Comparison between radioidine therapeutic and diagnostic whole body scans in postoperative differentiated thyroid carcinoma patients: correlation with serum thyroglobulin levels

Iman AL-SHAMMERI, Saad Al-Deen MAHMOOD, Shihab AL-MOHANNADI, Nasser BALLANI

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 undergone postoperative radiiodine 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 radiiodine 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 patients (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 against 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 radiiodine treatment. Despite recording a negative diagnostic scan, postoperative radiiodine 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 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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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 l’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.
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)**

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**SUBJECTS AND METHOD**

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 µIU/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**

<table>
<thead>
<tr>
<th>RESULTS of DIAGNOSTIC SCAN at HIGH &amp; LOW THYROGLOBULIN LEVEL ONLY 25/59 of NEGATIVE DIAGNOSTIC HAD THERAPEUTIC SCAN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnostic scan</strong></td>
</tr>
<tr>
<td><strong>High Thyroglobulin Level ≥ 10 ng/ml</strong></td>
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<tr>
<td><strong>Low Thyroglobulin Level &lt; 10 ng/ml</strong></td>
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<td><strong>Total</strong></td>
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**TABLE II**

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<tr>
<th>RESULTS of THERAPEUTIC SCAN at HIGH &amp; LOW THYROGLOBULIN LEVEL ONLY 97/119 of LOW SERUM THYROGLOBULIN HAD THERAPEUTIC SCAN</th>
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<tr>
<td><strong>Therapeutic scan</strong></td>
</tr>
<tr>
<td><strong>High Thyroglobulin Level ≥ 10 ng/ml</strong></td>
</tr>
<tr>
<td><strong>Low Thyroglobulin Level &lt; 10 ng/ml</strong></td>
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<tr>
<td><strong>Total</strong></td>
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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

<table>
<thead>
<tr>
<th>Therapeutic scan</th>
<th>Total</th>
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<tbody>
<tr>
<td>Diagnostic scan +ve</td>
<td>180</td>
</tr>
<tr>
<td>Diagnostic scan -ve</td>
<td>19</td>
</tr>
<tr>
<td>Total</td>
<td>199</td>
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#### 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 dissimilar 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