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Recurrence patterns in differentiated thyroid cancer (DTC) following adjuvant radioiodine therapy

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Abstract

Introduction: With an increasing incidence of differentiated thyroid cancer (DTC) diagnosis, questions emerge about the optimal duration of follow-up for detecting recurrent disease and its outcomes. The objective of this retrospective research was to assess the clinical course of differentiated thyroid cancer after radioiodine adjuvant treatment in patients monitored over an extended period. Special attention was paid to the analysis of the time from treatment to recurrence. We also assessed patient outcomes after recurrence.

Material and methods: A total of 650 patients with DTC after total/near-total thyroidectomy and adjuvant radioiodine post-recombinant human thyrotropin (post-rhTSH) stimulation were evaluated. All patients were followed up with neck ultrasound, serum thyroid-stimulating hormone (TSH), thyroglobulin (Tg), and antithyroglobulin antibody (anti-Tg) measurements at intervals of 6 to 18 months. Only structural recurrences were considered. They were defined as locoregional recurrence confirmed by biopsy or distant metastases [confirmed by computed tomography (CT) or magnetic resonance imaging (MRI), or abnormal foci on radioiodine scintigraphy or ^{18}F-gluorodeoxyglucose positron emission tomography [^{18}F] FDG-PET scan], regardless of thyroglobulin (Tg) or anti-Tg levels.

Results: The median follow-up was 12 years (5–15.5). Structural recurrence was observed in 47 out of 650 patients (7%). All but 3 locoregional recurrences were suitable for surgery. The median time to structural recurrence was 16 months, with only 9 (1.4%) patients presenting with recurrence after more than 60 months. At the time of the database closure, 601 patients (92%) had an excellent response, including 20 out of 47 (42%) patients with structural recurrence. Eighty-one out of 650 patients had died (12.5%) before the database closure. The median age at the last follow-up of the patients who died was 72 years (range 20–88). A second recurrence was diagnosed in 10 out of 650 patients (1.5%), corresponding to 21% (10 out of 47) of patients who had already experienced a recurrence. The median time from radioiodine (RAI) therapy to the second structural recurrence was 108 months.

Conclusions: Structural recurrences in DTC are uncommon, with most patients showing a favourable response to treatment. Improved understanding of recurrence timing may define the duration of patient surveillance at reference centres that can be safely discontinued after 5 years in low- and intermediate-risk groups, as indicated in our study. **(Endokrynol Pol 2024; 75 (5): 486–493)**

Key words: *DTC; recurrence; ^{131}I treatment; outcome; thyroid cancer*

Introduction

Over the past few decades, cancer registries worldwide have reported an increasing incidence of differentiated thyroid cancer (DTC) [1–6]. The reasons for such a significant rise remain controversial. Among potential factors, environmental influences [7] and overdiagnosis due to excessive use of neck ultrasound and fine needle aspiration cytology have been suggested [8].

For many years, total thyroidectomy and postoperative administration of iodine-131 (^{131}I) were advocated in all patients with tumours larger than 1.0–1.5 cm [9]. The American Thyroid Association (ATA) guidelines do not recommend routine radioiodine (RAI) therapy for ATA low-risk DTC patients but suggest considering RAI therapy for those at intermediate risk and recommend routine RAI treatment for ATA high-risk DTC patients [10]. Polish recommendations also indicate that in low-risk DTC patients, RAI therapy may be abandoned unless postoperative diagnosis reveals an increased risk of tumour recurrence [11].

While the significant benefits of RAI in high-risk patients are well recognised, debate continues regarding its use in low- and intermediate-risk patients. The European Association of Nuclear Medicine has declined to endorse the 2015 ATA management guidelines, indicating insufficient evidence to abandon postoperative ^{131}I therapy in patients with non-microcarcinomas [12]. In 2022, the authors of the European Thyroid Association Consensus Statement recommend that the decision on whether to perform RAI therapy in low-risk patients should be based on the presence of individual

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risk modifiers. In the intermediate-risk category, RAI therapy may be indicated and should be tailored according to particular cases [13]. Furthermore, the heterogeneity within the intermediate-risk group often necessitates case-by-case determination of the initial treatment [14]. A significant lack of prospective studies evaluating the efficacy of RAI treatment in low- and intermediate-risk patients has been highlighted by several authors [15, 16]. Recently, the ESTIMABL2 trial, a randomised, controlled noninferiority study in France, found no difference in recurrence-free survival between low-risk DTC patients undergoing total thyroidectomy with adjuvant RAI and those undergoing thyroidectomy alone [17]. The IoN trial (phase II/III) is currently ongoing. Both studies include patients with DTC with low and intermediate risk.

The availability of very sensitive diagnostic tools, such as ultrasensitive thyroglobulin (Tg) measurement and advanced neck ultrasonography, plays a crucial role in changing the approach to DTC. These tools are very accurate methods for detecting disease recurrence [18–21] and have become an important tool in posttreatment DTC surveillance [22]. However, the decisions of whether to employ adjuvant radioiodine and the determination of when to cease surveillance of DTC, particularly in patients with intermediate risk, remain unresolved. Due to the lack of prospective trials on adjuvant treatment for DTC, decisions regarding treatment protocols are primarily based on high-quality retrospective studies, particularly with long-term follow-ups and incorporating modern diagnostic techniques in both treatment and follow-up phases.

The objective of this retrospective research was to assess the clinical course of DTC after radioiodine adjuvant treatment in patients monitored over an extended period. Special attention was paid to the analysis of the time from treatment to recurrence. We also assessed patient outcomes after recurrence, which may contribute to a better understanding of DTC dynamics and improve treatment and monitoring strategies.

Material and methods

A total of 650 patients with DTC after total/near total thyroidectomy without persistent structural disease treated for the first time with recombinant human thyrotropin (rhTSH)-aided adjuvant RAI were included in the study. Most patients were female (n = 535; median age 53 years). Most patients underwent total or near-total thyroidectomy (n = 595) with central node dissection (n = 341). Table 1 summarises the patients' characteristics.

The study group was divided into risk groups based on the risk stratification guidelines of the ATA. Because the study was retrospective, the medical records of patients did not always include all the information necessary to precisely divide patients into ATA risk groups. Specifically, information on the diameter of lymph node metastases and angioinvasion was frequently missing and, consequently, was excluded from our analysis. Table 2 shows the criteria used to divide the whole cohort of patients into ATA risk groups and the number of patients in each group.

Table 1. *Patients' characteristics*

Parameter	Patients treated with RAI ablation (n = 650)
Sex: female/male	535 (82.3)/115 (17.3)
Age [yr]: median (minimum–maximum)	53 (13–85)
Total/near total thyroidectomy	595 (91.5)/55 (8.5)
Central lymph node dissection	341 (52.5)
Lateral lymph node dissection	68 (10,5)
TNM classification (7th edition)	
T0	3 (0.5)
T1	362 (55.7)
T2	82 (12.6)
T3	142 (21.8)
• Intrathyroidal tumour > 4 cm in greatest dimension	26 (4)
• Extrathyroidal extension	116 (17.8)
T4	7 (1.1)
TX	54 (8.3)
Lymph node	
N0	241 (37.1)
N1	137 (21.1)
• N1a	74 (11.4)
• N1b	63 (9.7)
• NX	272 (41.8)
Histology	
Papillary	577 (88.8)
Follicular	52 (8)
Poorly differentiated	6 (0.6)
Multifocality	153 (23.5)

RAI — radioiodine; TNM — tumour–node–metastasis

According to the institutional guidelines, all patients were referred to RAI adjuvant treatment except for those with papillary thyroid carcinoma (PTC) pT1aN0M0 during the analysed period. Median RAI activity was 3.7 GBq (range 3.7–5.55 GBq). All treatments were performed under rhTSH stimulation on 2 consecutive days, followed by radioiodine application on day 3. Figure 1 shows a detailed scheme of diagnostic procedures during radioiodine treatment.

After radioiodine treatment, all patients were followed up with neck ultrasound and the assessment of serum thyroid-stimulating hormone (TSH), Tg, and antithyroglobulin antibodies (anti-Tg) at intervals of 6 to 18 months. Stimulated Tg measurements and ^{131}I whole-body scan were performed 12 to 24 months post-RAI treatment to assess the efficacy of therapy. For the purpose of this study, only structural recurrences were considered. They were defined as locoregional recurrences confirmed by biopsy or distant metastases [confirmed by computed tomography (CT) or magnetic resonance imaging (MRI), or clearly abnormal foci on radioiodine scintigraphy or ^{18}F-gluorodeoxyglucose positron emission tomography [^{18}F] FDG-PET scan], regardless of Tg or anti-Tg levels.

Table 2. *Criteria used to divide the whole cohort of patients into American Thyroid Association (ATA) risk groups*

ATA risk group	Criteria	Number of patients
Low	pT1N0/NX; pT2N0NX	339 (52.1%)
Intermediate	pT3 (AJCC 2010); N1a/N1b; aggressive variant of papillary thyroid cancer, follicular thyroid cancer	263 (40.5%)
High	pT4; poorly differentiated thyroid cancer; Tg concentration on suppression ≥ 1 ng/mL and/or stimulated Tg level > 10 ng/mL	21 (3.2%)
Undefined (lack of data)	pTxN0/NX	27 (4.2%)

AJCC — American Joint Committee on Cancer; Tg — thyroglobulin

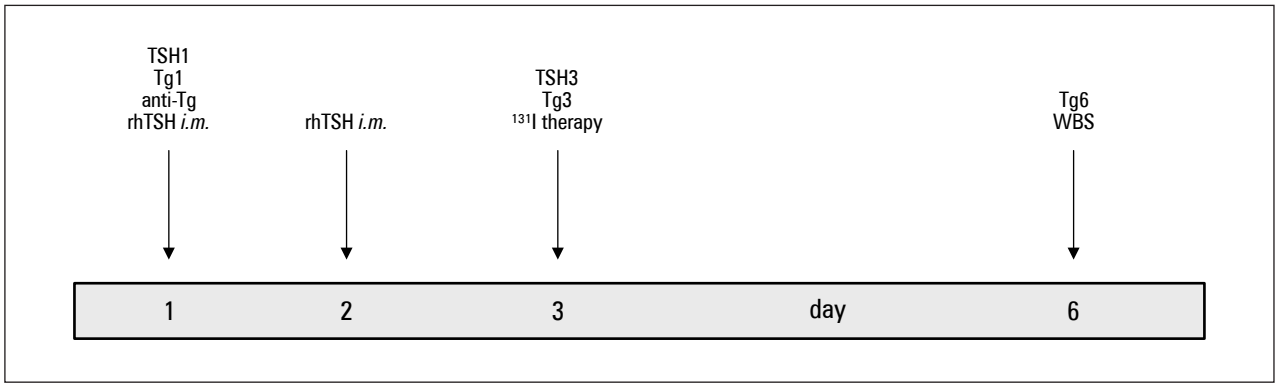

Figure 1. *Scheme of diagnostic procedures during radioiodine treatment. TSH — thyrotropic hormone; Tg — thyroglobulin; anti-Tg — antithyroglobulin antibodies; rhTSH — recombinant human thyroid-stimulating hormone; WBS — whole body scintigraphy; i.m. — intramuscular*

Statistical analysis

The retrospective analysis was concluded based on the data with the last update (December 1, 2023). Quantitative data are expressed as the median (minimum-maximum). Differences between the groups were assessed using a two-tailed unpaired t-test, with Fisher's correction applied if the number of cases was below 10.

Results

The median follow-up for the study group was 12 years (range 5–15.5). Structural recurrence was observed in 47 out of 650 patients (7%). The median size of local recurrence was 13 mm (2–35 mm). All but 3 locoregional recurrences were suitable for surgery. Palliative radiotherapy was performed in the other 3 cases. The median time to structural recurrence was 16 months, with only 9 (1.4%) patients presenting with recurrence after more than 60 months. At the time of the database closure, 81 out of 650 patients had died (12.5%). The median age at the last follow-up of the patients who died was 72 years (range 20–88).

A second recurrence was diagnosed in 10 out of 650 patients (1.5%), which corresponds to 21% (10 out of 47) of patients who had already experienced a recurrence. The median time from RAI therapy to the second structural recurrence was 108 months. Five relapses were found in the neck, 4 were distant, and one patient was diagnosed with both local recurrence and distant metastases. The results are given in Table 3.

Low-risk patients

The group of low-risk patients consisted of 339 out of 650 patients (52%). Structural recurrence was diagnosed in 8/339 patients (2.4%). All recurrences were local (3 occurred in the thyroid bed and 5 in the cervical lymph nodes). One patient was diagnosed with local recurrence and lung metastases (second recurrence) 117 months after the diagnosis of the first recurrence. Surgery was performed in all patients.

The median time from adjuvant RAI therapy to diagnosis of the first recurrence was 56 months (range: 11–154). Three patients presented with a recurrence after more than 60 months (Tab. 4). The percentage of recurrences diagnosed in specific time intervals after RAI treatment is presented in Table 4. At the last follow-up, 4 out of 8 patients (50%) had an excellent response, 3 out of 8 (37.5%) had a biochemical incomplete response, and 1 out of 8 (12.5%) had a structural incomplete response. Two out of 8 patients (25%) died; they had an incomplete biochemical response at the last follow-up and were 80 and 66 years of age at the time of their last follow-up. The median age among the survivors was 66 years (range 38–86).

Table 3. *The characteristics of second recurrences*

ATA risk group	Time interval after RAI therapy [years]			
	< 2	2– ≤ 5	5– ≤ 10	> 10
Low	0	0	0	1 local + lungs
Intermediate	0	1 lungs	1 local	1 local 2 lungs 1 bones
High	1 local	1 local	1 local	0

ATA — American Thyroid Association; RAI — radioiodine

Table 4. *Percentage of recurrences diagnosed in specific time intervals after radioiodine (RAI) treatment in a given American Thyroid Association (ATA) risk group*

Time interval after RAI therapy [yr]	Low-risk patients		Intermediate-risk patients		High-risk patients		Undefined-risk patients		All patients	
	No. at risk	No. of recurrences (n = 8) (%)	No. at risk	No. of recurrences (n = 31) (%)	No. at risk	No. recurrences (n = 6) (%)	No. at risk	No. recurrences (n = 2) (%)	No. at risk	No. recurrences (n = 47) (%)
< 2	339	2/8 (25)	263	19/31 (61)	21	4/6 (67)	27	1/2 (50%)	650	26/47 (55)
2 – ≤ 5	331	3/8 (37,5)	257	6/31 (19)	20	2/6 (33)	26	–	634	11/47 (23)
5 – ≤ 10	309	2/8 (25)	236	6/31 (19)	19	–	24	1/2 (50%)	588	9/47 (19)
> 10	234	1/8 (12.5)	186	–	14	–	17	–	451	1/47 (2)

Among the low-risk patients without recurrence at the last follow-up, 324 out of 331 (97.9%) showed an excellent response, 6 out of 331 (1.8%) had an indeterminate response, and 1 out of 331 (0.3%) had a biochemical incomplete response. Thirty-five out of 331 patients (10%) died, including 32 patients with a complete response. The median age at the last follow-up among the deceased patients was 71 years (range 28–88), while in the surviving group the median age was 63 years (range 21–86).

There was no difference in the number of deaths between the subgroups with or without recurrences (p = 0.2 Fisher exact test). Table 5 shows the response to treatment at the last follow-up and the number of deaths in each ATA risk group.

Intermediate-risk patients

In the study, 263 out of 650 patients (40%) were classified into the intermediate risk-group, and recurrence was diagnosed in 31 patients. Among these recurrences, 25 out of 31 (80%) were local: 17 in cervical lymph nodes, 7 in the thyroid bed, and one involved both the thyroid bed and neck lymph nodes. Four out of 31 patients (13%) developed lung metastases, one patient (3%) presented with bone metastases, and one was diagnosed with a local recurrence and lung metastases. The median time to structural recurrence was 13 months (range: 2–83). Six out of 31 patients (19%) presented with a second structural recurrence: 2 patients (6%) had a second local recurrence, 3 patients (10%) developed lung metastases, and one patient (3%) presented with bone metastases. The median time from the first to the second recurrence was 70 months.

At the last follow-up, 15 out of 31 patients (48%) showed an excellent response, 9 (29%) had a biochemical incomplete response, one patient (3%) had an indeterminate response, and 6 (19%) had a structural incomplete response. A total of 10 out of 31 patients (32%) had died, including 4 with an excellent response at their last follow-up, 2 with a biochemical incomplete response, and 4 with a structural incomplete response (one of whom had a second structural recurrence). Among 6 patients with an incomplete structural response, 3 died due to DTC. The median age at the last follow-up was 78 years (range: 54–84) for the patients who had died and 70 years (range: 39–89) for those who were alive at the time of the database closure.

Among intermediate-risk patients without diagnosed recurrence at the last follow-up, 219 out of 232 (94%) showed an excellent response, 9 (4%) had an indeterminate response, and 4 (1.5%) had a biochemical incomplete response. Twenty-five out of 232 patients

Table 5. *The response to treatment at the last follow-up and the number of deaths in each American Thyroid Association (ATA) risk group*

Response to treatment at last follow-up	Low risk (n = 339)				Intermediate risk (n = 263)				High risk (n = 21)				Undefined (n = 27)			
	With recurrence (n = 8) (%)		Without recurrence (n = 331) (%)		With recurrence (n = 31) (%)		Without recurrence (n = 232) (%)		With recurrence (n = 6) (%)		Without recurrence (n = 15) (%)		With recurrence (n = 2) (%)		Without recurrence (n = 25) (%)	
	Response	Number of deaths	Response	Number of deaths	Response	Number of deaths	Response	Number of deaths	Response	Number of deaths	Response	Number of deaths	Response	Number of deaths	Response	Number of deaths
Excellent	4 (50)	0	324 (97.9)	32/324 (9.9%)	15 (48)	4/15 (26.6%)	219 (94)	23/219 (10.5%)	0	0	13 (87)	0	1 (50)	1	25 (100)	4/25 (16%)
Biochemical incomplete	3 (37.5)	2/3 (66.6%)	1 (0.3)	1/1 (100%)	9 (29)	2/9 (22.2%)	4 (1.5)	1 /4 (25%)	0	0	0	0	0	0	0	0
Structural incomplete	1 (12.5)	0	0	0	6 (19)	4/6 (66.6%)	0	0	5 (83)	3/5 (60%)	0	0	0	0	0	0
Indeterminate	–	0	6 (1.8)	2/6 (33.3%)	1 (3)	0	9 (4)	1/9 (11%)	1 (17)	1/1 (100%)	2 (13)	0	1 (50)	0	0	0

(11%) died, including 23 subjects with a complete response.

The median age at the last follow-up was 73 years (range: 20–85) for the deceased patients and 61 years (range: 24–86) for survivors.

A significant difference was found in the number of deaths between the subgroups with and without recurrence (p = 0.009). However, the deceased patients in the recurrence group were older (74 *vs*. 67 years; p = ns). The results are given in Table 5.

High-risk patients

The high-risk group included 21 out of 650 patients (3%). Structural recurrence was identified in 6 of 21 patients (28%), with 3 recurrences occurring in the thyroid bed, one in cervical lymph nodes, and one in the lung. The median time from RAI therapy to structural recurrence was 9 months. A second structural recurrence was diagnosed in 3 patients: 2 in cervical lymph nodes and one in the thyroid bed (median time from the first to the second recurrence was 20 months).

At the last follow-up, 5 out of 6 patients (83%) showed a persistent disease, and one patient (17%) had an indeterminate response. Four out of 6 patients (67%) died, including the patient with an indeterminate response. One survivor was referred to palliative care.

Out of 21 high-risk patients, 15 (72%) were without structural recurrence, of whom 13 (87%) showed an excellent response, and 2 (13%) had an indeterminate response at the last follow-up. The median age for high-risk patients with structural recurrence was 60 years (range: 51–73), as opposed to 44 years (range: 22–68) for those without structural recurrence. As summarised in Table 5, a significant difference was found in the number of deaths between the subgroups with and without recurrence (p = 0.003, Fisher exact test).

Undefined-risk patients

Due to insufficient data, 27 out of 650 patients (4%) could not be classified into the ATA risk group. Recurrence in neck lymph nodes was diagnosed in one patient 84 months after RAI therapy, and another patient developed lung metastases 15 months post-RAI treatment. The patient with regional recurrence (aged 74 years at the last follow-up) had achieved an excellent response by the time of the final evaluation. However, the subject died of an unknown reason. The patient with lung micrometastases treated with RAI was 39 years old at the final follow-up and exhibited an indeterminate response (elevated Tg levels).

All 25 patients with no structural recurrence showed an excellent response at the last follow-up [4 of them (16%) died due to other reasons].

The median age at the last follow-up for the group of patients who died was 53 years (range: 31–78), as opposed to 63 years (range: 24–85) for survivors. The results are summarised in Tables 4 and 5.

Discussion

Over the past decades, the management of thyroid cancer has undergone a significant transformation. Although the overall prognosis for DTC is excellent, a subset of DTC patients suffers from disease recurrence or may not respond to standard therapies [10, 23]. To enhance treatment efficacy and minimise unnecessary interventions, an initial assessment of the risk of disease-specific mortality and persistent/recurrent disease is essential [24]. This is also crucial for determining the necessity of postoperative RAI therapy [25].

Patients with high-risk DTC constitute 5–10% of all patients [14]. In our study, this group accounted for 3.2% of the cohort. The lower proportion of patients in the high-risk category can be attributed to the inclusion criteria, which required complete remission post-surgery, thereby restricting the cohort to those receiving RAI as an adjuvant treatment. The risk of structural recurrence in these patients is over 20% [10], which is in line with our 28% recurrence rate. As opposed to low- and intermediate-risk groups, the vast majority of recurring patients did not achieve a complete structural response and 67% died. Patients without structural recurrence were younger, almost 90% of them achieved an excellent response to treatment, and no one died. Given the poor prognosis, our findings stress the utility of radioactive iodine in this group of patients and highlight the necessity for intensive follow-up, particularly among older patients, because age is a significant prognostic factor [26, 27].

Conversely, among low-risk and intermediate-risk patients, the risk of structural recurrence is ≤ 5% and 5–20%, respectively [10]. In our group, structural recurrence was diagnosed only in 2% of low-risk and 11% of intermediate-risk patients. These were predominantly locoregional recurrences, and only 6 out of 31 patients in the intermediate-risk group presented with distant metastases. It is noteworthy that 77% (30/39) of recurrences were diagnosed within 5 years after primary treatment, which indicates a very low rate of late recurrence and high economic cost of the diagnosis. Conducting annual follow-up visits from the 5th to the 10th year after the primary treatment would require 6020 visits to diagnose 9 recurrences. Durante et al. found that 75% of recurrences were diagnosed within 5 years of follow-up, including 50% within the first 3 years [28]. Similarly, Seejore et al. found that the vast majority of tumour recurrences (85%) were identifiable within 5 years of diagnostic surgery [29], which is similar to the findings of Polish authors [21].

Retrospective studies have not demonstrated decreased mortality after postoperative administration of ^{131}I and have shown conflicting results on recurrence rates [10, 30–35]. The results of the ESTIMABL2 study showed that a follow-up strategy that did not involve the use of RAI was non-inferior to ablation with RAI regarding the occurrence of functional, structural, and biochemical events at 3 years [17]. Despite the significance of ESTIMABL2 study, some researchers highlighted its limitations [36]. One is the 3-year follow-up, which is probably inadequate for conclusive results. Not many studies show the number of recurrences and time to recurrence as well as the post-recurrence fate of patients. As stated above, in our retrospective study, the recurrence rate was low and the prognosis was good. Death in the low- or intermediate-risk groups typically occurred in patients without structural disease. More importantly, out of 72 deaths during the follow-up, only 12 (16.6%) occurred after recurrence. A lower number of deaths occurred in patients with structural disease at the last follow-up (n = 4). It is also important to underline that surgery of recurrence resulted in complete structural response in most cases. Only 14 patients (0.6% in low- and 4.5% intermediate-risk groups of patients) presented with a second recurrence or had persistent disease.

The indolent nature of DTC and its long-term survival rates have limited the availability of randomised clinical trials assessing the benefit of RAI therapy in improving survival among intermediate-risk patients. Retrospective studies have yielded divergent results [31–34, 37]. There are even fewer data on the effect of RAI therapy on the risk of recurrence. Nixon et al. found no significant benefit of RAI therapy on disease-specific or recurrence-free survival [38]. On the other hand, Tian et al. concluded that postoperative RAI therapy decreased the risk of structural and biochemical recurrence in patients with intermediate-risk DTC with low Tg levels (unstimulated Tg ≤ 1 ng/mL or stimulated Tg ≤ 10 ng/mL) [39]. These results are striking because such low postoperative Tg levels are typically viewed as a favourable prognostic factor for disease-free survival. Tian et al. emphasised the need to conduct prospective randomised studies with a follow-up of sufficient duration to assess the effectiveness of adjuvant iodine treatment in intermediate-risk patients. Van Velsen and Verburg indicated that a decision to abandon adjuvant RAI therapy in patients with low Tg levels should be carefully considered. [40]. These doubts are reflected in the results of our study, which seem to confirm the necessity of RAI adjuvant therapy in view

of a relatively high risk of recurrence in the intermediate-risk group.

The management of DTC is changing and moving toward personalized medicine: from active surveillance to advanced, molecular targeted therapy [41]. This applies particularly to the intermediate-risk DTC group, which is very heterogenous. Theranostic medicine could be a part of this strategy with pre-RAI treatment imaging by low activity of ^{131}I. It has potential benefits to change the disease stage from M0 to M1 status or from N0 to N1. However, it is important to remember the biological, technical, and practical limitations of this approach [42].

The question of how long patients with DTC should be monitored remains open, and current practice guidelines offer no clear recommendations in this respect. Most patients are on lifelong oncologic follow-up, which negatively affects their quality of life and burdens the healthcare system [43]. In their study, Durante et al. reported a recurrence rate of 1.4%. Half of the recurrences were detected within the first 3 years of follow-up, and more than 75% were identified within the first 5 years [28]. These results are consistent with the findings of Polish authors who diagnosed recurrence in the same percentage of patients (1.4%). Most recurrences occurred within the first 5 years of the follow-up [21]. In our study with a median follow-up of 12 years, we diagnosed recurrence in 7% of patients. Regardless of the ATA risk group, most recurrences in our study were diagnosed within 5 years of RAI therapy (62% in low risk, 89% in intermediate risk, 100% in high risk). These results differ from a study of Mazzaferri and Jhiang, who reported a recurrence rate of 30%. 43.3% of the recurrences were identified after more than 5 years of follow-up, while 19% more than 10 years after treatment [9]. These differences may result from various definitions of recurrence and the changing demography of DTC patients. In our study, only 6 recurrences were diagnosed more than 10 years after RAI treatment, of which 5 were second structural recurrences. Two patients were classified as low risk, and 4 as intermediate risk. The above results support the possibility of earlier cessation of patient surveillance in tertiary referral care centres, especially in low-risk patients, as reported in previous studies [43].

This study benefits from a robust sample size of 650 patients, which enhances the statistical validity of the study findings on long-term recurrence patterns in DTC following radioiodine therapy. The median follow-up of 12 years provides substantial insights into the extended clinical outcomes of DTC. However, the retrospective nature of the study may introduce biases linked to historical data collection and lack of information on some prognostic factors such as angioinvasion.

Conclusion

Structural recurrences in DTC after surgery followed by radioiodine therapy are uncommon, with most patients showing a favourable response to the treatment of recurrent disease. Improved understanding of recurrence timing may define the duration of patient surveillance at reference centres, which can be safely discontinued after 5 years in low- and intermediate-risk groups, as indicated in our findings.

Data availability statement

The data presented in this study are available on request from the corresponding author. The data are not publicly available.

Ethics statement

All data were anonymised, and given the retrospective nature of the data, the need for bioethical committee approval was waived.

Author contributions

Conceptualisation: A.L., D.H.-J.; methodology: A.L., A.K. D.H-J; formal analysis: A.L., D.H.-J.; investigation: A.L., A.K. E. P.-C., A.B. A.S. T.O., resources: A.L., A.K., E.P-C., A.B. A.S., T.O., data curation: A.L., A.K., E.P.-C., A.B.; writing — original draft preparation: A.L., writing — review and editing: A.L.D. H.-J., visualisation: A.L., supervision: D.H-J.

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Conflict of interest

A.L. and E.P.-C. declare travel grants from Genzyme. D.H.-J. and A.K. declare travel grants and lecture fees from Genzyme. A.B., A.S., and T.O. declare no conflict of interest.

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