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Review

Pretreatment prognostic nutritional index as a prognostic factor in lung cancer: Review and meta-analysis

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ABSTRACT

Background: Numerous studies have explored the association between pretreatment prognostic nutritional index (PNI) and prognosis in lung cancer (LC), but the results are still inconclusive. We systematically evaluated the prognostic value of pretreatment PNI in LC patients by conducting a meta-analysis.

Methods: A comprehensive literature search was performed by retrieving PubMed, EMBASE, and Web of Science, Wan Fang and CNKI databases. We used hazard ratios (HRs) and their 95% confidence intervals (CIs) to assess the associations of PNI with overall survival (OS), disease-free survival/recurrence-free survival (DFS/RFS) and progression-free survival (PFS) in LC patients.

Results: A total of 21 studies were enrolled into this meta-analysis, with 17 about no-small cell lung cancer (NSCLC) and 4 about on small-cell lung cancer (SCLC). The results indicated that NSCLC patients with low PNI had shorter OS (HR: 1.59, 95% CI: 1.28–1.96, P = 0.001), DFS/RFS (HR = 1.74, 95% CI = 1.08–2.80, P = 0.017), and PFS (HR = 1.52, 95% CI = 1.26–1.83, P = 0.002) than patients with high PNI. The robustness of these pooled results were verified by our stratified analysis and sensitivity analysis. Besides, a pooled analysis of 4 studies about SCLC suggested that low PNI was closely associated with worse OS in SCLC patients as well.

Conclusion: Low PNI predicts poor survival in LC patients.

1. Introduction

Lung cancer (LC) is the most common cancer and is one of main causes of cancer-associated death worldwide [1]. Despite substantial advance in therapy during the past decades, LC patients still have unsatisfying long-term survival [2]. In present, Tumor-node-metastasis (TNM) staging system, histological subtype, and genetic biomarker have been widely applied to assess survival in LC patients. Nonetheless, some LC patients with identical TNM stage and histological subtype sometimes had different prognosis. Additionally, detection of genetic biomarker is rather expensive and inconvenient, especially for patients in developing country. Hence, it is very urgent to develop easily accessible, inexpensive and effective indicators for predicting survival outcomes in LC patients, which may contribute to improving individualize therapy for LC patients.

Nutrition and immune status play critical roles in disease progression and prognosis in cancer patients [3,4]. The prognostic nutritional index, calculated using serum albumin levels and total lymphocyte count in peripheral blood [5], is an effective indicator for assessing nutritional and immunological conditions of cancer patients. Numerous recent studies revealed that there was association between pretreatment PNI and survival in various cancer, including LC [6–26]. Nevertheless, the results are still conflicting.

2. Materials and methods

2.1. Search strategy

We performed an exhaustive literature search in five electronic databases including PubMed, Web of Science, EMBASE, CNKI, and Wan Fang. The most recent search was performed on April 1, 2018. The search terms included: “prognostic nutritional index” (abstract/title), and “cancer or tumor or carcinoma or neoplasm” (abstract/title), and “lung and pulmonary” (abstract/title). Additionally, we also tried to find out other pertinent publications through checking the reference lists of the identified literature.

2.2. Eligibility criteria

Studies were included according to the following criteria: (1) The LC

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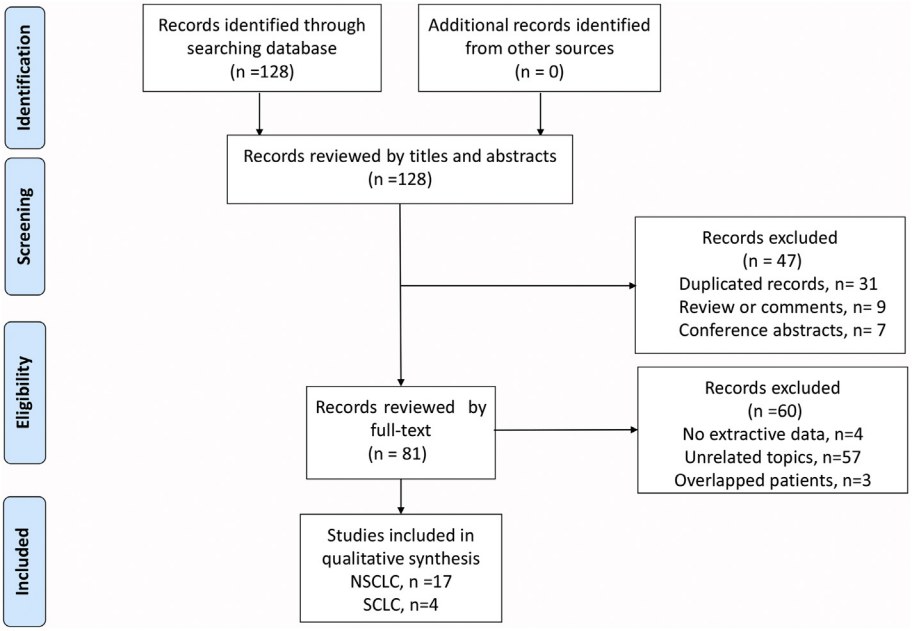

Fig. 1. Flow diagram of literature selection process.

patients were diagnosed by pathological confirmation; (2) The articles reported HRs and CIs for evaluating the associations of PNI with OS, DFS/RFS or PFS. (3) Only articles in English or Chinese were considered. The articles meeting one of the following criteria were excluded: (1) The articles were case reports, reviews, editorials, and conference reports; (2) The articles enrolled the overlapped or same population. (3) The articles did not directly present HRs for survival results in text.

2.3. Data extraction

Two authors independently (ZW and XZ) extracted data. When there were discrepancies in extracting data, another author (YW) extracted relevant data again, and then discussed with Wang and Zhang for a consensus. We extracted the first name of author, publication year, ethnicity, accrual period, median age, gender, histological type, cut-off value, means of determining cut-off value, follow-up, treatment method, survival analysis method and HRs and their 95% confidence intervals (CIs) for OS, DFS/RFS or PFS. In this meta-analysis, considering that the majority of the included studies reported OS in NSCLC, we took OS of NSCLC patients as primary ending point.

2.4. Quality assessment

We assessed the methodological quality of each eligible study based on the Newcastle-Ottawa Scale (NOS). In NOS system the total score awarded to a study varies from 0 to 9 [27]. The study scored 6 or more was considered as high quality.

2.5. Statistical analysis

The STATA 12.0 software was applied for all the statistical process in our meta-analysis. HRs and 95% CIs were used to evaluate the relationship between PNI and survival in LC patients. Heterogeneity among the included studies was assessed using the $\chi 2$ and I^2 test. $I^2 > 50\%$ and $P < 0.05$ suggested that there was significant heterogeneity. Random effects model was used to pooling analysis of data, if significant heterogeneity existed. When significant heterogeneity was not detected, a fixed effects model was used for pooling analysis of data. The concurrence of HR > 1 (low/high PNI) and upper limit of its 95% CI > 1 indicated worse survival in LC patients with low PNI. Stratified analyses was conducted by country, number of patients, TNM stage, cut-off value, methods of cut-off determination, and survival analysis method to explore the sources of heterogeneity. The sensitivity analysis was conducted to test the robustness of our pooled HRs by sequentially omitting each eligible. The Begg's and Egger's tests were used to evaluate publication bias [28,29].

3. Result

3.1. Study characteristics

The literature selection process was summarized in Fig. 1. In the first step, a total of 128 potentially relevant studies were identified through searching databases. We excluded 47 articles after screening titles and abstracts, including conference abstracts, reviews, comments, and duplicated studies. Then we carefully reviewing the full texts of the rest of studies and excluded another 60 studies, since they have no available data of our interest,enrolled overlapped patients or focused on unrelated topics. Ultimately, a total of 21 studies were included into our meta-analysis.

The baseline characteristics of the included studies were summarized in Table 1. Among all included studies, 4 reported SCLC [30–33] and 17 focused on NSCLC [10–26]. Eleven studies were performed in China, 8 studies were conducted in Japan and two studies were performed in Turkey and Korean. All included studies were of retrospective nature and published in recent five years (2014–2018). All the included studies were awarded to a score of ≥6 (Table 2) based on NOS system, indicating that these studies had high quality.

3.2. Pooling analysis

3.2.1. Association between PNI and OS in NSCLC patients

Fourteen studies with a total of 4922 patients reported OS in NSCLC patients [10–18,20–23,26]. As there was statistically significant heterogeneity ($I^2 = 81.1\%$, $P < 0.0001$), random-effects model was used for to pooling analysis of OS. The pooled result showed that NSCLC patients with a low PNI had worse OS as compared with those with high PNI (HR: 1.59, 95% CI: 1.28–1.96, P = 0.001, Fig. 2).

Aiming to explore the sources of heterogeneity, we conducted