INPLASY PROTOCOL

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Support: **No**

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

Conflicts of interest: **No.**

Survival comparison of different treatment options for patients with locally advanced nasopharyngeal carcinoma: a systematic review and network meta-analysis of randomized clinical trials

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Review question / Objective: **What are the best options for various interventions for locally advanced nasopharyngeal carcinoma? What is the difference between accelerated radiotherapy and traditional radiotherapy? Is there any difference between using targeted drugs or not? Our goal is to use network meta-analysis to generate clinically useful summaries of different interventions based on different survival outcomes.**
Condition being studied: **In the past few decades, several network meta-analysis in nasopharyngeal carcinoma patients has shown that adding adjuvant chemotherapy to concurrent chemoradiotherapy can obtain higher survival benefits. However, the authors did not include different radiation patterns and target drug interventions. According to the guidelines, there is still no standard treatment option, and patients are recommended to undergo clinical trials. So we conducted this study to compare the survival differences of different options.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 May 2020 and was last updated on 08 May 2020 (registration number INPLASY202050027).

INTRODUCTION

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METHODS

Participant or population: This study includes patients with locally advanced nasopharyngeal carcinoma.

Intervention: Interventions include concurrent chemoradiotherapy, neoadjuvant chemotherapy plus concurrent chemoradiotherapy, concurrent chemoradiotherapy plus adjuvant chemotherapy, accelerate radiotherapy, with target drug and so on.

Comparator: Comparators include radiotherapy alone, concurrent chemoradiotherapy, neoadjuvant chemotherapy plus concurrent chemoradiotherapy, concurrent chemoradiotherapy plus adjuvant chemotherapy, traditional radiotherapy, without target drug and so on.

Study designs to be included: Randomized controlled trials will be included.

Eligibility criteria: (1) The research object is locally advanced nasopharyngeal carcinoma; (2) The research type is randomized controlled trial; (3) The document language is limited to English; (4) The intervention is the comparison of different treatment options; (5) The research ending is at least one of overall survival, progression-free survival, loco-regional control, distant control.

Information sources: All data comes mainly from the original article and the survival curve in the article. When we are unable to obtain the necessary data from the article, we will try to contact the author via email for data support. When two emails were not contacted within a month, the study will be abandoned and explained in the result or discussion.

Main outcome(s): The main outcomes were overall survival, progression-free survival, loco-regional control, distant control.

Data management: Two authors will independently extract data. Any disagreement will be resolved by discussion until consensus is reached or by consulting a third author. The following data will be extracted: author, year of publication, country where the study was conducted, original inclusion criteria, total number of people included in the study, median age, doses of radiotherapy, chemotherapy regimens and so on.

Quality assessment / Risk of bias analysis: The details of the search terms for each database are given in the extension of the PRISMA statement for quality of the reporting methods. Risk of bias was assessed as per the Cochrane Collaboration tool. The quality of the evidence and its strength were rated as per the recommendations of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group.

Strategy of data synthesis: We plan to compared the results of two different methods including bayesian model and frequentist approach.Heterogeneity was quantified using the I2. The Q statistic is the sum of a statistic for heterogeneity and a statistic for inconsistency. The use of random-effects models and the performance of sensitivity analyses after the exclusion of trials that were considered as outliers in the standard meta-analysis. Within the Bayesian framework, the treatments are ranked using the surface under the cumulative ranking curve. A frequentist analog to surface under the cumulative ranking curve was named P-score. P-score would be 100% when a treatment is certain to be the best and 0% when a treatment is certain to be the worst. P values=0.05 were considered significant for the difference between treatments. All

analyses were performed using the R software (version 4.0.0) and Stata software (version 15.0).

Subgroup analysis: Subgroup analyses were performed on HRs using a mixed effects model. The Q value,degree of freedom, and P value were computed for each of the subgroups evaluated.

Sensibility analysis: A sensitivity analysis was performed for trials with low selective reporting bias. The protocol for the NMA stated that a fixed-effects model had to be used first and that in case of significant heterogeneity, two solutions would be investigated: the use of random-effects models and the performance of sensitivity analyses after the exclusion of trials that were considered as outliers in the standard meta-analysis.

Keywords: Locally advanced nasopharyngeal carcinoma, randomized controlled trials, network meta-analysis.

Contributions of each author:

Author 1 - Yu-Qin Liang - Yu-Qin Liang will search the databases, independently extract data and draft the manuscript.
Author 2 - Sen-Quan Feng - Sen-Quan Feng will search the databases, independently extract data and draft the manuscript.
Author 3 - Peng Huang - Peng Huang will conduct analyses.
Author 4 - Ren-Liang Xue - Ren-Liang Xue will independently extract data.
Author 5 - Wen-Jia Xie - Wen-Jia Xie will design and supervise the study.
Author 6 - Liang-Xi Xie - Liang-Xi Xie will design, supervise the study.