ORIGINAL ARTICLE

Medical Journal of Western Black Sea
Batı Karadeniz Tıp Dergisi

Med J West Black Sea 2025;9(2): 231-238
DOI: 10.29058/mjwbs.1671819

Evaluation of Thyroid Functions After Radiotherapy in Primary Head and Neck Malignancies without Surgery

Ameliyatsız Primer Baş ve Boyun Malignitelerinde Radyoterapi Sonrası Tiroid Fonksiyonlarının Değerlendirilmesi

Özlem ELMAS[1], **Ramazan KOZAN**[2], **Özlem APSAR BAŞARAN**[1]

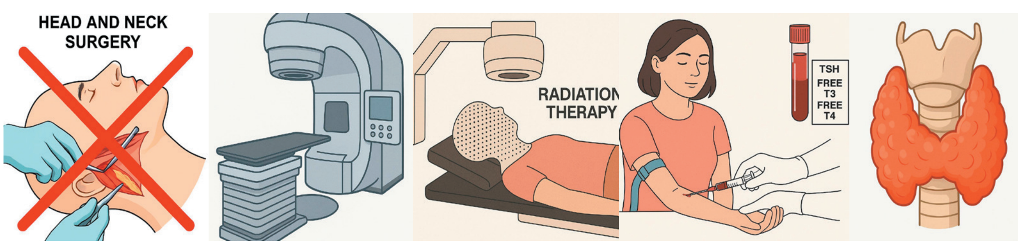
[1]Zonguldak Bülent Ecevit University Faculty of Medicine, Department of Radiation Oncology, Zonguldak, Türkiye
[2]Gazi University Faculty of Medicine, Department of General Surgery, Ankara, Türkiye

ORCID ID: *Özlem Elmas 0000-0001-8039-9610, Ramazan Kozan 0000-0002-3835-8759, Özlem Apsar Başaran 0009-0006-5767-1456*

Cite this article as: *Elmas Ö et al. Evaluation of thyroid functions after radiotherapy in primary head and neck malignancies without surgery. Med J West Black Sea. 2025;9(2): 231-238.*

GRAPHICAL ABSTRACT

The Importance of Examining Thyroid Function Tests in Routine Follow-Up of Patients with Head and Neck Malignancy Receiving Radiotherapy



In this study, it was aimed to investigate thyroid dysfunction in patients who underwent radiotherapy due to primary head and neck malignancy.

The study was conducted with patients who received radiotherapy and did not undergo surgery due to primary malignancy of the head and neck region.

In the routine follow-up of patients with head and neck malignancies receiving radiotherapy, examination of thyroid function tests may be important for early detection of subclinical cases.

Medical Journal of Western Black Sea | Özlem Elmas, Ramazan Kozan, Özlem Apsar Başaran | Elmas Ö et al. Evaluation of Thyroid Functions ... Med J West Black Sea. 2025;9(2).

ABSTRACT

Aim: In this study, it was aimed to investigate thyroid dysfunction in patients who underwent radiotherapy due to primary head and neck malignancy.

Material and Methods: The study was carried out between January 1, 2008 and January 31, 2017 at Zonguldak Bulent Ecevit University Health Practice and Research Hospital with patients who received radiotherapy due to primary malignancy of the head and neck region and did not undergo surgery. The data were recorded retrospectively from hospital records. All analyses were performed on SPSS v21 (SPSS Inc., Chicago, IL, USA). Two-tailed p-values of less than 0.05 were considered statistically significant.

Corresponding Author: Özlem Apsar Başaran ozlemapsar@gmail.com
Received: 08.04.2025 **Revision:** 09.07.2025 **Accepted:** 17.07.2025

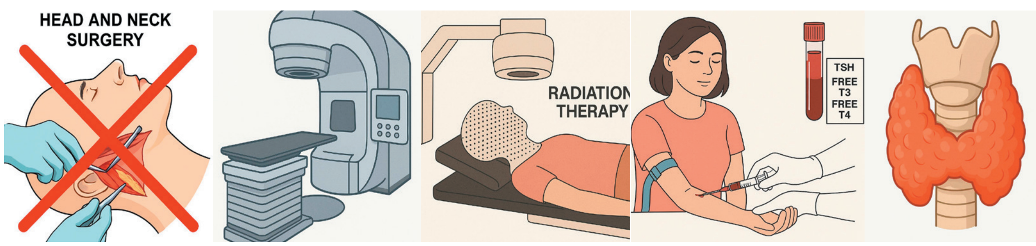
Results: The results of a total of 132 cancer patients were examined. Cancers examined mostly consisted of 52.28% (n = 69) glottic / supraglottic larynx cancer, 15.15% (n = 20) nasopharynx cancer, and 6.06% (n = 8) hodgkin lymphoma patients. In addition to ;78.8% (n = 104) of the patients were male and the median age was 60.5 (min = 15, max = 84) years. Median duration of treatment was 44 (min = 8, max = 354) days. It was determined that 28.8% (n = 38) of the patients had abnormal TSH value. Hypothyroidism developed in 15.9% (n = 21) of the individuals and hyperthyroidism developed in 12.9% (n = 17). And 29.0% (n = 11) of the TSH abnormalities determined in the pre-radiotherapy period and 71.0% in the post-radiotherapy period. There was no significant difference in age and gender between the normal TSH group and those that had abnormal TSH after radiotherapy; however, the age of patients with abnormal TSH value before radiotherapy was significantly higher (p <0.001).

Conclusion: Thyroid dysfunction in head and neck malignancies may also be seen before treatment, but the frequency of thyroid dysfunction increases after radiotherapy. The effect of radiotherapy on the thyroid gland is not affected by variables such as age and gender. Patients who develop thyroid dysfunction after radiotherapy were younger than patients with thyroid dysfunction before radiotherapy. In the routine follow-up of patients with head and neck malignancy who receive radiotherapy, the examination of thyroid function tests could be important for the early detection of particularly subclinical cases.

Keywords: Head and neck malignancies, radiotherapy, thyroid dysfunction

GRAFİKSEL ÖZET

Radyoterapi Alan Baş-Boyun Maligniteli Hastaların Rutin Takibinde Tiroid Fonksiyon Testlerinin İncelenmesinin Önemi



Bu çalışmada primer baş ve boyun malignitesi nedeniyle radyoterapi uygulanan hastalarda tiroid fonksiyon bozukluğunun araştırılması amaçlandı

Çalışma baş ve boyun bölgesinin primer malignitesi nedeniyle radyoterapi alan ve ameliyat geçirmeyen hastalarla gerçekleştirildi.

Radyoterapi alan baş ve boyun malignitesi olan hastaların rutin takibinde, subklinik vakaların erken saptanması için tiroid fonksiyon testlerinin incelenmesi önemli olabilir.

Batı Karadeniz Tıp Dergisi

Özlem Elmas, Ramazan Kozan, Özlem Apsar Başaran

Elmas Ö ve ark. Ameliyatsiz Primer Baş ve Boyun ... Med J West Black Sea. 2025;9(2).

ÖZ

Amaç: Bu çalışmada primer baş ve boyun malignitesi nedeniyle radyoterapi uygulanan hastalarda tiroid fonksiyon bozukluğunun araştırılması amaçlandı.

Gereç ve Yöntemler: Çalışma 1 Ocak 2008 ile 31 Ocak 2017 tarihleri arasında Zonguldak Bülent Ecevit Üniversitesi Tıp Fakültesi Hastanesi'nde baş ve boyun bölgesinin primer malignitesi nedeniyle radyoterapi alan ve ameliyat geçirmeyen hastalarla gerçekleştirildi. Veriler retrospektif olarak hastane kayıtlarından kaydedildi.

Bulgular: Toplam 132 kanser hastasının sonuçları incelendi. İncelenen bireylerin %52.28 (n = 69) glottik / supraglottik larinks kanseri, %15.15 (n = 20) nazofarenks kanseri ve %6.06 (n = 8) hodgkin lenfoma hastalarından oluşuyordu. Hastaların %78.8'i (n = 104) erkekti ve ortanca yaş 60.5 idi. Medyan tedavi süresi 44 (min = 8, maks = 354) gündü. Hastaların %28.8'inde (n = 38) anormal TSH değeri saptandı. Bireylerin %15.9'unda (n = 21) hipotiroidizm, %12.9'unda (n = 17) hipertiroidizm gelişti. Radyoterapi öncesi dönemde TSH anormalliği %29.0'ında (n = 11) ve radyoterapi sonrası dönemde %71.0'ında tespit edildi. Normal TSH grubu ile radyoterapi sonrası anormal TSH'si olanlar arasında yaş ve cinsiyet açısından anlamlı fark yoktu; ancak radyoterapi öncesi anormal TSH değeri olan hastaların yaşı anlamlı olarak daha yüksekti (p <0.001).

Sonuç: Radyoterapi alan baş ve boyun malignitesi olan hastaların rutin takibinde, özellikle subklinik vakaların erken saptanması için tiroid fonksiyon testlerinin incelenmesi önemli olabilir.

Anahtar Sözcükler: Baş ve boyun maligniteleri, radyoterapi, tiroid disfonksiyonu

INTRODUCTION

Thyroid dysfunction is among the most common endocrine disorders. Symptoms encountered in clinical practice vary depending on increasing or decreasing blood levels of thyroid hormones (1). Thyroid dysfunction can be caused by various conditions, such as autoimmune factors, use of various drugs, surgical removal of the thyroid gland, and radiotherapy (RT) (2).

Thyroid dysfunction is common after radiotherapy applied to patients with primary head and neck malignancy (HNM) (3). Although it is reported at different frequencies, the average frequency is around 40% (4-7). Risk is particularly high in patients diagnosed with nasopharyngeal cancer (8). Thyroid dysfunction after radiotherapy can be affected by many variables such as race, age, gender, thyroid gland size, radiotherapy applied area, radiotherapy dose (9-13). Radiotherapy applied to the head and neck region also negatively affects other healthy tissues in this region (3). Since the thyroid gland –which secretes and stores thyroid hormones crucial for metabolism– is located in this region, the damage caused by radiotherapy in this tissue should be investigated. Unlike other tissues in this region, thyroid dysfunctions can be monitored with various hormonal values such as thyroid-stimulating hormone (TSH), T3 and T4 levels. For this reason, TSH concentration should be followed up at routine intervals in patients undergoing radiotherapy due to HNM (5). It is recommended to evaluate thyroid functions in 3 to 6-month periods after the start of treatment. Another approach is to evaluate thyroid function twice in the first year and once in the following years (14).

It is important to consider the negative effects of radiotherapy on thyroid functions during follow-up studies due to the possibility of severe negative effects. In this study, we aimed to investigate thyroid dysfunction in patients who underwent radiotherapy due to primary HNM.

MATERIALS and METHODS

This retrospective cohort study was carried out between January 1, 2008 and January 31, 2017 at Zonguldak Bulent Ecevit University Health Practice and Research Hospital with patients who received radiotherapy due to a primary malignancy of the head and neck region and did not undergo surgery. The data were recorded retrospectively from hospital records. Patients with a history of thyroid surgery for any reason, those who were not deemed to be euthyroid at the time of diagnosis, and patients whose radiotherapy could not be completed were excluded from the study.

Measurements

All patients attended follow up studies regularly with thyroid function tests before and after treatment. Normally, thyroid function values are checked before treatment to understand whether thyroid dysfunction is due to radiotherapy during patient follow-up. Demographic findings, follow-up duration, thyroid dysfunction duration, and the development of hyperthyroidism or hypothyroidism were recorded. Patients were not given steroid treatment after radiotherapy.Iodinated contrast material was not used in the follow-up of the patients.Patients with head and neck cancer do not have thyroid tissue invasion. In short, other factors that could cause thyroid dysfunction were excluded.

Ethical Issues

Ethics committee approval was obtained from the Ethics Committee of Zonguldak Bulent Ecevit University (Approval no: 2018/22, Date: 21/11/2018).

Statistical Analysis

All analyses were performed on SPSS v21 (SPSS Inc., Chicago, IL, USA). For the normality check, the Kolmogorov-Smirnov test was used. Data are given as median (minimum - maximum) for continuous variables since they were non-normally distributed, and as frequency (percentage) for categorical variables. Continuous variables were compared with the Mann Whitney U test. Categorical variables were evaluated by using the Chi-square test or Fisher's exact test. Two-tailed p-values of less than 0.05 were considered statistically significant.

RESULTS

In the current study, the results of a total of 132 cancer patients were examined. The most common cancers examined in this study were as follows: 52.28% (n = 69) glottic / supraglottic larynx cancer, 15.15% (n = 20) nasopharynx cancer, and 6.06% (n = 8) hodgkin lymphoma (Table 1). In addition to this, 78.8% (n = 104) of the patients were male and the median age was 60.5 (min = 15, max = 84) years. Median duration of treatment was 44 (min = 8, max = 354) days. It was determined that 28.8% (n = 38) of the patients had abnormal TSH value. Hypothyroidism developed in 15.9% (n = 21) of the individuals and hyperthyroidism developed in 12.9% (n = 17). While 29.0% (n = 11) of the abnormal TSH values were determined in the pre radiotherapy period, 71.0% were detected in the post radiotherapy period (Table 2).

There was no significant difference in age and gender between patients whose TSH values were normal and those with abnormal TSH values ($p > 0.05$) (Table 3). All (n = 11) of the patients with abnormal TSH value before radiotherapy were male and the median age was 69 (min = 53, max = 84) years. In addition to 70.4% (n = 19) of the patients with abnormal TSH after radiotherapy were male and the median age was 52 (min = 23, max 77) years. Compared to patients with abnormal TSH value after radiotherapy, the age of patients with abnormal TSH value before radiotherapy was significantly higher ($p < 0.001$, Table 4).

Table 1: Location of Cancers / Tumors.

Malignancy	Frequency (n)	Percentage (%)
Glottic / Supraglottic Larynx Ca	69	52.27
Nasopharynx Ca	20	15.15
Hodgkin Lymphoma	8	6.06
Hypopharyngeal Ca	6	4.55
Non-Hodgkin Lymphoma	5	3.79
Submandibular Gland Ca	4	3.03
Tongue / Base of Tongue Ca	4	3.03
Tonsil Ca	4	3.03
Palate Ca	2	1.52
Parotid Gland Ca	2	1.52
Floor of Mouth Ca	1	0.76
Lower Lip Ca	1	0.76
Buccal Mucosa Ca	1	0.76
Maxillary Sinus Tumor	1	0.76
Nasal Cavity Ca	1	0.76
Oropharynx Ca	1	0.76
Cervical Esophageal Ca	1	0.76
Sino-nasal Neuroendocrine Tumor	1	0.76
Total	132	100.00

DISCUSSION

Radiotherapy applied for the treatment of HNM can affect other tissues in the target area.The thyroid gland is in this region and its functions are critical for normal metabolism. In this study, which examined thyroid dysfunctions before and after radiotherapy in cancers of this region, hypothyroidism was found in 15.9% (n = 21) of patients, and hyperthyroidism was detected in 12.9% (n = 17). It was interesting that a considerable percentage of TSH abnormalities (29.0%, n = 11) were present before radiotherapy; however, the majority of abnormalities(71.0%) developed after radiotherapy. Compared to patients with abnormal TSH value after radiotherapy, the age of patients with abnormal TSH value before radiotherapy was significantly higher.

Thyroid dysfunctions in cancer patients may be seen before radiotherapy as well as after treatment. Approximately one-third of the abnormal TSH values determined in our study were recorded in the pre-treatment period. Krashin et al. examined the relationship between thyroid hormones and cancer and reported that thyroid hormones affect various processes such as cancer development, proliferation, apoptosis and metastasis (15). In many studies, it has been shown that the increase in thyroid hormones is associated with an increase in the incidence of various types of cancer and a worse cancer prognosis (16-21). Therefore, determin-

Table 2: Summary of Patients' Characteristics.

Age	60.5 (15 - 84)
Gender	
Male	104 (78.79)
Female	28 (21.21)
Duration of Treatment (day)	44 (8 - 354)
Abnormal TSH	38 (28.79)
Hypothyroidism	21 (15.91)
Hyperthyroidism	17 (12.88)
Abnormal TSH Time	
Before RT	11 (28.95)
After RT	27 (71.05)
Abnormal TSH Time (day)	
Before RT	111 (12 - 476)
After RT	255 (4 - 1497)
TSH values	5.87 (0.01 - 100)
Hypothyroidism	8.7 (5.81 - 100)
Hyperthyroidism	0.24 (0.01 - 0.33)
Abnormal T3	38 (28.79)
Low T3	21 (15.91)
High T3	17 (12.88)
Abnormal T3 Time	
Before RT	11 (28.95)
After RT	27 (71.05)
Abnormal T3 Time (day)	
Before RT	111 (12 - 476)
After RT	255 (4 - 1497)
T3 values	3.9 (0.9 - 4.55)
Low T3	1.87 (0.9 - 4.35)
High T3	4.31 (3.98 - 4.55)
Abnormal T4	15 (11.36)
Normal	2 (1.52)
Low T4	9 (6.82)
High T4	4 (3.03)
Abnormal T4 Time	
Before RT	5 (33.33)
After RT	10 (66.67)
Abnormal T4 Time (day)	
Before RT	81 (12 - 127)
After RT	454 (160 - 1277)
T4 values	0.49 (0 - 4.6)
Normal	2.76 (0.92 - 4.6)
Low T4	0.25 (0 - 1.37)
High T4	2.01 (1.42 - 2.9)

Data are given as median (minimum - maximum) for continuous variables and as frequency (percentage) for categorical variables.

Table 3: Age and gender comparison results with regard to presence of abnormal TSH values.

	Normal TSH	Abnormal TSH	p
Age	61 (15 - 83)	59.5 (23 - 84)	0.782
Gender			
Male	74 (78.72)	30 (78.95)	1.000
Female	20 (21.28)	8 (21.05)	

Data are given as median (minimum - maximum) for continuous variables and as frequency (percentage) for categorical variables

Table 4: Age and gender comparison results with regard to presence of abnormal TSH values before or after treatment.

	Before RT (n=11)	After RT (n=27)	p
Age	69 (53 - 84)	52 (23 - 77)	<0.001
Gender			
Male	11 (100.00)	19 (70.37)	0.077
Female	0 (0.00)	8 (29.63)	

Data are given as median (minimum - maximum) for continuous variables and as frequency (percentage) for categorical variables

ing whether the disorder in thyroid functions has occurred before or after the cancer (and radiotherapy) may elucidate the causal characteristics of this relationship. Hercbergs et al. reported that hyperthyroidism has cancer-inducing properties; whereas hypothyroidism was found to have the opposite effect,a reduction in proliferation (22). In addition, there are studies reporting that hypothyroidism in HNM may enhance survival and could also reduce the risk of recurrence(23-25).

The thyroid gland is a tissue that is very sensitive to radiation exposure. The effects of radiotherapy on the thyroid are various, and it has been demonstrated that nodule formation, cancer development and hypothyroidism may be associated with radiotherapy application. Studies have shown that these effects are associated with the dose of radiation applied. Several studies have reported that higher doses of radiotherapy applied for HNM increase the risk of hypothyroidism in patients (26-28). At lower doses, radiotherapy has been reported to cause an increase in the incidence of autoimmune diseases of thyroid (26-28). Various studies have suggested that follicular epithelial cells in the thyroid gland are damaged due to radiotherapy, subsequently leading to thyroid dysfunction (27). As a result of the damage, hypothyroidism or hyperthyroidism can be seen, while autoimmune conditions have also been shown to be triggered, possibly due to the accumulation of lymphocytes (29, 30). It should not be forgotten that the effects of radiotherapy can continue for 2-3 years –albeit depending on the area and dose of radiotherapy(13, 31-33). In addition, since the negative effects may regress over time, it has been suggested that the actual frequency of these problems after radiotherapy may not be determined in cases (especially those without symptoms) in the absence of temporal investigations(34). It has been shown that chemotherapy applied without radiotherapy does not affect thyroid function (35, 36). El-Shebiney et al., in HNM patients with normal TSH before radiotherapy, reported that hypothyroidism developed in 24.6% of patients in the first year, 36.5% in the second year and 42.3% in the third year after radiotherapy (31). Although the follow-up period of the patients evaluated in our study was heterogeneous, abnormal TSH value was found in 28.2% of patients after radiotherapy. This frequency is compatible with the literature. We also found that hypo- and hyperthyroidism were present in our study group. It was thought that the development of hyperthyroidism could be associated with early damage leading to thyroiditis.

Damage to the thyroid due to radiotherapy applied for the treatment of HNM may vary depending on the various features of the patient. Murthy et al. examined the frequency of hypothyroidism after radiotherapy applied to 89 patients with head and neck squamous cell carcinoma, and reported that hypothyroidism developed more frequently in younger patients (12). Similarly, Wu et al. reported that being younger than 30 years old increased the frequency of hypothyroidism as a result of their studies evaluating the effect of radiotherapy applied to 408 patients with nasopharyngeal cancer (37). In different studies, the negative effect of radiotherapy on the thyroid has been shown to be inversely related to age (32, 38, 39). This may be related to the reduction of mitotic activity with aging (40). In contrast to these studies, Lo Galbo et al. reported that the frequency of hypothyroidism after radiotherapy increased with higher age in their study of 137 patients with larynx and hypopharynx cancer (33). Similarly, Diaz et al. reported that thyroid dysfunction was associated with higher age after radiotherapy applied to 144 patients with HNM (32). Colevas et al. determined that patients with a head and neck squamous cell carcinoma over 60 years of age had a higher frequency of post- radiotherapy hypothyroidism (41). Finally, Hancock et al. suggested that higher age was significantly associated with hypothyroidism in 1460 Hodgkin lymphoma patients who had undergone radiotherapy (42). In our study, no significant relationship was found between the presence of thyroid dysfunction and age; however, very interestingly, the age of patients with abnormal TSH before radiotherapy was found to be significantly higher than those with abnormal TSH after radiotherapy. When the conflicting results of published studies and our findings are evaluated together, it seems feasible to suggest that age has a more complex role in the development of thyroid dysfunction. We believe future studies could benefit from temporal evaluation of thyroid function in patients with HNM, both before and after treatment with radiotherapy. In regard to gender differences, prior studies have shown that women are less affected by radiotherapy due to the smaller size of the thyroid gland (43-45). In our study, the frequency of thyroid dysfunction was not different between the males and females.

Many studies have shown that the size of the thyroid gland is associated with thyroid dysfunction (9, 10). In this study, thyroid gland size was not evaluated. In addition, different studies have shown that radiotherapy dose, application area and duration of treatment are associated with thyroid dysfunction (11,12). The effects of factors such as chemotherapy drugs applied with radiotherapy, time after radiotherapy treatment, and smoking of tobacco products were shown to be influential in this regard (13); but these variables were not evaluated in this study. In many other studies, while only hypothyroidism was examined, in our study, hypothyroidism and hyperthyroidism were evaluated; thus, an overall 'thyroid dysfunction' category was also investigated. Although this may have caused erroneous interpretations in comparison with other studies, we believe this assessment could provide important real-life data to physicians. Finally, we must note that, in studies where different types of cancers observed in the head and neck region are examined under a single heading, it is difficult to draw healthy conclusions due to the heterogeneity of the cancer types and stages.

Conclusion

Thyroid dysfunction in HNM may be seen before treatment, but the frequency of thyroid dysfunction increases after radiotherapy. The effect of radiotherapy on the thyroid gland does not seem to be influenced by age and gender in the current study. However, patients who developed thyroid dysfunction after radiotherapy were younger than patients with thyroid dysfunction before radiotherapy. In the routine follow-up of radiotherapy recipients due to HNM, the examination of thyroid function tests may be crucial for the early detection of subclinical cases. In future studies, a higher number of patients in each disease category should be included, and features such as cancer type, stage, radiotherapy dose, thyroid gland size, gender and age should be recorded for more detailed analysis. In addition, our results show that it may be useful to examine both hypothyroidism and hyperthyroidism in those who undergo radiotherapy for HNM.

Acknowledgments

None.

Author Contributions

Concept, Analysis or Interpretation; **Özlem Elmas,** Design, Literature Search **Ramazan Kozan,** Data Collection or processing; **Özlem Apsar Başaran.**

Conflicts of Interest

There is no conflict of interest between the authors.

Financial Support

No financial support was received from any institution.

Ethical Approval

Ethics committee approval was obtained from the Clinical Research Ethics Committee of Zonguldak Bulent Ecevit University (Approval no: 2018/22, Date: 21/11/2018).

Review Process

Extremely and externally peer-reviewed

REFERENCES

1. Feller M, Snel M, Moutzouri E, Bauer DC, de Montmollin M, Aujesky D, Ford I, Gussekloo J, Kearney PM, Mooijaart S, Quinn T, Stott D, Westendorp R, Rodondi N, Dekkers OM. Association of Thyroid Hormone Therapy With Quality of Life and Thyroid-Related Symptoms in Patients With Subclinical Hypothyroidism: A Systematic Review and Meta-analysis. JAMA.2018;320(13):1349-59. doi: 10.1001/jama.2018.13770
2. Vanderpump MP, Tunbridge WM. Epidemiology and prevention of clinical and subclinical hypothyroidism. Thyroid. 2002;12(10):839-47. doi: 10.1089/105072502761016458
3. Boomsma MJ, Bijl HP, Langendijk JA. Radiation-induced hypothyroidism in head and neck cancer patients: a systematic review. Radiother Oncol. 2011;99(1):1-5. doi: 10.1016/j.radonc.2011.03.002
4. Lin CL, Wu SY, Huang WT, Feng YH, Yiu CY, Chiang WF, Ho SY, Lin SH. Subsequent thyroid disorders associated with treatment strategy in head and neck cancer patients: a nationwide cohort study. BMC Cancer. 2019;19(1):461. doi: 10.1186/s12885-019-5697-y
5. Feen Rønjom M. Radiation-induced hypothyroidism after treatment of head and neck cancer. Dan Med J. 2016;63(3):B5213
6. Mulholland GB, Zhang H, Nguyen NT, Tkacyzk N, Seikaly H, O'Connell D, Biron VL, Harris JR. Optimal detection of hypothyroidism in early stage laryngeal cancer treated with radiotherapy. J Otolaryngol Head Neck Surg. 2015;44(1):34. doi: 10.1186/s40463-015-0085-3
7. Fujiwara M, Kamikonya N, Odawara S, Suzuki H, Niwa Y, Takada Y, Doi H, Terada T, Uwa N, Sagawa K, Hirota S. The threshold of hypothyroidism after radiation therapy for head and neck cancer: a retrospective analysis of 116 cases. J Radiat Res. 2015;56(3):577-82. doi: 10.1093/jrr/rrv006
8. Fan CY, Lin CS, Chao HL, Huang WY, Su YF, Lin KT, Tsai IJ, Kao CH. Risk of hypothyroidism among patients with nasopharyngeal carcinoma treated with radiation therapy: A Population-Based Cohort Study. Radiother Oncol. 2017;123(3):394-400. doi: 10.1016/j.radonc.2017.04.025
9. Kamal M, Peeler CR, Yepes P, Mohamed ASR, Blanchard P, Frank S, Chen L, Jethanandani A, Kuruvilla R, Greiner B, Harp J, Granberry R, Mehta V, Rock C, Hutcheson K, Cardenas C, Gunn GB, Fuller C, Mirkovic D. Radiation-Induced Hypothyroidism After Radical Intensity Modulated Radiation Therapy for Oropharyngeal Carcinoma. Adv Radiat Oncol. 2019;5(1):111-9. doi: 10.1016/j.adro.2019.08.006

10. Chyan A, Chen J, Shugard E, Lambert L, Quivey JM, Yom SS. Dosimetric predictors of hypothyroidism in oropharyngeal cancer patients treated with intensity-modulated radiation therapy. Radiat Oncol. 2014;9:269. doi: 10.1186/s13014-014-0269-4
11. Akgun Z, Atasoy BM, Ozen Z, Yavuz D, Gulluoglu B, Sengoz M, Abacioglu U. V30 as a predictor for radiation-induced hypothyroidism: a dosimetric analysis in patients who received radiotherapy to the neck. Radiat Oncol. 2014;9:104. doi: 10.1186/1748-717X-9-104
12. Murthy V, Narang K, Ghosh-Laskar S, Gupta T, Budrukkar A, Agrawal JP. Hypothyroidism after 3-dimensional conformal radiotherapy and intensity-modulated radiotherapy for head and neck cancers: prospective data from 2 randomized controlled trials. Head Neck. 2014;36(11):1573-80. doi: 10.1002/hed.23482
13. Koc M, Capoglu I. Thyroid dysfunction in patients treated with radiotherapy for neck. Am J Clin Oncol. 2009;32(2):150-3. doi: 10.1097/COC.0b013e3181845517
14. Garcia-Serra A, Amdur RJ, Morris CG, Mazzaferri E, Mendenhall WM. Thyroid function should be monitored following radiotherapy to the low neck. Am J Clin Oncol. 2005;28(3):255-8. doi: 10.1097/01.coc.0000145985.64640.ac
15. Krashin E, Piekiełko-Witkowska A, Ellis M, Ashur-Fabian O. Thyroid Hormones and Cancer: A Comprehensive Review of Preclinical and Clinical Studies. Front Endocrinol (Lausanne). 2019;10:59. doi: 10.3389/fendo.2019.00059
16. Khan, S. R., Chaker, L., Ruiter, R., Aerts, J. G., Hofman, A., Dehghan, A., Franco, O. H., Stricker, B. H., & Peeters, R. P. (2016). Thyroid Function and Cancer Risk: The Rotterdam Study. The Journal of clinical endocrinology and metabolism, 2019;101(12), 5030–6.doi:10.3389/fendo.2019.00059
17. Søgaard M, Farkas DK, Ehrenstein V, Jørgensen JO, Dekkers OM, Sørensen HT. Hypothyroidism and hyperthyroidism and breast cancer risk: a nationwide cohort study. Eur J Endocrinol. 2016;174(4):409-14. doi: 10.1530/EJE-15-0989
18. Fang Y, Yao L, Sun J, Yang R, Chen Y, Tian J, Yang K, Tian L. Does thyroid dysfunction increase the risk of breast cancer? A systematic review and meta-analysis. J Endocrinol Invest. 2017;40(10):1035-47. doi: 10.1007/s40618-017-0679-x
19. Chan YX, Knuiman MW, Divitini ML, Brown SJ, Walsh J, Yeap BB. Lower TSH and higher free thyroxine predict incidence of prostate but not breast, colorectal or lung cancer. Eur J Endocrinol. 2017;177(4):297-308. doi: 10.1530/EJE-17-0197
20. Mondul AM, Weinstein SJ, Bosworth T, Remaley AT, Virtamo J, Albanes D. Circulating thyroxine, thyroid-stimulating hormone, and hypothyroid status and the risk of prostate cancer. PLoS One. 2012;7(10):e47730. doi: 10.1371/journal.pone.0047730
21. Minlikeeva AN, Freudenheim JL, Cannioto RA, Eng KH, Szender JB, Mayor P, Etter JL, Cramer DW, Diergaarde B, Doherty JA, Dörk T, Edwards R, deFazio A, Friel G, Goodman MT, Hillemanns P, Høgdall E, Jensen A, Jordan SJ, Karlan BY, Kjær SK, Klapdor R, Matsuo K, Mizuno M, Nagle CM, Odunsi K, Paddock L, Rossing MA, Schildkraut JM, Schmalfeldt B, Segal BH, Starbuck K, Terry KL, Webb PM, Zsiros E, Ness RB, Modugno F, Bandera EV, Chang-Claude J, Moysich KB. History of thyroid disease and survival of ovarian cancer patients: results from the Ovarian Cancer Association Consortium, a brief report. Br J Cancer. 2017;117(7):1063-9. doi: 10.1038/bjc.2017.267
22. Hercbergs AH, Ashur-Fabian O, Garfield D. Thyroid hormones and cancer: clinical studies of hypothyroidism in oncology. Curr Opin Endocrinol Diabetes Obes. 2010;17(5):432-6. doi: 10.1097/MED.0b013e32833d9710
23. Patil VM, Noronha V, Joshi A, Bhattacharjee A, Goel A, Talreja V, Chandrasekharan A, Pande N, Mandal T, Ramaswamy A, Prabhash K. Influence of Hypothyroidism After Chemoradiation on Outcomes in Head and Neck Cancer. Clin Oncol (R Coll Radiol). 2018;30(10):675. doi: 10.1016/j.clon.2018.07.002
24. Smith GL, Smith BD, Garden AS, Rosenthal DI, Sherman SI, Morrison WH, Schwartz DL, Weber RS, Buchholz TA. Hypothyroidism in older patients with head and neck cancer after treatment with radiation: a population-based study. Head Neck. 2009;31(8):1031-8. doi: 10.1002/hed.21066
25. Nelson M, Hercbergs A, Rybicki L, Strome M. Association between development of hypothyroidism and improved survival in patients with head and neck cancer. Arch Otolaryngol Head Neck Surg. 2006;132(10):1041-6. doi: 10.1001/archotol.132.10.1041
26. Cella L, Conson M, Caterino M, De Rosa N, Liuzzi R, Picardi M, Grimaldi F, Solla R, Farella A, Salvatore M, Pacelli R. Thyroid V30 predicts radiation-induced hypothyroidism in patients treated with sequential chemo-radiotherapy for Hodgkin's lymphoma. Int J Radiat Oncol Biol Phys. 2012;82(5):1802-8. doi: 10.1016/j.ijrobp.2010.09.054
27. Hancock SL, McDougall IR, Constine LS. Thyroid abnormalities after therapeutic external radiation. Int J Radiat Oncol Biol Phys. 1995;31(5):1165-70. doi: 10.1016/0360-3016(95)00019-U
28. Yoden E, Soejima T, Maruta T, Demizu Y, Nishimura H, Ejima Y, Sasaki R, Yamada K, Sugimura K. (Hypothyroidism after radiotherapy to the neck). Nihon Igaku Hoshasen Gakkai Zasshi. 2004;64(3):146-50. Japanese
29. Thomas O, Mahé M, Campion L, Bourdin S, Milpied N, Brunet G, Lisbona A, Le Mevel A, Moreau P, Harousseau J, Cuillière J. Long-term complications of total body irradiation in adults. Int J Radiat Oncol Biol Phys. 2001;49(1):125-31. doi: 10.1016/s0360-3016(00)01373-0
30. Nagayama Y, Kaminoda K, Mizutori Y, Saitoh O, Abiru N. Exacerbation of autoimmune thyroiditis by a single low dose of whole-body irradiation in non-obese diabetic-H2h4 mice. Int J Radiat Biol. 2008;84(9):761-9. doi: 10.1080/09553000802345910
31. El-Shebiney M, El-Mashad N, El-Mashad W, El-Ebiary AA, Kotkat AE. Radiotherapeutic factors affecting the incidence of developing hypothyroidism after radiotherapy for head and neck squamous cell cancer. J Egypt Natl Canc Inst. 2018;30(1):33-38. doi: 10.1016/j.jnci.2018.01.004
32. Diaz R, Jaboin JJ, Morales-Paliza M, Koehler E, Phillips JG, Stinson S, Gilbert J, Chung CH, Murphy BA, Yarbrough WG, Murphy PB, Shyr Y, Cmelak AJ. Hypothyroidism as a consequence of intensity-modulated radiotherapy with concurrent taxane-based chemotherapy for locally advanced head-and-neck cancer. Int J Radiat Oncol Biol Phys. 2010;77(2):468-76. doi: 10.1016/j.ijrobp.2009.05.018
33. Lo Galbo AM, Kuik DJ, Lips P, von Blomberg BME, Bloemena E, Leemans CR, deBree R. A prospective longitudinal study on endocrine dysfunction following treatment of laryngeal or hypopharyngeal carcinoma. Oral Oncol. 2013;49(9):950-955. doi: 10.1016/j.oraloncology.2013.03.450

34. Kim MY, Yu T, Wu HG. Dose-volumetric parameters for predicting hypothyroidism after radiotherapy for head and neck cancer. Jpn J Clin Oncol. 2014;44(4):331-7. doi: 10.1093/jjco/hyt235

35. Sinard RJ, Tobin EJ, Mazzaferri EL, Hodgson SE, Young DC, Kunz AL, Malhotra PS, Fritz MA, Schuller DE. Hypothyroidism after treatment for nonthyroid head and neck cancer. Arch Otolaryngol Head Neck Surg. 2000;126(5):652-7. doi: 10.1001/archotol.126.5.652

36. Mercado G, Adelstein DJ, Saxton JP, Secic M, Larto MA, Lavertu P. Hypothyroidism: a frequent event after radiotherapy and after radiotherapy with chemotherapy for patients with head and neck carcinoma. Cancer. 2001;92(11):2892-7. doi: 10.1002/1097-0142(20011201)92:11<2892::aid-cncr10134>3.0.co;2-t

37. Wu YH, Wang HM, Chen HH, Lin CY, Chen EY, Fan KH, Huang SF, Chen IH, Liao CT, Cheng AJ, Chang JT. Hypothyroidism after radiotherapy for nasopharyngeal cancer patients. Int J Radiat Oncol Biol Phys. 2010;76(4):1133-9. doi: 10.1016/j.ijrobp.2009.03.011

38. Tell R, Sjödin H, Lundell G, Lewin F, Lewensohn R. Hypothyroidism after external radiotherapy for head and neck cancer. Int J Radiat Oncol Biol Phys. 1997;39(2):303-8. doi: 10.1016/s0360-3016(97)00117-x

39. Çelik M, Meral R, Kanlıada D, Aydemir L, Başaran B, Kıyak E. Post-radiotherapy hypothyroidism in head and neck cancers: When should we be concerned?. Tr-ENT. 2017;27(6):269-275. doi: 10.5606/kbbihtisas.2017.93902

40. Lochhead, J.N., Care of the Patient in Radiotherapy. 1983: Blackwell Scientific.

41. Colevas AD, Read R, Thornhill J, Adak S, Tishler R, Busse P, Li Y, Posner M. Hypothyroidism incidence after multimodality treatment for stage III and IV squamous cell carcinomas of the head and neck. Int J Radiat Oncol Biol Phys. 2001;51(3):599-604. doi: 10.1016/s0360-3016(01)01688-1

42. Hancock SL, Cox RS, McDougall IR. Thyroid diseases after treatment of Hodgkin's disease. N Engl J Med. 1991;325(9):599-605. doi: 10.1056/NEJM199108293250902

43. Elzahry M, Wahman M. Radiotherapy-Induced Structural and Functional Changes in the Thyroid Gland. Journal of Cancer Science and Clinical Therapeutics 2020;032-041. doi:10.26502/jcsct.5079047

44. Chyan A, Chen J, Shugard E, Lambert L, Quivey JM, Yom SS. Dosimetric predictors of hypothyroidism in oropharyngeal cancer patients treated with intensity-modulated radiation therapy. Radiat Oncol. 2014;9:269. doi: 10.1186/s13014-014-0269-4

45. Cella L, Liuzzi R, Conson M, D'Avino V, Salvatore M, Pacelli R. Development of multivariate NTCP models for radiation-induced hypothyroidism: a comparative analysis. Radiat Oncol. 2012;7:224. doi: 10.1186/1748-717X-7-224