INPLASY PROTOCOL

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None declared.

Diagnostic Value of Circulating LncRNAs for Gastric Cancer: A Systematic Review and Meta-analysis

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Review question / Objective: **With the prevalence of the next generation sequencing (NGS) technology, a large number of long non-coding RNAs (lncRNAs) has been attracted attention and received extensive researches on gastric cancer (GC). It was revealed that lncRNAs not only participate the transduction of various singling pathways and thus influencing GC genesis and development, but also have the potential for GC diagnosis. Compared with CEA, CA199, CA724 and other tumor markers, what is the diagnostic value of circulating lncRNAs in GC? Therefore, we aimed to conduct a meta-analysis on previous studies on GC.**

Condition being studied: **Compared with CEA, CA199, CA724 and other tumor markers, what is the diagnostic value of circulating lncRNAs in GC? Therefore, we aimed to conduct a meta-analysis on previous studies on GC.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 November 2022 and was last updated on 06 November 2022 (registration number INPLASY2022110024).

INTRODUCTION

Review question / Objective: **With the prevalence of the next generation sequencing (NGS) technology, a large number of long non-coding RNAs (lncRNAs) has been attracted attention and received extensive researches on gastric cancer (GC). It was revealed that lncRNAs not only participate the transduction of various singling pathways and thus influencing GC genesis and development, but also have the potential for GC diagnosis. Compared with CEA, CA199, CA724 and other tumor markers, what is the diagnostic value of circulating lncRNAs**

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in GC? Therefore, we aimed to conduct a meta-analysis on previous studies on GC.

Condition being studied: Compared with CEA, CA199, CA724 and other tumor markers, what is the diagnostic value of circulating lncRNAs in GC? Therefore, we aimed to conduct a meta-analysis on previous studies on GC.

METHODS

Participant or population: For the enrolled articles, the following inclusion criteria must be fulfilled: (1) comparison were made between GC and healthy controls; (2) the diagnosis of GC was confirmed by pathologist; (3) the detection technique had to be quantitative real-time PCR and test samples were from serum of plasma; (4) sufficient data were provided to calculate 2 × 2 tables including TP (true positive), FP (false positive), TN (true negative), and FN (false negative).The exclusion criteria were as follows: (1) duplicate articles; (2) reviews, meta-analysis, bioinformatics, case reports and laboratory studies; (3) irrelevant to the diagnostic value of lncRNAs or GC; (4) the full text was not available.

Intervention: The gastric cancer was confirmed by pathological examination and the expression level of circulating lncRNAs was examed by RT-PCR.

Comparator: Healthy controls: None of the them have any gastric caner or any other types of malignancy.

Study designs to be included: All enrolled researches should be discussed in our meta-analysis. We will caculate the overall sensitivity, specificity and the area under the curve (AUC). The value of pooled diagnostic odds ratios (DOR) will also be caculated.

Eligibility criteria: (1) comparison were made between GC and healthy controls; (2) the diagnosis of GC was confirmed by pathologist; (3) the detection technique had to be quantitative real-time PCR and test samples were from serum of plasma; (4) sufficient data were provided to calculate 2 × 2 tables including TP (true positive), FP (false positive), TN (true negative), and FN (false negative).

Information sources: To identify potentially eligible articles which published before August 2021. Two authors independently searched online databases, include PubMed, Embase, the Cochrane Library, and Web of Science. All the English publications will be searched without any restriction of countries.

Main outcome(s): All enrolled researches should be discussed in our meta-analysis. We will caculate the overall sensitivity, specificity and the area under the curve (AUC). The value of pooled diagnostic odds ratios (DOR) will also be caculated.

Data management: Two authors will screened the full text of every study and extract relevant information or data including independently: (1) basic information of the enrolled articles: the first author, publication year, country of origin, ethnicity, specimen type (serum or plasma), lncRNA type, cases and healthy controls group size, mean age, gender distribution and (2) sensitivity, specificity, TP, FP, FN, and TN values were also extracted from each article.

Quality assessment / Risk of bias analysis: Quality of assessment: We will use the Quality Assessment of diagnostic Accuracy studies (QUADAS-2) to assess the quality of the studies included.
Bias of publication: Q test and Higgins I^2 statistic (I^2) will be used to estimate the heterogeneity among all include studies. If $I^2 > 50\%$, it signifies the existence of heterogeneity, then the random effect model will be needed for data consolidation. Otherwise, the fixed effect model will be needed. Finally, the potential bias of publication was estimated by Deeks' funnel plot. $P < 0.05$ was considered statistically significant.

Strategy of data synthesis: 1. Quality assessment - The Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2)

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was applied to evaluate all enrolled articles in meta-analysis, which mainly depend on the following domains: patient selection, index test, reference standard, and flow and timing.

2. Data extraction - Two authors independently screened the full text of every study and extracted relevant information or data including: (1) basic information of the enrolled articles: the first author, publication year, country of origin, ethnicity, specimen type (serum or plasma), lncRNA type, cases and healthy controls group size, mean age, gender distribution and (2) sensitivity, specificity, TP, FP, FN, and TN values were also extracted from each article.

3. Statistical methods - STATA 16.0 (Stata Corporation, College Station, TX, USA) and Revman 5.4 (The Nordic Cochrane Centre, Copenhagen, Denmark) were used to analyze extracted data. In this diagnostic meta-analysis, forest plots were applied to estimate sensitivity, specificity. The area under the curve (AUC) of the summary receiver operating curve (SROC) were used to calculate the diagnostic efficiency of serum or plasma lncRNAs in GC. According to previous report, the diagnostic efficiency can be divided into low, good, very good, and excellent in terms of AUC values:< 0.75, 0.75~0.92, 0.93~0.96, and 0.97 or above[22]. Meanwhile, Q test and Higgins I^2 statistic (I^2) were used to estimate the heterogeneity among all include studies. If $I^2 > 50\%$, it signified the existence of heterogeneity, then the random effect model was needed for data consolidation. Otherwise, the fixed effect model was needed. Finally, the potential bias of publication was estimated by Deeks' funnel plot. $P < 0.05$ was considered statistically significant.

Subgroup analysis: We will divide the extracted data into few subgroups for stratified analyses, including sample types, sample size, lncRNA expression profiling, expression level of lncRNA, and countries to assess their impact on diagnostic value. In order to clarify the sources of heterogeneity between studies and explore the influence of covariables on the merger effect, we will use regression analysis to explore the influence of the characteristics of the included studies on the combination effect.

Sensitivity analysis: STATA 16.0 (Stata Corporation, College Station, TX, USA) and Revman 5.4 (The Nordic Cochrane Centre, Copenhagen, Denmark) were used to analyze extracted data. In this diagnostic meta-analysis, forest plots were applied to estimate sensitivity, specificity. The area under the curve (AUC) of the summary receiver operating curve (SROC) were used to calculate the diagnostic efficiency of serum or plasma lncRNAs in GC. According to previous report, the diagnostic efficiency can be divided into low, good, very good, and excellent in terms of AUC values:< 0.75, 0.75~0.92, 0.93~0.96, and 0.97 or above.

Language restriction: English.

Country(ies) involved: China.

Keywords: Gastric cancer; lncRNA; diagnosis; systematic review; meta-analysis.

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