Iran J Nucl Med. 2023;31(1):49-53 [Serial No. 60]

Homepage: https://irjnm.tums.ac.ir/

ORIGINAL RESEARCH ARTICLE

The prevalence of pre-thyroidectomy thyroid function test abnormalities among patients with differentiated thyroid carcinoma: A descriptive study

Somayeh Barashki, Atena Aghaei, Seyed Rasoul Zakavi, Fatemeh Mohammad Bagherpour, Susan Shafiei, Hadis Mohammadzadeh Kosari

Nuclear Medicine Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

ARTICLE INFO

Article History:
Received: 18 June 2022
Revised: 09 October 2022
Accepted: 11 October 2022
Published Online: 17 October 2022

Keyword:
Thyroid cancer
Prevalence
Thyroid stimulating hormone
Differentiated thyroid cancer

*Corresponding Author:
Hadis Mohammadzadeh Kosari, MD
Address: Nuclear Medicine Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
Email: hmohammadzadekosari@gmail.com

ABSTRACT

Introduction: The present study aims to assess pre-thyroidectomy thyroid hormone disturbances among patients suffering from differentiated thyroid carcinoma (DTC).

Methods: This retrospective study was performed from September 2020 to March 2021. We analyzed the hospital files of 710 patients with DTC who underwent thyroidectomy and referred to nuclear medicine department from April 2013 to September 2019. Demographics, TNM stage, pre-surgery thyroid function tests, time-interval to achieve a complete response, recurrence rate, one-year response, final response, and the need for alternative treatment modalities were extracted. Then, we analyzed the potential association of pre-surgery TSH levels with the initial disease stage and treatment response. Chi-Square, Analysis-of-variance, and Kruskal-Wallis tests were used where appropriate.

Results: The mean age of participants was 40.39 ± 13.85 years. History of Hashimoto's disease was detected in 130 (18.3%) patients. Multi-focal DTC was found in 221 (31.2%) patients. Lymph node involvement was significantly higher among men (p = 0.001). Men also had significantly higher thyroglobulin levels (p = 0.025). No statistically significant association was found between pre-surgery thyroid function status and TNM stage or multifocality of the malignancy. Baseline thyroid function tests also did not show a statistically significant relationship with thyroglobulin, anti-thyroglobulin antibody, time to first excellent response, and follow-up duration.

Conclusion: Baseline thyroid function status may not change the outcome of DTC. It could also be plausible that thyroid dysfunction before surgery would not increase invasiveness nor impact the treatment-response of the tumor compared to euthyroid patients.

Use your device to scan and read the article online

How to cite this article: Barashki S, Aghaei A, Zakavi SR, Mohammad Bagherpour F, Shafiei S, Mohammadzadeh Kosari H. The prevalence of pre-thyroidectomy thyroid function test abnormalities among patients with differentiated thyroid carcinoma: A descriptive study. Iran J Nucl Med. 2023;31(1):49-53.

https://doi.org/10.22034/IRJNM.2022.40040

INTRODUCTION

It is estimated that thyroid cancer will represent 2.3% of new cancer diagnoses and 0.4% of cancer-related mortality in 2022 [1]. Women are affected three times more than men [1, 2]. Differentiated thyroid carcinoma, namely papillary and follicular types, makes up more than 90% of thyroid cancer types [2]. Although the survival rate is relatively high (about 98%), the economic burden of this cancer on the health systems is growing [3]. The total cost of one-year care for well-differentiated thyroid carcinoma in the United States exceeds 1.5 billion dollars which is predicted to grow to 3.5 billion in 2030 [3]. By 2030, thyroid cancer would be the fourth cause of cancer death [4]. Such increment in thyroid cancer patients is secondary to the increased usage of more sensitive diagnostic methods [2]. Although routine thyroid cancer screening has been discouraged in recent years and is advised to be replaced by the "unintentional screening event," the need for data to develop more cost-benefit approaches for managing these patients is crucial [5, 6].

The present study aims to determine the prevalence of pre-surgical thyroid function abnormalities in DTC patients, mainly to elucidate its probable effects on the disease stage and treatment response.

METHODS

We performed this retrospective study to assess the thyroid hormone disturbance before thyroidectomy and its potential effects on the surgery outcomes. During the implementation of this study, from September 2020 to March 2021, the files of 1274 patients referred to our tertiary clinic from April 2013 to September 2019 were examined, and 986 patients with DTC who underwent thyroidectomy (total or partial) were found. We excluded 276 cases with missed pre-surgical records of thyroid hormones or those without documented follow-up visits within one year of surgery. Hospital files of 710 remaining patients were reviewed retrospectively. Demographic characteristics, TNM stage, pre- and post-surgical TSH, time interval to achieve a complete response, recurrence rate, one-year response, final response, and the need for alternative treatment modalities were extracted. Then, we analyzed the potential association of TSH levels with the initial stage of the disease and response to treatment via SPSS software (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). Chi-Square, Analysis-of-variance, and Kruskal-Wallis tests were used where appropriate.

RESULTS

The mean age of participants was 40.39 ± 13.85 years. The mean age of women and men were 39.64 ± 13.19 and 43.21 ± 15.82, respectively, which differed significantly (p = 0.005; independent sample t-test). Most patients were women (79.01%). The mean age of hypothyroid, euthyroid, and hyperthyroid participants were 39 ± 14, 40 ± 13, and 42 ± 13, respectively. As shown in Table 1, 668 (94.08%) cases suffered from papillary thyroid carcinoma, while 42 (5.92%) had the follicular type. History of Hashimoto's disease was detected in 130 (18.3%) participants, and 572 (80.6%) cases reported no previous conditions. Multi-focal DTC was found in 221 (31.2%) patients. The tumor size of 254 (38.8%) participants was in the range of 2-4 centimeters (equal to the T2 stage). Lymph node involvement was significantly higher among women than men (p = 0.001; Chi-Square test). Men had significantly higher first thyroglobulin levels (p = 0.025; independent sample t-test).

Table 1. Demographic characteristics of participants

Variable	Explanation	Men (%) (Mean ± SD)	Women (%) (Mean ± SD)	Total (%)/ (Mean ± SD)	p-value
History of previous disease	None	134 (23.40)	438 (76.60)	572 (80.60)	0.011
	Hashimoto	14 (10.80)	116 (89.20)	130 (18.30)	
	Graves/Basedow	0 (0.00)	3 (100)	3 (0.40)	
	Iodine therapy	1 (20.00)	4 (80.00)	5 (0.70)	
Cancer type	Papillary	141 (21.10)	527 (78.90)	668 (94.10)	0.464
	Follicular	8 (19.00)	34 (81.00)	42 (5.90)	
Multifocal	No	101 (20.70)	387 (79.30)	488 (68.80)	0.414
	Yes	48 (21.70)	173 (78.30)	221 (31.20)	
Size (T)	Tx	5 (41.70)	7 (58.30)	12 (1.70)	0.068
	T1a	16 (16.50)	81 (83.50)	97 (13.70)	
	T1b	29 (16.30)	149 (83.70)	178 (25.10)	
	T2	60 (23.60)	194 (76.40)	254 (35.80)	

	T3a	18 (17.80)	83 (82.20)	101 (14.20)	
	T3b	6 (27.30)	16 (72.70)	22 (3.10)	
	T4a	10 (29.40)	24 (70.60)	34 (4.80)	
	T4b	5 (45.50)	6 (56.50)	11 (1.50)	
	T0	0 (0)	1 (100)	1 (0.10)	
Lymph node involvement (N)	Nx	6 (19.40)	25 (80.60)	31 (4.40)	0.001
	N0a	8 (9.30)	78 (90.70)	86 (12.10)	
	N0b	34 (15.30)	188 (84.70)	222 (31.30)	
	N1a	29 (19.70)	118 (80.30)	147 (20.70)	
	N1b	71 (32.60)	147 (67.40)	218 (30.70)	
	N1x	1 (16.70)	5 (83.30)	6 (0.80)	
Metastasis (M)	Mx	18 (18.90)	77 81.10()	95 (13.40)	0.105
	M0	121 (20.60)	467 (79.40)	588 (82.80)	
	M1	10 (37.00)	17 (63.00)	27 (3.80)	
Thyroid Function test	Hypothyroid	17(19.10)	72 (80.90)	27 (3.8)	0.808
	Hyperthyroid	12(19.00)	51 (81.00)	89 (12.50)	
	Euthyroid	120 (24.5)	438 (78.5)	558 (78.60)	
Age		43.21 ± 15.82	39.64 ± 13.19	40.39 ± 13.85	0.005
Hormonal evaluations	TSH	2.40 ± 2.86	2.58 ± 6.17	2.54 ± 5.63	0.727
	T3	72.36 ± 66.31	69.35 ± 68.14	70.06 ± 67.63	0.729
	T4	14.07 ± 22.30	15.11 ± 23.82	14.88 ± 23.48	0.664
	First TSH	76.29 ± 46.80	79.55 ± 55.01	78.86 ± 53.36	0.524
	First Tg	59.27 ± 145.79	33.65 ± 108.40	39.09 ± 117.68	0.025
	First Anti-Tg Antibody	190.27 ± 565.94	236.18 ± 652.50	226.28 ± 634.60	0.460

TSH: Thyroid Stimulation Hormone; Tg: Thyroglobulin; T3: Tri-iodo-thyronine; T4: Tetra-iodo-thyronine

Table 2 represents the features of DTC patients based on their hormonal status (hypo-, hyper-, or euthyroid). No statistically significant association was found between thyroid function status with TNM stage and multifocality of the malignancy. Although the most DTC patients have papillary thyroid carcinoma (94.1%), the only statistical significance shown in Table 2 clarifies that hypothyroid patients with DTC are more likely to suffer from the follicular type compared to hyperthyroid and euthyroid patients (p = 0.022; Chi-Square test); but still, the higher overall prevalence of papillary type in all groups should be noted.

Table 2. Features of differentiated thyroid carcinoma patients based on their hormonal status (hypo-, hyper-, or euthyroid)

Variable	Explanation	Hypothyroidism (%)	Hyperthyroidism (%)	Euthyroid	p-value
Cancer type	Papillary	78 (87.60)	60 (95.20)	530 (95.00)	0.022
	Follicular	11 (12.40)	3 (4.80)	28 (5.00)	
Multifocal	No	62 (69.70)	42 (66.70)	384 (68.90)	0.919
	Yes	27 (30.30)	21 (33.30)	173 (31.10)	
Size (T)	Tx	4 (4.5)	2 (3.2)	6 (1.10)	0.559
	T1a	10 (11.20)	12(19.00)	75 (13.40)	
	T1b	24 (27.00)	18 (28.60)	136 (24.40)	
	T2	29 (32.60)	17 (27.00)	208 (37.30)	
	T3a	15 (16.90)	7 (11.10)	79 (14.20)	
	T3b	4 (4.50)	3 (4.80)	15 (2.70)	
	T4a	2 (2.20)	3 (4.80)	29 (5.20)	
	T4b	1 (1.1)	1 (1.6)	9 (1.60)	
	T0	0 (0)	0 (0)	1 (0.20)	
Lymph node involvement (N)	Nx	3 (3.40)	3 (4.80)	25 (4.50)	0.173
	N0a	16 (18.00)	9 (14.30)	61 (10.90)	
	N0b	37 (41.60)	19 (30.20)	166 (29.70)	
	N1a	13 (14.60)	16 (25.40)	118 (21.10	
	N1b	19 (21.30)	16 (25.40)	183 (32.80)	
	N1x	1 (1.10)	0 (0)	5 (0.90)	
Metastasis (M)	Mx	8 (9.00)	9 (14.30)	78 (14.00)	0.449
	M0	79 (88.80)	53 (84.10)	456 (81.70)	
	M1	2 (2.20)	1 (1.60)	24 (4.30)	

Table 3 signifies the baseline thyroid function of DTC patients grouped by their first TSH, thyroglobulin, follow-up duration, and first time to excellent treatment response. Baseline thyroid function was not related significantly with thyroglobulin, anti-thyroglobulin antibody, time to first excellent response, and follow-up duration.

Table 3. Baseline thyroid function of differentiated thyroid carcinoma patients grouped by their first TSH, thyroglobulin, follow-up duration, and first time to excellent treatment response

Variables	Thyroid Function Status	Cases	Mean SD	F	p-value
First TSH	Hypothyroidism	82	90.84 ± 66.18	2.826	0.060
	Hyperthyroidism	58	70.76 ± 48.16		
	Euthyroid	512	77.85 ± 51.41		
First Tg	Hypothyroidism	80	28.70 ± 99.83	0.453	0.636
	Hyperthyroidism	58	34.16 ± 96.43		
	Euthyroid	498	41.33 ± 122.55		
First anti-Tg antibody	Hypothyroidism	78	373.28 ± 850.16	2.662	0.071
	Hyperthyroidism	58	261.28 ± 651.21		
	Euthyroid	484	198.40 ± 558.59		
Time to first excellent response	Hypothyroidism	33	14.97 ± 8.76	0.936	0.293
	Hyperthyroidism	24	15.08 ± 7.79		
	Euthyroid	220	17.87 ± 15.11		
Follow-up duration	Hypothyroidism	89	25.98 ± 23.85	0.594	0.552
	Hyperthyroidism	63	24.46 ± 22.84		
	Euthyroid	558	27.58 ± 23.99		

TSH: Thyroid Stimulation Hormone; Tg: Thyroglobulin

DISCUSSION

Our study was designed to observe the prevalence of pre-surgery thyroid hormone disturbances among DTC patients and to assess the potential relationship between baseline thyroid function test and TNM stage of the patients and the response to treatment. Most DTC patients were women (79.01%). We found that 94.08% of participants suffered from papillary thyroid carcinoma. DTC with baseline hypothyroidism was less likely to develop papillary thyroid cancer than those with euthyroid and hyperthyroid status at baseline; of note, papillary thyroid carcinoma was the main type in all groups. Lymph node involvement was significantly higher among women. No statistically significant relation was found regarding the baseline thyroid function tests and response to treatment or TNM stage.

Most articles we found in our searches had evaluated hyperthyroidism/Graves' as a risk factor for DTC. A meta-analysis by Staniforth et al. found that Graves' disease has an event rate of 0.07 for thyroid cancer; however, the odds of thyroid cancer in Graves' did not differ significantly from that of toxic multinodular goiter and toxic uninodular goiter [7]. Namely, any hyperthyroid state probably increases the odds of thyroid cancer. We did not find such findings probably due to the less sensitive methods compared to their meta-analysis as they declared insightfully in their conclusion that over-detection of papillary microcarcinoma caused such a high event rate.

Similar to our findings, Ömür et al. assessed 1800 patients with DTC and found 76 (4.2%) were hyperthyroid at baseline [8]. Most of them (90.8%) were papillary type. Their results are comparable to ours as both patient populations lived in an iodine-deficient area. Although they claimed that the DTC in hyperthyroid patients is diagnosed at earlier stages, the frequency of lymph node metastasis and the clinical course and complete remission ratio of DTCs did not differ. Premoli et al. showed that Graves' disease did not alter the clinical outcome of DTC patients, except for those with ≥ 1-centimeter tumors [9]. Similar results from a pediatric study showed that 2-year outcomes of DTC pediatric patients were not affected by Graves' disease [10].

Zhang et al. assessed 500 patients with thyroid nodules (250 benign and 250 DTC) and observed that pre-operative thyroglobulin-antibody and serum TSH levels were significantly higher among the DTC group [11]. They also reported significantly higher TSH levels among DTC patients with lymph node metastasis than those without such findings. This study affirmed the results of previous studies, which concluded that higher TSH levels and antithyroglobulin-antibody are associated with increased chances of DTC, higher stages, and more aggressive histological features in pathologic studies [12, 13].

18.3% of our participants were previously diagnosed with Hashimoto's. Molnár et al. considered Hashimoto's as a preneoplastic state [14]. Of their 230 participants with DTC, 40 suffered from coexisting Hashimoto's; female to male ratio was higher (78.1% versus 88.4%) in the coexisting group. They found that Hashimoto's thyroiditis coexisting with thyroid carcinoma increases the chances of multifocality (40.0% versus 23.7% in PTC patients)

and papillary morphology. On the contrary, Ma and colleagues assessed 563 PTC patients and grouped them based on pathological findings (PTC alone and PTC with other thyroid diseases) and claimed that simultaneous Hashimoto's, follicular adenoma, or nodular goiter is not only a protective factor against PTC, but also have less lymph node invasion and BRAF mutation among the PTC sufferers [15].

Although our study was strengthened by its high sample size, unfortunately, missing data in the hospital files caused many exclusions. We also failed to provide a clear drug history (especially previous thyroid hormone replacement) from some patients' medical records, which also caused some exclusions. Future studies are suggested to implement as a case-control design to provide more robust results.

CONCLUSION

Baseline thyroid function status may not change the outcome of DTC. It could also be plausible that thyroid dysfunction before surgery would not increase invasiveness nor impact the treatment-response of the tumor compared to euthyroid patients.

Acknowledgment

We are deeply grateful for the support of the Clinical Research Development Unit of Ghaem University Hospital for contributing to this study.

REFERENCES

1. Cancer Stat Facts: Thyroid Cancer. National Cancer Institute [cited 2022 Apr 20]. Available from: https://seer.cancer.gov/statfacts/html/thyro.html.
2. Schmidbauer B, Menhart K, Hellwig D, Grosse J. Differentiated thyroid cancer—treatment: state of the art. Int J Mol Sci. 2017 Jun;18(6):1292.
3. Barrows CE, Belle JM, Fleishman A, Lubitz CC, James BC. Financial burden of thyroid cancer in the United States: An estimate of economic and psychological hardship among thyroid cancer survivors. Surgery. 2020 Feb;167(2):378-84.
4. Rahib L, Smith BD, Aizenberg R, Rosenzweig AB, Fleshman JM, Matrisian LM. Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States. Cancer Res. 2014 Jun;74(11):2913-21.
5. Bibbins-Domingo K, Grossman DC, Curry SJ, Barry MJ, Davidson KW, Doubeni CA, Epling Jr JW, Kemper AR, Krist AH, Kurth AE, Landefeld CS, Mangione CM, Phipps MG, Silverstein M, Simon MA, Siu AL, Tseng CW. Screening for thyroid cancer: US Preventive Services Task Force recommendation statement. *J Am Med Assoc*. 2017 May;317(18):1882-7.
6. Davies L, Morris LG. The USPSTF recommendation on thyroid cancer screening: don't "check your neck". JAMA Otolaryngol Head Neck Surg. 2017 Aug;143(8):755-6.
7. Staniforth JU, Erdirimanne S, Eslick GD. Thyroid carcinoma in Graves' disease: a meta-analysis. Int J Surg. 2016 Mar;27:118-25.
8. Ömür Ö, Yazc B, Akgün A, Özcan Z, Akyldz M, Argon M, Ozklç H. Concomitant hyperthyroidism in patients with thyroid carcinoma and the effects of iodine supplementation in an iodine-deficient area. Clin Nucl Med. 2008 Nov;33(11):769-72.
9. Premoli P, Tanda M, Piantanida E, Veronesi G, Gallo D, Masiello E, Rosetti S, Cusini C, Boi F, Bulla J, Rodia R, Mariotti S, Capelli V, Rotondi M, Magri F, Chiovato L, Rocchi R, Campopiano MC, Elisei R, Vitti P, Barbato F, Pilli T, Castagna MG, Pacini F, Bartalena L. Features and outcome of differentiated thyroid carcinoma associated with Graves' disease: results of a large, retrospective, multicenter study. J Endocrinol Invest. 2020 Jan;43(1):109-16.
10. MacFarland SP, Bauer AJ, Adzick NS, Surrey LF, Noyes J, Kazahaya K, Mostoufi-Moab S. Disease burden and outcome in children and young adults with concurrent graves disease and differentiated thyroid carcinoma. J Clin Endocrinol Metab. 2018 Aug;103(8):2918-25.
11. Zhang X, Zhang X, Chang Z, Wu C, Guo H. Correlation analyses of thyroid-stimulating hormone and thyroid autoantibodies with differentiated thyroid cancer. J BUON. 2018 Sep;23(5):1467-71.
12. Haymart MR, Repplinger DJ, Leverson GE, Elson DF, Sippel RS, Jaume JC, Chen H. Higher serum thyroid stimulating hormone level in thyroid nodule patients is associated with greater risks of differentiated thyroid cancer and advanced tumor stage. J Clin Endocrinol Metab. 2008 Mar;93(3):809-14.
13. Morand G, da Silva S, Mlynarek A, Black M, Payne R, Hier M. Clinicopathological relevance of antithyroglobulin antibodies in low-risk papillary thyroid cancer. Clin Otolaryngol. 2017 Dec;42(6):1130-4.
14. Molnár C, Molnár S, Bedekovics J, Mokánszki A, Győry F, Nagy E, Méhes G. Thyroid carcinoma coexisting with Hashimoto's thyreoiditis: clinicopathological and molecular characteristics clue up pathogenesis. Pathol Oncol Res. 2019 Jul;25(3):1191-7.
15. Ma H, Li L, Li K, Wang T, Zhang Y, Zhang C, Xu Y, Xu X, Yu J, Wang H, Xiang B, Zhang R, Wang W. Hashimoto's thyroiditis, nodular goiter or follicular adenoma combined with papillary thyroid carcinoma play protective role in patients. Neoplasma. 2018 Mar;65(3):436-40.