

INPLASY PROTOCOL

To cite: Sun et al. MicroRNAs as Potential Biomarkers for the Diagnosis of Inflammatory Bowel Disease: A Systematic Review and Meta-analysis. Inplasy protocol 202220027. doi: 10.37766/inplasy2022.2.0027

Received: 10 February 2022

Published: 10 February 2022

Corresponding author:
Lina Sun

sunln13@163.com

Author Affiliation:

Xi'an Children's Hospital, Shaanxi Research Institute for Pediatric Diseases, The Affiliated Children's Hospital of Xi'an Jiaotong University, and National Regional Medical Center for Children (Northwest).

Support: Shaanxi.

Review Stage at time of this submission: Completed but not published.

Conflicts of interest:
None declared.

MicroRNAs as Potential Biomarkers for the Diagnosis of Inflammatory Bowel Disease: A Systematic Review and Meta-analysis

Sun, L¹; Han, Y²; Wang, H³; Liu, H⁴; Liu, S⁵; Yang, H⁶; Ren, X⁷; Fang, Y⁸.

Review question / Objective: The purpose of this systematic review was to systematically review the clinical studies regarding miRNAs as diagnostic biomarkers for inflammatory bowel disease and assess the overall diagnostic accuracy of miRNAs.

Condition being studied: The symptoms of inflammatory bowel disease (IBD) are highly variable. The diagnosis of IBD must be made through medical history, physical, laboratory, radiologic, endoscopic, and histological examinations. However, these diagnostic techniques are not specific and sometimes even equivocal. Therefore, reliable biomarkers are urgently needed in the diagnosis of IBD. Several clinical and preclinical researches have shown that dysregulated microRNAs (miRNAs) play a crucial role in IBD development. miRNAs, as single-stranded noncoding RNAs that contain 22-24 nucleotides, can post-transcriptionally regulate gene expression by blocking mRNA translation or degrading target mRNAs. miRNAs are widely involved in physiological and pathological cellular processes, such as differentiation, proliferation and apoptosis. Besides, they are stable, noninvasive, and resistant to degradation by ribonucleases, making them valuable targets in the diagnosis, monitoring, prognosis, and treatment of diseases. To date, inconsistent results have been found about miRNA expression profiling in the patients with IBD. Moreover, the diagnostic accuracy of miRNAs for IBD has not been reported in any meta-analysis.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 February 2022 and was last updated on 10 February 2022 (registration number INPLASY202220027).

INTRODUCTION

Review question / Objective: The purpose of this systematic review was to systematically review the clinical studies regarding miRNAs as diagnostic

biomarkers for inflammatory bowel disease and assess the overall diagnostic accuracy of miRNAs.

Condition being studied: The symptoms of inflammatory bowel disease (IBD) are

highly variable. The diagnosis of IBD must be made through medical history, physical, laboratory, radiologic, endoscopic, and histological examinations. However, these diagnostic techniques are not specific and sometimes even equivocal. Therefore, reliable biomarkers are urgently needed in the diagnosis of IBD. Several clinical and preclinical researches have shown that dysregulated microRNAs (miRNAs) play a crucial role in IBD development. miRNAs, as single-stranded noncoding RNAs that contain 22-24 nucleotides, can post-transcriptionally regulate gene expression by blocking mRNA translation or degrading target mRNAs. miRNAs are widely involved in physiological and pathological cellular processes, such as differentiation, proliferation and apoptosis. Besides, they are stable, noninvasive, and resistant to degradation by ribonucleases, making them valuable targets in the diagnosis, monitoring, prognosis, and treatment of diseases. To date, inconsistent results have been found about miRNA expression profiling in the patients with IBD. Moreover, the diagnostic accuracy of miRNAs for IBD has not been reported in any meta-analysis.

METHODS

Participant or population: Inflammatory bowel disease.

Intervention: miRNAs expression.

Comparator: Patients that are not related to inflammatory bowel disease or healthy controls. Patients that was not related to inflammatory bowel disease or healthy controls.

Study designs to be included: No restrictions.

Eligibility criteria: Inclusion criteria: Studies included in this systematic review should be reports on miRNAs expression in participants diagnosed with IBD. Studies reporting miRNA diagnostic accuracy that could be used to construct the 2x2 contingency table for IBD diagnosis are included in meta-analysis. Exclusion

criteria: Studies meeting one or more of the following criteria are excluded: 1) duplicate publications or articles with republished data; 2) reviews, letters, comments, replies, erratum, and conference abstracts; 3) case reports, database, or methodological studies; 4) cell, animal, or microbiological trials; 5) studies focusing on IBD-related diseases; 6) studies of miRNA polymorphism or methylation; 7) studies without control individuals who were healthy or whose normal tissues were used.

Information sources: We search articles in PubMed, EMBASE, Web of Science, the Cochrane Library, and the Cochrane IBD Group Specialized Register.

Main outcome(s): The pooled sensitivity, specificity, positive and negative likelihood ratios, diagnostic odds ratio and area under the curve.

Quality assessment / Risk of bias analysis: The quality of each study evaluates independently by two reviewers according to the Quality Assessment for Studies of Diagnostic Accuracy (QUADAS-2) tool.

Strategy of data synthesis: We combine data from individual datasets for meta-analysis using the software Meta-DiSc v1.4 (Clinical Biostatistics Unit, Ramón y Cajal Hospital, Madrid, Spain). The number of true positive (TP), false positive (FP), false negative (FN), and true negative (TN) of each study is calculated to obtain summary receiver operating characteristic (sROC) curve and pooled sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR) with 95% confidence interval (CI). The heterogeneity of included studies caused by a threshold effect is assessed by Spearman's correlation analysis and ROC plane plots. Statistical heterogeneity of non-threshold effects is assessed based on visual inspection of forest plots, the Higgins's inconsistency index (I²) statistic and the P value for the Chi² test. A random effects model (the DerSimonian-Laird method) is used when heterogeneity presented (I²>50% and/or P<0.05).

Otherwise, the fixed-effects model (the Mante-Haenszel method) is used.

Subgroup analysis: We carry out the following a priori subgroup analyses: IBD subtype (UC versus CD), age of participants (pediatric population (<18 years of age) versus adult (≥ 18 years of age), sample source (blood versus others), and method of quantifying miRNA expression (qPCR versus only microarray).

Sensitivity analysis: To evaluate the stability of our results, we perform sensitivity analyses that analysis the overall outcome after removing individual study one by one.

Country(ies) involved: China.

Keywords: inflammatory bowel disease; microRNAs; meta-analysis; systematic review; diagnosis.

Contributions of each author:

Author 1 - Lina Sun.

Author 2 - Yanan Han.

Author 3 - Hua Wang.

Author 4 - Huanyu Liu.

Author 5 - Shan Liu.

Author 6 - Hongbin Yang.

Author 7 - Xiaoxia Ren.

Author 8 - Ying Fang.