INPLASY PROTOCOL

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None declared.

Diagnostic Value of CircRNAs as Potential Biomarker in Oral Squamous Cell Carcinoma: A Meta-analysis

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Review question / Objective: **The purpose of this meta-analysis is to comprehensively evaluate the diagnostic performance of circular non-coding RNA as potential biomarker in oral squamous cell carcinoma on the basis of available observational studies.**
Condition being studied: **This review primarily focuses on the correlation between the diagnostic value of circRNAs and oral squamous cell carcinoma. Oral squamous cell carcinoma ranks the most common malignant neoplasm in head-and-neck squamous cell carcinoma, posing a serious threat to human health. The most widely applied therapy includes surgery, chemotherapy and radiotherapy which largely comprise the patients' quality of life. However, the prognosis is still poor with a five-year survival rate of lower than 50%. Currently, the gold standard for OSCC diagnosis is still constituted by conventional oral examination and histological evaluation of biopsy, which is limited clinically for the discomfort of patients and sampling bias that lead to misdiagnosis. Therefore, it is of profound significance to explore novel biomarkers to enhance efficacy of early detection of OSCC.**

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 INPLASY202160037).

INTRODUCTION

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squamous cell carcinoma ranks the most common malignant neoplasm in head-and-neck squamous cell carcinoma, posing a serious threat to human health. The most widely applied therapy includes surgery, chemotherapy and radiotherapy which largely comprise the patients' quality of life. However, the prognosis is still poor with a five-year survival rate of lower than 50%. Currently, the gold standard for OSCC diagnosis is still constituted by conventional oral examination and histological evaluation of biopsy, which is limited clinically for the discomfort of patients and sampling bias that lead to misdiagnosis. Therefore, it is of profound significance to explore novel biomarkers to enhance efficacy of early detection of OSCC.

METHODS

Participant or population: Patients with oral squamous cell carcinoma that have not received any chemotherapy and radiotherapy before surgery.

Intervention: CircRNAs were found to be differently expressed in patients with oral squamous cell carcinoma.

Comparator: Not applicable.

Study designs to be included: Randomaized controlled trials(RCTs), case-control studies and cohort studies involved with circRNA will be included.

Eligibility criteria: The eligibility criteria were as follows: (a) Case-control study or cohort study, (b) the diagnosis of oral squamous cell carcinoma was confirmed by histological examinations, (c) the studies analyzed the relationship between circRNAs and oral cancers, (d) circRNAs expression levels were assessed with qRT-PCR, (e) the sample size, sensitivity, specificity, and AUC were provided to calculate true positives (TP), false positives (FP), false negatives (FN), and true negatives (TN).

Information sources: The bibliography searching will be carried out in four electronic databases, PubMed, Web of Science, Embase and Cochrane Library.

Main outcome(s): SROC curve and AUC, Sensitivity, Specificity, Diagnostic odds ratio, positive likelihood ratio, negative likelihood ratio, Fagan's nomogram and scatter plot, subgroup of analysis and sensitivity analysis for diagnostic power of circRNAs. Trial Sequential Analysis for analyzing the reliability of the meta-analysis.

Quality assessment / Risk of bias analysis: Quality of every individual study will be assessed by two authors independently(WR and SL) with Quality Assessment of Diagnostic Accuracy Studies-2 tool (QUADAS-2) on the basis of four aspects (“Patient Selection”, “Flow and Timing”, “Reference Standard” and “Index Test”) in two dimensions (“Risk of Bias” and “Applicability Concerns”).

Strategy of data synthesis: The heterogeneity will be estimated using I^2 statistics. The meta-analysis will apply a random-effect model if the percentage of I^2 is more than 50%, otherwise a fixed-effect model will be applied. Meta-regression analysis will be conducted to identify the potential source of heterogeneity. To test the reliability of our research, we will use sensitivity analysis by omitting individual studies. Meta-analysis will be planned utilizing statistical softwares of STATA 15.1 and Review Manager 5.4 in order to analyze the diagnostic performance of circRNAs in OSCC, including specificity, sensitivity, negative likelihood ratio (NLR), positive likelihood ratio (PLR), diagnostics odds ratio (DOR). Summary receiver operator characteristics curve (SROC) will be plotted to calculate the area under SROC curve (AUC) as well as 95% confidence intervals (95%CIs) for the qualitative assessment of diagnostic value.

Subgroup analysis: Subgroup analysis will be based on specimen type, sample size and the expression status of circRNAs.

Sensitivity analysis: A sensitivity analysis will be carried out to explain the

heterogeneity of each study by omitting individual study to test whether the results are credible and reliable.

Country(ies) involved: China.

Keywords: circular RNA, OSCC, oral oncology, meta-analysis, biomarker, diagnosis.

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