INPLASY PROTOCOL

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Review Stage at time of this submission: **Preliminary searches.**

Conflicts of interest:
None declared.

Prognostic value of EGFR/p-EGFR in nasopharyngeal carcinoma: a protocol for systematic review and meta-analysis

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Review question / Objective: **Nasopharyngeal carcinoma (NPC) is one kind of malignant cancer occurring in epithelial cells of the nasopharynx and with high incidence among head and neck cancers in South China, Southeast Asia, and North Africa. Epidermal growth factor receptor (EGFR) is a member of the tyrosine kinase growth factor receptor family. Most nasopharyngeal cancer cell lines and patients overexpress EGFR. When a growth factor binds to EGFR, EGFR is self-phosphorylated by tyrosine kinase, and phosphorylated EGFR(p-EGFR) activates cell-signaling pathway involved in the regulation of cell cycle, apoptosis, angiogenesis, and cellular proliferation. The prognostic value of EGFR in NPC has been reported. However, conflicting results were reported in these studies. So we will conduct a systematic review and meta analysis to evaluate the prognostic impact of the EGFR/p-EGFR and assess their clinical usefulness.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 02 May 2021 and was last updated on 02 May 2021 (registration number INPLASY202150010).

INTRODUCTION

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cell-signaling pathway involved in the regulation of cell cycle, apoptosis, angiogenesis, and cellular proliferation. The prognostic value of EGFR in NPC has been reported. However, conflicting results were reported in these studies. So we will conduct a systematic review and meta analysis to evaluate the prognostic impact of the EGFR/p-EGFR and assess their clinical usefulness.

Condition being studied: According to PRISMA to reporting this review and meta-analysis.We will conduct a systematic search in the databases of six databases. Data collection and analysis will be evaluated by two researchers independently. And the third researcher will resolve the disagreement among the two researchers in literatures. Review manager 5.3, stata 15.0 statistical software will be used for the statistical analysis. Significant heterogeneity will be explored trough subgroup analysis and sensitivity analysis.

METHODS

Participant or population: Patients with pathologically confirmed to have NPC.

Intervention: EGFR/p-EGFR positive group.

Comparator: EGFR/p-EGFR negative group.

Study designs to be included: Randomised controlled trial (RCT).

Eligibility criteria: Inclusion criteria:(1)all patients were pathologically confirmed to have NPC. (2)EGFR/p-EGFR was detected in nasopharyngeal carcinoma tissues. (3)the relationship between EGFR/p-EGFR expression and prognosis of nasopharyngeal carcinoma was included. (4)the hazard ratio (HR) of OS, DFS, PFS and DMFS is reported in the article or can be calculated from the relevant.

Information sources: Six databases: PubMed, Embase, Wan-fang Database, Chinese Scientific Journal Database, China National Knowledge Infrastructure Database and Chinese Biomedical Literature Database will be searched from the construction of the database to May, 2021.

Main outcome(s): Overall survial(OS), disease free survival (DFS), progression-free survival (PFS), and distant metastasis-free survival (DMFS) will be used as the main outcome.

Quality assessment / Risk of bias analysis: Two researchers in our team will use the Prognosis studies Evaluation Quality Scale used by Hayden JA et al to ensure the quality of the included studies. Assessment of biases refers to the assessment of potential biases within the studies included in a review. Including 6 potential biases: Study participation, Study attrition, Prognostic factor measurement, Outcome measurement, Confounding measurement and account and Analysis. Three levels will be used to assess the risk of bias, namely, Yes, Partly, and No or Unsure. If they cannot got the same score, the third researcher will resolve the disagreement among the two researchers in literatures.To obtain complete information, we will contact the first author of the article when the information is vague.

Strategy of data synthesis: Data synthesis will be completed using RevMan5.3 and stata 15.0. HR and corresponding 95% CI were used to analyze pooled data. On one hand, if there is no heterogeneity among all included trials(I2<50%), models in fixed-effects will be used. On the other hand, models in random-effects will be used when there is significant heterogeneity(I2≥50%). And then, sensitivity analysis and subgroup analysis will be conducted.

Subgroup analysis: The grouping was based on NPC stages of patients, the population origin of samples and so on. In order to explain the source of heterogeneity.

Sensitivity analysis: Sensitivity analysis will be performed if significant heterogeneity still exists after subgroup analysis.

Language: Chinese and English.

Country(ies) involved: China.

Keywords: EGFR, p-EGFR, Nasopharyngeal carcinoma, prognosis, systematic review, meta analysis.

Contributions of each author:
Author 1 - Hong Xiaohua conceived and designed the protocol, and drafted the protocol manuscript.
Author 2 - Wang Guangyao provided statistical expertise.
Author 3 - Mo Chunmei contributed to the development of the selection criteria, and the risk of bias assessment strategy.
Author 4 - Rong Zhen read, provided feedback and approved the final manuscript.