Review Article

Association between blood inflammatory indicators and prognosis of papillary thyroid carcinoma: a narrative review

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Background and Objective: Papillary thyroid carcinoma (PTC) is the most common subtype of thyroid cancer, accounting for up to 85–90% of cases, with the best overall prognosis and mostly inert tumors. However, some tumors are aggressive, causing metastasis, recurrence, and other bad outcomes. Preoperative inflammation indices, such as lymphocyte-to-monocyte ratio (LMR), neutrophil-to-lymphocyte ratio (NLR), and systemic immune inflammation index (SII) in peripheral blood, have recently gained attention as nonspecific markers of inflammatory response in thyroid. In this study, we reviewed the interactions between preoperative inflammatory factors and outcomes in patients with PTC.

Methods: This is a narrative review. We searched for English articles published between January 2014 and December 2023 on PubMed and Web of Science to identify how do these blood indicators affect the prognosis of patients with papillary thyroid cancer.

Key Content and Findings: All retrievable indicators that have predictive significance for the prognosis of PTC were included, and the prognosis mainly included tumor-node-metastasis (TNM) staging, survival rate, recurrence, clinical and pathological risk factors such as lymph node metastasis (LNM), etc. From the general evidence, the prognostic predictive value of cell count alone was unknown, and low LMR was usually associated with poor prognosis, high NLR and high platelet-to-lymphocyte ratio (PLR) usually indicated poor prognosis.

Conclusions: These minimally invasive, low-cost, and easily obtainable blood indicators provide convenience for precise prognosis management of PTC patients, but many of the findings are conflicting and need to be validated by prospective studies that are more multi-sample, multi-centre and incorporate factors such as age that affect the immune response.

Keywords: Inflammation indices; papillary thyroid carcinoma (PTC); prognosis; metastasis

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Introduction

Background

Thyroid cancer is the most frequently occurring tumour in the head and neck region, ranking ninth in terms of tumor incidence in 2020. The global incidence for females is 10.1 per 100,000, which is roughly thrice the rate for males (1). In China, the occurrence of thyroid cancer markedly increased between 2000 and 2016, with approximately 202,600 new cases of thyroid cancer in 2016. The overall age-standardized incidence rate according to the World Standardized Population was $10.37/10^5$, with the standardized incidence rate of $5.11/10^5$ and $15.81/10^5$ for males and females, respectively (2). Of all thyroid cancers, papillary thyroid carcinoma (PTC) is the most commonly occurring subtype, constituting 85–90% of the thyroid cancer cases (3); moreover, it has the best prognosis. PTC demonstrates inert behavior, relatively low disease-specific mortality, early lymph node metastasis (LNM), and local and distant recurrences. Approximately 37% of patients with PTC have cancer cells that metastasize to the perithyroidal lymph nodes (4), including central and lateral lymph nodes; this is an essential prognosis indicator of PTC and an eminent risk indicator for high recurrence rates and poor survival (5).

Accurate prognostic assessment is important for treatment planning and longitudinal management of patients with PTC. It not only affects the selection of treatment strategies, such as surgery, radiotherapy, drug therapy, or combination therapy, but also relates to the long-term prediction of disease progression and quality of life. Nowadays, with personalized medicine receiving increasing attention, a precise prognostic assessment for each patient is crucial.

Objectives

Inflammation indicators, particularly hematologic components implicated in the holistic inflammatory response, have predictive significance in various malignancies. Inflammatory mediators in the blood include neutrophils, lymphocytes, monocytes, and platelets. Further calculations generated composite indicators, such as the lymphocyte-to-monocyte ratio (LMR), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune inflammation index (SII). It is generally accepted that lymphocytes are a fundamental component of the immune system, serving as the cellular basis for immunosurveillance and immunoediting, and acting as anti-tumour agents. While the role of monocytes in cancer is controversial, macrophages are distinct from monocytes and both pro- and anti-cancer potentials of monocytes/macrophages have been identified. Tumour-associated macrophages (TAMs) are classified according to their function as classical M1-type and alternative M2-type, with M1-macrophages involved in inflammatory responses, pathogen clearance and anti-tumour immunity, and M2-macrophages influencing anti-inflammatory responses, wound healing and possessing pro-tumourigenic properties (6). Tumour-associated neutrophils (TANs) are similar to monocytes, with N1 anti-tumour and N2 pro-tumour types, and in untreated tumours, N2-neutrophils support tumour growth through angiogenic factors and stromal degrading enzymes that promote the acquisition of a metastatic phenotype and suppress anti-tumour immunity (7-9), yet, upon blockade of the transforming growth factor-β (TGF-β) pathway or upon immune or cytokine activation, N1- neutrophils are generated with tumour cell killing and growth inhibiting potentials (10-12). Platelets participate in tumorigenesis through production of inflammation-promoting cytokines, such as vascular endothelial growth factor, tumor necrosis factor-alpha (TNF-α), interleukin-2 (IL-2), IL-6, and IL-10 (6).

The abovementioned indicators have become a topic of research interest in the field of thyroid cancer; these indicators are expected to predict the invasive clinical pathological characteristics, survival rate, and recurrence of patients with PTC. However, the role of these indicators in thyroid cancer has not been clarified, and there have been conflicting reports about their predictive significance for the prognosis of PTC. For this reason, this article reviewed the association between preoperative inflammatory indicators and the prognosis of papillary thyroid cancer. We present this article in accordance with the Narrative Review reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-24-72/rc).

Methods

This review was performed on PubMed and Web of Science database. Articles between January 2014 and December 2023 were searched. The search string was as follows: ((papillary thyroid carcinoma) OR (thyroid tumor) OR (thyroid papillary carcinoma)) AND ((blood immune indexes) OR (systemic immune inflammation index) OR (lymphocyte-to-monocyte ratio) OR (neutrophil-

Table 1 The search strategy summary

Items	Specification
Date of search	December 4th, 2023
Databases and other sources searched	PubMed, Web of Science
Search terms used	1#: (papillary thyroid carcinoma) OR (thyroid tumor) OR (thyroid papillary carcinoma) 2#: (blood immune indexes) OR (SII) OR (LMR) OR (NLR) OR (PLR) OR (FIB) OR (MPV) OR (PNI) OR (GLR) 3#: (prognosis) OR (recurrence) OR (survival) OR (lymph node metastasis) OR (stage) 4#: Review[Publication Type] Final search formula: 1# AND 2# AND 3# NOT 4#
Timeframe	January 2014–December 2023
Inclusion and exclusion criteria	We focused on English-language literature, and review literature was eliminated in all languages
Selection process	Selected by the principal authors (Y.C. and L.Z.)

SII, systemic immune inflammation index; LMR, lymphocyte-to-monocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; MPV, mean platelet volume; PNI, prognostic nutritional index; GLR, glucose-to-lymphocyte ratio.

to-lymphocyte ratio) OR (platelet-to-lymphocyte ratio) OR (FIB) OR (mean platelet volume) OR (prognostic nutritional index) OR (glucose-to-lymphocyte ratio)) AND ((prognosis) OR (recurrence) OR (survival) OR (lymph node metastasis) OR (stage)) NOT (Review[Publication Type]). As inclusion criteria, articles must provide a correlation analysis between preoperative blood indicators and the prognosis of patients with PTC. Some of the articles were excluded due to irrelevance to the topic in question, such as using blood indicators to distinguish between benign and malignant nodules. For summary of search strategy see *Table 1*.

Peripheral blood inflammation indicators

Cell count

Lymphocyte and neutrophil counts

In general, tumor infiltration of lymphocytes indicates an efficacious anti-tumour cells immune response and an increase in their infiltration has been linked to a better prognosis. Conversely, a decrease in lymphocytes signifies a generalised state of immunosuppression and compromised innate cellular immunity to malignant tumours, which worsens the prognosis (13).

Wen *et al.* (14) retrospectively analyzed 558 patients with PTC, 82 of whom were aged ≥55 years, and conducted univariate and multivariate analyses as well as receiver operating characteristic (ROC) study and revealed that in patients with PTC aged ≥55 years, elevated neutrophils were a predictive factor for bilateral and LNM, and elevated lymphocytes were a prognostic factor for advanced tumor-node-metastasis (TNM) staging. Liu *et al.* (15) revealed higher lymphocyte counts in patients aged <45 years compared to those aged ≥45 years with PTC as well as lower lymphocyte counts in clinical stage III/IV compared to patients with stage I/II PTC.

The two studies appeared contradictory regarding the correlation between lymphocytes and staging. On the one hand, it might be because the study by Wen *et al.* (14) used the revised differentiated thyroid cancer (DTC)-TNM staging system of American Joint Committee on Cancer (AJCC), in which the cut-off age for predicting mortality was increased from 45 to 55 years, and the effects of tumor size and LNM on staging were significantly decreased, thereby decreasing some patients' TNM staging (e.g., stage III T3N0M0, T1–3N1aM0, and stage IVA T1–3N1bM0 in the seventh edition staging were classified as stage II in the eighth edition). On the other hand, the complex role of lymphocytes in PTC remains unclear, and some studies have indicated that an increase in the number of lymphocytes facilitates the aggressive behavior of the tumor (16,17).

Platelet count (PLT)

Liu *et al.* (18) revealed that patients with a low PLT had a high risk of poor prognosis group (PPG) [by the Guidelines of 2015 American Thyroid Association (ATA), patients' response to treatment was divided into two groups: the 'good prognosis group (GPG)' and the 'PPG']. However, both the

odd ratio (OR) and 95% confidence intervals (CIs) were too close to 1; thus, the statistical difference was not clinically significant. Subsequently, patients were categorized into two groups by a PLT of 302×10^9/L, and the analyses revealed that patients with PLT $\leq302\times10^9$/L had a higher incidence of PPG. It was consequently concluded that the lower PLT group had a poorer outlook.

In general, platelets are considered to promote tumorigenesis, whereas in the present study, we achieved the opposite result in PTC. This may be because platelets synthesize, store, and release platelet-derived growth factor, which influences tumor cell radiosensitivity, especially because some patients with PTC received radioactive iodine (RAI) therapy postoperatively, and the reduced radiosensitivity caused resistance to RAI therapy, resonating with a poor prognosis (3).

LMR

Wen *et al.* (14) revealed an elevated LMR as a predictor of advanced TNM staging. Advanced (stages III–IV) was defined as patients with PTC aged ≥55 years and who fulfilled T4a/4b or M1. Additionally, logistic regression modeling indicated that an LMR of ≥5.45 was an independent risk factor for advanced TNM.

However, low LMR appears to be associated with a poorer prognosis. A study by Yokota *et al.* (19) revealed that preoperative low LMR in patients with PTC effectively predicted recurrence. Multivariate analysis revealed that low LMR independently predicted a poorer prognosis. Furthermore, low LMR was significantly associated with recurrence, especially in patients with advanced PTC. Kim *et al.* (20) determined that high LMR was prominently associated with prolonged recurrence-free survival (RFS) in low-intermediate-risk PTC. Multifactorial analysis revealed low LMR as an independent prognostic marker for worsening RFS in patients with PTC. Moreover, lower LMR was associated with more aggressive clinicopathological features (tumor size, LNM, multifocal PTC, and advanced N/M stage), whereas higher LMR was associated with significantly better overall survival (OS), PTC-free survival, and lower risk of recurrence in patients with PTC. Song *et al.* (21), Zhou *et al.* (22), Huang *et al.* (23), and Li *et al.* (24) retrospectively analyzed inflammatory indices in 212 patients with a postoperative diagnosis of intermediate- to high-risk PTC and revealed that LMR predicted peritumoral infiltration, although the actual mechanism is unknown at this time. Possible contributing factors include that circulating monocytes could develop into TAMs and myeloid-derived suppressor cells, which promote tumour cell proliferation, infiltration and transfer by hastening the transformation between the epithelium and the mesenchyme, whereas lymphocytes can promote the release of cytotoxic substances, for instance, perforin, as well as a variety of inflammatory mediators which exert anti-tumour effects (25-27).

In summary, most studies have concluded that a lower preoperative LMR in patients with PTC is associated with poorer outcome indicators such as recurrence, reduced survival, and aggressive clinicopathologic features, whereas a higher LMR portends a better prognosis.

NLR

Kim *et al.* (28) revealed that patients with stage III or IV PTC who had an NLR of ≥1.5 demonstrated significantly lower 5-year disease-free survival (DFS) than those with an NLR of <1.5. The model in this study suggests that a higher NLR is independently associated with a poorer prognosis and is a marker of poorer DFS in patients with PTC, especially in advanced stages. Gong *et al.* (29) demonstrated higher NLR in patients with PTC with LNMs, large tumors, and multifocal lesions. A higher number of patients with advanced TNM stage was reported in the high NLR group than in the low NLR group for patients aged ≥45 years. Linear regression analysis revealed a positive correlation between preoperative NLR and AJCC-TNM stage.

He *et al.* (30) revealed a high preoperative NLR level as an independent predictor of central LNM in patients with PTC and type 2 diabetes. Chae *et al.* (31) reported high NLR as an independent predictor of LNM in the lateral neck region. Analogously, Huang *et al.* (23), and Han *et al.* (32) revealed that high preoperative NLR was associated with a high risk of recurrence in patients with PTC.

Oba *et al.* (33) revealed that NLR may reflect the proportion of poorly differentiated components (PDCs), with the PTC group containing ≥50% PDCs having a significantly higher NLR than the pure PTC and PTC containing <50% PDC groups. In addition, the ≥50% PDC group was more aggressive than the other two groups.

In summary, several studies have reported that a high preoperative NLR predicts PTC progression and is correlated with a poor prognosis. This may be due to activated neutrophils stimulating tumour growth.

Some studies reported negative results, such as Lang *et al.* (34) who revealed that although higher NLRs may imply poorer tumour characteristics, it was not strongly related to poorer DFS or higher risk of occult central LNM in cN0 PTCs. One possible explanation for this is that the prognosis for cN0 PTC is usually quite promising, and thus its NLR is anticipated to be in the lower region. Kim *et al.* (35) indicated that NLR may not be a predictor of clinical aggressiveness or prognosis in PTC patients with LNM. Shin *et al.* (36) revealed that NLR was not relevant to DFS in PTC.

However, Chen *et al.* (37) revealed that a reduced NLR predicted recurrence, and an NLR of ≤1.6 was an independent predictor of recurrence. This may be because of the significantly lower NLR values for PTC than those for most other tumors as well as the relatively weak association between inflammation and PTC. In addition, the OR value (1.596) of NLR for predicting recurrence was relatively low, and the specificity (46.9%) and sensitivity (63.4%) were unsatisfactory.

PLR

Huang *et al.* (23) revealed that PLR was closely associated with aggressive clinicopathologic features of PTC [e.g., tumor size, lesion (unifocal or multifocal), LNM, and LNM rate] and postoperative recurrence. The higher the PLR value, the higher the risk of recurrence. Lee *et al.* (38) similarly concluded that a high PLR for PTC in group Y [patients in this research were divided into two groups based on their age: Y-group (age <45 years) and O-group (age ≥45 years)] was an independent predictor of disease recurrence. Kim *et al.* (39) revealed that high preoperative PLR was significantly associated with lateral LNM in female patients with PTC. Similar results have been widely reported in other cancers, such as hepatocellular carcinoma (40) and ovarian cancer (41). High PLR is associated with invasive lesions and negative prognostic effects (such as decreased survival rate and recurrence).

However, Li *et al.* (24) concluded that a PLR of ≤128.1 was a potential independent risk factor for the recurrence of intermediate- to high-risk PTC, where more specifically, patients with a PLR ≤128.1 had almost 3 times the risk of recurrence than patients with a PLR >128.1.

SII

Zhao *et al.* (42) revealed tumor diameter and preoperative SII as independent risk factors for lateral LNM in patients with PTC based on the results of univariate and multivariate logistic regression analyses. SII was calculated as PLT × neutrophil count/lymphocyte count. Zhang *et al.* (43) revealed that age, gender, tumor location, and SII levels were independently associated with central LNM in patients with cN0 PTC based on the results of univariate and multivariate analyses.

Platelet-related markers: mean platelet volume (MPV) and platelet distribution width (PDW)

In recent years, it has been reported that platelet volume is more tightly linked to platelet mobilisations than platelet number (14). MPV suggests the rate and spurs of platelet production. Several studies revealed that larger platelets appear to have higher metabolic and enzymatic activity than smaller platelets (44). Hence, the crucial role of MPV in tumor assessment has been increasingly emphasized.

Wen *et al.* (14) revealed that lower MPV and PDW were prognostic factors for the coexistence of PTC and Hashimoto's thyroiditis. Lower MPV and PDW may be protective indicators in older (≥55 years) patients with PTC. Li *et al.* (24) revealed that MPV predicted a maximum lymph node size of ≥1 cm in intermediate- to high-risk PTC, and MPV of >9.4 was significantly associated with recurrence. While a study of 158 PTC patients by Yu *et al.* (45) found no correlation between MPV and PDW with TNM stage, LNM and distant metastasis in PTC patients.

Fibrinogen (FIB)

The coagulation and fibrinolytic systems are usually impaired in patients with PTC, with FIB being the most abundant coagulation factor in plasma. Thus, there is a rationale for FIB being tapped as a tumour indicator in patients with PTC.

Li *et al.* (24) revealed that FIB was predictive of LNM in intermediate- to high-risk PTC, and FIB of ≤2.6 and peritoneal invasion were identified as independent risk factors for LNM by multivariate analysis.

Glucose-to-lymphocyte ratio (GLR)

Diabetes mellitus is known to be closely associated with cancer because it causes increased mortality in patients with cancer, and hyperglycemic states might impair the duration of survival and outcomes in cancer patients (46). Jin *et al.* (47)

revealed that a high preoperative GLR was an independent predictor of LNM in the central region in patients with PTC accompanied by type 2 diabetes.

Prognostic nutritional index (PNI)

PNI was calculated as 10 × albumin (g/dL) + 0.005 × lymphocyte count. Chen *et al.* (37) revealed that reduced PNI predicted advanced TNM staging, and PNI of ≤53.1 was an independent predictor of relapse.

Albumin-to-globulin ratio (AGR)

Huang *et al.* (23) revealed that AGR was closely associated with aggressive clinicopathological features (e.g., tumor size, lesions, LNM, and LNM rate) and postoperative recurrence. The higher the AGR value, the lower the risk of recurrence.

Conclusions

In the field of research and clinical practice in the prognostic assessment of thyroid cancer, the importance of serum markers, especially immune/inflammation-related markers, has become clear. These indicators reflect the immune and inflammatory status of the tumor microenvironment, which is strongly correlated with patient prognosis, thereby emphasizing the important role of immunomodulation in thyroid cancer development. Traditional methods of prognostic assessment, including TNM staging and clinicopathologic features, have limitations in revealing the biological properties of tumors and the immune microenvironment despite playing a pivotal role in clinical applications, thereby highlighting the complementary value of serum indices.

In our opinion, the predictive value of a single cell count is hardly certain. The immune profile of a tumour patient is influenced by a multitude of circumstances, and different mechanisms of the same immune cells, as well as different typologies, can alter the effect on the tumour. Analysed from mainstream research findings, low LMR may be caused by a decrease in lymphocytes due to immunocompromise or by an increase in monocytes in the peripheral circulation, which reflects increased tissue macrophage production and is a surrogate marker of high tumour burden. In general, low LMR is associated with a poor prognosis. High NLR reflects a high number of neutrophils or a low number of lymphocytes, with increased N2-neutrophils promoting tumourigenesis and metastasis, and fewer lymphocytes representing impaired immune function, so a high NLR typically indicates a poor prognosis. Analogously, high PLR is caused by high PLTs and/or low lymphocyte counts, and the pro-carcinogenic effect of high platelets suggests that high PLR is correlated with a poor prognosis. The remaining indicators such as SII, MPV, and PDW may not yet suggest contradictory results due to insufficient research, and their conclusions need to be verified by larger sample studies.

The prognostic significance of various blood indices in PTC is not entirely consistent across studies, and until this problem is resolved, the beautiful vision of using inexpensive, minimally invasive, and conveniently available preoperative blood indices as predictors of PTC prognosis, and thus helping patients with PTC to make accurate prognostic assessments and formulate individualised treatment plans, would be difficult to achieve in the field. Possible reasons for the contradictory study outcomes include, first, lack of sufficient sample size and insufficient follow-up time in previous studies, and the fact that patients with PTC rarely relapse and die, requiring larger samples and longer follow-up time to assess the effect of various blood markers on the prognosis of PTC. Second, differences in the statistical methods applied, and in the cut-off values of the blood indicators are also possible influencing factors. Third, some of the studies did not take into account changes in the immune system due to age, and the prognostic value of blood markers may change with age. When patients are grouped by age, the blood markers that have more prognostic value may be different for different age groups, and the same marker may even have opposite prognostic effects for different age groups. For example, in a study by Lee *et al.* (38), for PTC aged ≥45 years, NLR was an independent risk factor for DFS, higher NLR was associated with a poor prognosis, whereas for patients <45 years of age there was a trend towards a better prognosis for higher NLR, but there was no statistically significant difference, and PLR was an independent predictor of DFS in younger patients. In the 8th edition of the AJCC-TNM staging guidelines, the age cut-off point was raised from 45 to 55 years. Further prospective studies with larger sample sizes, longer follow-up times, more centres, and including age as an influencing factor, are expected to explore the predictive significance of various haematological-immunological markers on the prognosis of PTC and thereby minimise the heterogeneity of the results of the studies, for instance, by using 55 years

as a threshold subgroup.

In recent years, there are no unique reviews and meta-analyses in the field related to this study, such as the systematic review by Detopoulou *et al.* (48) published in March 2023, which showed that MPV was associated with cardiovascular complications in patients with thyroid tumours, and lower MPV was associated with metastasis, which lacked a breakdown of the types of thyroid tumours, and the summaries were too general, with even some ambiguities with the conclusions of the original study. Russo *et al.* (49), published in October 2023, included 12 studies with a total of 7,599 patients with DTC and conducted a meta-analysis of the relationship between preoperative blood levels of NLR, LMR, and PLR with DFS, which revealed that no significant correlation was found between these three blood markers and DFS. Our study explored the prognostic value of a more comprehensive set of blood markers, but it cannot be denied that we lacked the statistical tools to analyse them in a more scientific manner, making it difficult to arrive at a definitive result. In future studies, it is important to pay attention to the changing trend of immune response, bringing influencing factors such as age and stage into consideration, and selecting individualised immune prediction markers. In addition to the above blood indices, changes in various immune cell subpopulations in the blood can be further investigated, as well as further studies on the association between immune-related cells outside the blood and the prognosis of thyroid tumours, such as the immune cells within the tumour tissue, the immune cells in the normal tissues surrounding the tumour tissues and the various proportionality changes, etc., which can then guide the post-surgical treatment plan. Research should focus on improving the accuracy and clinical applicability of serum indices, including the development of precise detection techniques and construction of comprehensive multiparameter assessment models, on a prospective basis. In terms of individualization and dynamic monitoring, adapting to personalized needs will be crucial in the treatment and management of PTC. Considering all these findings, future research should focus on significantly improving the accuracy of prognostic assessment and effectiveness of clinical management of patients with thyroid cancer.

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Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-24-72/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-24-72/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71:209-49.
2. Zheng R, Zhang S, Zeng H, et al. Cancer incidence and mortality in China, 2016. J Natl Cancer Cent 2022;2:1-9.
3. Cabanillas ME, McFadden DG, Durante C. Thyroid cancer. Lancet 2016;388:2783-95.
4. Mao J, Zhang Q, Zhang H, et al. Risk Factors for Lymph Node Metastasis in Papillary Thyroid Carcinoma: A Systematic Review and Meta-Analysis. Front Endocrinol (Lausanne) 2020;11:265.

5. Zhao Q, Ming J, Liu C, et al. Multifocality and total tumor diameter predict central neck lymph node metastases in papillary thyroid microcarcinoma. Ann Surg Oncol 2013;20:746-52.
6. Chanmee T, Ontong P, Konno K, et al. Tumor-associated macrophages as major players in the tumor microenvironment. Cancers (Basel) 2014;6:1670-90.
7. Tazawa H, Okada F, Kobayashi T, et al. Infiltration of neutrophils is required for acquisition of metastatic phenotype of benign murine fibrosarcoma cells: implication of inflammation-associated carcinogenesis and tumor progression. Am J Pathol 2003;163:2221-32.
8. Pekarek LA, Starr BA, Toledano AY, et al. Inhibition of tumor growth by elimination of granulocytes. J Exp Med 1995;181:435-40.
9. Shojaei F, Singh M, Thompson JD, et al. Role of Bv8 in neutrophil-dependent angiogenesis in a transgenic model of cancer progression. Proc Natl Acad Sci U S A 2008;105:2640-5.
10. van Gisbergen KP, Geijtenbeek TB, van Kooyk Y. Close encounters of neutrophils and DCs. Trends Immunol 2005;26:626-31.
11. Di Carlo E, Forni G, Lollini P, et al. The intriguing role of polymorphonuclear neutrophils in antitumor reactions. Blood 2001;97:339-45.
12. Hicks AM, Riedlinger G, Willingham MC, et al. Transferable anticancer innate immunity in spontaneous regression/complete resistance mice. Proc Natl Acad Sci U S A 2006;103:7753-8.
13. Yamanaka T, Matsumoto S, Teramukai S, et al. The baseline ratio of neutrophils to lymphocytes is associated with patient prognosis in advanced gastric cancer. Oncology 2007;73:215-20.
14. Wen W, Wu P, Li J, et al. Predictive values of the selected inflammatory index in elderly patients with papillary thyroid cancer. J Transl Med 2018;16:261.
15. Liu J, Du J, Fan J, et al. The Neutrophil-to-Lymphocyte Ratio Correlates with Age in Patients with Papillary Thyroid Carcinoma. ORL J Otorhinolaryngol Relat Spec 2015;77:109-16.
16. Qing W, Fang WY, Ye L, et al. Density of tumor-associated macrophages correlates with lymph node metastasis in papillary thyroid carcinoma. Thyroid 2012;22:905-10.
17. Yu H, Huang X, Liu X, et al. Regulatory T cells and plasmacytoid dendritic cells contribute to the immune escape of papillary thyroid cancer coexisting with multinodular non-toxic goiter. Endocrine 2013;44:172-81.
18. Liu X, Huang Z, He X, et al. Blood prognostic predictors of treatment response for patients with papillary thyroid cancer. Biosci Rep 2020;40:BSR20202544.
19. Yokota M, Katoh H, Nishimiya H, et al. Lymphocyte-Monocyte Ratio Significantly Predicts Recurrence in Papillary Thyroid Cancer. J Surg Res 2020;246:535-43.
20. Kim K, Pak K, Kim IJ, et al. Lymphocyte-to-monocyte ratio prior to radioiodine ablation in low- and intermediate-risk, papillary thyroid cancer. Endocrine 2020;70:364-71.
21. Song L, Zhu J, Li Z, et al. The prognostic value of the lymphocyte-to-monocyte ratio for high-risk papillary thyroid carcinoma. Cancer Manag Res 2019;11:8451-62.
22. Zhou C, Duan D, Liu S. Predictive Value of a Prognostic Model Based on Lymphocyte-to-Monocyte Ratio Before Radioiodine Therapy for Recurrence of Papillary Thyroid Carcinoma. Technol Cancer Res Treat 2021;20:15330338211027910.
23. Huang Y, Liu Y, Mo G, et al. Inflammation Markers Have Important Value in Predicting Relapse in Patients with papillary thyroid carcinoma: A Long-Term Follow-Up Retrospective Study. Cancer Control 2022;29:10732748221115236.
24. Li C, Li J, Li S, et al. Prognostic significance of inflammatory markers LMR, PLR, MPV, FIB in intermediate-and high-risk papillary thyroid carcinoma. Front Endocrinol (Lausanne) 2022;13:984157.
25. Katoh H, Watanabe M. Myeloid-Derived Suppressor Cells and Therapeutic Strategies in Cancer. Mediators Inflamm 2015;2015:159269.
26. Marvel D, Gabrilovich DI. Myeloid-derived suppressor cells in the tumor microenvironment: expect the unexpected. J Clin Invest 2015;125:3356-64.
27. Thibodeau J, Bourgeois-Daigneault MC, Lapointe R. Targeting the MHC Class II antigen presentation pathway in cancer immunotherapy. Oncoimmunology 2012;1:908-16.
28. Kim JY, Park T, Jeong SH, et al. Prognostic importance of baseline neutrophil to lymphocyte ratio in patients with advanced papillary thyroid carcinomas. Endocrine 2014;46:526-31.
29. Gong W, Yang S, Yang X, et al. Blood preoperative neutrophil-to-lymphocyte ratio is correlated with TNM stage in patients with papillary thyroid cancer. Clinics (Sao Paulo) 2016;71:311-4.
30. He C, Lu Y, Wang B, et al. Development and Validation of a Nomogram for Preoperative Prediction of Central Compartment Lymph Node Metastasis in Patients with

Papillary Thyroid Carcinoma and Type 2 Diabetes Mellitus. Cancer Manag Res 2021;13:2499-513.
31. Chae IH, Kim EK, Moon HJ, et al. Preoperative High Neutrophil-Lymphocyte Ratio May Be Associated with Lateral Lymph Node Metastasis in Patients with Papillary Thyroid Cancers. Int J Thyroidol 2018;11:41-8.
32. Han SW, Kang SY, Kim SK, et al. Clinical Significance of Blood Neutrophil-to-Lymphocyte Ratio in Patients with Papillary Thyroid Carcinoma. Korean J Endocr Surg 2014;14:184-9.
33. Oba T, Maeno K, Kiyosawa N, et al. Neutrophil-to-Lymphocyte Ratio Is Associated With the Proportion of Poorly Differentiated Components in Papillary Thyroid Carcinoma. J Surg Res 2023;287:47-54.
34. Lang BH, Ng CP, Au KB, et al. Does preoperative neutrophil lymphocyte ratio predict risk of recurrence and occult central nodal metastasis in papillary thyroid carcinoma? World J Surg 2014;38:2605-12.
35. Kim HB, Lee HS, Kim SW, et al. Clinical Value of Blood Neutrophil to Lymphocyte Ratio in Patients with Papillary Thyroid Carcinoma with Neck Lymph Node Metastasis. International Journal of Thyroidology 2017;10:89-95.
36. Shin Y, Cho JY, Lee Y, et al. Clinical Meaning of Neutrophil-to-Lymphocyte Ratio (NLR)in Papillary Thyroid Carcinoma. Korean Journal of Endocrine Surgery 2016;16:31-5.
37. Chen W, Wei T, Li Z, et al. Association of the Preoperative Inflammation-Based Scores with TNM Stage and Recurrence in Patients with Papillary Thyroid Carcinoma: A Retrospective, Multicenter Analysis. Cancer Manag Res 2020;12:1809-18.
38. Lee KH, Seok EY, Kim EY, et al. Different prognostic values of individual hematologic parameters in papillary thyroid cancer due to age-related changes in immunity. Ann Surg Treat Res 2019;96:70-7.
39. Kim SM, Kim EH, Kim BH, et al. Association of the Preoperative Neutrophil-to-ymphocyte Count Ratio and Platelet-to-Lymphocyte Count Ratio with Clinicopathological Characteristics in Patients with Papillary Thyroid Cancer. Endocrinol Metab (Seoul) 2015;30:494-501.
40. Xia W, Ke Q, Wang Y, et al. Predictive value of pre-transplant platelet to lymphocyte ratio for hepatocellular carcinoma recurrence after liver transplantation. World J Surg Oncol 2015;13:60.
41. Ceran MU, Tasdemir U, Colak E, et al. Can complete blood count inflammatory parameters in epithelial ovarian cancer contribute to prognosis? - a survival analysis. J Ovarian Res 2019;12:16.
42. Zhao L, Zhou T, Zhang W, et al. Blood immune indexes can predict lateral lymph node metastasis of thyroid papillary carcinoma. Front Endocrinol (Lausanne) 2022;13:995630.
43. Zhang Z, Xia F, Wang W, et al. The systemic immune-inflammation index-based model is an effective biomarker on predicting central lymph node metastasis in clinically nodal-negative papillary thyroid carcinoma. Gland Surg 2021;10:1368-73.
44. Mangalpally KK, Siqueiros-Garcia A, Vaduganathan M, et al. Platelet activation patterns in platelet size sub-populations: differential responses to aspirin in vitro. J Thromb Thrombolysis 2010;30:251-62.
45. Yu YJ, Li N, Yun ZY, et al. Preoperative mean platelet volume and platelet distribution associated with thyroid cancer. Neoplasma 2017;64:594-8.
46. Barone BB, Yeh HC, Snyder CF, et al. Long-term all-cause mortality in cancer patients with preexisting diabetes mellitus: a systematic review and meta-analysis. JAMA 2008;300:2754-64.
47. Jin L, Zheng D, Mo D, et al. Glucose-to-Lymphocyte Ratio (GLR) as a Predictor of Preoperative Central Lymph Node Metastasis in Papillary Thyroid Cancer Patients With Type 2 Diabetes Mellitus and Construction of the Nomogram. Front Endocrinol (Lausanne) 2022;13:829009.
48. Detopoulou P, Panoutsopoulos GI, Mantoglou M, et al. Relation of Mean Platelet Volume (MPV) with Cancer: A Systematic Review with a Focus on Disease Outcome on Twelve Types of Cancer. Curr Oncol 2023;30:3391-420.
49. Russo E, Guizzardi M, Canali L, et al. Preoperative systemic inflammatory markers as prognostic factors in differentiated thyroid cancer: a systematic review and meta-analysis. Rev Endocr Metab Disord 2023;24:1205-16.

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