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Factors Affecting Ablation outcome in Low and Intermediate Risk Patients with Differentiated Thyroid Cancer.

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ABSTRACT:

Aim: To evaluate factors affecting ablation outcome in low- and intermediate-risk patients with differentiated thyroid cancer (DTC) as classified by the American Thyroid Association (ATA). **Methods:** Patients with pathologically proven ATA low- or intermediate-risk-DTC were retrospectively recruited. Those with incomplete tumor-resection or distant metastases were excluded. Demographic and clinical data were collected from the patient's medical records. Prior to receiving I-131 ablation-therapy, each patient underwent a post-operative Tc^{99m}-thyroid scan, baseline neck ultrasonography, baseline TG level (BTG), and anti-TG antibodies (TG-Abs). Patients received variable doses of I131 ablation, post-therapy I-131 whole body scan (WBS) was then performed. Six months later, laboratory testing, neck-ultrasound and WBS were conducted to evaluate the ablation outcome. *A* successful ablation outcome is defined as undetectable stimulated thyroglobulin with negative TG-Abs, free neck-ultrasound, and negative I-131-WBS. **Results:** Two hundred and fifty patients, 128 low-and 122 intermediate-risk, were included. The successful ablation rate was 62.5% in low-risk, compared to 59% in intermediate-risk group. Patients with negative ^{99m}Tc-thyroid scans and absent thyroid-capsule infiltration in the low-risk group have significantly higher successful-ablation rates (76.7% vs. 55.3 %, p:0.01and 66.6 vs

62.5 %, p:0.03). In the intermediate-risk group, the successful-ablation rate in cases with low BTG was significantly higher than those with high BTG (67.7 % vs. 50%, P:0.04). Regression analysis revealed that negative thyroid scan and lower BTG are the significant predictor factors in low-risk patients (P: 0.03 and 0.04, respectively), while in intermediate-risk group, BTG was the only significant predictor factor (P: 0.007).

Conclusion: In ATA-low-risk DTC patients, an intact thyroid capsule, and a-negative thyroid scan were linked to a significantly higher successful-ablation outcome. Additionally, a negative thyroid scan and lower BTG were the significant predictor factors for successful-ablation outcome. BTG was the only significant predictive factor in the intermediate-risk group, and it was linked to a-higher successful-ablation rate.

Keywords: DTC, Extra thyroidal extension, Ablation outcome, Basal TG, radioactive iodine dose.

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INTRODUCTION:

Differentiated thyroid carcinoma (DTC) includes papillary thyroid carcinoma which is the most common thyroid neoplasm (80% - 90%) followed by the follicular carcinoma (10% - 40%) [1, 2]. DTC, has a favorable prognosis with a 5- and 10-year survival rates of 97% and 93%, respectively [3]. The primary treatment strategy for thyroid carcinoma is surgery, followed by radioactive iodine therapy (RAIT), which can destroy any remnant thyroid tissue. Additional therapies include chemotherapy, radiation therapy, and targeted therapy. A successful first-time radioactive iodine ablation therapy may result in lower costs and an improvement in quality of life at the same time. However, not all patients benefit from the first RAIT. Proper knowledge about factors associated with successful ablation, each patient can get the best possible care by altering treatment and follow-up schedules for individual patients according to risk factors. Risk-modulated therapy aims to reduce radiation damage while preserving success rates (4).

DTC risk classification utilizing several staging methods based on a combination of the main tumor's size, specific histology, extra thyroidal dissemination, and age at diagnosis. It predicts the likelihood of local recurrence, developing metastases, and mortality in patients with DTC (5). Several studies evaluated the prognostic factors in DTC patients(6, 7), **Amin et al.** concluded that proper ablation dose of RAIT and absence of distant metastasis are the significant predictors for excellent outcome in DTC patients(8). **Husseini** found that stimulated BTG level is clinically essential and had a strong predictive value for successful ablation; consequently, increased pre-ablation TG could potentially be incorporated in the decision making for ^{131}I dosage and for prediction of ablation outcome**(6)**.

This study aimed to investigate different factors impacting the ablation outcome in low- and intermediate-risk DTC patients, according to the American Thyroid Association 2015 (ATA)(9).

PATIENTS and METHODS:

After the Institutional Review Board approved this retrospective study (IRB.no: 04-2023300264), we reviewed files of thyroid cancer patients presented to the nuclear medicine unit at Assiut University Hospital during the period from January 2015 to December 2021. Two hundred and fifty patients with pathologically verified ATA low- and intermediate-risk DTC were enrolled. The 2015 ATA thyroid cancer recommendation is followed when determining the patient risk, either low or intermediate (9). **Criteria of ATA low risk** (9)***:*** Well differentiated thyroid carcinoma with No local or distant metastases, resection of all macroscopic tumors, no loco-regional tumor invasion, no aggressive histology (columnar cell carcinoma, tall cell, or hobnail variant), no RAI-avid metastatic foci outside the thyroid bed on the first post-therapy I-131 WBS, no vascular invasion, clinical N0 or <5 pathologic N1 micro metastases (<0.2cm in its largest dimension), encapsulated follicular variant of papillary thyroid cancer, intra thyroidal, well differentiated follicular thyroid cancer with capsular invasion and no or minimal vascular invasion (<4foci) and uni focal or multifocal papillary micro carcinoma.

Criteria of ATA intermediate risk:

Microscopic invasion of tumor into the peri-thyroidal soft tissues, radioactive iodine avid metastatic foci in the neck on the first post-therapy WBS, aggressive histology, papillary thyroid carcinoma with vascular invasion, clinical N1or >5 pathologic N1 with all involved LNs <3cm in its largest dimension and multifocal papillary micro carcinoma with ETE.

All patients who underwent a total or nearly total thyroidectomy, along with or without regional lymph node dissection, were included in this study. Patients with incomplete tumor resection, distant metastases or incomplete data in the medical records were excluded. All data about age, gender, family history of thyroid cancer , thyroid stimulating hormone (TSH) level, baseline serum TG level (BTG), thyroglobulin antibodies (TG-Abs), neck ultrasound (N-US), lympho- vascular invasion (LVI), focality of the tumor (uni focal or multifocal), type of surgery, Tc-99m thyroid scan and uptake value, dose of RAIT, and the time between diagnosis and I131 ablation therapy, diagnostic I-131 whole body scan (Dx WBS) and post-therapy whole body scan as well as results of follow up laboratory and radiological data were collected. Furthermore, the Tumor node and Metastasis (TNM) staging system was recorded for each individual patient. Patients were categorized into two subgroups according to their BTG level, group I had BTG <5 ng/ml, and Group II had BTG >5. Also, as regards RAIT dose, patients were grouped into those who received a low dose of 30 mCi of I131 or those who received a high dose of I131 (80 mCi or more). All collected data were tabulated and statistically analyzed.

Follow-up and assessment of the ablation outcome.

Patients' follow-up was obtained six months after therapy based on physical examination as well as laboratory and radiological evaluation, including serum levels of TSH, stimulated serum TG, TG-Abs, N-US, and diagnostic I131 WBS, to evaluate the ablation outcome. According to the 2015 ATA guidelines [9], ablation outcome was divided into two categories.

1- Successful ablation: Is defined as undetectable stimulated serum TG (< 1 ng/mL), negative TG-Abs, free N-US (neither detectable pathological cervical LNs nor thyroid tissue), absence of RAI-131 uptake at the thyroid bed region or elsewhere in the scanned body at Dx WBS.

2- Unsuccessful ablation:

. Indeterminate response: defined as a non-specific imaging result, faint thyroid bed uptake at the diagnostic I-131 scan, detectable stimulated TG, but < 10 ng/mL, detectable non-stimulated TG, but >1 ng/mL, and TG-Abs are either constant or decreasing without evidence of structural disease. Biochemical incomplete response: negative imaging results with stimulated TG > 10 ng/mL or non-stimulated TG > 1 ng/mL or rising serum TG-Abs. Structural incomplete response: persistent or newly identified structural disease in the thyroid bed in diagnostic I131 WBS, N-US or in cross-sectional imaging modalities with or without elevated TG.

Statistical tests:

The data analysis software utilized was SPSS 26.0. Frequencies and percentages were used to express qualitative data, while mean ± SD was used to summarize quantitative data. The Chi-square test was employed to compare qualitative variables. To compare medians, we utilized the Mann-Whitney-U test. The study employed univariate and multivariate regression analyses to identify the significant predictor factors associated with a successful outcome. Receiver operating characteristic (ROC) analysis with areas under the curve (AUCs) was conducted to determine the best BTG and thyroid uptake cutoff values concerning the outcome. When the P-value was less than 0.05, it was deemed significant.

RESULTS:

We recruited 250 patients (43 males and 207 females) aged 14 to 70 years, with a mean age of 38.9 ± 11.6 years, out of them 178 patients aged ≤ 45 years. Only eight patients possessed a positive family history of thyroid cancer.

One hundred thirty-five patients underwent total or near total thyroidectomy without lymph node dissection, and the remaining 115 patients underwent thyroidectomy with lymph node dissection (67/115 patients had positive nodal metastasis). Regarding histopathological types, papillary carcinoma accounted for 94.8% of cases, while follicular carcinoma comprised the remaining 5.2%. One hundred twenty-eight patients have low risk compared to 122 with intermediate risk (**Table 1 and 2**). A successful ablation rate was 62.5 % in the low-risk group compared to 59 % for the intermediate-risk group (P:0.5). 48/128 patients with low-risk had unsuccessful ablation (22 cases had an incomplete response regarding structure, 8 had an incomplete response regarding biochemistry, and the remaining 18 cases had an indeterminate response) compared to 50/122 of those with intermediate-risk (12 had an incomplete response regarding structure, 14 had an incomplete response regarding biochemistry, and the remaining 24 cases had an indeterminate response) (**Table 3**). **Figures 1 and 2** represent successful and unsuccessful ablation outcomes, respectively.

Table 1: **clinical and laboratory characteristics in patients with differentiated thyroid cancer in respect to their response to RAIT.**

	Low Risk			**Intermediate Risk**		
	Successful	Unsuccessful	P	Successful	Unsuccessful	P
Age: • ≤45 • >45	55 (64 %) 25(59.5%)	31 (36%) 17 (40.5%)	0.6	53 (57.6%) 19 (63.3%)	39 (42.4%) 11 (36.7%)	0.5
Sex: • Male • Female	9 (64.3%) 71(62.3%)	5 (35.7%) 43 (37.7%)	0.8	14 (48.3%) 58 (62.4%)	15 (51.7%) 35 (37.6%)	0.1
Family history • Positive • Negative	2 (66.7%) 78(62.4%)	1 (33.3%) 47 (37.6 %)	0.8	1 (20%) 71 (60.7%)	4 (80 %) 46 (39.3%)	0.07
Thyroid scan: • **Negative** • **Positive**	33(76.7%) 47(55.3%)	10 (23.3%) 38 (44.7%)	***0.01***	37 (63.8%) 35 (54.7%)	21 (36.2%) 29 (45.3%)	0.3
BTG group: • **<5 ng/ml** • **>5 ng/ml**	38(64.4%) 42(60.8%)	21 (35.6%) 27 (39.2%)	0.6	42 (67.7%) 30 (50 %)	20 (32.3%) 30 (50 %)	**0.04**
Anti TG: • **Negative** • **Positive** • **Border line**	58(%59.8) 19(70.4%) 3 (75%)	39 (40.2%) 8 (29.6%) 1 (25%)	0.5	51 (60.7%) 19 (57.6%) 2 (40%)	33 (39.3 %) 14 (42.4 %) 3 (60 %)	0.6
Baseline neck US: • Free • Residual ± LNs	38(61.3%) 42(63.6%)	24 (38.7%) 24 (36.7%)	0.7	33 (63.5 %) 39 (55.7 %)	19 (36.5%) 31 (44.3%)	0.3

Table 2: Pathological characteristics and RAIT in patients with differentiated thyroid cancer in respect to their response to RAIT.

	Low Risk			Intermediate Risk		
	Successful	Unsuccessful	P	Successful	Unsuccessful	P
Surgery:						
• Total thyroidectomy	56(60.9%)	36 (39.1%)	0.5	26(60.5%)	17 (39.5%)	0.8
• Total thyroidectomy +LN dissection	24(66.7%)	12 (33.3%)		46(58.2%)	33 (41.8%)	
Pathology:						
• Papillary	75 (62%)	46 (38%)	0.6	68(58.6%)	48 (41.4%)	0.6
• Follicular	5 (71.4%)	2 (28.6%)		4 (66.7%)	2 (33.3%)	
N-stage:						
• **Nx**	56(60.9%)	36 (39.1%)	0.7	26(60.5%)	17 (39.5%)	0.9
• **N0**	23(67.6%)	11 (32.4%)		8 (57.1%)	6 (42.9%)	
• **N1**	1 (50%)	1 (50 %)		38(58.5%)	27 (41.5%)	
Thyroid capsule infiltration:						
• **Not reported**	2 (22.2%)	7 (77.8%)	***0.03****	*9* (69.2%)	*4* (30.8%)	0.7
• **Present**	15(62.5%)	9 (37.5%)		*32*(58.2%)	23 (41.8%)	
• **Absent**	63(66.3%)	32 (33.7%)		*31*(57.4%)	*23* (42.6%)	
Focality:						
• Uni focal	59(65.6%)	31 (34.4%)	0.2	27(61.4%)	17 (38.6%)	
• Multifocal	20(58.8%)	14 (41.2%)		40 (58%)	29 (42%)	0.9
• Not reported	1 (25%)	3 (75%)		5 (55.6%)	4 (44.4%)	
Lympho vascular invasion:						
• **Absent**	80(62.5%)	48 (37.5 %)	--	46(63.9%)	26 (36.1%)	0.1
• **Present**	--			26 (52 %)	24 (48 %)	
interval from surgery to initial RAI dose:						
• **<3 month**	67(60.9%)	43 (39.1%)	0.3	56(55.4%)	45 (44.6%)	0.07
• **>3 month**	13(72.2%)	5 (27.8%)		16(76.2%)	5 (23.8%)	
Dose of I-131:						
• **Low**	40(66.7%)	20 (33.3%)	0.3	14 (56%)	11 (44%)	0.7
• **High**	40(58.8%)	28 (41.2%)		58(59.8%)	39 (40.2%)	

Table 3: The overall ablation outcome rates.

Final outcome		**Total sample**	**Low risk**	**Intermediate risk**
		No. (10)=250	**No. 128**	**No. 122**
Successful	Excellent response	152 (60.8 %)	80 (62.5%)	72 (59%)
Unsuccessful	Biochemical incomplete response	22 (8.8 %)	8 (6.3 %)	14 (11.5%)
	Structural incomplete response	34 (13.6)	22 (17.2 %)	12 (9.8%)
	Indeterminate response	42 (16.8 %)	18 (14.1 %)	24 (19.7%)

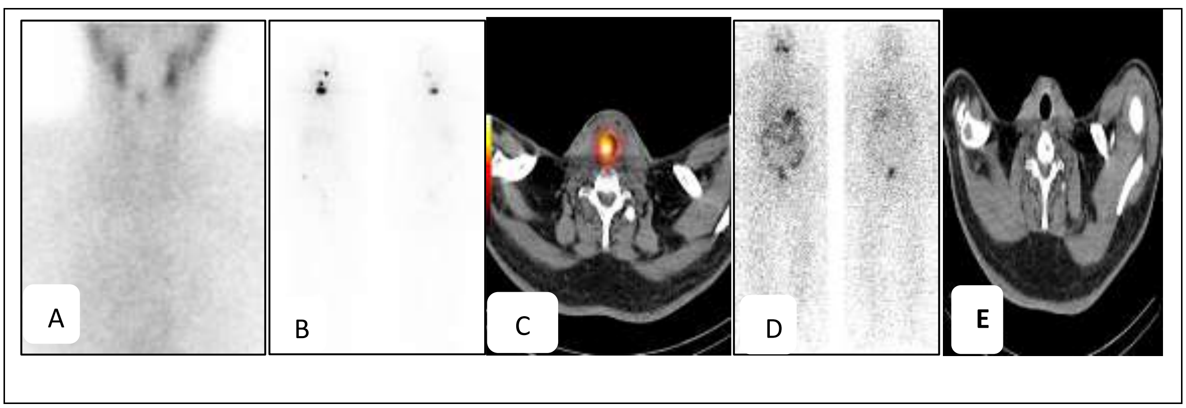

Figure (1): A 48-yrs-old female patient with ATA intermediate-risk papillary thyroid cancer underwent total thyroidectomy. Basal TSH=75.32 uIU/ml, BTG= 38.3ng/ml, TG-Abs was positive, and free N-US. (A): Tc99m-thyroid scan shows no residual functioning thyroid tissue, (B): post-therapy WBS, and (C) SPECT/CT images after receiving a RAI dose of 120 mCi, revealed residual active thyroid tissue at the right thyroid bed region. Six months later, TSH=59 uIU/ml, TG=0.04 ng/ml, TG- Ab was negative, and N-US was free, (D) Diagnostic I131 WBS and (E) the corresponding SPECT/CT images show no evidence of functioning iodine avid residual thyroid tissue denoting successful ablation.

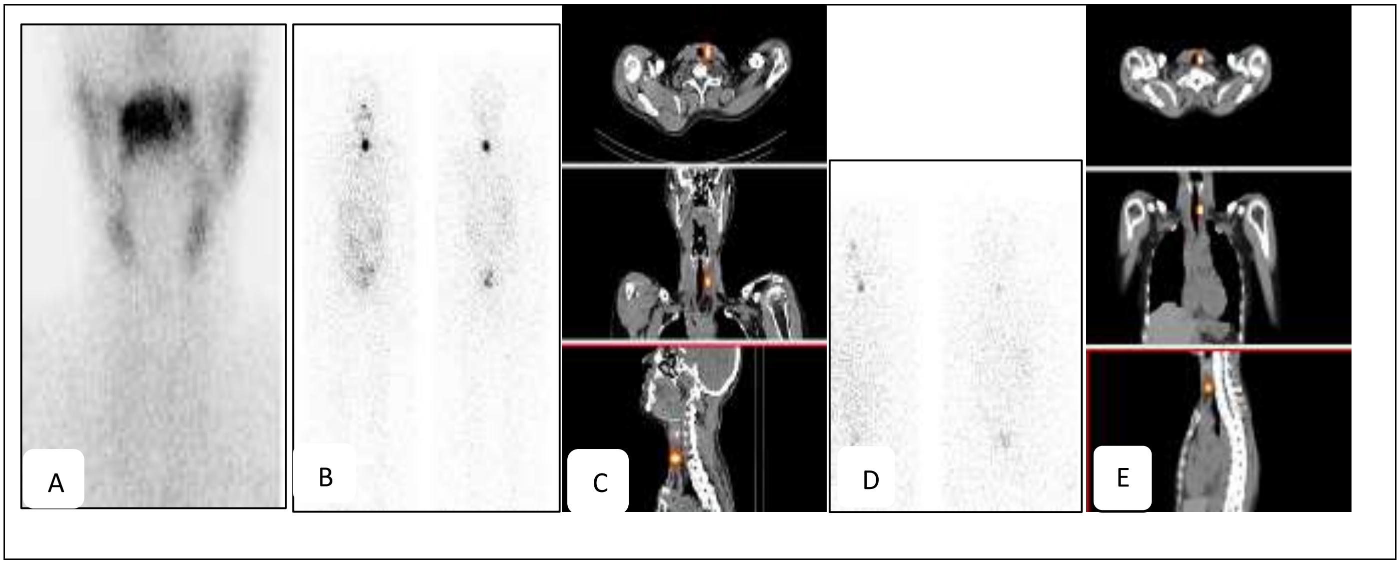

Figure (2) A 56-yrs-old female patient with ATA-low risk papillary thyroid carcinoma, basal investigation after surgery was TSH >150, TG= 0.25 ng/ml, Anti-TG Abs =787.87 (positive), and N-US was free. (A) Tc-99m thyroid scan showing no residual functioning thyroid tissue. (B) Post-therapy I WBS after receiving 30 mCi of RAI shows residual thyroid tissue (C) SPECT/CT images of the post-therapy I 131WBS show that uptake corresponded to residual thyroid tissue at the left thyroid bed, follow-up after sixth month, TSH was 150, TG 0.04, TG-Abs 573 and N-US was free, image (D)Diagnostic I131 WBS revealed focal active tracer uptake at the neck corresponding to residual active thyroid tissue at the SPECT/CT images (E) denoting **unsuccessful ablation.**

Based on ATA risk stratifications, gender, type of surgery, LN stage, lympho-vascular invasion(LVI), capsule infiltration, focality, thyroid scan, and the first ablation dose of RAIT were significantly different between the two risk groups (p:0.007, <0.01, <0.01, <0.01, <0.01, <0.01, 0.02, and <0.01, respectively) (**Table 4 and 5).** However, the age group, family history, pathologic variant, N-US, BTG, TG-Abs, and the interval between surgery and RAIT dose were insignificantly different between the two risk groups (p:0.1, 0.4, 0.7, 0.3, 0.6, 0.4, and 0.4, respectively). Additionally, the median value of TSH, BTG, and thyroid uptake showed insignificant differences between the two risk groups **(Table 6).**

Table 4: clinical and laboratory characteristics in patients with differentiated thyroid cancer according to ATA risk.

	Low risk	Intermediate risk	P
Age			
• ≤45	86	92	0.1
• >45	42	30	
Sex:			
• Male	14	29	**0.007***
• Female	114	93	
Family history			
• Positive	3	5	0.4
• Negative	125	117	
Thyroid scan:			
• **Negative**	43	58	**0.02***
• **Positive**	85	64	
BTG group:			
• **<5 ng/ml**	59	62	
• **>5 ng/ml**	69	60	0.6
Anti Tg:			
• **Negative**	97	84	
• **Positive**	27	33	0.4
• **Border line**	4	5	
Baseline neck US:			
• Free			
• Residual ± LNs	62	52	0.3
	66	70	

Table 5: Pathological characteristics and RAIT in patients with differentiated thyroid cancer according to ATA risk.

	Low risk	Intermediate risk	P value
Surgery:			
• Total thyroidectomy	92	43	**< 0.01***
• Total thyroidectomy +LN dissection	36	79	
Pathology:			
• Papillary	121	116	0.7
• Follicular	7	6	
N-stage:			
• **Nx**	92	43	**< 0.01***
• **N0**	34	14	
• **N1**	2	65	
Thyroid capsule infiltration:			
• **Not reported**	9	13	**< 0.01***
• **Present**	24	55	
• **Absent**	95	***54***	
Focality:			
• Uni focal	90	44	**< 0.01***
• Multifocal	34	69	
• Not reported	4	9	
Lympho vascular invasion:			
• **Absent**	128	72	**< 0.01***
• **Present**	0	50	
Time interval from surgery to the initial RAI dose:			
• **<3 month**	110	101	0.4
• **>3 month**	18	21	
Dose of I-131:			
• **Low**	60	25	**< 0.01***
• **High**	68	97	

Table 6: Descriptive analysis of postoperative baseline TSH, TG, Tc-99m uptake, and RAI dose:

	Total study population		Low risk	Intermediate risk	P-value
	Mean ± SD	Range	Mean ± SD	Mean ± SD	
TSH	82± 40.1	(3-253)	79.8 ± 41.2	86.2 ±38.8	0.1
Baseline TG	17.1 ± 33.35	(0.02-238.30)	14.3 ±25.8	20.1 ± 39.7	0.8
Thyroid uptake	0.31± 0.52	(0-3.4)	0.3 ±0.5	0.3 ±0.5	0.06
First RAI dose	87.9± 51.1	(30-175)	72.0 ± 48.3	104.6 ± 48.8	**< 0.01***

According to age, patients under 45 had a successful ablation rate of 64 % in the low-risk patients compared to 57.6 % in the intermediate-risk group. For those over 45, the successful ablation rates were 59.5 % and 63.3 % for the low and intermediate groups, respectively (P:0.6 and 0.5). The female gender represents 114/128 and 93/122 of low- and intermediate-risk patients, respectively, yet the ablation outcome was insignificantly different between gender types (P: 0.8 and 0.1, respectively).

Three cases with low risk have a positive family history of thyroid cancer compared to 5 cases in the intermediate risk group with insignificant differences in the ablation rate (P:0.8 and 0.07, respectively). 85/128 low-risk patients have positive residual at the thyroid scan with a significantly lower successful ablation rate than those with negative thyroid scans

(55.3 % vs. 76.7 %, P:0.01), this is also applicable to median thyroid uptake (0.1 Vs. 0.2, with p:0.03). On the other hand, no significant difference was observed regarding the intermediate-risk group (p:0.3).

According to BTG subgroups, no significant differences were found in the ablation outcome among low-risk patients (64.4 % vs 60.8 %, P:0.6), while in the intermediate group the ablation outcome in group I was significantly higher than group II (67.7 % vs 50 %, P:0.04). In addition, the median BTG value in low-risk patients with successful ablation outcomes was insignificantly lower than in patients with unsuccessful outcomes (4.8 versus 7.1 ng/ml, respectively, with P: 0.1); the same was true for the intermediate-risk group (3.6 vs. 9.1 ng/ml, respectively with p:0.06). Concerning TG-Abs status, no significant differences were found in the ablation outcome either for low- or intermediate-risk groups (in low-risk patients; successful ablation rates were 59.8 % and 70 % for patients with negative and positive TG-Abs, respectively while in intermediate-risk group the rates were 60.7 % and 57.6 % for patients with negative and positive TG-Abs, respectively (p:0.5 and p:0.6, respectively). Again, we found no significant differences in the ablation outcome for both risk groups between patients with free N-US and those with residual/LN (successful ablation rates were 61.3 % vs 63.6 %, p:0.7 in the low-risk and 63.5 % vs 55.7 % in the intermediate-risk group, p:0.3, respectively).

The type of surgery and the pathologic variant have no significant difference in the ablation outcome either in the low or intermediate-risk groups (p: 0.5 and 0.6 for low-risk, 0.8 and 0.6 for intermediate-risk, respectively). Among the low-risk group, the successful outcome was higher in patients with the N0-stage than those with the N1-stage, yet no statistical significance was found (67.6 % and 50 %, p:0.7). Still, among the intermediate risk group, there was no significant difference (57.1 % and 58.5, with P: 0.9).

In patients with low risk and absent thyroid capsule infiltration, the successful ablation rate was significantly higher than those with positive thyroid capsule infiltration

(66.6 % vs 62.5 %, p:0.03); this is not valid for the intermediate risk group (p:0.7). The uni focal tumor had an insignificantly higher successful ablation rate than the multifocal one regardless of the patient's risk (65.6 % vs. 58.8 %, P:0.2 for low-risk groups, and 61.4 % vs. 58 %, P:0.9 for the intermediate risk).

All low-risk patients have no evidence of LVI, with the successful ablation rate being 62.5 %. In the intermediate-risk patients, the successful ablation rate was insignificantly higher in patients without LVI than those with positive LVI (p:0.1). 110/128 low-risk patients and 101/122 intermediate patients received their first RAIT within three months of thyroidectomy with successful ablation rates of 60.9 % (P:0.3) and 55.4 % (P:0.07), respectively. Comparatively, 68/128 low-risk and 97/122 intermediate-risk patients received a high dose of RAI with a successful outcome rate of 58.8 % and 59.8 %, respectively, with no statistical significance (P:0.3 and 0.7, respectively).

Univariate regression analysis for the low-risk group revealed that absent thyroid capsule infiltration, negative thyroid scan and lower BTG were the significant predictor factors for successful outcome (P: 0.02, 0.02 and 0.04) (**Table 7**), yet in multivariate regression analysis, negative thyroid scan and lower BTG (<5ng/ml) maintained such significance (P: 0.03 and 0.04, respectively). Univariate regression analysis for the intermediate-risk group revealed that BTG was the only significant predictor factor for successful outcome (P:0.02) which maintained significance again in multivariate regression analysis (P: 0.007) (**Table 8)**.

Table 7: **Regression analysis for the low-risk group.**

Variable	Univariate regression			Multivariate regression		
	B	95 %CI	P-value	B	95 %CI	P-value
Age	0.82	0.38-1.76	0.6	0.796	0.32- 1.95	0.6
Sex	0.91	0.28-2.91	0.8	0.843	0.20- 3.46	0.8
Family history	0.83	0.07-9.40	0.8	0.74	0.05-10.64	0.8
Thyroid scan	0.37	0.16-0.85	**0.02***	0.32	0.11-0.90	**0.03***
BTG group	0.30	0.09-0.95	**0.04***	0.28	0.08-0.99	**0.04***
Anti TG	2.0	0.20-20.1	0.5	1.18	0.09-15.41	0.8
Baseline neck US	1.1	0.54-2.26	0.7	1.255	0.52-2.99	0.6
Type of surgery	1.2	0.57-2.88	0.5	0.92	0.34-2.49	0.8
Pathology	1.53	0.28-8.23	0.6	1.10	0.18-6.68	0.9
N-stage	0.59	0.03-9.73	0.7	0.57	0.02-13.04	0.7
Thyroid capsule infiltration	6.8	1.35-35.1	**0.02***	1.310	0.44-3.85	0.6
Focality	4.2	0.40-45.5	0.2	0.57	0.22-1.45	0.2
Time interval from surgery to the initial RAI dose	1.66	0.55-5.01	0.3	3.45	.90-13.18	0.07
Dose of I-131	0.71	0.34-1.47	0.3	0.95	.38-2.35	0.9

Table 8: **Regression analysis for the intermediate-risk group.**

Variable	Univariate regression			Multivariate regression		
	B	95 %CI	P-value	B	95 %CI	P-value
Age	1.2	0.54-2.97	0.5	1.390	0.50- 3.80	0.5
Sex	1.7	0.76-4.11	0.1	1.905	0.66- 5.48	0.2
Family history	6.1	0.66-56.98	0.1	8.56	0.58-125.8	0.1
Thyroid scan	0.68	0.33-1.41	0.3	0.88	0.35-2.23	0.7
BTG group	0.30	0.17-0.88	**0.02***	0.22	0.08-0.99	**0.007***
Anti TG	0.43	0.06-2.72	0.3	1.32	0.14-12.45	0.8
Baseline neck US	0.72	0.34-1.51	0.3	0.75	0.30-1.84	0.5
Type of surgery	0.91	0.42-1.94	0.8	1.03	0.24-4.35	0.9
Pathology	1.4	0.24-8.02	0.6	2.57	0.25 -25.81	0.4
N-stage	0.59	0.46-1.96	0.8	0.81	0.20-3.28	0.7
Thyroid capsule infiltration	0.59	0.16-2.18	0.4	1.23	0.48-3.15	0.6
Focality	1.1	0.272-4.47	0.8	1.06	0.04-2.82	0.8
Lympho- vascular invasion	0.61	0.29-1.27	0.1	0.78	0.33-1.87	0.5
Time interval from surgery to the initial RAI dose	2.57	0.87-7.55	0.08	3.44	0.91-12.93	0.06
Dose of I-131	1.16	0.48-2.83	0.7	2.38	0.69-8.15	0.1

In the low-risk group, ROC analysis found nearly equal AUCs for thyroid uptake and BTG (0.607 Vs. 0.575, p: 0.04 and 0.1, respectively) with a BTG cutoff value 0.2 ng/ml, giving 85 % sensitivity and 83 % specificity in predicting the ablation outcome. In contrast, a cutoff value for the thyroid uptake of 0.2% gives a lower sensitivity and specificity than BTG (65 % and 35 %, respectively). In the intermediate-risk group, using the same cut off values, ROC analysis again found nearly equal AUCs for BTG and thyroid uptake (0.590 vs 0.541 with P:0.06 and 0.44, respectively) with BTG giving 86 % sensitivity and 87 % specificity. In contrast, while thyroid uptake gives a lower sensitivity (40 %) and specificity (35 %) than BTG (**Figure 3**).

Figure (3) ROC curve analysis of BTG and % thyroid uptake according to the outcome for both risk groups.

DISCUSSION:

DTC has a good prognosis; however, at the time of diagnosis, it is essential to identify patients who are at a high risk of progressive illness and death from DTC. The best management of DTC, including the extent of thyroid surgery and the rationale for postoperative radioiodine therapy, depends on the identification of prognostic factors. Treatment plans are customized based on each patient's unique clinico pathological characteristics. Using recognized clinico pathological risk factors, such as advanced age at diagnosis, male sex, lymph node metastasis, and distant metastasis (DM), risk stratification is used to customize a therapeutic approach for each patient [11].

We observed an overall rate of successful ablation of 60.8% in the current study (62.5 % in the low-risk group compared to 59 % for the intermediate-risk group, P:0.5), which is slightly different from those reported by **Thientunyakit et al.** (49.69%) [12] and **Jung et al.,** who stated that 74% of ablations were successful overall; the study population's varied demographics might have brought about this discrepancy (they did not include TG-Abs positive patients) **[13]**. Many studies were done in Egypt about the ablation outcome, with ablation outcome figures in Egyptian patients of 58.9% up to 79.2% [8, 14, 15].

Nearly half the cases (42 patients; 18 low and 24 intermediate-risk cases) with unsuccessful ablation outcomes had indeterminate responses, structurally incomplete response was present in 34 cases (22 low and 12 intermediate-risk patients), a biochemically incomplete response was present in 22 (8 low and 14 intermediate-risk patients). Like our findings, **Li, Hui, et al.** discovered a greater prevalence of indeterminate responses (71%) in their work; the frequency variation may be related to the study population's various clinical and pathologic features **[16]**.

Age is one of the most critical and reliable risk factors for the ablation outcome of thyroid cancer[17]. Our study's findings indicate 86 and 92 cases with low and intermediate-risk respectively aged less than 45 and only 72 (42 low and 20 intermediate-risk) patients aged >45. This outcome is consistent with the study that found the diagnosis was made before age 45. Thyroid cancer is typically found in younger age as a risk factor for ablation outcome [18].

Over the past few decades, thyroid cancer has become more common. This rise in thyroid cancer cases is more likely to worry women than men [19]. Thyroid cancer is the only non-reproductive cancer where there is a discernible female preponderance, with a three- to four-fold higher incidence among females, even though males frequently have more aggressive disease [20]. We discovered in our cohort that the incidence was higher in females (81.2% versus 18.8%, respectively) than in males, regardless of the risk group. Given that the male-to-female ratio is 1 to 5, this difference did not significantly affect the disease's ablation outcome (P:0.2). This is consistent with other research that found no relationship between sex and the ablation outcome [21-23].

Several studies reported that patients with negative uptake at the Tc-99m pertechnetate thyroid scan have a higher rate of successful ablation [12, 24-27], this is similar to our results in patients in the low-risk category. Conversely, **Thientunyakit et al.** found no significant association between the percentage of Tc-99m pertechnetate uptake and the final ablation outcome [12]; this may be attributed to different sample sizes and demographics.

Husseini stated that baseline-stimulated TG level is clinically essential and had a strong predictive value for successful ablation; consequently, increased pre-ablation TG could potentially be incorporated in the decision making for ^{131}I dosage or other treatment [6]. **Lan et al.** concluded that a successful ablation rate is negatively correlated with the level of BTG; in line with this, we found that the median BTG value in low- and intermediate-risk patients with successful ablation outcomes was insignificantly lower than in patients with unsuccessful outcomes (4.8 versus 7.1 ng/ml, respectively, with P:0.1 in low-risk and 3.6 vs. 9.1 ng/ml, respectively with p:0.06 in intermediate risk). Additionally, we encountered higher successful ablation rates for groups I compared to group II for both risk groups (64.4 % vs 60.8 %, P:0.6 for low risk patients and 67.7 % vs 50 %, P:0.04 for intermediate risk group)[27].

Based on the study populations and the method of serological assays, up to 10% of the general population and ≥ 20% of patients with DTC have anti-TG in their serum. Several researchers have demonstrated that elevated anti-TG may be a tumor marker for persistent or recurrent DTC [28]; however, Gorges et al. did not support this finding [29]. The current work found no significant differences in the ablation outcome between patients with low or high levels of anti-TG for either low- or intermediate-risk groups (p:0.5 and 0.6, respectively).

Neck ultrasound is an easy, non-invasive, and highly sensitive method for detecting either abnormal cervical lymph nodes or any thyroid remnant post-thyroidectomy for DTC. It gained a particular emphasis in the American Thyroid Association's guidelines for monitoring DTC patients [30], yet we found no significant difference in the ablation outcome between those with negative or positive neck ultrasound for either low- or intermediate-risk groups (p: 0.7 and 0.3, respectively); this may be attributed to the smaller number of patients who had a free N-US and also by the fact that N-US is an operator dependent.

Like **Lan et al. and Li et al**., we found no significant effect of multi focality and pathologic type on the disease outcome among both risk groups[16, 31].

Although most of the study population (110/128 low-risk and 101/122 intermediate-risk patients) received their first therapy within three months of thyroidectomy, there were no significant differences in the ablation outcome between those who were ablated within three months and those who received ablation dose more than three months post operatively (P:0.3 and P:0.07, respectively). These results are different from Li et al., who found that in low- or intermediate-risk DTC patients, delayed initial RAI therapy (≥ three months after thyroidectomy) was associated with an incomplete response (indeterminate, structural incomplete, or biochemical incomplete response)[16]; this may be attributed to different patient demographics.

It is debatable how much radioactive iodine is required to successfully ablate the post-thyroidectomy functioning remnants, with estimates ranging from less than 1110–7400 MBq (30-200 mCi) [9]. **Amin et al.** concluded that proper ablation dose of RAIT is a significant predictor for excellent outcome in DTC patients [8]. In the present study, 85 patients (60 low-risk and 25 intermediate-risk) received a low dose of RAIT, with a successful ablation rate significantly higher in the low-risk group, 66.7 % versus 56 %, respectively. One hundred sixty-five patients (68 low and 97 intermediate-risk) received a high dose of RAIT, with a successful ablation rate nearly similar in both risk groups, 58.8 % for low and 59.8% for intermediate-risk. These findings agree with **Du et al.** [32], who found no conclusive evidence that 3700 MBq activity is more effective for ablation of the thyroid remnant than 1110 MBq activity. We evaluate the prognostic factors of independent features on the ablation outcome by univariate regression analysis; the significant predictor factors associated with successful ablation outcome in the low-risk group were absent thyroid capsule infiltration, negative thyroid scan and lower BTG (P: 0.02, 0.02 and 0.04), yet in multivariate regression analysis, negative thyroid scan and lower BTG maintained such significance (P: 0.03 and 0.04, respectively). Univariate regression analysis for the intermediate-risk group revealed that lower BTG was the only significant predictor factor for successful ablation outcome (P:0.02) which maintained significance again in multivariate regression analysis (P: 0.007). This agrees with the results of previous research [27, 33, 34].

Atilgan et al. found that serum TG's cutoff value of ≥ 0.2, gives 92.5% had sensitivity and 60% specificity as a predictor of successful ablation outcome (35). We found that the same cutoff value (≥ 0.2) gives 85 % sensitivity and 83 % specificity for predicting successful ablation outcome in the low-risk group compared to 86 % sensitivity and 87 % specificity in the intermediate-risk group.

We encountered a cutoff value for the thyroid uptake of 0.2 that gives 65 % sensitivity and 35 % specificity as a predictor of successful ablation outcome in the low-risk group compared to 40 % sensitivity and 35 % specificity in the intermediate-risk group, which are lower than those of **Giovanella et al.**, who found a cutoff value of thyroid uptake of 0.9 %, giving 70%, 55% sensitivity, and specificity respectively[36]. This discrepancy may be attributed to the difference in thyroidectomy skills and different surgeons.

CONCLUSIONS:

In ATA-low-risk DTC patients, an intact thyroid capsule and a negative post-operative ^{99m}Tc thyroid scan were linked to a significantly higher successful ablation outcome. Additionally, a negative thyroid scan and lower BTG (<5 ng/ml) were the only significant predictor factors for a successful ablation outcome. For the intermediate-risk group, BTG <5 ng/mL was the only significant predictive factor that was significantly linked to a higher successful ablation outcome. Although the percentage of thyroid uptake with a 0.2% cutoff value and BTG with a cutoff value of 0.2 ng/ml had nearly equal AUCs, BTG has a higher sensitivity and specificity than thyroid uptake in predicting the success of ablation outcomes in DTC patients in both low and intermediate risk categories.

Limitations:

The small sample size, and the retrospective design of the current study were among study limitations.

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