Is Routine Diagnostic Radioiodine Whole-Body Scintigraphy Needed in Patients who Received Ablative doses of Radioiodine for Differentiated Thyroid Carcinoma?

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Abstract: *Aim:* The present large-series retrospective sought to assess DWBS findings 6–12 weeks after RIAT in DTC patients in various risk groups. In addition, the study compared patients' simultaneous sTg levels.

Material and Methods: The follow-up data of 2879 patients who had received RIAT for DTC between 1998 and 2016 were evaluated for inclusion in the study. The study retrospectively evaluated the following: age at the time of diagnosis; gender; histopathological features of thyroidectomy materials (histological subtype, variant, dimension, multi-focality, thyroid capsule, and vascular invasion of tumors); TNM stage; ATA classification; sTg, suppressed-serum Tg, and antiTg antibody levels; and DWBS findings. Patients were categorized according to sTg level (undetectable, 1–10 ng/ml, and >10 ng/ml). Then, the DWBS findings were analyzed according to sTg level.

Results: The study analyzed 2184 patients (1805 F, 379 M; mean age: 43.54±12.64). In 2077 (95%) patients, the DWBSs performed 6–12 months after RIAT had shown no pathological uptake throughout the entire body. Pathological uptake had been detected in the neck and outside the neck in 88 (4%) and 19 (1%) patients, respectively. All patients who had had normal DWBSs also had had undetectable simultaneous sTg levels. In addition, the DWBSs had been normal in 187 (8%) patients who had had simultaneous sTg levels> 1 ng/ml and in 286 (13%) patients who had had levels > 10 ng/ml. In all patients who had pathological uptake in DWBSs, simultaneous sTg levels were > 1ng/ml, and in 47, they were> 10 ng/ml.

Conclusion: Routine DWBS seems to be unnecessary, even in high-risk DTCs. However, in patients who have detectable levels of serum sTg, it could be performed to localize the disease and plan patient management.

Keywords: Differentiated thyroid carcinoma, Diagnostic radioiodine whole-body scintigraphy, Serum thyroglobulin measurement.

INTRODUCTION

Differentiated thyroid carcinoma (DTC), which compromises papillary and follicular cancers, is one of the most common malignancies [1-3]. Traditionally, if it is indicated, radioiodine ablation treatment (RIAT) has been given following total or near-total thyroidectomy. Because DTCs have excellent survival rates, routine lifetime follow-up is needed [4-6]. Generally, follow-up includes periodic measurement of serum thyroglobulin (Tg), anti-thyroglobulin antibody (antiTg), and thyroid stimulating hormone (TSH)-stimulated serum thyroglobulin (sTg) along with simultaneous diagnostic radioiodine whole-body scintigraphy (DWBS) from6–12 weeks after RIAT.

Currently, guidelines of the American Thyroid Association (ATA) and the European Thyroid Association (ETA) do not recommend follow-up with DWBSs for low-risk patients [4, 7]. For intermediate- and high-risk patients, the role of routine DWBS is controversial [8]. There are claims that measuring sTg is more sensitive than DWBS and that DWBS might be combined with neck ultrasound (US) to check the success of RIAT. However, the additional information that DWBS can provide could help to localize recurrent or persistent disease and to evaluate the possibility of additional radioiodine treatments.

The present large-series retrospective sought to assess DWBS findings 6–12 weeks after RIAT in DTC patients in various risk groups. In addition, the study compared patients' simultaneous sTg levels.

MATERIALS AND METHODS

Patients

The follow-up data of 2879 patients who had received RIAT for DTC between 1998 and 2016 were evaluated for inclusion in the study. The study excluded patients who had undergone subtotal thyroidectomy, had not had a detailed histopathological examination of thyroidectomy material, had received RIAT within the previous 2 years, or had been lost to follow-up. Therefore, the study included 2184 patients in the analysis. All 2184had received RIAT following total or near-total thyroidectomy ± central ± lateral-compart-

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ment lymph-node dissection. In all patients, after 6–12 months of RIAT, a DWBS with 185 MBq of Iodine-131 (I-131) had been performed. In all patients, neck US and suppressed-serum Tg measurements had been evaluated yearly. In cases of clinical suspicion of recurrence, computed tomography (CT) of the thorax, 18F-Flourodeoxyglucose (FDG) positron emission tomography (PET)/CT, and additional DWBSs had been performed. In cases of documented persistent or recurrent disease, patients had undergone additional surgeries and additional radioiodine treatments.

Data and Statistical Analysis

The study retrospectively evaluated the following: age at the time of diagnosis; gender; histopathological features of thyroidectomy materials (histological subtype, variant, dimension, multi-focality, thyroid capsule, and vascular invasion of tumors); TNM stage; ATA classification; sTg, suppressed-serum Tg, and antiTg antibody levels; and DWBS findings. Patients were categorized according to sTg level (undetectable, 1–10 ng/ml, and >10 ng/ml). Then, the DWBS findings were analyzed according to sTg level. Continuous data are expressed as the mean and standard deviation or as the median and interquartile range. Categorical data are presented as numbers of patients and percentages. Compatibility of the DWBS findings with the sTg levels was analyzed using the Chi-square test. SPSS software (version 20.0; SPSS Inc.; Chicago, IL, USA) was used for statistical analysis.

RESULTS

Patients

The study analyzed 2184 patients (1805F, 379M; mean age: 43.54±12.64). Table **1** shows the patients' descriptive data. All patients had received RIAT at doses of from 30–150 mCi, according to the risk group they were in. In the post-ablative DWBSs obtained 5–8 days after RIAT, accumulation of radioactivity had been detected in the neck and outside the neck in 2061 (94%) and 83 (4%) patients, respectively. In 40 (2%) patients, the post-ablative DWBSs had been normal. Mean pre-ablative TSH sTg levels were calculated as 28.1±49.4 (min–max: 0.22–300) ng/ml.

In 2077 (95%) patients, the DWBSs performed 6–12 months after RIAT had shown no pathological uptake throughout the entire body. Pathological uptake had been detected in the neck and outside the neck in 88 (4%) and 19 (1%) patients, respectively. All patients who had had normal DWBSs also had had undetectable simultaneous sTg levels. In addition, the DWBSs had been normal in 187 (8%) patients who had had simultaneous sTg levels> 1 ng/ml and in 286 (13%) patients who had had levels > 10 ng/ml. In all patients who had pathological uptake in DWBSs, simultaneous sTg levels were > 1ng/ml, and in 47, they were> 10 ng/ml.

Table 1: Patients' Demographic and Follow-Up Data Parameter

Age	
F	1805 (83%)
M	379 (17%)
Subtype	
Papillary	1969 (90%)
Follicular	134(6%)
Mixed	32(1%)
Well-differentiated carcinoma with unknown malign potential	49(3%)
Multi-centricity	
Positive	1415 (65%)
Negative	769 (35%)
Thyroiditis	
Positive	611 (28%)
Negative	1573 (72%)
Thyroid capsule invasion	
Positive	749 (34%)
Negative	1435 (66%)
Vascular invasion	
Positive	169 (8%)
Negative	2015 (92%)
TNM stage	
1	1779 (81%)
2	153 (7%)
3	165 (8%)
4	87 (4%)
ATA classification	
Low-risk	1604 (73%)
Intermediate-risk	477 (22%)
High-risk	103 (5%)
ETA classification	
Very low	433 (20%)
Low	1324 (60%)
High	427 (20%)

(ATA: American Thyroid Association; ETA: European Thyroid Association)

Table **2** summarizes additional data on the comparison of DWBS findings and simultaneous serum sTg levels based on ATA risk groups. One examples for positive and negative DWBS were shown in Figure **1**.

DISCUSSION

DWBS is recommended as a simple, cost-effective, highly accurate method of following up DTC patients after RIAT [9]. It is recommended to be performedusing74–185 MBq of I-131 and endogenous or exogenous TSH stimulation in combination with simultaneous serum sTg measurements. However, because serum Tg measurement kits are highly sensitive, sensitivity and the role of routine DWBS are controversial. Because of radiation dosimetry and potential side effects, the role of DWBS should be redefined in managing DTCs.

Table 2: Comparison of DWBS Findings and Simultaneous Serum sTg Levels Based on ATA Risk Classifications

		Simultaneous Serum sTg Levels		
ATA Risk Group	**DWBS**	**<1 ng/ml**	**1–10 ng/ml**	**>10 ng/ml**
Low	Normal	1417	116	27
	Uptake in the neck	0	34	9
	Uptake outside the neck	0	1	0
Intermediate	Normal	344	64	35
	Uptake in the neck	0	20	14
	Uptake outside the neck	0	0	0
High	Normal	30	7	37
	Uptake in the neck	0	3	8
	Uptake outside the neck	0	2	16

(ATA: American Thyroid Association; Tg: Thyroglobulin;ng/ml: nanogram per milliliter; DWBS: diagnostic whole-body scintigraphy).

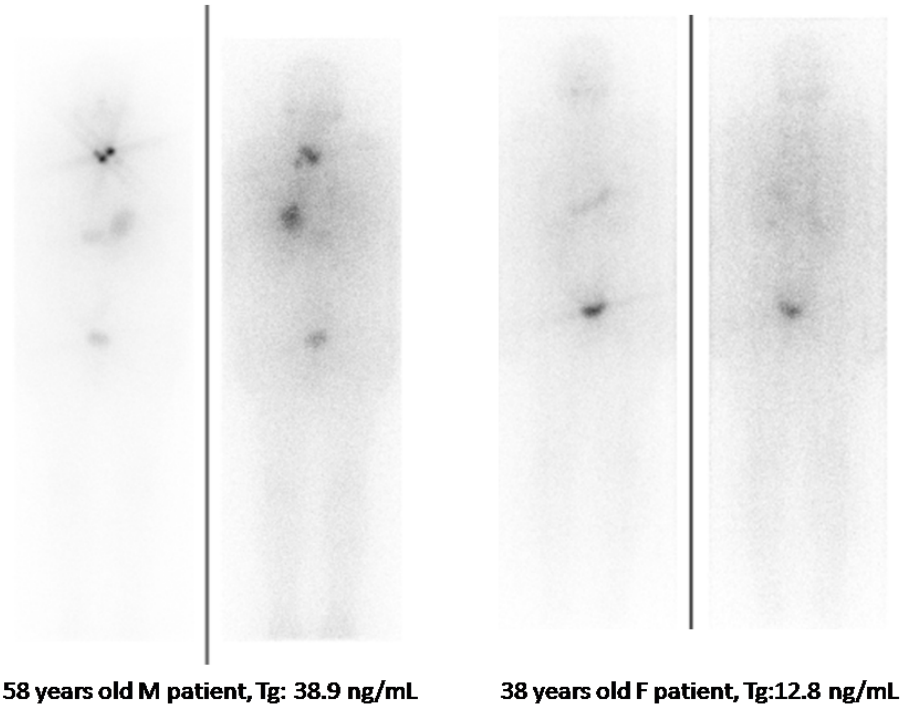

Figure 1: Examples for patients with elevated serum Tg level and positive and negative DWBS.

ATA guidelines do not recommend routine DWBS in low-risk patients. In intermediate- and high-risk patients, the role of DWBS is unclear. It may be of value in following up these groups. However, it is only an expert opinion, and application time is not stated [10]. Furthermore, the literature includes limited studies in this area [8, 11-13]. Meer *et al*. evaluated DWBS findings and simultaneous serum sTg levels in 112 high-risk patients [8], concluding that DWBSs offered no information in addition to that provided by the sTg levels. Similarly, Verburg *et al*. concluded that routine DWBS could be omitted in high-risk patients in their 44-patient group [11]. In the present retrospective study, 103 patients were in the high-risk group, and the results were similar to those of other studies: the present study found no differences in the sensitivity of DWBSs between high- and low-risk groups. However, Robbins *et al*. advocated performing routine DWBS in all DTCs, claiming that serum Tg measurements alone could not detect all the metastases that could be detected by DWBSs [13]. The present study analyzed the DWBS findings and simultaneous serum sTg levels in a large patient group, finding no additional recurrence or persistent disease that could be seen on DWBSs but not detected by serum sTg measurements. Undetectable serum Tg levels have high negative-predictive value in the absence of serum antiTg antibodies. However, in the case of the presence of circulating antiTg antibodies, DWBSs could become more important [14]. In patients with no detectable antiTg antibodies, it is quite rare to detect disease recurrence by a DWBS without accompanying serum sTg levels. In such cases, false-positive reasons that could trap I-131should be considered [9].

To our knowledge, the present retrospective study is the largest in the literature comparing serum sTg measurements and DWBSs. The present study found that a routine DWBS after 6–12 months of RIAT did not detect any recurrent of persistent disease in addition to that detected by serum sTg measurements, even in intermediate- and high-risk patients. Therefore, sTg seems more sensitive to persistent or recurrent disease. The amount of residual or recurrent disease and its I-131 avidity are very important to detectability by DWBSs. However, when a DWBS is positive, it can localize the disease and can give information about its radioiodine avidity, which is an important prognostic factor (15). For these reasons, DWBSs could be performed for patients who have detectable levels of serum sTg.

CONCLUSIONS

Routine DWBS seems to be unnecessary, even in high-risk DTCs. However, in patients who have detectable levels of serum sTg, it could be performed to localize the disease and plan patient management.

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