INPLASY PROTOCOL

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Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest: **NO.**

Association between microRNA 21 expression in serum and lung cancer: a protocol of systematic review and meta-analysis

Qiao, F[1]; Luo, P[2]; Liu, CH[3]; Fu, K[4]; Zhao, YB[5].

Review question / Objective: **Is microRNA 21 (mRNA 21) expression in serum associated with lung cancer (LC)?**
Condition being studied: **MicroRNA 21 and lung cancer.**
Information sources: **Electronic searches We will search Cochrane Library, PubMed, EMBASE, Allied and Complementary Medicine Database, WANGFANG database, and China National Knowledge Infrastructure from the inception to the present. We will search all these electronic databases with no language and geographical location restrictions. We will create detailed search strategy of Cochrane Library and will present it. We will also adapt similar search strategies of other electronic databases. Other resources Besides the electronic databases, we will search conference proceedings, dissertations, and reference lists of included studies.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 April 2020 and was last updated on 10 April 2020 (registration number INPLASY202040055).

INTRODUCTION

Review question / Objective: **Is microRNA 21 (mRNA 21) expression in serum associated with lung cancer (LC)?**

Condition being studied: **MicroRNA 21 and lung cancer.**

METHODS

Participant or population: **Patients diagnosed as histopathology-proven LC and normal participants without LC will be included without any restrictions related to the race, age, and gender.**

Intervention: **Experimental group: All patients with histopathology-proven LC examined with the levels of mRNA 21 expression in serum.**

Comparator: Control group: All normal participants were detected with the levels of mRNA 21 expression in serum.

Study designs to be included: All case-controlled studies reporting association between mRNA 21 expression in serum and patients with LC will be included.

Eligibility criteria: All case-controlled studies compared the association between mRNA 21 expression in serum of LC patients or normal participants.

Information sources: Electronic searches We will search Cochrane Library, PubMed, EMBASE, Allied and Complementary Medicine Database, WANGFANG database, and China National Knowledge Infrastructure from the inception to the present. We will search all these electronic databases with no language and geographical location restrictions. We will create detailed search strategy of Cochrane Library and will present it. We will also adapt similar search strategies of other electronic databases. Other resources Besides the electronic databases, we will search conference proceedings, dissertations, and reference lists of included studies.

Main outcome(s): The primary outcome is levels of serum mRNA-21 (as measured by real-time quantitative real-time polymerase chain reaction).

Additional outcome(s): The secondary outcomes are pathological types, tumor tumor-node-metastasis stages, lymph node metastasis, and tumor markers.

Data management: Two authors will independently collect the information from each included study. Any conflicts between them will be solved by consensus with the help of a third experienced author. The extracted information consists of manuscript title, name of first author, journal, year of publication, country, race, age, gender, eligibility criteria, sample size, study setting, study design, index and reference tests, and outcome indicators. We will contact primary authors to obtain any missing or unclear information in the included studies.

Quality assessment / Risk of bias analysis: In this study, two authors will independently assess the study quality for all included studies. Any different opinions will be solved by another experienced author through discussion. We will utilize Newcastle-Ottawa Scale to investigate the methodological quality for observational studies.

Strategy of data synthesis: We will employ RevMan V.5.3 software for statistical analysis. We will calculate continuous data as mean difference or standardized mean difference and 95% confidence intervals (CIs), and dichotomous data using risk ratio and 95% CIs. We will examine heterogeneity across included studies using I^2 test. I^2 ≤50% shows homogeneity and a fixed-effect model will be used, and I^2 >50% suggests remarkable heterogeneity and a random-effect model will be applied. If possible, we will perform a meta-analysis if we collected ample data from eligible trials with homogeneity. If there is obvious heterogeneity, we will test the sources of heterogeneity. We will also carry out a narrative summary. We will report this study results as a narrative summary by providing detailed written commentary to present study findings, study quality, and outcome indicators (e.g. mRNA-21 expression).

Subgroup analysis: We will carry out subgroup analysis to explore the possible sources of significant heterogeneity based on the different types of study information, types of patients and outcomes.

Sensibility analysis: In case of the sufficient data, sensitivity analysis will be performed to test the robustness of merged results by excluding low quality studies.

Country(ies) involved: China.

Keywords: Lung cancer; microRNA 21; case-controlled study; association.