

MEDICAL SCIENCE

To Cite:

My TT, Phuong LD, Hiep DV, Huy HQ. Role of Computed Tomography in evaluation of invasion and regional lymph nodes metastasis in patients with thyroid cancer. *Medical Science* 2023; 27: e278ms3113. doi: <https://doi.org/10.54905/disssi/v27i136/e278ms3113>

Authors' Affiliation:

¹Pham Ngoc Thach University of Medicine, Ho Chi Minh city, Vietnam

²HCMC Oncology Hospital, Ho Chi Minh city, Vietnam

³Trung Vuong Hospital, Ho Chi Minh city, Vietnam

*Corresponding author

Pham Ngoc Thach University of Medicine, Ho Chi Minh city, Vietnam
and Trung Vuong Hospital, Ho Chi Minh city,
Vietnam

Email: huyhq@pnt.edu.vn

Peer-Review History

Received: 14 May 2023

Reviewed & Revised: 18/May/2023 to 19/January/2023

Accepted: 24 June 2023

Published: 27 June 2023

Peer-review Method

External peer-review was done through double-blind method.

Medical Science

pISSN 2321-7359; eISSN 2321-7367

This open access article is distributed under [Creative Commons Attribution License 4.0 \(CC BY\)](https://creativecommons.org/licenses/by/4.0/).

Role of Computed Tomography in evaluation of invasion and regional lymph nodes metastasis in patients with thyroid cancer

Trương Thụy My^{1,2}, Lam Diem Phuong^{1,3}, Dang Vinh Hiep¹, Huynh Quang Huy^{1,3*}

ABSTRACT

Background: Vietnam reported 5471 new thyroid cancer patients which rank tenth in 2020. The sensitivity of computed tomography (CT) is higher than ultrasound in evaluation of invasive thyroid cancer and the lymph nodes metastasis. **Materials and methods:** One hundred and four patients (72 women, 32 men; age range 16 – 80 years; mean 44 years) with 116 malignant tumors of the thyroid were enrolled in this descriptive study. All patients were performed a neck contrast-enhanced CT and the results were compared with the surgical and histopathologic findings. **Results:** The features of thyroid cancer on CT include irregular margins, unclear boundaries, calcification and strong contrast enhancement after injection. The sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) of CT were as follows: 99%, 84.6%, 98.1% and 91.7% for capsular invasion; 98.7%, 97.4%, 98.7% and 97.4% for invasion of strap muscles; 85.7%, 97.2%, 66.7% and 99% for invasion of subcutaneous soft tissues; 77.3%, 98.9%, 94.4% and 94.9% for tracheal invasion; 76.5%, 98.9%, 92.9% and 96.1% for esophageal invasion; 83.3%, 100%, 100% and 99% for invasion of blood vessels. The rate of lymph node metastasis in thyroid cancer was high and the central cervical lymph node group predominates. **Conclusion:** CT can be a valuable tool for evaluation of invasive thyroid cancer and the lymph nodes metastasis.

Keyword: Thyroid cancer, computed tomography, invasion, lymph nodes metastasis.

1. INTRODUCTION

Thyroid cancer ranks ninth in the prevalence among common cancers and has about 586,000 cases worldwide in 2020. In Vietnam, thyroid cancer ranks tenth in the high incidence group with 5471 cases, 642 deaths were recorded in 2020. According to statistics, the incidence rate in women is 7.6/100,000 and

four times higher in male is 1.9/100,000 (Sung et al., 2021). Currently, ultrasonography is widely used to assess the risk of malignancy of thyroid nodules and to guide fine-needle aspiration (FNA) to look for abnormal cells (Haugen et al., 2016; Raslan et al., 2020).

However, ultrasound only evaluates about 50% of regional lymph nodes detected during surgery (Yeh et al., 2015). Therefore, computed tomography (CT) or magnetic resonance imaging (MRI) with intravenous contrast is indicated preoperatively in clinical cases of suspected disease progression, invasive primary tumor or evaluation entire regional lymph nodes (Haugen et al., 2016; Yeh et al., 2015; Jambi, 2022). Although MRI is better in tissue contrast than CT, it is affected by respiratory and swallowing artefacts, artifact due to different magnetic sensitivities between cervical soft tissue and tracheal air (Haugen et al., 2016; Miyakoshi et al., 2007).

In Vietnam, CT is a common imaging tool, non-invasive, not time consuming, not too expensive and especially popular in most medical facilities. CT has better sensitivity than ultrasound in evaluating regional lymph nodes, especially mediastinal, retropharyngeal and paratracheal nodes (Haugen et al., 2016; Suh et al., 2016; Ahn et al., 2008). Besides, CT is superior in evaluating primary tumors that invade nearby organs such as larynx, trachea and esophagus; invasion of blood vessels or muscles of the neck; evaluate the size of large tumor hanging into the mediastinum (Haugen et al., 2016; Yeh et al., 2015).

Therefore, we carried out this study to describe the characteristics of thyroid cancer on CT scan and compare it with the results of surgery and pathology to determine the value of CT in the assessment of invasion and metastasis of regional lymph nodes in patients with thyroid cancer.

2. METHODS

Participants

All patients with a clinical diagnosis of thyroid cancer underwent CT, had surgery with full reports and had histologically confirmed malignant tumor in the thyroid gland.

Exclusion criteria

Patient did not have a complete surgical report; Patients with pathological results are not clear to confirm the diagnosis; The operated and treated patient has retaken a CT to monitor the progression of the disease.

Study design

A descriptive, retrospective and prospective cross-sectional study was carried out between August 2022 and March 2023.

Methods of selection of participants

All cases that met the sampling criteria were included in the study sample.

Research facilities

64-row computer tomography machine with Optima 660 generation receiver and 16-row computerized tomography machine with BrightSpeed Elite generation of GE at Ho Chi Minh City Oncology Hospital.

Multi-probe CT scanning procedure in thyroid cancer patients

Patient position: Supine on the scanning table, head placed symmetrically on both sides. Scout shooting: Anteroposterior 700mm survey area (AP). Place the axial cut along the body, taking from the cranial base to the adrenal gland.

Reading of results

The results of CT are read together with experienced radiologist. Use techniques such as window change, thin-slice reconstruction with multi-plane... to identify and evaluate tumor

Determine the location, size, structure and characteristics of the tumor to be investigated. Assess the extent and invasion of the suspected lesions with adjacent structures.

Determine lymph node location, lymph node group distribution, contrast enhancement properties and surrounding lymph node involvement.

Data collection method

Collect other information from the medical record: Clinical diagnosis, imaging results, cytology and pathology and procedure reports. View the CT images stored on the PACS system. Compare CT images with surgical and pathological results to determine the value of CT in the assessment of regional lymph node invasion and metastasis in patients with thyroid cancer.

Statistical methods

Data was analyzed by SPSS 26.0. Qualitative variables are presented as frequencies and percentages. Quantitative variables are presented as mean and standard deviation. χ^2 is used to compare two proportions. A p value < 0.05 is considered to be significance.

3. RESULTS

There were 104 patients diagnosed with thyroid cancer, of which 116 thyroid tumors were surveyed.

Imaging characteristics of thyroid cancers on CT

The tumors distributed mainly in two lobes of the thyroid gland, in which the right lobe is 58 lesions, accounting for 50%. The left lobe is less with 54 lesions, accounting for 46.6% and the isthmus has only 3 lesions (2.6%). Recorded 1 lesion outside the thyroid gland (soft part of the anterior neck area, accounting for 0.8%) (Figure 1).

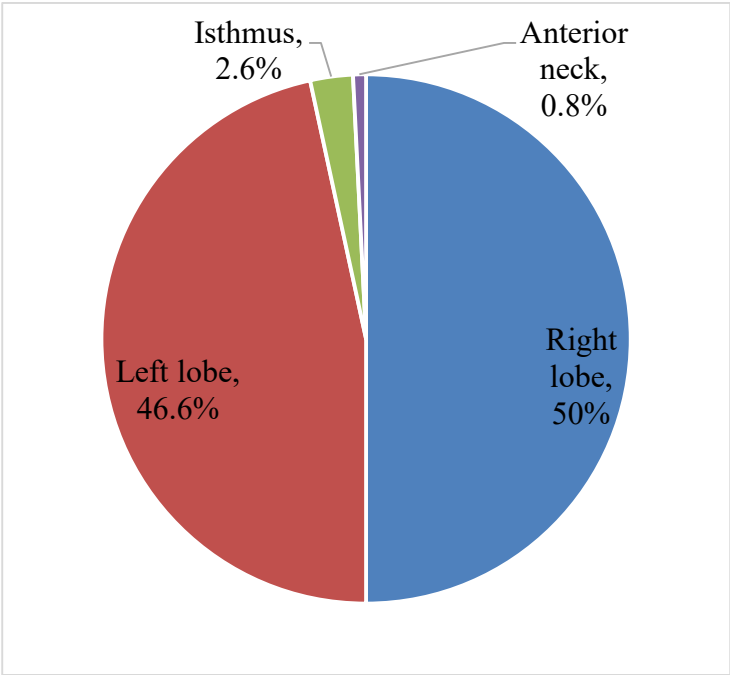


Figure 1 Location of thyroid cancers

Lesions ranging in size from 9mm to 160mm were divided into three main groups. Lesions are mainly > 40mm with the rate of 35.4%. Lesions ≤ 20mm and 20-40mm have the rate of 21% and 33.6%, respectively (Table 1). Most of the tumors share common features such as: Irregular margins, unclear boundaries, calcifications and strong contrast enhancement after injection (Table 2).

Table 1 Characteristics of thyroid cancers size

Size	n	%
≤ 20mm	36	31
20 – 40mm	39	33.6
> 40mm	41	35.4
Overall	116	100

Table 2 Other characteristics of thyroid cancers on CT

Characteristics	n	%
Irregular margins	116	100
Unclear boundaries	111	95.7
Calcification	75	64.7
Strong contrast enhancement	107	92.2

Invasive and metastatic characteristics of thyroid cancer: CT vs. surgery

Most of the lesions evaluated on CT were characterized by capsular invasion (89.7%), followed by invasion of the anterior neck muscle with 66.4%. Lesions invading the trachea and esophagus are more than 10%. Subcutaneous soft tissue invasion, vascular invasion were uncommon and there was no mediastinal invasion (Table 3).

Table 3 Invasive characteristics of thyroid cancers on CT

Characteristics on CT		Characteristics on surgery		Overall
		Yes	No	
Capsular invasion	Yes	102	2	104
	No	1	11	12
Anterior neck muscles invasion	Yes	76	1	77
	No	1	38	39
Subcutaneous soft tissue invasion	Yes	6	3	9
	No	1	106	107
Tracheal invasion	Yes	17	1	18
	No	5	93	98
Esophageal invasion	Yes	13	1	14
	No	4	98	102
Angioinvasion	Yes	5	0	5
	No	1	110	111
Mediastinal invasion	Yes	0	0	0
	No	0	116	116

Among 104 patients with thyroid cancer: 70 patients with cervical lymph node metastasis, accounting for 67.3%; 34 patients had no cervical lymph node metastasis, accounting for 32.7%. The rate of metastasis of cervical lymph node in thyroid cancer was quite high.

Value of CT to evaluate the invasion

Invasive features investigated on computed tomography mostly have high sensitivity and specificity over 70%. The esophageal invasive feature had the lowest sensitivity with 76.5%. The feature of vascular invasion has the highest specificity with 100% and the feature with the lowest specificity is capsule invasion with 84.6% (Table 4).

Table 4 Values of CT in invasive evaluation of thyroid cancer

Characteristics	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Capsular invasion	99.0	84.6	98.1	91.7	97.4
Anterior neck muscles invasion	98.7	97.4	98.7	97.4	98.2
Subcutaneous soft tissue invasion	85.7	97.2	66.7	99.0	96.6
Tracheal invasion	77.3	98.9	94.4	94.9	94.8
Esophageal invasion	76.5	98.9	92.9	96.1	95.7
Angioinvasion	83.3	100	100	99.0	99.1

The overall sensitivity and specificity when examining all groups of lymph nodes is higher than 80%. Particularly, the lateral cervical lymph node group has higher sensitivity and specificity than the central cervical lymph node group. The positive predictive values were all higher than 90%. However, the NPV was much lower even though all groups are above 60%. Accuracy for lateral cervical lymph node group was the highest with 90.9% (Table 5).

Table 5 Values of CT in evaluation the metastasis of lymph node in thyroid cancer

Characteristics	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Lymph node overall	89.8	84.8	96.5	64.5	88.9
Central cervical lymph node group	87.2	75.0	90.7	67.7	84.0
Lateral cervical lymph node group	90.7	92.1	98.6	62.5	90.9

4. DISCUSSION

Characteristics of thyroid cancer on computed tomography

The lesions were mainly located in both lobes of the gland that the right lobe was 58 lesions (50%) and the left lobe was 54 lesions (46.6%). Lesions in the isthmus area were rare (2.6%) and only one lesion outside the thyroid gland was investigated. According to Ramundo et al., (2019) investigated 44 malignant thyroid nodules, the lesions in the right lobe accounted for 52.3%, the left lobe accounted for 45.5% and the isthmus accounted for 2.2%. Zhang et al., (2020) studied 49 thyroid malignancies which they found that most of them were detected in the right lobe (46.9%) and left lobe (49%). They rarely found lesions in the isthmus region (4.1%) (Zhang et al., 2020).

We noted an extrathyroidal lesion in the neck region, which may be an ectopic thyroid tissue and a malignant lesion. According to Klubo-Gwiedzinska et al., (2011) and Lianos et al., (2013), ectopic thyroid cancer is quite rare, accounted for < 1%. Our results about the location of thyroid lesions are similar to those of other authors around the world, which tumors are mainly located in two thyroid lobes, rarely in the isthmus and very rarely in extrathyroidal lesions. 116 lesions had sizes ranging from 9mm to 160mm and most of these lesions were > 40mm (35.4%). Lesions from 20-40mm also have the same rate as 33.6% and lesions ≤ 20mm account for only 21%.

According to Cramer et al., (2010) reported on 29,425 thyroid malignant lesions, the proportion of tumors with size ≤ 20mm accounted for 66.9%, size 20-50mm accounted for 29.5%. The difference in lesion size distribution in our study and that of Cramer et al., (2010) may be due to our much smaller sample size (116 vs. 29425) and we only studied the lesions on CT, does not investigate all thyroid lesions detected by ultrasound. Heterogeneous margins features were present in all 116 lesions. Besides, the characteristic of unclear boundaries could not be determined and strong contrast treatment accounted for a high rate with 95.7% and 92.2%, respectively. Particularly, the calcification in the lesion accounted for only 64.7%. Thus, most thyroid cancer lesions have common features such as: Irregular margins, unclear boundaries, calcification and strong contrast enhancement after injection.

According to Wu et al., (2012) calcification is present in approximately 57% of thyroid malignancies on computed tomography. Zhang et al., (2020) concluded that the malignant thyroid nodules on computed tomography often have features such as: Irregular margins (57.1%), unclear boundaries (75.5%) and strong contrast enhancement (75.5%). Our study is similar to other authors when describing malignant thyroid lesions on computed tomography.

Invasive features of thyroid cancer on computed tomography

Most of the lesions evaluated in our study have the features of capsular invasion, accounting for 89.7%. Lesions located close to the capsule tend to be more invasive. Se, Sp, PPV and NPV were 99%, 84.6%, 98.1% and 91.7%, respectively, p value < 0.001. Chung et al., (2020) reported the encapsulation rate of 47.3% (783/1656) in papillary thyroid cancer on ultrasound. According to Lee et al., (2014), the rate of capsular invasion is (46.2%) when evaluated simultaneously on ultrasound and computed tomography. Liu et al., (2018) studied 381 patients and recorded the encapsulation rate of 62.2%.

The higher rate of capsular invasion in our study may be due to the limited sample survey (116 versus 1,656 lesions) and the larger proportion of lesions >20mm (69%), in the study of Chung et al., (2020) the lesion size was mainly ≤ 10mm (55.6%). Out of a total of 116 lesions surveyed, 77 lesions invaded the anterior neck muscle, accounting for 66.4%. The values were 98.7%, 97.4%, 98.7% and 97.4% for Se, Sp, PPV, NPV, respectively, p value < 0.001. In previous study on 4045 patients, there were 371 patients with thyroid lesions invading the anterior neck muscle (accounting for 9.2%). The study also showed that this invasion is associated with large lesions, multiple lesions, with lymph node metastasis and distant metastasis (Li et al., 2020).

Rosario et al., (2019) studied 182 patients and showed signs of invasion of the anterior neck muscle, accounting for 44%. According to Jin et al., (2015), a survey of 967 papillary thyroid cancer patients who were indicated with surgery recorded 476 patients with invasion beyond the thyroid gland, in which the rate of invasion of the anterior neck muscle was 25.4%. The characteristics of soft tissue invasion on computed tomography were only 7.8% in our study. The diagnostic values were 85.7% (Se), 97.2% (Sp), 66.7% (PPV) and 99% (NPV), respectively, p value < 0.001 .

The characteristics of tracheal invasion on computed tomography accounted for 15.5% in our study. The values were 77.3%, 98.9%, 94.4% and 94.9% (Se, Sp, PPV and NPV respectively), p value < 0.001 . Features of esophageal invasion on computed tomography were determined with 12.1%. The values were 76.5%, 98.9%, 92.9% and 96.1%, respectively, p value < 0.001 . In terms of vascular invasion, we evaluated including invasion of common carotid artery, internal jugular vein or internal carotid artery, our study showed that vascular invasion accounted for 4.3%. The values were 83.3%, 100%, 100% and 99%, respectively, p value < 0.001 .

Seo et al., (2010) studied 86 malignant thyroid lesions with invasive manifestations on computed tomography, showing that 25.6% invaded the trachea; 8.1% invaded the esophagus; 5.8% invaded vascular invasion. In a study by Kim et al., (2014) on 75 patients, the rate of tracheal invasion was 13.3%, esophageal invasion was 9.3% and vascular invasion was 9.3%. According to Ibrahimasic et al., (2013), they evaluated on 91 patients and the results showed that tracheal invasion accounted for 19.8%, esophageal invasion was 16.5% and vascular invasion was 3.3%.

Of the total 104 patients we studied, 70 patients had cervical lymph node metastasis; accounting for 67.3% and 371 groups of lymph nodes were dissected. Of which, 305 groups of lymph nodes were identified as metastatic lymph nodes on pathology. The data show that the central cervical lymph node (group VI) predominates with 78/371 groups of nodes. In the group of lateral cervical lymph nodes, group IV lymph nodes have the highest rate, accounting for 19.8%. The lateral cervical lymph node group Va was presented as the lowest percentage and there was no cervical lymph node group I. The metastasis rate of the central cervical lymph node group was 73.6%; the metastasis rate in the lateral cervical lymph node group was 85.7%.

According to Lee et al., (2013), evaluating on 410 groups of lymph nodes showed that the metastasis rate of lymph nodes in the central and the lateral cervical was 32.4% and 50%, respectively. According to Ahn et al., (2008), the metastasis rate of lymph node in cervical is 64%. In which, the rate of metastasis to the central cervical lymph nodes is 67.3%, the lateral cervical lymph nodes are 62.7% (Ahn et al., 2008).

5. CONCLUSION

The features of thyroid cancer on CT include irregular borders, unclear boundaries, calcification and strong contrast enhancement after injection. The lesions in the study were mainly $> 40\text{mm}$ in size with the rate of 35.4%. Thyroid cancer invades the capsule and anterior neck muscle more often than invades the trachea and esophagus and rarely invades blood vessels and subcutaneous soft tissue. There were no mediastinal invasion lesions in our study. The metastasis rate of lymph node is high and the central cervical lymph node group predominates. CT has high value in the assessment of regional invasion of lymph node and metastasis in thyroid cancer patients.

Acknowledgement

We thank the participants who were all contributed samples to the study.

Ethical approval

The study was approved by the Medical Ethics Committee of Ho Chi Minh city Oncology Hospital (IRB number: 15.2022-OH).

Author contributions

TTM and DVH contributed equally to this work

Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Funding

This study has not received any external funding.

Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

REFERENCES AND NOTES

1. Ahn JE, Lee JH, Yi JS, Shong YK, Hong SJ, Lee DH, Choi CG, Kim SJ. Diagnostic accuracy of CT and ultrasonography for evaluating metastatic cervical lymph nodes in patients with thyroid cancer. *World J Surg* 2008; 32(7):1552-8. doi: 10.1007/s00268-008-9588-7
2. Chung SR, Baek JH, Choi YJ, Sung TY, Song DE, Kim TY, Lee JH. Sonographic Assessment of the Extent of Extrathyroidal Extension in Thyroid Cancer. *Korean J Radiol* 2020; 21(10):1187-1195.
3. Cramer JD, Fu P, Harth KC, Margevicius S, Wilhelm SM. Analysis of the rising incidence of thyroid cancer using the Surveillance, Epidemiology and End Results national cancer data registry. *Surgery* 2010; 148(6):1147-1153.
4. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, Pacini F, Randolph GW, Sawka AM, Schlumberger M, Schuff KG, Sherman SI, Sosa JA, Steward DL, Tuttle RM, Wartofsky L. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid* 2016; 26(1):1-133. doi: 10.1089/thy.2015.0020
5. Ibrahimasic T, Ghossein R, Carlson DL, Chernichenko N, Nixon I, Palmer FL, Lee NY, Shaha AR, Patel SG, Tuttle RM, Balm AJ, Shah JP, Ganly I. Poorly differentiated thyroid carcinoma presenting with gross extrathyroidal extension: 1986-2009 Memorial Sloan-Kettering Cancer Center experience. *Thyroid* 2013; 23(8):997-1002. doi: 10.1089/thy.2012.0403
6. Jambi LK. Treatment of Thyroid Carcinoma with Radioactive Iodine (¹³¹I) following total thyroidectomy with incomplete neck dissection. *Medical Science* 2022; 26:ms473e2571. doi: 10.54905/disssi/v26i129/ms473e2571
7. Jin BJ, Kim MK, Ji YB, Song CM, Park JH, Tae K. Characteristics and significance of minimal and maximal extrathyroidal extension in papillary thyroid carcinoma. *Oral Oncol* 2015; 51(8):759-763.
8. Kim H, Kim JA, Son EJ, Youk JH, Chung TS, Park CS, Chang HS. Preoperative prediction of the extrathyroidal extension of papillary thyroid carcinoma with ultrasonography versus MRI: A retrospective cohort study. *Int J Surg* 2014; 12(5):544-548.
9. Klubo-Gwiedzinska J, Manes RP, Chia SH, Burman KD, Stathatos NA, Deeb ZE, Wartofsky L. Clinical review: Ectopic Cervical Thyroid Carcinoma—Review of the Literature with Illustrative Case Series. *J Clin Endocrinol Metab* 2011; 96(9):2684-2691.
10. Lee DW, Ji YB, Sung ES, Park JS, Lee YJ, Park DW, Tae K. Roles of ultrasonography and computed tomography in the surgical management of cervical lymph node metastases in papillary thyroid carcinoma. *Eur J Surg Oncol* 2013; 39(2):191-196.
11. Lee DY, Kwon TK, Sung MW, Kim KH, Hah JH. Prediction of Extrathyroidal Extension Using Ultrasonography and Computed Tomography. *Int J Endocrinol* 2014; 2014:351058.
12. Li G, Li R, Song L, Chen W, Jiang K, Tang H, Wei T, Li Z, Gong R, Lei J, Zhu J. Implications of Extrathyroidal Extension Invading Only the Strap Muscles in Papillary Thyroid Carcinomas. *Thyroid* 2020; 30(1):57-64.
13. Lianos G, Bali C, Tatsis V, Anastasiadi Z, Lianou E, Papathanasiou V, Messinis T. Ectopic thyroid carcinoma. Case report. *G Chir* 2013; 34(4):114-116.
14. Liu L, Oh C, Heo JH, Park HS, Lee K, Chang JW, Jung S, Koo BS. Clinical significance of extra thyroidal extension according to primary tumor size in papillary thyroid carcinoma. *Eur J Surg Oncol* 2018; 44(11):1754-1759.
15. Miyakoshi A, Dalley RW, Anzai Y. Magnetic resonance imaging of thyroid cancer. *Top Magn Reson Imaging* 2007; 18(4):293-302. doi: 10.1097/RMR.0b013e318572b76
16. Ramundo V, Lamartina L, Falcone R, Ciotti L, Lomonaco C, Biffoni M, Giacomelli L, Maranghi M, Durante C, Grani G. Is thyroid nodule location associated with malignancy risk? *Ultrasonography* 2019; 38(3):231-235.
17. Raslan IKI, Farahat MS, Hessein ASE, El-badawy N, Abdelsamad AM, El-shafie MA. Efficacy of neck ultrasound in the detection of cervical lymph node metastasis from thyroid carcinoma. *Medical Science* 2020; 24(105):3083-3092
18. Rosario PW, Mourão G, Calsolari MR. Risk of recurrence in patients with papillary thyroid carcinoma and minimal extrathyroidal extension not treated with radioiodine. *J Endocrinol Invest* 2019; 42(6):687-692.
19. Seo YL, Yoon DY, Lim KJ, Cha JH, Yun EJ, Choi CS, Bae SH. Locally Advanced Thyroid Cancer: Can CT Help in Prediction of Extrathyroidal Invasion to Adjacent Structures? *AJR Am J Roentgenol* 2010; 195(3):W240-W244.

20. Suh CH, Baek JH, Choi YJ, Lee JH. Performance of CT in the Preoperative Diagnosis of Cervical Lymph Node Metastasis in Patients with Papillary Thyroid Cancer: A Systematic Review and Meta-Analysis. *AJNR Am J Neuroradiol* 2016; 38(1):154-161.
21. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021; 71(3):209-249. doi: 10.3322/caac.21660
22. Wu CW, Dionigi G, Lee KW, Hsiao PJ, Paul-Shin MC, Tsai KB, Chiang FY. Calcifications in thyroid nodules identified on preoperative computed tomography: Patterns and clinical significance. *Surgery* 2012; 151(3):464-470.
23. Yeh MW, Bauer AJ, Bernet VA, Ferris RL, Loevner LA, Mandel SJ, Orloff LA, Randolph GW, Steward DL; American Thyroid Association Surgical Affairs Committee Writing Task Force. American Thyroid Association statement on preoperative imaging for thyroid cancer surgery. *Thyroid* 2015; 25(1):3-14. doi: 10.1089/thy.2014.0096
24. Zhang F, Qiao Y, Zhang H. Value of CT Features in the Diagnosis of Papillary Thyroid Tumors in Incidental Thyroid Nodules. *Int J Endocrinol* 2020; 2020:9342317.