Radiation Oncology

REVIEW Open Access

Clinical implications of the serum platelet-to-lymphocyte ratio in the modern radiation oncology era: research update and literature review

Dong Soo Lee[1*]

Abstract
Radiation therapy (RT) continues to be the primary approach for treating cancer, and numerous cancer biomarkers associated with oncological outcomes have been investigated in the context of RT. The serum platelet-to-lymphocyte ratio (PLR) is one of the emerging landmark biomarker in the oncologic field. Mounting evidence indicates that an elevated serum PLR may function as a marker of unfavorable tumor characteristics, adverse treatment outcomes and treatment-related toxicities among individuals undergoing RT. However, the findings of these investigations have revealed a few disparities among researchers, highlighting the need for further meticulously planned studies to draw conclusive results. This article provides a comprehensive literature review and in-depth discussion regarding the clinical implications of the serum PLR in the modern RT era.

Keywords Biomarker, Cancer, Platelet-to-lymphocyte ratio, Radiation therapy

Introduction

Radiation therapy (RT) has been the cornerstone of numerous cancer treatments [1] since the discovery of its biological efficacy against cancer cells via a variety of mechanisms [2]. Moreover, the recent development of RT technologies has enabled the broad application and supply of RT equipment globally for cancer treatment [3–7].

There are a variety of indices and landmarks available for estimating the benefits and outcomes of RT [8–11]. Blood markers are commonly and regularly tested in cancer patients and have merits in their simplicity, cost-effectiveness, and repeatability [12, 13].

More recently, a number of inflammatory indices based on blood cells have been reported. The lymphocyte-to-monocyte ratio (LMR), neutrophil-to-lymphocyte ratio (NLR), platelet-to- lymphocyte ratio (PLR), and albumin-to-alkaline phosphatase ratio (AAR) are representative examples of widely studied blood inflammatory indices [14–17]. Inflammatory biomarkers are being rigorously investigated because the host immune system and cancer-related inflammation are believed to be linked to the progression and prognosis of a number of malignancies [18]. Furthermore, systemic immune and inflammatory cells, such as lymphocytes, monocytes, neutrophils, and platelets, are thought to play crucial roles in the development of cancer via multiple mechanisms [19, 20].

There is substantial evidence that platelets contribute to cancer development and metastasis [19]. A number of

*Correspondence:
Dong Soo Lee
dreamdoc77@catholic.ac.kr
[1]Department of Radiation Oncology, College of Medicine, The Catholic University of Korea, Seoul 06591, Republic of Korea

platelet-expressed proteins have been shown to be crucial for tumor spreading in experimental animal models, and platelets have also been implicated in the mechanisms that drive tumor angiogenesis [20–23]. In addition, platelets are considered to protect circulating tumor cells (CTCs) from antitumor immune responses and thereby promote CTC metastasis [12, 24]. Lymphocytes, a well-known type of blood cell, play a vital role in antitumor immune effects and inhibit tumor proliferation and migration [25]. The PLR can therefore serve as one of the primary markers of cancer outcomes.

A number of studies have examined the prognostic relevance of the PLR in different types of cancer [12, 19, 26–30]. However, as multimodal approaches are commonly used in cancer treatment, the role of the PLR in the population of patients who undergo RT has not been well studied. Similarly, during our literature search for this study, we also found that most of the related studies involved patients treated with a variety of management options [31–36]. The objective of this review is to summarize the PLR outcomes in different cancer cohorts of patients who underwent RT.

Summary of research investigating PLR according to cancer type

We examined the studies related to the PLR in patients with each type of cancer who underwent various therapeutic modalities including RT. The primary emphasis of the search for research articles was on RT as a treatment modality. However, the majority of cancer patients are treated using a combination of various approaches. Our aim in this review was to identify and include studies or articles from which important findings were reported and recently published.

Brain malignancies

Among brain tumors, primary radical resection is the most essential part of treatment, and studies have also included patients who underwent primary surgery and postoperative RT (PORT) in their treatment sequence. Yersal et al. [37] reported negative results for the PLR in glioblastoma patients. Treatment also varied considerably, and progression-free survival (PFS) and overall survival (OS) did not significantly differ according to the PLR. Gao et al. [38] analyzed 274 atypical meningioma patients. The preoperative PLR was significantly associated with PFS according to the receiver operating characteristic curve. The PLR, included in the risk model, was also significantly correlated with PFS in multivariate analysis. Hsu et al. [39] analyzed the results of 182 malignant glioma patients. A Post-RT PLR > 200 but not an intra-RT PLR > 200 was significantly associated with improved OS and PFS in multivariate analysis. A summary of the studies is shown in Table 1.

Breast malignancies

In an early study by Krenn-Pilko et al. [40], 793 nonmetastatic breast cancer patients were analyzed. In accordance with traditional treatment guidelines, most of the included patients underwent breast-conserving surgery and adjuvant RT. An increased preoperative PLR was significantly associated with decreased cause-specific survival (CSS) and OS in multivariate analysis. An increased PLR was significantly associated with the occurrence of distant metastases (DM) in univariate analysis. Although treatment methods and disease stages were heterogeneous because of the meta-analysis feature, a high PLR was associated with poor disease-free survival (DFS) and OS in the study by Zhang et al. [41]. A greater incidence of high PLR was noted in the stage II–IV subgroup than in the stage I subgroup. In addition, the incidence of high PLR was significantly different between the lymph node-positive and lymph node-negative groups and between the metastasis-positive and metastasis-negative groups. Although treatment types were not specified in detail, a lower PLR (≤210) correlated with a better DFS among patients with inflammatory breast cancer [29]. The results of these studies on breast cancer are summarized in Table 2.

Gastrointestinal malignancies

The PLR has been widely studied in various gastrointestinal (GI) malignancies. Like in other studies, an increased PLR was associated with inferior outcomes in most of

Table 1 PLR studies in brain malignancies

Year	Article	Total *N*	Study end-point(s)	Disease(s)	Treatment(s)	Important results
2018	Yersal et al. [37]	104	PFS, OS	Glioblastoma	S-> CRT/RT/CTx/No Tx	PFS and OS did not differ significantly according to PLR values
2021	Gao et al. [38]	274	PFS	Atypical Meningioma	S-> RT	Preop PLR was significantly associated with PFS (ROC analysis); PLR including risk score significantly correlated with PFS in multivariate analysis
2022	Hsu et al. [39]	182	OS, PFS	Malignant gliomas	S-> RT	Post-RT PLR > 200 was significantly associated with improved OS and PFS in multivariate analysis

PFS: Progression free survival; OS: Overall survival; S: Surgery; CRT: Chemoradiation therapy; RT: Radiation therapy; CTx: Chemotherapy; Tx: Treatment; PLR: Platelet to lymphocyte ratio; ROC: Receiver Operating Characteristic

Table 2 PLR studies in breast malignancies

Year	Article	Total *N*	Study end-point(s)	Disease(s)	Treatment(s)	Important results
2014	Krenn-Pilko et al. [40]	793	CSS, OS, DMFS	Breast ca.	BCS + RT (90%), MRM (10%)	The elevated preoperative PLR was significantly associated with CSS and OS in multivariate analysis; increased PLR showed a significant association with the occurrence of distant metastases in univariate analysis
2017	Zhang et al. [41]	5542 (12 studies)	DFS, OS	Breast ca.	Not specified	High PLR was associated with poor DFS and OS; higher incidence of high levels of PLR was noted in the stage II–IV group relative to the stage I group; the incidence of high levels of PLR was significantly different between the lymph node-positive and lymph node-negative groups and between the metastasis-positive and metastasis-negative group
2020	Van Berckelaer et al. [29]	127	RFS, DMFS, OS	Inflammatory breast ca.	Not specified except NACT	A lower PLR (≤ 210) was correlated with better RFS and DMFS; a high PLR was significantly associated with metastatic disease in multivariate analysis

CSS: Cause specific survival; OS: Overall survival; DMFS: Distant metastasis free survival; BCS: Breast conserving surgery; RT: Radiation therapy; MRM: Modified radical mastectomy; PLR: Platelet to lymphocyte ratio; DFS: Disease free survival; RFS: Relapse free survival; NACT: Neoadjuvant chemotherapy; DMFS: Distant metastasis free survival

these studies. Several types of study endpoints demonstrated a close relationship with the PLR. The major results of GI malignancy studies are summarized in Table 3.

In esophageal cancer, pathological tumor response, DFS, PFS and OS were the main study endpoints. The pretreatment and post-treatment PLR or the change in PLR was investigated. The pretreatment PLR was significantly correlated with lymph node (LN) and distant organ metastasis according to Wang et al. [42]. In contrast to most related studies, Tseng et al. [43] reported that an elevated PLR after treatment was associated with better disease-specific survival (DSS). Changes in the PLR have also shown prognostic significance in several studies [43–45]. A greater change in the PLR was associated with inferior DFS and OS in the studies by Khin et al. [44] and Zhang et al. [45], whereas an elevated PLR after treatment was associated with better DSS in the study by Tseng et al. [43]. Results indicating no correlation or statistical significance in only univariate analysis between PLR and study endpoints (OS and DFS) were also reported [46, 47]. Correlation between high PLR and worse pathological or clinical tumor response was also illustrated [28, 48].

In hepatocellular carcinoma (HCC), the baseline PLR (pretreatment), post-treatment PLR and change in PLR were also correlated with OS and intrahepatic relapse-free survival [12, 31, 49–51]. Lee et al. [12] reported that the highest post-treatment PLR was an independent prognostic indicator of distant control rates among patients who underwent curative intent trans-arterial chemoembolization followed by fractionated or stereotactic ablative RT. Post-treatment worsening (increase) of the PLR was significantly related to intrahepatic recurrence in Bae et al. [31]. The results of other studies on HCC are described in Table 3.

In rectal cancer, both positive and negative results have been described. In positive studies, a high PLR was significantly associated with worse outcomes with decreased OS and DFS [26, 52]. Lateral LN recurrence was also correlated with high PLR in the study by Miyakita et al. [53]. The relationship between tumor response and the PLR was also studied [54–56]. In studies with negative results, the PLR was not associated with OS, DFS or tumor response [54, 57]. The opposite results were also reported in relation to other studies, in which a high PLR was associated with a better prognosis (better OS) [33].

Genitourinary and gynecological malignancies

PLR studies also demonstrated similar results as other site malignancies in genitourinary and gynecological malignancies. In a large-scale study by Langsenlehner et al. [19], high pretreatment PLR (PLR ≥ 190) was independently associated with poor metastasis-free survival (HR = 2.24), CSS (HR = 3.99), and OS (HR = 1.87) in multivariate analysis among prostate cancer patients who underwent definitive RT. However, in Huszno et al. [58], pretreatment PLR was not associated with OS among prostate cancer cohorts comprised with patients who underwent RT or surgery. Cervix cancer was vigorously studied for PLR investigation in gynecological cancer. Meta-analysis by Ma et al. [34] has shown that elevated pretreatment PLR was significantly correlated with poor major study outcomes such as OS, DFS or PFS. The PLR was also meaningfully correlated with lymphovascular invasion, LN metastasis, large tumor size (> 4 cm) and high grade (G3) tumors. The results were statistically significant although the study population was mixed. Clinical response was also another significant end-point in Chauhan et al. [59] and high pretreatment PLR significantly associated with poor response. Statistically significant and independent inferior OS or PFS was reported resulting from high pretreatment PLR in other literatures

Table 3 PLR studies in gastrointestinal malignancies

Year	Article	Total *N*	Study end-point(s)	Disease(s)	Treatment(s)	Important results
2017	McLaren et al. [28]	60	pCR, OS	Esophageal ca.	nCRT-> S	Increased pretreatment PLR was the predictor of poor pCR; only pretreatment PLR was predictive of decreased OS in Cox model
2021	Khin et al. [44]	53	OS, PFS	Esophageal ca.	dCRT	PLR significantly increased after CRT; higher levels of PLR before and after CRT were associated with inferior OS; post-CRT PLR ≥ 420 had inferior OS and PFS compared to PLR < 420 in univariate analysis; greater increase in PLR (ΔPLR ≥ 230) after CRT was associated with inferior OS and PFS in univariate analysis
2021	Wang et el [42].	113	OS, PFS	Esophageal ca.	S only/CRT	Pretreatment PLR was significantly correlated with LN and distant organ metastasis; pretreatment PLR (> 183.06) was independently associated with poor OS or PFS in multivariate analysis
2022	Ran et al. [47]	80	OS, PFS	Esophageal ca.	dCRT	Pretreatment dichotomized PLR was not significantly correlated with OS or PFS
2022	Zhang et al. [45]	106	OS, DFS	Esophageal ca.	dCRT	The change of PLR (ΔPLR) was the independent prognostic factors in OS and DFS; higher ΔPLR was related to poor OS and DFS; high ΔPLR was associated with radiation pneumonitis
2022	Du et al. [46]	245	OS, PFS	Esophageal ca.	dCRT	Pretreatment PLR > 148 was associated with inferior OS in only univariate analysis
2022	Tseng et al. [43]	420	OS, DSS	Esophageal ca.	dCRT	Low levels of pretreatment PLR (< 375) was independently associated with better OS and DSS; elevated PLR after treatment had better DSS in univariate analysis
2023	Sun et al. [48]	353	cTR	Esophageal ca.	dCRT	High PLR was independently associated with worse RT tumor response
2021	Ajdari et al. [49]	89	LF, OS	HCC	SBRT for liver metastasis	Baseline PLR significantly associated with OS
2022	Li et al. [50]	309	OS	HCC	IMRT for unresectable HCC/TACE before IMRT (66%), resection (48.2%)	PLR significantly increased after IMRT; pre-PLR, post-PLR and delta-PLR were significantly associated with OS in univariate analysis
2022	Park et al. [51]	39	LC, OS, PFS	HCC	SBRT	PLR increased after SBRT, and decreased slowly to the pre-SBRT value at 6-months; the PLR change was significantly associated with OS in multivariate analysis; post-SBRT PLR > 90 was associated with poorer OS and PFS in univariate analysis
2022	Bae et al. [31]	4076	IHRFS, OS	HCC	LT/S/RFA/TACE + RFA/TACE + RT/RT	Pretreatment PLR and post-treatment worsening of PLR was independently associated with IHRFS; post-treatment worsening of PLR was significantly related to both early and late IHR
2023	Lee et al. [12]	76	OS, DC, LC, IHC	HCC	TACE/RT, RT	The highest post-treatment PLR was the independent prognostic indicator of DC rates; higher post-treatment PLR (> 235.7) was associated with poor DC rates
2018	Lee et al. [55]	297	pCR	Rectal ca.	nCRT-> S	PLR during CRT and change of PLR during CRT were the independent predictors of pCR in multivariate logistic regression
2021	Partl et al. [57]	363	Sphincter preserving surgery	Rectal ca.	nCRT-> S	PLR was not significantly associated with the type of surgery
2022	Miyakita et al. [53]	168	Lateral LN recurrence	Rectal ca.	nCRT-> S	High pre- and post-CRT PLR were significantly associated with lateral LN recurrence
2022	Ergen et al. [52]	53	pTR, DFS, OS	Rectal ca.	nCRT-> S	PLR was the significant prognostic factor for OS and DFS in ROC analysis; high PLR was significantly associated with poor OS and DFS in multivariate analysis
2022	Duque-Santana et al. [26]	100	pCR, DFS, OS	Rectal ca.	nCRT-> S	High pretreatment PLR (> 133) was the significant predictor of inferior DFS in multivariate analysis
2022	Huang et al. [33]	69	OS, DFS	Rectal ca.	nCRT-> S	The median OS was significantly higher among patients with a high post-CRT PLR than among those with a low post-CRT PLR

Table 3 (continued)

Year	Article	Total *N*	Study end-point(s)	Disease(s)	Treatment(s)	Important results
2022	Xu et al. [56]	205	pTR, OS, DFS	Rectal ca.	nCRT-> S	After propensity score matching, good response group displayed significantly lower pre-CRT PLR; there were no significant difference of post-CRT PLR according to response groups
2022	Chiloiro et al. [54]	808	pCR, OS, DFS	Rectal ca.	nCRT-> S	Pretreatment PLR was not associated with pCR, OS or DFS

pCR: Pathological complete response; OS: Overall survival; nCRT: Neoadjuvant chemoradiation therapy; S: Surgery; PLR: Platelet to lymphocyte ratio; PFS: Progression free survival; dCRT: Definitive chemoradiation therapy; LN: Lymph node; DFS: Disease free survival; DSS: Disease specific survival; cTR: Clinical tumor response; RT: Radiation therapy; LF: Local failure; HCC: Hepatocellular carcinoma; SBRT: Stereotactic body radiation therapy; IMRT: Intensity modulated radiation therapy; TACE: Transarterial chemoembolization; LC: Local control; IHRFS: Intrahepatic relapse free survival; LT: Liver transplantation; S: Surgery; RFA: Radiofrequency ablation; DC: Distant control; IHC: Intrahepatic control; pCR: Pathological complete response; nCRT: Neoadjuvant chemoradiation therapy; LN: Lymph node; pTR: Pathological tumor response; DFS: Disease free survival; ROC: Receiver operating characteristic

Table 4 PLR studies in genitourinary and gynecological malignancies

Year	Article	Total *N*	Study end-point(s)	Disease(s)	Treatment(s)	Important results
2015	Langsenlehner et al. [19]	374	MFS, CSS, OS, Biochemical DFS	Prostate ca.	RT	High pretreatment PLR (PLR ≥ 190) was associated with poor MFS, CSS and OS in multivariate analysis
2022	Huszno et al. [58]	152	OS	Prostate ca.	RT (81.6%)/S (13.8%)	Pretreatment PLR was not associated with OS
2018	Ma et al. [34]	3668 (12 studies)	OS, DFS, PFS	Cervix ca.	CRT, mixed, surgery	Elevated pretreatment PLR was significantly correlated with poor OS, DFS/PFS; elevated pretreatment PLR was highly correlated with lymphovascular invasion (+), lymph node metastasis (+), tumor size (> 4 cm), and grade (G3)
2022	Chauhan et al. [59]	90	Clinical response	Cervix ca.	CRT	High pretreatment PLR was significantly associated with poor response (AUC = 0.626)
2023	Gao et al. [27]	110	OS, PFS	Cervix ca.	RT	High pretreatment PLR (PLR > 187.88) was the independent risk factor for inferior OS; high PLR was associated with LN metastasis
2023	Li et al. [60]	795	OS	Cervix ca.	CRT	High pretreatment PLR (> 164.29) was independently associated with inferior OS

MFS: Metastasis free survival; CSS: Cause specific survival; OS: Overall survival; DFS: Disease free survival; RT: Radiation therapy; PLR: Platelet to lymphocyte ratio; S: Surgery; PFS: Progression free survival; CRT: Chemoradiation therapy; AUC: Area under the curve; LN: Lymph node

Table 5 PLR studies in hematological malignancies

Year	Article	Total *N*	Study end-point(s)	Disease(s)	Treatment(s)	Important results
2014	Wang et al. [61]	252	OS	Extranodal NK/T-cell lymphoma, nasal type	CRT/CTx/RT/No Tx	PLR significantly correlated with AAS, IPI, KPI and ALC; high PLR (> 185) was the independent prognostic factor of inferior OS, and PLR including prognostic model significantly predicted OS
2018	Reddy et al. [62]	338	FFP	Hodgkin lymphoma (classic type)	Unspecified	High pretreatment PLR was the independent prognostic factor of FFP in multivariate analysis
2023	Wen et al. [63]	183	PFS	MALT lymphoma	At least 1 antitumor therapy (S/RT/CTx /TT/Anti-HP therapy)	High pretreatment PLR (> 131.47) was the independent prognostic factor of PFS; PLR-based nomogram significantly predicted PFS

OS: Overall survival; NK: Natural killer; CRT: Chemoradiation therapy; CTx: Chemotherapy; RT: Radiation therapy; Tx: Treatment; PLR: Platelet to lymphocyte ratio; AAS: Ann arbor stage; IPI: International prognostic index; KPI: Korean prognostic index; ALC: Absolute lymphocyte count; FFP: Freedom from progression; PFS: Progression free survival; MALT: Mucosa-associated lymphoid tissue; S: Surgery; TT: Targeted therapy; HP: Helicobacter pylori

[27, 60]. The major study results of genitourinary and gynecological malignancies are summarized in Table 4.

Hematological malignancies

The PLR has not been broadly studied in hematological malignancies. In Wang et al. [61], the PLR was significantly correlated with various lymphoma staging systems and a high PLR was an independent prognostic factor for inferior OS in patients with extranodal NK/T-cell lymphoma. In Hodgkin and mucosa-associated lymphoid tissue (MALT) lymphoma, a high PLR was independently linked to worse outcomes [62, 63]. The study results for patients with hematological malignancies are summarized in Table 5.

Head and neck malignancies

The PLR was widely investigated in various types of head and neck malignancies. Nasopharyngeal, oropharyngeal and hypopharyngeal cancers were routinely treated with definitive RT and chemotherapy as known treatment guidelines. Upfront surgery was preceded in oral and salivary gland cancers. In meta-analysis published in 2020, 3459 patients were included among 9 nasopharyngeal cancer studies [30]. An increased pretreatment PLR predicted poor OS, PFS and DM free-survival (DMFS) in non-metastatic disease, whereas an increased PLR was not significantly associated with poor OS in patients with metastatic disease. A high PLR was significantly related to worse OS, PFS or DMFS in majority of the studies [30, 35, 64–67]. However, opposite [68] and negative results [69, 70] have also been reported. In 418 patients with salivary gland cancer by Yan et al. [67], a high PLR before PORT was significantly associated with worse DMFS in multivariate analysis, and PLR-based nomogram also conveyed accurate individual predictions of DMFS. In oral squamous cell cancers, a high preoperative PLR was associated with inferior DFS or OS [65, 71]. The summarized results are described in Table 6.

Lung malignancies

The PLR has also been extensively investigated in small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). In SCLC, a high PLR was associated with inferior OS or PFS in several studies [36, 72, 73], while no correlation was also reported [25, 74]. In NSCLC, a variety kind of study cohorts were enrolled in the studies. Pre- or mid-treatment PLR was correlated with OS or PFS [75, 76]. In early-stage NSCLC, low pretreatment PLR was significantly associated with superior non-local failure following stereotactic body radiation therapy (SBRT) [77]. Delikgoz Soykut et al. [75] described interaction between the PLR and loco-regional relapse free survival. Negative results with no correlation between the PLR and clinical outcomes were also depicted [25, 78]. Pavan et al. [79] explored tumor immune-milieu among patients with superior sulcus NSCLC who underwent conformal RT followed by surgery. CD68+tumor infiltrating immune cells were associated with a higher PLR and higher PLR values seemed to be linked with fewer residual viable tumor cells. However, the presurgical PLR was not associated with a radiological or metabolic response. The results are described in Table 7.

Table 6 PLR studies in head and neck malignancies

Year	Article	Total *N*	Study end-point(s)	Disease(s)	Treatment(s)	Important results
2018	Jiang et al. [69]	247	NPC	OS, PFS, DMFS, LRFS	(C)RT	Pretreatment PLR was significantly associated with T-stage and tumor stage; pretreatment PLR was not significantly associated with OS, PFS, DMFS and LRFS
2020	Tazeen et al. [71]	130	Oral ca.	DFS, OS	S, S-> RT/CTx/CRT	Preoperative high PLR (> 142) was the independent factor for DFS and OS
2020	Zhang et al. [30]	3459 (9 studies)	NPC	OS, PFS, DMFS	(C)RT	Increased pretreatment PLR predicted poor OS, PFS and DMFS in non-metastatic disease; increased PLR was not significantly associated with poor OS in patients with metastatic disease
2021	Chen et al. [68]	216	NPC	OS, RRFS, LRRFS, DMFS	(C)RT	Low pre-treatment PLR (≤ 140.065) remained significantly related to worse OS and DMFS
2021	Li et al. [64]	342	NPC	OS, PFS	(C)RT	High PLR (≥ 184.91) was significantly associated with poor OS and PFS
2021	Peng et al. [35]	1661	NPC	OS, PFS	(C)RT, CTx-> CRT, CRT-> CTx	High pretreatment PLR (> 157.14) was significantly associated with inferior OS and PFS; PLR-including risk score significantly predicted OS and PFS
2021	Staniewska et al. [70]	208	OPC	OS	(C)RT, CTx-> RT	Pretreatment PLR was not associated with OS
2022	Wan et al. [66]	103	HPC	OS, PFS	(C)RT, CTx-> RT	After PSM, high pretreatment PLR (≥ 133.06) was significantly associated with inferior OS, PFS and LF
2023	Yan et al. [67]	418	SGC	DMFS	S-> RT	Pre-PORT high PLR was significantly associated with worse DMFS in multivariate analysis; PLR-based nomogram presented accurate individual prediction of DMFS
2023	Liu et al. [65]	418	Oral ca.	OS	S-> RT and/or CTx	High preoperative PLR (> 135) was associated with inferior OS

NPC: Nasopharyngeal cancer; OS: Overall survival; PFS: Progression free survival; DMFS: Distant metastasis free survival; LRFS: Local relapse free survival; CRT: Chemoradiation therapy; PLR: Platelet to lymphocyte ratio; DFS: Disease free survival; S: Surgery; RT: Radiation therapy; CTx: Chemotherapy; RRFS: Regional recurrence free survival; LRRFS: Locoregional recurrence free survival; OPC: Oropharyngeal cancer; HPC: Hypopharyngeal cancer; PSM: Propensity score matching; LF: Local failure; SGC: Salivary gland cancer; PORT: Postoperative radiation therapy

Table 7 PLR studies in lung malignancies

Year	Article	Total *N*	Study end-point(s)	Disease(s)	Treatment(s)	Important results
2015	Cannon et al. [77]	149	OS, Nonlocal failure	ES-NSCLC	SBRT	Low pretreatment PLR (< 250) was significantly associated with superior nonlocal failure in multivariate analysis
2019	Suzuki et al. [72]	122	OS	LS-SCLC	(C)RT	High pretreatment PLR (≥ 140.1) was associated with inferior OS in multivariate analysis
2019	Zhang et al. [36]	286	OS, PFS	LS-SCLC	CTx, (C)RT, CTx-> RT, Surgery	High pretreatment PLR (> 152.1) was associated with inferior OS and PFS in multivariate analysis
2020	Xia et al. [76]	244	OS, PFS	LA-NSCLC	(C)RT	PLR 1-month after initiation was significantly associated with OS and PFS; 1-month PLR was associated with baseline count and mean body dose in multivariate analysis
2020	Yu et al. [73]	544	OS	LS-SCLC	CRT	Pretreatment PLR (continuous variable) was significantly correlated with OS in multivariate analysis; PLR-including model more accurately predicted OS than conventional model
2021	Qi et al. [74]	344	OS	LS-SCLC	CRT, CTx-> CRT	Pretreatment PLR was not significantly associated with OS
2022	Delikgoz Soykut et al. [75]	392	OS, PFS, LRRFS	LA-NSCLC	CRT	Low (< 166) pretreatment PLR was significantly associated with improved OS, PFS and LRRFS in multivariate analysis
2022	Abravan et al. [25]	2513	OS	NSCLC, SCLC	fRT, SBRT	Pretreatment PLR was not significantly associated with OS
2022	Pavan et al. [79]	8	TIIC, PD-L1-TPS, RVTC	SS-NSCLC	CRT-> S	CD68+-TIICs were associated with higher PLR; presurgery PLR was not linked to radiologic or metabolic response; higher PLR values seemed linked with lower RVTC
2022	Aduquaye et al. [78]	72	OS, RFS	ES-NSCLC	SBRT	Pretreatment PLR was not associated with RFS or OS in multivariate analysis

OS: Overall survival; ES-NSCLC: Early stage non-small cell lung cancer; SBRT: Stereotactic body radiation therapy; PLR: Platelet to lymphocyte ratio; LS-SCLC: Limited stage small cell lung cancer; CRT: Chemoradiation therapy; PFS: Progression free survival; CTx: Chemotherapy; RT: Radiation therapy; LA: Locally advanced; LRRFS: Locoregional relapse free survival; fRT: Fractionated radiation therapy; TIIC: Tumor immune infiltrating cell; PD-L1: Programmed death ligand 1;TPS: Tumor proportion score; RVTC: Residual viable tumor cells; SS: Superior sulcus; RFS: Relapse free survival

Soft tissue malignancies

The PLR was not studied well in soft tissue sarcomas. In the study by Fiore et al. [32], 423 patients with retroperitoneal sarcoma were examined who underwent preoperative RT or RT and chemotherapy. Prognostic index comprised with initial (pretreatment) PLR significantly discriminated OS and served as an available prognostic tool in that study. Tepper et al. [80] reported treatment outcomes of 86 patients with undifferentiated pleomorphic sarcoma (UPS). All included patients underwent resection of the UPS and RT was performed via by neoadjuvant or adjuvant sequence. A high pretreatment PLR was associated with worse OS in univariate analysis but not in multivariate analysis.

Toxicities

Notably, significant correlation between the PLR and treatment toxicity has been illustrated in several studies. Among 379 esophageal cancer patients who underwent chemoradiation treatment (CRT), Han et al. [81] reported that a high pretreatment PLR was an independent predictor of esophageal fistula, and a nomogram including the PLR significantly predicted esophageal fistula. Yang et al. [82] reported that an increased PLR during 3–4 weeks of RT was the independent indicator of symptomatic radiation pneumonitis among patients with esophageal cancer who underwent RT or CRT, and PLR-based nomogram also significantly predicted symptomatic radiation pneumonitis. In contrast, an increased 6-week PLR was associated with a decreased risk of radiation pneumonitis among patients with NSCLC in Huang et al. [83]. Radiation esophagitis was investigated by Qui et al. [84]. A high pretreatment PLR was the significant predictor of severe esophagitis among SCLC patients. Table 8 provides a summary of studies.

Discussion

Because of the variety of cancer types, treatment modalities, and timepoints of blood tests, consistent conclusions and results could not be drawn from the review of studies. Although we sought to include, examine and analyze RT-related studies in this review, cancer types treated by RT alone are confined to several diseases only, and most of the malignancies were managed with multidisciplinary and multimodal options. Therefore, we cannot arrive at concrete and constant conclusions from these studies. Multiple blood tests are repeatedly performed even within a short period of time for chronic diseases such as cancer. Accurate quantification of the timing of blood tests seems critical, but there is a possibility of variation among studies. However, despite this heterogeneity, we can focus on several concordant conclusions and results among studies. A summary of the clinical implications of the PLR is illustrated in Fig. 1.

Table 8 PLR studies related to treatment toxicities

Year	Article	Total *N*	Study end-point(s)	Disease(s)	Treatment(s)	Important results
2020	Han et al. [81]	379	EF	Esophageal ca.	CRT	High pretreatment PLR (> 153) was the independent factor of EF in multivariate analysis; PLR-based nomogram significantly predicted EF
2021	Yang et al. [82]	174	RP	Esophageal ca.	(C)RT	PLR (≥ 523.78) during 3–4 weeks of RT was the independent predictor of symptomatic RP in multivariate analysis; PLR including nomogram significantly predicted symptomatic RP
2022	Huang et al. [83]	84	OS, PFS, RP	NSCLC	(C)RT/(C)RT + durvalumab	Week 6 PLR ≥ 180 was associated with a lower risk of pneumonitis; week 6 PLR (continuous) was the independent indicator of PFS.
2022	Qui et al. [84]	187	Severe radiation esophagitis (≥ Gr2)	SCLC	(C)RT	Pretreatment high PLR (≥ 231.1) was the predictor of severe RE in univariate analysis only

CRT: Chemoradiation therapy; PLR: Platelet to lymphocyte ratio; EF: Esophageal fistula; RT: Radiation therapy; RP: Radiation pneumonitis; OS: Overall survival; PFS: Progression free survival; NSCLC: Non-small cell lung cancer; Gr: Grade; SCLC: Small cell lung cancer; RE: Radiation esophagitis

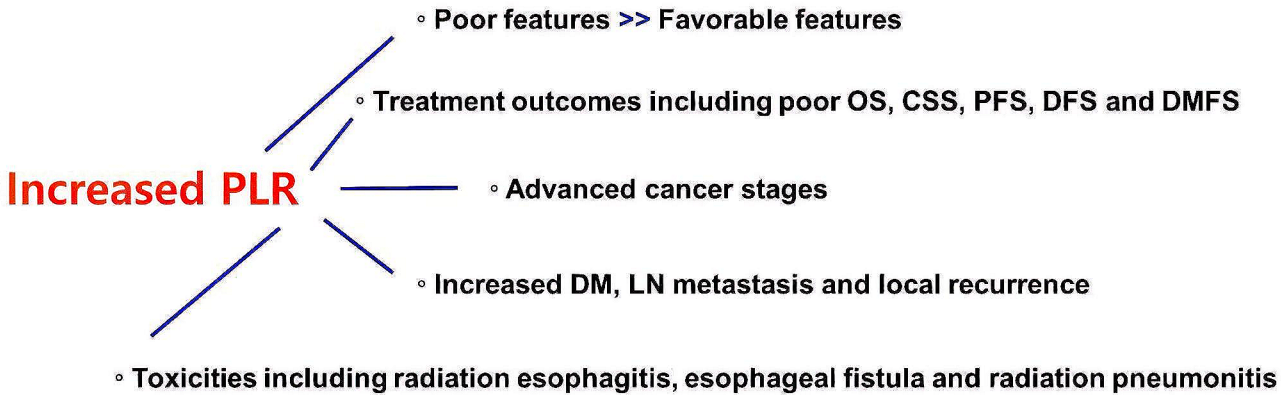

Fig. 1 A summary of the clinical implications of the increased PLR

The connection between systemic inflammation and cancer development was described in the 19th century [59]. Since then, the known link between inflammation and cancer has recently undergone a renaissance as a result of investigations of the role of inflammation in cancer [59]. The inflammatory microenvironment is now regarded as the seventh hallmark of cancer according to the numerous clinical and translational studies [85]. Blood parameters such as platelets, leukocytes, lymphocytes, macrophages, monocytes and dendritic cells are regularly measured and compose a paramount part of the immune system. When triggered, these cells release a variety of cytokines and tumor growth-promoting factors. Platelets are among the important tumor-promoting blood cells. They release epidermal growth factor, hepatocyte growth factor, insulin-like growth factor, platelet-derived growth factor, transforming growth factor β, vascular endothelial growth factor and many cytokines that promote epithelial-to-mesenchymal transition and metastasis [86, 87]. Lymphocytes are also an integral part of host's cellular immunity and are involved in antitumor immune responses. Lymphocytes can induce cell death and impede the proliferation and migration of cancer cells [33]. The presence of lymphocytes in the tumor is associated with improved treatment responses and favorable prognosis, whereas low lymphocyte counts are linked to diminished antitumor immune responses, which can lead to tumor growth and progression [88].

When we summarized the results, most studies illustrated association between a high PLR and poor outcomes even though consistent conclusions and trends were not found. The majority of the included studies investigated OS, DFS or PFS as primary study endpoints, and a high PLR was correlated with deteriorated outcomes at these endpoints. An association with LC has been observed in few studies, whereas a close relationship with DM has been described in several studies. Connection between a high PLR and worse clinical and pathological factors as well as disease stages have also been demonstrated. The specific relevance of the PLR in particular cancer types can be determined through well-designed studies with fixed and predefined PLR measurement timepoints.

When we examined the results according to disease site, some concordant results were observed despite the heterogeneous composition of the study groups. Among the brain tumors, atypical meningioma and malignant gliomas were included. The preoperative or Post-RT PLR was associated with PFS or OS. The PLR-including risk score also significantly correlated with PFS. In breast cancer, the PLR was

investigated from diverse perspectives. In the meta-analysis, the associations of a high PLR with advanced disease stage, LN metastasis, and DM, as well as poor DFS and OS, were reported. Interactions of the preoperative PLR with CSS and OS and a very strong association between a high PLR and DM were also depicted. In GI malignancies, the PLR has been more broadly investigated. In esophageal cancer, most included studies involved patients who underwent definitive CRT. However, studies on the heterogeneity of treatment therapeutics and studies on patients treated with neoadjuvant CRT followed by surgery were also included. Although most of the endpoints were OS, DFS or PFS, tumor response or complete response was another endpoint in some studies. In most of those studies, elevated PLRs were associated with poor clinical outcomes and poor pathological responses. In some studies, the PLR increased after CRT, and a high post-treatment PLR was related to poor OS. Changes in the PLR were also related to OS and DFS in several studies. The assessment timepoints of the PLR in relation to treatment time varied among studies and were linked to treatment outcomes in various aspects. LN metastasis and DM were also linked to a high PLR in some studies. The results for HCC patients were similar to those of other PLR-related studies. The highest PLR among the collected data was associated with DM, and worsening of the PLR after treatment was connected to intrahepatic recurrence. In rectal cancer, according to the standard treatment paradigm, treatment proceeded via the sequence of neoadjuvant CRT followed by radical surgery in all included studies. The results were also divided into positive (close relationship) and negative (no relationship) outcomes. An elevated PLR was related to poor OS, DFS, PFS and lateral LN recurrence. A favorable response after CRT was associated with a low PLR in some studies. In hematologic malignancies, investigations of the PLR have rarely been conducted. Extranodal NK/T-cell lymphoma, Hodgkin's lymphoma and MALT lymphoma were the disease entities studied. An increased PLR was consistently related to poor OS or PFS in all the included studies. A number of studies on head and neck malignancies have been performed for various types of cancer. In the study population of patients who underwent definitive CRT, an elevated PLR was related to poor OS, PFS or DMFS in most of the studies. Opposite or negative (no relationship) results have been reported from several studies. In the study cohorts of salivary gland cancer or oral cancer, in which upfront surgery was followed by PORT, the PLR before surgery or PORT was connected to DMFS, DFS or OS. Many investigational studies related to the PLR in lung cancer have been carried out in both SCLC and NSCLC. Similar to the finding of other studies, an elevated pretreatment PLR was related to inferior OS and PFS. The relationship with the mid-treatment PLR was also depicted. In one study, a close association with local recurrence was described. PLR-related studies of soft tissue sarcomas have rarely been performed. The pretreatment PLR demonstrated a close relationship with OS. Interestingly, a close connection between the PLR and treatment toxicitiy has been reported in several articles. Esophageal fistula, radiation esophagitis and radiation pneumonitis are representative examples of toxicities that have shown a close relationship with the PLR, and pretreatment or mid-treatment PLR values were significantly linked to toxicities.

Conclusions

In summary, the PLR was associated with basic tumor characteristics, various oncologic factors, treatment outcomes and toxicities in cancer treatment involving RT. Although the results were not consistent, increased PLR mostly correlated with poor clinical features and prognosis. These features include baseline tumor characteristics; clinical study endpoints such as DFS, DM, DMFS, OS and PFS; and partly LN metastasis or local recurrence. However, some studies have shown negative or opposite results. The consistency of the PLR measurement time points in relation to the treatment and the consistency of treatment types and modalities in the study design should be paramount for drawing more accurate and firm conclusions. Future studies with results that may support more concrete and definitive conclusions are anticipated.

Abbreviations

RT	Radiation therapy
LMR	Lymphocyte-to-monocyte ratio
NLR	Neutrophil-to-lymphocyte ratio
PLR	Platelet-to- lymphocyte ratio
AAR	Albumin-to-alkaline phosphatase ratio
CTCs	Circulating tumor cells
PFS	Progression-free survival
OS	Overall survival
PORT	Postoperative RT
CSS	Cause-specific survival
DM	Distant metastases
DFS	Disease-free survival
LN	Lymph node
DSS	Disease-specific survival
HCC	Hepatocellular carcinoma
MALT	Mucosa-associated lymphoid tissue
DMFS	DM free-survival
SCLC	Small cell lung cancer
NSCLC	Non-small cell lung cancer
SBRT	Stereotactic body radiation therapy
UPS	Undifferentiated pleomorphic sarcoma

Author contributions

DSL designed and wrote the main manuscript text, figure and tables.

Funding

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (No. RS-2023-00246209).

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethical approval and consent to participate

Due to its nature of review article, it is not applicable.

Consent for publication
Yes.

Competing interests
None/DSL contributed to the conception and design of the study, the methodology, surveyed the literature data, and drafted the manuscript.

Received: 30 May 2024 / Accepted: 1 July 2024
Published online: 13 August 2024

References

1. Baskar R, Lee KA, Yeo R, Yeoh KW. Cancer and radiation therapy: current advances and future directions. Int J Med Sci. 2012;9:193–9.
2. Baskar R, Dai J, Wenlong N, Yeo R, Yeoh KW. Biological response of cancer cells to radiation treatment. Front Mol Biosci. 2014;1:24.
3. Chetty IJ, et al. Technology for Innovation in Radiation Oncology. Int J Radiat Oncol Biol Phys. 2015;93:485–92.
4. Feain IJ, Court L, Palta JR, Beddar S, Keall P. Innovations in Radiotherapy Technology. Clin Oncol (R Coll Radiol (G B)). 2017;29:120–8.
5. Jaffray DA. Image-guided radiotherapy: from current concept to future perspectives. Nat Rev Clin Oncol. 2012;9:688–99.
6. Jiang GL. Particle therapy for cancers: a new weapon in radiation therapy. Front Med. 2012;6:165–72.
7. Welsh JS, et al. Helical tomotherapy: an innovative technology and approach to radiation therapy. Technol Cancer Res Treat. 2002;1:311–6.
8. Blomain ES, Moding EJ. Liquid biopsies for Molecular Biology-based Radiotherapy. Int J Mol Sci 22 (2021).
9. Huang C, et al. The pretherapeutic systemic inflammation score is a prognostic predictor for elderly patients with oesophageal cancer: a case control study. BMC Cancer. 2023;23:505.
10. Ree AH, Redalen KR. Personalized radiotherapy: concepts, biomarkers and trial design. Br J Radiol. 2015;88:20150009.
11. Tran PT, et al. Tissue biomarkers for prostate cancer radiation therapy. Curr Mol Med. 2012;12:772–87.
12. Lee DS et al. Association between Posttreatment Serum Platelet-to-Lymphocyte Ratio and distant metastases in patients with Hepatocellular Carcinoma receiving curative Radiation Therapy. Cancers 15 (2023).
13. Li A, et al. Prognostic value of lymphocyte-to-monocyte ratio and systemic immune-inflammation index in non-small-cell lung cancer patients with brain metastases. Future Oncol (London England). 2020;16:2433–44.
14. An L, Yin WT, Sun DW. Albumin-to-alkaline phosphatase ratio as a promising indicator of prognosis in human cancers: is it possible? BMC Cancer. 2021;21:247.
15. Gasparyan AY, Ayvazyan L, Mukanova U, Yessirkepov M, Kitas GD. The platelet-to-lymphocyte ratio as an inflammatory marker in Rheumatic diseases. Annals Lab Med. 2019;39:345–57.
16. Li P, Li H, Ding S, Zhou JNLR. PLR, LMR and MWR as diagnostic and prognostic markers for laryngeal carcinoma. Am J Translational Res. 2022;14:3017–27.
17. Lin ZX, et al. Lymphocyte-to-monocyte ratio predicts survival of patients with hepatocellular carcinoma after curative resection. World J Gastroenterol. 2015;21:10898–906.
18. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell. 2011;144:646–74.
19. Langsenlehner T, et al. Evaluation of the platelet-to-lymphocyte ratio as a prognostic indicator in a European cohort of patients with prostate cancer treated with radiotherapy. Urol Oncol. 2015;33:e201209–216.
20. Pinedo HM, Verheul HM, D'Amato RJ, Folkman J. Involvement of platelets in tumour angiogenesis? Lancet (London England). 1998;352:1775–7.
21. Bakewell SJ, et al. Platelet and osteoclast beta3 integrins are critical for bone metastasis. Proc Natl Acad Sci USA. 2003;100:14205–10.
22. Boucharaba A, et al. Platelet-derived lysophosphatidic acid supports the progression of osteolytic bone metastases in breast cancer. J Clin Investig. 2004;114:1714–25.
23. Sabrkhany S, Griffioen AW, Oude Egbrink MG. The role of blood platelets in tumor angiogenesis. Biochim Biophys Acta. 2011;1815:189–96.
24. Leone K, Poggiana C, Zamarchi R. The interplay between circulating Tumor cells and the Immune System: from Immune escape to Cancer Immunotherapy. Diagnostics (Basel Switzerland) 8 (2018).
25. Abravan A, Salem A, Price G, Faivre-Finn C, van Herk M. Effect of systemic inflammation biomarkers on overall survival after lung cancer radiotherapy: a single-center large-cohort study. Acta Oncol (Stockholm Sweden). 2022;61:163–71.
26. Duque-Santana V, et al. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio as prognostic factors in locally advanced rectal Cancer. Oncology. 2023;101:349–57.
27. Gao Z, Zhao M, Yang X, Fu J. Assessment of Peripheral platelet to lymphocyte ratio and Prognostic Nutritional Index in the efficacy and prognosis of Radiotherapy for Cervical Cancer. Curr Oncol (Toronto Ont). 2023;30:2834–44.
28. McLaren PJ, et al. Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios can predict treatment response to Neoadjuvant Therapy in Esophageal Cancer. J Gastrointest Surgery: Official J Soc Surg Aliment Tract. 2017;21:607–13.
29. Van Berckelaer C, et al. A high neutrophil-lymphocyte ratio and platelet-lymphocyte ratio are associated with a worse outcome in inflammatory breast cancer. Breast (Edinburgh Scotland). 2020;53:212–20.
30. Zhang J, et al. Prognostic significance of platelet-to-lymphocyte ratio in patients with nasopharyngeal carcinoma: a meta-analysis. Future Oncol (London England). 2020;16:117–27.
31. Bae BK et al. The significance of systemic inflammation markers in Intrahepatic Recurrence of Early-Stage Hepatocellular Carcinoma after Curative Treatment. Cancers 14 (2022).
32. Fiore M, et al. Preoperative neutrophil-to-lymphocyte ratio and a new inflammatory biomarkers Prognostic Index for primary retroperitoneal sarcomas: Retrospective Monocentric Study. Clin cancer Research: Official J Am Association Cancer Res. 2023;29:614–20.
33. Huang YM et al. Histopathological and Haemogram Features Correlate with prognosis in rectal Cancer patients receiving Neoadjuvant Chemoradiation without Pathological Complete response. J Clin Med 11 (2022).
34. Ma JY, Ke LC, Liu Q. The pretreatment platelet-to-lymphocyte ratio predicts clinical outcomes in patients with cervical cancer: a meta-analysis. Medicine. 2018;97:e12897.
35. Peng RR, et al. Nomogram based on Lactate dehydrogenase-to-albumin ratio (LAR) and platelet-to-lymphocyte ratio (PLR) for Predicting Survival in Nasopharyngeal Carcinoma. J Inflamm Res. 2021;14:4019–33.
36. Zhang Q, et al. Initial platelet-to-lymphocyte count as prognostic factor in limited-stage small cell lung cancer. Biomark Med. 2019;13:249–58.
37. Yersal Ö, Odabaşi E, Özdemir Ö, Kemal Y. Prognostic significance of pre-treatment neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in patients with glioblastoma. Mol Clin Oncol. 2018;9:453–8.
38. Gao P, et al. A clinical prognostic model based on preoperative hematological and clinical parameters predicts the progression of primary WHO Grade II Meningioma. Front Oncol. 2021;11:748586.
39. Hsu EJ, et al. Neutrophilia and post-radiation thrombocytopenia predict for poor prognosis in radiation-treated glioma patients. Front Oncol. 2022;12:1000280.
40. Krenn-Pilko S, et al. The elevated preoperative platelet-to-lymphocyte ratio predicts poor prognosis in breast cancer patients. Br J Cancer. 2014;110:2524–30.
41. Zhang M et al. High Platelet-to-Lymphocyte Ratio Predicts Poor Prognosis and Clinicopathological Characteristics in Patients with Breast Cancer: A Meta-Analysis. BioMed research international. 2017;2017:9503025.
42. Wang C, et al. Pretreatment neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio as prognostic factors and reference markers of Treatment options for locally advanced squamous cell carcinoma located in the Middle and Upper Esophagus. Cancer Manage Res. 2021;13:1075–85.
43. Tseng RH, Lai KM, Tsai CY, Yan SL. Elevated platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio after first cycle of Chemotherapy and Better Survival in Esophageal Cancer patients receiving concurrent Chemoradiotherapy. Curr Oncol (Toronto Ont). 2022;29:8825–34.
44. Khin NS, et al. Chemoradiation-induced changes in systemic inflammatory markers and their prognostic significance in oesophageal squamous cell carcinoma. Br J Radiol. 2021;94:20200314.
45. Zhang Y, et al. Impact of platelets to lymphocytes ratio and lymphocytes during Radical Concurrent Radiotherapy and Chemotherapy on patients with nonmetastatic esophageal squamous cell carcinoma. J Oncol. 2022;3412349. 2022.
46. Du X, et al. Novel nomograms predicting the survival of patients with non-surgical thoracic esophageal squamous cell carcinoma treated with IMRT: a retrospective analysis. Medicine. 2022;101:e30305.
47. Ran JJ, Shen JJ, Ma J, Li XY. Survival analysis of 80 elderly patients with esophageal squamous cell carcinoma receiving definitive concurrent

chemoradiotherapy with S-1. Cancer Radiotherapie: J De La Societe francaise de radiotherapie oncologique. 2022;26:1064–9.
48. Sun L, et al. A nomogram based on hematological markers to predict radiosensitivity in patients with esophageal squamous cell carcinoma. Medicine. 2023;102:e33282.
49. Ajdari A, et al. Toward Personalized Radiation Therapy of Liver Metastasis: importance of serial blood biomarkers. JCO Clin cancer Inf. 2021;5:315–25.
50. Li JX, et al. Prognostic value of a nomogram based on peripheral blood immune parameters in unresectable hepatocellular carcinoma after intensity-modulated radiotherapy. BMC Gastroenterol. 2022;22:510.
51. Park Y, Chang AR. Neutrophil to lymphocyte ratio and platelet to Lymphocyte Ratio in Hepatocellular Carcinoma Treated with stereotactic body Radiotherapy. Korean J Gastroenterol = Taehan Sohwagi Hakhoe Chi. 2022;79:252–9.
52. Ergen Ş, Barlas A, Yıldırım C, C., Öksüz D. Prognostic role of Peripheral Neutrophil-Lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) in patients with rectal Cancer undergoing Neoadjuvant Chemoradiotherapy. J Gastrointest cancer. 2022;53:151–60.
53. Miyakita H, et al. Predictors and histological effects of preoperative chemoradiotherapy for rectal cancer and control of lateral lymph node metastasis. BMC Gastroenterol. 2022;22:334.
54. Chiloiro G, et al. Predictive and prognostic value of inflammatory markers in locally advanced rectal cancer (PILLAR) - a multicentric analysis by the Italian Association of Radiotherapy and Clinical Oncology (AIRO) gastrointestinal Study Group. Clin Translational Radiation Oncol. 2023;39:100579.
55. Lee JH, et al. Predicting Pathological Complete regression with haematological markers during Neoadjuvant Chemoradiotherapy for locally advanced rectal Cancer. Anticancer Res. 2018;38:6905–10.
56. Xu N, et al. Systemic inflammation-based predictors of pathological response to neoadjuvant chemoradiotherapy in locally advanced rectal cancer patients. J Cancer Res Ther. 2022;18:438–44.
57. Partl R et al. Can Pre-Treatment Inflammatory Parameters Predict the Probability of Sphincter-Preserving Surgery in Patients with Locally Advanced Low-Lying Rectal Cancer? Diagnostics (Basel, Switzerland). 2021;11.
58. Huszno J, et al. Role of neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, lymphocyte-monocyte ratio and platelets in prognosis of patients with prostate cancer. Oncol Lett. 2022;24:305.
59. Chauhan R, Trivedi V, Rani R, Singh U, Singh K. Pre-treatment hematological parameters as a cost effective predictive marker for response to concurrent chemo radiation in locally advanced cervical cancer. Cancer Treat Res Commun. 2022;31:100539.
60. Li N, et al. Analysis of systemic inflammatory and coagulation biomarkers in advanced cervical cancer: prognostic and predictive significance. Int J Biol Mark. 2023;38:133–8.
61. Wang KF, et al. A prognostic model based on pretreatment platelet lymphocyte ratio for stage IE/IIE upper aerodigestive tract extranodal NK/T cell lymphoma, nasal type. Med Oncol (Northwood Lond Engl). 2014;31:318.
62. Reddy JP, et al. Pre-treatment neutrophil/lymphocyte ratio and platelet/lymphocyte ratio are prognostic of progression in early stage classical Hodgkin lymphoma. Br J Haematol. 2018;180:545–9.
63. Wen Q, et al. A new prognostic nomogram in patients with mucosa-associated lymphoid tissue lymphoma: a multicenter retrospective study. Front Oncol. 2023;13:1123469.
64. Li Q, Yu L, Yang P, Hu Q. Prognostic value of inflammatory markers in nasopharyngeal carcinoma patients in the intensity-modulated Radiotherapy Era. Cancer Manage Res. 2021;13:6799–810.
65. Liu B, Li M, Chen S, Cui Q. A study on the survival prediction for patients with oral cancer in southwest China. Oral Dis (2023).
66. Wan M, et al. Pretherapy platelet-to-lymphocyte ratio as a prognostic parameter for locally advanced hypopharyngeal cancer patients treated with radiotherapy combined with chemotherapy. Eur Archives oto-rhino-laryngology: Official J Eur Federation Oto-Rhino-Laryngological Soc (EUFOS) : Affiliated German Soc Oto-Rhino-Laryngology - Head Neck Surg. 2022;279:5859–68.
67. Yan W, Ou X, Shen C, Hu C. A nomogram involving immune-inflammation index for predicting distant metastasis-free survival of major salivary gland carcinoma following postoperative radiotherapy. Cancer Med. 2023;12:2772–81.
68. Chen Y, et al. Predictive value of pretreatment lymphocyte-to-monocyte ratio and platelet-to-lymphocyte ratio in the survival of nasopharyngeal carcinoma patients. Cancer Manage Res. 2021;13:8767–79.
69. Jiang Y, Qu S, Pan X, Huang S, Zhu X. Prognostic value of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in intensity modulated radiation therapy for nasopharyngeal carcinoma. Oncotarget. 2018;9:9992–10004.
70. Staniewska E, Tomasik B, Tarnawski R, Łaszczych M, Miszczyk M. The prognostic value of red cell distribution width (RDW), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) in radiotherapy for oropharyngeal cancer. Rep Practical Oncol Radiotherapy: J Greatpoland Cancer Cent Poznan Pol Soc Radiation Oncol. 2021;26:1010–8.
71. Tazeen S, et al. Assessment of Pretreatment Neutrophil/Lymphocyte Ratio and Platelet/Lymphocyte Ratio in prognosis of oral squamous cell carcinoma. J oral Maxillofacial Surgery: Official J Am Association Oral Maxillofacial Surg. 2020;78:949–60.
72. Suzuki R, et al. Prognostic significance of total lymphocyte Count, Neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio in limited-stage small-cell lung Cancer. Clin Lung Cancer. 2019;20:117–23.
73. Yu Y, et al. Pre-radiotherapy lymphocyte count and platelet-to-lymphocyte ratio may improve survival prediction beyond clinical factors in limited stage small cell lung cancer: model development and validation. Translational lung cancer Res. 2020;9:2315–27.
74. Qi J, et al. The addition of peripheral blood inflammatory indexes to Nomogram improves the predictive accuracy of Survival in Limited-Stage Small Cell Lung Cancer patients. Front Oncol. 2021;11:713014.
75. Delikgoz Soykut E, et al. Prognostic impact of immune inflammation biomarkers in predicting survival and radiosensitivity in patients with non-small-cell lung cancer treated with chemoradiotherapy. J Med Imaging Radiat Oncol. 2022;66:146–57.
76. Xia WY, et al. Neutrophil-lymphocyte ratio and platelet-lymphocyte ratio associations with heart and body dose and their effects on patient outcomes in locally advanced non-small cell lung cancer treated with definitive radiotherapy. Translational lung cancer Res. 2020;9:1996–2007.
77. Cannon NA, et al. Neutrophil-lymphocyte and platelet-lymphocyte ratios as prognostic factors after stereotactic radiation therapy for early-stage non-small-cell lung cancer. J Thorac Oncology: Official Publication Int Association Study Lung Cancer. 2015;10:280–5.
78. Aduquaye M, et al. Impact of Pre-treatment NLR and other hematologic biomarkers on the outcomes of Early-Stage Non-small-cell Lung Cancer treated with stereotactic body Radiation Therapy. Curr Oncol (Toronto Ont). 2022;29:193–208.
79. Pavan A, et al. Tumor Immune-Infiltrate Landscape after Chemo-Radiotherapy in a Case Series of patients with non-small cell lung Cancer: pretreatment predictors and correlation with outcome. Oncologist. 2022;27:e199–202.
80. Tepper SC, et al. Association between neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, and survival in undifferentiated pleomorphic sarcoma (NLR, PLR, and overall survival in UPS). Surg Oncol. 2023;49:101949.
81. Han D, et al. Platelet-to-lymphocyte ratio is an independent predictor of chemoradiotherapy-related esophageal fistula in esophageal cancer patients. Annals Translational Med. 2020;8:1163.
82. Yang LT, et al. Establishment and Verification of a Prediction Model for Symptomatic Radiation Pneumonitis in patients with esophageal Cancer receiving Radiotherapy. Med Sci Monitor: Int Med J Experimental Clin Res. 2021;27:e930515.
83. Huang Y, et al. Real-world experience of consolidation durvalumab after concurrent chemoradiotherapy in stage III non-small cell lung cancer. Thorac cancer. 2022;13:3152–61.
84. Qiu J, et al. Using inflammatory indexes and clinical parameters to predict radiation esophagitis in patients with small-cell lung cancer undergoing chemoradiotherapy. Front Oncol. 2022;12:898653.
85. Colotta F, Allavena P, Sica A, Garlanda C, Mantovani A. Cancer-related inflammation, the seventh hallmark of cancer: links to genetic instability. Carcinogenesis. 2009;30:1073–81.
86. Contursi A, Sacco A, Grande R, Dovizio M, Patrignani P. Platelets as crucial partners for tumor metastasis: from mechanistic aspects to pharmacological targeting. Cell Mol Life Sci. 2017;74:3491–507.
87. Tesfamariam B. Involvement of platelets in tumor cell metastasis. Pharmacol Ther. 2016;157:112–9.
88. Ménétrier-Caux C, Ray-Coquard I, Blay JY, Caux C. Lymphopenia in Cancer patients and its effects on response to Immunotherapy: an opportunity for combination with cytokines? J Immunother Cancer. 2019;7:85.

Publisher's Note