INPLASY PROTOCOL

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Prognostic value of nutritional risk index in patients with esophageal cancer

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Review question / Objective: A systematic review and metaanalysis about the prognostic value of nutritional risk index in esophageal cancer.

Eligibility criteria: Studies were included as they met the following inclusion criteria: (1) studies reporting the prognosis value of NRI in esophageal cancer; (2) Outcomes of trails include survival index or the relationship between NRI and clinical characteristic variables; (3) adequate data to calculate hazard ratio (HR) and 95% confidence interval (95% CI); (4) To avoid the publication bias, only studies whose sample size was \geq 30 were included.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 June 2021 and was last updated on 12 June 2021 (registration number INPLASY202160038).

INTRODUCTION

Review question / Objective: A systematic review and meta-analysis about the prognostic value of nutritional risk index in esophageal cancer.

Condition being studied: Esophageal cancer is the second most common tumor of the digestive system after gastric

cancer, and one of the ten most common malignant tumors in the world. Although the treatments for esophageal cancer have achieved some progress in recent years, the 5-year survival rate of locally advanced EC is unsatisfied, ranging from 15% to 25%. Malnutrition is a common state in esophageal cancer patients, especially during radiation therapy, the frequency of malnutrition is as high as 90%. Malnutrition

could impair the immune function, muscle function, the quality of life and response to chemotherapy, and so on. The European Society of Clinical Nutrition and Metabolism guideline indicated that a comprehensive nutritional assessment and adequate nutrition counseling is necessary for every patient undergoing radiation therapy for gastrointestinal cancers. There are many methods for assessing the nutritional status, such as PNI, POSSUM, and E-PASS. However, these scores are not convenient for clinical use because they are complex and many items need to be calculated. Serological indicators such as albumin, C-reactive protein (CRP), and neutrophil-lymphocyte ratio (NLR) are also commonly used to assess the nutritional status of patients with digestive system tumors. Unfortunately, these markers are easily affected by various conditions, including inflammation and hydration status. Nutritional risk index (NRI) was firstly proposed by Buzby and improved by Bouillanne to get the modified geriatric NRI (GNRI). It was initially used to assess patients with total parenteral nutrition, and later it was discovered that NRI was also a specific indicator to assess the risk of surgical complications. NRI is composed of only two objective parameters, body mass index (BMI) and albumin. and its calculation method is simple. NRI and GNRI are usually calculated according to the following formulas: NRI = $(1.519 \times \text{albumin}, \text{g/I}) +$ (41.7 × present/ideal body weight); GNRI = (1.489 × albumin, g/l) + (41.7 × present/ideal body weight). Although their formulas are slightly different, the corresponding criteria for judging malnutrition have also changed accordingly. One previous study compared the NRI values calculated by the two formulas and found that there was little difference between these two values. In that case, we combined the two indicators in this meta-analysis. In recent years, NRI and the improved NRI have been tools to predict the prognosis of diseases such as alzheimer, chronic heart failure, systemic lupus erythematosus, chronic renal failure, sepsis. Regarding tumors, some studies reported that NRI was independently associated with the survival rates for patients with colorectal cancer, head and

neck cancer and non-small cell lung cancer. Furthermore, the area under curve(AUC) value of GNRI is slightly higher than the three models of PNI, POSSUM, and E-PASS. There are some studies exploring the prognostic significance of NRI in esophageal cancer, but the results are not consistent. In this study, we searched available articles and carried out this meta-analysis to comprehensively evaluate the prognostic value of NRI in esophageal cancer and explore relevant clinicopathological factors.

METHODS

Search strategy: The objective of searching was to collect all literatures related to NRI with esophageal cancer. Literatures were searched on Pubmed, Embase, Cochrane library and Web of science databases from their inception to the present. The search keywords were "Esophageal Neoplasms", "NRI" and "nutrition assessment". The search and usability assessment of the integrated databases was carried out by the two evaluators separately, and if there was a controversy, it was judged by the third evaluator. A second manual search on the retrieved documents were performed after the comprehensive search.

Participant or population: Adults with esophageal cancer.

Intervention: Nutritional risk index.

Comparator: The low NRI and high NRI.

Study designs to be included: Comparative trials will be included.

Eligibility criteria: Studies were included as they met the following inclusion criteria: (1) studies reporting the prognosis value of NRI in esophageal cancer; (2) Outcomes of trails include survival index or the relationship between NRI and clinical characteristic variables; (3) adequate data to calculate hazard ratio (HR) and 95% confidence interval (95% CI); (4) To avoid the publication bias, only studies whose sample size was \geq 30 were included.

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Information sources: Electronic databases and trial registers.

Main outcome(s): Overall survival and progression-free survival.

Quality assessment / Risk of bias analysis: The quality assessment will be assessed according to the Newcastle-Ottawa Scale (NOS). Studies will be divided into 0-9 scores, and studies aboved 6 scores will be thought as high quality. The funnel plot, Begg's test and Egger's test were used to evaluate the publication bias of this metaanalysis.

Strategy of data synthesis: I2 statistics will be used to assess the heterogeneity between studies. If there was no significant heterogeneity (I2 < 50%), we will rather choose a fixed effect model to combine data. Otherwise, a random effect model will applied. Subgroup analysis and sensitivity analysis will be performed to find the source of heterogeneity. If there was publication bias among studies, the trim and fill method was applicated to adjust the HR. P value < 0.05 is considered statistically significant. All statistical analysis will be performed using stata statistical software 15.0 (Stata Corporation, College Station, TX, USA).

Subgroup analysis: This meta-analysis will conduct a subgroup analysis in terms of areas, NRI/GNRI, sample sizes, critical values, tumor pathological types and therapeutic methods.

Sensitivity analysis: We will delete individual test results, merge the remaining test results, and observe whether a single test has a significant impact on the overall result.

Country(ies) involved: China.

Keywords: Nutritional risk index; Esophageal neoplasms; Prognosis; Survival analysis; Meta-analysis.

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