TURKISH JOURNAL OF INTERNAL MEDICINE

ISSN:2687-4245

Internal Medicine

Evaluation of the relationship between papillary thyroid cancer and radiation exposure

Deniz Gezer[1], **Seval Müzeyyen Ecin**[2]

[1]Departman of Internal Medicine, Mersin City Training and Research Hospital, Mersin, Turkey
[2]Departman of Occupational Diseases, Mersin City Training and Research Hospital, Mersin, Turkey

ABSTRACT

Background It has been identified that ionising radiation is the definitive cause of human cancer. One-third of the tumours that develop after radiation exposure are malignant, with papillary thyroid cancer (PTC) being the most common cancer type. This study investigated the relationship between total radiation dose (TRD) received during imaging tests and thyroid cancer occurrence in patients diagnosed with PTC.

Methods The study was designed to retrospectively review the data of adult patients aged ≥18 years diagnosed with PTC between 2005 and 2022. Patients diagnosed with a condition other than PTC were excluded from the study.

Results Three hundred seven patients with papillary thyroid cancer were 256 (83.4%) women, with a mean age of 44.7±13.5 years. A statistically significant relationship was observed between TRD and multifocality (p=0.02). Tumour size (r=0.200, p=0.07) weakly correlated with TRD, and TRD (OR: 0.9, 95% CI: 1.0-1.1, p=0.006) was found to be significant according to multifocality.

Conclusion This study found an association between TRD taken during imaging tests and multifocality. As a result, the authors aimed to remind clinicians that the disease may progress more aggressively and that thyroid cancer may develop in patients exposed to radiation due to excessive imaging tests.

Turk J Int Med 2023;5(4):7-11
DOI: 10.46310/tjim.1255695
Original Article

Keywords: *.Thyroid cancer, papillary thyroid cancer, radiation, multifocality*

Received: *February 24, 2023;* ***Accepted:*** *July 11, 2023;* ***Published Online:*** *29 October 2024*

How to cite this article: *Geze D, Ecin SM.Evaluation of the relationship between papillary thyroid cancer and radiation exposure. Turk J Int Med 2024;6(1):7-11. DOI: 10.46310/tjim.1255695*

Address for Correspondence:
Deniz Gezer, Mersin City Training and Research Hospital, Korukent Mah. 96015 Sok. Mersin Entegre Sağlık Kampüsü, 33240 Toroslar, Mersin, Turkey
E-mail: drdenizgezer@gmail.com

INTRODUCTION

The incidence of thyroid cancer is increasing worldwide,[1] with over diagnosis being one of the most common causes.[2] However, over diagnosis cannot be ruled out as the sole reason. Furthermore, occupational exposure and several environmental factors are thought to be important risk factors.[3] The International Cancer Organization has identified ionising radiation as the definitive cause of human cancer.[4] One-third of the tumors that develop after radiation exposure are malignant, with papillary thyroid cancer (PTC) being the most common cancer type. Cancer develops at least 5-10 years after radiation exposure.[5] Meta-analysis and studies show a relationship between radiation and thyroid cancer.[6,7]

The present study aimed to investigate the relationship between the total radiation dose (TRD) received during imaging tests and the occurrence of thyroid cancer in patients diagnosed with PTC by retrospectively reviewing direct X-ray and computed tomography (CT) examinations performed for diagnostic purposes between 2005 and the time of diagnosis.

MATERIAL AND METHODS

The study was designed to retrospectively review the data of adult patients aged ≥18 years who were diagnosed with PTC at Mersin City Training and Research Hospital between 2005 and 2022. Data related to age, gender, year of diagnosis, tumour size, multifocality, presence of invasion, hemogram (haemoglobin and hematocrit) results, and the availability and number of X-rays and CT scans performed before the diagnosis was recorded. Patients diagnosed with a condition other than PTC were excluded from the study. Radiation is exposed during imaging methods such as X-ray and CT scans taken for imaging purposes. The Turkish Society of Radiation Oncology has declared a radiation exposure of 0.02 mSv from an X-ray and 8 mSv from a CT scan.8 The TRD was calculated using the following formula: TRD = (number of X-rays × 0.02) + (number of CT scans × 8).

Statistical Analysis

The data was processed using the SPSS 21.0 statistical software package (IBM Corp., Armonk, NY, USA). The conformity of the variables in the study to the normal distribution was examined using the Kolmogorov–Smirnov test. Numerical variables were expressed as median±standard deviation, and categorical variables were expressed as numbers and percentages. The t-test and Mann–Whitney U test were used for intergroup comparisons of numerical variables, and categorical variables were compared using the chi-square test or Fisher's exact chi-square test. When showing the relationship between total radiation dose, univariable and multivariable logistic regression, and other independent variables, the direction and degree of the relationship between the variables can be obtained by using a proportional or interval scale.

Pearson correlation analysis was used if variables showed normal distribution. If it did not show a normal distribution, Spearman correlation analysis was used.

RESULTS

Between 2005 and 2022, 307 patients with papillary thyroid cancer were 256 (83.4%) women, with a mean age of 44.7±13.5 years. Invasion was detected in 16.3% of the patients, and multifocality was detected in 31.9%; the number of direct X-rays taken before diagnosis was 1.0 (0-24), and the number of CT scans was 0.0 (0-12). Demographic and laboratory data of the patients with papillary thyroid cancer was given in Table 1.

Table 1. Demographic and laboratory data of the patients with papillary thyroid cancer (n: 307)

Variables	Values
Gender (Female/Male)	256 (83.4%)/51 (16.6%)
Age (years)	44.7±13.5
Diagnosis (years)	3.2±1.8
Tumor size (cm)	1.2±1.2
Tumor invasion	50 (16.3%)
Multifocality	98 (31.9%)
Haemoglobin (g/dL)	13.2±1.6
Hematocrit (%)	40.1±4.9
X-ray numbers	1.0 (0:24)
CT numbers	0.0 (0:12)
X-ray radiation dose (mSv)	0.02 (0:0.48)
CT radiation dose (mSv)	0.0 (0:96.0)

CT: computed tomography.
The values were expressed as n (%), mean ± standard deviation or median (minimum:maximum).

A statistically significant relationship was observed between TRD and multifocality (p=0.02). TRD was found to be 5.6±11.3 in those with low haemoglobin levels and 12.0±19.9 in those with normal

haemoglobin levels, which was significant (p=0.010). TRD was found to be 6.6±13.9 in patients with low hematocrit levels and 11.8±18.9 in patients with normal hematocrit levels, which was found to be significant (p=0.030). The association between total radiation dose and clinicopathological characteristics in papillary thyroid cancers was given in Table 2.

Table 2. Association between total radiation dose and clinicopathological characteristics in papillary thyroid cancers

Features	Total radiation dose (mSv)	*P*-value
Gender		0.258
Female	8.05±15.1	
Male	10.9±20.4	
Tumour size		0.251
<1 cm	7.5±14.9	
≥1 cm	9.9±17.6	
Invasion		0.289
Yes	9.2±16.1	
No	8.4±16.2	
Multifocality		0.022
Yes	11.5±19.5	
No	7.2±14.1	

The values were expressed as mean ± standard deviation.

In papillary thyroid cancer, tumour size (r=0.200, p=0.070) and haemoglobin (r=0.200, p=0.090) weakly correlated with total radiation dose. There was no significant correlation between age (r=0.08, p=0.100) and total radiation dose. The correlation between total radiation dose and age, tumour size and haemoglobin was given in Figure 1.

In the adjusted multivariable logistic regression analysis, total radiation dose (OR: 0.9, 95% CI: 1.0-1.1, p=0.006) according to multifocality was significant. The adjusted multivariable logistic regression analysis according to tumor size and multifocalty in papillary thyroid cancers was given in Table 3.

DISCUSSION

In our study, invasion was detected in 16.3% of the patients and multifocality was detected in 31.9%. A statistically significant relationship was observed between TRD and multifocality. Tumour size had a weak correlation with TRD, and TRD was significant based on multifocality.

In our study, the frequency was five times higher in females than in males. Thyroid cancer is 4-5 times more common in women.[9] It was found that it is 2-3 times more common in cancers caused by external radiation exposure.[10] However, gender influence could not be found in people who were exposed to radiation after the Chernobyl disaster or in a pooled analysis of 12 studies.[10,11] Consistent with the literature data, the present study found no significant relationship between gender and TRD.

The present study found no significant relationship between TRD and age when it examined the relationship between radiation exposure associated with imaging tests and the occurrence of PTC in adult patients aged ≥18 years who presented to the internal medicine outpatient clinic. It has been determined that the risks associated with radiation exposure are the highest if the exposure has occurred in the first years of life. Furthermore, the related risk decreases with age and is the lowest if the exposure occurred in adulthood.[5,6]

The tumors measuring 1 cm or less were classified as papillary microcarcinoma by the World Health Organization, and a better understanding of the biological and etiological factors responsible for its development has emphasized the importance of revealing the reasons behind the overall increase in the incidence of thyroid cancer.[12] In our study, a weak correlation was found between TRD and tumor size, and no statistically significant correlation was found between papillary microcancer and TRD. Similar to our study, the

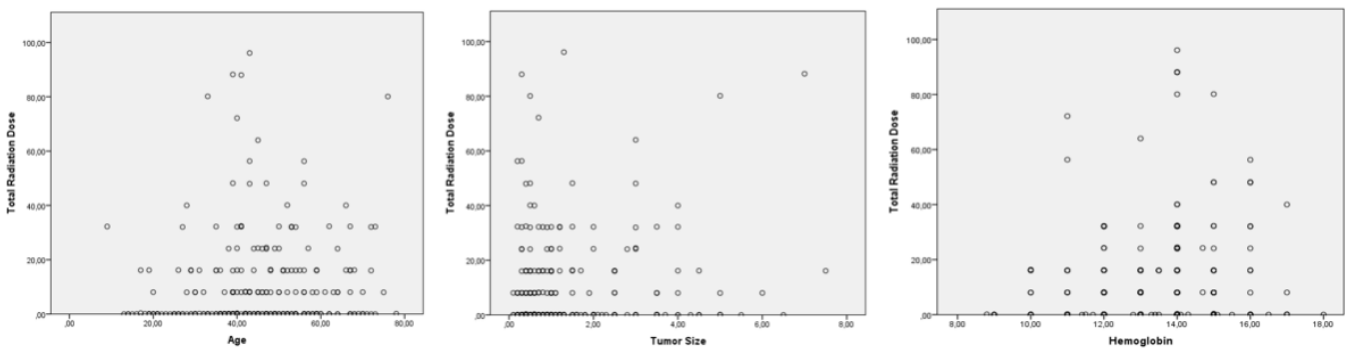

Figure 1. Correlation between total radiation dose and age, tumour size and haemoglobin

Table 3. The adjusted multivariable logistic regression analysis according to tumour size and multifocalty in papillary thyroid cancers

Features	Tumour size		Multifocality	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age	0.9 (0.9-1.0)	0.100	1.0 (0.9-1.0)	0.113
Gender	0.6 (0.3-1.2)	0.200	0.0 (0.0-)	0.997
Total radiation dose	1.0 (1.0-1.1)	0.100	0.9 (1.0-1.1)	0.006
Haemoglobin	0.8 (0.5-1.3)	0.400	1.1 (0.6-1.8)	0.835

study carried out after the atomic bombing of Japan in 1945 determined that radiation exposure might be associated with the development of papillary microcarcinoma.[13]

The present study included 340 patients with PTC and TRD was evaluated in addition to the radiation history. TRD was significantly higher among those with multifocal tumors, indicating a more severe disease progression. A study conducted in Toronto with 125 patients diagnosed with thyroid cancer found that the incidence of multifocality increased with a positive history of radiation exposure in the last three years, indicating a more aggressive disease course in these patients.[14]

In a pooled analysis of seven studies examining the relationship between external radiation and thyroid cancer, post- atomic bombing survivors, thymus, thyroid hypertrophy treatment, or children who received external radiotherapy for the treatment of tinea capitis were examined.[5] Another study found no increased risk of developing thyroid cancer associated with radiation exposure caused by diagnostic X-rays or occupational exposure.[15] To the best of our knowledge, there are not many studies examining the relationship between radiation exposure from imaging tests and PTC. The present study is one of those examining the relationship between TRD associated with imaging tests and PTC.

The limitations of our study; that it is a retrospective study. Therefore, environmental and occupational exposure to radiation in childhood and later periods could not be evaluated. The strength of the present study is that it examines the relationship between pathological markers and the radiation exposure associated with imaging tests.

CONCLUSIONS

PTC is a cancer with an increasing incidence and one of the most important causes is radiation exposure. Previous studies have examined the relationship PTC and radiation exposure after atomic bombing or high-dose irradiation for therapeutic purposes. There has been a significant increase in the number of imaging tests performed for diagnostic purposes, and the impact of this exposure cannot be ignored. The present study found a relationship between TRD received during imaging tests and multifocality. As a result, the authors intended to remind clinicians that the disease may progress more aggressively and that patients exposed to radiation due to excessive imaging tests may develop thyroid cancer.

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

The protocol of the study was approved by the Medical Ethics Committee of Mersin University, Mersin, Turkey. (Decision number: 20227453, date: 06.07.2022).

Authors' Contribution

Study Conception: DG, SME,; İI; Study Design: DG, SME,; Literature Review: DG, SME,; Critical Review: DG, SME,; Data Collection and/or Processing: DG, SME,; Analysis and/or Data Interpretation: DG, SME,; Manuscript preparing: DG, SME.

REFERENCES

1. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973–2002. JAMA. 2006 May 10;295(18):2164-7. doi: 10.1001/jama.295.18.2164.
2. Ito Y, Nikiforov YE, Schlumberger M, Vigneri R. Increasing incidence of thyroid cancer: controversies explored. Nat Rev Endocrinol. 2013

Mar;9(3):178-84. doi: 10.1038/nrendo.2012.257.
3. Zhu C, Zheng T, Kilfoy BA, Han X, Ma S, Ba Y, Bai Y, Wang R, Zhu Y, Zhang Y. A birth cohort analysis of the incidence of papillary thyroid cancer in the United States, 1973-2004. Thyroid. 2009 Oct;19(10):1061-6. doi: 10.1089/thy.2008.0342.
4. IARC. IARC Monograph Volume 100D: A review of human carcinogens—radiation. Monographs on the Evaluation of Carcinogenic Risks to Humans. Lyon, France: IARC Publications; 2012.
5. Ron E, Lubin JH, Shore RE, Mabuchi K, Modan B, Pottern LM, Schneider AB, Tucker MA, Boice JD Jr. Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies. 1995. Radiat Res. 2012 Aug;178(2):AV43-60. doi: 10.1667/rrav05.1.
6. Schneider AB, Ron E, Lubin J, Stovall M, Gierlowski TC. Dose-response relationships for radiation-induced thyroid cancer and thyroid nodules: evidence for the prolonged effects of radiation on the thyroid. J Clin Endocrinol Metab. 1993 Aug;77(2):362-9. doi: 10.1210/jcem.77.2.8345040.
7. Iglesias ML, Schmidt A, Ghuzlan AA, Lacroix L, Vathaire F, Chevillard S, Schlumberger M. Radiation exposure and thyroid cancer: a review. Arch Endocrinol Metab. 2017 Mar-Apr;61(2):180-187. doi: 10.1590/2359-3997000000257.
8. Türk Radyasyon Onkolojisi Derneği. Görüntüleme Teknikleri - Radyasyon Dozu (2022). Available at: https://www.trod.org.tr/app_society_patient?id=14. Acsessed May 23, 2022.
9. Casella C, Fusco M. Thyroid cancer. Epidemiol Prev. 2004 Mar-Apr;28(2 Suppl):88-91.
10. Veiga LH, Holmberg E, Anderson H, Pottern L, Sadetzki S, Adams MJ, Sakata R, Schneider AB, Inskip P, Bhatti P, Johansson R, Neta G, Shore R, de Vathaire F, Damber L, Kleinerman R, Hawkins MM, Tucker M, Lundell M, Lubin JH. Thyroid cancer after childhood exposure to external radiation: An updated pooled analysis of 12 studies. Radiat Res. 2016 May;185(5):473-84. doi: 10.1667/RR14213.1.
11. Boice JD Jr. Thyroid disease 60 years after Hiroshima and 20 years after Chernobyl. JAMA. 2006 Mar 1;295(9):1060-2. doi: 10.1001/jama.295.9.1060.
12. DeLellis RA, Lloyd RV, Heitz PU, Eng C, eds. Pathology and Genetics of Tumours of Endocrine Organs Volume 8. WHO Classification of Tumours. 3rd ed. IARC Publications; 2004.
13. Harach HR, Franssila KO, Wasenius VM. Occult papillary carcinoma of the thyroid. A "normal" finding in Finland. A systematic autopsy study. Cancer. 1985 Aug 1;56(3):531-8. doi: 10.1002/1097-0142(19850801)56:3<531::aid-cncr2820560321>3.0.co;2-3.
14. Seaberg RM, Eski S, Freeman JL. Influence of previous radiation exposure on pathologic features and clinical outcome in patients with thyroid cancer. Arch Otolaryngol Head Neck Surg. 2009 Apr;135(4):355-9. doi: 10.1001/archoto.2009.13.