INPLASY PROTOCOL

Corresponding author:
Baojun Qiao

ybcxax@163.com

Author Affiliation:
PLA General Hospital.

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

Conflicts of interest: None declared.

Prognostic significance of long noncoding RNA HOTAIR in hepatocellular carcinoma: A protocol for systematic review and meta-analysis

Feng, L[1]; Liu, W[2]; Lv, Y[3]; Qiao, B[4].

Review question / Objective: This systematic review and meta-analysis is conducted to answer the following two questions: (1) Is high homeobox transcript antisense intergenic RNA (HOTAIR) expression associated worse overall survival (OS) and progression-free survival (PFS) in hepatocellular carcinoma (HCC)? (2) Is high HOTAIR expression associated with worse clinical features (e.g. more advanced clinical stage)?

Condition being studied: Hepatocellular carcinoma (HCC).

Eligibility criteria: The study selection will be conducted according to the following eligibility criteria by two researchers independently, and the dispute will be solved by the discussion with the third researcher. (1) The inclusion criteria are as follows: (a) Participants: Patients with HCC older than 18 years; (b) Intervention: Patients in the high HOTAIR expression; (c) Comparison: Patients in the low HOTAIR expression;(d) Outcomes: OS, PFS, and clinical features, including age, gender, tumor size, tumor number, histopathologic grading, α-fetoprotein level, cirrhosis, portal invasion, lymph node metastasis, distant metastasis, and clinical stage. (e) Study design: Prospective or retrospective studies. (2) The exclusion criteria include case reports, reviews, animal or cell experiments, incomplete data, and duplications.

INTRODUCTION

Review question / Objective: This systematic review and meta-analysis is conducted to answer the following two questions: (1) Is high homeobox transcript antisense intergenic RNA (HOTAIR) expression associated worse overall

survival (OS) and progression-free survival (PFS) in hepatocellular carcinoma (HCC)? (2) Is high HOTAIR expression associated with worse clinical features (e.g. more advanced clinical stage)?

Condition being studied: Hepatocellular carcinoma (HCC).

METHODS

Participant or population: Patients with HCC.

Intervention: Patients in the high HOTAIR expression.

Comparator: Patients in the low HOTAIR expression.

Study designs to be included: Prospective or retrospective studies.

Eligibility criteria: The study selection will be conducted according to the following eligibility criteria by two researchers independently, and the dispute will be solved by the discussion with the third researcher. (1) The inclusion criteria are as follows: (a) Participants: Patients with HCC older than 18 years; (b) Intervention: Patients in the high HOTAIR expression; (c) Comparison: Patients in the low HOTAIR expression;(d) Outcomes: OS, PFS, and clinical features, including age, gender, tumor size, tumor number, histopathologic grading, α-fetoprotein level, cirrhosis, portal invasion, lymph node metastasis, distant metastasis, and clinical stage. (e) Study design: Prospective or retrospective studies. (2) The exclusion criteria include case reports, reviews, animal or cell experiments, incomplete data, and duplications.

Information sources: PubMed, Cochrane Library, and Embase will be comprehensively searched to seek the relevant studies.

Main outcome(s): OS, PFS, and clinical features, including age, gender, tumor size, tumor number, histopathologic grading, α-fetoprotein level, cirrhosis, portal invasion, lymph node metastasis, distant metastasis, and clinical stage.

Quality assessment / Risk of bias analysis: Two tools are used to evaluate the quality of included studies. For the randomized controlled trial (RCT), the "risk of bias assessment" tool in Cochrane System Assessment Manual will be used to evaluate the risk of bias of included studies. Using this standard, one RCT study will be divided into three classes: high, unclear, or low risk of bias. For non-RCT study, the quality of included study will be assessed with the Newcastle-Ottawa Scale (NOS) score, and the study with NOS score ≥7 is considered to have the high quality. The quality assessment of included studies is conducted by two researchers independently, and any disagreement will be solved by the discussion with the third researchers.

Strategy of data synthesis: All analyses in this study will be performed with Review Manager (RevMan) 5.3 and Stata 12.0 (Stata Corp, College Station, TX). A combination of hazard ratio (HR) and 95% confidence interval (CI) is used to estimate the impact of HOTAIR expression on the OS and PFS in HCC. The relationships between HOTAIR expression and clinical features of HCC are evaluated using the odds ratio (OR) and 95% CI. If one study only reported the Kaplan–Meier curves, the HR and corresponding 95% CI will be calculated using the methods provided by Tierney et al [14]. All results will be showed in the form of forest plots. A two-side p-value less than 0.05 indicates there is a statistically significant result. A test of heterogeneity of combined HR or OR was conducted using the Cochran Q test and Higgins I2 statistic. A p-value for heterogeneity less than 0.10 or I2 larger than 50% indicates there is an obvious heterogeneity among included studies, as a result, a random-effect model should be used. On the contrary, a p-value for heterogeneity larger than 0.10 or I2 less than 50% indicates there is no obvious heterogeneity among included studies, and a fixed-effect model should be used.

Subgroup analysis: To comprehensively evaluate the relationship between HOTAIR expression and OS, the subgroup analyses will be performed using different grouping standards, such as country, sample size, treatment therapy, and quality of included studies.

Sensitivity analysis: The sensitivity analysis is performed to determine that whether one of the included studies has the decisive effect on the pooled results. The sensitivity analysis will be conducted using the Stata 12.0 by removal of one study one time to observe the change of pool results.

Country(ies) involved: China.

Keywords: homeobox transcript antisense intergenic RNA, HOTAIR, hepatocellular carcinoma, prognosis, meta-analysis.

Contributions of each author:
Author 1 - Lei Feng.
Author 2 - Wenqing Liu.
Author 3 - Yunhuo Lv.
Author 4 - Baojun Qiao.