

The Role of Neutrophil to Lymphocyte and Platelet to Lymphocyte Ratios in Diagnosing Thyroid Nodule

Haider Salim Mihson, Ayad Khani Maikhan, Ali Rodan Shuwelif

Department of Surgery, Al-Kindy Teaching Hospital, Baghdad, Iraq

Abstract

Background: Thyroid nodule is a common clinical finding and may be associated with a 5%–7% risk for malignancy. Methods for the detection of malignancy had their own drawbacks, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) may give a promising result to solve this dilemma. **The Aim of the Study:** This study aims to evaluate NLR and PLR as predictors of malignancy in solitary thyroid nodules. Also, to estimate their effect on tumor size, lymph node metastasis, and extrathyroidal extension. **Patient and Methods:** Prospective cohort study conducted at Major Teaching Hospital over a period of 1 year. Patients with solitary thyroid nodules were included in the study and according to histopathological results divided into two groups (A: Malignant and B: Benign), blood samples were drawn from participants, and measurement of lymphocyte, neutrophil, platelet, NLR, and PLR was done. **Results:** Both NLR and PLR were higher in cases of malignancy with a cutoff point for NLR >2.9 associated with 84.8% sensitivity (SN) and 71.4% specificity (SP), while PLR >140.15 associated with 87.9% SN and 71.4% SP. High NLR is further associated with larger tumor size. **Conclusion:** Both NLR and PLR are good predictors of malignancy of thyroid nodules. NLR of more than 2.9 is associated with larger-size tumors.

Keywords: Benign thyroid nodules, malignant thyroid nodules, Neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio

INTRODUCTION

Newly discovered solitary thyroid nodule was increasing in rate recently with detection rate may reach 65%.^[1] Yet only 5%–7% risk of being malignant,^[2] methods of detection of malignancy mostly invasive (fine-needle aspiration cytology [FNAC] or lobectomy), yet ultrasound had proved to be useful in some instances but also lacks specificity (SP).^[3] The result of FNAC is diagnostic in cases of papillary thyroid cancer but still class 3 Bethesda further workup (in the form of genetic testing or lobectomy) proved to be mandatory.^[2] The pathology behind thyroid malignancy may be linked to the inflammatory process as described by previous studies,^[4,5] these results take attention to investigate the level of inflammatory markers to aid in diagnosing malignancy in thyroid nodules.^[6–8] The widely available easily performed complete blood count gives good predictors of malignancy in the form of mean platelet volume,^[9] and red blood cell distribution width.^[10] While, the new hematological parameters neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) proved to

be of diagnostic value in many inflammatory and autoimmune conditions (inflammatory bowel disease^[11] and thyroiditis^[12]) and recently many malignancies such as breast cancer,^[13] lung cancer,^[14] gastric cancer,^[15] and many other diseases. Although NLR and PLR had been studied by previous researchers, no clear estimation for sensitivity (SN), and SP at a specified cutoff point was found.

The aim of the study

The aim of the study is to evaluate NLR and PLR as predictors of malignancy in a solitary thyroid nodule. Also, to estimate their relationship with tumor size, lymph node (LN) metastasis, and extrathyroidal extension.

Address for correspondence: Dr. Ali Rodan Shuwelif,
Al-Kindy Teaching Hospital, Palestine Street, Baghdad, Iraq.
E-mail: ali_rawdhan_farttoosi@yahoo.com

Submitted: 16-Sep-2022 Revised: 06-Oct-2022 Accepted: 21-Oct-2022 Published: 02-Jan-2023

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Mihson HS, Maikhan AK, Shuwelif AR. The role of neutrophil to lymphocyte and platelet to lymphocyte ratios in diagnosing thyroid nodule. *Mustansiriyah Med J* 2022;21:155-9.

Access this article online

Quick Response Code:



Website:
<http://www.mmjonline.org>

DOI:
10.4103/mj.mj_46_22

PATIENTS AND METHODS

A prospective cohort study was conducted at a major teaching hospital over a period extended over 1 year (March 1, 2021– March 1, 2022). The study included all euthyroid patients diagnosed to have solitary thyroid nodules and would be subject to lobectomy, or total thyroidectomy (cases were chosen for surgery if they have Bethesda class 3, 4, or 5). Patients with medical comorbidity or chronic drug users, and patients with thyroiditis, or abnormal thyroid function test were excluded from the study. All participants were informed about the nature of the study and informed consent was obtained. Data collected from participants include age, gender, previous history of malignancy, or chronic medical conditions for identification of exclusion criteria. Before induction of anesthesia, 1 ml of venous blood was drawn and kept in an EDTA tube for measuring hematological parameters (NLR and PLR) using ABX Micros ES 60 hematology analyzer (Horiba, France). All participants undergo ultrasound examination of the neck to assess for LN enlargement, and the size of thyroid nodule enlarged LN s undergoing FNAC. Patients were subjected to surgery (lobectomy or thyroidectomy) and the thyroid samples were sent for histopathological study (HP), the information gathered from the HP report were the type of nodule (benign or malignant), size, and extrathyroidal extension. According to the HP results, the patients have divided into two groups group A were HP showed malignancy, and group B were HP showed benign nodules.

The study proposal was reviewed and accepted by the scientific committee of the same hospital.

Statistical analysis

Data were entered into IBM– SPSS V26 (IBM Corporation, Armonk, NY, USA) for statistical analysis, and data were presented in the form of counts, percentages, mean, and standard deviation appropriate. Chi-square, Fisher's exact test, and student *t*-test were used as applicable. Predictive abilities were checked using the receiver operator characteristic curve (ROC).

RESULTS

Total cases enrolled in the study was 82 cases, and according to the HP study, 33 cases (40.2%) were diagnosed as malignant thyroid nodule (Group A), and 49 cases (59.8%) were diagnosed as benign thyroid nodule (Group B). Group A included 3 cases (3.6%) of follicular thyroid cancer, 1 case (1.2%) had anaplastic thyroid cancer and 29 case (35.4%) with papillary thyroid cancer. The HP of thyroid specimen also showed that five cases had extrathyroidal extension, and ultrasound showed six cases to have enlarged LN (the FNAC of all cases showed metastatic papillary thyroid cancer).

Regarding age, gender, neutrophil count, and platelet counts there was no significant difference between the two groups.

Lymphocyte count was significantly lower in cases of malignancy than in benign cases. Higher NLR and PLR were

found in cases of thyroid malignancy and these results were significantly different from benign thyroid nodules [Table 1].

After the application of ROC curve analysis [Figures 1 and 2], predictive abilities of NLR and PLR were obtained as explained in Table 2.

According to the cutoff points, comparison of the characteristic of tumor showed that NLR more than 2.9 was associated with mean tumor size 2.4 ± 0.71 cm. LN and extrathyroidal extension of the tumor involvement were not different regarding NLR. While all the three-tumor characteristic were not different regarding PLR. Table 3 shows the tumor characteristics according to the cutoff points of both NLR and PLR.

DISCUSSION

The widely available use of thyroid FNAC fall into the trap of over-diagnosing thyroid malignancy with consequential increased rate of thyroid surgery.^[16,17] This concept raises a red flag to investigate another predictor of malignancy in addition to FNAC.

The current study showed no difference in regard to the age of presentation of the cases, similar result found by Ceylan *et al.*^[18] and Offi *et al.*^[19] Although some studies showed that old age patients would be more prone for the risk of malignant

Table 1: The distribution of study variables according to the diagnostic groups

Variables	Mean $\pm$ SD		P
	Group A	Group B	
Age (years)	51.21 $\pm$ 5.41	52.71 $\pm$ 5.68	0.981
Male	7 (21.2)	8 (16.3)	0.576
Female	26 (78.8)	41 (83.7)	
Lymphocyte count ($\times 10^3/\mu\text{L}$)	1.29 $\pm$ 0.34	1.76 $\pm$ 0.61	0.003
Neutrophil count ($\times 10^3/\mu\text{L}$)	4.42 $\pm$ 0.86	4.58 $\pm$ 0.84	0.761
Platelet count ($\times 10^3/\mu\text{L}$)	236.18 $\pm$ 37.9	220.84 $\pm$ 41.5	0.094
NLR	3.53 $\pm$ 0.47	2.34 $\pm$ 0.87	<0.0001
PLR	154.21 $\pm$ 14.92	136.5 $\pm$ 11.88	<0.0001

NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, SD: Standard deviation

Table 2: Predictive ability of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio

Predictor	NLR	PLR
AUC (95% CI)	0.885 (0.789-0.940)	0.840 (0.736-0.943)
Cutoff point	2.9	140.15
Sensitivity (%)	84.8	87.9
Specificity (%)	71.4	71.4
PPV (%)	66.7	67.4
NPV (%)	87.5	89.7
Accuracy (%)	76.8	78
Relative risk (95% CI)	2.97 (1.87-4.74)	3.08 (1.94-4.87)

NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, AUC: Area under the curve, CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value

Table 3: Relationship between neutrophil-to-lymphocyte ratio and platelet-to -lymphocyte ratio with tumor size, lymph node status, and extrathyroidal extension

Variables	NLR			PLR		
	≤2.9	>2.9	P	≤140.15	>140.15	P
Tumor size (cm)	1.68±0.43	2.4±0.71	0.015	2.78±0.62	2.22±0.71	0.174
Involvement of LN (n=6), n (%)	0	6 (21.4)	0.556	1 (25.0)	5 (17.2)	1.00
Extrathyroidal extension (n=5), n (%)	1 (20.0)	4 (14.3)	1.00	1 (25.0)	4 (13.8)	0.500

NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, LN: lymph node

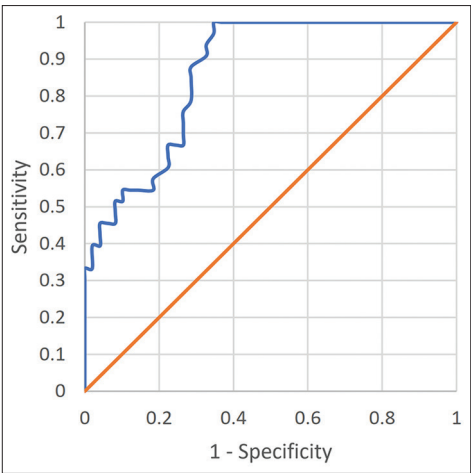


Figure 1: ROC curve for NLR. ROC: Operator characteristic curve, NLR: Neutrophil-to-lymphocyte ratio

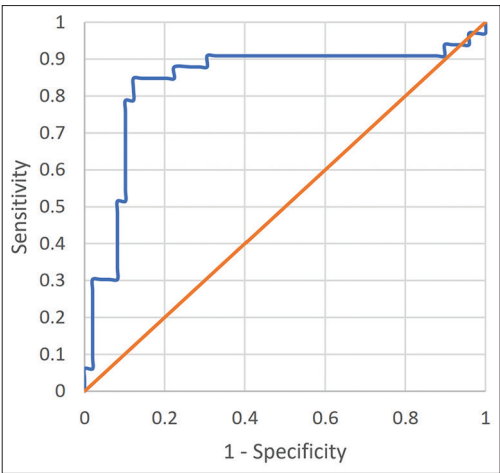


Figure 2: ROC curve for PLR. ROC: Operator characteristic curve, PLR: Platelet-to-lymphocyte ratio

thyroid nodules and also increased risk for aggressive form of malignancy as suggested by Deng *et al.*^[20] These differences in the result may attributed to the small sample size used in the current study.

There was no difference between the two groups in regard to gender, similar results also found by Ceylan *et al.*^[18] and Offi *et al.*^[19] while Bessey *et al.*^[21] in their large study (n = 3730) found that thyroid disorders were more common in females but malignancy rate were higher in male. Du *et al.*^[22] also found that age-standardized incidence of thyroid cancer was higher in males than females. This difference in the results may attributed to the large sample size of these studies in comparison to the current study (only 15 males were included in this study), thus increase in the likelihood of type II error.

Lymphocyte count was lower in cases of thyroid malignancy than benign, similar result found by Offi *et al.*^[19] Neutrophil count was not different statistically similar result found by Offi *et al.*^[19] Liu *et al.*^[23] The mechanism by which malignancy associated with lymphopenia still under investigation, this lymphopenia was found of poor prognosis in many malignancies as found by Sawa *et al.*^[24] in their study that conducted on patients with breast cancer, and in the study conducted by Ray-Coquard *et al.*^[25] who included different types of carcinomas, sarcomas, and lymphomas and found that lymphopenia is a poor prognostic factor for these types of malignancies.

This study showed that neutrophil count was not different between the two groups. Similarly, Sit *et al.*^[26] found that no significant difference in the neutrophil count between benign and malignant thyroid nodules. This result highlights the unormal changes in the neutrophile count in thyroid nodules, but it is important to note that the high neutrophile count should be associated with lymphopenia for the increase the risk of malignancy, as neutrophil act as an escort for malignant cell and involved in the progression of cell cycle as found by Szczerbe *et al.*^[27]

Platelet count was not different statistically in this study, Offi *et al.*^[19] and Martin *et al.*^[28] found similar result.

NLR was higher in cases of malignant thyroid nodule, with level of NLR more than 2.9 the SN for detecting malignancy was 84.8% and SP of 71.4%, with relative risk for the malignancy was 2.97 time those with NLR <2.9.

This result was supported by studies conducted by Ozmen *et al.*^[29] Ceylan *et al.*^[18] with an estimated cut-off point of 1.92 but they did not estimate the predictive ability in their studies, Gong *et al.*^[30] also found a significant difference with cut-off point of 2 again no estimation for predictive ability, Ozmen *et al.*^[29] applied ROC curve analysis but only estimated the area under the curve (AUC) to be 0.831, a result comparable to our result (in this study AUC was 0.885).

NLR highlights the effect of the proinflammatory nature of the thyroid malignancy, as it was found by Zhang *et al.*^[31] that malignant cells tend to activate neutrophil through multiple

interleukins and tumor necrosis factors, this lead to the promotion of malignant cells and increased the ability of cell migration.

On the other hand Offi *et al.*^[19] found that NLR was not different between cases of benign and malignant thyroid nodules, this result may be explained by the type of nodule included in their study (only Bethesda class 3: Follicular lesion of undetermined significance, or atypia of undetermined significance), while in the current study class 3, 4, and 5 were included.

PLR was higher in cases of malignant thyroid nodule, with level of PLR more than 140.15 the SN for detecting malignancy was 87.9% and SP of 71.4%, with relative risk for the malignancy was 3.08 time those with PLR <140.15.

Offi *et al.*^[19] found a significant difference in the level of PLR in cases of Bethesda 3 between benign and malignant thyroid nodules, with cutoff point more than 121.665 were associated with 69.5% SN and 48.1% SP. This variation of SN and SP may be attributed to inclusion of cases of Bethesda 3, 4, and 5 in the current study that gives wider range for PLR measurement than in their study.

The malignant cells tend to activate both the inflammatory cells and platelets,^[32] the inflammatory cells additionally activate platelet by release of chemoattractant for platelets, that lead to serial conformational changes and activation of the platelets,^[33] the ratio between inflammatory cells to platelets reflect the abnormality that occurred in malignancy, as higher ratio in malignant than in benign nodule reflect the additional activation of platelet (mediated by tumor cells) rather than the usual activation by inflammatory cells alone.

Regarding tumor characteristics tumor size was larger in cases of NLR more than 2.9 this result was supported by the results found by Ceylan *et al.*^[18] who studied the relationship of NLR with tumor size and found that NLR higher than 1.92 was associated with mean tumor size of 2.79 ± 1.48 cm and this result may mark inflammatory process in the behavior of these tumors. Liu *et al.*^[23] also found significant correlation of the tumor size with NLR. Gong *et al.*^[30] found that mean tumor size was larger in cases of NLR more than 2. On the other hand, Kim *et al.*^[34] found no difference in regard to tumor size but they predefined the size into two groups <1 and more than 1 cm this result making room for information bias.

The PLR was not different regarding tumor size similar result found by Ceylan *et al.*^[18]

LN involvement was not different in regard to the levels of both NLR and PLR similar result found by Ceylan *et al.*^[18] and Kim *et al.*^[34]

Only five cases had extrathyroidal extension in the current study, no significant difference in regard both NLR and PLR was found. Kim *et al.*^[34] ($n = 1066$) also found no significant difference in their study. While Ceylan *et al.*^[18] ($n = 201$), found a significant difference in the level of NLR but no difference

in PLR. This variation may be attributed to the samples size of these studies.

Limitation of the study was the small sample size, also the unavailability of genetic testing as all cases subjected for diagnostic lobectomy or thyroidectomy, that it could be avoided by such study. The other limitation was the difficulty in follow-up of the patients, as our center does not have a specialized oncologist, so we had to refer the patient to other hospitals, this lead to difficult follow-up and inability to estimate the effect of these parameters on survival of the patients.

CONCLUSION

Both NLR and PLR are good predictors of malignancy of thyroid nodule. NLR more than 2.9 is associated with larger-size tumors.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Zhou H, Jin Y, Dai L, Zhang M, Qiu Y, Wang K, *et al.* Differential diagnosis of benign and malignant thyroid nodules using deep learning radiomics of thyroid ultrasound images. *Eur J Radiol* 2020;127:108992.
2. Pasha HA, Dhanani R, Mughal A, Ahmed KS, Suhail A. Malignancy rate in thyroid nodules with atypia or follicular lesion of undetermined significance. *Int Arch Otorhinolaryngol* 2020;24:e221-6.
3. Persichetti A, Di Stasio E, Guglielmi R, Bizzarri G, Taccogna S, Misischì I, *et al.* Predictive value of malignancy of thyroid nodule ultrasound classification systems: A prospective study. *J Clin Endocrinol Metab* 2018;103:1359-68.
4. Ferrari SM, Fallahi P, Galdiero MR, Ruffilli I, Elia G, Ragusa F, *et al.* Immune and inflammatory cells in thyroid cancer microenvironment. *Int J Mol Sci* 2019;20:4413.
5. Revilla G, Corcoy R, Moral A, Escolà-Gil JC, Mato E. Cross-talk between inflammatory mediators and the epithelial mesenchymal transition process in the development of thyroid carcinoma. *Int J Mol Sci* 2019;20:2466.
6. Bertol BC, de Araújo JN, Sadissou IA, Sonon P, Dias FC, Bortolin RH, *et al.* Plasma levels of soluble HLA-G and cytokines in papillary thyroid carcinoma before and after thyroidectomy. *Int J Clin Pract* 2020;74:e13585.
7. Zheng R, Chen G, Li X, Wei X, Liu C, Derwahl M. Effect of IL-6 on proliferation of human thyroid anaplastic cancer stem cells. *Int J Clin Exp Pathol* 2019;12:3992-4001.
8. Zhao X, Ma W, Li X, Li H, Li J, Li H, *et al.* ANXA1 enhances tumor proliferation and migration by regulating epithelial-mesenchymal transition and IL-6/JAK2/STAT3 pathway in papillary thyroid carcinoma. *J Cancer* 2021;12:1295-306.
9. Baldane S, Ipekci SH, Sozen M, Kebapcilar L. Mean platelet volume could be a possible biomarker for papillary thyroid carcinomas. *Asian Pac J Cancer Prev* 2015;16:2671-4.
10. Sevinc B, Karahan O, Ay S, Aksoy N, Okus A. Red cell distribution width as a marker of thyroid papillary carcinoma. *Transl Surg* 2016;1:41.
11. Bertani L, Costa F, Barberio B, Savarino E. Reply to letter to the editor: NLR and PLR as novel prognostic biomarkers of mucosal healing in ulcerative colitis patients treated With Anti-TNF. *Inflamm Bowel Dis* 2020;26:e104.
12. Calapkulu M, Sencar ME, Sakiz D, Duger H, Ozturk Unsal I, Ozbek M, *et al.* The prognostic and diagnostic use of hematological parameters in

- subacute thyroiditis patients. *Endocrine* 2020;68:138-43.
13. Guo W, Lu X, Liu Q, Zhang T, Li P, Qiao W, *et al.* Prognostic value of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio for breast cancer patients: An updated meta-analysis of 17079 individuals. *Cancer Med* 2019;8:4135-48.
14. Russo A, Russano M, Franchina T, Migliorino MR, Aprile G, Mansueto G, *et al.* Neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and outcomes with Nivolumab in pretreated non-small cell lung cancer (NSCLC): A large retrospective multicenter study. *Adv Ther* 2020;37:1145-55.
15. Zhang Y, Lu JJ, Du YP, Feng CX, Wang LQ, Chen MB. Prognostic value of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in gastric cancer. *Medicine (Baltimore)* 2018;97:e0144.
16. McDow AD, Saucke MC, Marka NA, Long KL, Pitt SC. Thyroid lobectomy for low-risk papillary thyroid cancer: A national survey of low- and high-volume surgeons. *Ann Surg Oncol* 2021;28:3568-75.
17. Kitahara CM, Sosa JA. Understanding the ever-changing incidence of thyroid cancer. *Nat Rev Endocrinol* 2020;16:617-8.
18. Ceylan Y, Kumanlioğlu K, Oral A, Ertan Y, Özcan Z. The correlation of clinicopathological findings and neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios in papillary thyroid carcinoma. *Mol Imaging Radionucl Ther* 2019;28:15-20.
19. Offi C, Romano RM, Cangiano A, Filograna Pignatelli M, Candela G, Docimo G. Evaluation of LMR, NLR and PLR as predictors of malignancy in indeterminate thyroid nodules. *Acta Otorhinolaryngol Ital* 2021;41:530-6.
20. Deng Y, Li H, Wang M, Li N, Tian T, Wu Y, *et al.* Global burden of thyroid cancer from 1990 to 2017. *JAMA Netw Open* 2020;3:e208759.
21. Bessey LJ, Lai NB, Coorrough NE, Chen H, Sippel RS. The incidence of thyroid cancer by fine needle aspiration varies by age and gender. *J Surg Res* 2013;184:761-5.
22. Du L, Wang Y, Sun X, Li H, Geng X, Ge M, *et al.* Thyroid cancer: Trends in incidence, mortality and clinical-pathological patterns in Zhejiang Province, Southeast China. *BMC Cancer* 2018;18:291.
23. Liu CL, Lee JJ, Liu TP, Chang YC, Hsu YC, Cheng SP. Blood neutrophil-to-lymphocyte ratio correlates with tumor size in patients with differentiated thyroid cancer. *J Surg Oncol* 2013;107:493-7.
24. Sawa A, Bando H, Kamohara R, Takeuchi N, Terasaki A, Okazaki M, *et al.* Absolute lymphocyte count (ALC) as an independent prognostic factor in metastatic breast cancer: a retrospective study. *Oncology*. 2022. doi: 10.1159/000526963.
25. Ray-Coquard I, Cropet C, Van Glabbeke M, Sebban C, Le Cesne A, Judson I, *et al.* Lymphopenia as a prognostic factor for overall survival in advanced carcinomas, sarcomas, and lymphomas. *Cancer Res* 2009;69:5383-91.
26. Sit M, Aktas G, Erkol H, Yaman S, Keyif F, Savli H. Neutrophil to lymphocyte ratio is useful in differentiation of malign and benign thyroid nodules. *P R Health Sci J* 2019;38:60-3.
27. Szczerba BM, Castro-Giner F, Vetter M, Krol I, Gkoutela S, Landin J, *et al.* Neutrophils escort circulating tumour cells to enable cell cycle progression. *Nature* 2019;566:553-7.
28. Martin S, Mustata T, Enache O, Ion O, Chifulescu A, Sirbu A, *et al.* Platelet activation and inflammation in patients with papillary thyroid cancer. *Diagnostics (Basel)* 2021;11:1959.
29. Ozmen S, Timur O, Calik I, Altinkaynak K, Simsek E, Gozcu H, *et al.* Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) may be superior to C-reactive protein (CRP) for predicting the occurrence of differentiated thyroid cancer. *Endocr Regul* 2017;51:131-6.
30. Gong W, Yang S, Yang X, Guo F. Blood preoperative neutrophil-to-lymphocyte ratio is correlated with TNM stage in patients with papillary thyroid cancer. *Clinics (Sao Paulo)* 2016;71:311-4.
31. Zhang W, Gu J, Chen J, Zhang P, Ji R, Qian H, *et al.* Interaction with neutrophils promotes gastric cancer cell migration and invasion by inducing epithelial-mesenchymal transition. *Oncol Rep* 2017;38:2959-66.
32. Palacios-Acedo AL, Mège D, Crescence L, Dignat-George F, Dubois C, Panicot-Dubois L. Platelets, thrombo-inflammation, and cancer: Collaborating with the enemy. *Front Immunol* 2019;10:1805.
33. Dib PR, Quirino-Teixeira AC, Merij LB, Pinheiro MB, Rozini SV, Andrade FB, *et al.* Innate immune receptors in platelets and platelet-leukocyte interactions. *J Leukoc Biol* 2020;108:1157-82.
34. Kim SM, Kim EH, Kim BH, Kim JH, Park SB, Nam YJ, *et al.* Association of the preoperative neutrophil-to-lymphocyte count ratio and platelet-to-lymphocyte count ratio with clinicopathological characteristics in patients with papillary thyroid cancer. *Endocrinol Metab (Seoul)* 2015;30:494-501.