Clinica Chimica Acta 486 (2018) 44–48

Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/cca

Review

Lymphocyte-to-monocyte ratio in esophageal squamous cell carcinoma prognosis

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ARTICLE INFO

Keywords:
Esophageal squamous cell carcinoma
Lymphocyte-to-monocyte ratio
Prognosis
Meta-analysis

ABSTRACT

Introduction: Recently, the prognostic value of the lymphocyte-to-monocyte ratio (LMR) has been widely evaluated in multiple malignancies. However, its prognostic value in patients with esophageal squamous cell carcinoma (ESCC) remains controversial. Herein, we perform a meta-analysis to assess the prognostic value of the preoperative LMR in ESCC.

Methods: Relevant studies were systematically retrieved from the online Cochrane, MEDLINE, and EMBASE databases published until March 2018. Data from studies reporting a hazard ratio (HR) and 95% confidence interval (CI) were weighted by generic inverse-variance and pooled in either fixed-effects models or random effects meta-analysis. Seven eligible studies involving 1701 patients were analyzed in this meta-analysis.

Results: The synthesized analysis showed that patients with low LMR had a significantly shorter overall survival (OS) (HR: 0.67, 95% CI: 0.58–0.78, $p < 0.001$) and disease-free survival (DFS)/progression-free survival (PFS) (HR: 0.67, 95% CI: 0.50–0.92, $p = 0.01$). Additionally, low LMR was correlated with TNM stage (III-IV vs. I-II; HR = 1.94, 95% CI: 1.16–3.22, $P = 0.01$) and tumor recurrence (yes vs. no; HR = 1.71, 95% CI: 1.06–2.77, $P = 0.03$).

Conclusion: Low LMR was associated with advanced clinicopathological features and poor prognosis as a predicative biomarker in patients with ESCC.

1. Introduction

Esophageal cancer (EC) is a highly aggressive disease and is usually fatal. It is estimated that it is the 8th leading cancer in incidence and 4th in mortality worldwide [1].

Esophageal squamous cell carcinoma (ESCC), accounting for around 90% of EC, is the most common histologic subtype [2]. Radical esophagectomy with complete lymph node dissection is the mainstay of curative treatment for patients with ESCC. Nevertheless, most patients eventually develop local or distant tumor recurrence, even after esophagectomy. Thus, the prognosis is still poor. Recently, several factors have been widely regarded as prognostic biomarkers of ESCC, including clinicopathological features (such as tumor differentiation and TNM stage). However, the prognosis differs even in patients with the same TNM stage [3]. Therefore, a new and accurate prognostic prognostic biomarker is required to identify risk classification and even guide the treatment.

A growing body of evidence has reported cancer-related inflammation leads to worse prognosis. It is clear that systemic inflammation plays a key role in cancer development, progression, and metastasis [4]. Various inflammatory biomarkers, such as the Glasgow prognostic score (GPS), cytokine, C-reactive protein-to-albumin ratio (CAR), neutrophil to lymphocyte ratio (NLR), and platelet to lymphocyte ratio (PLR) have been investigated in a variety of solid tumors [5–9]. The lymphocyte-to-monocyte ratio (LMR), calculated as lymphocyte counts divided by monocyte counts, has been associated with poor survival in various cancers, including breast cancer, pancreatic cancer, ovarian cancer, and hepatocellular carcinoma [10–13]. However, due to the inconsistent results, the prognostic role of LMR in ESCC remains controversial [14–17]. Thus, we aimed to quantify the prognostic effect of LMR and analyse the relationship between LMR and clinicopathological parameters in patients with ESCC.

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https://doi.org/10.1016/j.cca.2018.07.029
Received 13 June 2018; Received in revised form 14 July 2018; Accepted 16 July 2018
Available online 17 July 2018
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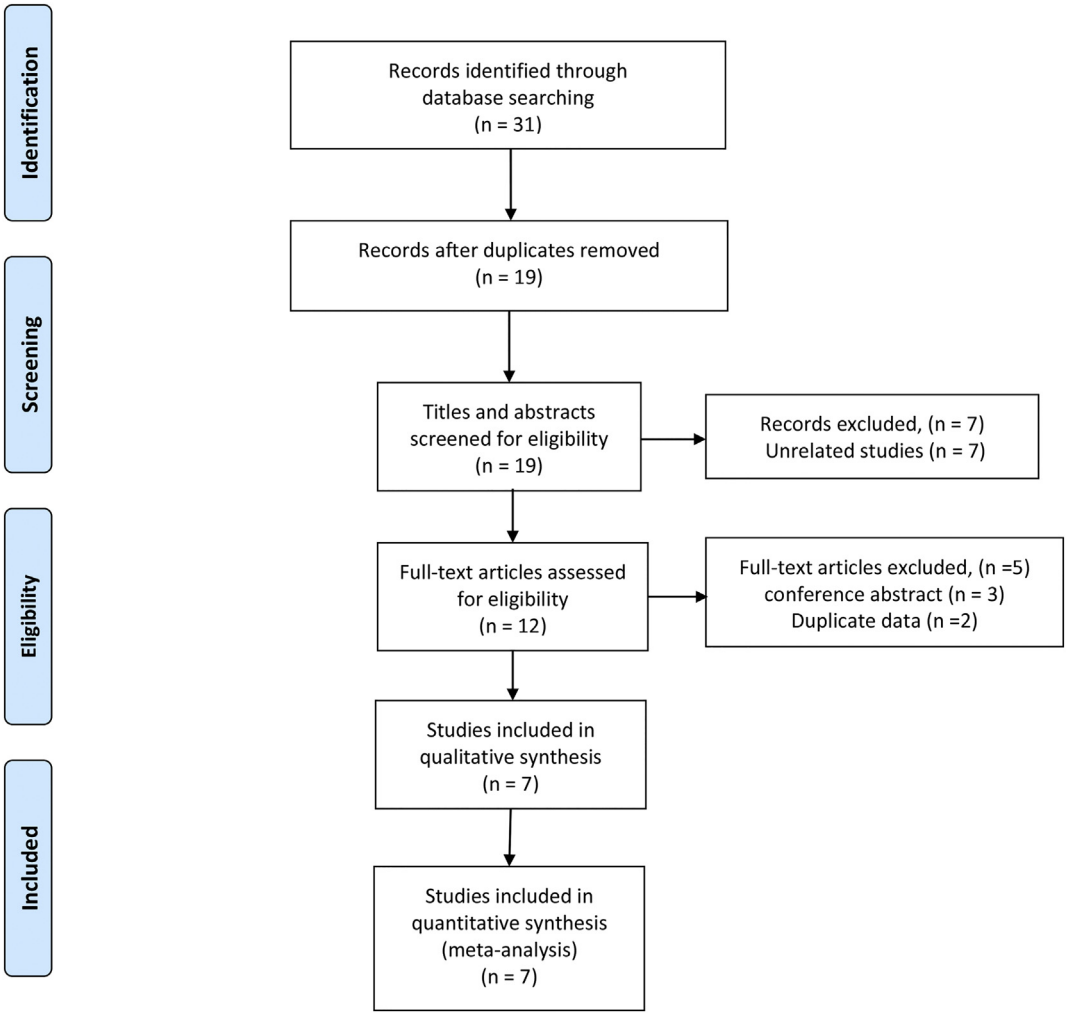

Fig. 1. Flow diagram of the study selection process.

2. Materials and methods

2.1. Search strategies

An electronic search of MEDLINE, EMBASE, and Cochrane Library was performed up to March 2018 in this research. The following search terms were used: “lymphocyte-to-monocyte ratio” or “LMR” or “lymphocyte to monocyte ratio” or “lymphocyte monocyte ratio” and “esophageal carcinoma” or “esophageal neoplasm” or “esophageal tumor” or “esophageal squamous cell carcinoma” or “ESCC”. The bibliographies cited in the selected articles were also examined to identify other relevant studies.

2.2. Study selection

The following eligibility criteria were utilized: (1) the LMR was measured from serum; (2) the diagnosis of ESCC were pathologically confirmed; (3) studies investigated LMR and clinicopathologic features or survival in ESCC; (4) reported a cut-off value for LMR; and (5) sufficient data were provided to calculate the hazard ratio (HR) and 95% confidence interval (CI). Studies were excluded if they meet the following criteria: (1) studies were reviews, case reports, letters, or conference abstracts; (2) studies with insufficient data; and (3) duplicate publication.

2.3. Data extraction and quality assessment

All eligible studies were reviewed and extracted independently by two reviewers. We extracted data including: the first author, country, ethnicity, publication year, number of patients, age, time of follow-up, treatment, tumor location, tumor length, depth of invasion, tumor differentiation, TNM stage, lymph node status, vessel invasion, recurrence, cut-off values, survival analysis methods,clinicopathological parameters, and HRs and associated 95% CIs for OS or DFS/PFS. The Quality Assessment of Newcastle-Ottawa Scale (NOS) was adopted to evaluate the methodological quality of included studies [18]. It included three main parts –Selection, Comparability and Outcome, which were scored separately. The NOS scores ≥ 6 are considered as high-quality studies. Two reviewers completed their own evaluation which then were crosschecked.

2.4. Statistical analysis

Extracted data were pooled using Review Manager 5.3 software (Cochrane Collaboration, Copenhagen, Denmark). Odds ratios (ORs) and their 95% CIs were applied to estimate the correlation between LMR and clinicopathological features. HRs and their 95% CIs were used to evaluate the effect of LMR on prognosis. If HRs and 95% CIs were obtained from individual articles, we extracted them directly. Otherwise, they were calculated with Kaplan-Meier survival curves according to the methods described by Parmar and Tierney [19, 20].

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