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Meta-Analysis

Association between platelet to lymphocyte ratio (PLR) and overall survival (OS) of hepatocellular carcinoma (HCC): A meta-analysis

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Abstract: Some studies investigated the association between platelet-to-lymphocyte ratio (PLR) and the survival of hepatocellular carcinoma (HCC). However, the results remained inconclusive. Thus, we performed this meta-analysis. Published studies were searched in PubMed and EMBASE. The strength of association was assessed by calculating odds ratios (OR) and 95% confidence interval (CI). In total, 6 studies with 1446 HCC patients were included in this meta-analysis. HCC with higher PLR showed an increased death risk (OR = 1.59; 95%CI, 1.15–2.20; P < 0.0001). However, the heterogeneity was high (I^2=89.2%). When the study by Li et al. was excluded, the heterogeneity decreased (I^2=20%). Further, the result was still positive (OR = 1.70; 95%CI, 1.42–2.04; P < 0.00001). In conclusion, this meta-analysis suggested that PLR was significantly associated with the OS of HCC.

Key words: Hepatocellular carcinoma; Platelet-to-lymphocyte ratio; Survival.

Introduction

Hepatocellular carcinoma (HCC) is one of the most common causes of cancer death worldwide (1). HCC is among a group of tumors that have the highest mortality rate (1). Since the early symptoms of liver cancer are not obvious, early diagnosis is difficult. Therefore, identifying biomarkers that predict survival of HCC can improve their management.

Systemic inflammatory response can impact tumor development through the inhibition of apoptosis, promotion of angiogenesis, and damage to the DNA (2). Recently, many studies suggested that increased systemic inflammation could lead to poor prognosis of some types of cancers (3,4). Platelet-to-lymphocyte ratio (PLR) is a biomarker to evaluate systemic inflammatory responses. Some studies investigated the association between PLR and the survival of HCC. However, the results remained inconclusive (5-10). Thus, we performed this meta-analysis to determine the association of PLR and the overall survival (OS) of HCC.

Materials and Methods

Search for publications

Published studies were searched in PubMed and EMBASE up to Feb 2017, with the following key words: “hepatocellular carcinoma”, “liver cancer”, “platelet-to-lymphocyte ratio” and “PLR”. Publication language and time of publication were not restricted in this search. Reference lists of articles retained for review were examined manually to further identify potentially relevant reports. Unpublished studies were not considered.

Inclusion and exclusion criteria

Studies should meet the following criteria: (1) evaluate the association between PLR and the OS of HCC; (2) the diagnosis of HCC should be confirmed by pathology; (3) reported adjusted odds ratios (OR) and 95% confidence interval (CI). Studies should be excluded if the following criteria existed: (1) Reviews and abstracts; (2) not evaluate of the association between PLR and the OS of HCC; (3) without sufficient data. When authors reported two or more publications on the same patient population, only the largest study was selected.

Data extraction and Qualitative assessment

Two authors extracted the data independently. These data included: the first author, year, race, age, outcome, and sample size. The Newcastle–Ottawa Scale (NOS) was used to assess the methodological quality.

Statistical analysis

The strength of association was assessed by calculating OR with 95% CI. A statistical test for heterogeneity was performed based on the Q statistic. The P>0.10 of the Q-test indicated a lack of heterogeneity among studies. If heterogeneity was observed among the studies, the random-effects model was used to estimate the pooled HR (the DerSimonian and Laird method). Otherwise, the fixed-effects model was adopted (the Mantel–Haenszel method). Sensitivity analysis and cumulative analysis were performed. All statistical tests were performed with Stata software 11.0 (Stata Corporation, College Station, TX). A P value <0.05 was considered statistically significant.

Table 1. Characteristics of the included studies.

Study	Year	Race	Age	No. of patients	Outcome	Quality score	Adjusted
Li	2014	Asian	57	243	OS	8	Yes
Fan	2015	Asian	49	132	OS	8	Yes
Xue	2015	Asian	53	291	OS	8	Yes
Ji	2015	Asian	51	321	OS	7	Yes
Tian	2016	Asian	56	122	OS	8	Yes
Dong	2016	Asian	NA	337	OS	8	Yes

Results

Characteristics of the included studies

According to the inclusion criteria, 6 studies were included in this meta-analysis. The publication year of involved studies ranged from 2014 to 2016. In total, 1446 HCC patients were included in this meta-analysis, which evaluated the relationship between PLR and the OS of HCC. All this studies came from Asia and all studies reported adjusted results. The quality of the studies were high. The characteristics of the included studies are summarized in Table 1.

Meta-analysis

As shown in Figure 1, HCC with higher PLR showed an increased death risk (OR = 1.59; 95%CI, 1.15–2.20; P < 0.0001). However, the heterogeneity was high (I^2=89.2%). When the study by Li et al. (5) was excluded, the heterogeneity decreased (I^2=20%). Further, the result was still positive (OR = 1.70; 95%CI, 1.42–2.04; P < 0.00001; Figure 2).

Cumulative analysis was performed and showed that the result was stable (Figure 3). In order to assess the stability of the results of the meta-analysis, we performed a sensitivity analysis by omitting one study at a time. As shown in Figure 4, the results were not materially altered. There were only five studies in this meta-analysis, thus we did not check publication bias.

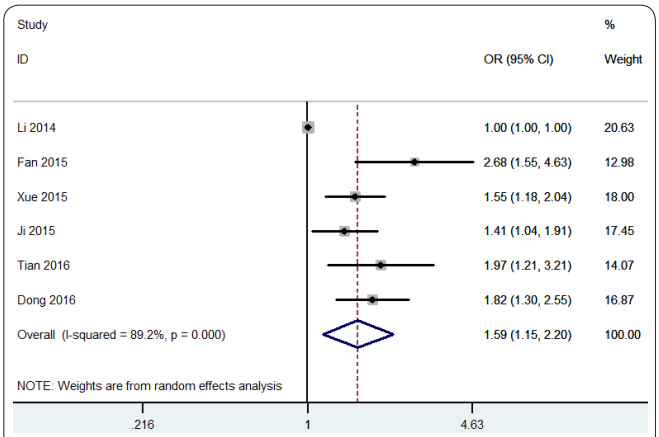

Figure 1. The association between PLR and OS of HCC.

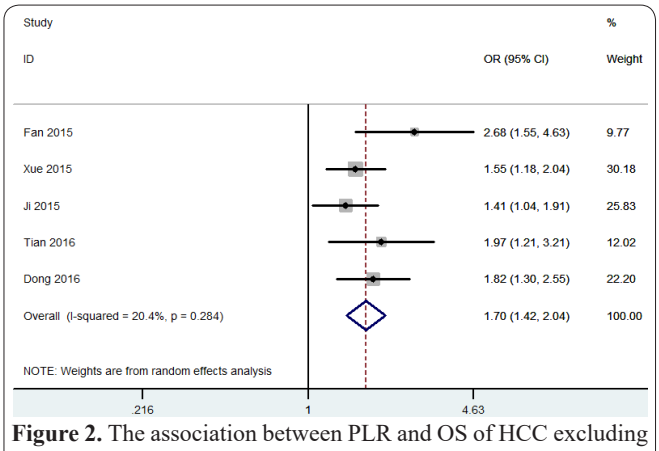

Figure 2. The association between PLR and OS of HCC excluding one study.

Discussion

This study with 6 studies (n=1446) assessed the relationship between PLR and the OS of HCC. The result suggested that PLR was significantly associated with the OS of HCC. This result indicated that HCC patients with high PLR might have shorter OS. Two previous meta-analysis also found similar results (11, 12). However, this present study included only adjusted results and included new study. Thus, our result was more reliable and the power of the meta-analysis was high.

Inflammatory process might affect the overall survival of the patients with cancers. Guo et al. found that elevated PLR was associated with poor prognosis of

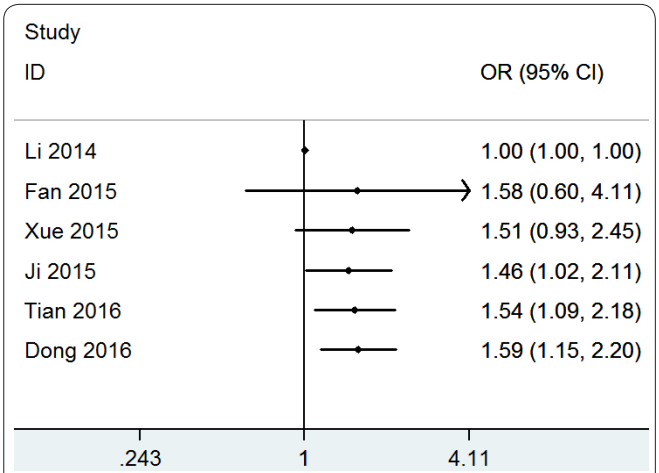

Figure 3. Cumulative analysis of the association between PLR and OS of HCC.

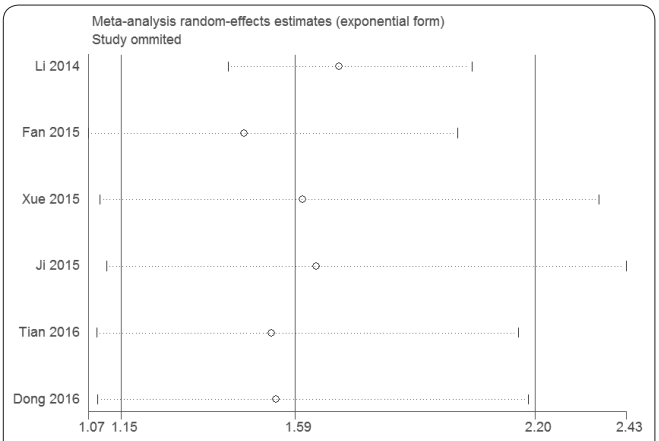

Figure 4. Sensitivity analysis of the association between PLR and OS of HCC.

colorectal cancer (13). Hu et al. suggested that a high PLR was related to a two-fold increase in risk of death in resected high-grade serous ovarian carcinoma (14). Turri-Zanoni et al. indicated that high pretreatment PLR was associated with poor prognosis in patients affected by epithelial advanced-stage sinonasal cancer (15).

Our meta-analysis also had some limitations. First, the numbers of published studies were small. Second, All included studies used retrospective design. No prospective studies confirmed our result. Third, as a meta-analysis of observational studies, it was prone to bias (e.g., recall and selection bias) inherent in the original studies.

In conclusion, this meta-analysis suggested that PLR was significantly associated with the OS of HCC.

Disclosure of conflict of interest

The authors have declared that no competing interests exist.

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