

ARTICLE ORIGINAL/ORIGINAL ARTICLE

COMPARISON BETWEEN RADIOIODINE THERAPEUTIC AND DIAGNOSTIC WHOLE BODY SCANS IN POSTOPERATIVE DIFFERENTIATED THYROID CARCINOMA PATIENTS

Correlation With Serum Thyroglobulin Levels

<http://www.lebanesemedicaljournal.org/articles/65-1/original5.pdf>

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Al-Shammeri I, Mahmood S, Al-Mohannadi S, Ballani N. Comparison between radioiodine therapeutic and diagnostic whole body scans in postoperative differentiated thyroid carcinoma patients : correlation with serum thyroglobulin levels. J Med Liban 2017; 65 (1): 25-28.

ABSTRACT • Purpose: It has been reported that high image quality and high sensitivity can be achieved by the I-131 post-therapy scan. We aim to demonstrate through our clinical experience the efficacy of I-131 therapeutic whole body scans (WBSs) compared to diagnostic scans in detecting lesions and to appraise whether the differentiated thyroid carcinoma patient has to undergo postoperative radioiodine therapy based on the diagnostic scan and/or thyroglobulin level. **Method:** 263 patients (193 females, 70 males, 19-67 years old) with well-differentiated thyroid carcinoma (208 papillary, 55 follicular) underwent postoperative diagnostic radioiodine scan. All patients (263) were imaged 48 hours after receiving a diagnostic I-131 dose of 111-185 MBq (3-5 mCi). Two hundred seven (207) with a postoperative thyroid ablation and I-131 uptake above 2% received an 1110-4440 MBq (30-120 mCi) therapeutic I-131 dose and were imaged 72 hours thereafter. Images from both scans, diagnostic and therapeutic, were compared for the presence and the intensity of thyroid cancer lesions (recurrences and metastases) and correlated to the serum thyroglobulin level. **Results:** Compared to negative diagnostic WBSs (25 patients) and those with high serum thyroglobulin level (110 patients), therapeutic scans revealed positive lesions in 19/25 patients (76%). Almost all lesions (104/110) were detected and more clearly defined in the therapeutic scan than the diagnostic scan. Sensitivity was calculated to be 96% for therapeutic WBS and 88% for diagnostic WBS, respectively. Only 7/207 patients (3.4%) who received a high therapeutic dose (4440 MBq) showed a greater lesion uptake in the diagnostic scan than the therapeutic scan. **Conclusion:** The findings indicate that therapeutic scans are more effective than diagnostic scans for follow-up studies in differentiated thyroid carcinoma patients undergoing postoperative radioiodine treatment. Despite recording a negative diagnostic scan, postoperative radioiodine therapy still had to be performed for those patients with high serum thyroglobulin levels.

Keywords: radioactive iodine I-131; therapeutic scan; diagnostic scintigraphy; differentiated thyroid carcinoma; serum thyroglobulin level

INTRODUCTION

It has been reported that distant metastases are the main cause of death in patients with thyroid carcinoma [1,2]. The whole body I-131 scan has been reported to be an efficient tool to follow up thyroid carcinoma [3]. Post-therapeutic and diagnostic scans can be used to evaluate the presence of recurrent thyroid cancer or the presence of

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RÉSUMÉ • Objectif : Il a été démontré qu'une bonne qualité d'images ou un dépistage de certaines lésions peuvent être obtenus par l'analyse de scans post-dose thérapeutique d'I-131. L'objectif de notre étude est de comparer l'efficacité des scans corps entier (WBS) à l'I-131 thérapeutique aux scans diagnostiques dans la détection des lésions. Notre étude vise également à examiner si un patient souffrant d'un cancer de la thyroïde doit subir, en postopératoire, un traitement à l'iode radioactif en se basant sur les tests diagnostiques et/ou sur le taux élevé de thyroglobuline dans le sérum. **Méthode :** 263 patients (193 femmes et 70 hommes de 19 à 67 ans) ayant un carcinome thyroïdien bien différencié (papillaire : 208; folliculaire : 55) ont subi un scan postopératoire par iode radioactif. Tous les patients (263) ont été imagés 48 h après l'administration d'une dose diagnostique I-131 de 111-185 MBq (3-5 mCi). Deux cent sept (207) avec une ablation postopératoire de la thyroïde et absorption de I-131 supérieure à 2% ont reçu une dose thérapeutique I-131 de 1110-4440 MBq (30-120 mCi) et ont été imagés 72 heures par la suite. Les images provenant des deux balayages, diagnostique et thérapeutique, ont été comparées pour déterminer la présence et l'intensité des lésions de cancer de la thyroïde (récidives et métastases) et en corrélation avec le taux de thyroglobuline dans le sérum. **Résultats :** Comparés aux WBSs diagnostiques négatifs (25 patients) et ceux qui ont un taux de thyroglobuline sérique élevé (110 patients), les scans diagnostiques ont été positifs et ont détecté des lésions thérapeutiques chez 19/25 patients. Les lésions (104/110) ont été presque totalement détectées et plus clairement définies dans le scan thérapeutique que dans le scan diagnostique. La sensibilité a été calculée à 96% et 88% respectivement pour WBS thérapeutique et diagnostique. Seuls 7/207 patients (3,4%) ayant reçu une dose thérapeutique élevée (4440 MBq) ont montré une plus grande absorption de la lésion dans le scan diagnostique. **Conclusion :** Les résultats de cette étude indiquent que les scans thérapeutiques sont plus efficaces que les scans diagnostiques dans les études longitudinales sur des patients souffrant d'un cancer de la thyroïde qui subissent un traitement postopératoire à l'iode radioactif. Cependant, la thérapie postopératoire à l'iode radioactif doit toujours être effectuée pour les patients avec des taux élevés de thyroglobuline sérique.

thyroid distant metastases. However, a higher image quality or better detection of additional lesions can be achieved in the therapeutic scan by a delayed imaging of 4-7 days [4,5]. Additional lesions could be seen in immediate post-therapeutic dose [6]. Minimizing the risk of recurrence and metastases can be achieved in patients with differentiated thyroid cancer undergoing high-dose I-131 [1,6].

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SUBJECTS AND METHOD

False positive or false negative results can occur in I-131 diagnostic imaging while therapeutic dose imaging can improve the detection of both true and spurious lesions [7]. Diagnostic dose imaging is well documented for metastatic diseases and a therapeutic dose should follow [8]. For example, a liver metastatic case was found and reported in therapy scan images [9].

Maximizing the benefit of the therapeutic dose is possible by imaging the patient for better detection of metastasized lesions. In less functioning thyroid metastatic tissues a lesser response to the I-131 dose occurs [10].

Using I-131 therapeutic dose imaging to follow these cases could be useful [2,11]. However, low uptake of very high I-131 therapeutic doses (up to 200 mCi)* might occur with a stunning effect [12] especially if preceded immediately by a diagnostic scan. The usefulness of I-131 to function as both a therapeutic and diagnostic tool in differentiated carcinoma has been documented [13], however, imaging a therapeutic dose could be more beneficial. Various imaging techniques could be also useful for patient care [14], which can be obtained by using the I-131 therapeutic dose for imaging.

However, radioiodine therapy is usually performed depending on a high thyroglobulin level and/or positive diagnostic I-131 scan. It has been suggested to combine both markers to improve the need of a therapeutic course [15,16].

Wartofsky *et al.* [17] suggest that radioiodine therapy might be justified based on high thyroglobulin in high-risk differentiated thyroid cancer patients with a negative I-131 diagnostic scan. Meanwhile, high-risk patients with significant positive thyroglobulin and a negative diagnostic scan undergoing radioiodine treatment should be considered for long-term trials [18].

A previous attempt to emphasize the pathology of differentiated thyroid carcinoma behind the discordance between a diagnostic scan and serum thyroglobulin levels was recently conducted [19,20]. The results showed that the serum thyroglobulin was high in papillary thyroid carcinoma when the diagnostic scans were negative. Also, different rates of differentiated thyroid cancer subtypes, papillary and follicular, were detected according to iodine nutrient intake amounts. However, this is currently beyond the scope of this study.

In this work the attempt was to add our clinical experience to the existing evidence and to allow a more informed consideration to maneuver postoperative radioiodine treatment in patients with well differentiated carcinoma. In particular, a retrospective assessment was performed to compare and contrast between therapeutic and diagnostic I-131 scans and scheme whether a high serum thyroglobulin level as an indicator for postoperative therapeutic I-131 should be considered when it is combined with a negative diagnostic scan.

*mCi (millicurie) = 37 MBq (megabecquerel)

Under official departmental research committee permission, this study was performed retrospectively in our nuclear medicine department. Two hundred and sixty-three postoperative differentiated thyroid carcinoma (208 papillary and 55 follicular) patients, 193 females and 70 males, 19 to 67 years old, who had TSH levels greater than 100 μ IU/ml were included in the study. All patients underwent whole body I-131 scans (WBS) 48 hours after receiving a diagnostic I-131 dose of ~111 MBq* (~3 mCi). Two hundred seven (207) patients, with a thyroid uptake greater than 2%, were sent to radioiodine ablation therapy and underwent WBS 72 hours after receiving a therapeutic I-131 dose of 1110-4440 MBq (30-120 mCi). Before dose administration, all imaged patients were four weeks off thyroid hormones and one week on an advised low iodine diet. Images from both scans, diagnostic and therapeutic, were compared for the presence and the intensity of thyroid residual lesions. In addition, both scans were correlated with serum thyroglobulin levels that were considered significantly high at ≥ 10 ng/ml.

RESULTS

Diagnostic scans revealed the ability to detect thyroid lesions as a local recurrence as well as distant metastases. While all 110 patients with high serum thyroglobulin levels revealed a positive thyroid uptake percentage, 85/110 patients (Table I) and 104/110 (Table II) showed positive diagnostic and therapeutic WBS, respectively. However, most lesions that were shown in diagnostic radioiodine WBSs were better defined and more clearly seen in the therapeutic scans.

TABLE I
RESULTS of DIAGNOSTIC SCAN at HIGH & LOW THYROGLOBULIN LEVEL
ONLY 25/59 of NEGATIVE DIAGNOSTIC HAD THERAPEUTIC SCAN

	Diagnostic scan		Total
	+ve	-ve	
High Thyroglobulin Level ≥ 10 ng/ml	85	25	110
Low Thyroglobulin Level < 10 ng/ml	119	34	153
Total	204	59	263

TABLE II
RESULTS of THERAPEUTIC SCAN at HIGH & LOW THYROGLOBULIN LEVEL
ONLY 97/119 of LOW SERUM THYROGLOBULIN HAD THERAPEUTIC SCAN

	Therapeutic scan		Total
	+ve	-ve	
High Thyroglobulin Level ≥ 10 ng/ml	104	6	110
Low Thyroglobulin Level < 10 ng/ml	95	2	97
Total	199	8	207

Qualitatively, only 7/207 patients (3.4%) who received a therapeutic dose showed fewer lesions in therapeutic compared to diagnostic WBS. While revealing positive diagnostic WBS, two cases were reported as having a negative therapeutic scan. These were explained by the stunning effect that can be avoided by giving smaller diagnostic doses. There were 34/59 patients with a negative diagnostic scan and low serum thyroglobulin levels who were not sent into radioiodine ablation therapy. Those could be considered true negative (TN ~58%) diagnostic scans, hence no thyroid I-131 uptake. This was confirmed by 25/59 false negative results (FN ~42%). On the other hand, there were 22 patients with a positive diagnostic scan and low serum thyroglobulin level who were also not sent into radioiodine ablation therapy. Those could be considered false positive (FP ~11%) diagnostic scans, hence no thyroid I-131 uptake. Despite false positives and negatives, diagnostic radioiodine postoperative WBS showed very good sensitivity (182/207 = 88%) when compared to a positive uptake > 2%, and good sensitivity (85/110 = 77) when compared to high serum thyroglobulin levels (Table III). On the other hand, therapeutic WBS sensitivity was calculated to be 96% (199/207) when compared to a thyroid uptake > 2% and 95% (104/ 110) when compared to high serum thyroglobulin levels.

TABLE III
RESULTS of DIAGNOSTIC versus THERAPEUTIC SCAN

	Therapeutic scan		Total
	+ve	-ve	
Diagnostic scan +ve	180	2	182
Diagnostic scan -ve	19	6	25
Total	199	8	207

DISCUSSION

Woodruff *et al.* [19] concluded that follicular thyroid cancer is more common in iodine-deficient intake developing countries, whereas papillary thyroid cancer is the main subtype in other developed countries. They also suggest that reducing iodine intake deficiency may produce a less aggressive subtype. We have found that papillary thyroid cancer in Kuwait is predominant when compared to the follicular subtype. In this study, there were 208/263 (79%) papillary compared to 55/263 (21%) of the follicular thyroid cancer subtype. Hence, iodine-sufficient intake is predominant in Kuwait.

Despite a good correlation between the existence of thyroid tissue and serum thyroglobulin levels, a dissonant result has been found between the I-131 diagnostic scan and serum thyroglobulin levels. Previous reports have shown that 15-20% of differentiated thyroid cancer patients with negative diagnostic I-131 scans demonstrated a high serum thyroglobulin level [1,21,22]. Despite the high serum thyroglobulin cut-off value (≥ 10 ng/ml instead of > 5 ng/ml), nearly the same results have been

obtained in this study. Twenty-five patients showed negative diagnostic scans out of 110 high serum thyroglobulin levels (~23%).

Detection of differentiated thyroid carcinoma lesions for local recurrence would be the purpose of an I-131 scan [8,20,22]. Distant metastases were also detected using diagnostic imaging [9,10]. In this study, the routine diagnostic scintigraphy detection was comparable to those previously reported [23]. For example, all 204 patients with positive diagnostic scans were detected by therapeutic radioiodine scans. In addition, the efficacy of the diagnostic scans was demonstrated over serum thyroglobulin. In this retrospective assessment work, out of 204 positive diagnostic scans, 119 negative serum thyroglobulin patients were found.

Radioiodine diagnostic scintigraphy is also possible with the early administration of a high dose of I-131 [5]. Increasing the detection rate can be achieved by imaging with a therapeutic dose [7]. It has been found in this work, that more lesions can be detected using the therapeutic dose scintigraphy. In addition, better lesion visualization has been achieved. Out of 25 negative diagnostic scans at high serum thyroglobulin levels, 19 patients showed positive therapeutic scans.

False positive or negative testing can be associated with high dose imaging [10,14]. Previous case reports have indicated such an effect [4,24,25].

Stunning effect is also associated with high dose of diagnostic scanning [12]. We have experienced such an effect in our research. This can be avoided by using a lesser dose for the diagnostic scan when the therapeutic dose is expected to be given shortly thereafter, and/or when more time is allowed between the diagnostic and therapeutic doses. For this purpose, it might be useful to avoid any intake amount of iodine, either stable or unstable. Thus, effective radioiodine treatment half-life would be prolonged and therefore an efficient therapeutic success rate could be achieved.

Chong *et al.* [26] showed that imaging at 7 days post therapeutic radioiodine dose would reveal better I-131 avid lung or bone metastatic lesions than at a 3-day imaging. However, we demonstrated better efficiency by therapeutic scan (sensitivity = 96%) than diagnostic scan (sensitivity = 8%) and it might be worthwhile to consider such a method for further research. Hence, no additional patient radiation dose would need to be administered.

A positive diagnostic radioiodine scan in postoperative differentiated thyroid cancer patients clearly indicates a straightforward need for radioactive iodine to treat the remnant and/or distant metastases. The results obtained from this study confirm the previous published results in this regard. On the other hand, to answer the question of whether to treat postoperative differentiated thyroid carcinoma patients when they have a negative diagnostic scan associated with a high serum thyroglobulin level is not clear yet. This study will hopefully provide more insight relative to this issue and assist in clarifying suggestions for further research.

CONCLUSION

Either combined negative diagnostic WBS/high serum thyroglobulin level or positive diagnostic WBS should be selected as a marker for postoperative iodine therapy in patients with differentiated thyroid carcinoma. The therapeutic WBS might be preferred for follow-up since it reveals better lesion detection compared to the diagnostic WBS.

CONFLICT OF INTEREST

The authors indicated no conflict of interest.

REFERENCES

1. Cooper DS, Doherty GM, Haugen BR et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2009; 19: 1167-214.
2. Mazzaferri EL, Kloos RT. Clinical review 128: current approaches to primary therapy for papillary and follicular thyroid cancer. *J Clin Endocrinol Metab* 2001; 86: 1447-63.
3. Marinuzzi G, Bellini V, Antimi M. Differentiated thyroid carcinomas. *Clin Ter* 2000; 151: 365-9.
4. Briele B, Hotze A, Grunwald F, Overbeck B, Biersack HJ. Increased sensitivity of whole-body scintigraphy with I131 for the detection of iodine-accumulating metastases by means of delayed imaging. *Nuklearmedizin* 1990 Dec; 29 (6): 264-8.
5. Chong A, Song HC, Min JJ et al. Improved detection of lung or bone metastases with an I-131 whole body scan on the 7th day after high-dose I-131 therapy in patients with thyroid cancer. *Nucl Med Mol Imaging* 2010 Dec; 44 (4): 273-81.
6. Souza Rosário PW, Barroso AL, Rezende LL et al. Post I-131 therapy scanning in patients with thyroid carcinoma metastases: an unnecessary cost or a relevant contribution? *Clin Nucl Med* 2004 Dec; 29 (12): 795-8.
7. Greenler DP, Klein HA. The scope of false-positive iodine-131 images for thyroid carcinoma. *Clin Nucl Med* 1989; 14: 111-17.
8. Watne AL, Starke J, McQuitty D, Sohrabi A. Follicular carcinoma of the thyroid. *Semin Surg Oncol* 1991; 7: 87-91.
9. Konez O, Hanelin LG, Jenison EL, Goyal M, Randolph W. Functioning liver metastases on an I-131 whole-body scan: a case of malignant struma ovarii. *Clin Nucl Med* 2000; 25: 465-96.
10. Kasagi K, Miyamoto S, Endo K et al. Increased uptake of iodine-131 in metastases of differentiated thyroid carcinoma associated with less severe hypothyroidism following total thyroidectomy. *Cancer* 1993; 72: 1983-90.
11. Amdur RJ, Mazzaferri EL. The value of a post treatment whole body scan. In: Amdur RJ, Mazzaferri EL, editors. *Essentials of Thyroid Cancer Management*. New York: Springer, 2005: 65-8.
12. Kao CH, Yen TC. Stunning effects after a diagnostic dose of iodine-131. *Nuklearmedizin* 1998; 37: 30-2.
13. Huang TS, Chieng PU, Chang CC, Yen RF. Positron emission tomography for detecting iodine-131 nonvisualized metastasis of well-differentiated thyroid carcinoma: two case reports. *J Endocrinol Invest* 1998; 21: 392-8.
14. Krausz Y. Nuclear endocrinology as a monitoring tool. *Semin Nucl Med* 2001; 31 (3): 238-50.
15. Degrossi OJ, Rozados IB, Damilano S et al. Serum thyroglobulin and whole-body scanning as markers in the follow-up of differentiated thyroid carcinomas. *Medicina (B Aires)* 1991; 51: 291-5.
16. Wang SJ, Liu TJ. Use of fractionated doses of iodine-131 for ablation of thyroid remnants. *Zhonghua Yi Xue Za Zhi (Taipei)* 2002; 65: 336-40.
17. Wartofsky L, Sherman SI, Gopal J, Schlumberger M, Hay ID. The use of radioactive iodine in patients with papillary and follicular thyroid cancer. *J Clin Endocrinol Metab* 1998 Dec; 83 (12): 4195-203.
18. Fatourech V, Hay ID. Treating the patient with differentiated thyroid cancer with thyroglobulin-positive iodine-131 diagnostic scan-negative metastases: including comments on the role of serum thyroglobulin monitoring in tumor surveillance. *Semin Nucl Med* 2000 Apr; 30 (2): 107-14.
19. Woodruff SL, Arowolo OA, Akute OO, Afolabi AO, Nwariaku F. Global variation in the pattern of differentiated thyroid cancer. *Am J Surg* 2010 Oct; 200 (4): 462-6.
20. Ansari M, Babaei AA, Shafiei B et al. Pathological evaluation of differentiated thyroid cancer in patients with positive serum thyroglobulin and negative iodine scan. *Eur Rev Med Pharmacol Sci* 2014 Jul; 18 (13): 1925-9.
21. Baudin E, Do Cao C, Cailleux AF, Leboulleux S, Travagli JP, Schlumberger M. Positive predictive value of serum thyroglobulin levels, measured during the first year of follow-up after thyroid hormone withdrawal, in thyroid cancer patients. *J Clin Endocrinol Metab* 2003 Mar; 88 (3): 1107-11.
22. Saghari M, Gholamrezanezhad A, Mirpour S et al. Efficacy of radioiodine therapy in the treatment of elevated serum thyroglobulin in patients with differentiated thyroid carcinoma and negative whole-body iodine scan. *Nucl Med Commun* 2006 Jul; 27 (7): 567-72.
23. Hamby LS, McGrath PC, Schwartz RW, Sloan DA, Simpson WG, Kenady DE. Management of local recurrence in well-differentiated thyroid carcinoma. *J Surg Res* 1992; 52 (2): 113-17.
24. Nam MS, Chu YC, Choe WS et al. Metastatic follicular thyroid carcinoma to the thymus in a 35-year-old woman. *Yonsei Med J* 2002; 43 (5): 665-9.
25. Wu SY, Kollin J, Coodley E et al. I-131 total-body scan: localization of disseminated gastric adenocarcinoma. Case report and survey of the literature. *J Nucl Med* 1984; 25: 1204-9.
26. Chong A, Song HC, Min JJ et al. Improved detection of lung or bone metastases with an I-131 whole body scan on the 7th day after high-dose I-131 therapy in patients with thyroid cancer. *Nucl Med Mol Imaging* 2010 Dec; 44 (4): 273-81.