BMC Cancer

RESEARCH

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RAI therapy in low-risk papillary thyroid cancer: recurrence reduction and long-term outcomes in the Turkish population

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Abstract

Purpose Papillary thyroid cancer (PTC) is the most common thyroid malignancy, characterized by its slow progression and favorable prognosis. This study re-evaluates the efficacy of radioactive iodine (RAI) therapy versus no RAI in low-risk PTC patients following total thyroidectomy.

Methods A retrospective analysis was conducted on 588 patients treated between 2010 and 2016 at a major tertiary center in Turkey. Patients were divided into two cohorts: those receiving total thyroidectomy (TT) with high-dose RAI (100 mCi) and those receiving TT alone. A matched cohort of 138 patients per group was analyzed to minimize bias.

Results Follow-up data indicated that at 24 months, the RAI group demonstrated a higher percentage of excellent treatment responses (86%) compared to the non-RAI group (74%). Long-term follow-up showed that 99.3% of the RAI group achieved no evidence of disease (NED), versus 90.6% in the non-RAI group. Recurrence rates were significantly lower in the RAI group (1%) compared to the non-RAI group (5.8% with a > 2.0 ng/ml cut-off for biological events).

Conclusion In summary, the findings from this study underscore the efficacy of RAI therapy in reducing recurrence rates and enhancing long-term disease control in low-risk papillary thyroid cancer patients. While total thyroidectomy alone is effective, the addition of RAI therapy provides a marked improvement in treatment responses and reduces the risk of disease recurrence. This indicates that personalized treatment plans incorporating RAI may offer significant advantages in managing low-risk PTC.

Keywords Papillary thyroid cancer, Radioactive iodine therapy, Total thyroidectomy, Recurrence, Thyroglobulin levels, Low-risk PTC

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Introduction

Papillary thyroid cancer (PTC) accounts for approximately 90% of all cases and stands as the most prevalent form of thyroid malignancy [1]. Recognized for its slow growth and limited spread PTC has an excellent prognosis with a ten-year survival rate exceeding 95% [2]. The standard treatment for PTC is surgery to remove the whole or most of the thyroid gland, total or near total thyroidectomy, (TT, NTT) followed by radioactive Iodine (RAI) therapy to eradicate the remaining residual tissue [3]. However, this strategy has been modified according to the 2015 American Thyroid Association (ATA 2015) guidelines, which introduced categories of Low, Intermediate, and High Risk (Table 1) [4]. Low-risk PTC includes cases with no local or distant metastases, no remaining

Table 1 2015 American Thyroid Association Risk stratification System

Category	Complete Features
ATA low-risk	PTC with all of the following
	No local or DM
	All macroscopic tumor has been resected
	No tumor invasion of loco-regional tissues or structures
	No aggressive cytotype (e.g., tall cell, hobnail variant, columnar cell carcinoma)
	No vascular invasion
	Clinical N0 or ≤ 5 pathologic N1 micro-metastases (< 0.2 cm in largest dimension)
	If RAI given, there are no RAI-avid metastatic foci outside the thyroid bed on the first post treatment WBS
	Intra-thyroidal EFVPTC
	Intra-thyroidal MPTC, unifocal or multifocal, including BRAFV600E mutated (if known)
ATA intermediate-risk	Microscopic ETE
	Aggressive cyto-type (e.g., tall cell, hobnail variant, columnar cell carcinoma)
	PTC with vascular invasion
	Clinical N1 or > 5 pathologic N1 with all involved LN < 3 cm in largest dimension
	Multifocal MPTC with ETE and BRAFV600E mutated (if known)
	RAI-avid metastatic foci in the neck on the first post-treatment WBS
ATA high-risk	Gross ETE
	Incomplete tumor resection
	Distant metastases
	Postoperative serum thyroglobulin suggestive of DM
	Pathologic N1 with any metastatic LN ≥ 3 cm in largest dimension

ATA, American Thyroid Association; PTC, papillary thyroid cancer; DM, distant metastases; RAI, radioactive iodine; WBS, whole body scan; N0, no evidence of regional lymph node metastasis; N1, metastasis to regional node; EFVPTC, encapsulated follicular variant of papillary thyroid cancer; MPTC, papillary microcarcinoma; ETE, extrathyroidal extension; LN, lymph nodes; Gross ETE, macroscopic invasion of tumor into the perithyroidal soft tissues

macroscopic tumor tissue, no invasion into loco-regional tissues or structures, and no aggressive histology [5]. Specifically, this category encompasses tumors with no vascular invasion, clinical N0 or ≤5 N1 metastases smaller than 0.2 cm, intrathyroidal follicular variant PTC, intra-thyroidal papillary microcarcinoma, and unifocal or multifocal tumors with or without the BRAFV600E mutation. When RAI treatment is applied, it is indicated if there are no RAI-avid metastatic foci outside of the thyroid bed on the first post-treatment whole-body RAI scan. The ATA 2015 guidelines do not recommend routine RAI treatment for low-risk PTC patients. This approach has been causing an ongoing debate among the clinicians. In our clinic, some clinicians advocate the idea of postponing or omitting RAI treatment to mitigate its possible side effects [6], while others are reluctant to forgo this treatment, which has been a key approach in thyroid cancer care for over 75 years with minimal morbidity [7].

The outcomes of papillary thyroid cancer (PTC) in the Turkish population show notable differences from those observed in Western countries. Publications have reported that PTC exhibits variations in Middle Eastern populations [8]. Turkey, located in Asia Minor, has historically faced widespread iodine deficiency, leading to the endemic occurrence of multinodular goiter. Secondly, unlike in Western countries, thyroid surgeries in Turkey are predominantly performed by general surgeons rather than endocrine-specific surgeons. Additionally, in patients with low-risk features during pre-operative evaluation, prophylactic lymph node dissection is rarely performed, which further complicates the applicability of international guidelines to the specific conditions of our country. These factors highlight the necessity of region-specific studies to better understand the distinct characteristics and outcomes in the Turkish population.

Therefore, we re-analyzed the data by considering both early and long-term follow-up results in low-risk PTC patients treated and monitored at our institute, one of the largest tertiary centers in Turkey. This retrospective study involves matching two cohorts: those treated with total thyroidectomy (TT) and a high dose of 100 mCi (3.7 GBq) RAI, and those who underwent TT only.

Materials and methods

Study design and patients

Between 2010 and 2016, a total of 588 patients who underwent total or near-total thyroidectomy in multiple centers and were referred to our clinic for RAI treatment evaluation were included in the study. The inclusion criteria were age 18 or older, having undergone total or near-total thyroidectomy, having a diagnosis of papillary or micropapillary thyroid cancer, having pre-treatment blood Tg, anti-Tg, and TSH values available, and a minimum follow-up duration of at least 40

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months. Individuals whose last follow-up time exceeded 12 months were invited for a new check-up, and those with a lapse in follow-up exceeding 3 years were excluded from the study. Exclusion criteria are lobectomy, unclear pathology information due to missing or unavailable institutional revision, lack of subtype information, and lost to follow-up.

All patients' pathology specimens were re-evaluated by endocrine pathologists at our institute. As a result, approximately 10% of the patients were reclassified as intermediate risk. All intermediate and high-risk patients were excluded from the study. All cases underwent a low-iodine diet program for 4 weeks and were off levothyrox-ine. All cases have been evaluated in thyroid tumor board for the decision of necessity of RAI ablation with their basal investigation panel including I-131 radioiodine with 2- and 24-hour uptake values and the neck ultrasound (US) examination as well as serum assays of TSH, Tg and anti-Tg, at least on a four-weeks T4-off (TSH-stimulated) situation after the thyroidectomy operation. The median interval between the surgery and the RAI ablation deci-sion meeting was 60 days. The day of attendance at the RAI treatment planning meeting is considered as 'day zero' of the treatment.

The patients were followed up with 6-month inter-vals during the first two years (According to Dynamic risk stratification method) and afterward, the follow-up period was extended to 1 year interval [9]. At each fol-low-up examination, the patients were assessed with stimulated Tg, Anti-Tg, and TSH as well as the neck US. Treatment response evaluations have been reclassified based on the information obtained from the assess-ments. Table 2 shows the treatment response catego-ries according to the ATA 2015 classification (Excellent, Indeterminate, Biochemically Incomplete, Structur-ally Incomplete). The median follow-up period was 79 months, ranging from 40 to 173. The last control time was required within the last 1 year.

In long-term follow-up, the disease can present in four different states. No evidence of disease (NED). Recur-rence is defined as either a structural event (SE) or a biological event (BE). SE is identified by imaging stud-ies, such as ultrasound, or other imaging modalities, and includes recurrence in the thyroid bed, nearby struc-tures, or lymph node metastases or fine needle aspira-tion (FNA). BE is defined as follows in patients who have undergone RAI treatment: Elevation of suppressed Tg levels > 1 ng/ml, without imaging evidence of recurrence. For patients who have not received RAI treatment: sup-pressed Tg levels > 2 ng/ml.

Statistical analyses

The Statistical Package for the Social Sciences version 25.0 for Windows (IBM Corp., Armonk, NY, USA) and version 4.4.1 of the R statistical application were used for data evaluation and analysis. To examine the normality distribution of the data, we employed the Kolmogorov-Smirnov normality test. Numerical data are presented as mean and standard deviation or as median and range. Categorical data are presented as frequencies (n) and percentages (%). The Chi-square test and the Fisher test were used to compare categorical data. The Receiver

Table 2 Therapy Response According to the ATA 2015 Guideline

2015 ATA Response-to-Therapy classification	Description	
Excellent response	Negative imaging	1–4% recurrence
	Sti-Tg < 1 ng/ml	< 1% DSS
	Sup-Tg < 0 0.2 ng/ml	
Indeterminate response	Non-specific image findings	15–20% will have structural disease in follow-up
	Faint thyroid bed uptake	< 1% DSS
	Sti-Tg < 10 ng/ml	
	Sup-Tg < 1 ng/ml	
	or Anti-Tg antibodies	
	stable/declining	
Biochemical incomplete response	Negative imaging	20% develop structural disease
	Sti-Tg ≥ 10 ng/ml	< 1% DSS
	Sup-Tg ≥ 1 ng/ml	30% spontaneously NED
	Rising anti-Tg antibody levels	%20 achieve NED after additional therapy
Structural incomplete response	Structural or functional evidence of disease	50–85% persistent disease
	-With any Tg level	DSS:
	-With any level of Anti-Tg	11% Loco-regional M.
		50% Distant M.

TSH, Thyroid Stimulating Hormone. Sti-Tg, TSH stimulated Tiroglobulin. Sup-Tg, TSH suppressed Tiroglobulin. Anti-Tg, anti-thyroglobulin. DSS, disease specific death. NED, no evidence of disease. M., metastases

Operating Characteristic (ROC) analysis was used to obtain the area under the curve (AUC) for postoperative serum thyroglobulin (Tg) levels. The difference in median values between groups was assessed by Mann-Whitney U test. The Mahalanobis distance matching (MDM) was utilized for patient matching [10]. Given the need to mitigate bias, reduce the probability of confounding, and exclude extreme cases from the study group due to the abundance of obtained patient data, Mahalanobis distance matching (MDM) was preferred over Propensity Score Matching (PSM). The "E1071" package was employed for these computations [11]. Hazard ratios (HR) and 95% confidence intervals (CI) were reported. For the significance level, p-values less than 0.05 were considered statistically significant.

Results

Patients

The study enrolled 588 patients with low-risk PTC. In our pre-matched cohort, $n=396$ patients received radioactive iodine (RAI) therapy, while $n=196$ patients were followed without RAI treatment. Both groups were followed with mild TSH suppression keeping the serum TSH values between 0.1 and 0.5 IU/ml. Figure 1 displays the patient flow diagram. The non-RAI group consists of patients who are slightly smaller in median tumor size compared to the RAI group and are characterized by factors that are not listed as risk factors (e.g., bilateral, multifocal, Hashimoto thyroiditis, etc.). No parameter in the non-RAI group poses a greater risk compared to the RAI group.

Due to the retrospective nature of the data, it was necessary to adjust certain parameters between the two
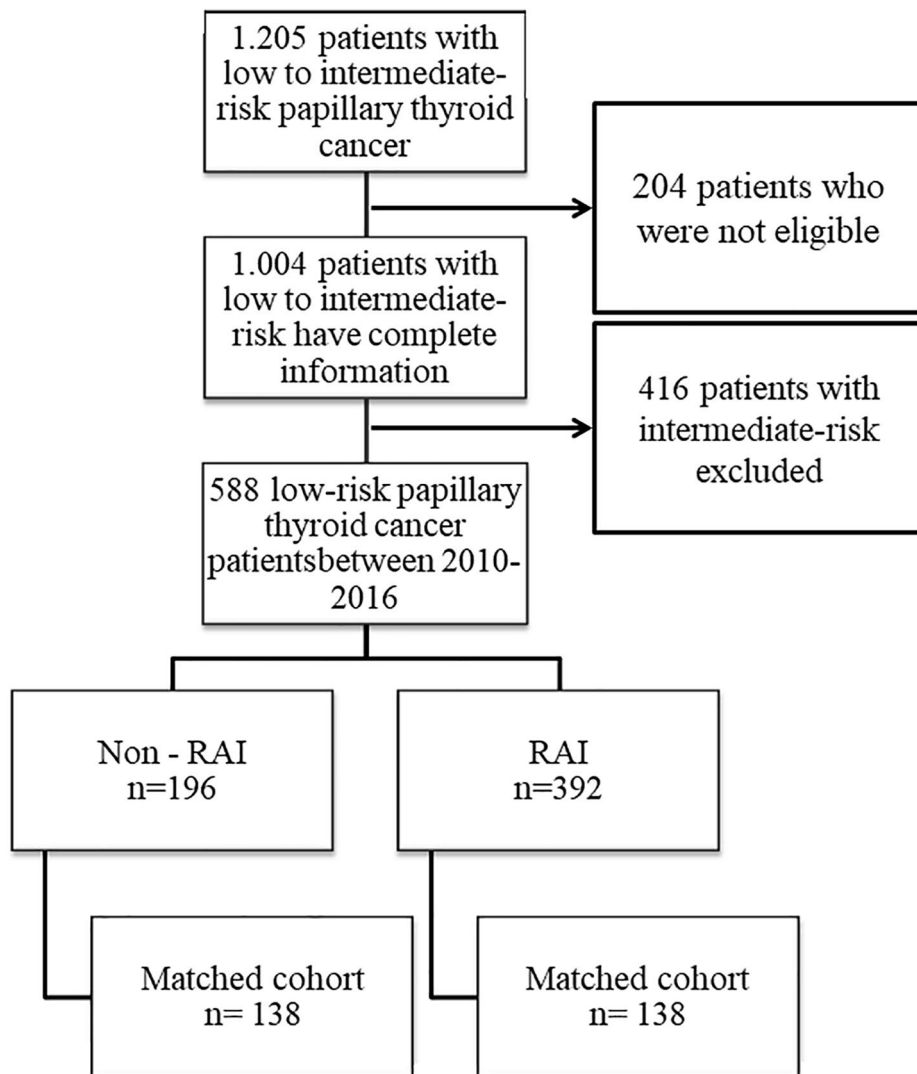

Fig. 1 Flow chart. RAI, Radioiodine treatment; Non – RAI, papillary thyroid cancer patient without RAI treatment

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groups to assess the effectiveness of the treatment. Before matching, 85% of the patients were females. Due to the small number and uneven distribution of patients who underwent near-total thyroidectomy ($n=9$), as well as the limited number of male subjects, both factors were excluded from the matching process. Since almost all tumors larger than 15 mm were treated with RAI, we set the upper limit for tumor size at 15 mm to maintain homogeneity within our study group. Anti-Tg values below 135 IU/ml appear within normal limits. Patients with Anti-Tg values above this threshold were excluded from matching due to the increased difficulty in detecting biochemical recurrence. Postoperative Tg level was matched as a critical blood parameter for the detection of recurrence.

After matching, we obtained $n=138$ patients from both groups. Characteristics of the matched cohorts are provided in Table 3. There was no significant difference between the age at diagnosis and postoperative Tg level. When evaluating the RAI and Non-RAI groups, the median age was 47.0 (20.0–69.0) and 47.0 (20.0–77.0), respectively ($p=0.82$). The mean postoperative Tg level in the RAI group was slightly higher at 5.30 ng/ml (95% CI : 3.95–6.66) compared to 3.96 ng/ml (95% CI: 2.95–4.96) in the Non-RAI group ($p=0.34$). Similarly, the majority of patients did not undergo neck dissection. In the RAI group, central dissection was performed in $n=8$ (6%) patients, with $n=3$ (2%) undergoing both central and lateral dissection. In the Non-RAI group, $n=3$ (2%) patients underwent central dissection, and $n=1$ (1%) patient underwent both central and lateral dissection ($p=0.99$). The median follow-up duration is 78.82 months for the RAI group and 78.62 months for the Non-RAI group, respectively ($p=0.93$).

However, even after matching, the tumor size of patients in the RAI group was significantly larger (8.0 mm vs. 5.9 mm, $p<0.001$). Consequently, histological analysis revealed a significantly higher ratio of papillary tumors in the RAI group compared to micropapillary tumors (36% vs. 14%, $p<0.001$). The RAI group has a significantly higher proportion of bilateral (30% vs. 9%), and multifocal (33% vs. 7%) cases ($p<0.001$). The Hashimoto ratio is slightly higher in the RAI group (33% vs. 30%, $p=0.99$). When analyzed unidirectionally, none of the pathological factors in the Non-RAI group are worse compared to the RAI group.

RAI treatment protocol
Patient selection for RAI was done in a non-randomized manner. The potential impact of RAI on recurrence was explained to the patients, and the decision was made based on patient preference. The treatment doses for patients receiving RAI were planned in accordance with the EANM 2008 guidelines during the treatment period from 2010 to 2016 [12]. Four patients received a 30 mCi (1.1 GBq) RAI dose, and two patients received a 50 mCi (18.5 GBq) RAI dose. 123 patients received a 100 mCi (3.7 GBq) dose, while 9 patients with high remnant tissue (mean postoperative Tg: 9.00 ng/ml) were treated with a 150 mCi (5.5 GBq) dose. None of the patients received a second or subsequent RAI treatment.

Dynamic risk assessment
According to dynamic risk stratification, at follow-up up to 24 months, the excellent response was observed at 86%; indeterminate response occured at 11%; and 3% of patients had an incomplete response in the RAI group. Whereas, in the Non-RAI group patients, the excellent response recorded at 74%; the indeterminate response reached 20%; and the incomplete response was observed in 6% of patients (Fig. 2).

Long-term follow-up
At long-term follow-up, 137 patients (99.3%) in the RAI group achieved NED. Only less than 1% of patients had a SE. No BE were observed in patients from the RAI group.
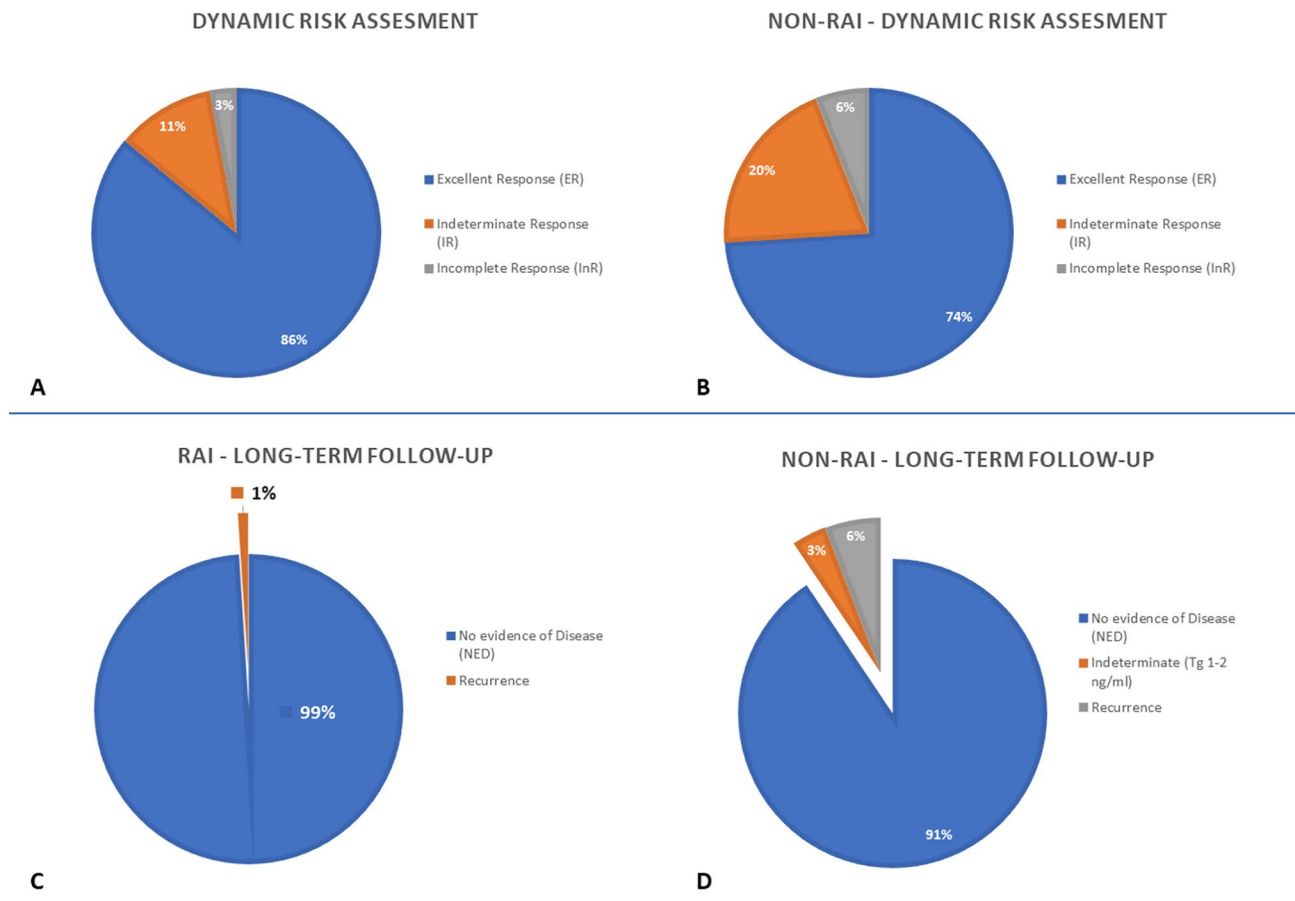
Table 3 Characteristics of Matched Cohorts

Variable	RAI (n = 138)	Non-RAI (n = 138)	P-Value
Age at diagnosis (years)	47 (20–69)	47 (20–77)	0.82
Histology			
Micropapillary	88 (64%)	118 (86%)	0.01[a]
Papillary	50 (36%)	20 (14%)	
Tumor size, largest diameter (mm)	8.0 (1.0–15)	5.9 (1.0–15)	0.01[a]
Bilateral	42 (30%)	12 (9%)	0.01[a]
Multifocal	45 (33%)	9 (7%)	
Hashimoto's	46 (33%)	42 (30%)	0.99
Primary TNM			0.01[a]
pT1aN0	3 (2%)	3 (2%)	
pT1aNx	85 (62%)	126 (88%)	
pT1bN0	8 (6%)	1 (1%)	
pT1bNx	40 (29%)	13 (9%)	
Neck dissection			
None	127 (92%)	134 (97%)	0.99
Central only	8 (6%)	3 (2%)	
Central and lateral	3 (2%)	1 (1%)	
Post operative labs			
Thyroglobulin (ng/ml)	5.30 (3.95–6.66)	3.96 (2.95–4.96)	0.34[b]
Anti-Thyroglobulin (IU/ml)	15.6 (0.10–125)	14.2 (0.00–120)	0.72
TSH (µIU/ml)	100	69	0.82

*Two-tailed analysis. In a one-tailed analysis, any value in the non-RAI group is greater. Tx, total thyroidectomy; TNM, the tumor (T), node (N), and distant metastasis (M); TSH, Thyroid Stimulating Hormone. Results are presented as *n (%)* for categorical data. [b]*Mean* (95% CI) for serum thyroglobulin and *median (range)* for other continuous data

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Fig. 2 Low-Risk Papillary Thyroid Cancer Treatment Responses in RAI and Non-RAI Groups: Dynamic Risk Assessment Results (**A** and **B**), and Long-Term Follow-Up Outcomes (**C** and **D**)

Table 4 Univariate analysis of variables assossiated with low-risk papillary thyroid cancer recurrence

	RAI (n = 138)		Non-RAI (n = 138)	
	HR (%95 CI)	*P*-Value	HR (%95 CI)	P-Value
Age at diagnosis	1.08 (1.06–1.11)	**< 0.001**	0.97 (0.94–1.01)	0.14
Tumor size, largest diameter (mm)	0.90 (0.86–0.94)	**< 0.001**	0.94 (0.79–1.12)	0.48
Post-operative Thyroglobulin (ng/ml)	1.04 (1.02–1.07)	**< 0.001**	1.08 (1.04–1.12)	**< 0.001**

HR: Hazard ratio, %95 CI: Confidence interval, P-Value < 0.05 considered as significant

In the Non-RAI group, NED was observed in 125 patients (90.6%), while structural events were noted in 4 patients (2.9%). BE were observed in 9 patients (6.5%) when applying the classical cut-off value of suppressed thyroglobulin > 1.0 ng/ml. If the cut-off value is increased to > 2.0 ng/ml, the number of BE decreases to 4 patients (2.9%), reducing the recurrence rate to 5.8% (*p* = 0.018). An approximately 7 to 10-fold difference in recurrence rates was observed between the two treatment groups.

Prognostic factors

Table 4 analyzes the prognostic factors of the RAI and Non-RAI groups. Age at diagnosis, the largest diameter of the tumor, and post-operative Tg levels were examined as prognostic factors.

In the RAI group, the age at diagnosis has increased the recurrence risk by 8.3% [HR: 1.083 (1.057–1.110, *p* < 0.001)]; with each 1 mm increase in the largest diameter of the tumor, the recurrence rate decreases by 10.2% [HR: 0.898 (0.859–0.940, *p* < 0.001)]; and each unit increase in post-operative Tg level increases the recurrence risk by 4.1% [HR: 1.041 (1.018–1.065, *p* < 0.001)].

In the Non-RAI group, each unit increase in post-operative Tg level increases the recurrence risk by %7.7 [HR: 1.077 (1.040–1.116) *p* < 0.001]. Age at diagnosis and

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largest tumor size were not significantly different in this group.

The postoperative serum Tg levels demonstrated an AUC of 0.658 (95% CI: 0.478–0.837, $p=0.062$) with a sensitivity and specificity of 62% each at a cut-off of 2.4 ng/ml in the non-RAI group, and an AUC of 0.646 (95% CI: 0.481–0.810, $p=0.066$) with a sensitivity of 64% and specificity of 65% at a cut-off of 3.1 ng/ml in the combined patient group.

Univariate analysis was conducted for prognostic factors, revealing that the factors of multifocality and nodal status did not conform to the analysis model due to a limited number of samples.

Discussion

During the period when treatments were planned, numerous randomized controlled trials (RCTs) with conflicting results regarding the ablation success of 30 mCi (1.1 GBq) and 100 mCi (3.7 GBq) doses were published [13–17]. Despite the ATA 2015 guidelines recommend a 30 mCi (1.1 GBq) dose for remnant ablation, clinicians quickly adopted a strategy of 'saving a chance of definitive treatment for a later occasion' by opting for the full dose of RAI. As a result, the majority of patients received an adjuvant treatment dose of 100 mCi (3.7 GBq).

Our matched patient cohort primarily aims to evaluate the effectiveness of RAI therapy in patients who have undergone total thyroidectomy (TT) in our country. Even though the ATA 2015 guidelines do not recommend routine RAI ablation in low-risk cancer patients, and suggest using low-dose RAI if ablation is performed, certain factors may cause different outcomes in our country [4]. The patient group included in our study comprises individuals from various regions of the country, most of whom underwent TT not performed by endocrine-specific surgeons. Only approximately 6% of the patients in our study underwent central neck dissection, and 2% underwent lateral neck dissection. The mean postoperative Tg levels are 5.30 ng/ml (95% CI: 3.95–6.66) for the RAI group and 3.96 ng/ml (95% CI: 2.95–4.96) for the Non-RAI group, respectively. The recently published prospective phase-3 ESTIMABL2 study reported that 42% of patients underwent lymph node dissection (LND), with up to 25% undergoing lateral neck dissection, which is unusual for low-risk patients. In contrast, the ESTIMABL2 study, while the mean or median postoperative serum Tg levels were not specified, it was reported that out of 555 patients with postoperative serum Tg results, 507 had levels below 1 ng/ml [18]. Previously, the HiLo study, which investigated the difference between low and high RAI doses, included patients who had undergone LND in 75% of cases, with median postoperative serum Tg levels at 2.3 ng/ml [19]. Along with these randomized studies, various studies and meta-analyses have examined the success of RAI therapy based on results from patients who underwent LND in 50% or more of cases [20, 21]. In these studies, the presence of a very small thyroid remnant likely made TT combined with LND sufficient on its own, or a low dose of RAI therapy was adequate. However, this was insufficient for our study group.

Notably, The long-term recurrence rate in our RAI group is around 1%, which is similar to the 2% rate reported in the ESTIMABL1 study. However, the recurrence rate in our Non-RAI group differs from that in the ESTIMABL2 study. In the ESTIMABL2 study, during a 36-month follow-up period, 4.1% of Non-RAI patients experienced recurrence (BE with Tg levels > 2.0 ng/ml). Although the ATA 2015 guidelines have established treatment response categories for patients receiving RAI, there is currently no standardization for the Non-RAI group. In our Non-RAI group, a significant proportion of patients experienced BE, with rates of 5.8% when using a cut-off of Tg > 2.0 ng/ml and 9.4% with a cut-off of Tg > 1.0 ng/ml.

With a median follow-up period of 6.5 years, we observed an increased ablation rate in the RAI group, while a lower proportion of patients in the Non-RAI group achieved NED (99.3% vs. 90.6%, $p<0.002$). Although the ESTIMABL2 study has only published 36-month follow-up data, showing that 95.6% of RAI patients achieved NED, it is likely that long-term outcomes will reach around 98%, as seen in the ESTIMABL1 study. Nevertheless, given that our study cohort had a higher postoperative remnant level compared to the surgical group in these studies, achieving statistical significance in comparisons is unlikely.

Our study, similar to these prospective studies, found that postoperative serum Tg levels are a significant predictor of recurrence in both patient groups ($p<0.001$). In the non-RAI group, the area under the curve (AUC) was 0.658 (95% CI: 0.478–0.837), with a cut-off of 2.4 ng/ml yielding a sensitivity and specificity of 62%. For the overall patient cohort, the AUC was 0.646 (95% CI: 0.481–0.810), with a cut-off of 3.1 ng/ml, resulting in a sensitivity of 64% and specificity of 65%. These AUC values indicates that while Tg levels are a useful marker, their predictive accuracy is moderate, but statistically, they are not significant. This suggests that while Tg levels are a useful marker, their accuracy in predicting recurrence is limited.

Our study aims to guide clinics in the treatment of low-risk thyroid cancer with a focus on achieving a low LND rate and minimizing incisions. The low recurrence rates achieved with standard RAI treatment highlight this situation clearly, showing a recurrence difference of up to 7–10 times. Studies that perform a high frequency of central and even lateral LNDs on low-risk patients are far from guiding daily practice. Many guidelines,

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including those from the American Thyroid Association, do not recommend routine central LND and state that lateral LND should be recommended only with proof of metastatic disease through fine-needle aspiration biopsy. Extensive surgery leads to more significant issues compared to RAI-related salivary gland problems, such as vocal cord paralysis, permanent tracheostomy, permanent hypoparathyroidism, and extensive neck scarring [22–25]. Although the ESTIMABL2 study did not provide data on complications from extensive surgery, it aims to protect against the potential side effects of RAI. However, its results could only be applied to centers with high-volume endocrine spesific surgeons, whereas a wider range of thyroid surgeons, including general surgeons, could benefit from our findings.

Our study has certain limitations, mainly stemming from its retrospective design and the absence of a multicenter approach. The applicability of the findings may not be universally generalizable due to varying genetic and societal background factors, including differences in iodine deficiency status at the time of diagnosis compared to countries like the USA, France, or the United Kingdom, which have adequate iodine levels [26–28]. Additionally, the use of Mahalanobis distance matching in our study introduces specific limitations, notably Dimensionality bias. This bias occurs when the number of variables considered in the matching process is high relative to the sample size, potentially leading to inaccurate or suboptimal matches. As a result, the effectiveness of matching might be compromised, affecting the robustness of our findings.

Conclusions

In summary, the findings from this study underscore the efficacy of RAI therapy in reducing recurrence rates and enhancing long-term disease control in low-risk papillary thyroid cancer patients. While total thyroidectomy alone is effective, the addition of RAI therapy provides a marked improvement in treatment responses and reduces the risk of disease recurrence. This indicates that personalized treatment plans incorporating RAI may offer significant advantages in managing low-risk PTC.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-024-12986-0.

Supplementary Material 1

Declarations

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