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Platelet-lymphocyte ratio acts as an independent predictor of prognosis in patients with renal cell carcinoma

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ABSTRACT

Background: The prognostic value of plated-lymphocyte ratio (PLR) in multiple malignancies had been investigated in previous studies; however, its prognostic value in renal cell carcinoma (RCC) remains controversial. This study was performed to assess the prognostic value of preoperative PLR in RCC patients.

Methods: Literature was searched from PubMed, Embase, Web of Science and Cochrane database, which evaluated the relationships between preoperative PLR and prognosis in RCC patients. Hazard ratios (HRs) for overall survival (OS) and progression-free survival (PFS) were extracted from eligible studies. Heterogeneity was assessed using the I^2 value. The fixed-effects model was used if there was no evidence of heterogeneity; otherwise, the random-effects model was used. Publication bias was evaluated using Begg's funnel plots and Egger's regression test.

Results: A total of 1528 patients from seven studies were included in the analysis. The pooled analysis showed that an elevated PLR was an effective prognostic marker of both OS (pooled HR = 2.10, 95%CI: 1.38–3.19, $p = 0.001$) and PFS (pooled HR = 3.45, 95%CI: 1.61–7.40, $p = 0.001$). Subgroup analysis revealed that a high PLR significantly predicted worse OS and PFS in Asian studies (OS, pooled HR = 2.72, 95%CI: 1.06–7.03, $p = 0.038$; PFS, pooled HR = 6.0, 95%CI: 3.12–11.54, $p < 0.001$), in metastatic RCC patients receiving mixed therapies (OS, pooled HR = 3.69, 95%CI: 1.93–11.42, $p = 0.023$; PFS, pooled HR = 6.05, 95%CI: 1.34–27.37, $p = 0.019$) and targeted therapy (OS, pooled HR = 1.59, 95%CI: 0.97–2.62, $p = 0.067$), in sample size > 100 (OS, pooled HR = 1.83, 95%CI: 1.49–2.25, $p < 0.001$; PFS pooled HR = 6.05, 95%CI: 1.34–27.37, $p < 0.019$), and in cut-off value of PLR ≤ 195 (OS, pooled HR = 3.65, 95%CI: 1.06–12.60, $p = 0.04$; PFS pooled HR 4.46, 95%CI: 1.68–11.87, $p = 0.003$).

Conclusions: This study suggests that a high preoperative PLR is correlated with poor prognosis in RCC patients.

1. Introduction

Renal cell carcinoma (RCC) is one of the most common cancer worldwide [1,2]. As changes in the lifestyle and environment over past decades, the incidence of RCC has increased. Despite multiple treatment methods have been applied to treat this disease, the long-term outcome is still unsatisfactory [3]. Nearly 20–30% of RCC patients have distant metastasis when diagnosed, and 20% of patients with localized RCC will finally progress to metastatic RCC [4]. But it is unfortunate that metastatic RCC is a treatment-resistant malignant tumor. Therefore, a novel and reliable prognostic biomarker to distinguish high-risk patients and to improve clinical outcomes of RCC are urgent to develop.

Tumor development and progression is associated with host inflammatory responses [5]. Some inflammatory factors, such as C-reactive protein, neutrophil to lymphocyte ratio (NLR), lymphocyte to monocyte ratio (LMR) are identified as valuable indicators for predicting the prognosis in solid tumors [6–8]. Furthermore, these factors which function as hematological biomarkers are costless and easily available. Recently, the platelet-lymphocyte ratio (PLR) has been identified as a valuable prognostic factor in multiple cancers [9,10]. However, the prognostic values of PLR in RCC are inconsistent [11–14].

2. Materials and methods

2.1. Search strategy and selection criteria

We did this meta-analysis using a predefined protocol in accordance with the preferred reporting items for systematic reviews and meta-analyses guidelines [15]. We searched PubMed, Embase, Cochrane, and the Web of Science from inception up to September 15, 2017. The

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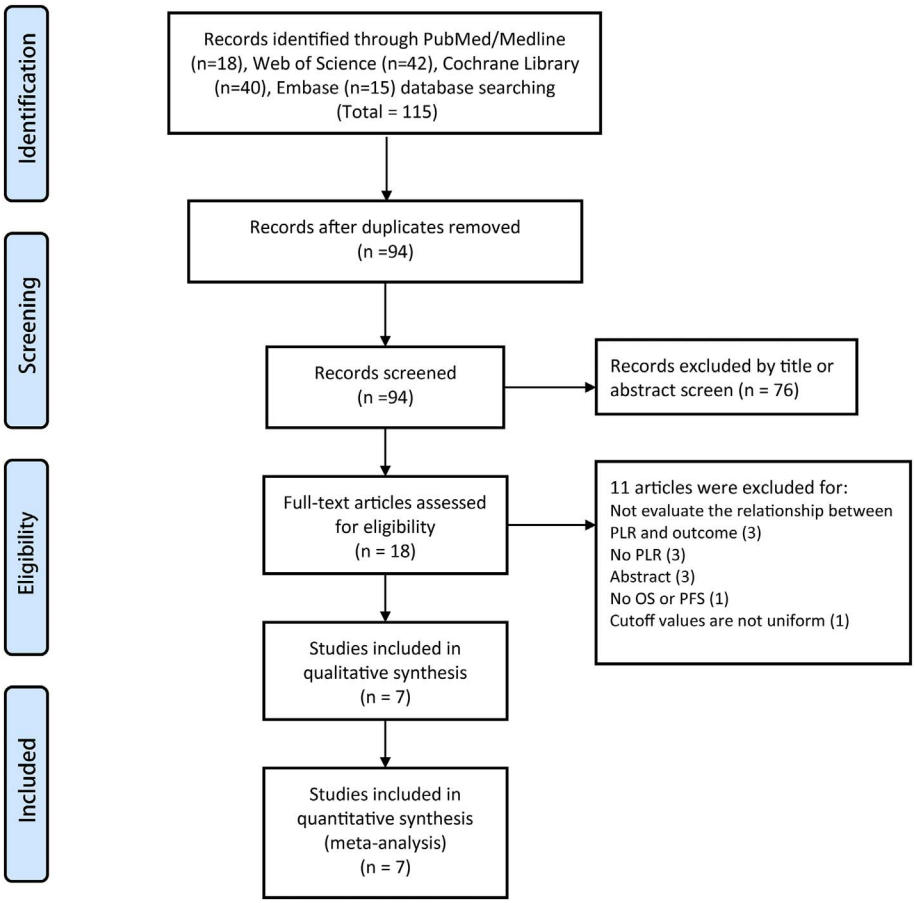

Fig. 1. Flow diagram of the study selection process.

following search terms were used “renal cell carcinoma,” “renal cell cancer,” “renal cell adenocarcinoma,” or “kidney tumor,” as well as “Plated-lymphocyte ratio,” “PLR”; and “prognosis,” “survival,” or “outcome” in humans. The language of publications was restricted to English. Two reviewers (ZW and SHP) independently screened the titles and abstracts of all initially identified studies according to the selection criteria. Full-text articles of studies that met all selection criteria were retrieved. The eligible studies were required to meet the follow criteria: (1) RCC was pathologically confirmed; (2) retrospective of prospective studies on the value of PLR in predicting prognosis in RCC patients; (3) the hazard ratios (HRs) and their 95%CIs for overall survival or progression-free survival analysis were reported in text or could be computed from given data; (4) cut-off value for PLR was reported in the text. When multiple reports describing the same population were published, the most recent or complete report was used. The followings were excluded: abstracts, reviews, case reports or comment letters; laboratory studies; animal studies; duplicate publications; or studies published in a language other than English.

2.2. Data extraction and quality

Two authors (ZW and SHP) independently reviewed all eligible studies and extracted data, and a consensus was reached in the case of any inconsistency with the involvement of a third author (AXW). Quality assessment of included studies was using the Newcastle-Ottawa Quality Assessment Scale (NOS) [16]. NOS score of 6 or higher was considered as a high-quality study. We used a predesigned data extraction form to obtain relevant information. The data extracted from the eligible studies included the following items: first author, year of publication, country of origin, number of patients, histopathological information, cut-off value, number of increased CRP expression, HR for survival (OS and/or PFS), and follow-up time. For articles that only provided survival data in a Kaplan-Meier curve, software designed by Jayne F Tierney and Matthew R Sydes was used to digitize and extract the OR and its 95%CI [17].

2.3. Statistical analysis

Data were analyzed using Stata SE12.0. The hazard ratio (HR) with a 95%CI was selected as the effect to measure prognosis outcomes. Interstudy heterogeneity was evaluated using the chi-square test and I^2 statistic (100% × [(Q-df)/Q]) [18,19]; the value of $P_{heterogeneity} < 0.1$ and $I^2 > 50\%$ represents significant heterogeneity. A fixed-effects model was used when the value of $P_{heterogeneity} > 0.1$ or $I^2 < 50\%$; otherwise, a random-effects model was applied. Subgroup analysis was performed for OS and PFS analysis. Begg's funnel plot and Egger linear regression tests evaluated the potential for publication bias. A 2-tailed $p < 0.05$ was considered statistically significant.

3. Results

3.1. Features of included studies

The work flow chart for this study is shown in Fig. 1. One hundred fifteen potentially relevant studies were identified through systematic literature searches after removing duplicates, 94 articles remained to be screened. Of these 94 studies, 76 articles were excluded, including reviews, letters, meeting abstracts, laboratory studies, and other articles irrelevant to our study. After assessing the full text of the remaining articles, 11 additional articles were excluded. Finally, 7 retrospective studies [11–14,20–22] were included in the following meta-analysis.

Summary characteristics of these studies were shown in Table 1.