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REVIEW

Prognostic value of platelet-to-lymphocyte ratio in pancreatic cancer: a comprehensive meta-analysis of 17 cohort studies

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Background and aims: Several studies were conducted to explore the prognostic value of platelet-to-lymphocyte ratio (PLR) in pancreatic cancer and have reported contradictory results. This study aims to summarize the prognostic role of PLR in pancreatic cancer.

Materials and methods: Embase, PubMed and Cochrane Library were completely searched. The cohort studies focusing on the prognostic role of PLR in pancreatic cancer were eligible. The overall survival (OS) and progression-free survival (PFS) were analyzed.

Results: Fifteen papers containing 17 cohort studies with pancreatic cancer were identified. The results showed patients that with low PLR might have longer OS when compared to the patients with high PLR (hazard ratio=1.28, 95% CI=1.17–1.40, $P<0.00001$; $I^2=42\%$). Similar results were observed in the subgroup analyses of OS, which was based on the analysis model, ethnicity, sample size and cut-off value. Further analyses based on the adjusted potential confounders were conducted, including CA199, neutrophil-to-lymphocyte ratio, modified Glasgow Prognostic Score, albumin, C-reactive protein, Eastern Cooperative Oncology Group, stage, tumor size, nodal involvement, tumor differentiation, margin status, age and gender, which confirmed that low PLR was a protective factor in pancreatic cancer. In addition, low PLR was significantly associated with longer PFS when compared to high PLR in pancreatic cancer (hazard ratio=1.27, 95% CI=1.03–1.57, $P=0.03$; $I^2=33\%$).

Conclusion: In conclusion, it was found that high PLR is an unfavorable predictor of OS and PFS in patients with pancreatic cancer, and PLR is a promising prognostic biomarker for pancreatic cancer.

Keywords: platelet-to-lymphocyte ratio, pancreatic cancer, prognostic, progression-free survival, overall survival, biomarker

Introduction

It was estimated that 53,670 cases would be newly diagnosed with pancreatic cancer and 43,090 cases would die from pancreatic cancer in the USA in 2017.[1] Although great development of the diagnosis and treatment of pancreatic cancer has been made in recent years, the prognosis of patients with pancreatic cancer remains disappointing.[2,3] In 2016, there were an estimated 53,070 patients newly diagnosed with pancreatic cancer and an estimated 41,780 deaths from pancreatic cancer in the USA.[4]

In view of the poor prognosis outcome of patients with various cancers, more and more attention was paid to explore the predictive factors of cancers.[5–8] Regarding pancreatic cancer, several factors might be involved in the prognosis of patients, including mRNA, protein, clinical index and so on.[9–12]

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In recent years, several studies have reported that inflammatory pathways might play an important role in the tumorigenesis and metastasis.[13–16] Meanwhile, inflammatory biomarkers are expected to be a prognostic index of pancreatic cancer, including neutrophil-to-lymphocyte ratio (NLR), C-reactive protein (CRP), platelet-to-lymphocyte ratio (PLR) and so on.[17–19] Yang et al performed a meta-analysis and found that high peripheral blood PLR suggested a poor prognosis for patients with pancreatic cancer.[19] However, there was no consistent conclusion on the role of PLR in pancreatic cancer. Kishi et al analyzed 65 patients with pancreatic cancer and drew the conclusion that PLR was not associated with the prognosis of these patients.[20] Nevertheless, other researchers focusing on pancreatic cancer found opposite results, which indicated that patients with low PLR might have longer overall survival (OS) when compared to the patients with high PLR.[20–22] On account of these controversies, we performed this meta-analysis to explore the prognostic value of PLR in pancreatic cancer.

Materials and methods

Literature search strategy

The Cochrane Library, PubMed and Embase database were comprehensively searched up to May 2, 2017. The search terms included "pancreatic neoplasm", "pancreatic cancer", "PLR", "platelet-to-lymphocyte ratio", "platelet lymphocyte ratio" and "platelet-lymphocyte ratio". The relevant conference papers were also carefully assessed. All the retrieved papers were carefully checked. After scanning the abstracts or titles, the distinctly irrelevant articles were excluded. For the remaining papers, the full text was carefully reviewed.

Inclusion criteria

The study would be included into this meta-analysis if it met all the following criteria: 1) cohort study; 2) focusing on the prognostic value of PLR in pancreatic cancer; 3) enough data to obtain the hazard ratio (HR) for OS, along with their 95% CIs or *P*-values and 4) published in English.

Exclusion criteria

The exclusion criteria were as follows: 1) comments, reviews, case reports and expert opinions; 2) data deficiencies of the HR; 3) not focusing on the prognostic value of PLR in pancreatic cancer; 4) lacking key information for further analysis; 5) duplicate publications; 6) reporting the overlapping data and 7) non-human research.

Data extraction

Two investigators evaluated and extracted the data independently. For each included study, the following data were abstracted: the first author, year of publication, country of the study, ethnicity, number of patients, percentage of males, cut-off value, survival outcomes and analysis model. It should be noted that patients in each original study were divided into two groups based on the cut-off value of PLR: high PLR group and low PLR group. The HRs of prognostic outcomes obtained directly or indirectly from the published articles were integrated in the meta-analysis according to the study conducted by Tierney et al.[23] If the HR was assessed with both multivariate analysis and univariate analysis, the results of multivariate analysis were applied in the current study. The quality of the included studies was assessed using the Newcastle–Ottawa Scale (NOS). Also, studies with NOS score $\geq$6 were considered to be of high quality. Any other disputes were discussed with the third investigator.

Statistical analysis

The main results of this meta-analysis were analyzed by Review Manager Version 5.3 software. The prognosis outcomes were assessed using the HR, along with the corresponding 95% CI or *P*-values. The main prognostic outcome was the OS. Cochran's Q test and Higgins I^2 were applied to evaluate the heterogeneity among included studies. Heterogeneity should be considered if $I^2>50\%$, and the random-effect model was applied; if not, the fixed-effect model was applied. In addition, to explore the publication bias, the funnel plot was drawn using Review Manager Version 5.3 software. To validate the credibility of outcomes in this meta-analysis, the sensitivity analysis was performed using Stata 12.0. Nonetheless, the subgroup analysis was carried out to further explore the association between the PLR and prognosis of patients with pancreatic cancer. The difference was considered to be statistically significant when the *P*-value was <0.05.

Results

Literature search

As shown in Figure 1, the literature search process is summarized in a flow diagram according to Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA).[24] One hundred seventy-one papers were initially retrieved from the Cochrane Library, PubMed and Embase database. One hundred thirty-six papers remained after duplicates were removed. For the remaining 136 papers, 112 papers with significantly diverse topics were directly excluded by

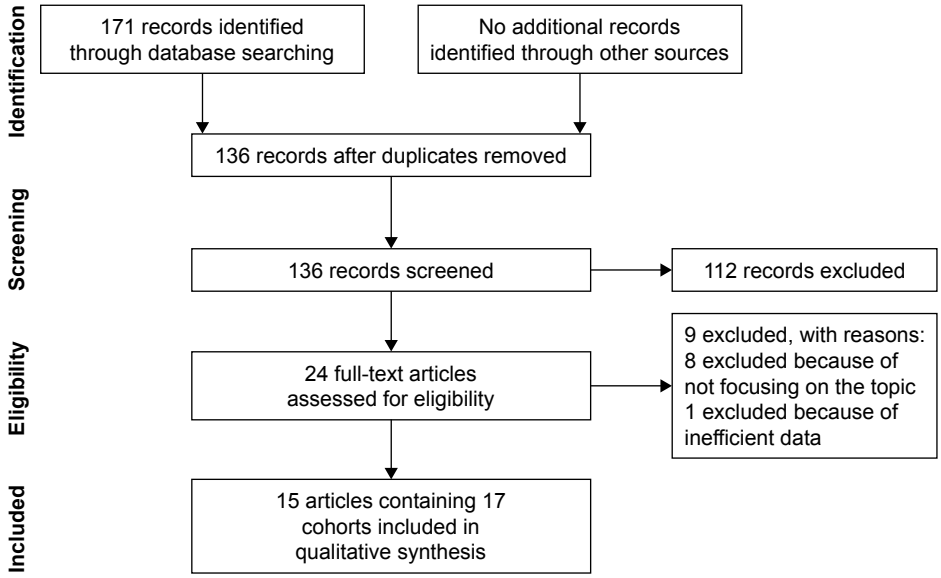

Figure 1 Flow diagram of the study selection process.

scanning the titles or abstracts. Among the rest of the papers, eight papers were excluded for not focusing on the topic and one paper was excluded for inefficient data. Therefore, 15 papers containing 17 cohort studies were finally included in this meta-analysis.[20–22,25–36]

Characteristics of included studies

The clinical details of the included studies are presented in Table 1. Regarding the 17 included cohort studies, 5 were performed in China,[30,32,34,36] 5 in Japan,[20,21,26,28,35] 2 in USA,[22,25] 2 in Austria,[33] 1 in Australia,[31] 1 in Singapore[27] and 1 in South Korea.[29] Besides, sample size of the included cohort studies varied from 37 to 440. As for the gender information in the included studies, the percentage of males among the cohort studies varied from 39.5% to 88.8%. As for clinical outcomes, all the included cohort studies reported the OS,[20–22,25–36] two studies reported the disease-free survival (DFS),[20,21] one study presented the recurrence-free survival (RFS)[22] and one study

Table 1 Main information of the included studies in the meta-analysis

Study	Country	Ethnicity	Patients (n)	Male n (%)	Age (years)	Outcome	Analysis	Cut-off value	Therapy	NOS
Wang et al 2012[34]	China	Asian	177	120 (67.8)	<65.0 (70.1%)	OS	U	300	NA	7
Stotz et al 2013[33] (1)	Austria	Caucasian	261	103 (39.5)	<65.0 (42.5%)	OS	U	150	NA	6
Stotz et al 2013[33] (2)	Austria	Caucasian	110	51 (46.4)	<65.0 (50.0%)	OS	U	150	Surgery	6
Martin et al 2014[31]	Australia	Caucasian	124	66 (53.2)	68.5 (35–90)	OS	M	200	NA	7
Qi et al 2015[32]	China	Asian	211	134 (63.5)	<60.0 (75.4%)	OS	M	126	NA	7
Goh et al 2015[27]	Singapore	Asian	120	49 (40.8)	60.5 (24–84)	OS	M	208.1	NA	8
Inoue et al 2015[28]	Japan	Asian	440	249 (56.6)	67.0 (32–88)	OS	U	150	NA	6
Kishi et al 2015[20]	Japan	Asian	65	39 (60.0)	65.0 (35–85)	OS, DFS	U	150	Chemoradiotherapy	7
Shirai et al 2015[21]	Japan	Asian	131	81 (61.8)	66.5±10.2[a]	OS, DFS	M	150	Surgery	6
Spolverato et al 2015[22]	USA	Caucasian	420	208 (49.5)	NA	OS, RFS	M	190	Surgery	8
Alagappan et al 2016[25]	USA	Caucasian	208	109 (52.4)	75.2 (65.9–86.1)	OS	U	200	Radiotherapy	7
Asari et al 2016[26]	Japan	Asian	37	20 (54.0)	<70.0 (62.0%)	OS	M	225	Surgery	6
Lee et al 2016[29]	South Korea	Asian	82	49 (60.0)	63.5±10.7[a]	OS, PFS	U	150	Chemotherapy	8
Watanabe et al 2016[35]	Japan	Asian	46	26 (56.5)	NA	OS	M	200	Surgery	6
Liu et al 2017[30]	China	Asian	386	238 (61.7)	<65.0 (64.2%)	OS	U	165.5	NA	6
Yu et al 2017[36] (1)	China	Asian	139	83 (59.7)	<60.0 (38.8%)	OS	U	154	Chemotherapy	7
Yu et al 2017[36] (2)	China	Asian	225	146 (64.9)	<60.0 (34.7%)	OS	U	154	Chemotherapy	6

Notes: (1) cohort I; (2) cohort II. Data presented as range unless otherwise indicated. [a]Data presented as mean ± SD.
Abbreviations: DFS, disease-free survival; M, multivariate analysis; NA, not available; NOS, Newcastle–Ottawa scale; OS, overall survival; PFS, progression-free survival; RFS, recurrence-free survival; U, univariate analysis.

covered the progression-free survival (PFS).[29] Moreover, the OS of 10 cohort studies was assessed with univariate analysis;[20,25,28–30,33,34,36] however, the other studies evaluated it with multivariate analysis.[21,22,26,27,31,32,35] Besides, the NOS score of each included study was ≥6, which meant that the included studies were of relatively high quality. Regarding the seven studies assessed with multivariate analysis, the main adjusted potential confounders included CA199, NLR, modified Glasgow Prognostic Score (mGPS), albumin, CRP, Eastern Cooperative Oncology Group (ECOG), stage, tumor size, nodal involvement, tumor differentiation, margin status, age and gender, and the details are listed in Table S1.

The meta-analysis of OS

All the included studies covered the OS of patients with pancreatic cancer. Therefore, 17 cohort studies were finally gathered into the meta-analysis of OS. As shown in Figure 2, in view of low heterogeneity (I^2=42%), fixed-effect model was used. And the results indicated that there was statistically significant relationship between the PLR and prognosis of patients with pancreatic cancer, and patients with low PLR might have longer OS when compared to the patients with high PLR (HR=1.28, 95% CI=1.17–1.40, P<0.00001). Furthermore, funnel plot was conducted to explore the bias among the included studies, and the results demonstrated that no obvious publication bias was detected (Figure 3). Furthermore, sensitivity analysis conducted by Stata 12.0 confirmed the robustness of the results (Figure S1).

To further explore the prognostic value of PLR in pancreatic cancer, subgroup analyses were performed based on the analysis model, ethnicity, sample size and cut-off value. The main results were presented in Table 2. In terms of analysis model, when only the studies with multivariate analysis were included into the meta-analysis, significant association between the PLR and OS was observed, with low heterogeneity (HR=1.76, 95% CI=1.45–2.14, P<0.00001; I^2=9%). Similarly, when only considering the studies with univariate analysis, obvious correlation was detected between the PLR and prognosis of pancreatic cancer (HR=1.18, 95% CI=1.07–1.30, P=0.001; I^2=0%). Subgroup analyses by ethnicity revealed that negative predictor of high PLR for OS was found both in Asian cases (HR=1.35, 95% CI=1.14–1.61, P=0.0006; I^2=52%) and in Caucasian populations (HR=1.25, 95% CI=1.08–1.45, P=0.004; I^2=17%). Regarding sample size, distinct association between the PLR and OS was detected not only when the sample size ≤150 (HR=1.49, 95% CI=1.14–1.94, P=0.003; I^2=52%) but also when the sample size >150 (HR=1.26, 95% CI=1.11–1.42, P=0.0003; I^2=31%). Additionally, considering different cut-off values, PLR was a negative prognostic biomarker for the cut-off value ≤150 (HR=1.19, 95% CI=1.02–1.40, P=0.002; I^2=29%) and the cut-off value >150 (HR=1.39, 95% CI=1.23–1.56, P<0.00001; I^2=43%). As for treatment, obvious association between the PLR and OS was detected not only when the treatment was surgery (HR=1.86, 95% CI=1.22–2.84, P=0.004; I^2=63%) but also when the treatment was not surgery (HR=1.24, 95% CI=1.13–1.36, P<0.0001; I^2=22%).

The further analysis was conducted based on the 7 studies assessed with multivariate analysis. As listed in Table 3,

Study or subgroup	Log (hazard ratio)	SE	% weight	Hazard ratio IV, fixed, (95% CI)	Year
Wang et al 2012[34]	0.1848	0.1561	8.1	1.20 (0.89–1.63)	2012
Stotz et al 2013[33] (2)	0.1249	0.1681	7.0	1.13 (0.81–1.58)	2013
Stotz et al 2013[33] (1)	0.0686	0.135	10.9	1.07 (0.82–1.40)	2013
Martin et al 2014[31]	0.4574	0.1989	5.0	1.58 (1.07–2.33)	2014
Inoue et al 2015[28]	0.0469	0.1141	15.2	1.05 (0.84–1.31)	2015
Kishi et al 2015[20]	–0.1393	0.2725	2.7	0.87 (0.51–1.48)	2015
Goh et al 2015[27]	1.1099	0.6286	0.5	3.03 (0.89–10.40)	2015
Spolverato et al 2015[22]	0.5822	0.2722	2.7	1.79 (1.05–3.05)	2015
Shirai et al 2015[21]	0.5235	0.2447	3.3	1.69 (1.04–2.73)	2015
Qi et al 2015[32]	0.4523	0.1653	7.2	1.57 (1.14–2.17)	2015
Lee et al 2016[29]	0.3577	0.3028	2.2	1.43 (0.79–2.59)	2016
Alagappan et al 2016[25]	0.2546	0.1561	8.1	1.29 (0.95–1.75)	2016
Asari et al 2016[26]	1.1151	0.4893	0.8	3.05 (1.17–7.96)	2016
Watanabe et al 2016[35]	1.5149	0.4903	0.8	4.55 (1.74–11.89)	2016
Yu et al 2017[36] (1)	0.0989	0.2146	4.3	1.10 (0.72–1.68)	2017
Yu et al 2017[36] (2)	0.116	0.1567	8.1	1.12 (0.83–1.53)	2017
Liu et al 2017[30]	0.4055	0.1224	13.2	1.50 (1.18–1.91)	2017
Total (95% CI)			**100**	**1.28 (1.17–1.40)**	

Heterogeneity: χ^2=27.68, df=16 (P=0.03); I^2=42%
Test for overall effect: Z=5.53 (P<0.00001)

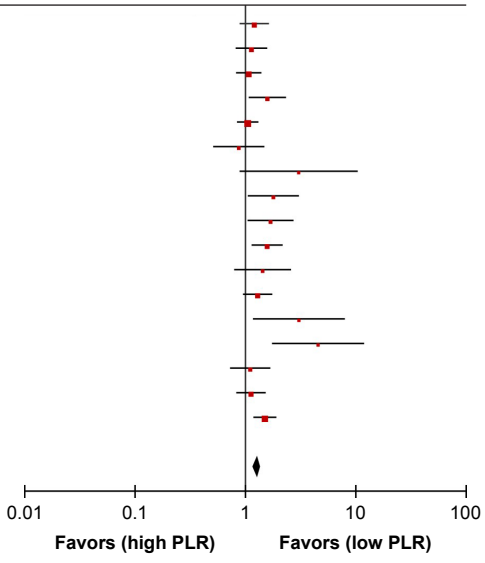

Figure 2 Meta-analysis of overall survival.
Abbreviations: *df*, degrees of freedom; PLR, platelet-to-lymphocyte ratio; SE, standad error.

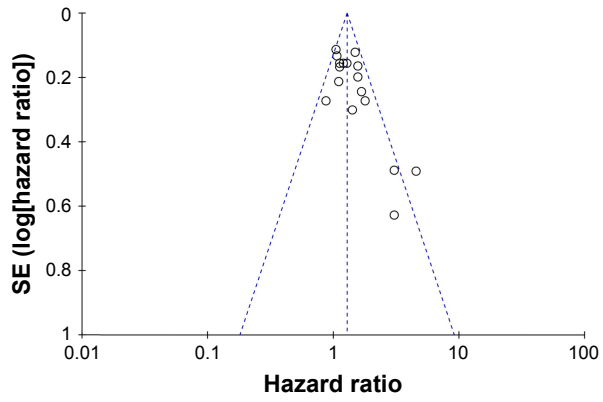

Figure 3 Funnel plot of overall survival.
Abbreviation: SE, standard error.

obvious relationship between the PLR and OS in pancreatic cancer was detected based on the subgroup analyses regarding the main adjusted potential confounders, including CA199, NLR, mGPS, albumin, CRP, ECOG, stage, tumor size, nodal involvement, tumor differentiation, margin status, age and gender.

The meta-analysis of PFS

Among the included studies, two studies reported the DFS, one study presented the RFS and one study covered the PFS. Also, these four studies were finally included into the meta-analysis of PFS. As shown in Figure 4, the results indicated that low PLR was significantly associated with longer PFS when compared to high PLR, with low heterogeneity (HR=1.27, 95% CI=1.03–1.57, P=0.03; I^2=33%). In addition, funnel plot indicated that there was no obvious bias of included studies (Figure 5).

Discussion

Inflammation is a hallmark of various cancers. Increasing evidences have shown that systemic inflammatory response was involved in tumorigenesis, malignant transformation and metastasis.[37,38] Platelet has been proved to be associated with the diagnosis and treatment of cancers.[39,40] Besides, lymphocyte infiltration in advanced stages is lower than that in the early stages of pancreatic cancer. In recent years, more and more researchers have started to pay attention to the prognostic role of PLR in various cancers, including liver cancer,[41] lung cancer[42] and colorectal cancer,[43] as well as esophageal cancer.[44] Similarly, the prognostic value of PLR in pancreatic cancer was also being investigated; however, the results were controversial.[21,26,28,31]

In the current study, the results demonstrated that PLR was significantly associated with the OS of patients with pancreatic cancer, which was similar to the conclusion in other cancers.[42,44–48] Patients with low PLR had longer OS when compared to the patients with high PLR, indicating that low PLR might be a protective factor for pancreatic cancer. Besides, the subgroup analysis based on analysis model, ethnicity, sample size and cut-off value also presented similar results. It is worth mentioning that we conducted further analysis based on the adjusted potential confounders, including CA199, NLR, mGPS, albumin, CRP, ECOG, stage, tumor size, nodal involvement, tumor differentiation, margin status, age and gender, which was not reported in the earlier similar meta-analysis.[19,44] Also, the results confirmed that low PLR was associated with longer OS in pancreatic cancer. We further explored the association between PLR, PFS, RFS and DFS; the results similarly demonstrated that

Table 2 Subgroup analysis of the association between the PLR expression and OS

Survival analysis	Included cohorts	HR (95% CI)	*P*-value	I^2 (%)	*P*-value for heterogeneity	Analysis model
Analysis model						
Multivariate	7	1.76 (1.45–2.14)	<0.00001*	9	0.36	Fixed
Univariate	10	1.18 (1.07–1.30)	0.001*	0	0.57	Fixed
Ethnicity						
Caucasian	5	1.25 (1.08–1.45)	0.004*	17	0.31	Fixed
Asian	12	1.35 (1.14–1.61)	0.0006*	52	0.02	Random
Sample size						
≤150	9	1.49 (1.14–1.94)	0.003*	52	0.03	Random
>150	8	1.26 (1.11–1.42)	0.0003*	31	0.18	Fixed
Cut-off value						
≤150	7	1.19 (1.02–1.40)	0.03*	29	0.21	Fixed
>150	10	1.39 (1.23–1.56)	<0.00001*	43	0.07	Fixed
Treatment						
Surgery	5	1.86 (1.22–2.84)	0.004*	63	0.029	Random
Not surgery	12	1.24 (1.13–1.36)	<0.00001*	22	0.229	Fixed

Note: *P<0.05, the difference was statistically significant.
Abbreviations: HR, hazard ratio; OS, overall survival; PLR, platelet-to-lymphocyte ratio.

Table 3 Subgroup analysis of OS based on the adjusted potential confounders of the seven studies assessed with multivariate analysis

Analysis	Included cohorts	HR (95% CI)	*P*-value	I^2 (%)	*P*-value for heterogeneity	Model
CA19-9						
Yes	3	1.64 (1.29–2.09)	<0.0001*	0	0.43	Fixed
No	4	2.01 (1.45–2.77)	<0.0001*	23	0.27	Fixed
NLR						
Yes	6	1.88 (1.48–2.39)	<0.00001*	14	0.33	Fixed
No	1	1.57 (1.14–2.17)	0.0006*	NA	NA	Fixed
mGPS						
Yes	2	1.73 (1.21–2.49)	0.003*	36	0.13	Fixed
No	5	1.78 (1.41–2.23)	<0.0001*	20	0.29	Fixed
Albumin						
Yes	2	1.73 (1.21–2.49)	0.003*	36	0.13	Fixed
No	5	1.78 (1.41–2.23)	<0.0001*	20	0.29	Fixed
CRP						
Yes	1	1.58 (1.07–2.33)	0.02*	NA	NA	Fixed
No	6	1.83 (1.46–2.29)	<0.0001*	19	0.29	Fixed
Tumor size						
Yes	2	1.73 (1.21–2.48)	0.005*	0	0.87	Fixed
No	5	1.78 (1.41–2.24)	<0.00001*	39	0.16	Fixed
Gender						
Yes	1	1.79 (1.05–3.05)	0.03*	NA	NA	Fixed
No	6	1.76 (1.43–2.17)	<0.0001*	24	0.26	Fixed
ECOG						
Yes	1	1.58 (1.07–2.33)	0.02*	NA	NA	Fixed
No	6	1.83 (1.46–2.29)	<0.0001*	19	0.29	Fixed
Stage						
Yes	1	1.57 (1.14–2.17)	0.01*	NA	NA	Fixed
No	6	1.88 (1.48–2.39)	<0.0001*	14	0.33	Fixed
Nodal involvement						
Yes	2	1.73 (1.21–2.48)	0.003*	0	0.87	Fixed
No	5	1.78 (1.41–2.24)	<0.00001	39	0.16	Fixed
Albumin						
Yes	2	1.73 (1.21–2.49)	0.003*	36	0.13	Fixed
No	5	1.78 (1.41–2.23)	<0.0001	20	0.29	Fixed
Margin status						
Yes	3	1.86 (1.33–2.59)	0.0003*	0	0.55	Fixed
No	4	1.72 (1.36–2.18)	<0.00001*	43	0.61	Fixed
Tumor differentiation						
Yes	1	1.69 (1.04–2.73)	0.03*	NA	NA	Fixed
No	6	1.78 (1.44–2.20)	<0.00001*	23	0.26	Fixed
Age						
Yes	1	1.79 (1.05–3.05)	0.03*	NA	NA	Fixed
No	6	1.76 (1.43–2.17)	<0.0001*	24	0.26	Fixed

Note: *$P<0.05$, the difference was statistically significant.
Abbreviations: CRP, C-reactive protein; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; mGPS, modified Glasgow Prognostic Score; NA, not available; NLR, neutrophil-to-lymphocyte ratio; OS, overall survival.

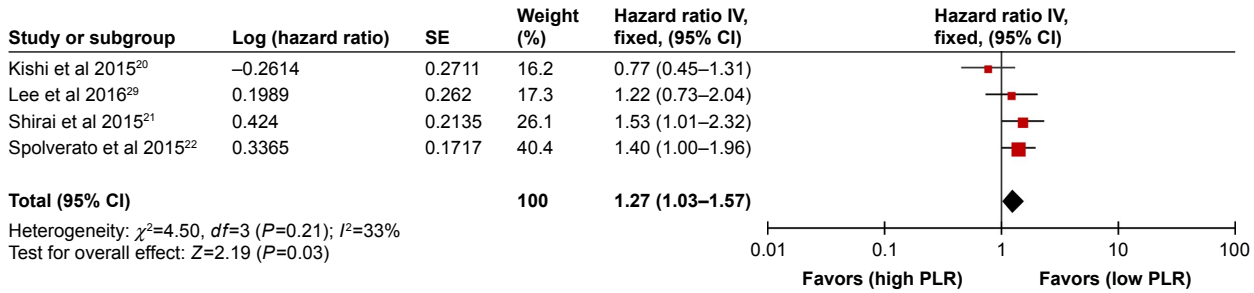

Figure 4 Meta-analysis of progression-free survival.
Abbreviations: *df*, degrees of freedom; PLR, platelet-to-lymphocyte ratio; SE, standard error.

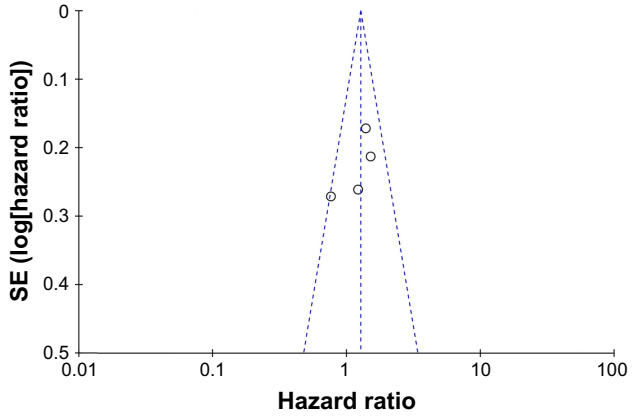

Figure 5 Funnel plot of progression-free survival.
Abbreviation: SE, standard error.

low PLR was a protective factor for patients with pancreatic cancer. Zhou et al performed a meta-analysis to explore the prognostic value of PLR in various cancers and found that PLR was not associated with OS in pancreatic cancer, which was inconsistent with our study.[49] It should be noted that only three studies were included in the meta-analysis of OS in Zhou et al's study.[49] Nevertheless, 17 cohort studies were finally included in the meta-analysis of OS; therefore, our conclusion was more convincing.

In spite of the conclusion arrived at in our study, the underlining mechanism of the prognostic value of PLR in pancreatic cancer remains unclear. Platelets might promote tumor growth, angiogenesis, metastasis and cancer-associated thrombosis.[50,51] Moreover, Abiko et al reported that interferon-gamma from the lymphocytes induced PD-L1 expression and promoted the progression of ovarian cancer.[52] Besides, He et al declared that lymphocyte promoted tumorigenesis by activating gene-3, an important immune checkpoint in cancer.[53] Xu et al found that circulating CD3+CD8+ T lymphocytes might be used as a prognostic biomarker for lung cancer.[54] Based on the platelet and lymphocyte counts, PLR might be related to the prognosis of patients with pancreatic cancer.

To the best of our knowledge, this is the first meta-analysis to explore the prognostic value of PLR in pancreatic cancer. Besides, our study contained 17 cohort studies involving 3,182 patients; therefore, the conclusion was convincing. Nonetheless, our meta-analysis is not without any limitation. First, all the data were obtained from the published articles and the original data of included patients were unavailable. Second, patients in the meta-analysis received several therapies and we cannot get the details, which may lower the applicability of this study. Third, the cut-off value of the included studies varied a lot, which might increase the heterogeneity. Fourth, some included studies lacked assessment of the confounding factors.

Conclusion

PLR could be used as a prognostic predictor in patients with pancreatic cancer. High PLR was associated with poor prognosis, especially shorter OS. In contrast, low PLR obviously was correlated with favorable OS in pancreatic cancer. More studies should be carried out to investigate the underlying mechanism.

Author contributions

Study concepts and design: YZZ, HXQ, YPZ; literature search: YPZ, SJC; data extraction: YZZ, YPZ; manuscript preparation and revision: AHF, SJC, YPZ, HXQ. All authors have participated sufficiently in the study and approved the final version. All authors contributed toward data analysis, drafting and revising the paper and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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Supplementary materials

Table S1 Adjustment for potential confounders of the seven included studies assessed with multivariate analysis

Study	CA199	NLR	mGPS	Albumin	CRP	ECOG	Stage	Tumor size	Nodal involvement	Margin status	Tumor differentiation	Age	Gender
Martin et al 2014[10]	√	√	√	√	√	√							
Qi et al 2015[11]	√						√						
Goh et al 2015[6]		√											
Shirai et al 2015[2]		√						√	√	√	√		
Spolverato et al 2015[3]		√						√	√	√		√	√
Asari et al 2016[5]	√	√	√	√						√			
Watanabe et al 2016[14]		√											

Abbreviations: CRP, C-reactive protein; ECOG, Eastern Cooperative Oncology Group; mGPS, modified Glasgow Prognostic Score; NLR, neutrophil-to-lymphocyte ratio.

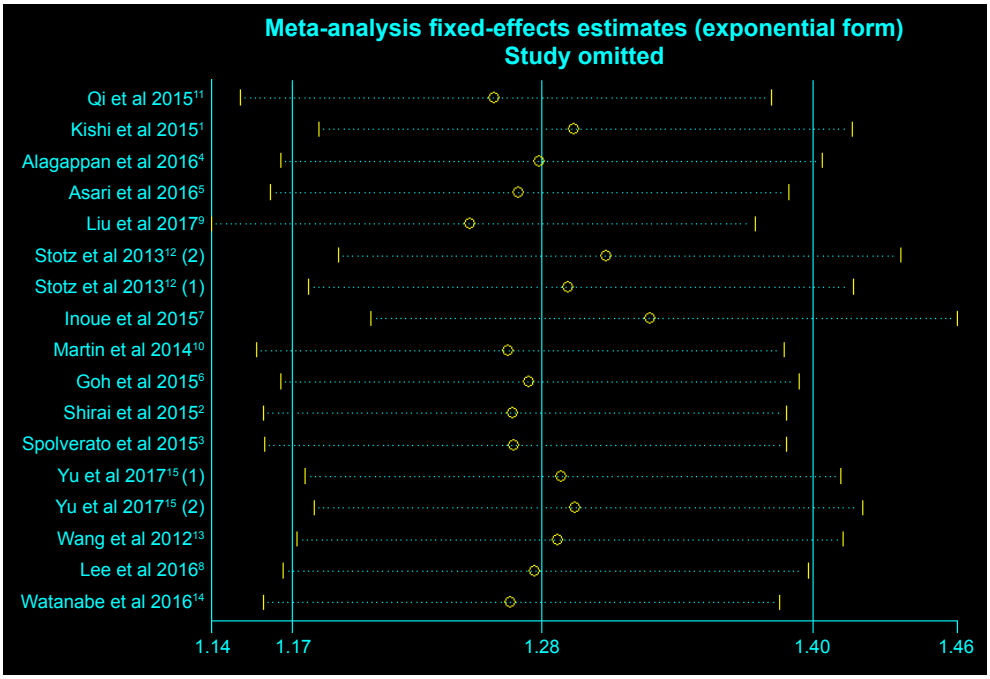

Figure S1 Sensitivity analysis of overall survival.
Note: (1) cohort I; (2) cohort II.

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