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The serum platelet-to-lymphocyte ratio as a predictor of outcomes in bladder cancer patients: an updated meta-analysis

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There is conflicting evidence regarding the association between platelet-lymphocyte ratio (PLR) and the prediction of outcomes in bladder cancer (BCa). Due to the rapidly increasing availability of data to explore this issue, this updated meta-analysis investigates how pretreatment PLR influences the outcomes of BCa. Literature was retrieved from Embase, Cochrane Library, Web of Science, and PubMed from 2015 to April 2025. The 95% confidence intervals (CIs) and pooled hazard ratio (HR) have been employed in the exploration of the link across BCa prediction and PLR. The 95% CIs and pooled odds ratios (ORs) examined the connection between PLR and clinicopathological features of BCa. Subgroup analysis and meta-regression were conducted to identify the main sources of heterogeneity. Sensitivity analysis was used to assess the robustness of the results. The Egger's test and "trim and fill" method have been used in evaluating publication bias. This study incorporated 20 studies comprising 5,594 participants. Elevated PLR was conspicuously linked to inferior overall survival (OS) (HR = 1.51, 95% CI 1.23–1.85, *P* < 0.001) and recurrence-free survival (RFS) (HR = 1.68, 95% CI 1.26–2.24, *P* < 0.001). A marginally significant association was observed between high PLR and progression-free survival (PFS) (HR = 1.61, 95% CI1.00–2.59, *P* = 0.052). No strong correlation between PLR and cancer-specific survival (CSS) (HR = 1.14, 95% CI 0.96–1.35, *P* = 0.138). Additionally, elevated PLR was significantly associated with tumor stage ≥T2 (OR = 1.92, 95% CI 1.24–2.97, *P* = 0.003). The PLR can be regarded as an indicative predictor of the destitution of individuals suffering from BCa.

Keywords Platelet-lymphocyte ratio, Systemic inflammatory response, Meta-analysis, Predictive value, Bladder cancer

Bladder cancer (Bca) presents a type of malignant tumor occurring frequently, and whose elevated morbidity and mortality rates pose a significant healthcare burden[1]. Annually, it affects 600,000 people, with about 66% experiencing recurrence within five years[2]. During the early phase, Bca might not show any symptoms or may manifest as minor blood in the urine, which is often unnoticed by patients. At present, the most frequently employed technique for diagnosing Bca is the invasive cystoscopic biopsy[3]. Of all Bca, non-muscle-invasive bladder cancer (NMIBC)[4] represents 75%, and its prognosis is significantly better than that of muscle-invasive bladder cancer (MIBC), marking the timely diagnosis of Bca as a hallmark for halting this disease. NMIBC is treated with transurethral resection of bladder tumor (TURBT), then a risk-based intravesical therapy (IVe), achieving a 90% overall survival rate[5]. In contrast, MIBC is characterized by a high risk of progression, distant metastasis, and poor survival outcomes, often requiring radical cystectomy (RC) and systemic chemotherapy[6]. However, despite rigorous treatment, they still have a high recurrence rate, making long-term monitoring essential and early detection beneficial for improving prognosis[7]. Managing the prognosis of Bca continues to be a challenge for clinicians[8]. Therefore, a feasible instrument for making predictions and diagnoses is required.

Inflammation associated with cancer manifests in the cellular microenvironment surrounding the tumor and occupies a key position in prognosticating disease advancement and survival outcomes across various malignancies[9]. Systemic inflammation can be evaluated using blood biomarkers, including neutrophil-to-lymphocyte ratio (NLR)[10], Lymphocyte-C-reactive protein ratio (LCR)[11], and platelet-lymphocyte ratio (PLR)[12].

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These serum and tissue biomarkers, indicating systemic inflammatory response, are promising candidates for developing non-invasive immuno-oncology assays[13]. The PLR is determined by dividing the platelet count by the lymphocyte count.

Studies have revealed PLR's predictive significance in solid tumors like Perihilar Cholangiocarcinoma[14], laryngeal, gastric[15], and neuroendocrine neoplasms[16]. The link between PLR and BCa prognosis was initially revealed by a meta-analysis executed by Wang et al.[17], however, its findings were constrained by the limited data. In the present study, we updated the evidence base by incorporating 12 additional articles comprising 2,291 more patients and by including progression-free survival as an outcome indicator, thereby strengthening the robustness and generalizability of our findings.

Methods

Study registration

This investigation has been carried out per the regulations of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[18], and it is registered in PROSPERO under the identifier CRD420251071198. The study protocol can be accessed upon reasonable request.

Literature search strategy

The literature was derived from Cochrane Library, Web of Science databases, PubMed, as well as Embase from 2015-April 2025. Bibliographies of incorporated studies were reviewed. The search strategies are presented in Supplementary Table 1.

Inclusion and exclusion criteria

The inclusion criteria covered these points: (1) research that included BCa diagnosis was confirmed through pathological analysis; (2) studies whose participants were categorized as elevated and diminished PLR strata; (3) research that provided precise cut-off values for PLR; (4) studies investigating studies that examined a link of PLR, overall survival (OS), cancer-specific survival (CSS), recurrence-free survival (RFS), and progression-free survival (PFS); (5) studies that provided adequate information for determining the hazard ratio (HR) as well as 95% confidence intervals (CIs); (6) studies published in the English language. The exclusion criteria comprised: (1) reviews, editorials, conference abstracts without full text, letters, and case reports; (2) duplicate or overlapping cohorts; (3) studies not reporting OS, CSS, RFS, and PFS; (4) studies not providing sufficient data to obtain an effect size.

Data extraction

Two investigators (ZBN and YZY) independently selected the studies for this analysis. Discussions were carried out to resolve any disagreements until a consensus was reached. The following details have been derived from every research: first author, publication year, country, quantity of cases, age, thresholds, study design, study period, therapeutic approach, and survival results. Most HR parameters were extracted directly from the included publications. For studies that did not provide HR explicitly, we digitized the published Kaplan–Meier curves using Engauge Digitizer to extract time-survival coordinates, and individual patient data were subsequently reconstructed with the IPDfromKM algorithm to estimate HR[19].We contacted the first and/or corresponding authors to acquire any missing information as necessary.

Quality assessment and risk of bias

Considering that the nature of all included studies was retrospective, two reviewers (ZBN and YZY) independently assessed the methodological quality and potential risk of bias using the Newcastle–Ottawa Scale (NOS) [20]. The NOS is a semi-quantitative rating system that utilizes a star-based scale, with a total score ranging from 0 to 9 stars. It evaluates the quality of studies across three domains: selection (up to 4 stars), comparability (up to 2 stars), and outcome assessment (up to 3 stars). Studies achieving a score of 6 stars or more were considered high quality. Scoring discrepancies were reviewed and resolved by the corresponding author (ZZB).

Statistical analyses

Pooled HR for OS, CSS, RFS and PFS were computed for the evaluation of the link between PLR and predictive value among individuals exhibiting BCa. According to Barraclough et al.[21], an HR greater than 1 indicates an increased risk of adverse outcome in the exposed group. To explore the link between PLR and clinical traits involving tumor stage and metastasis, OR with 95%CIs were employed. Chen et al.[22] suggested that an OR below 1.68 represents a very small effect, values between 1.68 and 3.47 indicate a small effect, 3.47 to 6.71 reflect a moderate effect, and values above 6.71 correspond to a large effect. Furthermore, the Higgins' I^2 statistic and Cochran's Q test have been employed in determine heterogeneity across research; the findings denoted significant heterogeneity. Since the primary studies are inherently heterogeneous in their methodology, a random-effects model should be employed in all analyses[23,24]. To identify potential sources of heterogeneity, subgroup analysis (ethnicity, publication year, sample size, cut-off values, treatment) and meta-regression were conducted. In line with common practice in previous oncological meta-analyses, we adopted 200 cases as threshold for sample size stratification in order to assess the impact of study scale on heterogeneity[25,26]. The robustness of the results was examined through sensitivity analysis. Publication bias was estimated using funnel plot assessment, Egger's test and "trim and fill" method. Statistical analyses were executed on Stata 14.0, and findings having two-tailed $P < 0.05$ were regarded as significant.

Results

Search outcomes

Figure 1 depicts a flowchart of the literature selection processes. The first database search resulted in 336 records and 189 studies after removing the duplicates. After reviewing titles and abstracts, 149 papers were dismissed, resulting in 40 full-text articles sought for retrieval. Of these, 39 were assessed for eligibility, with 27 subsequently excluded (Fig. 1). Ultimately, 20 studies[27–46] involving 5594 participants were considered for this analysis.

Baseline characteristics and patient demographics

Of the 20 retrospective cohort studies, published between 2015 and 2024, 8 studies were from China[30,32,34,39,41–44], 5 from Turkey[36–38,40,46], and 1 from Canada[27], 2 from Korea[28,35], 1 from UK[29], 1 from Japan[31], 1 from Poland[33] and 1 from Iran[45]. Together, these studies included a total of 5594 patients (4684 males and 910 females), with median ages ranging from 61 to 75 years The threshold of PLR varied between 93 and 218. Table 1 portrays the initial features of the research covered.

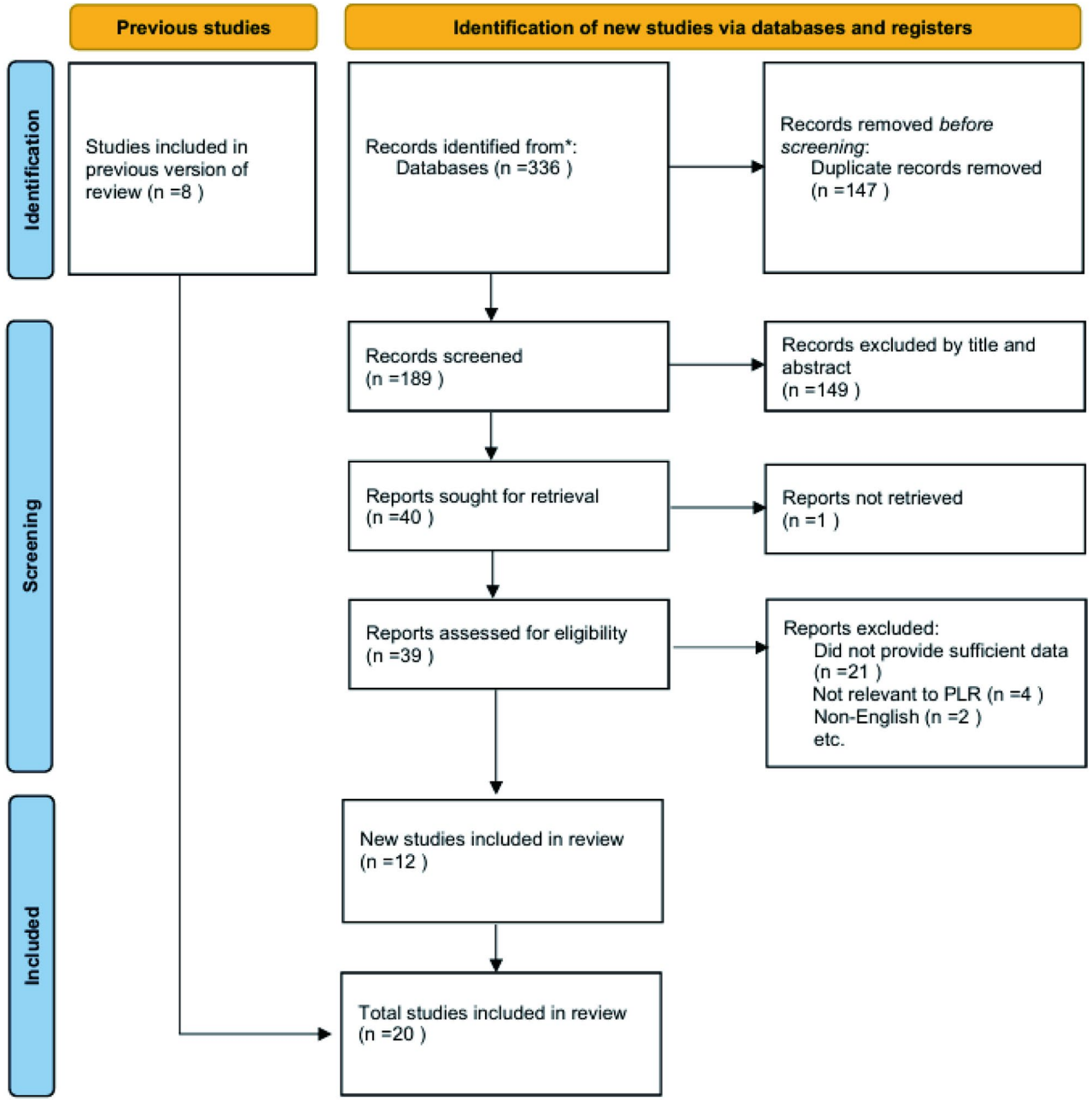

Fig. 1. Flow diagram of the included studies.

References	Country	Dominant ethnicity	Sample size	Male N %)	Median/ mean age	Study design	Treatment	Cut-off value	Study period	Survival outcome
B. Bhindi	Canada	Caucasian	418	322(77.0%)	70	R	RC	150	1992–2012	OS, CSS, RFS
M. Kang	Korea	Asian	1551	1302(83.9%)	65	R	TURBT	124	1990–2013	OS, CSS
S. Lee	UK	Caucasian	226	174(77.0%)	75	R	TURBT	218	2011–2013	OS
S. Mao	China	Asian	207	169(81.6%)	66	R	TURBT	123	2010–2012	RFS, PFS
M. Miyake	Japan	Asian	117	95(81.2%)	72	R	RC	150	2006–2016	OS, CSS
D. Peng	China	Asian	516	436(84.5%)	66	R	RC	214	2004–2016	OS
P. Rajwa	Poland	Caucasian	144	115(79.9%)	NA	R	RC	160	2003–2015	OS, CSS
G. Zhang	China	Asian	124	100(80.6%)	65	R	RC	140	Jan–Dec, 2009	OS
H. Yuk	Korea	Asian	385	327(84.9%)	73	R	TURBT + BCG	171	1991–2015	OS, CSS
A Caglayan	Turkey	Caucasian	74	64(86.5%)	67	R	TURBT	123	2016–2020	OS, CSS, RFS, PFS
R. kayar	Turkey	Caucasian	119	105(88.2%)	65	R	RC	150	2014–2022	OS
C. Karan	Turkey	Caucasian	226	207(91.6%)	67	R	Chemotherapy	169	2008–2020	OS
X. Wang	China	Asian	99	88(88.9%)	68	R	TURBT	133	2018–2020	RFS
M. Avci	Turkey	Caucasian	231	202(87.5%)	62	R	TURBT	114	2016–2022	RFS, PFS
W. Zhang	China	Asian	127	110(86.6%)	66	R	RC	124	2005–2017	OS, PFS
R. Wu	China	Asian	197	170(86.3%)	64	R	TURBT + BCG	100(RFS) /113(PFS)	2012–2019	RFS, PFS
X. Yi	China	Asian	348	274(78.7%)	68	R	TURBT	150	NA	RFS
C. Wang	China	Asian	222	180(81.1%)	NA	R	TURBT + chemotherapy or CHT	93	2016–2020	RFS
A.Salari	Iran	Caucasian	187	179(95.7%)	61	R	RC	104	2016–2022	OS
I. Yilmaz	Turkey	Caucasian	76	65(85.5%)	66	R	TURBT	150	2006–2018	RFS, PFS

Table 1. Baseline characteristics of studies included in the meta-analysis. *NA* not available, *RC* radical cystectomy, *TURB* transurethral resection of bladder tumor, *OS* overall survival, *CSS* cancer-specific survival, *RFS* recurrence-free survival, *PFS* progression-free survival.

Quality assessment of included studies

All 20 retrospective studies included in the analysis achieved NOS scores of six or above, suggesting a generally high methodological quality (Table 2).

Predictive importance of PLR for OS

A total of 13 articles were analyzed to evaluate the relationship between PLR and poor OS in individuals suffering from BCa. Unlike the previous investigation, this updated meta-analysis included data from six additional studies. As illustrated in Table 3 and Fig. 2A, the HR for high PLR was 1.51 (95% CI 1.23–1.85, $P < 0.001$), displaying a significant link. In addition, a considerable heterogeneity was observed ($I^2 = 84.5\%$, $P < 0.001$). When stratified by year of publication, a significant between-subgroup difference was detected (Pbetween = 0.019). Notably, the heterogeneity within studies published after 2020 markedly decreased ($I^2 = 13.1\%$), representing a reduction of 71.4 percentage points compared with the overall analysis, and this subgroup demonstrated a stronger effect size (HR 2.14 vs. 1.21). These findings suggest that publication year may partially account for the observed heterogeneity. In contrast, stratifications by ethnicity, sample size, cut-off value, and treatment did not reveal significant between-subgroup differences, and the heterogeneity within these subgroups remained high, indicating the presence of residual heterogeneity. Strata analyses also portrayed a significant association between high PLR and OS in patients receiving RC. Furthermore, the prognostic value of PLR for OS remained significant in subgroups of Caucasian patients and studies with a sample size of fewer than 200 participants (Table 3).

Predictive importance of PLR for CSS

For the association between PLR and CSS, we incorporated the 6 articles[27,28,31,33,35,36]. Despite the inclusion of additional literature, no significant association between PLR and CSS was observed. The relevant data can be found in Table 3 and Fig. 2B.

Predictive importance of PLR for RFS

Data from 9 articles[27,30,36,39,40,42–44,46] were included in the examination of the link across PLR and RFS in participants with BCa. The pooled analysis suggested that PLR has a considerable prognostic impact on RFS, exhibiting HR = 1.68 (95% CI 1.26–2.24, $P < 0.001$) (Fig. 2C). Subgroup analyses and meta-regression indicated that ethnicity and cut-off value may contribute to the observed heterogeneity. However, it cannot be conclusively identified as the main source, as shown in Table 3.

	Selection				Comparability	Exposure			
Studies	1	2	3	4	5	6	7	8	Total score
B. Bhindi	★	★	★	★	★	★		★	7
M. Kang	★	★	★		★	★		★	6
S. Lee	★	★	★	★	★	★		★	7
S. Mao	★	★	★	★	★	★	★	★	8
M. Miyake	★	★	★	★	★		★	★	7
D. Peng	★	★	★	★	★	★	★	★	8
P. Rajwa	★	★	★	★	★	★	★	★	8
G. Zhang	★	★		★	★	★		★	6
H. Yuk	★	★	★	★	★	★	★	★	8
A. Caglayan	★	★		★	★	★		★	6
R. kayar	★	★	★	★	★	★	★		7
C. Karan	★	★	★	★	★	★		★	7
X. Wang	★	★	★	★	★	★	★	★	8
M. Avci	★	★	★	★	★	★	★	★	8
W. Zhang	★	★	★	★	★	★	★	★	8
R. Wu	★	★	★	★	★	★	★	★	8
X. Yi	★	★	★	★	★	★	★	★	8
C. Wang	★	★	★	★	★	★	★	★	8
A. Salari	★	★	★	★	★	★		★	7
I. Yilmaz	★	★	★	★	★	★	★	★	8

Table 2. The Newcastle–Ottawa Scale was used to assess the quality of the included studies. 1. Representativeness of the exposed cohort; 2. Selection of the non-exposed cohort; 3. Ascertainment of exposure; 4. Demonstration that the outcome of interest was not present at the start of the study; 5. Comparability of cohorts based on the design or analysis; 6. Assessment of outcome; 7. Sufficiency of follow-up duration for outcomes to occur; 8. Adequacy of follow-up of cohorts.

Predictive importance of PLR for PFS

A total of 6 studies[30,36,40–42,46] examined the relationship between PLR and PFS. The pooled analysis indicated a marginally significant association between elevated PLR and poorer PFS (HR = 1.61, 95% CI 1.00–2.59, $P = 0.052$). Notably, a significant association between PLR and PFS was identified in the subgroup of patients undergoing TURBT (HR = 1.90, 95% CI 1.21–2.99, $P = 0.006$). It is noteworthy that this subgroup analysis included only five studies, and thus the reliability of its findings may be limited. Detailed results are provided in Table 3 and Fig. 2D.

Relationship between PLR and clinical pathological factors

According to 8 studies[29,30,33,34,38,41,44,45], there is a connection between PLR and clinicopathological factors like smoking status, chemotherapy, diabetes, age, distant metastasis, sex, tumor grade, tumor size, and tumor stage. Figure 3 and Table 4 demonstrate a significant link between high PLR and individuals aged ≥ 65 years (OR = 1.77, 95% CI 1.22–2.59, $P = 0.003$), as well as with tumor stage ≥ T2 (OR = 1.92, 95% CI 1.24–2.97, $P = 0.003$) and tumor size ≥ 3 cm (OR = 2.26, 95% CI 1.17–4.37, $P = 0.016$). However, PLR showed no correlation with sex (OR = 0.78, 95% CI 0.53–1.14, $P = 0.135$), tumor grade (OR = 1.21, 95% CI 0.62–2.35, $P = 0.583$), diabetes (OR = 0.98, 95% CI 0.60–1.60, $P = 0.943$), distant metastasis (OR = 1.03, 95% CI 0.48–2.21, $P = 0.932$), smoking status (OR = 1.38, 95% CI 0.44–4.34, $P = 0.580$), or chemotherapy (OR = 1.29, 95% CI 0.40–4.22, $P = 0.672$). In our analysis, the ORs for tumor stage, age, and tumor size were all within the range classified as small.

Sensitivity analysis

To assess the robustness of our findings, we performed leave-one-out sensitivity analyses. The sequential exclusion of each individual study did not result in notable changes in the pooled effect estimates, thereby supporting the stability and reliability of the results (Fig. 4).

Publication bias

As shown in Fig. 5, the two sides of the funnel plot appeared slightly asymmetric upon visual inspection. Therefore, we conducted Egger's tests, as presented in Supplementary Fig. 1. The P values obtained were 0.002 for OS, 0.093 for RFS. Moreover, we applied "trim and fill" procedure and the results suggested that there were 3 potentially missing studies for the association PLR and OS (Supplementary Fig. 2). The adjusted pooled effect was HR = 1.30 (95% CI 1.08–1.57, $P = 0.006$), directionally consistent and remained statistically significant, but was attenuated relative to the unadjusted estimate.

Survival analysis	No. of studies	HR (95% CI)	p	I^2 (%)	*P*-value for heterogeneity	Analysis model	Meta Regression *P*
OS							
Total	13	1.51 (1.23, 1.85)	< 0.001	84.5	< 0.001	Random	
Ethnicity							0.819
Asian	6	1.45 (0.98,2.16)	0.063	76.2	0.001	Random	
Caucasian	7	1.54 (1.19,1.98)	0.001	86.4	< 0.001	Random	
Publication year							0.019
Before 2020	8	1.21 (1.00,1.47)	0.050	78.8	< 0.001	Random	
After 2020	5	2.14 (1.67,2.76)	< 0.001	13.1	0.330	Random	
Sample size							0.202
< 200	7	1.97 (1.22,3.17)	0.006	87.8	< 0.001	Random	
≥ 200	6	1.26 (0.98,1.62)	0.073	68.1	0.008	Random	
Cut-off value							0.941
< 150	5	1.73 (1.06,2.83)	0.030	77.4	0.001	Random	
≥ 150	8	1.44 (1.13,1.82)	0.003	86.4	< 0.001	Random	
Treatment							0.424
TURBT	4	1.30 (0.67,2.53)	0.438	77.0	0.005	Random	
RC	9	1.61 (1.25,2.06)	< 0.001	87.9	< 0.001	Random	
CSS							
Total	6	1.14 (0.96,1.35)	0.138	56.2	0.044	Random	
Ethnicity							0.312
Asian	3	1.42 (0.98,2.07)	0.063	0	0.459	Random	
Caucasian	3	1.08 (0.91,1.28)	0.371	68.9	0.040	Random	
Sample size							0.244
< 200	3	1.23 (0.73,2.09)	0.440	50.2	0.134	Random	
≥ 200	3	1.21 (1.05,1.39)	0.007	0	0.964	Random	
Cut-off value							0.870
< 150	2	1.20 (0.78,1.85)	0.413	0	0.775	Random	
≥ 150	4	1.14 (0.93,1.40)	0.197	71.9	0.014	Random	
Treatment							0.733
TURBT	3	1.22 (0.80,1.86)	0.358	0	0.925	Random	
RC	3	1.14 (0.92,1.41)	0.220	80.8	0.005	Random	
RFS							
Total	9	1.68 (1.26,2.24)	< 0.001	68.6	0.001	Random	
Ethnicity							0.080
Asian	5	2.00 (1.40,2.85)	< 0.001	55.4	0.062	Random	
Caucasian	4	1.26(0.97,1.64)	0.080	22.3	0.277	Random	
Publication year							0.935
Before 2020	2	1.72 (0.79,3.77)	0.175	83.7	0.013	Random	
After 2020	7	1.70 (1.22,2.38)	0.002	54.4	0.040	Random	
Sample size							0.138
< 200	5	1.64 (1.09,2.49)	0.019	68.2	0.014	Random	
≥ 200	4	1.76 (1.07,2.88)	0.026	65.5	0.034	Random	
Cut-off value							0.075
< 150	6	2.02 (1.48,2.77)	< 0.001	46.4	0.097	Random	
≥ 150	3	1.21 (1.08,1.36)	0.002	0	0.779	Random	
Treatment							0.576
TURBT	8	1.81 (1.32,2.47)	< 0.001	53.4	0.036	Random	
PFS							
Total	6	1.61 (1.00,2.59)	0.052	58.3	0.035	Random	
Ethnicity							0.446
Asian	3	1.81 (0.79,4.11)	0.159	74.5	0.020	Random	
Caucasian	3	1.44 (0.71,2.92)	0.306	51.8	0.126	Random	
Sample size							0.387
< 200	4	1.20(0.71,2.03)	0.501	45.2	0.140	Random	
≥ 200	2	2.62(1.61,4.27)	< 0.001	2.1	0.312	Random	
Cut-off value							0.539
Continued							

Survival analysis	No. of studies	HR (95% CI)	p	I^2 (%)	*P*-value for heterogeneity	Analysis model	Meta Regression *P*
< 150	5	1.81 (1.12,2.93)	0.016	55.6	0.061	Random	
Treatment							0.282
TURBT	5	1.90 (1.21,2.99)	0.006	40.9	0.149	Random	

Table 3. Subgroup analysis of the association between PLR and OS, CSS, RFS, PFS. *NA* not available, *HR* hazard ratios, *OS* overall survival, *CSS* cancer-specific survival, *RFS* recurrence-free survival, *PFS* progression-free survival.

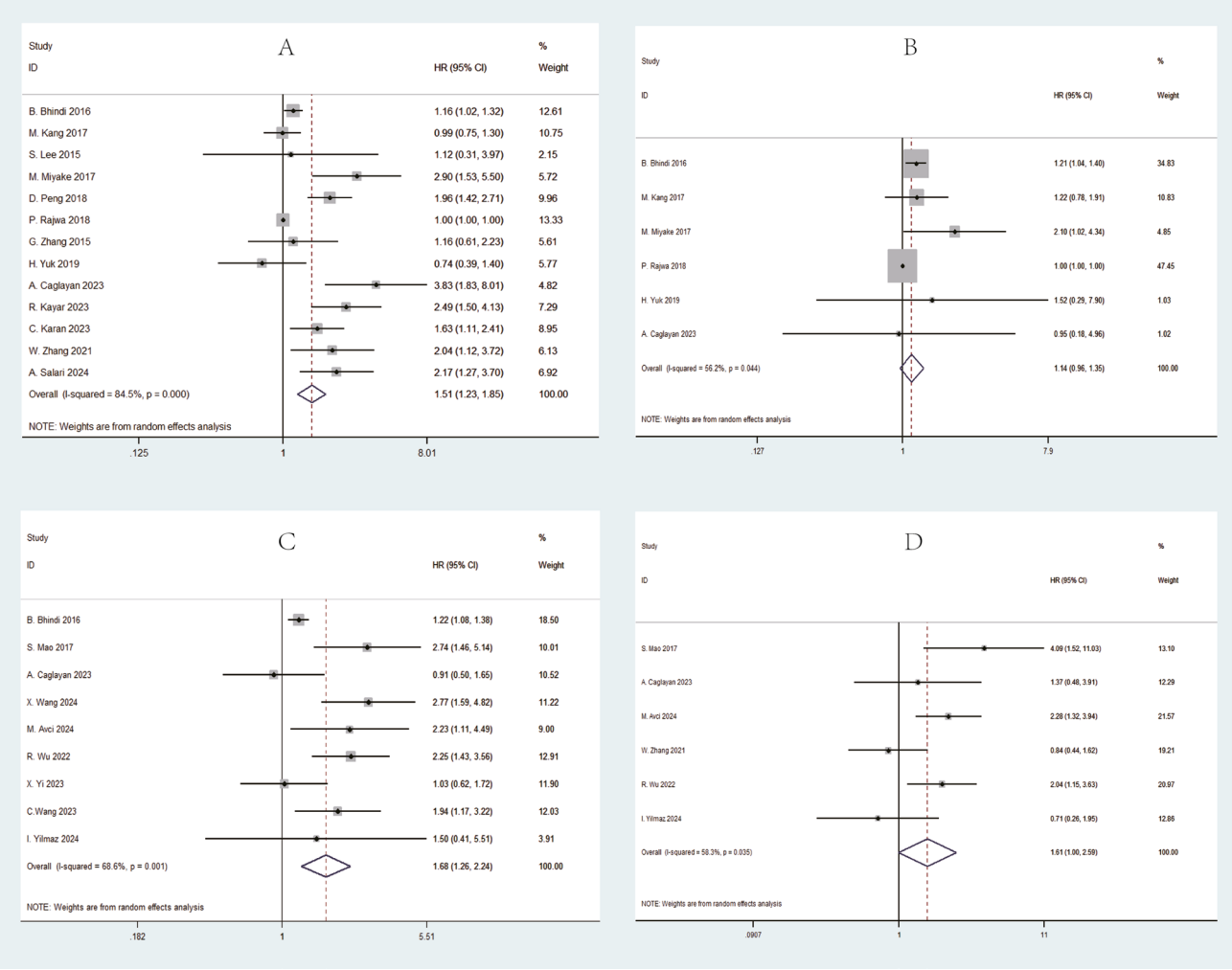

Fig. 2. Meta-analysis of the association between PLR and (**A**) OS, (**B**) CSS, (**C**) RFS, and (**D**) PFS mortality of bladder cancer.

Discussion

This updated meta-analysis analyzed 20 studies comprising 5594 BCa patients to determine the prognostic importance of PLR. Compared to the previous meta-analysis, our study incorporated an additional 12 articles encompassing 2291 patients, and further introduced PFS as an outcome measure. Concerning OS, despite the inclusion of a more extensive dataset, our findings replicated those of the previous meta-analysis, indicating that a high PLR is associated with inferior OS, consistent with previous study[17]. Regarding the correlation between PLR and age, we retained the data consistent with past investigations as well, suggesting that a high PLR is related to BCa patients aged ≥ 65 years. This finding may be attributed to the substantial remodeling and decline of the immune system that occurs with advancing age[47]. In addition, including more data enabled us to discover a statistically significant link between PLR and bad RFS. Moreover, elevated PLR was significantly correlated with higher tumor stage and increased tumor size, indicating its potential as a marker of tumor burden. Consequently, the serum PLR can function as a convenient and dependable biomarker for prognosing BCa.

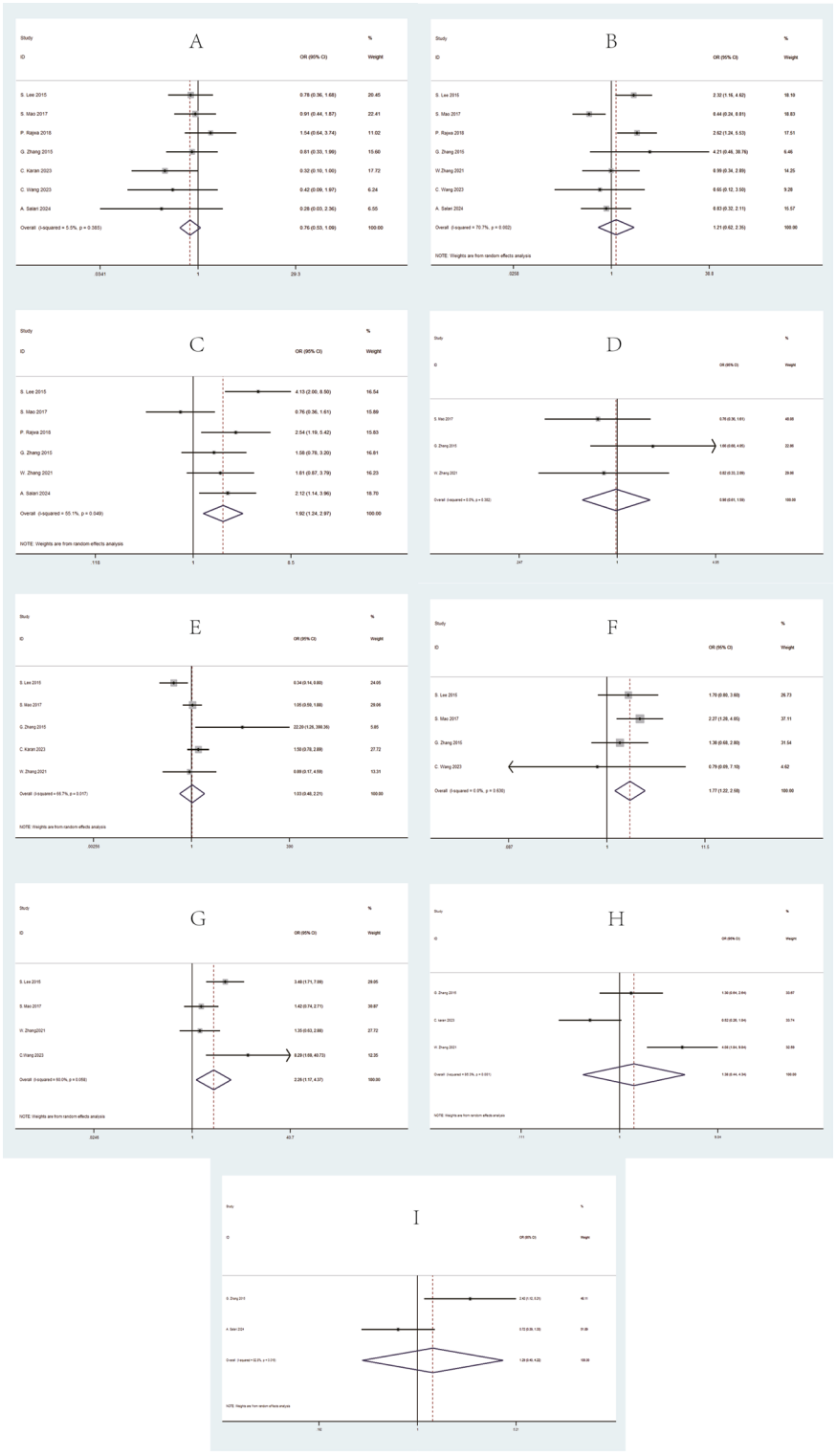

Fig. 3. Forest plots of associations between PLR and (**A**) sex, (**B**) tumor grade, (**C**) tumor stage, (**D**) diabetes, (**E**) distant metastasis, (**F**) age, (**G**) tumor size, (**H**) smoking status, and (**I**) with chemotherapy.

The ability of PLR to predict bladder cancer may involve the following mechanisms: PLR is calculated by dividing the number of platelets by the number of lymphocytes, and it primarily involves these two types of blood cells. First, a substantial body of experimental evidence indicates that platelets are integral to various physiological and pathophysiological processes beyond their traditional role of maintaining hemostasis. Mechanistic investigations have identified the platelet adenosine diphosphate (ADP) receptor P2Y12 as being indispensable for platelet aggregation within canine cancer models[48]. Additionally, platelets trigger Epithelial

Clinicopathological factors	No. of studies	OR (95% CI)	p	I^2 (%)	*P*-value for heterogeneity	Analysis model
Sex (M vs. F)	7	0.78 (0.53, 1.14)	0.135	5.1	0.388	Random
Tumor grade (G3 vs. G1/G2)	7	1.21 (0.62, 2.35)	0.583	70.7	0.002	Random
Tumor stage (T2-T4 vs. Ta-T1)	6	1.92 (1.24, 2.97)	0.003	55.1	0.049	Random
Diabetes (yes vs. no)	3	0.98 (0.60,1.60)	0.940	0	0.382	Random
Distant metastasis (yes vs. no)	5	1.03 (0.48, 2.21)	0.932	66.7	0.017	Random
Age (y) (≥ 65 vs. < 65)	4	1.77 (1.22,2.59)	0.003	0	0.630	Random
Tumor size (cm) (≥ 3 vs. < 3)	4	2.26 (1.17,4.37)	0.016	60.0	0.058	Random
Smoking (yes vs. no)	3	1.38 (0.44, 4.34)	0.580	86.3	0.001	Random
With chemotherapy(yes vs. no)	2	1.29 (0.40,4.22)	0.672	82.8	0.016	Random

Table 4. Meta-analysis results of PLR and clinicopathological parameters in patients with bladder cancer.

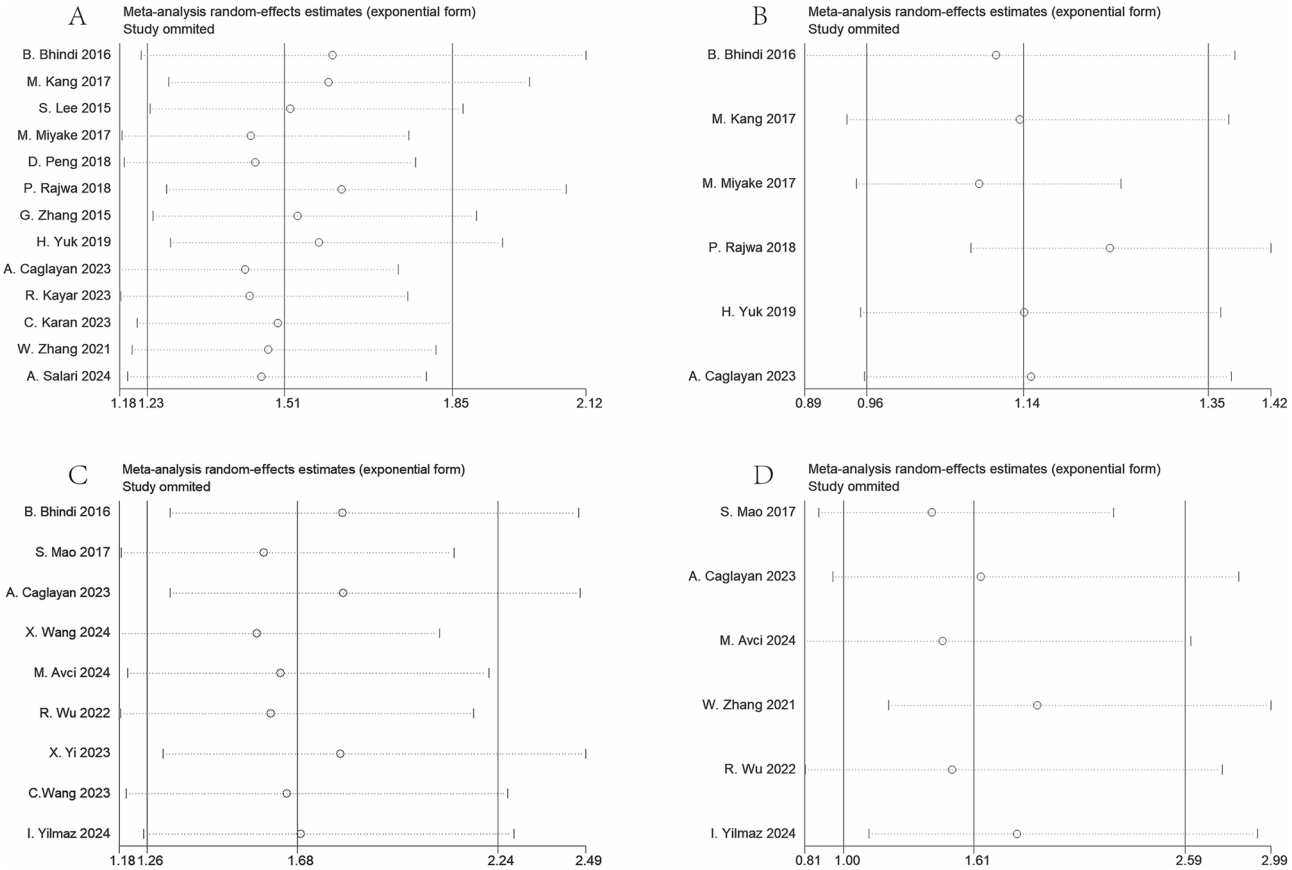

Fig. 4. Sensitivity analysis results. (**A**) OS, (**B**) CSS, (**C**) RFS, and (**D**) PFS.

Mesenchymal Transition (EMT) to foster cancer progression and invasiveness[49]. On the other hand, lymphocytes are widely recognized as indicators of systemic immune status, and their reduction serves as a hallmark of immunosuppression. A decreased lymphocyte count is closely linked to tumor immune evasion and unfavorable changes within the tumor immune microenvironment[50]. Taken together, PLR, as a composite inflammatory marker, reflects the balance between tumor-promoting and tumor-inhibiting immune mechanisms.

Previous investigations have demonstrated the prognostic value of PLR across diverse types of cancer. A comprehensive meta-analysis encompassing 49 studies entailing 28,929 participants suffering from gastric cancer demonstrated a considerable correlation between high levels of PLR and bad OS ($P < 0.001$) and DFS ($P < 0.001$)[51]. However, there is conflicting evidence regarding the association between PLR and the prediction of BCa. In this meta-analysis, we first found that elevated PLR levels serve as feasible predictive markers for both OS and RFS in adults with BCa. In addition, we observed a significant correlation between PLR and PFS in patients treated with TURBT ($P < 0.001$), which is consistent with the findings of Hu et al. [52]. It should be noted that both the study by Hu et al. and the present analysis included only five studies; hence, the findings should be interpreted with caution. In contrast, no association was found between PLR and PFS among patients undergoing RC, which we attribute to the limited number of available studies in this subgroup. Lastly, this meta-

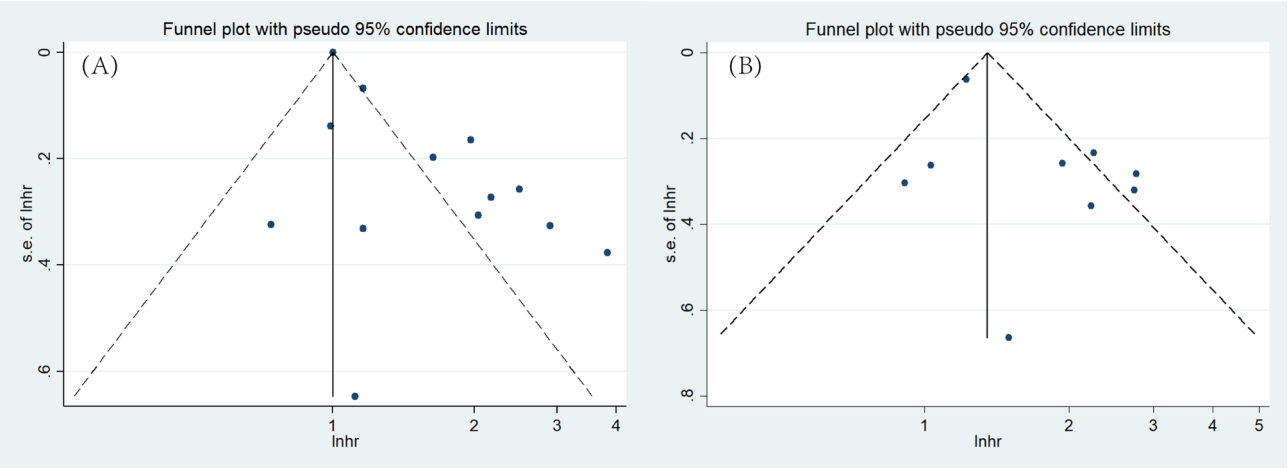

Fig. 5. Funnel plot of included studies. (**A**) OS and (**B**) RFS.

analysis did not find that PLR predicted CSS in BCa. In summary, elevated PLR may indicate the need for more intensive and individualized therapeutic approaches.

Regarding heterogeneity, we prioritized the between-subgroups *P* value as the primary indicator to determine whether a stratification factor could explain the observed variability, while the extent of I^2 reduction and improvements in within-subgroup homogeneity were considered as supporting evidence. For OS, the year of publication satisfied these criteria, whereas ethnicity and cut-off value in RFS showed only borderline trends. For CSS and PFS, certain subgroups demonstrated improved homogeneity; however, in the absence of significant between-subgroups *P* values, these observations should be interpreted as exploratory. Overall, the limited number of included studies and the uneven distribution of subgroups reduced the statistical power. Therefore, we interpreted these findings with caution and emphasized the need for further validation in future research.

Notably, our findings further suggest that in patients aged ≥ 65 years, with tumor stage ≥ T2, or with tumor size ≥ 3 cm, evaluation of the PLR may be particularly valuable for guiding treatment decisions and improving clinical outcomes. It is noteworthy that their OR were all within the small range. Our study also incorporated additional clinicopathological variables, including diabetes, smoking status and chemotherapy exposure. Although the associations between PLR and these factors did not reach statistical significance ($P = 0.943$, $P = 0.580$ and $P = 0.672$, respectively), their inclusion broadens the clinical context of the analysis and highlights potential directions for future investigations. As more data accumulate, these variables may emerge as significant modifiers of the prognostic value of PLR in BCa.

Finally, we acknowledge that this investigation has constraints. Firstly, ethnic groups in this research are relatively homogeneous, as all the participants were either from Caucasian or Asian backgrounds. Therefore, our conclusions are not generalizable to individuals of other ethnic groups. Second, all studies included in this analysis were retrospective, which inherently subjects the pooled results to selection bias, information bias, and confounding bias. Third, considerable heterogeneity was observed across studies, particularly in the analyses of OS and RFS ($I^2 > 60\%$). Although subgroup analysis and meta-regression were performed, the main source of heterogeneity in RFS could not be clearly identified. Forth, we chose the OR as the effect size for clinicopathological characteristics rather than the relative risk (RR). Several studies have noted that when the outcome is common, OR may appear larger than the corresponding RR[53], thus potentially exaggerating the results. Therefore, caution is warranted in their interpretation. Lastly, in the OR results of PLR with age and tumor size, only four studies were included in each, which is fewer than five. Therefore, the reliability of these findings remains limited and requires further validation with additional studies. Future investigations are required to address these shortcomings.

Conclusion

In summary, this updated meta-analysis is the first to demonstrate that elevated PLR levels may serve as reliable predictive markers for both OS and RFS. Additionally, we first revealed that high PLR was significantly associated with advanced tumor stage and larger tumor size. This further confirms that PLR is a valuable prognostic tool for individuals suffering from BCa.

Data availability

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

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Author contributions

ZZ and YZ designed the research and edited and revised the article. BZ and ZY performed the data extraction. BZ, ZY and ZZ carried out the meta-analysis. BZ and ZY drafted the article. All authors approved the submitted and final versions.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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