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Comparison of the diagnostic value of various microRNAs in blood for colorectal cancer: A Systematic Review and Network Meta-Analysis

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ADMINISTRATIVE INFORMATION

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

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 August 2023 and was last updated on 21 August 2023.

INTRODUCTION

Review question / Objective Participants: The population in the diagnostic test was divided into two groups, patients with colorectal cancer and healthy individuals. Intervention: levels of microRNA in peripheral blood of patients before any treatment. Comparison: gold standard test. Study design: Cohort studies or case-control studies. Outcome: sensitivity and specificity.

Condition being studied Colorectal cancer is the third most common cancer and the second leading cause of death worldwide. In developed countries such as Europe and the United States, colorectal cancer incidence and mortality rates are decreasing due to the availability of screening and early treatment; meanwhile, in some low- and middle-income countries, the incidence of colorectal cancer is increasing due to lack of diagnosis and treatment. Therefore, early detection and treatment can improve the cure rate of colorectal cancer.

METHODS

Participant or population The population in the diagnostic test was divided into two groups, patients with colorectal cancer and healthy individuals.

Intervention Levels of microRNA in peripheral blood of patients before any treatment.

Comparator Gold standard test.

Study designs to be included Cohort studies or case-control studies.

Eligibility criteria The exclusion criteria were as follows: (1) A minimum follow-up period of 1 year. (2) Limited to studies published after 2000. (3) Language of publication was English. (4) Report

status was published; reports such as unpublished manuscripts and conference abstracts were not eligible for inclusion. (5) Studies were excluded because sensitivity or specificity was not reported.

Information sources On February 1, 2023, we searched Pubmed, Embase, Web of Science, Scopus, and Cochrane databases to screen studies.On February 10, 2023, we also conducted a 'snowball' search by searching reference lists of publications eligible for full-text review and using Google Scholar to identify and screen studies that cite them to identify additional studies.

Main outcome(s) This review evaluates the diagnostic value of microRNA in three dimensions, namely sensitivity, specificity and accuracy. Studies that met the inclusion and exclusion criteria provided data for all three were eligible for synthesis.
The two review authors independently collected the sensitivity and specificity from the studies, while the accuracy of some of the studies could not be obtained directly from the literature directly. Therefore, we derived the accuracy indirectly by conversion. Sensitivity = A/(A+C), the probability of a positive diagnosis with disease; specificity = D/(B+D), the probability of a negative diagnosis without disease; accuracy = (A+D)/(A+B+C+D), the probability of total positives as a percentage of total. a+C is the number of patients with CRC, and B+D is the number of negative controls.

Quality assessment / Risk of bias analysis We used a scoring system based on the CASP checklist (designated for diagnostic studies). The purpose of the study, sources and measurements, statistical methods, data results, primary outcomes, and limitations of the study were assessed. The 12 questions in the checklist were scored as 0, 0.5, or 1 (yes: 1; indistinguishable: 0.5, no: 0). Based on these mean scores, the quality of the study was divided into three groups: high (receiving 70% of the total score), moderate (receiving 50-69% of the total score), and low quality (less than 50% of the total score). Overall, 94.4% of the studies were of high quality, while the others were of moderate quality.
The two review authors independently applied the tool to each of the included studies and recorded supporting information and rationale for the judgment of risk of bias for each domain (low; high; some concerns). Any differences in judgments of risk of bias or rationale for judgments were resolved by discussion to reach consensus between the two review authors, with a third review author acting as arbiter if necessary.

Strategy of data synthesis The main steps of the analysis in this paper are as follows: first, the traditional pairwise metaanalysis and then the network meta-analysis. In the first step, sensitivity, specificity, and accuracy were comparedwith the estimated odds ratios (ORs) and 95% confidenceintervals (CI). Also, I-square and Tau-square tests wererun to detect the amount of heterogeneity for each pairwisemeta-analysis. In the second step, to clarify directand indirect comparisons, a network plot of all the diagnostic panels was depicted. The size of nods and lines in the network plot showed the number of patients and involvedstudies, respectively, for each direct comparison. Pooledeffective sizes were estimated by using Bayesian networkmeta-analysis for all the direct and indirect comparisons.The Bayesian analysis used samples of Markov chain generating by Monte Carlo simulation by noninformative priorsfor both effect sizes and precision. Convergence was checkedand confirmed after four chains and a 10,000-simulation burn-in phase. Finally, direct probabilities were resultedfrom the additional 50,000-simulation phase. The estimates ORs and 95% credible interval (CrI) were considered for presenting the results; the ones not containing 1were considered statistically significant.

Subgroup analysis None.

Sensitivity analysis To check the publication bias of this study, we plotted a funnel plot. Figures 5a and 5b correspond to the funnel plots for sensitivity and specificity, respectively, and both of the 2 plots are relatively symmetrical, suggesting that the publication bias of the study is small and can be ignored.

Country(ies) involved China.

Keywords diagnostic value, circulating microRNA, colorectal cancer, Network Meta-Analysis.

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