

# Comparison of neutrophil–lymphocyte ratio and platelet–lymphocyte ratio in patients with thyroiditis and papillary tumors

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## Abstract

**Objective:** The neutrophil–lymphocyte ratio (NLR) and platelet–lymphocyte ratio (PLR) have recently been introduced as prognostic markers of thyroid cancer and strong inflammatory markers. The study was performed to investigate the association of the PLR and NLR with thyroid inflammation and papillary cancer.

**Methods:** Patients with thyroiditis and patients with papillary carcinomas were compared with sex-, age-, and body mass index-matched healthy controls. The NLR and PLR were calculated and compared among the three groups.

**Results:** The NLR was significantly higher in patients with thyroiditis and non-significantly higher in patients with papillary cancer than in healthy controls. The PLR was significantly higher in both patients with thyroiditis and papillary cancer than in healthy controls. Like the NLR, the PLR was not different between patients with thyroiditis and papillary cancer. The NLR was significantly and positively associated with the PLR and white blood cell count.

**Conclusion:** The PLR and NLR showed similar results in both thyroid inflammation and cancer. It seems difficult to obtain clear results in separating cancer from inflammatory events using these parameters. We suggest using them as supportive parameters of thyroid papillary cancer or inflammation.

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## Keywords

Neutrophil–lymphocyte ratio, platelet–lymphocyte ratio, thyroid cancer, thyroiditis, prognosis, biomarkers

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## Introduction

Recent studies have revealed novel evidence that inflammation is related to cancer pathophysiology.<sup>1</sup> The neutrophil–lymphocyte ratio (NLR) has recently been shown to serve as an independent prognostic factor in patients with cancer.<sup>2,3</sup> This parameter is readily available from routine analyses and is therefore a convenient prognostic marker in such patients. In contrast to the NLR, the platelet–lymphocyte ratio (PLR) has been accepted as a novel biomarker. Platelets are inflammatory markers and are used to monitor the progression of tumoral invasion.<sup>4</sup> Both of these markers are practical and reproducible at almost no extra cost and have been shown to improve the ability to assess the prognosis in patients with cancer.<sup>5</sup>

Papillary thyroid malignancy is the most common type of thyroid carcinoma.<sup>6</sup> Although the prognosis is generally good, the local and regional recurrence rates remain high.<sup>7</sup> Unlike other types of cancers, few studies of thyroid cancer and its association with inflammation have been published.<sup>8</sup> In a recent study, Seretis et al.<sup>9</sup> evaluated the NLR in patients with papillary carcinoma and reported higher NLR levels in carcinoma. Another study showed a correlation between the preoperative NLR and tumor characteristics, with a significantly higher NLR in larger thyroid tumors.<sup>10</sup> However, no further study has been performed to investigate the association between the PLR and papillary thyroid cancer in addition to the NLR. Although the NLR and PLR are currently accepted

as prognostic markers for thyroid cancer, both of these parameters also increase in patients with inflammatory conditions of the thyroid. Although no association between papillary cancers and thyroiditis has been proven, inflammation is the common point of these diseases.

The present study was performed to investigate the NLR and PLR in patients with papillary thyroid cancer and thyroiditis to clarify whether alterations in the NLR and PLR are mainly affected by papillary cancer or thyroiditis.

## Methods

The study involved patients with thyroiditis, patients with papillary carcinoma, and age-, sex-, and body mass index-matched healthy control subjects who visited the General Surgery Clinic at Istanbul Training and Research Hospital from 2014 to 2017. Approval for the study was granted by the Ethics Committee of Istanbul Research Hospital. All study participants provided written informed consent. All patients with thyroiditis and carcinoma were histopathologically diagnosed, and detailed demographic data were recorded.

### *Laboratory assessment*

Biochemical analyses and blood counts were measured on the day of surgery. The NLR and PLR were calculated from the neutrophil, platelet, and lymphocyte ratios after performing a full blood count, which was analyzed with the impedance method using an XT-2000i hematology analyzer

(Sysmex Corporation, Kobe, Japan). Other biochemical parameters were measured with standard methods on a clinical chemistry autoanalyzer (Cobas c501-e601; Roche, Basel, Switzerland) using the original test kits.

### Statistical analysis

All patient data are presented as mean  $\pm$  standard deviation. Multi-group analysis of variance was used to find significant differences among the mean values. Tukey's B test was used for post-hoc analysis on subgroup comparisons. The one-tailed Pearson's correlation test was applied to investigate correlations between variables. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22 (IBM Corp., Armonk, NY, USA).

### Results

This study included 50 patients with thyroiditis, 50 patients with papillary carcinoma, and 46 age-, sex-, and body mass

index-matched healthy control subjects. All participants' PLR, NLR, biochemical and hematological parameters, and demographic characteristics are shown in Table 1. There were no significant differences in demographic data among the groups. Each group was compared with the others using post-hoc analysis. The mean NLR was significantly higher in the thyroiditis group ( $2.42 \pm 1.40$ ,  $p=0.017$ ) and non-significantly higher in the papillary cancer group ( $2.14 \pm 0.90$ ) than in the healthy group ( $1.89 \pm 0.70$ ). No significant difference was observed between the thyroiditis and papillary cancer groups (Figure 1).

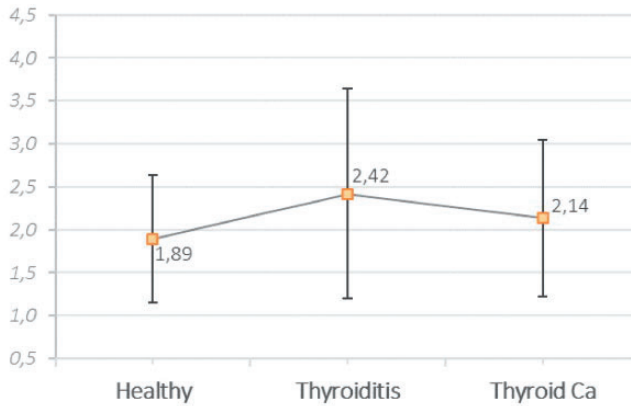
The mean PLR was significantly higher in both the thyroiditis group ( $139.1 \pm 52.0$ ,  $p<0.001$ ) and papillary cancer group ( $136.7 \pm 57.0$ ,  $p=0.003$ ) than in the healthy group ( $107.0 \pm 22.3$ ). No significant difference was observed between the thyroiditis and thyroid papillary cancer groups (Figure 2).

The fasting glucose, creatinine, aspartate transaminase, alanine transaminase, and

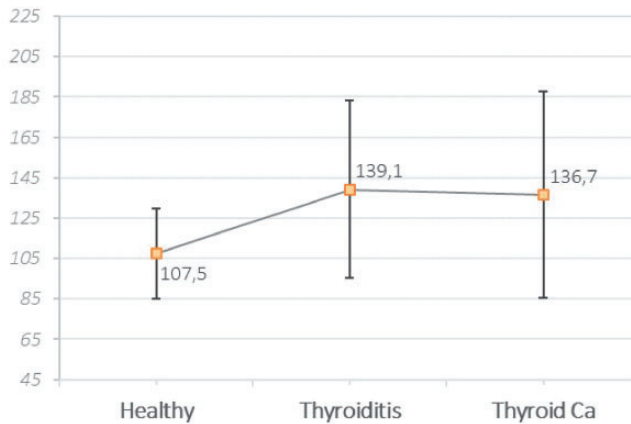
**Table 1.** NLR, PLR, laboratory parameters, and demographic characteristics of each group

Parameters	Healthy	Thyroiditis	Thyroid carcinoma
Age (years)	45 $\pm$ 10	48 $\pm$ 10	46 $\pm$ 12
Sex (female/male)	32/14	38/12	36/14
BMI (kg/m <sup>2</sup> )	26.8 $\pm$ 5.3	25.1 $\pm$ 6.2	28.3 $\pm$ 4.7
Nodule size (cm)	0.0 $\pm$ 0.0	3.4 $\pm$ 0.8	1.9 $\pm$ 1.0
Hemoglobin (g/dL)	12.8 $\pm$ 1.1	13.0 $\pm$ 1.2	12.8 $\pm$ 1.2
WBC (10 <sup>3</sup> / $\mu$ L)	7.02 $\pm$ 1.27	7.30 $\pm$ 1.93	7.62 $\pm$ 2.10
NEUT (10 <sup>3</sup> / $\mu$ L)	4.04 $\pm$ 1.05	4.42 $\pm$ 1.55	5.85 $\pm$ 10.00
PLAT (10 <sup>3</sup> / $\mu$ L)	260 $\pm$ 64	264 $\pm$ 71	272 $\pm$ 67
LYMP (10 <sup>3</sup> / $\mu$ L)	2.24 $\pm$ 0.57	2.17 $\pm$ 0.80	2.40 $\pm$ 1.05
NLR (Ratio)	1.89 $\pm$ 0.70	2.40 $\pm$ 1.40	2.14 $\pm$ 0.90
PLR (Ratio)	107.0 $\pm$ 22.3	139.1 $\pm$ 52.0	136.7 $\pm$ 57.0
FASTGLU (mg/dL)	95 $\pm$ 12	108 $\pm$ 36	97 $\pm$ 22
Creatinine (mg/dL)	0.92 $\pm$ 0.10	0.87 $\pm$ 0.18	0.82 $\pm$ 0.21
AST (IU/L)	22.0 $\pm$ 9.1	22.0 $\pm$ 11.4	20.0 $\pm$ 10.5
ALT (IU/L)	22.0 $\pm$ 9.3	22.0 $\pm$ 10.2	20.0 $\pm$ 12.7
TSH (mIU/L)	2.38 $\pm$ 1.10	1.71 $\pm$ 1.32	1.65 $\pm$ 1.23

Abbreviations: BMI, body mass index; WBC, white blood cells; NEUT, neutrophils; PLAT, platelets; LYMP, lymphocytes; AST, aspartate transaminase; ALT, alanine transaminase; TSH, thyroid-stimulating hormone; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; FASTGLU, fasting glucose



**Figure 1.** Neutrophil-lymphocyte ratio in each group. Ca, carcinoma



**Figure 2.** Platelet-lymphocyte ratio in each group. Ca, carcinoma

thyroid-stimulating hormone (TSH) concentrations were similar in all groups. As shown in Table 2, a Pearson test was performed on each variable to investigate the correlation of the variable with the NLR. A strong positive correlation was found between the NLR and PLR ( $r=0.682$ ,  $p<0.001$ ), a weak positive correlation was found between the NLR and the white blood cell count ( $r=0.285$ ,  $p=0.025$ ), and no correlation was found between the NLR and the nodule diameter, age, or

TSH level. In the thyroiditis group, significant correlations were found only between the NLR and PLR ( $r=0.711$ ,  $p<0.001$ ).

## Discussion

In this study, we investigated the relationships of thyroiditis and papillary tumors with the NLR and PLR, which are known indicators of inflammation. Recent studies have shown that inflammation is associated with the cancer prognosis.<sup>10</sup> Underlying

**Table 2.** Pearson correlation between NLR and other parameters in papillary cancer

Variables	Coefficient	p-value
Age	0.072	0.385
Nodule size	0.102	0.313
TSH	-0.015	0.856
WBC	0.286*	0.025
PLR	0.682**	0.001

Abbreviations: NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; WBC, white blood cells; TSH, thyroid-stimulating hormone.

\* $p < 0.05$ , \*\* $p < 0.001$

mechanisms and diagnostic biomarkers have been investigated in detail over the last decade. The results of these studies have suggested that the PLR and NLR are strong potential parameters for both cancer and inflammation of the thyroid because the assays are simple, inexpensive, and reproducible.<sup>11-13</sup> In the current study, the NLR and PLR were compared between healthy control subjects and patients with thyroiditis and papillary cancer to clarify this point, and the results showed that the NLR was significantly higher in patients with thyroiditis than in healthy controls while the PLR was higher in both patients with papillary cancer and thyroid inflammation than in healthy controls. However, these increases did not show evidence of being specific to inflammation or papillary cancer.

Increasing evidence supports the involvement of systemic inflammation in cancer development and progression.<sup>14</sup> In various types of cancer, the degree of systemic inflammation reflects the tumor burden.<sup>15</sup> Evidence of systemic inflammation, as marked by leukocytosis or an elevated C-reactive protein level, is a known poor prognostic factor in cancers; additionally, such markers portend a worse prognosis and response to therapy.<sup>16</sup> The NLR reflects the balance between innate (neutrophils) and adaptive (lymphocytes) immune

responses.<sup>17</sup> A high NLR reflects an augmented inflammatory reaction, which in turn correlates with decreased tumor-specific immunity.<sup>18</sup> Moreover, the NLR has been shown to be a convenient and inexpensive prognostic biomarker in human cancers.

The NLR has been investigated in patients with malignancies of the pancreas, colon, liver, and lung. Although conflicting results have been obtained,<sup>19</sup> a strong meta-analysis performed by Templeton et al.<sup>20</sup> showed that the NLR was associated with survival in several solid tumors. Measurement of the preoperative NLR might also indicate activation of the systemic inflammatory response. In a study by Gong et al.,<sup>21</sup> a positive association was demonstrated between a high NLR and advanced-stage disease in patients with papillary tumors. That report supports the importance of the NLR in evaluating thyroid carcinoma. In another related study, Seretis et al.<sup>9</sup> investigated the NLR in patients with incidental papillary tumors and those with benign goiter. Higher NLRs were reported in patients with carcinoma than in those with goiter. Similarly, in the current study, the NLR was significantly higher in the patients with papillary carcinoma than in the healthy individuals, but it was not higher than that in patients with thyroiditis.

The PLR is a valuable inflammatory index.<sup>22</sup> It has also been suggested as a prognostic marker in several types of cancers, including gastric, ovarian, colorectal, and pancreatic cancer and cholangiocarcinoma.<sup>23</sup> In breast cancer, an elevated PLR has been found to adversely impact survival in a few studies.<sup>3</sup> The PLR is being accepted as another novel inflammatory marker that has been reported to be biochemically involved in the progression of tumor invasion. Recent studies have shown the potential for use of the PLR in a diagnostic approach to inflammatory events and malignancy.<sup>24</sup> In the current study, the

PLR and NLR were higher in patients with papillary carcinoma than in healthy individuals. However, only the increased PLR was of statistical significance. In support of these results, Liu et al.<sup>25</sup> performed a systematic meta-analysis based on 7 prospective cohort studies comprising 7349 patients and reported that an elevated NLR was not a reliable indicator of differentiated thyroid cancers in patients with goiters. In addition, Manatakis et al.<sup>26</sup> reported that the NLR was not associated with sex, age, tumor size, tumor subtype, the presence of thyroiditis, or the TNM stage. Similarly, in the current study, no correlation was found between the NLR and age, nodule size, or TSH level, demonstrating that the PLR not only had a strong correlation with the NLR but was also significantly different from the NLR.

The findings of this study support previous findings in the literature showing that the NLR and PLR have potential in both malignancy and inflammatory events of thyroid tissue. However, this potential was stronger for the PLR than NLR. The present findings indicated a greater increase in the PLR than NLR in thyroid tissue. Even more importantly, both of these parameters showed similar results in thyroid inflammation and cancer. Therefore, it would appear to be difficult to obtain clear results from the measurement of these markers in the differentiation of cancer from inflammatory events.

## Conclusion

Because the PLR and NLR are routinely used and calculable biomarkers, they can be easily measured and are highly reproducible. This makes them optimal tools in the prognosis and assessment of thyroid-related events. In the present study, these two promising biomarkers showed similar results in thyroid inflammation and cancer. It would appear to be difficult to obtain clear results from the measurement of these markers in

the differentiation of cancer from inflammatory events; therefore, they might be useful as supportive or warning markers, not diagnostic markers, for thyroid papillary cancer or inflammation.

## Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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