-36.
2. Ledwon A, Paliczka-Cieślik E, Syguła A, Olczyk T, Kropińska A, Kotecka-Blicharz A, et al. Only peak thyroglobulin concentration on day 1 and 3 of rhTSH-aided RAI adjuvant treatment has prognostic implications in differentiated thyroid cancer. Annals of Nuclear Medicine. 2021;35:1214-22.
3. Wu K, Ozomaro U, Flavell R, Pampaloni M, Liu C. Causes of false-positive radioactive iodine uptake in patients with differentiated thyroid cancer. Curr Radiol Rep. 2021;9:6.
4. Liu S, Zuo R, Yang T, Pang H, Wang Z. A semiquantitative study of the optimal whole-body imaging time after 131I therapy for differentiated thyroid cancer. Front Endocrinol. 2022;13:955387.
5. Hussein E, Abd El-Aleem M, El-Refaei S. Re-exploration of Radio-iodine Diffuse Hepatic Uptake as Early Prognostic Indicator in Differentiated Thyroid Carcinoma. Egyptian J Nucl Med. 2019;19:123.
6. Chung JK, Park YJ, Kim TY, So Y, Kim SK, Park DJ, et al. Clinical significance of elevated level of serum antithyroglobulin antibody in patients with differentiated thyroid cancer after thyroid ablation. Clin Endocrinol. 2002;57:215-21.
7. Rosenbaum RC, Johnston GS, Valente WA. Frequency of hepatic visualization during I-131 imaging for metastatic thyroid carcinoma. Clin Nucl Med. 1988;13:657-60.
8. Tatar FA, Morita E, Ituarte PH, Cavalieri RR, Duh QY, Price DC, et al. Association between residual thyroid carcinoma and diffuse hepatic uptake of 131I following radioiodine ablation in postoperative total thyroidectomy patients. World J Surg. 2001;25:718-22.
9. Kim K, Kim SJ, Kim IJ, Kim YK, Kim BS, Pak K. Clinical significance of diffuse hepatic visualization and thyroid bed uptake on post-ablative iodine-131 whole body scan in differentiated thyroid cancer. Onkologie. 2012;35:82-6.
10. Jun S, Lee JJ, Park SH, Kim TY, Kim WB, Shong YK, et al. Prediction of treatment response to ^{131}I therapy by diffuse hepatic uptake intensity on post-therapy whole-body scan in patients with distant metastases of differentiated thyroid cancer. Ann Nucl Med. 2015;29:603-12.
11. Mazzaferri EL, Robbins RJ, Spencer CA, Braverman LE, Pacini F, Wartofsky L, et al. A consensus report of the role of serum thyroglobulin as a monitoring method for low-risk patients with papillary thyroid carcinoma. J Clin Endocrinol Metab. 2003;88:1433-41.
12. Muratet JP, Giraud P, Daver A, Minier JF, Gamelin E, Larra F. Predicting the efficacy of first iodine-131 treatment in differentiated thyroid carcinoma. J Nucl Med. 1997;38:1362-8.
13. Bernier MO, Morel O, Rodien P, Muratet JP, Giraud P, Rohmer V, et al. Prognostic value of an increase in the serum thyroglobulin level at the time of the first ablative radioiodine treatment in patients with differentiated thyroid cancer. Eur J Nucl Med Mol Imaging. 2005;32:1418-21.
14. Ferris HA, Williams G, Parker JA, Garber JR. Therapeutic implications of diffuse hepatic uptake following I-131 therapy for differentiated thyroid cancer. Endocr Pract. 2013;19:263-7.
15. Lee J, Yun MJ, Nam KH, Chung WY, Soh EY, Park CS. Quality of life and effectiveness comparisons of thyroxine withdrawal, triiodothyronine withdrawal, and recombinant thyroid-stimulating hormone administration for low-dose radioiodine remnant ablation of differentiated thyroid carcinoma. Thyroid. 2010;20:173-9.
16. Omür O, Akgün A, Ozcan Z, Sen C, OzkiIiç H. Clinical implications of diffuse hepatic uptake observed in postablative and post-therapeutic I-131 scans. Clin Nucl Med. 2009;34:11-4.