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SYSTEMATIC REVIEW

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Intensive blood pressure management for ischemic stroke patients following endovascular thrombectomy: a meta-analysis of randomized controlled trials

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Abstract

Objective This meta-analysis aimed to determine the potential benefits of intensive blood pressure management in ischemic stroke patients who have undergone endovascular thrombectomy (EVT).

Methods We comprehensively searched all relevant studies published before August 23, 2024, using multiple databases, including Cochrane Library, Embase, PubMed, Web of Science and China National Knowledge Infrastructure (CNKI) and Wangfang. The primary outcomes were favorable outcomes at 90 days (mRS score = 0–2), while the secondary outcomes comprised 90-day mortality, incidence of symptomatic intracranial hemorrhage (sICH), and 7-day mortality.

Results Six randomized controlled trials studies involving 1752 patients were included. The incidence of 90 days (mRS score = 0–2) score was significant difference between different blood pressure management (RR = 0.81, 95% CI [0.74, 0.89], $p < 0.01$) with heterogeneity ($I^2 = 0\%$, $p = 0.52$). No significant difference was perceived in the 90-day mortality (RR = 1.16, 95% CI [0.90, 1.48], $p = 0.28$; $I^{2=}$ 0%, $p = 0.89$). Additionally, there was no statistically significant difference in the incidence of sICH, (RR = 1.03, 95% CI [0.72, 1.48], $p = 0.86$; $I^{2=}$ 0%, $p = 0.42$). There was also no statistically significant discerned in the 7-day mortality (RR = 1.33, 95% CI [0.88, 2.01], $p = 0.17$; $I^{2=}$ 0%, $p = 0.67$).

Conclusion Our research results suggest that routine standard blood pressure management is more beneficial to the functional independence for patients, a more moderate intensive blood pressure management should be used.

Keywords Blood pressure, Endovascular thrombectomy, Ischemic stroke, Meta-analysis

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Introduction

Endovascular thrombectomy (EVT) is a reliable and effective intervention for individuals with acute ischemic stroke and notable vascular occlusion [1–3]. Despite achieving successful reperfusion in approximately 80% of the cases, at least 50% of patients bear adverse consequences such as mortality or disability within 90 days [1, 4, 5].

A previous observational study has demonstrated that blood pressure is an independent factor influencing postoperative EVT patients [6]. Although numerous guidelines advocate maintaining blood pressure < 180/105 mmHg following EVT [7, 8]; however, several observational studies have demonstrated an association between elevated blood pressure and unfavorable prognosis [9, 10]. Notably, nearly 70% of institutions adopt lower targets for managing systolic blood pressure (SBP) [11]. These divergent perspectives can be attributed to multiple factors. Elevated blood pressure might increase the risk of intracranial hemorrhage and malignant brain edema in stroke patients by increasing intracranial pressure and cerebral microvascular reperfusion injury in stroke patients [1, 6, 9]. Conversely, hypotension maintenance might lead to the infarcted area's progressive expansion due to inadequate reperfusion, thereby elevating the likelihood of stroke recurrence [1, 5, 10]. Intensive blood pressure management refers to maintaining blood pressure at a lower level through appropriate treatment [12], which is different from the conservative blood pressure control strategies after EVT [7, 8].

BP-TARGET was the pioneering randomized controlled trial (RCT) that targeted blood pressure management post-EVT and effectively controlled intensive blood pressure within the range of 100–129 mmHg [13]. However, its findings did not support the advantages of intensive blood pressure treatment modalities. Subsequently, a Chinese RCT, ENCHANTED2/MT, was prematurely terminated due to adverse effects associated with intensive blood pressure management [12]. Therefore, whether intensive blood pressure management can yield reasonable benefits is still unclear. However, data are available regarding the blood pressure management strategy after recanalization in large-vessel occlusion stroke patients [14]. Thus, we conducted a comprehensive analysis of large-scale multicenter RCTs and systematically reviewed the available evidence regarding blood pressure management following EVT. We also sought to ascertain whether intensive blood pressure control modality confers benefits on ischemic stroke patients.

Materials and methods

The present meta-analysis was conducted per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [15], adhering to established standards.

Search strategy

We extensively searched multiple databases including Cochrane Library, Embase, PubMed, Web of Science, China National Knowledge Infrastructure (CNKI) and Wangfang to identify relevant studies published before August 23, 2024. The PubMed search strategy included the terms "ischemic stroke", "mechanical thrombectomy", "endovascular thrombectomy", "intraarterial thrombectomy", "endovascular procedures", and "blood pressure". Additionally, we manually searched the references of selected studies and current field reviews to identify relevant literature. After Endnote software eliminated duplicate studies, the remaining articles were carefully reviewed.

Selection criteria

The inclusion criteria were: (1) Ischemic stroke patients who underwent successful EVT, defined as achieving a modified Thrombolysis in Cerebral Infarction (mTICI) score of ≥ 2b; (2) The studies that investigated different blood pressure management approaches and primarily focused on SBP; (3) Those with at least one of the following outcome measures: primary outcome index encompassing favorable outcome at 90-day, mRS (modified Rankin Scale) score = 0–2 whereas secondary outcome index included 90-day mortality, incidence of symptomatic intracranial hemorrhage (sICH), and 7-day mortality; (4) The studies incorporating RCTs.

The exclusion criteria were: (1) AIS patients who did not achieve successful reperfusion after EVT; (2) Studies without intensive blood pressure management, and (3) Meta-analyses, systematic reviews, case reports, editorials, animal experiments, letters, comments, and conference abstracts were excluded.

Data extraction and quality assessment

Two researchers independently screened the literature and extracted relevant data. Any discrepancies were resolved through discussion with a third researcher. The extracted data included authorship, publication date, study design, blood pressure target, sample size, and other pertinent data. RCTs were assessed using the Cochrane Risk of Bias Tool.

Statistical analysis

The statistical analysis was performed using StataMP (v.15) software. Dichotomous variables were represented by risk ratio (RR) and 95% confidence interval (CI). A p-value < 0.05 was considered statistically significant. The I^2 test was used to measure heterogeneity; an $I^2 < 50\%$ indicated high homogeneity and a fixed-effect model was employed. Furthermore, $I^2 > 50\%$ indicated lower homogeneity, and thus a random-effect model was utilized. Publication bias assessment was only performed in cases when the analysis included > 7 studies [16].

Results

After comprehensively searching multiple databases and eliminating duplicate studies, we reviewed 3,552 published studies based on their titles and abstracts. Among these, we examined entire texts of 89 studies and excluded those who lacked blood pressure target data. Eventually, six studies [12, 13, 17–20] were included in this meta-analysis (Fig. 1), encompassing 1,689 EVT patients. As there were two groups of interventions in the Mistry et al. [17], to reduce the risk of study bias, we included blood pressure management less than 140 mm Hg and excluded blood pressure management measures less than 160 mm Hg. Table 1 presents a summary of the key characteristics of the included studies. The studys' quality evaluation was illustrated in eFigure 1, supplement 1.

Favorable outcome at 90-day (mRS score = 0–2)

Six studies with 1,689 patients provided data on favorable outcomes at 90 days (mRS score = 0–2). After using a fixed-effect model for analysis, significant differences were observed in blood pressure management (RR = 0.81, 95% CI [0.74, 0.89], $p < 0.01$), without any heterogeneity ($I^2 = 0\%$, $p = 0.52$, Fig. 2). Subgroup analyses were performed because of the different blood pressure values. Subgroup analyses revealed statistically significant differences in SBP < 140 mmHg (RR = 0.79, 95% CI [0.67, 0.92]; $I^2 = 0\%$, $p = 0.65$), (eFigure 2, supplement 1).

90-day mortality

The results of 90-day mortality data were obtained from six studies encompassing 1,689 patients. As seen in Fig. 3, no statistically significant difference in 90-day mortality was observed across different blood pressure management strategies (RR = 1.16, 95% CI [0.90, 1.48], $p = 0.89$; $I^2 = 0\%$, $p = 0.89$) in a fixed-effect model analysis. Subgroup analyses revealed no significant differences (eFigure 3, supplement 1).

Symptomatic intracranial hemorrhage

The sICH data were extracted from five studies involving 1,609 patients. After using a fixed-effect model for analysis, there was no significant difference in sICH between different blood pressure management strategies (RR = 1.03, 95% CI [0.72, 1.48], $p = 0.86$; $I^2 = 0\%$, $p = 0.42$) as seen in Fig. 4. Subgroup analyses revealed no significant differences (eFigure 4, supplement 1).

7-day mortality

We extracted 7-day mortality data from two studies encompassing 1,134 patients. A fixed-effect model displayed no statistically significant difference in the occurrence of 7-day mortality among different blood pressure management (RR = 1.33, 95% CI [0.88, 2.01], $p = 0.17$; $I^2 = 0\%$, $p = 0.67$), Fig. 5.

Table 1 Baseline characteristics of the included studies

Author, Year	Country	Sample size[#]	Intensive/ Standard[*] (mm Hg)	Achieved SBP target[*] (mm Hg)	Onset to puncture (minutes)[*]	stroke severity (NIHSS)[*]	Primary outcomes	Antihypertensive drugs	Time of duration(h)
Mazighi,2021	France	318	100 ~ 129/130 ~ 180	128(11)/ 138(17)	285 (234,357) /297 (220,353)	18 (12 ~ 20)/ 17 (13 ~ 20)	abcd	Nicardipine	24
Yang,2022	China	816	< 120/ 140 ~ 180	NA	NA	15 (10 ~ 20)/ 15 (10 ~ 20)	abcd	--	72
Mistry,2023	USA	71	< 140/ < 180	122 (15)/ 129 (20)	NA	16 (11 ~ 23)/ 14 (11 ~ 17)	abc	Nicardipine	24
Nam,2023	South Korea	302	< 140/ 140 ~ 180	135(20)/ 141 (20)	388(224, 693)/ 356(208, 730)	13(6)/ 12(7)	abc	Nicardipine	24
Ma,2023	China	102	130 ~ 140/ 160 ~ 180	134(8)/ 153(4)		22/21	abc	Nitroglycerin	72
Guan,2024	China	80	110 ~ 140/<180	NA	NA	NA	ab	Urapidil	72

[#] The number of patient who finished the study and data was available

[*] Intensive systolic blood pressure target group VS. Standard systolic blood pressure target group

*a*Favorable outcome at 90-day (mRS score = 0–2), *b* 90-day mortality, *c* sICH, *d* 7-day mortality

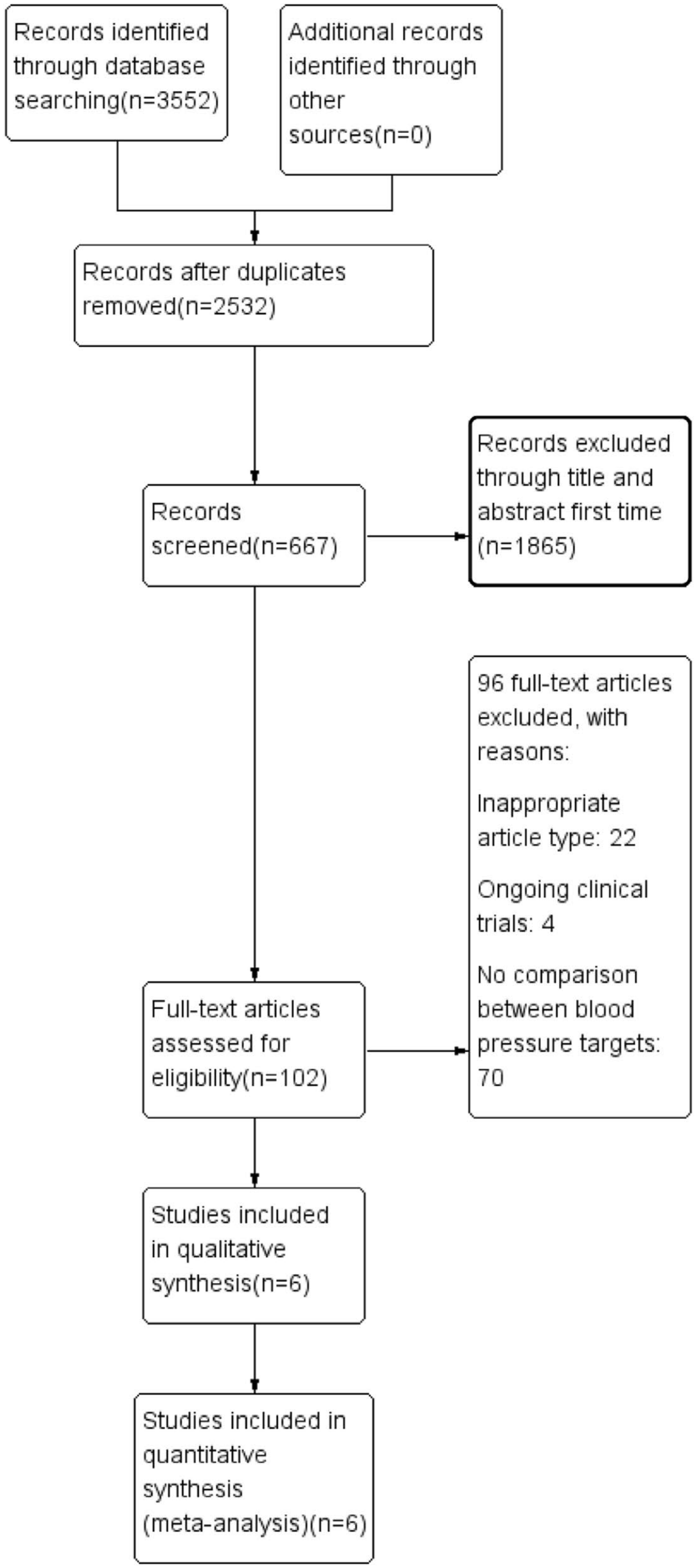

Fig. 1 Flow diagram: the study selection procedure

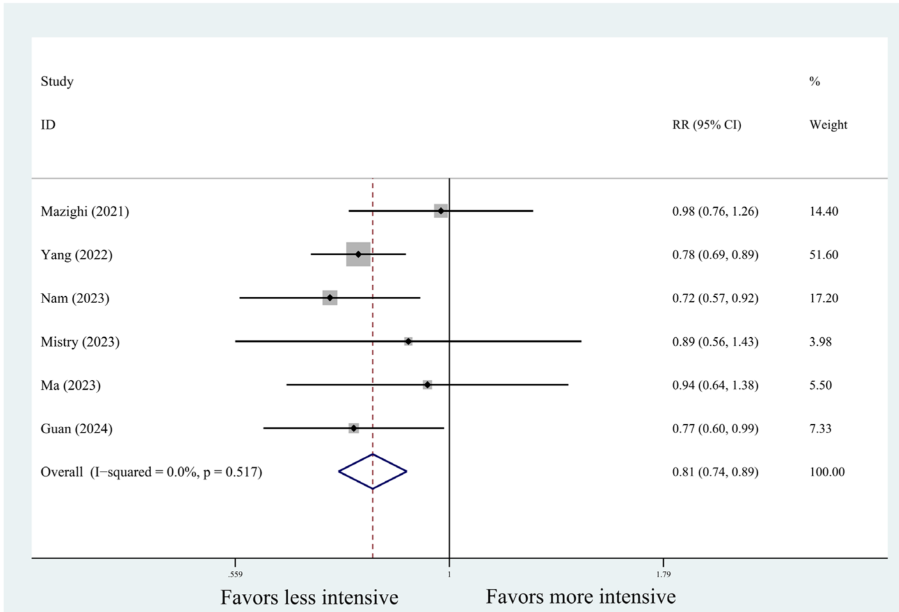

Fig. 2 Forest plot. Meta-analysis of favorable outcome at 90-day (mRS score = 0–2)

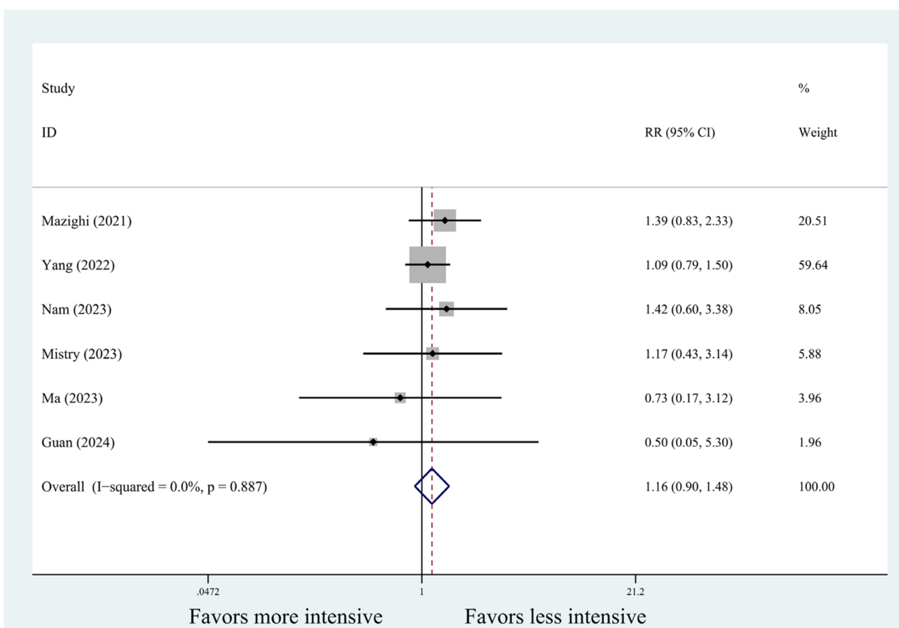

Fig. 3 Forest plot. Meta-analysis of 90-day mortality

Discussion

This study aimed to assess the safety and efficacy of intensive blood pressure management strategies on the clinical outcomes of ischemic stroke patients post-EVT. Hence, we included relevant high-quality RCTs [12, 13, 17–20]. In order to ensure similar baseline characteristics across the groups, all eligible patients were randomly assigned to either a managed blood pressure value or standard blood pressure management modality. Unlike previous meta-analyses incorporating observational studies [21, 22], this study is the first to include only RCTs that have investigated intensive blood pressure management following EVT. Our study mitigated selection bias and demonstrated higher methodological quality despite,

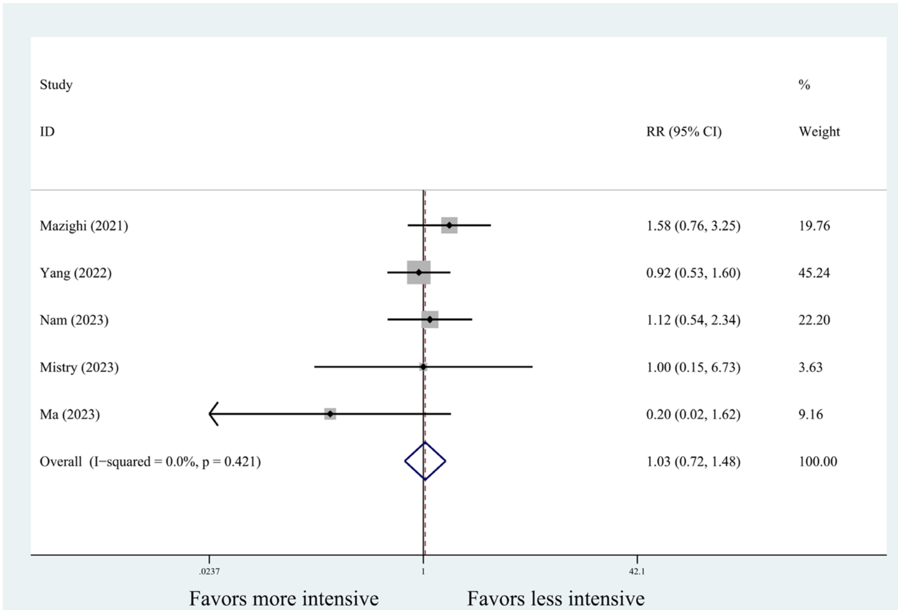

Fig. 4 Forest plot. Meta-analysis of sICH

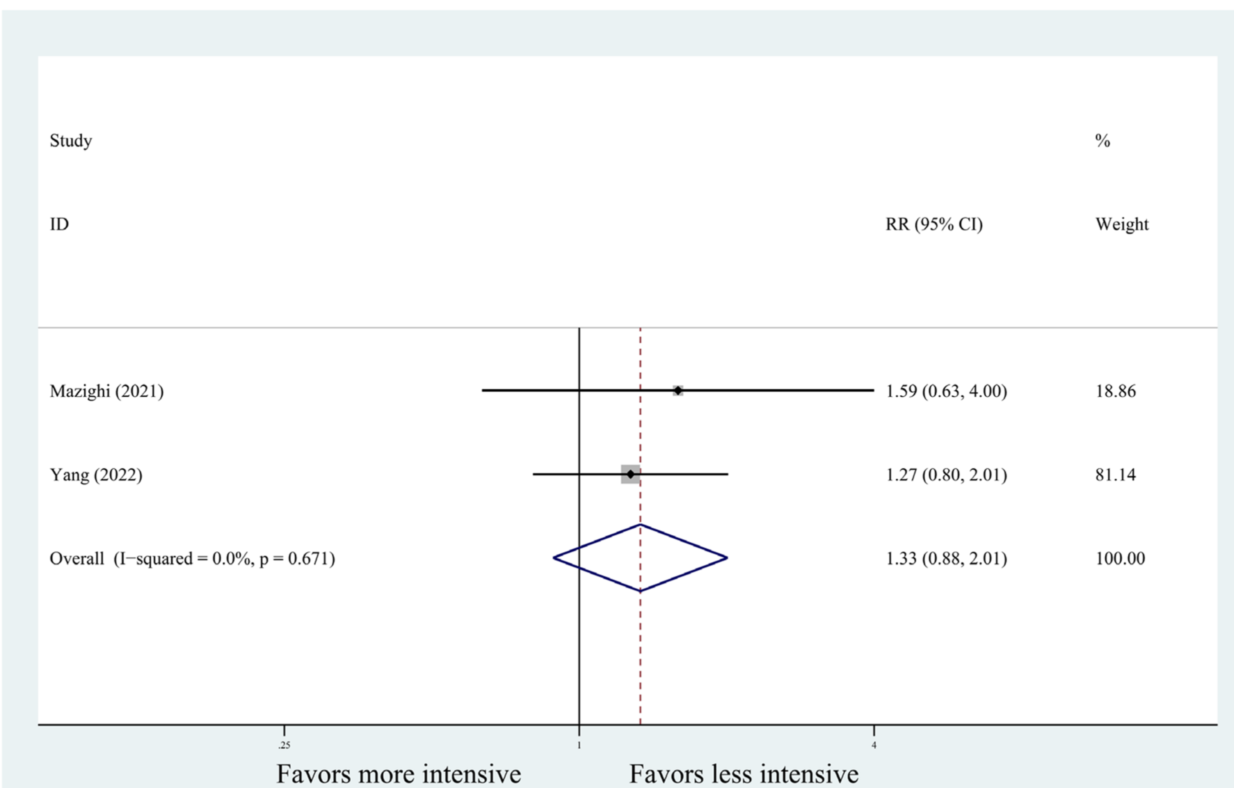

Fig. 5 Forest plot. Meta-analysis of 7-day mortality

including only six RCTS thereby enhancing our findings' reliability. Our findings demonstrate that standard blood pressure protocol provides more benefits than intensive blood pressure management, especially in terms of achieving a good 90-day functional outcome. Because of different blood pressure values, our subgroup analysis showed that SBP > 140mmHg was more beneficial to patients' 90-day functional independence. This is consistent with the research results of Zhou [21] et al. However, no discernible differences were observed in terms of 90-day mortality, sICH, and 7-day mortality, each outcome index showed low heterogeneity ($I^{2=}$ 0%). Notably, previous studies have established a strong association between progressive SBP elevation and the incidence of sICH [10, 23, 24]. However, our study did not observe any disparity in sICH occurrence among different blood pressure management targets, which might be attributed to interindividual variations within distinct patient cohorts. Hence, a sensitivity analysis was not performed because of the substantial number of included studies. Interestingly, three almost identical meta-analyses all included the same four randomized controlled trials, but our study also included studies from other databases. However, our findings all support standard blood pressure management rather than intensive blood pressure management [25–27].

Heterogeneity of stroke patients undergoing endovascular thrombectomy is a critical aspect that influences treatment outcomes and clinical decision-making [28]. Various factors contribute to this heterogeneity, including patient demographics, clinical presentations, comorbidities, and the specific characteristics of the stroke itself, such as the location and extent of the occlusion. For instance, age plays a significant role in the outcomes of endovascular thrombectomy (EVT) [28]. Studies have shown that elderly patients, particularly those aged 80 and above, tend to have poorer functional outcomes and higher mortality rates compared to younger patients [29]. This raises important considerations regarding the risk-benefit ratio of performing EVT in older populations, as their overall health status and the presence of comorbidities can complicate recovery [29]. Additionally, the timing of intervention is crucial. Delays in treatment can adversely affect outcomes, with evidence suggesting that shorter times from symptom onset to thrombectomy are associated with better functional recovery [28, 30]. This highlights the importance of efficient emergency response systems and protocols to minimize delays in treatment initiation.The quality of the thrombus itself also varies among patients and can impact the success of the procedure [30]. Research indicates that the composition and characteristics of the thrombus can influence the effectiveness of different thrombectomy devices, suggesting that personalized approaches based on thrombus quality may enhance recanalization success rates [31]. Moreover, the presence of comorbid conditions, such as diabetes and hypertension, can exacerbate the severity of stroke and complicate recovery. Elevated blood glucose levels have been associated with increased brain edema and worse clinical outcomes, indicating that metabolic factors should be considered when evaluating stroke patients for EVT [32]. Finally, the decision to use intravenous thrombolysis prior to thrombectomy remains a topic of debate. While some studies suggest that bridging therapy may improve outcomes, others indicate that direct thrombectomy could be equally effective, particularly in certain patient populations [33, 34]. This ongoing discussion underscores the need for individualized treatment strategies that take into account the unique characteristics of each patient.

Although the European Stroke Organization and the American Stroke Association recommend maintaining post-EVT blood pressure < 180/105 mmHg [7, 8], they acknowledge the dearth of RCTs assessing blood pressure management goals after EVT [35]. Consequently, the inaugural BP-TARGET RCT was initiated in 2021, suggesting that intensive blood pressure management was a viable approach [13]. Another meta-analysis proposed a specific target value for blood pressure management and suggested that maintaining SBP < 140 mmHg may yield superior benefits. However, the incorporation of observational studies and RCTs led to selection bias and compromised the research findings [21].

In contrast to previous studies [36, 37], we supported the implementation of standard blood pressure management following EVT for achieving favorable 90-day functional outcomes. Following successful reperfusion, the blood pressure target should be adjusted to mitigate reperfusion injury and facilitate penumbra recovery [35]. However, the recommended management target of 180/105 mmHg lacks valid evidence, and the adjustment of the appropriate blood pressure target based on individual patient factors (like reperfusion degree, overall hemodynamic state, and infarct area) remains uncertain [7, 8, 35]. Previous observational studies had demonstrated that lower postoperative blood pressure values were associated with improved patient prognosis [23, 38]. However, the ENCHANTED2/MT trial has provided additional evidence suggesting limited impairment when SBP<120 mmHg, leading to early termination due to poor 90-day mRS scores. Since this blood pressure management goal is uncommon in current clinical practice, this can also define a minimum target value for blood pressure management goals in future RCTs [12, 21]. Although our analysis revealed that standard blood pressure management yields greater benefits, the intensive blood pressure modality's target values were inconsistent across different trials (BP-TARGET < 130 mmHg [13]; ENCHANTED2/MT<120 mmHg [12]; BEST-II<140 or 160 mmHg [17], and OPTIMAL-BP < 140 mmHg [18]). Thus, establishing a unified target value for intensive blood pressure management is a challenge. In summary, our objective was to validate the intensive blood pressure's efficacy rather than focusing solely on specific blood pressure values, thereby suggesting a more conservative approach to managing intensive blood pressure in future studies.

The relationship between the reperfusion degree and BPV is of significant interest and can be determined by the mTICI scores. Previous studies have presented conflicting views on these findings. Some researchers argue that BPV in successful reperfusion patients (mTICI ≥ 2B) was closely associated with poor outcomes [39, 40], while another study suggested that this association was the strongest in inadequate recanalization patients (mTICI < 2B) [41]. However, all our patients achieved successful reperfusion (mTICI ≥ 2b), possibly due to the limited number of cases with poor reperfusion (mTICI < 2b) and insufficient study data.

Our study's primary strength lies in its pioneering meta-analysis of relevant RCTs that have investigated intensive blood pressure management strategies among stroke patients after EVT. This meta-analysis effectively addressed the limitations of previous studies, like substantial heterogeneity and selection bias. Considering the scarcity of previous RCTs (two RCTs [12, 13]), we also have incorporated two recently published high-quality trials to enhance our findings' reliability [17, 18] and two studies from Chinese database [19, 20]. However, subgroup analysis was not conducted due to the limited number of included studies.

Limitations

We solely investigated the potential benefits of intensive blood pressure. However, we could not ascertain the optimal blood pressure values due to limited RCTs. Furthermore, our findings do not apply to unsuccessful reperfusion patients, as indicated by mTICI < 2b. Thus, more RCTs focusing on blood pressure management in patients who do not achieve successful reperfusion should be undertaken in the future.

Conclusion

Our results show that routine standard blood pressure management can improve the functional independence of EVT patients' prognosis. However, for different blood pressure management targets, intensive blood pressure management with SBP < 140 mmHg resulted in the worst patient prognosis. Therefore, a mild and higher blood pressure management target should be adopted in subsequent trials. Additional large-scale multicenter RCTs should be undertaken to validate our findings.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12883-024-03976-7.

Supplementary Material 1

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Not applicable.

Authors' contributions
Shenglei Jiang and Yitao Zhou: Study Conceptualization; Data curation; Conducting research and design; data analysis; composing the initial draft, final approval.Yangbin Zhou: Data curation; Formal analysis; data analysis; composing the initial draft, final approval.Ganying Huang: Study Conceptualization; Project administration; Conducting research and design; data analysis; Supervision; Writing - review & editing; final approval.

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Data availability
All data can be found in articles and supplementary materials.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Every human participant provide their consent for publication.

Competing interests
The authors declare no competing interests.

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