Impact of lymphocytic thyroiditis on the outcome of papillary thyroid carcinoma treated with radioactive iodine I-131

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Abstract:

OBJECTIVES: Recently, the incidence of chronic lymphocytic thyroiditis (CLT) in patients with papillary thyroid carcinoma (PTC) has been increased, yet the effect of CLT on the outcome of PTC remains a matter of debate. The aim of this study was to evaluate the impact of CLT on the outcome of radioactive iodine I-131 remnant ablation (RRA) in patients with PTC.

METHODS: Fifty patients with pathologically proven PTC were retrospectively enrolled in the current study. Patients underwent total or subtotal thyroidectomy, followed by radioactive iodine-123 (I-123) whole-body scan (WBS), neck ultrasound (U/S), serum thyroglobulin (Tg) level and serum Tg antibodies (TgAb) assay. Subsequent RRA was done approximately 6 weeks after thyroid hormone withdrawal. A follow-up radioactive iodine 131 (I-131) WBS, neck U/S, serum Tg, and serum TgAb were performed 6 -12 months later following the suspension of levothyroxine for about one month in 39 cases and following recombinant human TSH (rhTSH) stimulation in 11 cases. TSH-stimulated Tg <1 ng/mL, within normal serum TgAb, negative WBS, and normal U/S were considered the criteria for successful ablation. Patients were categorized into two groups according to the presence or absence of CLT in their histopathology.

RESULTS: Twenty (40%) out of the 50 PTC patients had CLT. No significant difference was found between the 2 groups regarding gender, age, histopathology, the extent of surgery, and ablative dose of I-131. 19/20 patients with evidence of CLT and 23/30 patients without evidence of CLT had negative follow-up I-131 WBS. One patient of those with evidence of CLT and 4 of those without evidence of CLT had a negative follow-up I-131 WBS yet had serum Tg > 5 ng/ml with U/S findings suggestive of residual disease in the neck indicating unsuccessful ablation. The overall successful ablation rate was 90% in group1 compared to 63.3% in group 2 (P< .05).

CONCLUSION: PTC patients with histopathologic evidence of CLT had a higher success rate of RRA and a significantly better outcome as compared to those without evidence of CLT.

Keywords: Papillary thyroid carcinoma, lymphocytic thyroiditis, RRA, I-131.

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Introduction:

Thyroid cancer (TC) is the most common endocrine malignancy and accounts for about 3.1% of the global cancer incidence. An estimated 586,202 new cases of TC were diagnosed worldwide during 2020, including 448,915 new cases among women, and 137,287 in men, with differences by geographical area and age. The global age-adjusted incidence rate in women is more than three times higher than in men: 10.1 and 3.1 per 100,000, respectively [1, 2]. Papillary thyroid carcinoma (PTC) accounts for about 85% of TC [3]. Recently the incidence has increased progressively worldwide, mostly secondary to small papillary carcinomas as a consequence of better diagnostic accuracy and over-diagnosis of indolent disease [4]. The only well-established risk factor for TC is exposure to ionizing radiation during childhood, however, there is evidence that other factors, i.e., obesity, smoking, hormonal exposures, and some environmental pollutants, may play a role [5].

The increased incidence of TC is accompanied by a parallel rise in the incidence of autoimmune thyroid diseases (AITD), with chronic lymphocytic thyroiditis (CLT) being the most common AITD [6]. PTC on a background of CLT was first described by Dailey et al. [7] with a recent frequency ranges from 0.5 to 85% [8-11]. CLT is characterized by diffuse infiltration of the thyroid gland with autoreactive T and B lymphocytes, resulting in progressive destruction of the gland parenchyma, late-stage parenchymal atrophy of thyroid tissue, fibrosis, and eventually hypothyroidism. It is considered the most common cause of hypothyroidism in iodine-sufficient countries [7, 12, 13].

The mechanisms explaining the co-occurrence of PTC and CLT remain debatable, although a number of theories have been postulated. One suggestion is that CLT is induced as a response to a pre-existing PTC; the second is that PTC is induced or encouraged by a pre-existing chronic inflammatory process, and lastly, common mechanisms are responsible for both entities [14]. The co-existence of CLT and PTC may also be attributed to prolonged stimulation of the thyroid by high thyroid-stimulating hormone (TSH), which may initiate or promote the growth of thyroid neoplasm [15].

Several previous studies have shown that the coexistence of CLT and PTC is associated with less aggressive tumors, a better prognosis, and a lower recurrence rate [10, 16, and 17]. On the contrary, other studies have reported that the coexistence of CLT and PTC has no effect or even a negative impact on patient outcome [18, 19].

The 2015 guidelines of the American Thyroid Association (ATA) recommended radioactive-iodine remnant ablation (RRA) as adjuvant therapy after total thyroidectomy for certain patients with PTC [20]. However, CLT may reduce the success of attempted RRA as a result of its impact on the ability of thyroid tissues to trap radioactive iodine 131 (I-131) [21]. The aim of the current study was to assess the impact of CLT on the outcome of RRA in patients with PTC.

Patients and Methods:

Study Population

After approval by the local institutional ethics committee, with waiving the requirement for obtaining informed consent for this retrospective study, 50 consecutive patients with PTC, who underwent thyroidectomy, followed by RRA, were retrospectively enrolled in the current study. Patients were categorized into two groups according to the presence or absence of CLT.

Initial treatment was total or subtotal thyroidectomy ± selective neck dissection (SND). Postoperatively, all patients underwent radioactive I-123 whole-body scanning (I-123 WBS), neck ultrasound (U/S), serum thyroglobulin (Tg) and Tg antibodies (TgAb) assay after about 6 weeks of levothyroxine withdrawal to induce a hypothyroid state. The patients were on a low-iodine diet approximately 10–15 days before WBS.

Radioactive iodine whole-body scan and remnant ablation

WBS and static view of the neck were performed before RRA in all subjects to detect any residual thyroid tissues or metastatic lesions. Scans were acquired using a low-energy parallel-hole collimator fitted to the Forte dual-head gamma camera (Phillips Medical Systems) set at 159 keV with a 20% energy window, 24 h post-administration of 37–111 MBq (1–3 mCi) of I-123.

Patients received I-131 doses based on the findings of post-thyroidectomy I-123 WBS, Neck U/S, histologic findings, Tg, and TgAbs levels to ablate the normal thyroid and residual disease and to treat metastatic lesions. Subsequently, they maintained TSH-suppressive doses of levothyroxine. Post-ablation I-131 WBS and static view of the neck were acquired 5-10 days post-RRA using a high-energy parallel-hole collimator fitted to the Forte dual-head gamma camera set at 364 keV with a 20% energy window.

Neck ultrasonography

U/S evaluation of the thyroid bed and both central and lateral neck compartments was performed before administration of the diagnostic dose of radioiodine. Lymph node (LN) was considered suspicious based on the following criteria: Hyperechoic punctuations, cystic appearance, hypervascularization, round shape node without hyperechoic hilum, and a short axis >7 mm [22].

Follow-up and evaluation of successful RRA

Six months after RRA, follow-up including clinical assessment, I-131 WBS, neck U/S, Tg, and TgAb assay were performed following the suspension of levothyroxine for one month (TSH > 30 μIU/ml) in 39 patients and following recombinant human TSH (rhTSH) stimulation in 11 patients. A WBS and static views of the neck were acquired 48 hours post-administration of 92.5–137.64 MBq (2.5–3.72 mCi) of I-131, using the same acquisition parameters used for post-therapy WBS. TSH-stimulated Tg <1 ng/mL, within normal serum TgAb, negative WBS, and normal U/S were considered the criteria for successful ablation. Tg level was deemed to be inaccurate in the presence of TgAb. Serum Tg level of 1 – 2 ng/mL was considered borderline and Tg level > 2 ng/mL was considered positive. The normal value of TgAb was < 4.11 IU/mL.

Statistical analysis:

Data were analyzed using SPSS version 20.0 software (Statistical Package for the Social Sciences, IBM Inc., Armonk, NY). Continuous parametric variables were displayed in the form of mean ± standard deviation (SD). Non-parametric variables were expressed as the median and Interquartile range (IQR). Categorical data were reported as percentages. Independent sample t-test was used to compare between continuous variables. Mann-Whitney-U test was used to compare between non-parametric variables. Categorical variables were analyzed using a Chi-square or Fisher's exact test.

Univariate and multivariate regression analysis was performed to detect the significant independent predictor factors to predict successful ablation among clinicopathological prognostic factors of thyroid cancer. A P < .05 was considered statistically significant.

Results:

A total of 50 consecutive patients (age 39.36 ± 9.17 years, male: female = 20: 30) with PTC were retrospectively enrolled in the current study. All patients underwent total or near-total thyroidectomy ± SND. Of the studied PTC patients, 20/50 (40%) had CLT. 50 % (15/30) of the female patients and 25% (5/20) of the male patients were found to have CLT. Group 1 included (13/20, 65%) PTC Classic variant, (3/20, 15%) PTC follicular variant, (2/20, 10%) PTC with foci of classic and follicular variants, (1/20, 5%) PTC with foci of oncocytic (Hurthle cell) variant, and (1/20, 5%) PTC sclerosing variant. While, group 2 included (22/30, 73.3%) PTC Classic variant, (3/30, 10%) PTC follicular variant, (3/30, 10%) PTC with foci of classic and follicular variants, (1/30, 3.3%) PTC with foci of oncocytic (Hurthle cell) variant, and (1/30, 3.3%) PTC sclerosing variant. Demographic, histopathological findings and TNM staging are summarized in Table 1. There were no significant differences regarding age, gender, the extent of surgery, histopathology, and ablative dose of I-131 between the two groups.

All subjects were in the hypothyroid state with serum TSH level of more than 30 μIU/mL prior to the scintigraphic evaluation and ablation. The TSH levels were 80.04 ± 34.17 μIU/mL in group 1 and 102.35 ± 64.34 μIU/mL in group 2. The pre-ablation median serum Tg level was 1.5 (IQR= 3.5) ng/mL and median serum TgAb level was 7.35 (IQR= 47.15) IU/mL in group 1 compared to 5.2 (IQR= 9.4) ng/mL (P = 0.069), and 4.41 (IQR= 6.02) IU/mL (P = 0.068) in group 2 respectively (Table 2).

Table (1): Comparison of demographic, and histopathology findings among PTC patients studied with and without histopathological evidence of lymphocytic thyroiditis

	Thyroiditis group (n = 20)	***No-thyroiditis group (n = 30)***	***P-value***
Age	38.65 ± 9.74	39.83 ± 8.9	NS
Gender			
Female	15 (75%)	15 (50%)	NS
Male	5 (25%)	15 (50%)	
Histopathology			
PTC Classic variant	13 (65%)	22 (73.3%)	
PTC follicular variant	3 (15%)	3 (10%)	
PTC Classic and follicular variants	2 (10%)	3 (10%)	NS
PTC oncocytic (Hurthle cell) variant	1 (5%)	1 (3.3%)	
PTC sclerosing variant	1 (5%)	1 (3.3%)	
Maximum tumor size	1.55 ± 0.94 cm	2.1 ±1.28 cm	NS
Multiplicity	7/20 (35%)	12/30 (40%)	NS
Bilaterality	6/20 (30%)	10/30 (33.3%)	NS
Capsular invasion	6/20 (30%)	4/30 (13.33%)	NS
Extrathyroidal extension	2/20(10%)	2/30 (6.7%)	NS
Lymphatic invasion	2/20(10%)	1/30 (3.3%)	NS
Lymph node metastasis	7/20 (35%)	8/30 (26.67%)	NS
TNM staging			
T1	17 (85%)	19 (63.33%)	
T2	2 (10%)	9 (30%)	NS
T3	1 (5%)	2 (6.67%)	
N0	13 (65%)	22 (73.3%)	
N1a	4 (20%)	2 (6.67%)	NS
N1b	3 (15%)	6 (20%)	
M0	20 (100%)	30 (100%)	

PTC, Papillary thyroid carcinoma; NS, Non-significant

Table (2): Comparison of laboratory findings and ablative I-131 activity administered between papillary thyroid carcinoma patients with and without evidence of CLT

	Thyroiditis group	***No-thyroiditis group***	***P- value***
Pre-ablative TSH uIU/ml	80.04 ± 34.17	102.35 ± 64.34	NS
Pre-ablation serum Tg (ng/ml) Median (IQR)	1.5 (3.5)	5.2 (9.4)	NS
Pre-ablation serum TgAb (IU/ml) Median (IQR)	7.35 (47.15)	4.41 (6.02)	NS
Therapeutic dose [GBq (mCi)]	4.48 ± 1.124 (121.17 ± 30.38)	4.485 ± 1.163 (121.23 ± 31.43)	NS
Follow-up TSH uIU/ml	101.84±51.33	104.55 ± 59.5	NS
Follow-up serum Tg (ng/ml) Median (IQR)	0.8 (0)	0.8 (3.35)	0.027*
Follow-up serum TgAb (IU/ml) Median (IQR)	3.09 (3)	3.07 (4)	NS

Tg, thyroglobulin; TgAb, Thyroglobulin antibodies; GBq, Gigabecquerel; mCi, Millicurie; *, statistically significant

Neck US showed evidence of small residual thyroid tissues at the thyroid bed in 40% of group 1 patients (unilateral residual in 20% and bilateral residual in 20% of cases) and suspicious cervical LNs in 10% of cases. 60% of group 2 patients had small residual thyroid tissue (unilateral residual in 43.3% and bilateral residual in 16.7% of cases) and suspicious cervical LNs in 23.3% of patients (Table 3). No statistically significant difference was found in the size of the residual thyroid tissues between the two groups (1.47 ± 0.64 cm versus 1.24 ± 0.75 cm).

The overall U/S findings were abnormal in 40% (8/20) of group 1 patients [unilateral residual in 15% (3/20), bilateral residual in 15% (3/20), unilateral residual associated with suspicious ipsilateral cervical LN in 5% (1/20), and bilateral residual associated with suspicious cervical LN in 5% (1/20)] and in 70% (21/30) of group 2 patients [unilateral residual in 33% (10/30), bilateral residual in 13.33% (4/30), unilateral residual associated with suspicious ipsilateral cervical LN in 10% (3/30), and bilateral residual associated with suspicious cervical LN in 3.33% (1/30), and suspicious ipsilateral cervical LN without evidence of residual thyroid tissues at the surgical bed of thyroid gland in 10% (3/30)].

Post-thyroidectomy WBS revealed uptake in the neck, which is considered positive for residual functioning thyroid tissue in all cases without evidence of abnormal uptake at the lateral neck to suggest cervical LN metastasis or at the rest of the whole body to suggest distant metastasis.

Subsequently, 5 patients (2 from group 1 and 3 from group 2) underwent SND based on the presence of suspicious LNs on neck U/S, elevated post-thyroidectomy serum Tg, and positive fine-needle aspiration cytology.

The average I-131 ablation dose was 4.48 ± 1.124 GBq (121.17 ± 30.38 mCi) in group 1 and 4.485 ± 1.163 GBq (121.23 ± 31.43 mCi) in group 2 (P = 0.995). TSH-suppressive doses of levothyroxine followed this.

The average TSH level before the follow-up was (101.84±51.33 μIU/mL) in group 1 and (104.55 ± 59.5 μIU/mL) in group 2.

The follow-up median serum Tg level was 0.8 (IQR= 0) ng/mL and median serum TgAb level was 3.09 (IQR= 3) IU/mL in group 1 compared to 0.8 (IQR= 3.35) ng/mL (P = 0.027), and 3.07 (IQR= 4) IU/mL (P = 0.452) in group 2, respectively (Table 2).

95% (19/20) of group 1 patients and 76.7% (23/30) of group 2 patients had negative follow-up I-131 WBS (Figure 1). However, one patient of group 1, and 4 of group 2 who had a negative follow-up I-131 WBS, had serum Tg > 5 ng/ml, with U/S findings suggestive of residual thyroid tissue in the neck. The overall successful ablation rate was significantly higher among group 1 patients [90% (18/20) versus 63.3% (19/30) of group 2 patients (P< .05)].

Uni- and Multivariate Analyses:

In Univariate analysis of the prognostic clinicopathological factors; female gender (p=.017), and evidence of CLT on histopathology (p= 0.048), were significant predictor factors for successful I-131 ablation. Multivariate regression analysis again revealed that female sex (odds ratio [OR] = 4.304, 95%CI= 1.041 – 17.786 and P= .044), and evidence of CLT on histopathology (OR= 4.009, 95%CI= 0.732 – 21.962 and P= .035), were the significant independent predictor factors for successful I-131 ablation (Table 4).

Table (3): Comparison of Pre-ablation ultrasonographic findings of PTC between papillary thyroid carcinoma patients with and without evidence of CLT

	Thyroiditis group	***No-thyroiditis group***	***P- value***
Evidence of residual thyroid tissues on post-thyroidectomy U/S			
No residual	12 (60%)	12 (40%)	
Unilateral residual	4(20%)	13 (43.3%)	NS
Bilateral residual	4 (20%)	5 (16.67%)	
U/S size of residual thyroid tissues	1.47 ± 0.64	1.24 ± 0.75	NS
Lymph node involvement on post-thyroidectomy neck U/S	2/20 (10%)	7/30 (23.3%)	NS

NS, Non-significant

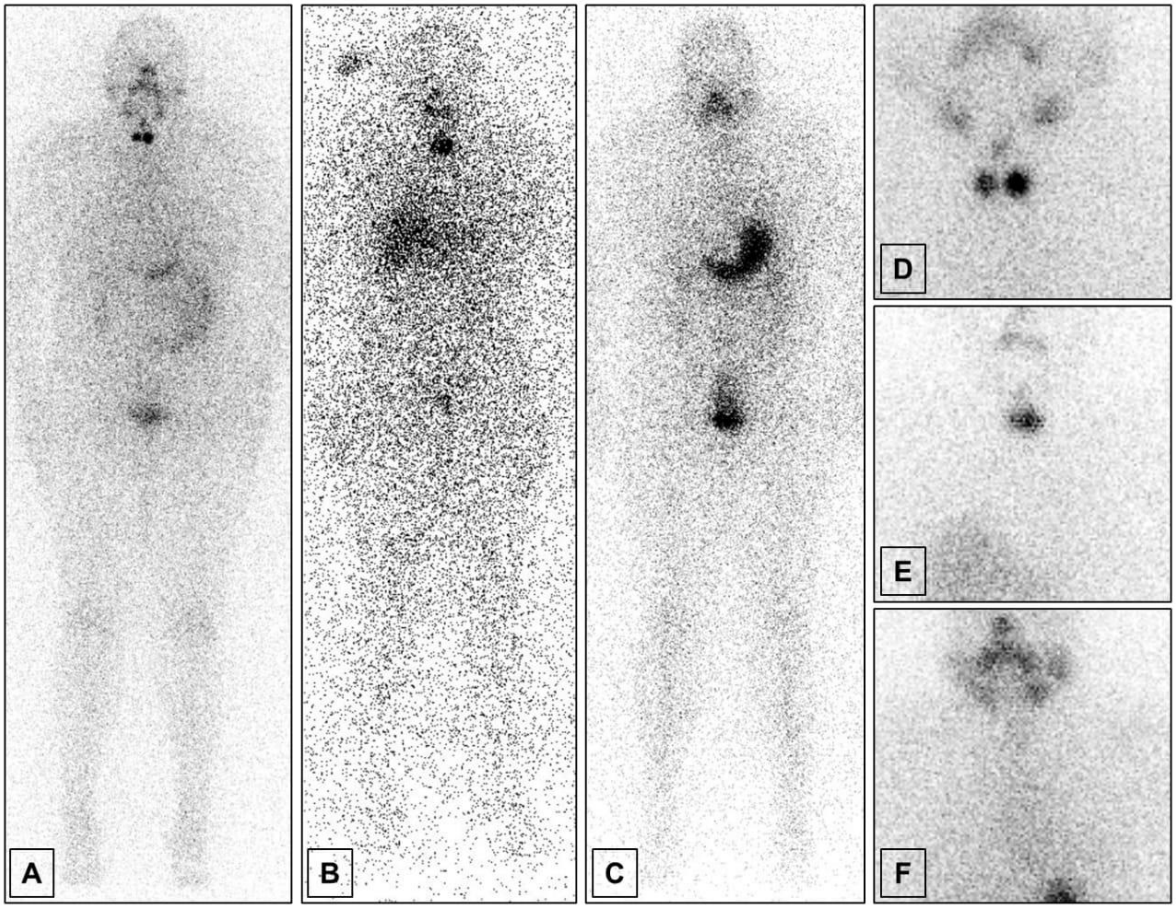

Figure 1. Whole body scans (WBS) of a 40-year-old female with classic papillary thyroid carcinoma, stage (pT3, pN1a), and evidence of Lymphocytic thyroiditis: Anterior WB (A) and anterior static neck images (D) of 1-123 post-thyroidectomy WBS showed abnormal radiotracer uptake at the bed of the thyroid gland. A post-therapy I-131 WBS (B & E) showed good tracer localization in residual thyroid tissue in the neck and no distant metastasis. Follow-up I-131 WBS after 6 months (C & F) showed unremarkable radiotracer localization and serum Tg was less than 0.8 ng/ml, suggest successful ablation

Table.4: Univariate and multivariate regression analyses for successful I-131 ablation prediction

Variable	Univariate analysis			Multivariate analysis		
	OR	95%CI	P	OR	95%CI	P
Age	0.977	0.911 – 1.048	0.517			
Gender	5.318	1.348 – 20.984	0.017*	4.304	1.041 – 17.786	0.044*
Histopathology						
Maximum tumor size	0.616	0.350 – 1.083	0.092			
Thyroiditis on pathology	5.211	1.012 – 26.828	0.048*	4.009	0.732 – 21.962	0.035*
Multiplicity	0.632	0.175 – 2.278	0.483			
Bilaterality	1.080	0.276 – 4.225	0.912			
Extrathyroidal extension	1.059	0.1 – 11.179	0.962			
Lymphatic invasion	0.686	0.057 – 8.257	0.766			
Lymph node metastasis	0.833	0.209 – 3.323	0.796			
U/S size of residual thyroid tissues	0.686	0.294 – 1.602	0.384			
Lymph node involvement on post-thyroidectomy neck U/S	1.12	0.187 – 6.720	0.901			
Post thyroidectomy serum Tg	0.911	0.822 – 1.01	0.077			

*, statistically significant

Discussion:

The prevalence of PTC with CLT in the literature ranges from 0.5- 85 %; we reported a prevalence of 40% in our study that comes in concordant with results reported by Lee et al. [16]. The wide range may be explained by several factors such as heterogeneous patient characteristics, different diagnostic criteria for CLT, and various sample size [9].

Similar to Babli et al. [23], we found that PTC patients with CLT presented at a younger age and more frequent in females. This could be attributed to the higher incidence of CLT in females than in males with a ratio of >10:1 and lower age incidence of CLT [16, 24]. The higher incidence of CLT in female patients than in males, in addition to the results of several studies that proved the male gender as having worse PTC prognosis, support the fact that the coexistence of CLT with PTC has a positive prognostic effect and more favorable outcome of PTC [25-27].

The 2015 ATA Guidelines reported the tumor size among the prognostic factors in DTC and that larger tumor size is associated with poor survival [20]. In line with the results of Zhang et al. [28], we found no significant difference between the two groups regarding tumor size, multifocality, cervical LN metastasis. However, Lee et al. [16] found a statistically significant difference; this discrepancy may be attributed to different sample size and different study populations.

Measurement of Tg and TgAb is an important step to assess the risk stratification [20]. Tg is a glycoprotein that is expressed only in normal thyroid tissues and in differentiated TC (DTC), and its clear organ specificity makes it a promising biomarker for monitoring DTC and detection of residual/recurrence in DTC patients [29, 30]. We found insignificantly lower median baseline Tg values in group 1 patients, which could be due to interference of TgAbs. TgAbs are produced by immune cells, mostly by lymphocytes that react against thyroid auto-antigens and progressively infiltrate the thyroid gland. It is present in about 30% of DTC patients and might interfere with Tg measurement [31]. Similar to Liang et al. [32], we reported a higher level of TgAb in group1 patients.

Although LN metastases are reported to have a substantial impact on local recurrence in patients with DTC [33], the association between nodal metastases and CLT is unclear and only a few studies have addressed this issue. In our cohort cervical nodal metastasis was insignificantly more frequent in group 1 (35% versus 26.67%, p = 0.39). Jeong et al. [34] reported no difference in cervical LN metastasis between the CLT and non-CLT groups. On the contrary, Aydogan et al. [35] reported that LN metastasis was insignificantly more frequent among non-CLT patients compared to the CLT group (35.4% versus 26.5%, p = 0.2). Kim et al. [36] demonstrated that patients with PTC and coexistent CLT had a lower incidence of LN metastasis when adjusted for gender, age, preoperative TSH level, tumor size, and the mean number of dissected LNs. Paulson et al. [37] showed that PTC patients with coexistent CLT had a lower incidence of LN metastasis compared with those without CLT.

ATA guidelines recommended using cervical U/S to evaluate the thyroid bed, central and lateral cervical nodal compartments after surgery and to be performed at 6–12 months and then periodically, depending on the patient's risk for recurrence and Tg level [20]. We found a higher frequency of abnormal ultrasound findings (either residual thyroid tissues or residual thyroid tissues and abnormal LN) among group 2 patients, yet an insignificantly larger size of the residual thyroid tissues was found in group 1 patients. Yoo et al. reported lower diagnostic accuracy of U/S for LN metastasis in CLT patients with PTC than it was in those without CLT. In this study, we found a lower frequency of LN involvement on post-thyroidectomy neck U/S among PTC patients with CLT [38].

In the present study, successful ablation was achieved in 90% of PTC patients with coexisting CLT compared to 63.3% of patients without CLT following initial RRA. On the other hand, previous studies showed a much lower success rate of the initial RRA in patients with PTC and coexisting CLT. Kwon et al. [39] reported that patients with coexisting CLT showed a lower rate of initial low-dose RRA success than patients without CLT (50.7% vs 67.4%, $P < .001$). These conflicting results could be attributed to their use of low-dose (1.1 GBq) I-131 for RRA. Wagieh et al. [40] also reported a lower success rate of about 34.9% in patients with CLT, compared to 80% in patients without CLT treated with high dose (3.7 GBq) I-131. One possible explanation for the lower rate of RRA success in these studies was lower sodium iodide symporter (NIS) expression in PTC with coexisting CLT and consequent decreased RAI-131 uptake into the remnant thyroid tissue [41, 42]. Although it has been reported that DTC patients with CLT were significantly more likely to have low or no radioiodine uptake demonstrated on the post-ablation scan [21], there was no significant difference in radioiodine uptake between the two patient groups in our study. This can be explained based on the use of high ablative doses in our study, as this reduced radioiodine uptake was reported more frequently after low-dose (1.1 GBq) I-131 than high-dose 3 GBq I-131 [21].

Female gender and coexisting CLT were significant independent predictor factors for successful I-131 ablation on univariate and multivariate regression analyses. Kebebew et al. [17] reported that CLT, gender, age, stage of PTC, tumor multicentricity, and tumor size were significant prognostic factors in univariate analysis, while in multivariate analysis, only age and tumor stage of PTC remained significant independent prognostic factors. On the other hand, Kwon et al. [39] reported that multivariate analysis, demonstrated coexisting CLT and elevated serum Tg were negative predictive factors for successful low-dose RRA treatment.

The presence of thyroid autoantibodies in CLT induces an autoimmune response to thyroid-specific antigens that may cause the destruction of thyroid cancer cells. These antibodies have been suggested as one of the mechanisms by which CLT may improve prognosis in DTC and further decrease the chances of metastasis or recurrence [9, 43-45]. Other reports have suggested that PTC, with evidence of thyroiditis exhibit cytotoxic T-cell-mediated reactions [46, 47]. Therefore, CLT may facilitate the destruction of cancer cells and prevent further tumor growth via both humoral and cytotoxic immune responses that may augment the therapeutic effect of I-131.

A unique feature of our study is the use of high-dose RRA in both groups that probably overcome the lower NIS-expression in PTC with coexisting CLT and improved RAI-131 uptake into the remnant thyroid tissues and outcome.

Limitations

A potential limitation of the current study was its retrospective single-centre study design with a limited number of subjects. Further prospective multi-centre studies with a larger sample size may be considered to validate our findings.

Conclusion:

We found a significantly better outcome and a higher success rate of I-131 ablation among PTC patients with histopathologic evidence of CLT compared to those without evidence of CLT.

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