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Comprehensive meta-analysis of the diagnostic potential of miRNAs and piRNAs in sperm abnormalities associated with male infertility

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ADMINISTRATIVE INFORMATION

Support - Yes.

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 25 December 2024 and was last updated on 25 December 2024.

INTRODUCTION

Review question / Objective The primary objective of this study was to evaluate the diagnostic potential of microRNAs (miRNAs) and piwi-interacting RNAs (piRNAs) as biomarkers for sperm abnormalities associated with maleinfertility.

Condition being studied This study aimed to assess the viability of ncRNAs, particularly focusing on miRNAs and piRNAs, as novel biomarkers with high diagnostic accuracy for detecting sperm abnormalities linked to male infertility. Nonetheless, the findings are constrained by the paucity and variable quality of existing literature, necessitating additional clinical validation.

METHODS

Participant or population This study primarily involves patients with infertility caused by various male sperm abnormalities, and non-coding RNA is used as a biomarker in the diagnosis of male infertility.

Intervention Not applicable.

Comparator Not applicable.

Study designs to be included This study will include literature written in either English or Chinese, and each included study must demonstrate the principle of randomization in its experimental design.

Eligibility criteria Inclusion Criteria:
(i) miRNAs and piRNAs play a role in the diagnosis of male sperm abnormalities; (ii) specific indicators of male infertility diseases are clearly defined, such as oligospermia, azoospermia, and asthenospermia; (iii) complete data are available to determine the True Positives (TP), False Positives (FP), True Negatives (TN), and False Negatives (FN) in this study; (iv) study types: cohort studies or case-control studies.
Exclusion Criteria:
(ii) Duplicate studies, review articles, animal experiments, etc.; (ii) literature from which the required data cannot be obtained and cannot be contacted with the authors; (iii) cases of male infertility with unknown causes; (iv) literature not published in Chinese or English.

Information sources Studies from databases such as PubMed, Embase, Web of Science, Cochrane Library, CNKI, Wanfang Data, and cqvip.

Main outcome(s) Studies were included if they involved miRNAs and piRNAs in the diagnosis of male sperm abnormalities, clearly defined specific indicators of male infertility diseases, and provided complete data to determine True Positives (TP), False Positives (FP), True Negatives (TN), and False Negatives (FN). Cohort studies or case-control studies were considered.

Quality assessment / Risk of bias analysis Deek's funnel plot is more appropriate for assessing publication bias. The p-values for publication bias in the diagnosis of male sperm abnormalities using miRNAs and piRNAs were 0.63 and 0.73, respectively. The plots were generally symmetrical, indicating no evidence of publication bias among the included studies.

Strategy of data synthesis A meta-analysis was conducted using RevMan 5.4 and Stata 16.0 software. Heterogeneity among the studies was assessed using the χ^2 test and I^2 statistic. A P value greater than 0.1 and an I^2 statistic less than 50% indicated good homogeneity, warranting the use of a fixed-effect model. Conversely, a P value of 0.1 or less and/or an I^2 statistic of 50% or more suggested heterogeneity, necessitating further subgroup analysis to explore its causes. After excluding obvious clinical and methodological heterogeneities, if significant heterogeneity remained, a random-effects model or descriptive analysis was employed. Based on the appropriate model, sensitivity, specificity, diagnostic odds ratio (DOR), positive likelihood ratio (PLR), negative likelihood ratio (NLR), area under the curve (AUC), and 95% confidence intervals (CI) for the combined literature or subgroups were calculated. As this was a diagnostic meta-analysis, Deek's funnel plot was used to evaluate publication bias, with a P value less than 0.05 indicating statistical significance. Additionally, a Fagan plot was utilized to assess the clinical utility of miRNAs and piRNAs in diagnosing male sperm abnormalities.

Subgroup analysis Given the substantial heterogeneity observed in diagnostic outcomes, conducting a subgroup analysis is imperative to elucidate the underlying sources of this variability. This entails categorizing patients based on specific disease types linked to sperm abnormalities, both individually and in combination, as well as by the ethnic backgrounds of the participants. A focused subgroup analysis on miRNAs in diagnosing sperm abnormalities will be undertaken. However, due to the paucity of research on piRNAs, the analysis for azoospermia and oligospermia will be limited to these conditions.

Sensitivity analysis Using a leave-one-out approach, each study was excluded one at a time, and a new meta-analysis was performed on the remaining studies. The results indicated that the final outcomes did not change significantly before and after the exclusion of individual studies, suggesting that the meta-analysis results are robust.

Country(ies) involved Changsha Maternal and Child Health Hospital, China.

Keywords miRNA, piRNA, Diagnostic potential, Sperm abnormality, meta-analysis.

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