Differentiated thyroid carcinoma : nuclear medicine studies
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Chapter 2

Radioiodine-131 in differentiated thyroid cancer: a retrospective analysis of an uptake-related ablation strategy

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Abstract

In our hospital, a 24-h radioiodine-131 (^{131}I) uptake-related ablation strategy is used in patients with differentiated thyroid cancer to destroy thyroid remnants after primary surgery. In this strategy, low doses of ^{131}I are used, but data in the literature on its efficacy are conflicting. Therefore, we performed the present study to evaluate the clinical outcome of this ablation strategy. In this study, patients (n=235) were selected who underwent thyroidectomy for differentiated thyroid cancer, followed by an ablative dose of ^{131}I. Approximately 6 months after ablation, treatment efficacy was evaluated using radioiodine scintigraphy and thyroglobulin (Tg) measurements. Successful ablation was defined as the absence of radioiodine uptake in the neck region (criterion 1). Tg values were determined 3-12 months after ablation (criterion 2). Based on criterion 1, unsuccessful ablation was found in 43.0% of cases. Pre-treatment uptake values were statistically significantly lower (p=0.003) in successfully ablated patients (mean 5.4%) than in unsuccessfully ablated patients (mean 8.2%). Based on criterion 2, unsuccessful ablation was found in 52.4% of patients. The uptake-related ablation strategy, using low doses of ^{131}I, shows a relatively high treatment failure rate. Based on these results it is suggested that a lower ablation failure rate could be achieved by applying higher ^{131}I doses in the ablation of thyroid remnants in differentiated thyroid carcinoma patients. In the case of lymph node metastases a further dose adjustment may be advisable.

Introduction

The therapy of choice in patients suffering from differentiated thyroid cancer, subdivided into papillary and follicular thyroid carcinoma, is (near-) total thyroidectomy. This is routinely followed by the administration of radioiodine-131 (^{131}I) to destroy any remaining benign or malignant thyroid tissue, so-called ablation. There are several reasons for routine ablation after surgery [1]: (a) to be able to detect a carcinoma recurrence by radioiodine scanning; (b) radioiodine can destroy microscopic foci of carcinoma in the thyroid remnant; (c) possible carcinoma outside the thyroid bed may be detected and treated by radioiodine; (d) to use thyroglobulin (Tg) as tumor marker of recurrent carcinoma all normal thyroid tissue has to be destroyed.

Iodine-131 has been used for many years to ablate thyroid remnants following thyroid surgery, but a single optimal dose has not yet been established [2]. According to Mazzaferri [3], more studies are required to establish the optimal dose necessary for ablation of the thyroid remnant. In this respect, data in the literature are inconsistent; some studies conclude that a dose of 1110 MBq of ^{131}I may be as effective as a high dose such as 3700 MBq [4-6], while other authors suggest that a higher dose of ^{131}I will improve the rate of successful remnant ablations [7-9].

In our hospital, relatively low doses of ^{131}I have been used for many years for ablation in patients without distant metastases. The applied ^{131}I dose, which was based on data in the literature [10-14], depends on the 24-h ^{131}I pre-treatment uptake value in the neck region and ranges from 1100 to 2800 MBq. To assess the outcome of this strategy and because of inconsistencies in the literature regarding the appropriate ablative dose of ^{131}I [4-9], we performed a retrospective study to evaluate the clinical outcome of this ablation strategy.

Materials and methods

Study population and equipment.

Patients were selected who received ablation treatment with ^{131}I at the Leiden University Medical Center (LUMC) between January 1986 and December 1999 (n=418), to destroy thyroid remnants after thyroidectomy for differentiated thyroid cancer. This period was selected as before 1986 standardised records regarding the applied dose of ^{131}I were not available. Furthermore, follow-up of at least 2 years was required.

Consecutive exclusion criteria were: first dose of ^{131}I before 1986 (n=37), a first dose of ^{131}I given in another hospital (n=15), radioiodine treatment more than 1 year after thyroidectomy (n=24), only hemi-thyroidectomy (n=6), ^{131}I doses not according to the standard protocol (n=64) and distant metastases (n=30). In ten cases, proper assessment for the presence of distant metastases by evaluating the post-ablative scintigram was not possible owing to scattered radiation on the post-ablative scintigram. In 11 patients, whole-body scintigraphy 3-10 days after ablation (post-ablative scintigram) was not performed. To assess whether these patients were free of distant metastases at the time of ablation, records of follow-up scintigrams and/or other data from the medical files were studied. Patients were excluded from analysis when these data revealed distant metastases (n=3) or when follow-up data were not available or incomplete (n=3). Histopathology in one of the 236 remaining patients revealed no malignancy in the thyroid gland, but only an ectopic localisation of thyroid carcinoma. This patient was also excluded. After withdrawal of 183 patients for the foregoing reasons, 235 patients were left for evaluation.

From the medical files, age, gender, histopathological data, treatment characteristics and laboratory data were recorded. Records of scintigrams were analysed and coded.

Tumor staging was scored according to the criteria of the TNM Atlas [15].

For all scintigrams, a Toshiba gamma camera (Tokyo, Japan) was used. A high-energy collimator (matrix sizes of 256x1,024 and 256x256, window of 20% centered at 360 keV) for the ^{131}I scintigrams, a low-energy collimator (matrix sizes of 256x1,024 and 256x256, window of 20% centered at 159 keV) for the ^{123}I scintigrams 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.

Radioiodine treatment.

The mean interval between thyroidectomy and the ablative dose was 7.0 weeks (standard deviation ±6.4 weeks). During this interval, no suppressive treatment with L-thyroxine was initiated. TSH values were measured at the time of ablation.

In patients treated from 1992, low-iodine diets were used approximately 4 days before the ablative dose was given. In patients 4 treated until 1992, low-iodine diets were not strictly applied according to the currently used protocol. The rationale of a low-iodine diet was to achieve a reduction in the iodide pool of the body, in order to achieve the highest possible entrance of ^{131}I ions into the thyroid remnant.

The 24-h ^{131}I pre-treatment uptake value in the neck region was measured using standard techniques (in %): 40 MBq of ^{131}I was given orally, followed by planar scintigraphy of the neck region 24 h later. A standard of 40 MBq ^{131}I that was calibrated on the day of admission and measured in a neck phantom after 24 h was used as a reference. Uptake of less than 5%, of between 5% and 10% and of more than 10% was followed by 2800, 1850 and 1100 MBq of ^{131}I in one dose, respectively. The rationale of this quantitative approach is to avoid unnecessary exposure [16] and local radioiodine side-effects [17;18]. In this regimen, no adjustments were made in the case of cervical lymph node metastases.

Documentation of treatment efficacy.

Treatment efficacy was evaluated approximately 6 months after ablation using low-dose radioiodine diagnostic whole-body scintigrams obtained 3 days after administration of ^{131}I or 24 h after administration of ^{123}I. For this purpose, hormonal supplementation was withdrawn. Records of these diagnostic radioiodine scintigrams were studied. The percentage of ^{131}I versus ^{123}I diagnostic scans was 87.6% versus 12.4%, respectively. For the ^{131}I scintigrams, doses of 40 (1.2%), 100 (7.6%) or 185 MBq (91.2%) were used. In patients who received a second therapeutic dose of ^{131}I (n=81), records of whole-body scintigrams obtained approximately 1 week after this second therapeutic dose (i.e. post-therapeutic scintigram) were also evaluated. In the case of a second therapeutic treatment with ^{131}I, the average dose was 6163 MBq (standard deviation ±449 MBq). Unsuccessful ablation of the thyroid remnant was defined as the visible presence of radioiodine uptake in the neck region on the diagnostic and/or post-therapeutic scintigram (criterion 1). Results of ablation are presented for the whole group, for patients without clinically lymph node metastases (N0) and for patients with histopathologically proven lymph node metastases (N1). Scintigrams obtained up to 2 years after ablation were included for analysis.

Available Tg values, determined 3-12 months after ablation, were also used to document ablation efficacy. Cut-off levels of ≤1μg/l (i.e. undetectable, criterion 2a) and ≤3 μg/l (criterion 2b) were applied. If anti-thyroglobulin antibodies (Tgab) were measurable, interference effects in the determination of Tg could be substantial [19]. As IRMA assays were used, these interference effects generally would have resulted in underestimation of the Tg value. Therefore, Tg values were excluded from analysis in the presence of measurable Tgab and a corresponding Tg value below the cut-off level.

Data collection and statistical analysis.

All collected data were put in a database using MS-Access97. For statistical analysis we used SPSS for Windows, version 10.0 and MS-Excel97. The quantitative data (continuous parameters) were analysed using Student's t test for normal distributed data or the Mann-Whitney *U* test for non-normal distributed data. For analysis of data on the nominal scale we used the Chi-squared test. Quantifiable data are given as minimal and maximal values as well as the mean ± standard deviation (SD). A statistically significant difference was considered when $p<0.05$.

Results

Study population

Papillary thyroid carcinoma was diagnosed in 184 patients, 38 men and 146 women (age at thyroidectomy 16.4-87.1 years; mean 42.1; SD ±14.2). Follicular thyroid carcinoma was diagnosed in 50 patients, 12 men and 38 women (age at thyroidectomy 14.8-85.5 years; mean 51.7; SD ±20.0). In one case, thyroid carcinoma was not otherwise specified (tcNOS) (Table 1).

At the histological study of the surgically excised material, lymph node metastases were diagnosed in 53 papillary thyroid carcinoma patients. In follicular thyroid carcinoma patients, no lymph node metastases were found (Table 1).

Table 1. Population characteristics including tumor and lymph node stage.

Differentiated thyroid carcinoma		No. of patients	No. of patients with lymph node metastases
Tumor stages in papillary thyroid cancer patients	T1	18	12
	T2	107	22
	T3	28	5
	T4	31	14
	Tx	0	0
	Total	**184**	**53**
Tumor stages in follicular thyroid cancer patients	T1	1	0
	T2	29	0
	T3	14	0
	T4	5	0
	Tx	1	0
	Total	**50**	**0**
Tumor stages in thyroid carcinoma not otherwise specified	T1	0	0
	T2	1	0
	T3	0	0
	T4	0	0
	Tx	0	0
	Total	**1**	**0**
Tumor stages: total numbers	T1	19	12
	T2	137	22
	T3	42	5
	T4	36	14
	Tx	1	0
	Total	**235**	**53**

Treatment efficacy (criterion 1)

In 200 patients, diagnostic and/or post-therapeutic scintigrams were available for evaluation. In the remaining 35 cases, scintigraphic follow-up was not performed for unknown reasons. There was no significant difference between the group of patients with (n=200) and without (n=35) scintigraphic follow-up with respect to age at thyroidectomy (p=0.249), sex (p=0.123), tumor stage (stages T1-T3 versus stage T4, p=0.906), lymph node stage (p=0.088) or pre-treatment uptake values (p=0.194). Therefore, we considered the outcome of ablation in the group of patients with follow-up scintigrams (n=200) as representative for the whole group of 235 patients.

In 86 cases (43.0%), radioiodine uptake was seen in the neck region on the diagnostic and/or post-therapeutic scintigram, implying unsuccessful ablation. In eight of these 86 cases, diagnostic scintigraphy revealed no evidence for a persistent thyroid remnant, while a subsequent post-therapeutic scintigram performed up to 2 years after ablation did indicate uptake.

Figure 1 demonstrates the percentage of unsuccessful ablations per histological type and tumor category without clinically lymph node metastases and with histopathologically proven lymph node metastases. No statistically significant differences could be found in ablation rates between papillary thyroid carcinoma and follicular thyroid carcinoma patients (p=0.738) or between tumor stages T1-T3 and tumor stage T4 (p=0.510).

In 59 of 151 clinically N0 patients (39.1%), ablation was unsuccessful, while in 27 of 49 patients (55.1%) with histopathologically proven lymph node metastases, ablation was unsuccessful. This difference in ablation rate was statistically significant (p=0.049).

As shown in Table 2, the frequency of unsuccessful ablations increased with rising 24-h ^{131}I pre-treatment uptake values: the uptake values were significantly lower (p=0.003) in successfully ablated patients (mean 5.4%; SD ±7.5%) than in unsuccessfully ablated patients (mean 8.2%; SD ±8.6%).

Table 2. Number of patients demonstrating uptake in the neck region on follow-up scintigraphy (criterion 1), in relation to the pre-treatment uptake values.

Pre-treatment uptake value (U)		**No. of patients**	**Uptake in neck region on follow-up scintigraphy**	
value	**mean ±SD**		**No.**	**%**
U ≤5	2.4 ±1.2	128	44	34.4*
5< U ≤10	7.7 ±1.4	31	17	54.8
U >10	21.9 ±8.5	33	20	60.6*
U unknown		8	5	62.5
Total		**200**	**86**	**43.0**

(* = statistically significant difference, p=0.006)

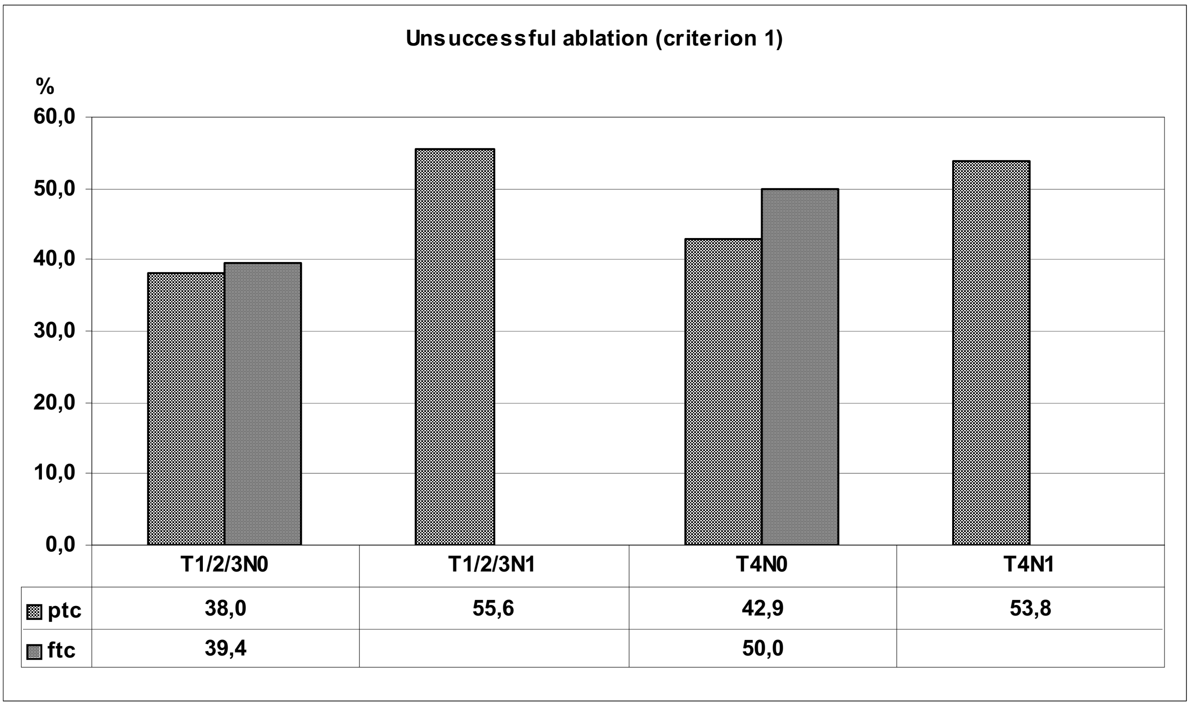

Figure 1. Percentage of unsuccessful ablations according to criterion 1 (radioiodine uptake in the neck region on follow-up scintigraphy). Papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC) patients. T1/2/3/N0: tumor stages T1, T2, T3 without clinically lymph node metastases; T1/2/3N1: tumor stages T1, T2, T3 with histopathologically proven lymph node metastases; T4N0: tumor stage T4 without clinically lymph node metastases; T4N1: tumor stage T4 with histopathologically proven lymph node metastases.

With respect to age, no statistically significant difference in ablation results was found (p=0.197). A statistically significant difference (p=0.014) in ablation failure rate was found between males (58.7%) and females (38.3%). However, in our population there was a statistically significantly (p=0.001) higher prevalence of lymph node metastases in male patients (43.5%) than in female patients (18.8%).

No significant differences in treatment results (p=0.84) were found between patients treated until 1992 (low-iodine diets not strictly applied) and those treated after 1992 (low-iodine diets used 1 week before ablation).

Treatment efficacy (criterion 2)

With respect to Tg values, 191 and 187 evaluable cases were available for cut-off levels of ≤1 and ≤3 µg/l respectively. This difference in evaluable cases is caused by exclusion of values in the presence of measurable Tgab and a corresponding Tg value below the cut-off level. In 100 cases (52.4%) a Tg value >1 µg/l was present, implying unsuccessful ablation (criterion 2a). A Tg value >3 µg/l was present in 38 cases (20.3%) (criterion 2b). In Tables 3 and 4 a subdivision is given according to the pre-treatment uptake value.

Table 3. Number of patients with Tg values >1 µg/l (criterion 2a) determined 3-12 months after ablation, in relation to the pre-treatment uptake values.

Pre-treatment uptake value (U)	**No. of evaluable cases**	**Tg >1 µg/l**	
		No.	**%**
U ≤5	123	62	50.4*
5< U ≤10	31	16	51.6
U >10	30	15	50.0*
U unknown	7	7	100.0
Total	**191**	**100**	**52.4**

(* = No statistically significant difference, p=0.968)

Table 4. Number of patients with Tg values >3 μg/l (criterion 2b) determined 3-12 months after ablation, in relation to the pre-treatment uptake values.

Pre-treatment uptake value (U)	No. of evaluable cases	Tg >3 μg/l	
		No.	%
U ≤5	120	23	19.2*
5< U ≤10	30	4	13.3
U >10	30	9	30.0*
U unknown	7	2	28.6
Total	**187**	**38**	**20.3**

(* = No statistically significant difference, p=0.195)

TSH values

TSH values at the time of ablation ranged from 3.1 to 330.0 mU/l (mean 71.0; SD ±42.2). In 15 patients, a TSH value below 20 mU/l was found at the time of ablation. Nine of these 15 patients had a pre-treatment uptake value ≥10%, and in only one of these nine was ablation successful according to criterion 1. In this patient there were no signs of residual thyroid tissue.

Discussion

In the present study the clinical outcome of a 24-h ^{131}I uptake-related ablation strategy to destroy thyroid remnants after primary surgery for differentiated thyroid cancer was evaluated. In this strategy, rather low ablative doses of ^{131}I are used. Depending on the extent of the thyroid remnant, unsuccessful ablation was found in 34%-61% of cases, which is relatively high.

One criterion for successful ablation was the visible absence of radioiodine uptake in the neck region on follow-up scintigraphy, routinely performed 6 months after ablation. Furthermore, Tg values were evaluated and cut-off levels of ≤1 and ≤3 μg/l were applied. The rationale for using a low cut-off level of ≤ 1 µg/l, in our laboratory defined as undetectable, is that in the case of circulating Tg, residual normal thyroid or tumor cells are present [20]. A cut-off level ≤3µg/l was based on data published by Duren *et al*. [21] and Ozata *et al*. [20].

Samaan *et al*. [22] retrospectively analysed 1599 patients who were treated for well-differentiated thyroid carcinoma. There were 736 patients who received radioiodine and this group was compared with the 863 patients who did not receive radioiodine. The authors concluded that treatment with radioactive iodine improves diseasefree interval and survival. In an article by Mazzaferri [3] on a large follow-up study, similar conclusions were reported. However, the optimal dose to achieve total ablation after one dose of ^{131}I is still controversial. As already mentioned, some investigators conclude that a low dose, such as 1110 MBq, may be as effective as a high dose, such as 3700 MBq, in achieving ablation [4-6] while others suggest that increasing the dose will improve the rate of successful remnant ablation [7;8]. However, the above-mentioned studies included a small number of patients, ranging from 13 to 63. Roos and Smith [2] concluded that the issue of the appropriate dose of ^{131}I for ablation of thyroid remnants postoperatively still remains undetermined. In a meta-analysis including 11 studies and two additional cohorts of their own, Doi and Wood-house [9] compared the efficacy of remnant ablation following a single low dose (1074-1110 MBq) versus a single high dose (2775-3700 MBq). Their results demonstrate that a single high dose of ^{131}I is more efficient in ablating residual thyroid tissue than a low dose. However, ablation rates are also influenced by remnant size [9; 16; 23]. In general, irrespective of the dose, the more extensive surgery is performed, the more likely ablation will be successful [9]. Arslan *et al.* [24] found a statistically significantly lower remnant thyroid volume (calculated by ultrasonography) in patients in whom ablation was achieved compared with patients in whom ablation failed. In patients with total ablation, partial ablation and no ablation, Beierwaltes *et al*. [25] found average preradioiodine treatment uptake of 5.22%, 9.91% and 13.11%, respectively. In the present study, we found statistically significantly lower pre-treatment uptake values in successfully ablated patients. This is in agreement with the above-mentioned studies. However, taking into account that better ablation results are achieved after more extensive surgery, Doi and Woodhouse [9] still concluded that the available data favor higher doses of ^{131}I (2775 - 3700 MBq) for remnant ablation.

In the study by Beierwaltes *et al*. [25], total ablation after thyroidectomy from the first dose of ^{131}I, not less than 3700 MBq, was achieved in 87% of 267 well-differentiated thyroid carcinoma patients with radioiodine uptake confined to the thyroid bed and an average pre-treatment percent uptake of 6.01%. Their results also demonstrated comparable ablation results when cervical lymph nodes were present (total ablation was achieved in 114 out of 129 patients after the first dose of more than 3700 MBq of ^{131}I). They treated patients with ^{131}I for ablation of remnants in the thyroid bed when there was significant 24-h ^{131}I uptake (generally >0.5%) after 74 MBq of ^{131}I. Within 1 year after ablation, they performed ^{131}I scintigraphy in the hypothyroid state. The thyroid remnant was judged to have been totally ablated when no residual uptake was seen in the thyroid bed and the measured percent uptake in the neck was <1%. De Klerk *et al*. [26] evaluated 93 differentiated thyroid carcinoma patients referred for their first ablative treatment after thyroidectomy. The patients were treated with 3700 MBq of ^{131}I in the absence of lymph node or distant metastases and 5550 MBq of ^{131}I in the presence of pre- or peri-operatively detected cervical lymph node metastases. Pre-ablative ^{131}I diagnostic scintigraphy was not performed. One year after ^{131}I ablation, a whole-body diagnostic ^{131}I (370 MBq) scintigram was performed after discontinuation of thyroid replacement therapy for 4-6 weeks. Their main criterion for successful ablation was the absence of visual ^{131}I residual neck uptake on diagnostic scintigraphy. This was achieved in 88% of the patients, with a mean uptake percentage in the neck of 0.23% (SD ±0.87%;

range 0.001-6.4%), measured 1 week after ablation. However, they reported a Tg value of <1 µg/l at 1-year follow-up in only 48% of the patients. We also found a discrepancy in ablation rate using criterion 1 (radioiodine uptake in the neck region) and criterion 2a (Tg value ≤1µg/l). This discrepancy amounted to 16% in patients with comparable pre-treatment uptake of ≤5%.

Factors that could have influenced the treatment results

Stunning effect. It has been shown that relatively low diagnostic doses of ^{131}I may lead to impaired ability of remnant thyroid tissue to concentrate the subsequent ablative dose of ^{131}I (so-called stunning effect) and thereby reduce therapeutic efficacy [27;28]. Muratet *et al*. [28] suggested that the threshold dose of ^{131}I above which the stunning phenomenon may have an adverse effect on treatment efficacy is between 37 and 111 MBq ^{131}I. In a study by Morris *et al*. [29], no significant difference was found in ablation rates between patients who received 111-185 MBq ^{131}I for diagnostic scanning before the ablative dose and patients who did not receive any ^{131}I before the initial treatment dose. Since in the present study a dose of 40 MBq was usually applied in the pre-ablative uptake measurements, we assume that the stunning phenomenon made at most a slight contribution to the ablation failure rate.

Low-iodine diet. For many years, low-iodine diets have been used to increase the ^{131}I dose delivered to the thyroid remnant [30;31]. The increase in thyroid ^{131}I uptake after a low-iodine diet theoretically implies that a low-iodine diet will increase the effectiveness of ablative doses [32]. Nevertheless, Morris *et al*. [32] did not find a significant difference in ablation rate between patients who followed a regular diet and patients who followed a low-iodine diet before ablation. Between 4 and 42 months after the ablative dose they determined success of ablation according to the visual absence of uptake in the thyroid bed and neck region on a low-dose ^{131}I diagnostic scintigram. However, significantly more patients were treated with 3700 MBq of ^{131}I in the low-iodine diet group and significantly more with 5550 MBq in the group of patients who followed a regular diet. In our study, low-iodine diets were not strictly applied in patients who were treated until 1992. In this group of patients we did not make a distinction in the analysis of treatment results between low-iodine diet and normal diet patients. However, no significant differences in treatment results according to criterion 1 were found between patients in whom low-iodine diets were not strictly applied (treated until 1992) and patients in whom low-iodine diets were applied according to the currently used protocol (treated from1992). One reason for the lack of difference in treatment results between low-iodine diet patients and patients in whom low-iodine diets were not strictly applied could be the short duration of iodine abstinence. Probably the iodide pool had not been significantly reduced.

Discontinuation of thyroid hormone supplementation.

The follicular cells of the thyroid gland trap and concentrate iodide from the blood, which is achieved by an active, energy-dependent transport process across the basolateral plasma membrane of the thyrocytes. The sodium/iodide symporter (*NIS*) gene encodes the protein responsible for the transport process [33]. Because thyroid cancers or metastases from thyroid cancer accumulate iodine to a lesser degree than normal thyroid tissue, intensive TSH stimulation is required in patients with thyroid cancer before administration of ^{131}I in order to increase *NIS* expression and thus the ability of thyroid cancer tissue to take up ^{131}I [33]. To achieve intensive TSH stimulation, discontinuation of thyroid hormone supplementation is necessary. As expected, the TSH stimulation varied between patients, which theoretically could have had an impact on the success of ablation of the thyroid remnant.

In the present study we did not take into account the effect of TSH values on the ablation results. It is possible that ablation results could be affected in the presence of an inadequate degree of hypothyroidism, for example a TSH value below 20 mU/l. As mentioned above, in 10 of 15 patients who had a TSH value below 20 mU/l at the time of ablation, treatment with ^{131}I was unsuccessful. In eight of these ten patients a pre-treatment uptake value of ≥10% was measured, probably indicating that a substantial amount of residual functioning thyroid tissue prevented sufficient TSH elevation.

Limitations of the study

In 35 patients scintigraphic follow-up was not performed, implying that presentation of treatment results for the whole patient group was not possible. No statistically significant differences in age, sex, tumor stage, lymph node stage or pre-treatment uptake values were found between the group of patients with (n=200) and the group without scintigraphic follow-up (n=35). We assumed that the similarity of the groups allowed inference of the same ablation results.

Scintigrams were not independently reviewed by one individual, causing an element of uncertainty. As we defined unsuccessful ablation as the presence of radioiodine uptake in the neck region, we did not distinguish between residual normal thyroid tissue in the thyroid bed, pyramidal lobe or thyroglossal duct region and residual functioning thyroid cancer in cervical lymph nodes.

Total ablation according to criterion 1 was considered as the absence of uptake in the neck region on follow-up scintigraphy. However, in our study population, follow-up scintigraphy indicated new uptake outside the neck region in two patients, likely corresponding to new distant metastases. Nevertheless, in the presented results these two patients were regarded as having had successful ablation of their thyroid remnant.

In this retrospective study, data regarding the remnant mass were not available. Consequently, we could not provide exact information about a possible relation between tumor dosimetry, which is based on uptake values and remnant masses, and subsequent failure rates. In our opinion, in current practice it is not feasible to correctly assess the size of small remnants by means of imaging techniques. Studies on the use of ultrasonography for the estimation of thyroid masses have been performed in hyperthyroidism, i.e. in patients with a thyroid in situ. Data on its use and, especially, on its accuracy and reproducibility in thyroidectomy patients are scarce or even not available.

Conclusion

The uptake-related ablation strategy as described in the present study shows relatively high failure rates. As we excluded Tg values from analysis in the presence of detectable Tgab and a Tg value below the cut-off level, the given ablation failure rate according to criterion 2 could actually be even higher. Furthermore, as described in our results, low-dose radioiodine diagnostic whole-body scintigraphy may give a false-negative outcome.

Based on these results and on studies in the literature, it is suggested that a lower ablation failure rate could be achieved when higher ^{131}I doses are applied in the ablation of thyroid remnants in differentiated thyroid carcinoma patients. Because our results show high unsuccessful ablation rates in the group of patients with uptake values above 10% (statistically significantly higher compared with the group of patients with uptake values below or equal to 5%), surgical re-exploration for additional thyroid tissue removal may be suggested for this group of patients. However, further studies are required in which higher ablation doses are tested, even in the case of high uptake values.

We found statistically different ablation results between male and female patients and between patients without and with lymph node metastases. In a study by Arslan *et al*. [24], a significantly higher total ^{131}I dose was needed for successful ablation in males and in patients with a higher stage of disease. This is probably related to the fact that the less differentiated the tumor, the lower the uptake function and hence the need for a higher activity for the ablation of possible malignant cells in the remnant. Therefore, in the case of lymph node metastases a further dose adjustment may be advisable.

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