INPLASY PROTOCOL

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

Conflicts of interest: None.

Long non-coding RNAs, one of candidate biomarkers in diabetic kidney disease A systematic review protocol of profiling studies

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Review question / Objective: The objective of this systematic review is to conduct a protocol for systematic review to summarize and analyse the approximately consistent differential expressed lncRNAs which have been cited in reproducible profiling results as candidate biomarkers for DKD.

Condition being studied: Diabetic kidney disease (DKD) is a unique serious microvascular complication of diabetes with increasing prevalence and accounts for approximately 40% of diagnosed end-stage renal disease (ESRD). Currently, there are few especially effective predictive methods for early diagnosis for DKD except microalbuminuria and declining of glomerular filtration rate (GFR). Long non-coding RNAs (LncRNAs), as emerging biomarkers, coming into people's vision. Currently, a number of studies have indicated that lncRNAs are concerning with the progression of DKD. This systematic review is aiming to conduct a protocol for systematic review to summarize and analyse the approximately consistent differential expressed lncRNAs which have been cited in reproducible profiling results as candidate biomarkers for DKD. And it helps to offer candidate biomarkers for early detection and early clinical management.

INTRODUCTION

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METHODS

Search strategy: (((Diabetic Kidney Disease) OR (Diabetic Nephropathy)) AND ((((LncRNA) OR (LncRNAs)) OR (Long non-coding RNA)) OR (Long non-coding RNAs))) AND (((expression) OR (profile)) OR (profiling)).

Participant or population: DKD participants of all ages will be included in the study regardless of nationality, gender, race, occupation, or education level. And DKD animal models regardless of spieces. Cell lines studies were excluded.

Intervention: This study focuses on the lncRNAs' function as candidate biomarkers for early detection for DKD, therefore, samples of DKD patients were glomerulus, plasma/serum, urine and exosome.et al. Besides, it is a technical challenge to analyze the lncRNAs owing to their relatively low and tissue-specific expression. Therefore, the lncRNA expression analysis methods were with high sensitivity, resolution and continuously optimized. Such as High-throughput sequencing serial analysis of gene expression (SAGE), microarray, next generation sequencing (NGS) , RNA-Seq, Cap analysis of gene expression (CAGE), PCR or Western blotting.

Comparator: Non-DKD patients or normal animals.

Study designs to be included: In order to ensure the quality of this systematic review, we will include all the relevant lncRNAs studies published in English or Chinese. The current research results will be objectively integrated to evaluate the offered candidate biomarkers for early detection and early clinical management.

Eligibility criteria: The inclusion and exclusion criteria were defined as follows: studies were included if (1) studies must have lncRNA expression profiling on humans or animal models of DKD; (2) studies have to compare DKD samples with healthy control samples; (3) studies have to report the relative lncRNA expression via lncRNA High-throughput sequencing serial analysis of gene expression (SAGE)[32, 33], microarray, next generation sequencing (NGS) , RNA-Seq [34], Cap analysis of gene expression (CAGE)[35], PCR or Western blotting; (4) studies have to report cut-off criteria of dysregulated lncRNAs; (5) sample sizes should be reported; and (6) fold changes should be reported (even if non-explicit). Studies were excluded if: (1) did not meet the inclusion criteria; (2) did not found significant interest results; (3) studies were about cell lines; (4) review articles; and (5) they compared lncRNA expression profiles in stages of DKD progression together.

Information sources: PubMed, Web of science, Springer Cochrane Library, EBASE, WHO International Clinical Trials Registry Platform ,Wanfang Database, China National Knowledge Infrastructure Database, Chinese Scientific Journal Database, and Chinese Biomedical Literature Database.

Main outcome(s): Highly significant and consistently dysregulated lncRNAs will be identified.

Quality assessment / Risk of bias analysis:
Two review authors will independently use the criteria outlined in theCochrane Handbook for Systematic Reviews of Interventions to assess the risk of bias in the included studies. The following 6 domains in the Cochrane "Risk of bias tool" will be assessed: random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other bias. We will grade each potential trial of bias as high, low, and unclear. Any disagreement will be resolved by discussing or by asking the 3rd author to make a final decision.

Strategy of data synthesis: RevManV.5.3.5 will be used for data analysis and synthesis. Continuous data will be expressed as MD/SMD with 95% CIs, while the dichotomous outcomes will be presented as RR with 95% CIs. When I2<50%, the fixed effect model will be adopted to analyze. Otherwise, the random effect model will be selected. Additionally, we will use the sensitivity analysis and subgroup analysis to explore the causes of heterogeneity.

Subgroup analysis: LncRNAs express differentially among species, disease and tissue types, with different properties and heterogeneities. Subgroup analyses divided and compared the differentially expressed lncRNAs according to species (human and animal), types of diabetes (T1DN and T2DN) and tissue type (kidney, blood and urine).

Sensibility analysis: If there are sufficient studies included, we will take sensitivity analyses to test the robustness and reliability of the results. The sensitivity analysis focuses on research characteristics or types such as methodological quality, and examines the effects of total effects by excluding certain low quality studies or unblinded studies.

Language: English.

Country(ies) involved: China.

Keywords: long non-coding RNA.

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