

Table S1. Database search strategy.

Database		Code
PubMed	First search (screening)	((("Myocardial Infarction"[Mesh] OR "ST Elevation Myocardial Infarction"[tiab] OR STEMI[tiab] OR "ST-segment elevation"[tiab] OR "ST elevation"[tiab] OR "acute myocardial infarction"[tiab] OR "acute MI"[tiab]) AND ("Percutaneous Coronary Intervention"[Mesh] OR "Angioplasty, Balloon, Coronary"[Mesh] OR "primary percutaneous coronary intervention"[tiab] OR "primary PCI"[tiab] OR PPCI[tiab] OR "primary angioplasty"[tiab] OR PCI[tiab]) AND (intracoronary[tiab] OR "intra-coronary"[tiab] OR "intracoronary administration"[tiab]) AND (prourokinase[tiab] OR "pro-urokinase"[tiab] OR "pro urokinase"[tiab] OR "recombinant human prourokinase"[tiab] OR rhProUK[tiab] OR rhPro-UK[tiab] OR ("Urokinase-Type Plasminogen Activator"[Mesh] OR urokinase[tiab])) AND (randomized controlled trial[pt] OR controlled clinical trial[pt] OR random*[tiab] OR placebo[tiab] OR trial[tiab]) NOT (animals[mh] NOT humans[mh]))
	Second search (sensible)	((("Myocardial Infarction"[Mesh] OR "ST Elevation Myocardial Infarction"[tiab] OR STEMI[tiab] OR "ST-segment elevation"[tiab] OR "ST elevation"[tiab] OR "acute myocardial infarction"[tiab]) AND ("Percutaneous Coronary Intervention"[Mesh] OR "Angioplasty, Balloon, Coronary"[Mesh] OR "primary percutaneous coronary intervention"[tiab] OR "primary PCI"[tiab] OR PPCI[tiab] OR "primary angioplasty"[tiab] OR PCI[tiab]) AND (prourokinase[tiab] OR "pro-urokinase"[tiab] OR "pro urokinase"[tiab] OR "recombinant human prourokinase"[tiab] OR rhProUK[tiab] OR rhPro-UK[tiab] OR ("Urokinase-Type Plasminogen Activator"[Mesh] OR urokinase[tiab]))) AND (randomized controlled trial[pt] OR controlled clinical trial[pt] OR random*[tiab] OR placebo[tiab] OR trial[tiab]) NOT (animals[mh] NOT humans[mh]))
LILACS	First search (screening)	tw:(prourokinase OR prouroquinasa OR "pro-urokinase" OR "pro-uroquinasa" OR rhProUK OR rhPro-UK OR "recombinant human prourokinase" OR urokinase OR uroquinasa) AND tw:(random* OR ensayo OR "ensayo clínico" OR "ensaio clínico" OR aleator* OR trial OR placebo) AND tw:(infarto OR "myocardial infarction" OR STEMI OR "ST elevation" OR "ST-segment elevation")
	Second search (sensible)	tw:(prourokinase OR prouroquinasa OR "pro-urokinase" OR "pro-uroquinasa" OR rhProUK OR rhPro-UK OR "recombinant human prourokinase")
CENTRAL (Cochrane)	Search manager code	#1 Myocardial Infarction explode all trees; #2 ('STEMI OR "ST elevation" OR "ST-segment elevation" OR "acute myocardial infarction"):ti,ab,kw; #3 Percutaneous Coronary Intervention explode all trees; #4 ("primary PCI" OR PPCI OR "primary percutaneous coronary intervention" OR PCI OR "primary angioplasty"):ti,ab,kw; #5 (intracoronary OR "intra-coronary"):ti,ab,kw; #6 (prourokinase OR "pro-urokinase" OR "recombinant human prourokinase" OR rhProUK OR "rh pro uk" OR urokinase):ti,ab,kw; #7 (#1 OR #2) AND (#3 OR #4) AND #5 AND #6.
Clinicaltrials.gov	General search	Prourokinase AND STEMI
WHO ICTRP	General search	Prourokinase myocardial infarction

Table S2. Search through citation in Google Scholar.

Study	Cited by	Potentially relevant	Could It be included?	Name	Observations
Cao et al. 2022 [1]	8	2	Yes	SH Che, et al. (2024) [2]	Full text not available (the same in databases screen)
			No	Zhao Lili, et al. (2025) [3]	Exclude
Geng et al. 2017 [4]	41	10	Yes	Huang et al. 2021 [5]	Already included
			Yes	Wang et al. 2020 [6]	Already included
			Yes	Cao et al. 2022 [1]	Already included
			Yes	Wu et al 2020 [7]	Already included
			No	Yin et al. 2022 [8]	Meta analysis
			No	Qin et al. 2020 [9]	Exclude
			No	Zhang et al. 2022 [10]	Wrong study design: non-randomized cohort study.
			No	Wang et al. 2021 [11]	Exclude
			No	Ma et al. 2020 [12]	Exclude
			No	Zhao et al. 2021 [13]	Wrong study design: observational multicenter cohort not randomized.
Huang et al. 2021 [5]	30	1	Yes	Cao et al. 2022 [1]	Already included
Jiang et al. 2021 [14]	24	2	Yes	SH Che, et al. (2024) [1]	Full text not available (the same in databases screen)
			No	Yin et al. 2022 [8]	Meta analysis
Wang et al. 2020 [6]	24	2	Yes	Cao et al. 2022 [1]	Already included
			No	Yin et al. 2022 [8]	Meta analysis
Wu et al,2020 [7]	22	3	No	SH Che, et al. (2024) [2]	Full text not available (the same in databases screen)
			No	Yin et al. 2022 [8]	Meta analysis
			No	Wang Jin, et al. (2021) [15]	Wrong study design (non-randomized cohort study).

This table details the manual search conducted via Google Scholar citation tracking to identify additional studies. It presents the screening process based on relevance and provides specific reasons for exclusion, such as study design or lack of full-text availability.

Table S3. Backward citation searching through references.

Study	References	Potentially relevant	Included	Name	Observations
Cao et al. 2022 [1]	33	5	0	Geng et al. 2017 [4]	Already included
				Huang et al. 2021 [5]	Already included
				Wang et al. 2020 [6]	Already included
Geng et al. 2017 [4]	33	0	0	None	-
Huang et al. 2021 [5]	43	1	0	Geng et al. 2017 [4]	Already included
Jiang et al. 2021 [14]	17	0	0	None	-
Wang et al. 2020 [6]	39	2	0	Geng et al. 2017 [4]	Already included
				Zhao et al. 2018 [16]	Wrong intervention
Wu et al,2020 [7]	23	1	0	Geng et al. 2017 [4]	Already included

This table presents the results of backward citation searching by reviewing the reference lists of included studies to identify further evidence. It tracks potentially relevant records and provides specific justifications for those not included, such as duplicate entries or incorrect interventions.

Table S4. Studies excluded after full text screening.

No.	Study	Year	Exclusion reason	Justification
1	ChiCTR1900022666 [17]	2019	Trial registry entry	Registry record only; no published trial results available for eligibility confirmation or data extraction.
2	ChiCTR1800015932 [18]	2018	Trial registry entry	Registry-only record without a full trial report or extractable outcome data.
3	Zhu TQ et al. [19]	2012	Intervention mismatch	Compared tirofiban vs urokinase, not prourokinase vs no intracoronary lytic control.
4	Zhao B et al. [20]	2015	Wrong drug	Evaluated intracoronary urokinase, whereas the protocol prespecified prourokinase.
5	Pelliccia F et al. [21]	2021	Wrong drug	Long-term follow-up of the DISSOLUTION urokinase trial; wrong fibrinolytic agent for this review.
6	Yu S et al. [22]	2024	Comparator mismatch	Both groups received intracoronary pro-urokinase; groups differed only by low-pressure balloon pre-dilatation.
7	Zhu TQ et al. [23]	2013	Intervention mismatch	Compared tirofiban vs urokinase rather than prourokinase vs placebo/saline/standard PCI.
8	ChiCTRINR16009135 [24]	2016	Trial registry entry	Registry entry only; no complete published results for inclusion.
9	ChiCTR2100042906 [25]	2021	Trial registry entry	Registry-only record without a full peer-reviewed trial report.
10	NCT02131220 [26]	2014	Trial registry entry	Trial registration only; no published randomized results available.
11	ChiCTRINR16010007 [27]	2016	Trial registry entry	Registry-only citation; no full study report with usable data.
12	Zhang R et al. [10]	2022	Wrong study design for review question	Did not evaluate adjunct intracoronary prourokinase during primary PCI versus no-lytic control; instead compared a thrombolysis-based strategy with conventional PCI.
13	ChiCTR1900022290 [28]	2019	Trial registry entry	Registration record only; no full published results.
14	ChiCTRIPR17010745 [29]	2017	Trial registry entry	Registry-only study record without a full report for inclusion.
15	ChiCTR2500103336 [30]	2025	Trial registry entry	Registry entry only. The population extended beyond STEMI to broader ACS, but registry-only status was sufficient for exclusion.
16	Fu Y et al. [31]	2019	Intervention mismatch	Experimental arm used pro-urokinase plus anisodamine, a bundled active co-intervention not matched in the control arm.
17	Schieman G et al. [32]	1990	Wrong population	Included acute ischemic syndromes with thrombus complicating angioplasty, not the target STEMI primary PCI population.
18	Sandø A et al. [33]	2020	Intervention mismatch	Biomarker/prognostic study of soluble urokinase receptor; not a trial of intracoronary prourokinase.
19	Zhao L et al. [16]	2017	Wrong study design	Phase IV clinical study not matching the prespecified randomized adjunct intracoronary prourokinase vs no-lytic control during primary PCI design.
20	Han YL et al. [34]	2013	Wrong study design	Evaluated pharmacoinvasive prourokinase therapy for delayed PCI.
21	Kereiakes DJ et al. [35]	1991	Wrong population	Concerned patients after thrombolytic therapy/CABG for acute MI, not adults undergoing primary PCI for STEMI.

This table lists the studies excluded from the meta-analysis after a full-text review, providing the specific reason and justification for each exclusion. Common reasons for removal include trial registry entries without published results, mismatched interventions, or incorrect study designs and populations. PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction; CABG: coronary artery bypass grafting; ACS: acute coronary syndrome; n: number.

Table S5. PRISMA 2020 – MAIN CHECKLIST [36]

Topic	No.	Item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title page.
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	INTRODUCTION.
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	INTRODUCTION.
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Methods - Eligibility criteria
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Methods - Information sources and search strategy
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Methods - Information sources and search strategy
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Methods - Selection process
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Methods - Data collection process
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Methods - Data items and outcomes
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Methods - Data items and outcomes
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Methods - Study risk of bias assessment
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Methods - Data synthesis and statistical analysis

Topic	No.	Item	Location where item is reported
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item 5)).	Methods - Data synthesis and statistical analysis
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Methods - Data synthesis and statistical analysis
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Methods - Data synthesis and statistical analysis
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Methods - Data synthesis and statistical analysis
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Methods - Data synthesis and statistical analysis
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Methods - Data synthesis and statistical analysis
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Methods - Study risk of bias assessment
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Methods - Certainty assessment
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Results - Study selection
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Results - Study selection
Study characteristics	17	Cite each included study and present its characteristics.	Results - Study characteristics
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Results - Risk of bias in studies
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured Tables or plots.	Results - Results of individual studies and synthesis
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Results - Results of individual studies and synthesis
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Results - Results of individual studies and synthesis
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Results - Results of individual studies and synthesis

Topic	No.	Item	Location where item is reported
Reporting biases Certainty of evidence	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Results - Results of individual studies and synthesis
	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Results - Reporting biases
	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Results - Certainty of evidence
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Discussion - General interpretation of findings
	23b	Discuss any limitations of the evidence included in the review.	Discussion - Limitations of the included evidence
	23c	Discuss any limitations of the review processes used.	Discussion - Limitations of the review process
	23d	Discuss implications of the results for practice, policy, and future research.	Discussion - Implications for practice, policy, and research
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Methods - Protocol, registration, and reporting framework
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Methods - Protocol, registration, and reporting framework
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Methods - Protocol, registration, and reporting framework
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Funding
Competing interests	26	Declare any competing interests of review authors.	Conflicts of interest
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Data availability.

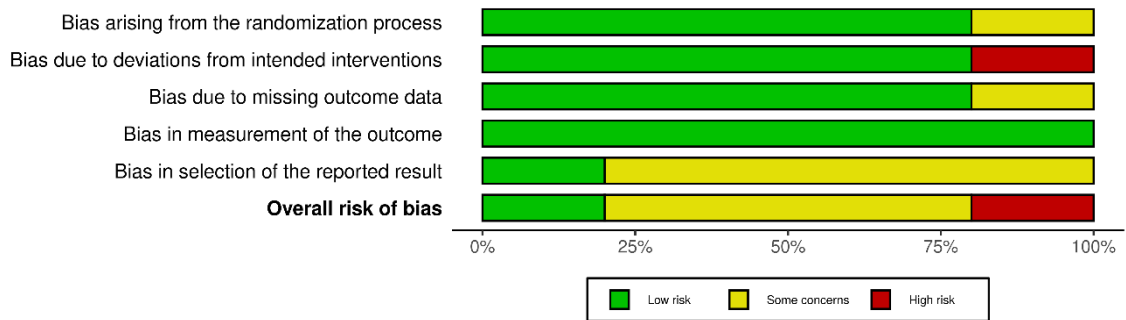
Table S6. PRISMA Abstract Checklist [1]

Topic	No.	Item	Reported?
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesize results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. MetaArXiv. 2020, September 14. DOI: 10.31222/osf.io/v7gm2. For more information, visit: www.prisma-statement.org

Risk of bias in studies (full domain-level assessments)^{37,38}

1) COMPLETE ST-RESOLUTION:



	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Study						
Wu et al., 2020	+	+	+	+	+	+
Wang et al., 2020	+	+	+	+	-	-
Cao et al., 2022	+	+	+	+	-	-
Huang et al., 2021	+	X	-	+	-	X
Geng et al., 2017	-	+	+	+	-	-

Domains:

D1: Bias arising from the randomization process.

D2: Bias due to deviations from intended intervention.

D3: Bias due to missing outcome data.

D4: Bias in measurement of the outcome.

D5: Bias in selection of the reported result.

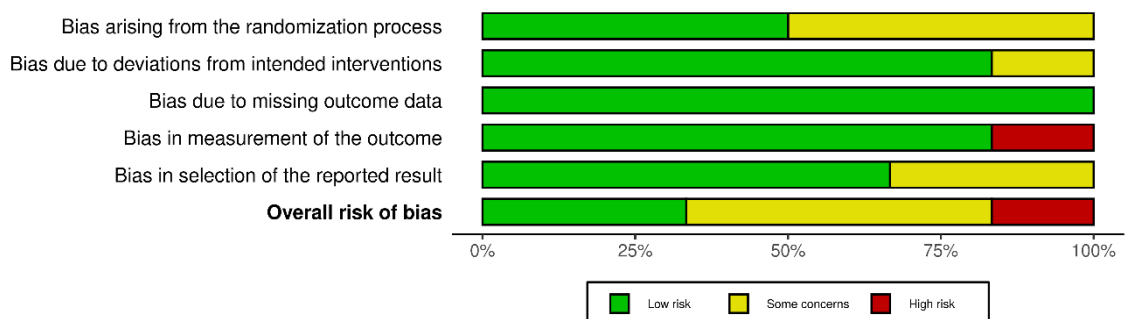
Judgement

X High

- Some concerns

+ Low

2) FINAL TIMI 3 FLOW:



		Risk of bias domains					
		D1	D2	D3	D4	D5	Overall
Study	Wu et al., 2020	+	-	+	+	+	-
	Cao et al., 2022	+	+	+	+	+	+
	Geng et al., 2017	-	+	+	+	+	-
	Huang et al., 2021	+	+	+	+	+	+
	Jiang et al., 2020	-	+	+	X	-	X
	Wang et al., 2020	-	+	+	+	-	-

Domains:

D1: Bias arising from the randomization process.

D2: Bias due to deviations from intended intervention.

D3: Bias due to missing outcome data.

D4: Bias in measurement of the outcome.

D5: Bias in selection of the reported result.

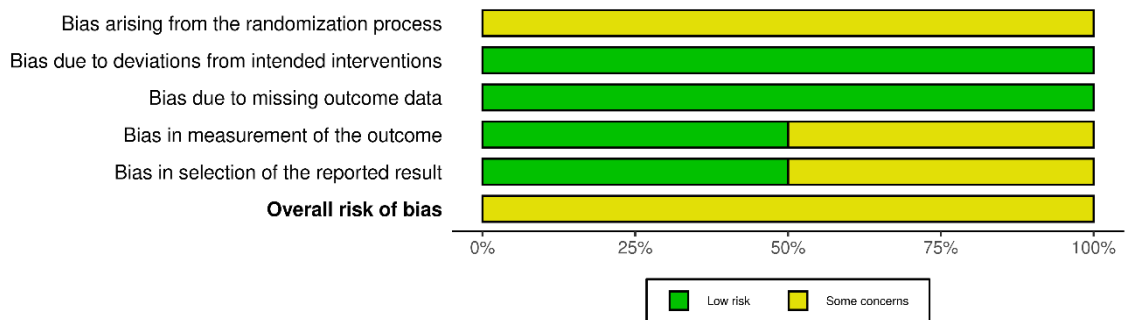
Judgement

X High

- Some concerns

+ Low

3) MAJOR BLEEDING:



		Risk of bias domains					
		D1	D2	D3	D4	D5	Overall
Study	Geng et al., 2017						
	Wang et al., 2020						

Domains:

D1: Bias arising from the randomization process.

D2: Bias due to deviations from intended intervention.

D3: Bias due to missing outcome data.

D4: Bias in measurement of the outcome.

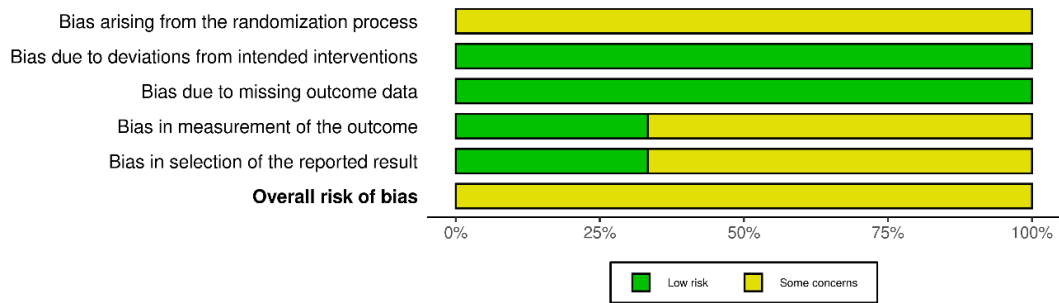
D5: Bias in selection of the reported result.

Judgement

 Some concerns

 Low

4) MACE:

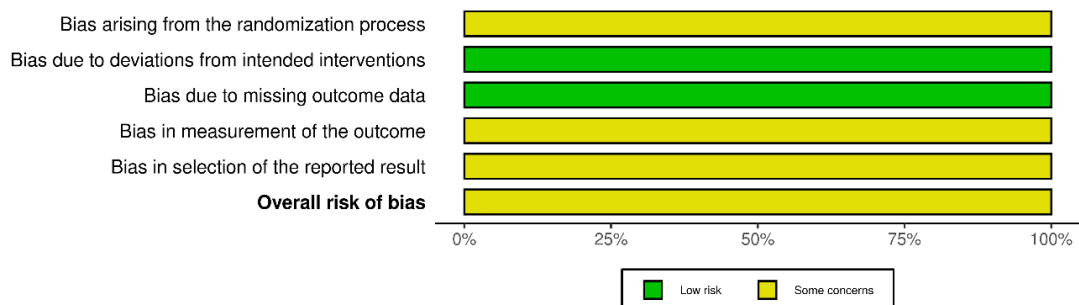


		Risk of bias domains					
		D1	D2	D3	D4	D5	Overall
Study	Geng et al., 2017	-	+	+	-	+	-
	Jiang et al., 2020	-	+	+	-	-	-
	Wang et al., 2020	-	+	+	+	-	-

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
- Some concerns
+ Low

5) LVEF:

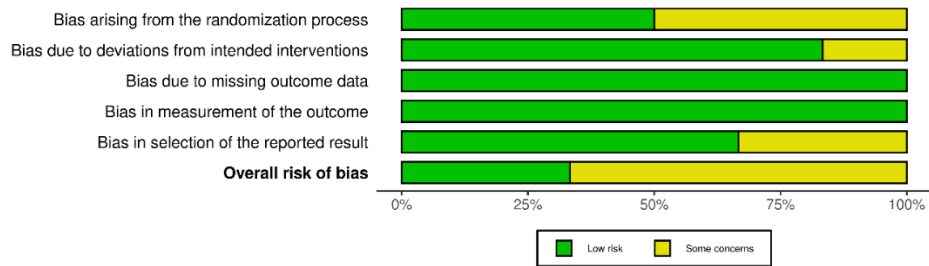


		Risk of bias domains					
		D1	D2	D3	D4	D5	Overall
Study	Jiang et al., 2020	-	+	+	-	-	-
	Wang et al., 2020	-	+	+	-	-	-

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
- Some concerns
+ Low

6) CKMB:

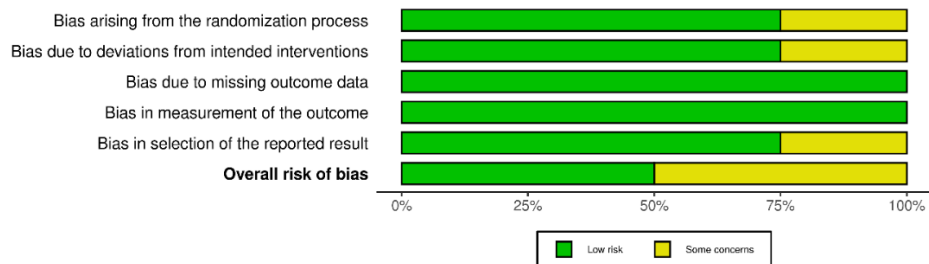


		Risk of bias domains					
		D1	D2	D3	D4	D5	Overall
Study	Wu et al., 2020	+	+	+	+	+	+
	Cao et al., 2022	-	+	+	+	+	-
	Geng et al., 2017	+	+	+	+	+	+
	Huang et al., 2021	-	+	+	+	-	-
	Jiang et al., 2020	-	+	+	+	-	-
	Wang et al., 2020	+	-	+	+	+	-

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
- Some concerns
+ Low

7) cTFC:



		Risk of bias domains					
		D1	D2	D3	D4	D5	Overall
Study	Wu et al., 2020	+	-	+	+	+	-
	Cao et al., 2022	+	+	+	+	+	+
	Huang et al., 2021	+	+	+	+	+	+
	Wang et al., 2020	-	+	+	+	-	-

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
- Some concerns
+ Low

Figure S1. Forest plot of an additional secondary analysis that included an additional trial using a >50% threshold for the outcome complete ST-segment resolution (STR).

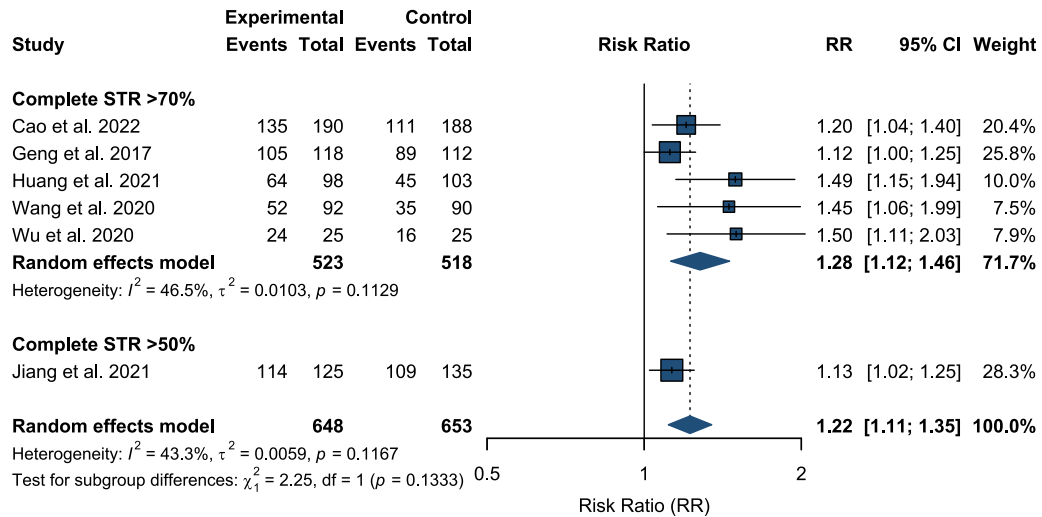


Figure S2. Forest plot of MACE at 30 days comparing intracoronary prourokinase versus control during primary PCI, pooled as risk ratios using a random-effects model.

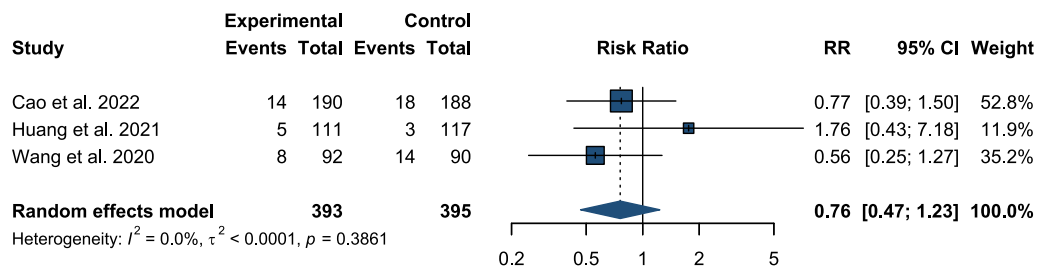


Figure S3. Forest plot of CK-MB peak comparing adjunct intracoronary low-dose prourokinase versus control during primary PCI, pooled as SMD using a random-effects model.

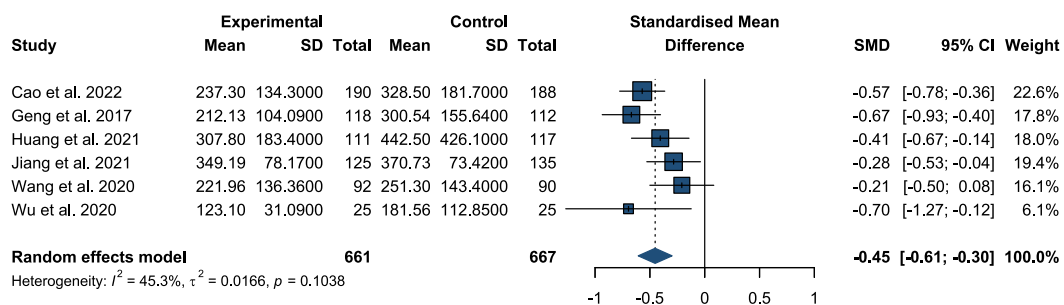


Figure S4. Forest plot of corrected TIMI frame count (cTFC) comparing adjunct intracoronary low-dose prourokinase versus control during primary PCI, pooled as MD using a random-effects model.

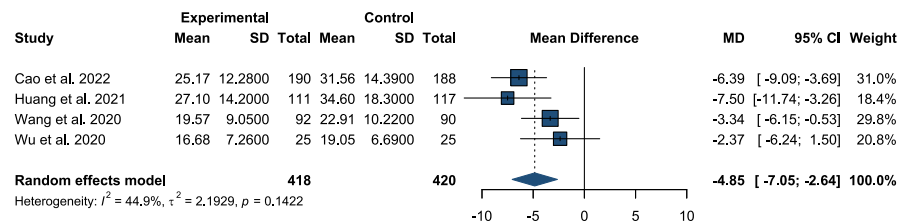
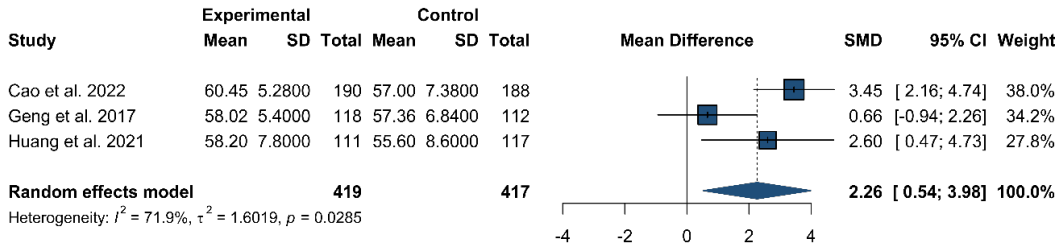
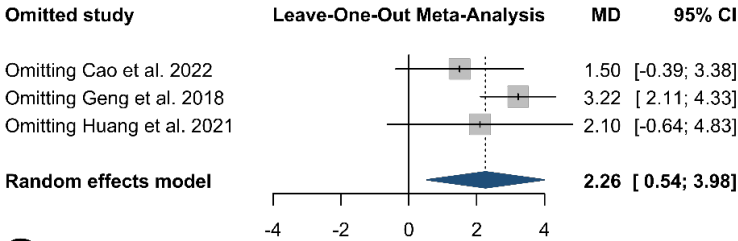


Figure S5. LVEF at 30 days and influence analysis comparing intracoronary prourokinase 4 versus control.

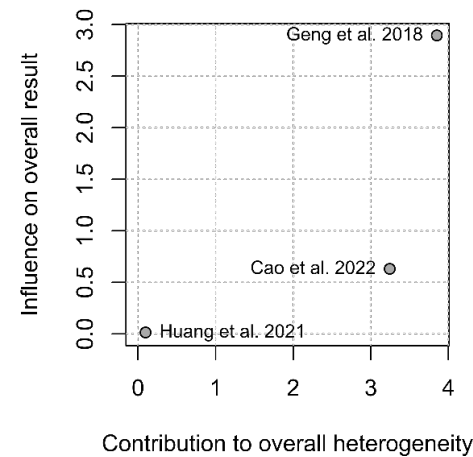
A



B



C



A) Forest plot of LVEF at 30 days pooled as mean differences using a random-effects model. B) Leave-one-out sensitivity analysis for 30-day LVEF. C) Baujat plot showing study contribution to heterogeneity and influence on the overall result.

Figure S6. Forest plot of LVEF at 6 months comparing intracoronary prourokinase versus control, pooled as mean differences (random-effects model).

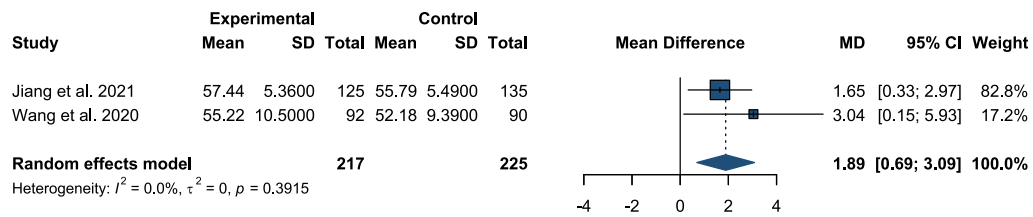
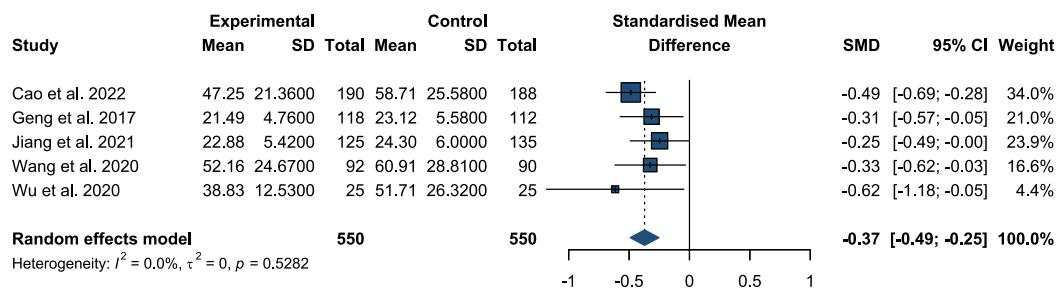


Figure S7. Forest plot of peak troponin levels comparing intracoronary prourokinase versus control, pooled as standardized mean differences (random-effects model).



Summary of findings³⁹

Table S7. GRADE Summary of Findings.

Author(s): Gabriel Andrés Reartes; Juan Eduardo Robledo Almonacid

Question: Intracoronary low-dose prourokinase compared to no intracoronary fibrinolytic (placebo/saline/usual care) in Reartes GA, Robledo Almonacid JE. Adjunct intracoronary low-dose prourokinase during primary PCI for ST-elevation myocardial infarction: systematic review and meta-analysis of randomized trials. PROSPERO (CRD420261284192; 2026).

Setting: Hospital-based acute cardiac care; cardiac catheterization laboratory (primary PCI setting)

Bibliography: Reartes GA, Robledo Almonacid JE. Adjunct intracoronary low-dose prourokinase during primary PCI for ST-elevation myocardial infarction: systematic review and meta-analysis of randomized trials. PROSPERO (CRD420261284192; 2026).

Certainty assessment						N° of patients		Effect		Certainty	Importance
N° of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Intervention	Control	Relative (95% CI)	Absolute (95% CI)		

Complete ST-segment resolution (STR) (follow-up: mean 2 hours; assessed with: Proportion with “complete” STR (≥70% reduction in summed ST-segment elevation), assessed 30–120 min post-PCI)

5	Randomised trials	Serious ^a	Not serious	Serious ^b	Not serious	380/523 (72.7%)	296/518 (57.1%)	RR 1.28 (1.12 to 1.46)	160 more per 1000 (from 69 more to 263 more)	⊕⊕○○ Low ^{a,b}	CRITICAL
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Final TIMI 3 flow (assessed with: Proportion with TIMI grade 3 flow on final angiography (post-PCI))

6	Randomised trials	Serious ^c	Not serious	Serious ^d	Not serious	611/661 (92.4%)	563/667 (84.4%)	RR 1.08 (1.03 to 1.14)	68 more per 1000 (from 25 more to 118 more)	⊕⊕○○ Low ^{c,d}	CRITICAL
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Major Adverse Cardiovascular Events (MACE) at 6 months (follow-up: median 6 months; assessed with: Stent thrombosis, recurrent MI, CHF, angina, cardiac death, etc.)

3	Randomised trials	Serious	Not serious	Not serious	Serious ^e	28/335 (8.4%)	47/337 (13.9%)	RR 0.59 (0.38 to 0.92)	57 fewer per 1000 (from 86 fewer to 11 fewer)	⊕⊕○○ Low ^e	CRITICAL
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Major Bleeding at 6 months (follow-up: median 6 months; assessed with: TIMI)

2	Randomised trials	Serious	Not serious	Not serious	Very serious ^f	5/210 (2.4%)	6/202 (3.0%)	RR 0.84 (0.23 to 3.03)	5 fewer per 1000 (from 23 fewer to 60 more)	⊕○○○ Very low ^f	CRITICAL
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CK-MB peak (assessed with: Peak)

6	Randomised trials	Not serious	Not serious	Serious ^g	Not serious	661	667	-	SMD 0.45 SD lower (0.61 lower to 0.3 lower)	⊕⊕⊕○ Moderate ^g	IMPORTANT
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Left Ventricular Ejection Fraction. (follow-up: median 6 months; assessed with: by echocardiography.)

Certainty assessment						N° of patients		Effect		Certainty	Importance
N° of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Intervention	Control	Relative (95% CI)	Absolute (95% CI)		
2	Randomised trials	S	Not serious	S ^g	S ^h	217	225	-	MD 1.89 SD higher (0.69 higher to 3.09 higher)	⊕○○○ Very low ^{g,h}	CRITICAL

Corrected TIMI Frame Count (assessed with: Frames)

4	Randomised trials	Not serious	Not serious	S ⁱ	Not serious	418	420	-	MD 4.85 MD lower (7.05 lower to 2.64 lower)	⊕⊕⊕○ Moderate ⁱ	IMPORTANT
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CI: confidence interval; MD: mean difference; RR: risk ratio; SMD: standardised mean difference

- One study is High risk overall (Huang 2021) and three are Some concerns overall.¹¹
- STR is a surrogate reperfusion endpoint, not a patient-important outcome.
- One study is High risk overall (Jiang et al. 2020) (Jiang et al. 2021) and three are Some concerns overall.¹⁵
- The 95% CI does not cross 1, and is reasonably narrow (small-to-moderate but consistent effect).
- < 300 events.
- Extremely rare events [4 in experimental vs 6 in control], very wide confidence interval that includes both substantial benefit and harm.
- Surrogate biomarker of infarct size.
- Wide CI including null effect and small sample size for this parameter.
- Surrogate angiographic index.

RStudio scripts

It is an example of the script utilized in Rstudio for the TIMI outcome.

```
library(meta)
datos_rr <- data.frame(estudio = c("Cao et al. 2022", "Geng et al. 2017", "Huang et al. 2021", "Jiang et al. 2021", "Wang et al. 2020", "Wu et al. 2020"),
evento_Prourokinase = c(174,109,101,123,82,22), total_Prourokinase = c(190,118,111,125,92,25),
evento_ctrl = c(155,96,90,130,72,20), total_ctrl = c(188,112,117,135,90,25))
meta_rr <- metabin(event.e = evento_Prourokinase, n.e = total_Prourokinase, event.c = evento_ctrl, n.c = total_ctrl, studlab = estudio, data = datos_rr, sm = "RR", random = TRUE, common = FALSE)
forest(meta_rr, leftcols = c("studlab", "event.e", "n.e", "event.c", "n.c"), leftlabs = c("Study", "Events", "Total", "Events", "Total"), rightcols = c("effect", "ci", "w.random"), rightlabs = c("RR", "95% CI", "Weight"), col.square = "black", col.square.lines = "black", col.diamond = "black", col.diamond.lines = "black", fontsize = 10)
```

Another real example for SMD (CK-MB):

```
library(meta)
datos_smd <- data.frame(estudio = c("Cao et al. 2022", "Geng et al. 2017", "Huang et al. 2021", "Jiang et al. 2021", "Wang et al. 2020", "Wu et al. 2020"), media_exp = c(237.3,212.13,307.8,349.19,221.96,123.10), sd_exp =
```

```
c(134.3,104.09,183.4,78.17,136.36,31.09),n_exp = c(190,118,111,125,92,25), media_ctrl =  
c(328.5,300.54,442.5,370.73,251.30,181.56),sd_ctrl =  
c(181.7,155.64,426.1,73.42,143.40,112.85), n_ctrl = c(188,112,117,135,90,25))  
  
meta_smd <- metacont(n.e = n_exp, mean.e = media_exp, sd.e = sd_exp, n.c = n_ctrl, mean.c =  
media_ctrl, sd.c = sd_ctrl,studlab = estudio,data = datos_smd,sm = "SMD",random =  
TRUE,common = FALSE)  
  
forest(meta_smd,leftcols = c("studlab", "mean.e", "sd.e", "n.e", "mean.c", "sd.c", "n.c"),leftlabs  
= c("Study","Mean","SD","Total","Mean","SD","Total"),rightcols = c("effect", "ci",  
"w.random"),rightlabs = c("SMD", "95% CI", "Weight"),col.square = "#1F4E79",col.square.lines  
= "black",col.diamond = "#1F4E79",col.diamond.lines = "#1F4E79",col.label.left =  
"black",col.label.right = "black",col.inside = "black",fontsize = 10,digits = 2,digits.pval = 3)
```

Another real example for MD (cTFC):

```
library(meta)  
  
datos <- data.frame(estudio = c("Cao et al. 2022", "Huang et al. 2021", "Wang et al. 2020", "Wu  
et al. 2020"),media_exp = c(25.17, 27.10, 19.57, 16.68),sd_exp = c(12.28, 14.2, 9.05,  
7.26),n_exp = c(190, 111, 92, 25),media_ctrl = c(31.56, 34.6, 22.91, 19.05),sd_ctrl = c(14.39,  
18.3, 10.22, 6.69),n_ctrl = c(188, 117, 90, 25))  
  
meta_md <- metacont(n.e = n_exp,mean.e = media_exp,sd.e = sd_exp,n.c = n_ctrl,mean.c =  
media_ctrl,sd.c = sd_ctrl,studlab = estudio,data = datos,sm = "MD",random = TRUE,common =  
FALSE)  
  
forest(meta_md,leftcols = c("studlab", "mean.e", "sd.e", "n.e", "mean.c", "sd.c", "n.c"),leftlabs  
= c("Study","Mean","SD","Total","Mean","SD","Total"),rightcols = c("effect", "ci",  
"w.random"),rightlabs = c("MD", "95% CI", "Weight"),col.square = "#1F4E79",col.square.lines =  
"black",col.diamond = "#1F4E79",col.diamond.lines = "#1F4E79",col.label.left =  
"black",col.label.right = "black",col.inside = "black",fontsize = 10,digits = 2,digits.pval = 3)
```

Excel files containing the extracted raw data used for the meta-analyses

1) Table S8. Study characteristics.

study_id	first_author	year	journal	country	registry_id	publication_type
1	Mingkun Cao [1]	2022	Journal of International Medical Research	China	ChiCTR1900022290	Prospective, randomized controlled trial
2	Wei Geng [4]	2018	Journal of Interventional Cardiology,	China	ChiCTR-INR-16009135	Single-center prospective randomized clinical trial.
3	Dong Huang [5]	2021	Frontiers in Cardiovascular Medicine,	China	NCT02131220	Multi-center, prospective, randomized, placebo-controlled, single-blind trial
4	Wenlong Jiang [14]	2021	Coronary Artery Disease,	China	SZXJ2018009-20170202	Single-center prospective randomized clinical trial
5	Xuechao Wang [11]	2020	Coronary Artery Disease,	China	Non reported	Randomized study involving consecutive patients
6	Yanqiang Wu [7]	2020	BMC Cardiovascular Disorders	China	ChiCTR1800016207	Randomized, controlled study

study_id	first_author	year	design
1	Mingkun Cao [1]	2022	This study is a prospective, randomized controlled trial. It employed simple randomized group allocation using computer-generated sequences and was conducted at a single hospital.
2	Wei Geng [4]	2018	The design is a single-center, prospective, randomized clinical trial. Patients were randomized into two groups using a computer-generated random-allocation system.
3	Dong Huang [5]	2021	This research is a multi-center, prospective, randomized, placebo-controlled, single-blind trial. Randomization was stratified by clinical center using central randomization and opaque sealed envelopes.
4	Wenlong Jiang [14]	2021	This is a single-center, prospective, randomized clinical trial. Participants were assigned to groups using a computer-generated random-allocation system.
5	Xuechao Wang [11]	2020	The study is a randomized controlled trial involving consecutive patients. Patients were randomized to either the study or control group by means of sealed envelopes.
6	Yanqiang Wu [7]	2020	This research is a randomized, controlled study. Consecutive patients were assigned to groups using a block randomization method with sequences created by statistical software.

study_id	first_author	year	analysis_type_reported
1	Mingkun Cao [1]	2022	Continuous data were analyzed using the independent samples t-test, while categorical data were compared via the chi-square test or Fisher's exact test. The Mann-Whitney U test was applied for ranked data, and all analyses were conducted using SPSS v.24.0.
2	Wei Geng [4]	2018	Statistical comparisons involved the Student's t-test for normally distributed values and the Mann-Whitney U test for non-normally distributed data. Categorical variables were assessed using the chi-square test or Fisher's exact test.
3	Dong Huang [5]	2021	This study explicitly performed an intention-to-treat (ITT) analysis. Methods included the Kolmogorov-Smirnov test for normality, one-way ANOVA or Kruskal-Wallis Test for three-group comparisons, and Student's t-test or Mann-Whitney U-test for pairwise comparisons.
4	Wenlong Jiang [14]	2021	Statistical analysis utilized the Student's t-test for normally distributed continuous variables and the Mann-Whitney U test for non-normally distributed data. Categorical variables were compared using the chi-square test or Fisher's exact test.

5	Xuechao Wang [11]	2020	Analysis included the two-tailed Student's t-test or Mann-Whitney U test for group means and the χ^2 or Fisher exact test for proportions. Additionally, Kaplan-Meier analysis was used for MACE-free survival and multivariate logistic regression to identify independent predictors of complete STR.	
6	Yanqiang Wu [7]	2020	Comparisons between groups were determined by the Student's t-test (normal distribution) or Mann-Whitney U test (non-normal distribution). Categorical values were analyzed using the Chi-squared test or Fisher's exact test.	

study_id	first_author	year	n_randomized_total	n_analyzed_primary_outcome	setting	enrollment_years
1	Mingkun Cao [1]	2022	390	378	Single hospital (Inner Mongolia People's Hospital, China).	July 2015 to June 2018.
2	Wei Geng [4]	2018	230	230	Single center (Baoding First Central Hospital, China).	January 2015 to May 2016.
3	Dong Huang [5]	2021	345	345	Multi-center (11 hospitals in China).	November 2015 to July 2017.
4	Wenlong Jiang [14]	2021	260	260	Single-center (Shenzhen Yantian People's Hospital, China).	July 2017 to December 2019.
5	Xuechao Wang [11]	2020	182	182	Single center (Hebei General Hospital, China).	January 2017 to March 2018.
6	Yanqiang Wu [7]	2020	50	50	Single Hospital (The Second Hospital of Hebei Medical University, China).	June 2017 to December 2017.

study_id	first_author	year	funding	conflicts_reported
1	Mingkun Cao [1]	2022	None ("received no specific grant").	Yes (No conflict of interest declared).
2	Wei Geng [4]	2018	Public/Government (Baoding Science and Technology Research Program).	Yes (No conflicts of interest reported).
3	Dong Huang [5]	2021	Public/Government (National Key Research and Development Program of China).	Yes (No commercial or financial relationships declared).
4	Wenlong Jiang [14]	2021	Public/Government (Shenzhen City Health Commission and District Bureau).	Yes (No conflicts of interest).
5	Xuechao Wang [11]	2020	NR (Not explicitly reported in the provided source excerpts).	Yes (No conflicts of interest).
6	Yanqiang Wu [7]	2020	None.	Yes (No competing interests declared).

study_id	first_author	year	stemi_definition
1	Mingkun Cao [1]	2022	"Electrocardiography (ECG) showing ST-segment elevation on two or more adjacent leads".
2	Wei Geng [4]	2018	"Patients... presented with ST segment elevation myocardial infarction (STEMI)".
3	Dong Huang [5]	2021	"Prolonged chest pain, persistent ST-segment elevation, and a clinical diagnosis of acute STEMI".
4	Wenlong Jiang [14]	2021	"Patients... presented with STEMI within 12 hours of symptom onset".
5	Xuechao Wang [11]	2020	"Typical ischemic chest pain lasted more than 30 min... ECG with new ST-segment elevation in two or more contiguous leads of ≥ 0.2 mV in precordial leads or ≥ 0.1 mV in extremity leads".
6	Yanqiang Wu [7]	2020	"Persistent chest pain more than 30min, and ST-segment elevation with the cut-off J points ≥ 1 mm in standard leads or ≥ 2 mm in contiguous precordial leads".

study_id	first_author	year	time_from_symptoms_limit_hours	high_thrombus_burden_enriched
1	Mingkun Cao [1]	2022	12 hours.	Yes (Required modified TIMI thrombus grades 4 or 5).
2	Wei Geng [4]	2018	12 hours.	No (Enrolled consecutive patients).
3	Dong Huang [5]	2021	12 hours.	No (Selected for TIMI flow 0–2, though 80% had high-grade thrombus).
4	Wenlong Jiang [14]	2021	12 hours.	No (Enrolled consecutive patients).
5	Xuechao Wang [11]	2020	12 hours.	Yes (Required modified TIMI thrombus grades 3–5).
6	Yanqiang Wu [7]	2020	6 hours.	No (Consecutive patients, but those with "no obvious thrombus burden" were excluded).

study_id	first_author	year	key_exclusions	infarct_location_included
1	Mingkun Cao [1]	2022	Urgent CABG, cardiogenic shock, liver or renal failure, pregnancy.	All (LAD, LCX, and RCA included).
2	Wei Geng [4]	2018	History of ICH, stroke within 3 months, aortic dissection, severe hypertension, major surgery.	All (LAD, LCX, RCA, and LM included).
3	Dong Huang [5]	2021	Rescue PCI, cardiogenic shock, stroke within 6 months, major surgery, liver/kidney failure.	All (Anterior, inferior, and other locations included).
4	Wenlong Jiang [14]	2021	ICH history, stroke within 3 months, aortic dissection, active hemorrhage, severe hypertension.	All (LAD, LCX, RCA, and LM included).
5	Xuechao Wang [11]	2020	Rescue PCI, urgent CABG, liver/renal failure, active bleeding, IRA diameter <2.25 mm.	Restricted (Excluded Left Main or saphenous vein graft lesions).
6	Yanqiang Wu [7]	2020	Cardiac shock, aortic dissection, ICH, stroke within 3 months, trauma/surgery within 4 weeks.	Restricted (Excluded Left Main disease with stenosis >50%).

2) Table S9. Study arms:

study_id	arm_id	arm_label	prourokinase_recombinant	dose_total	dose_unit	dose_per_bolus
Mingkun Cao [1]	A	Pro-UK group (10mg intracoronary)	Unclear ("natural fibrin-specific plasminogen activator")	10	mg	10
Mingkun Cao [1]	B	Control group (0.9% sodium chloride)	NA (Control arm)	0	NA	0
Wei Geng [4]	A	Intracoronary prourokinase (IP) group (10mg)	Yes,	10	mg	10
Wei Geng [4]	B	Control group (Saline)	NA (Control arm),	0	NA	0
Dong Huang [5]	A	Pro-UK group (20mg intracoronary)	Yes,	20	mg	20
Dong Huang [5]	B	Tirofiban group (10 µg/kg intracoronary)	NA (For active comparision),	10	µg/kg	10
Dong Huang [5]	C	Saline group (Control, 20mL)	NA (Control arm),	0	NA	0
Wenlong Jiang [14]	A	Intracoronary prourokinase (IP) group (10 mg)	Yes,	10	mg	10
Wenlong Jiang [14]	B	Control group (Saline)	NA (Control arm)	0	NA	0
Xuechao Wang [11]	A	Study group (Intracoronary prourokinase 20 mg)	Unclear	20	mg	20
Xuechao Wang [11]	B	Control group (Intracoronary 0.9% sodium chloride)	NA (Control arm),	0	NA	0
Yanqiang Wu [7]	A	Intracoronary prourokinase group (10 mg)	Unclear ("natural fibrin-specific plasminogen activator")	10	mg	10
Yanqiang Wu [7]	B	Control group (Saline)	NA	0	NA	0

study_id	arm_id	number_of_boluses	delivery_route	delivery_device	timing_relative_to_pci	infusion_duration
Mingkun Cao [1]	A	1	intracoronary	Thrombus aspiration catheter	After thrombus aspiration, before PCI	NR (Control: 5 min)
Mingkun Cao [1]	B	NA	intracoronary	Thrombus aspiration catheter	After thrombus aspiration, before PCI	5 min
Wei Geng [4]	A	1	intracoronary	Balloon catheter (punctured),	After balloon dilatation, before stent,	3 min
Wei Geng [4]	B	NA	intracoronary	Balloon catheter (punctured)	After balloon dilatation, before stent	3 min
Dong Huang [5]	A	1	intracoronary	Selective intracoronary catheter	After reperfusion (aspiration or balloon), before stent	3 min
Dong Huang [5]	B	1	intracoronary	Selective intracoronary catheter	After reperfusion (aspiration or balloon), before stent	3 min
Dong Huang [5]	C	NA	intracoronary	Selective intracoronary catheter	After reperfusion (aspiration or balloon), before stent	3 min
Wenlong Jiang [14]	A	1	intracoronary	Balloon catheter (punctured)	After balloon dilatation, before stent	3 min
Wenlong Jiang [14]	B	NA	intracoronary	Balloon catheter (punctured)	After balloon dilatation, before stent	3 min
Xuechao Wang [11]	A	1	intracoronary	Thrombus aspiration catheter	Immediately after thrombus aspiration	3 min

Xuechao Wang [11]	B	NA	intracoronary	Thrombus aspiration catheter	Immediately after thrombus aspiration	3 min
Yanqiang Wu [7]	A	1	intracoronary	Thrombus aspiration catheter	After thrombus aspiration, before stent	Slowly (NR numeric)
Yanqiang Wu [7]	B	NA	intracoronary	Thrombus aspiration catheter	After thrombus aspiration, before stent	Slowly (NR numeric)

study_id	arm_id	target_vessel_delivery	placebo_saline_given	heparin_type	heparin_dose	p2y12_inhibitor
Mingkun Cao [1]	A	Yes	Yes	NR	Standard care (NR)	Clopidogrel or Ticagrelor
Mingkun Cao [1]	B	Yes	Yes	NR	Standard care (NR)	Clopidogrel or Ticagrelor
Wei Geng [4]	A	Yes	Yes	UFH	3000 U + 70 U/kg	Ticagrelor
Wei Geng [4]	B	Yes	Yes	UFH	3000 U + 70 U/kg	Ticagrelor
Dong Huang [5]	A	Yes	Yes	UFH	70–100 U/kg	Ticagrelor or Clopidogrel
Dong Huang [5]	B	Yes	Yes	UFH	70–100 U/kg	Ticagrelor or Clopidogrel
Dong Huang [5]	C	Yes	Yes	UFH	70–100 U/kg	Ticagrelor or Clopidogrel
Wenlong Jiang [14]	A	Yes	Yes	UFH	3000 U + 100 U/kg	Ticagrelor
Wenlong Jiang [14]	B	Yes	Yes	UFH	3000 U + 100 U/kg	Ticagrelor
Xuechao Wang [11]	A	Yes	Yes	UFH	3000 U + ACT guided	Ticagrelor
Xuechao Wang [11]	B	Yes	Yes	UFH	3000 U + ACT guided	Ticagrelor
Yanqiang Wu [7]	A	Yes	Yes	UFH	5000 U (or weight-based) + ACT guided	Ticagrelor
Yanqiang Wu [7]	B	Yes	Yes	UFH	5000 U (or weight-based) + ACT guided	Ticagrelor

study_id	arm_id	p2y12_loading_dose	gpiib/iii_a_use	aspiration_thrombectomy	other_intracoronary_drugs
Mingkun Cao [1]	A	300 mg (Clopidogrel) / 180 mg (Ticagrelor)	Not used	yes (Protocol-mandated)	Nitroglycerin or Sodium Nitroprusside
Mingkun Cao [1]	B	300 mg (Clopidogrel) / 180 mg (Ticagrelor)	Not used	yes (Protocol-mandated)	Nitroglycerin or Sodium Nitroprusside
Wei Geng [4]	A	180 mg	bailout	no	None
Wei Geng [4]	B	180 mg	bailout	no	None
Dong Huang [5]	A	180 mg (Ticagrelor) / 600 mg (Clopidogrel)	not used	bailout (Used in ~52%)	None
Dong Huang [5]	B	180 mg (Ticagrelor) / 600 mg (Clopidogrel)	protocol-mandated (Tirofiban arm)	bailout (Used in ~50%)	None
Dong Huang [5]	C	180 mg (Ticagrelor) / 600 mg (Clopidogrel)	not used	bailout (Used in ~50%)	None
Wenlong Jiang [14]	A	180 mg	bailout	bailout (Used in ~8%)	None

Wenlong Jiang [14]	B	180 mg	bailout	bailout (Used in ~6%)	None
Xuechao Wang [11]	A	180 mg	bailout (Used in ~18%)	yes (Protocol-mandated)	None
Xuechao Wang [11]	B	180 mg	bailout (Used in ~13%)	yes (Protocol-mandated)	None
Yanqiang Wu [7]	A	180 mg	bailout (Used in 72%)	yes (Protocol-mandated)	None
Yanqiang Wu [7]	B	180 mg	bailout (Used in 56%)	yes (Protocol-mandated)	None

3) Table S10. Baseline data.

study_id	arm_id	n_baseline	age_mean	age_sd	age_median	age_iqr	female_n	diabetes_n	hypertension_n	smoker_n
Mingkun Cao [1]	A	190	58.17	10.39	NR	NR	42	40	101	112
Mingkun Cao [1]	B	188	59.12	9.99	NR	NR	44	37	95	105
Wei Geng [4]	A	118	53.52	11.41	NR	NR	41	26	84	50
Wei Geng [4]	B	112	55.17	10.39	NR	NR	42	22	69	58
Dong Huang [5]	A	111	59.4	10.1	NR	NR	11	21	52	67
Dong Huang [5]	B	117	60.6	9.7	NR	NR	16	27	62	65
Dong Huang [5]	C	117	58.5	9.9	NR	NR	12	21	58	75
Wenlong Jiang [14]	A	125	53.87	6.61	NR	NR	48	32	62	69
Wenlong Jiang [14]	B	135	55.08	6.77	NR	NR	47	35	69	77
Xuechao Wang [11]	A	92	61.12	11.25	NR	NR	16	20	54	51
Xuechao Wang [11]	B	90	58.81	10.98	NR	NR	17	22	46	55
Yanqiang Wu [7]	A	25	59.48	14.36	NR	NR	4	8	17	12
Yanqiang Wu [7]	B	25	60.96	12.56	NR	NR	3	6	19	13

study_id	arm_id	prior_mi_n	killip_class_reported	killip_ge_2_n	symptom_to_balloon_time	symptom_to_balloon_unit	initial_timi_flow_reported
Mingkun Cao [1]	A	28	Distribution (I, II, III, IV)	59	4.15	hours	Distribution (0, 1, 2)
Mingkun Cao [1]	B	25	Distribution (I, II, III, IV)	55	4.12	hours	Distribution (0, 1, 2)
Wei Geng [4]	A	No reportado	Distribution (I, II, III, IV)	40	4.06	hours	NR (Only Post-PCI reported)
Wei Geng [4]	B	No reportado	Distribution (I, II, III, IV)	38	4.15	hours	NR (Only Post-PCI reported)

Dong Huang [5]	A	5	NR	NR	3.9	hours	Distribution (0, 1, 2)
Dong Huang [5]	B	1	NR	NR	4.0	hours	Distribution (0, 1, 2)
Dong Huang [5]	C	5	NR	NR	4.3	hours	Distribution (0, 1, 2)
Wenlong Jiang [14]	A	No reportado	Distribution (I, II, III, IV)	60	5.10	hours	NR (Only Post-PCI reported)
Wenlong Jiang [14]	B	No reportado	Distribution (I, II, III, IV)	61	4.78	hours	NR (Only Post-PCI reported)
Xuechao Wang [11] [11]	A	8	Distribution (1, 2, 3, 4)	22	203.58	minutes	NR
Xuechao Wang [11] [11]	B	5	Distribution (1, 2, 3, 4)	18	193.80	minutes	NR
Yanqiang Wu [7]	A	No reportado	Distribution (I, II, III)	15	NR	NR	NR (Thrombus grade reported)
Yanqiang Wu [7]	B	No reportado	Distribution (I, II, III)	11	NR	NR	NR (Thrombus grade reported)

study_id	arm_id	initial_timi_0_1_n	thrombus_grade_definition	thrombus_grade_high_n	notes
Mingkun Cao [1]	A	173	Modified TIMI thrombus grade (High = 4–5)	190	All patients had high thrombus burden by inclusion criteria.
Mingkun Cao [1]	B	173	Modified TIMI thrombus grade (High = 4–5)	188	
Wei Geng [4]	A	NR	NR	NR	Time reported as "symptom onset to balloon dilatation".
Wei Geng [4]	B	NR	NR	NR	
Dong Huang [5]	A	103	TIMI thrombus grade (High = 4–5)	102	Thrombus graded after wire crossing,. Time defined as "Reperfusion time" (chest pain to wire crossing).
Dong Huang [5]	B	104	TIMI thrombus grade (High = 4–5)	102	,
Dong Huang [5]	C	111	TIMI thrombus grade (High = 4–5)	110	,
Wenlong Jiang [14]	A	NR	NR	NR	
Wenlong Jiang [14]	B	NR	NR	NR	
Xuechao Wang [11] [11]	A	NR	Modified TIMI thrombus grade (High = 3–5)	92	Study specifically enrolled high thrombus burden (grades 3–5),.
Xuechao Wang [11] [11]	B	NR	Modified TIMI thrombus grade (High = 3–5)	90	
Yanqiang Wu [7]	A	NR	TIMI thrombus grade (1–5)	21	High count calculated as sum of grades 4 and 5 from Table 2.
Yanqiang Wu [7]	B	NR	TIMI thrombus grade (1–5)	21	High count calculated as sum of grades 4 and 5 from Table 2.

4) Table S11. Dichotomous outcomes.

study_id	outcome_name	outcome_definition_in_study	Timepoint_value	Timepoint_unit	window_category	armA_id	n_armA	armA_events	armA_total
Mingkun Cao [1]	MACE	Cardiac death, non-fatal MI, urgent TVR	30	days	30d	A	190	14	B
Wei Geng [4]	MACE	Stent thrombosis, recurrent MI, CHF, angina, cardiac death	30	days	30d	A	118	3	B
Wei Geng [4]	MACE	Stent thrombosis, recurrent MI, CHF, angina, cardiac death	6	months	6m	A	118	10	B
Dong Huang [5]	MACE	Cardiac mortality, non-fatal myocardial reinfarction, TVR	30	days	30d	A	111	5	C
Wenlong Jiang [14]	MACE	Stent thrombosis, recurrent MI, CHF, angina, cardiac death	24	weeks	6m	A	125	8	B
Xuechao Wang [11] [11]	MACE	Cardiac mortality, reinfarction, TVR	30	days	30d	A	92	8	B
Xuechao Wang [11] [11]	MACE	Cardiac mortality, reinfarction, TVR	6	months	6m	A	92	10	B
Yanqiang Wu [7]	MACE	Cardiac death, HF, malignant arrhythmia, new MI, TVR	3	months	3m	A	25	3	B
Mingkun Cao [1]	Major_bleeding	Major hemorrhage (Table 4)	30	days	30d	A	190	5	B
Wei Geng [4]	Major_bleeding	TIMI Major bleeding	6	months	6m	A	118	1	B
Dong Huang [5]	Major_bleeding	TIMI Major bleeding	30	days	30d	A	111	2	C
Xuechao Wang [11] [11]	Major_bleeding	TIMI Major bleeding	6	months	6m	A	92	4	B
Yanqiang Wu [7]	Major_bleeding	Intracranial hemorrhage, Hematemesis, Hematuria (Table 5)	3	months	3m	A	25	0	B
Mingkun Cao [1]	STR_complete	ST-segment resolution $\geq 70\%$	2	hours	Post-PCI (Immediate)	A	190	135	B
Wei Geng [4]	STR_complete	ST-segment resolution $> 70\%$	1	hours	Post-PCI (Immediate)	A	118	105	B
Dong Huang [5]	STR_complete	Complete ST-segment resolution ($\geq 70\%$)	2	hours	Post-PCI (Immediate)	A	98	64	C
Wenlong Jiang [14]	STR_complete	ST-segment resolution $> 50\%$	2	hours	Post-PCI (Immediate)	A	125	114	B
Xuechao Wang [11] [11]	STR_complete	Complete ST-segment resolution $\geq 70\%$	90	min	Post-PCI (Immediate)	A	92	52	B
Yanqiang Wu [7]	STR_complete	Complete ST-segment resolution ($\geq 70\%$)	60	min	Post-PCI (Immediate)	A	25	24	B
Mingkun Cao [1]	TIMI3_final	TIMI flow grade 3 post-PCI	0	hours	Post-PCI (Immediate)	A	190	174	B

Wei Geng [4]	TIMI3_final	Post PCI TIMI grade 3	0	hours	Post-PCI (Immediate)	A	118	109	B
Dong Huang [5]	TIMI3_final	TIMI flow grade 3 after PCI	0	hours	Post-PCI (Immediate)	A	111	101	C
Wenlong Jiang [14]	TIMI3_final	Post-PCI TIMI grade 3	0	hours	Post-PCI (Immediate)	A	125	123	B
Xuechao Wang [11] [11]	TIMI3_final	TIMI flow grade 3	0	hours	Post-PCI (Immediate)	A	92	82	B
Yanqiang Wu [7]	TIMI3_final	TIMI grade 3	0	hours	Post-PCI (Immediate)	A	25	22	B

study_id	outcome_name	armB_id	armB_events	armB_total	analysis_population	source_locator	notes
Mingkun Cao [1]	MACE	188	18	188	Per-protocol / Completers	Table 4	
Wei Geng [4]	MACE	112	2	112	Randomized / Completers	Table 5	
Wei Geng [4]	MACE	112	14	112	Randomized / Completers	Table 5	
Dong Huang [5]	MACE	117	3	117	ITT	Table 3	
Wenlong Jiang [14]	MACE	135	13	135	Randomized / Completers	Table 5	Follow-up at 24 weeks.
Xuechao Wang [11] [11]	MACE	90	14	90	Randomized (post-exclusion)	Table 3	
Xuechao Wang [11] [11]	MACE	90	20	90	Randomized (post-exclusion)	Table 3	
Yanqiang Wu [7]	MACE	25	7	25	Randomized	Table 6	Follow-up is 3 months.
Mingkun Cao [1]	Major_bleeding	188	3	188	Per-protocol / Completers	Table 4	Defined as "Major hemorrhage".
Wei Geng [4]	Major_bleeding	112	3	112	Randomized / Completers	Table 5	Defined as "TIMI major".
Dong Huang [5]	Major_bleeding	117	0	117	ITT	Table 4	Defined as "TIMI major".
Xuechao Wang [11] [11]	Major_bleeding	90	3	90	Randomized (post-exclusion)	Table 3	Defined as "Major bleeding".
Yanqiang Wu [7]	Major_bleeding	25	0	25	Randomized	Table 5	"Intracranial hemorrhage" and other major categories are 0.
Mingkun Cao [1]	STR_complete	188	111	188	Per-protocol / Completers	Table 2	Analysis based on 190/188 patients who completed 30-day follow-up (Fig 1).
Wei Geng [4]	STR_complete	112	89	112	Randomized / Completers	Table 2	"230 enrolled... completed this study".
Dong Huang [5]	STR_complete	103	45	103	Available Case / ITT	Table 3, Fig 1	ECG data available for fewer patients than randomized (98 vs 111 in A; 103 vs 117 in C).
Wenlong Jiang [14]	STR_complete	135	109	135	Randomized / Completers	Table 3	Defined as >50% resolution (lower threshold than others).
Xuechao Wang [11] [11]	STR_complete	90	35	90	Randomized (post-exclusion)	Table 2	Figure 1 shows exclusions after initial assessment, leaving 92/90 for analysis.

Yanqiang Wu [7]	STR_complete	25	16	25	Randomized	Table 3
Mingkun Cao [1]	TIMI3_final	188	155	188	Per-protocol / Completers	Table 2
Wei Geng [4]	TIMI3_final	112	96	112	Randomized / Completers	Table 1
Dong Huang [5]	TIMI3_final	117	90	117	ITT	Table 3
Wenlong Jiang [14]	TIMI3_final	135	130	135	Randomized / Completers	Table 2
Xuechao Wang [11] [11]	TIMI3_final	90	72	90	Randomized (post-exclusion)	Table 2
Yanqiang Wu [7]	TIMI3_final	25	20	25	Randomized	Table 3

5) Table S12. Continuous outcomes.

study_id	outcome_name	outcome_units	outcome_definition_in_study	timepoint_value	timepoint_unit	window_category
Mingkun Cao [1]	CKMB_peak	U/L	Peak CK-MB concentration	0	hours	In-hospital (Peak)
Wei Geng [4]	CKMB_peak	U/L	CK-MB peak value	0	hours	In-hospital (Peak)
Dong Huang [5]	CKMB_peak	U/L	Peak CK-MB level	0	hours	In-hospital (Peak)
Wenlong Jiang [14]	CKMB_peak	U/L	CK-MB peak value	0	hours	In-hospital (Peak)
Xuechao Wang [11] [11]	CKMB_peak	U/mL	Peak CK-MB	0	hours	In-hospital (Peak)
Yanqiang Wu [7]	CKMB_peak	U/L	CK-MB peak value	0	hours	In-hospital (Peak)
Mingkun Cao [1]	cTFC	frames	Corrected TIMI frame count	0	hours	Post-PCI (Immediate)
Dong Huang [5]	cTFC	frames	Corrected TIMI frame count	0	hours	Post-PCI (Immediate)
Xuechao Wang [11] [11]	cTFC	frames	Corrected TIMI frame count	0	hours	Post-PCI (Immediate)
Yanqiang Wu [7]	cTFC	frames	Corrected TIMI frame count	0	hours	Post-PCI (Immediate)
Yanqiang Wu [7]	IMR	U	Index of microcirculatory resistance	0	hours	Post-PCI (Immediate)
Mingkun Cao [1]	LVEF	%	LVEF by echocardiography	30	days	30d
Wei Geng [4]	LVEF	%	LVEF by echocardiography	1	months	30d
Dong Huang [5]	LVEF	%	Echocardiographic LVEF	30	days	30d
Wenlong Jiang [14]	LVEF	%	LVEF by echocardiography	24	weeks	6m
Xuechao Wang [11] [11]	LVEF	%	LVEF by echocardiography	6	months	6m
Yanqiang Wu [7]	LVEF	%	LVEF by echocardiography	3	months	3m
Wei Geng [4]	MBF_MCE	mL/min/g	Myocardial blood flow by MCE	7	days	7d

Mingkun Cao [1]	NT-proBNP	ng/L	N-terminal-proBNP	30	days	30d
Mingkun Cao [1]	Troponin_peak	ng/mL	Peak Troponin I (TnI)	0	hours	In-hospital (Peak)
Wei Geng [4]	Troponin_peak	ng/L	TnI peak value	0	hours	In-hospital (Peak)
Wenlong Jiang [14]	Troponin_peak	ng/L	TnI peak value	0	hours	In-hospital (Peak)
Xuechao Wang [11] [11]	Troponin_peak	ng/mL	Peak TnI	0	hours	In-hospital (Peak)
Yanqiang Wu [7]	Troponin_peak	ng/L	cTnI peak value	0	hours	In-hospital (Peak)

study_id	outcome_name	armA_mean	armA_sd	armA_n	armB_mean	armB_sd	armB_n	data_type	conversion_method
Mingkun Cao [1]	CKMB_peak	237.3	134.3	190	328.5	181.7	188	Mean/SD	Reported as "Peak CK-MB".
Wei Geng [4]	CKMB_peak	212.13	104.09	118	300.54	155.64	112	Mean/SD	
Dong Huang [5]	CKMB_peak	307.8	183.4	111	442.5	426.1	117	Mean/SD	
Wenlong Jiang [14]	CKMB_peak	349.19	78.17	125	370.73	73.42	135	Mean/SD	
Xuechao Wang [11] [11]	CKMB_peak	221.96	136.36	92	251.30	143.40	90	Mean/SD	Unit reported as U/mL in source (likely U/L).
Yanqiang Wu [7]	CKMB_peak	123.10	31.09	25	181.56	112.85	25	Mean/SD	
Mingkun Cao [1]	cTFC	25.17	12.28	190	31.56	14.39	188	Mean/SD	Primary endpoint.
Dong Huang [5]	cTFC	27.1	14.2	111	34.6	18.3	117	Mean/SD	Arm A (Pro-UK) vs Arm C (Saline).
Xuechao Wang [11] [11]	cTFC	19.57	9.05	92	22.91	10.22	90	Mean/SD	
Yanqiang Wu [7]	cTFC	16.68	7.26	25	19.05	6.69	25	Mean/SD	
Yanqiang Wu [7]	IMR	34.56	7.48	25	49.00	8.98	25	Mean/SD	Measured by pressure-temperature guidewire.
Mingkun Cao [1]	LVEF	60.45	5.28	190	57.00	7.38	188	Mean/SD	
Wei Geng [4]	LVEF	58.02	5.40	118	57.36	6.84	112	Mean/SD	Reported at "1-month".
Dong Huang [5]	LVEF	58.2	7.8	111	55.6	8.6	117	Mean/SD	Total n=285 for Day 30 LVEF (missing data implied). Used randomized N as denominator is unclear.
Wenlong Jiang [14]	LVEF	57.44	5.36	125	55.79	5.49	135	Mean/SD	Reported at "6-month".
Xuechao Wang [11] [11]	LVEF	55.22	10.50	92	52.18	9.39	90	Mean/SD	
Yanqiang Wu [7]	LVEF	60.84							
Wei Geng [4]	MBF_MCE	34.13	15.59	118	14.28	9.44	112	Mean/SD	MCE = Myocardial Contrast Echocardiography.

Mingkun Cao [1]	NT-proBNP	452.3	259.4	190	632.7	278.3	188	Mean/SD	
Mingkun Cao [1]	Troponin_peak	47.25	21.36	190	58.71	25.58	188	Mean/SD	
Wei Geng [4]	Troponin_peak	21.49	4.76	118	23.12	5.58	112	Mean/SD	Unit reported as ng/L.
Wenlong Jiang [14]	Troponin_peak	22.88	5.42	125	24.30	6.00	135	Mean/SD	Unit reported as ng/L.
Xuechao Wang [11] [11]	Troponin_peak	52.16	24.67	92	60.91	28.81	90	Mean/SD	
Yanqiang Wu [7]	Troponin_peak	38.83	12.53	25	51.71	26.32	25	Mean/SD	Unit reported as ng/L.

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