Differentiated thyroid carcinoma : nuclear medicine studies

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Chapter 5

A new functional parameter measured at the time of ablation that can be used to predict differentiated thyroid cancer recurrence during follow-up

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Abstract

Background: This study addresses the questions whether patients with a high risk for recurrent thyroid cancer can be identified at initial stage, i.e. at the time of ablation.

Methods: We evaluated tumor recurrence in consecutive patients treated for differentiated thyroid cancer (DTC). Prognostic factors were statistically analyzed. We defined prognostic parameters based on thyroglobulin (Tg) levels, 24-h ^{131}I uptake rates and TSH levels: (a) Tg/TSH, (b) Tg/24-h ^{131}I uptake value, and (c) Tg/(TSHx24-h ^{131}I uptake).

Results: We included 190 patients (50 male, 140 female; mean age 47 years) with DTC for analysis, 146 without distant metastases and 44 with M1 tumor stage at initial presentation. The mean period of follow-up was 10.4 years (SD± 3.7 years). In 18 out of the 146 DTC patients with M0 disease (12.4%), tumor recurrence was found during follow-up. Although tumor stage, age, and standard biochemical values significantly differ between patients with and without recurrent disease or between patients with M0 and M1 tumor stage, the newly defined parameter Tg/(TSHx24-h ^{131}I uptake) was the best independent significant prognostic parameter in the assessment whether patients will develop a tumor recurrence during follow-up or not.

Conclusion: High Tg/(TSHx24-h ^{131}I uptake) ratios justify an adjustment of the ^{131}I activity for ablation therapy. To assess the optimal cut-off level for a dose adjustment, however, further studies are required in more patients, but the initial results are encouraging with respect to improving outcome in DTC patients.

Introduction

Differentiated thyroid cancer (DTC) is a rather uncommon tumor with a high survival rate. The therapy of choice consists of (near-) total thyroidectomy followed by ablation with radioiodine-131 (^{131}I). This combined treatment schedule is a prerequisite for an optimal tumor destruction as well as for an optimal patient follow-up [1]. The currently used follow-up strategy is based on regular thyroglobulin (Tg) measurements under thyroid stimulating hormone (TSH) stimulation (Tg-off levels) either using thyroid hormone withdrawal or rhTSH and ^{131}I whole body scintigraphy (WBS). Later on, Tg levels without TSH stimulation may guide the clinician during the follow-up of DTC. The purpose of optimal follow-up protocols in thyroid carcinoma is the early detection of recurrent or metastatic thyroid cancer, as it has a great impact on morbidity and mortality. Indeed, patients with recurrent DTC have a less favorable prognosis than those with primary disease, as more than 50% of patients with a recurrence experience tumor-related mortality. One of the major issues in such cases is the fact that a tumor recurrence may loose the ^{131}I uptake capacity [2]. In this respect, it has been stated that high ablation doses may be recommended to decrease the risk not only for persistent thyroid remnants but also for tumor recurrence. The question, however, could be raised whether this should be applied in all DTC patients or in subgroups only [3-6]. Therefore, it would be helpful to have one single or a combination of prognostic parameters at initial stage that can be used to identify patients with a high risk for tumor recurrence during follow-up. Thyroglobulin measured at initial stage may be of prognostic value, but its value cannot be disconnected from the TSH stimulation and the amount of residual disease after surgery, expressed as the 24-h ^{131}I uptake value. In the present study, this value is a surrogate value for remnant size. Although ultrasonography or computed tomography (CT)-scanning of the head and neck region would give a better estimation of the residual thyroid volume after surgery than the uptake value, these imaging techniques are less

reliable shortly after surgery due to edema. Furthermore, contrast administration is required for optimal CT-scanning of the neck which interferes with subsequent ^{131}I therapy.

In the present study, data from 190 patients with newly diagnosed DTC were analyzed in order to assess the prognostic value of commonly determined initial parameters in the prediction of a tumor recurrence during follow-up. Furthermore, we studied the prognostic value of three newly defined parameters which are based on Tg under endogenous TSH stimulation, TSH levels, and/or the 24-h ^{131}I uptake value, all measured at the time of ablation. With the results, we might be able to adjust the ^{131}I ablation activity to decrease the risk of a recurrence and to improve morbidity and mortality.

Material and methods

Study population

Data were collected from the records of consecutive patients with DTC who received ablation treatment with ^{131}I at the Leiden University Medical Center (LUMC) between January 1986 and December 1999. This included a total of 255 patients with pathologically verified DTC, i.e. either papillary, follicular, mixed papillary follicular, or follicular Hürthle carcinoma. For the current evaluation, a follow-up period of at least 1 year was required. Exclusion criteria were: missing biochemical parameters, the presence of Tg-antibodies (Tg-abs levels >50 μg/l), or TSH levels <20 U/l at the time of ablation (n=49), unknown uptake (n=17), and/or follow-up of <1 year (n=10). As a result, 65 patients were excluded, resulting in a total study population of 190 patients. Out of these 190 patients, 146 had no distant metastases, whereas 44 had metastases at the time of initial diagnosis.

Hospital records were reviewed and the following (prognostic) data were recorded: age, gender, histopathological data, treatment characteristics, and laboratory values. Records of scintigrams were analyzed and coded. Tumor

staging was scored according to the criteria of the fifth tumor node metastasis (TNM) Atlas. We defined three new parameters as follows: (i) Tg/24-h ^{131}I uptake, (ii) Tg/TSH, and (iii) Tg/(TSHx24-h ^{131}I uptake) (Tg is expressed in µg/l and TSH in U/l).

Radioiodine treatment

Therapy for DTC consists of (near-) total thyroidectomy, followed 4-6 weeks later by radioiodine ablation therapy. During this interval, no treatment with $_{L}$-thyroxin was initiated in order to increase TSH levels. The 24-h ^{131}I pre-treatment uptake value in the neck region was measured using standard techniques: 40 MBq of ^{131}I was given orally, followed by planar scintigraphy of the neck region 24 h later. This uptake value is regarded as a surrogate value for remnant size in the present study. Although stunning may occur during diagnostic scanning with ^{131}I, a recent study by Dam *et al*. [7] demonstrated that treatment efficacy is not influenced by activities <185 MBq [7-9]. In addition, follow-up studies and subsequent treatment are used to achieve a complete ablation. In case of a possible stunning effect, ablation failures will be depicted 6 months after initial treatment (see evaluation of treatment efficacy).

A standard ^{131}I activity of approximately 2800 MBq was given orally 24 h after the uptake measurement and adjusted in case of large thyroid remnants. The rationale of this quantitative approach is to avoid unnecessary exposure and local radioiodine side effects. In this regimen, no adjustments were made in the case of cervical lymph node metastases. Treatment of patients with M1 tumor stage at initial presentation as well as subsequent treatment for either initial ablation failures or recurrent disease was done with 6100 MBq of ^{131}I. Seven days after each treatment, whole-body scans were made according to the protocol described below to assess loco-regional uptake and the presence of metastases.

Evaluation of treatment efficacy

Six months after the ablation therapy, L-thyroxin was withdrawn for at least 4 weeks. Subsequently, radioiodine diagnostic whole-body scintigrams were obtained 3 days after the administration of 185 MBq of ^{131}I or 24 h after the administration of 370 MBq ^{123}I. For all scintigrams, a Toshiba gamma camera (Tokyo, Japan) was used. A high-energy collimator (matrix sizes of 256 X 1024 and 256 X 256, window of 20% centered at 360 keV) for the ^{131}I WBS, a low-energy collimator (matrix sizes of 256 X 1024 and 256 X 256, window of 20% centered at 159 keV) for the ^{123}I WBS was used.

Anterior and posterior whole-body and planar views of the neck region were routinely obtained. For the whole-body scintigrams, scanning rates of 15 (^{131}I) and 10 cm/min (^{123}I) were used. In addition, Tg levels were determined at the time of the diagnostic whole-body scan to document the ablation efficacy. For successful ablation, a cut-off level of Tg of ≤1 µg/l was applied. Patients with an unsuccessful ablation, documented by scintigraphy and/or a Tg level >1 µg/l during TSH stimulation after 4 weeks of L-thyroxin withdrawal, received a second treatment with ^{131}I.

Recurrent disease was defined as increased Tg levels, abnormal WBS, or both but not within 2 years after ablation and following at least one diagnostic session with normal test results. Persistent disease or ablation failures were defined if one or both tests remained abnormal after ablation, irrespective of the time interval.

Analytical methods

Until 1997, serum Tg was measured using an IRMA, the Dynotest TG (Brahms Diagnostica GmBH, Germany), with a detection limit of 1 µg/l. From 1997 onwards the Dynotest TG-s (Brahms Diagnostica GmBH) was used, with a detection limit of 0.5 µg/l. Recurrent disease, however, was defined as Tg levels >1 µg/l. TSH levels were measured by means of an immunofluorometric assay

(IFMA) with the Delfia (Wallac, Turku, Finland) until 1997. Thereafter, an immunoluminometric assay (ILMA) was used with the Elecsys (Boehringer Mannheim, Germany). Serum Tg-abs were determined by the Ab-HTGK-3 IRMA test (DiaSorin Biomedics, Italy).

Data collection and statistical analysis

All collected data were put in a database using MS-Access 2000. Statistical analysis was performed with SPSS 11.5 for Windows (SPSS Corporation, Chicago, IL, USA) and MS-Excel 2000. The quantitative data were analyzed using Cross-tabs with χ^2, Student's *t*-test, Cox regression, Cox regression forward stepwise, and by calculating curve coordinates. The prognostic value of the patient characteristics was quantified with the hazard ratio and its 95% confidence level. Throughout, a p value of 0.05 or less was considered statistically significant. Finally, three subgroups were identified for statistical analysis: patients with initially M0 stage DTC, irrespective of recurrent disease during follow-up; patients with initially M1 stage DTC; and finally, patients with initially M0 stage disease, but with recurrent DTC during follow-up. For the generation of the probability plot and prognostic stratification, only patients with initially M0 disease were used, whereas their results were compared with patients with M1 disease to assess the overall value of the study results.

Results

In the present study, 190 patients (50 male, 140 female; mean age 47.1 years) with DTC were included for further analysis, 146 without distant metastases and 44 with M1 tumor stage at initial presentation. Papillary thyroid carcinoma, consisting of papillary and mixed papillary follicular, was diagnosed in 102 patients. Follicular thyroid carcinoma was diagnosed in 44 patients. In the present study, 49 patients had lymph node involvement at the time of thyroidectomy. The mean period of follow-up was 10.4 ±3.7 years. In 18 out of

the 146 DTC patients with M0 disease (12.4%), tumor recurrence was found during follow-up. A total of 14 patients died in the group without metastases, 6 from the differentiated thyroid carcinoma, whereas 8 died from other causes, such as second primary tumors.

Table 1 shows subgroup characteristics of patients with initially M0 stage (n=146) and patients with M1 stage (n=44) DTC as well as for patients with initially M0 stage without (n=128) and with (n=18) recurrent disease respectively. Significant differences were found between almost all parameters tested between patients with M0 and M1 initial tumor stage. For age, we found a cut-off level of 59 years between those with a high and low risk for recurrent disease. In patients with M0 disease, age at diagnosis (>59 years), T stage, N stage, and all newly defined parameters were significantly different between those with and without tumor recurrence during follow-up. For the risk of recurrent disease, Tg levels (p=0.027), N stage (p=0.038), and Tg/TSH (p=0.021) were significant correlates for tumor recurrence. In stepwise analysis, an increased ratio of Tg/(TSHx24-h ^{131}I uptake) was selected as the most reliable variable (p=0.001) for tumor recurrence (Figure 1), with a Hazard rate of 12.1 (95% CI: 6.61-22.13). Initial ablation failure was not found to be a significant indicator for tumor recurrence. The number of patients with initial ablation failure was not significantly different between the groups with and without recurrent disease (p=0.522).

To assess whether the parameters studied may be indicative for bulky disease, we compared the parameters of patients having initially M1 disease with those having initially M0 disease and tumor recurrence during follow-up. In this respect, age at diagnosis was significantly different between these subgroups (p=0.021; see Table 2). Finally, we combined patients with M1 with patients with recurrent disease into one group to determine the accuracy of Tg/(TSHx24-h ^{131}I uptake) in the assessment of bulky disease at the time of ablation.

The area under the receiver operating characteristic (ROC) curve was 0.800 (95% CI: 0.714-0.866).

Table 1. Differences between differentiated thyroid cancer patients with and without metastases and between patients with and without recurrent disease during follow-up.

	Patients with initially M0 (SD) (n=146)	**Patients with initially M1** (SD) (n=44)	**p value**	**M0 without RD** (SD) (n=128)	**M0 with RD** (SD) (n=18)	**p value**
Gender: Male / Female	32 / 114	13 / 31	0.400	27 / 101	5 / 13	0.521
Age at diagnosis	42.6 (±14.87)	61.9 (±16.46)	0.001	41.5 (±14.02)	50.7 (±18.3)	0.013
Histology			0.007			0.700
Papillary carcinoma	120	27		104	16	
Follicular carcinoma	26	17		24	2	
T-stage			0.001			0.003
T1	7	1		5	2	
T2	89	16		85	4	
T3	25	5		20	5	
T4	25	22		18	7	
N-stage			0.001			0.001
N0	110	31		101	9	
N1	36	13		27	9	
TSH (U/l)	77 (±36)	62 (±17)	0.023	77 (±37)	78 (±34)	0.949
Tg (µg/l)	21 (±110)	1246 (±4066)	0.000	8 (±14)	120 (±321)	0.001
Uptake (%)	6.1 (±7.3)	6.7 (±7.8)	0.621	6.3 (±7.6)	4.7 (±5.3)	0.125
Tg/Uptake	3.9 (±9.2)	827.1 (±3312.3)	0.003	2.5 (±5.6)	15.3 (±19.9)	0.001
Tg/TSH	0.4 (±2.3)	51.2 (±207.9)	0.003	0.1 (±0.2)	2.7 (±6.6)	0.001
Tg/(TSHx24-h ^{131}I uptake)	0.07 (±0.19)	38.00 (±170.55)	0.007	0.04 (±0.07)	0.31 (±0.49)	0.001
Initial ablation failure *				43 (34%)	8 (44%)	0.522

RD, recurrent disease; T stage, tumor stage; N stage, node stage; TSH, thyroid stimulation hormone; Tg, thyroglobulin.
* Evaluation 6-12 months after the ^{131}I ablation therapy.

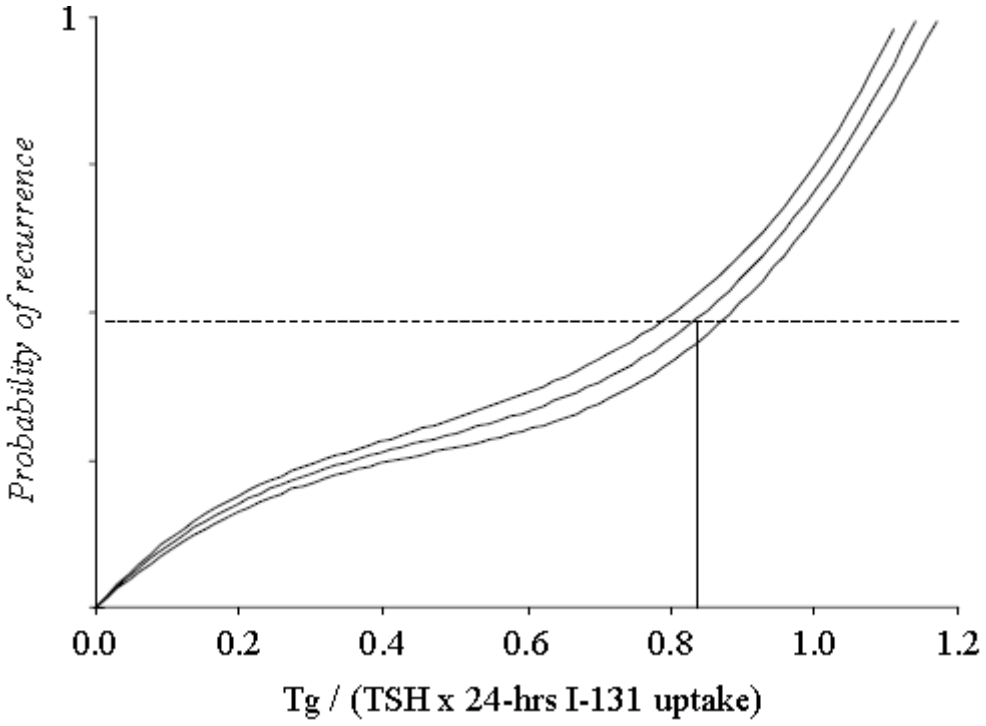

Figure 1. Probability plot of tumor recurrence with its 95% confidence interval in patients with initially MO tumor stage. Tg tryroglobulin; TSH, thyroid-stimulating hormone.

Table 2. Differences between differentiated thyroid cancer patients with initially distant metastases (M1) and with locoregional disease (M0) but a recurrence during follow-up.

		Patients with initially M1 (SD) (n=44)	**Patients with initially M0 and RD** (SD) (n=18)	**p value**
Gender: Male / Female		13 / 31	5 / 13	0.889
Age at diagnosis		62 (±16)	51 (±18)	0.021
Histology				0.061
	Papillary carcinoma	27	16	
	Follicular carcinoma	17	2	
T-stage				0.149
	T1	1	2	
	T2	16	4	
	T3	5	5	
	T4	22	7	
N-stage				0.217
	N0	31	9	
	N1	13	9	
TSH (U/l)		62 (±17)	78 (±34)	0.225
Tg (µg/l)		1246 (±4066)	120 (±321)	0.276
Uptake (%)		6.7 (±7.8)	4.7 (±5.3)	0.311
Tg/Uptake		827.1 (±3312.3)	15.3 (±20.0)	0.334
Tg/TSH		51.2 (±207.9)	2.7 (±6.6)	0.357
Tg/(TSH x 24-h ^{131}I uptake)		38.00 (±170.55)	0.31 (±0.49)	0.383

RD, recurrent disease; T stage, tumor stage; N stage, node stage; TSH, thyroid stimulating hormone; Tg, tryroglobulin.

Discussion

In the present study, we have assessed the value of clinical and biochemical parameters in prognostic stratification of patients with DTC at the time of ablation with radioiodine. Although T stage, N stage, age, and standard biochemical values at the time of diagnosis significantly differ between patients with and without recurrent disease or between patients with M0 and M1 tumor stage, we found a considerable overlap between these parameters to be of clinical value. Nevertheless, current study revealed the newly defined parameter Tg/(TSHx24-h ^{131}I uptake) determined at initial stage to be the strongest independent significant prognostic factor for tumor recurrence during follow-up.

The Leiden University Medical Center is a reference center for patients with relatively complicated DTC, which is reflected in the high number of patients (n=44) with M1 disease at initial stage. In 12% of the patients with initially M0 disease tumor recurrence was seen during follow-up, which is in agreement with previous publications by others [10-12]. All patients had been treated by near-total thyroidectomy and subsequent ablation with radioiodine approximately 6 weeks after surgery. In a recent report [3], we have described that the use of rather low ablation doses results in failure rates up to 60% and, consequently, in a high number of additional treatments up to more than a year after initial operation. Although a relation between the initial treatment failure and recurrent disease was suggested, this could not be established in the present study, as differences in failure rates between patients with and without recurrent DTC were not statistically significant. This finding is in agreement with the data published by Falvo *et al*. [13].

In a recent report by Haigh *et al*. it was shown that survival of patients with DTC was not significantly influenced by the extent of initial thyroidectomy [14]. The authors found 10-year survival rates of 72 and 78% respectively for total and partial thyroidectomy. In contrast to these results, however, Cushing *et al*. [15] reported on the prognostic value of the extension of initial surgery. They

studied 333 patients with a mean age of 39.7 years and found that a total thyroidectomy revealed better results than a near-total or partial thyroidectomy. Regarding the number of patients with advanced disease at initial presentation in their study, it is not surprising that non-total thyroidectomy did not only result in a high frequency of large thyroid remnants, but also in a high number of patients with tumor remnants.

The fact that the presence of lymph node metastases is a predictive factor for recurrence, irrespective of initial surgery (partial or total thyroidectomy) [16], again underlines the issue that an optimal assessment and subsequent resection of the total tumor mass at initial stage is highly important for prognosis and survival. In addition, subsequent treatment with radioiodine, therefore, is almost a prerequisite for an optimal starting point, especially in extensive disease, as it destroys normal thyroid tissue as well as small tumor remnants. Indeed, Haq *et al*. [17] clearly showed the superior value of a combined therapeutic approach over surgery alone. Despite the low number of patients with recurrent disease in the present study, we found a significant difference in N stage between patients with and without recurrent disease ($p=0.001$).

Different staging classifications have been proposed over the past decades in hopes of a better identification of high risk patients, i.e. patients with bulky disease. In this respect, the TNM tumor staging system is still the most commonly used system. Although it can be used to differentiate low-risk from high-risk patients, it was found to be less valuable in identifying intermediate-risk groups [10;18]. The age for men, gender and histological subtype (AMES) classification, a system based on age, gender, and histological parameters, as well as the European Organization for Research and Treatment of Cancer (EORTC) classification were both tested in a prognostic study on 499 DTC patients by Jukkola *et al*. [10], revealing that these methods were not reproducible. Finally, the metastasis, age, completeness of resection, local invasion, tumor size (MACIS) scoring classification, which is based on age,

tumor size, incomplete surgery, extra-thyroidal invasion, and distant metastases, was found to leave the definition of the intermediate and high risk groups too wide. Consequently, most of the staging classifications are found to have more or less practical limitations.

One of the most well-known prognostic parameters is age at the time of diagnosis. In this respect, we observed not only a significant difference between patients with M0 disease (42.6 years) and those with M1 disease (61.9 years; p=0.001), but also between M0 tumor stage patients with (50.7 years) and without (41.5 years; p=0.013) recurrent disease. Falvo *et al*. [13] performed a study on biologically aggressiveness of DTC in elderly patients, in which an age exceeding 70 years represented the most unfavorable prognosis. Haq *et al*. [17] reported a comparable age of 70 years and older in relation to a poor outcome. Both Volante *et al*. [19] and Siironen *et al*. [20] described an age of >45 years in close relation to an aggressive tumor behavior. Based on the present data, however, it can be concluded that age at initial diagnosis is indicative for tumor extension, but it is not an independent prognostic parameter that can be used to identify patients with a high risk for tumor recurrence. Indeed, regarding age, the overlap between the subgroups defined is too much to be useful in clinical practice.

As tumor extension at initial presentation is highly important for the assessment of prognosis and clinical outcome, it would be helpful to have a test that better reflects tumor burden than current staging and imaging techniques. In one of the most interesting publications on this subject, a clear relation between tumor burden and thyroglobulin levels was described [21]. The authors reported not only that the number of metastatic lesions was linked with serum Tg/TSH levels, but also their total volume. The diagnostic value of Tg was confirmed and established in subsequent reports and it was demonstrated that the value of stimulated Tg levels, i.e. levels measured after hormonal withdrawal, clearly identifies persistent or recurrent disease. In a study by Giovanella *et al*. [11],

post-surgery Tg levels above 4.5 μg/l identified 94% of patients with metastasis, which, according to the authors, could be taken into account in treatment planning. Bernier *et al*. showed that Tg levels measured at the time of ablation and 5 days later expressed as TgD5/TgD0 ratio were highly suggestive for treatment failure [22]. The larger the ratio, the better the final outcome. In other studies, Tg levels measured at 3 or 6 months after ablation were found to be strongly correlated with metastatic disease and the authors concluded that levels measured at these time intervals are indicative for an intensive follow-up scheme or additional treatment [23;24]. Others have shown that the best positive predictive value for the detection of a local recurrence is brought by the slope of the Tg levels [25;26]. Finally, Kim *et al*. [27] showed that Tg levels measured at the time of immediate postoperative ^{131}I remnant ablation correlated well with serum Tg levels at the time of diagnostic whole-body scanning during follow-up. High Tg levels were indicative for tumor persistence or recurrence of disease in the earliest postoperative period.

Under normal circumstances, i.e. in normal thyroid tissue, an optimal re-uptake and storage mechanism should prevent leakage of Tg into the bloodstream. In clinical practice, however, it has been found that this physiologic mechanism is not fulfilling this task completely with measurable Tg levels as a consequence in patients with normal function of the thyroid gland. Increased Tg production and a distortion of the physiological process, as seen in infection and malignancy, results in a misbalance and in increased serum Tg levels compared with normal circumstances, a phenomenon that is enhanced by TSH stimulation. Indeed, from data in literature, it is known that Tg measurements after hormonal withdrawal have a higher accuracy than Tg-on levels in the detection of malignancy. In this respect, a TSH stimulation >20 U/l is regarded as prerequisite for an optimal Tg measurement. In general, patients who are admitted for ablation with radioiodine have normal thyroid tissue remnants in the neck region. Despite the optimal TSH stimulation at that time to facilitate an

optimal ^{131}I uptake, Tg levels should be relatively low in the case of a normal function of the remnant, as the re-uptake and storage mechanisms are intact. On the other hand, the levels may be significantly increased in remnants harboring malignant cells. In the present study, we have evaluated whether an increased Tg level is caused by a large nearly stimulated thyroid remnant or a small remnant with stimulated thyroid cancer cells. For this purpose, we have normalized the Tg levels for both the amount of functional thyroid tissue, expressed in a 24-h uptake value, and the amount of TSH stimulation. Although we used a low dose ^{131}I 24-h uptake scan before therapy, it has become more and more common practice to perform a post-therapy scan with uptake measurements over the neck region. In this respect, one of the major issues for discussion is the possible stunning effect that may occur even when using activities of ^{131}I in the range of 40 MBq [7-9]. Since therapeutic activities of ^{131}I are nowadays more based on tumor stage instead of uptake values, post-treatment uptake values may be advised for prognostic stratification to avoid stunning effects by pre-treatment scans.

We found significant differences in Tg levels at initial presentation between patients with (mean level, 8 μg/l) and without (mean level, 120 μg/l) recurrent disease during follow-up, whereas TSH stimulation and 24-h uptake values were not different. In the univariate analysis, T and N stage were significantly different between the two groups, but, using the stepwise forward multivariate analysis, Tg/(TSHx24-h uptake) remained the most significant independent parameter, irrespective of N and T stage. Moreover, except from age, we did not find significant differences in all parameters tested between patients with initially M1 disease and patients with M0 stage demonstrating recurrent disease during follow-up. Even the newly defined parameters that were based on Tg levels did not show any significance anymore, suggesting that high values indicate bulky DTC. Consequently, patients with M0 stage and high Tg/(TSHx24-h uptake) ratios at initial presentation should be regarded as

patients with initially M1 disease and therefore be treated with higher ^{131}I doses. In addition, a close clinical follow-up scheme is recommended for these patients. Finally, it has to be realized that at severe malignancy the Tg production may be low and not high as found in the present study, which may cause a false negative effect on this new parameter. In such cases, radioiodine uptake is often also severely diminished, as the expression of the sodium-iodine symporter is commonly the first factor being affected in a dedifferentiation process of thyroid cancer. This condition, however, is very rare at initial presentation, whereas such features are more common in anaplastic tumors, which were excluded in the present study.

Conclusion

In the present study, we have evaluated the prognostic value of clinical and biochemical parameters measured at the time of ablation for DTC. Based on these values, we have defined a new parameter, Tg/(TSHx24-h uptake), which was hypothesized to be a better prognostic indicator for the presence of malignant cells after total or near-total thyroidectomy for DTC. Although T stage, N stage, age at the time of diagnosis, and standard biochemical values significantly differ between patients with and without recurrent disease or between patients with M0 and M1 tumor stage, the newly defined parameter was the best independent significant prognostic parameter in the assessment whether patients will develop a tumor recurrence during follow-up or not. From the present data, it can be concluded that high ratios justify an adjustment of the ^{131}I doses as ablation dose and a close clinical follow-up.

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