

Appendix 1

Search strategies

CNKI

1. (主题=高血压) OR (主题=原发性高血压) OR (主题=高血压病)
2. (主题=外泌体) OR (主题=细胞外囊泡)
3. 1 AND 2

CNKI

1. (term=hypertension) OR (term=essential hypertension) OR (term=high blood pressure)
2. (term=exosome) OR (term=essential hypertension)
3. 1 AND 2

WanFang Database

1. 主题:(高血压) or 主题:(高血压病) or 主题:(原发性高血压)
2. 主题:(外泌体) or 主题:(细胞外囊泡)
3. 1 AND 2

WanFang Database

1. term:(hypertension) or term:(high blood pressure) or term:(essential hypertension)
2. term:(exosome) or term:(extracellular vesicles)
3. 1 AND 2

PubMed

- #1 ("essential hypertension"[Mesh]) OR ("essential hypertension" [Title/Abstract]) OR ("primary hypertension" [Title/Abstract]) OR ("isolated systolic hypertension" [Title/Abstract]) OR ("hypertension" [Title/Abstract]) OR ("high blood pressure" [Title/Abstract])
- #2 ("extracellular vesicles"[Mesh]) OR ("exosomes"[Mesh]) OR ("extracellular vesicles "[Title/Abstract]) OR ("exosomes"[Title/Abstract]) OR ("EVs"[Title/Abstract])
- #3 #1 AND #2

EMBASE

- #1 'essential hypertension'/exp OR 'primary hypertension'/exp OR 'hypertension'/exp OR 'isolated systolic hypertension'/exp OR 'high blood pressure'/exp
- #2 'extracellular vesicles'/exp OR 'exosomes'/exp OR 'EVs'/exp
- #3 #1 AND #2

Web of Science

- #1 TS=(essential hypertension) or (primary hypertension) or (hypertension) or (isolated systolic hypertension) OR (high blood pressure)
- #2 TS=(extracellular vesicles) or (exosomes) or (EVs)
- #3 #1 and #2

The Cochrane Library

#1 (exosome): ti, ab, kw

#2 (extracellular vesicles): ti, ab, kw

#3 (EVs): ti, ab, kw

#4 #1 OR #2 OR #3

#5 (essential hypertension): ti, ab, kw

#6 (primary hypertension): ti, ab, kw

#7 (hypertension): ti, ab, kw

#8 (isolated systolic hypertension): ti, ab, kw

#9 (high blood pressure): ti, ab, kw

#10 #5 OR #6 OR #7 OR #8 OR #9

#11 #4 AND #10

Chinese Clinical Trial Registry (ChiCTR)

1. 研究疾病: 高血压 OR 原发性高血压

2. 研究内容: 外泌体 OR 细胞外囊泡

3. 试验状态: 已完成 OR 进行中

4. 1 AND 2 AND 3

Chinese Clinical Trial Registry (ChiCTR)

1. Research Diseases: Hypertension OR Essential hypertension

2. Study Content: Exosomes OR Extracellular vesicles

3. Trial status: Completed OR In progress

4. 1 AND 2 AND 3

Table S1 JBI Quality Assessment Scale

No.	JBI critical appraisal checklist The score is 1 for “Yes”, 0 for “no”, and U for “unclear”	Included Studies									
		Zhang J	Song H	Kong L	Liu D	Wang C <i>et al.</i>	Santelli A <i>et al.</i>	Perez- Hernandez J <i>et al.</i> (2021)	Ma J <i>et al.</i>	Lugo- Gavidia LM <i>et al.</i>	Perez- Hernandez J <i>et al.</i> (2018)
1	Were the criteria for inclusion in the sample clearly defined?	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes
2	Were the study subjects and the setting described in detail?	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Unclear
3	Was the exposure measured in a valid and reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4	Were objective, standard criteria used for measurement of the condition?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5	Were confounding factors identified?	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes
6	Were strategies to deal with confounding factors stated?	No	No	No	No	No	Yes	Yes	Yes	Yes	Unclear
7	Were the outcomes measured in a valid and reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8	Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Total score (%)		6 (75)	6 (75)	6 (75)	6 (75)	4 (50)	8 (100)	7 (87.5)	8 (100)	8 (100)	6 (75)
Quality of review		Moderate	Moderate	Moderate	Moderate	Moderate	High	High	High	High	Moderate

Answers: Yes, No, Unclear or Not Applicable. To classify a JBI score out of 8 into low, moderate, or high categories. Interpretation of the score: 1–3 (low quality), 4–6 (moderate quality), and 7–8 (high quality).

Table S2 ROBINS-I assessment

Study	ROBINS-I domain							Overall ROBINS-I assessment
	Bias due to confounding	Bias in selection of participants	Bias in measurement of interventions	Bias due to departures from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of reports results	
Damkjaer M <i>et al.</i>	Moderate	Low	Low	Low	Moderate	Low	Low	Moderate

ROBINS-I, risk of bias in nonrandomized studies of interventions.

Table S3 Potential exosomal biomarkers in blood

No.	Study	Race	Significant biomarker
1	Kong L (25)	Han	Upregulated: hsa-miR-154-5p, hsa-miR-200c-3p, hsa-miR-376b-3p, hsa-miR-424-5p, hsa-miR-744-5p, hsa-miR-335-3p, hsa-miR-487b-3p, hsa-miR-145-5p, novel-hsa-miR285-5p, novel-hsa-miR247-5p, hsa-miR-339-3p, hsa-miR-205-5p, hsa-miR-143-3p, hsa-miR-5010-3p, hsa-miR-326, hsa-miR-495-3p novel-hsa-miR100-5p, hsa-miR-499a-5p, hsa-miR-153-3p Downregulated: hsa-miR-122-5p
		Uighur	Upregulated: hsa-miR-199a-5p, hsa-miR-23b-3p, hsa-miR-376c-3p, hsa-miR-7-1-3p, hsa-miR-223-3p, hsa-miR-589-5p, hsa-miR-27b-3p, hsa-miR-19b-3p, hsa-miR-411-5p, hsa-miR-379-5p, hsa-miR-199b-3p, hsa-miR-199a-3p novel-hsa-miR223-5p, hsa-miR-363-3p, hsa-miR-21-5p novel-hsa-miR260-5p, hsa-miR-20a-5p, hsa-miR-431-5p novel-hsa-miR105-5p, hsa-miR-148b-3p, hsa-miR-27a-3p novel-hsa-miR316-3p, hsa-miR-155-5p, hsa-miR-146a-5p, hsa-miR-337-3p, hsa-miR-4662a-5p, hsa-miR-323a-3p, hsa-miR-425-3p, hsa-miR-3613-5p, hsa-miR-98-5p, hsa-miR-22-3p, hsa-miR-29c-5p, hsa-miR-410-3p, hsa-miR-548j-5p, hsa-miR-30b-5p, hsa-miR-30a-5p, hsa-miR-185-5p, hsa-miR-196b-5p, hsa-let-7i-5p, hsa-let-7d-5p, hsa-miR-145-5p novel-hsa-miR289-5p, hsa-miR-1271-5p, hsa-miR-30d-5p, hsa-miR-146b-5p, hsa-let-7g-5p, hsa-miR-1284, hsa-let-7f-5p, hsa-miR-576-5p, hsa-miR-15b-5p, hsa-let-7a-5p
		Kazakh	Upregulated: hsa-miR-192-5p, hsa-miR-140-5p, hsa-miR-7-1-3p, hsa-miR-30a-3p Downregulated: hsa-miR-877-5p, novel-hsa-miR285-5p
2	Lugo-Gavidia LM <i>et al.</i> (19)	ND	The mean level of platelet derived EVs were higher in patients with hypertension compared to healthy reference group. Similar results were obtained when comparing only treated hypertensive patients with healthy participants
3	Wang C <i>et al.</i> (23)	ND	Upregulated: hsa-miR-320d, hsa-miR-423-5p, hsa-miR-378a-3p, hsa-miR-134-5p, hsa-miR-2110, hsa-miR-378c, hsa-miR-4732-3p, hsa-miR-7706, hsa-miR-1180-3p, hsa-miR-1307-3p Downregulated: hsa-miR-22-5p, hsa-miR-363-3p, hsa-miR-103a-3p, hsa-miR-24-3p, hsa-miR-194-5p, hsa-miR-199a-3p, hsa-let-7i-5p, hsa-miR-30e-5p, hsa-miR-140-3p
4	Perez-Hernandez J <i>et al.</i> (21)	ND	Upregulated: miR-126-3p, miR-191-5p Downregulated: miR-26a-5p, miR-222-3p Compared with UAE patients, healthy individuals had significantly different miR-191-5p and miR-222-3p levels in plasma exosomes.
5	Ma J <i>et al.</i> (20)	ND	Upregulated: miRNA-6852-3p Downregulated: miRNA-625-3p Hypertensive patients with cognitive impairment (HT-CI) group had lower miRNA-330-3p and miRNA-432-5p than the hypertensive patients with normal impairment (HT-NC) group.
6	Liu D (24)	ND	Upregulated: hsa-miR-372-5p, hsa-miR-552-3p, hsa-miR-891a-5p, hsa-miR-4745-5p, hsa-miR-655-3p, hsa-miR-99a-3p, hsa-miR-1275, hsa-miR-3131, hsa-miR-1284, hsa-miR-431-5p, hsa-miR-365b-5p, hsa-miR-122-3p, hsa-miR-30b-3p, hsa-miR-454-5p, hsa-miR-203a-3p, hsa-miR-4433b-3p Downregulated: hsa-miR-502-5p, hsa-miR-6820-3p, hsa-miR-1537-3p, hsa-miR-548ar-3p, hsa-miR-1236-5p, hsa-miR-8061, hsa-miR-663a, hsa-miR-7106-5p, hsa-miR-216b-3p, hsa-miR-4433a-5p, hsa-miR-1185-2-3p, hsa-miR-6826-5p, hsa-miR-937-5p, hsa-miR-33a-5p, hsa-miR-1185-1-3p, hsa-miR-3152-5p, hsa-miR-3140-3p, hsa-miR-215-3p, hsa-miR-3920, hsa-miR-4726-5p

EH, essential hypertension; HC, healthy control; miRNA, microRNA; ND, not determined; EV, extracellular vesicle; BP, blood pressure; PWV, pulse wave velocity; UAE, urinary albumin excretion.

Table S4 Potential exosomal biomarkers in urine

No.	Study	Race	Significant biomarker
1	Zhang J (27)	ND	Downregulated: miR-29-5p, miR-200a-3p
2	Song H (26)	Mongol	NCC protein (EH/HC ratio)
3	Santelli A <i>et al.</i> (22)	ND	Overall percentage of urinary p16 ⁺ EVs, p16 ⁺ /urate transporter 1 ⁺ , p16 ⁺ /prominin-2 ⁺
4	Perez-Hernandez J <i>et al.</i> (21)	ND	Downregulated: miR-26a-5p
5	Damkjaer M <i>et al.</i> (18)	ND	RAIG-2, syntenin-1
6	Perez-Hernandez J <i>et al.</i> (12)	ND	miR-146a, miR-335

EH, essential hypertension; HC, healthy control; ND, not determined; mRNA, messenger RNA; NCC, Na-Cl cotransporter; EV, extracellular vesicle; UAE, urinary albuminuria.