Blood Pressure Reduction Among Acute Stroke Patients
A Randomized Controlled Clinical Trial

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Background

- Stroke is the second leading cause of death and the leading cause of serious, long-term disability worldwide.
- Clinical trials have documented that lowering BP reduces the risk of stroke in hypertensives and normotensives with a history of stroke or transient ischemic attack.
- The effect of immediate antihypertensive treatment in acute ischemic stroke patients with elevated BP is uncertain.

Objectives

- The primary objective is to test whether an immediate BP reduction within the first 48 hours after the onset of an acute ischemic stroke would reduce death and major disability at 14 days or hospital discharge.
- The secondary objective is to test the effects of antihypertensive treatment during the acute phase of ischemic stroke on mortality, major disability, and vascular events at 3 months.

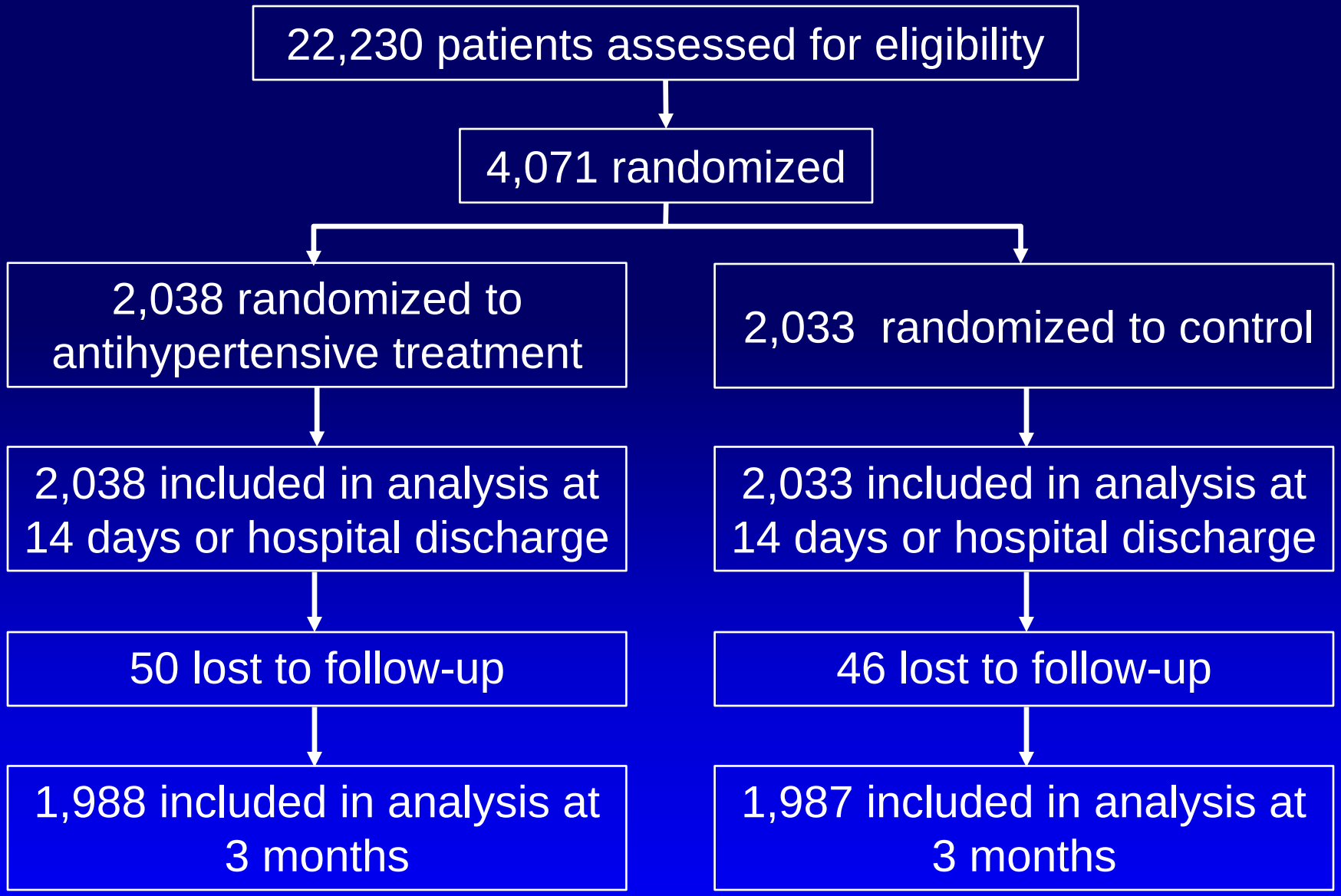
Study Participants

- China Antihypertensive Trial in Acute Ischemic Stroke (CATIS) was a multicenter, randomized, single-blind, blinded end-points trial.
- 4,071 patients aged ≥22 years who had ischemic stroke, confirmed by brain CT or MRI, within 48 hours of symptom onset and who had an elevated systolic BP between 140 and <220 mm Hg were included.
- Patients were recruited from 26 hospitals across China between August 2009 and May 2013.

Exclusion Criteria

- Severe heart failure (NYHA class III and IV), acute myocardial infarction, unstable angina, atrial fibrillation, aortic dissection, and severe cerebrovascular stenosis
- Patients in a deep coma
- Blood pressure ≥220/120 mm Hg
- Resistant hypertension
- Intravenous thrombolytic therapy
- Current pregnant women
- Unable to participate in the follow-up examination

Study Participant Flow Diagram



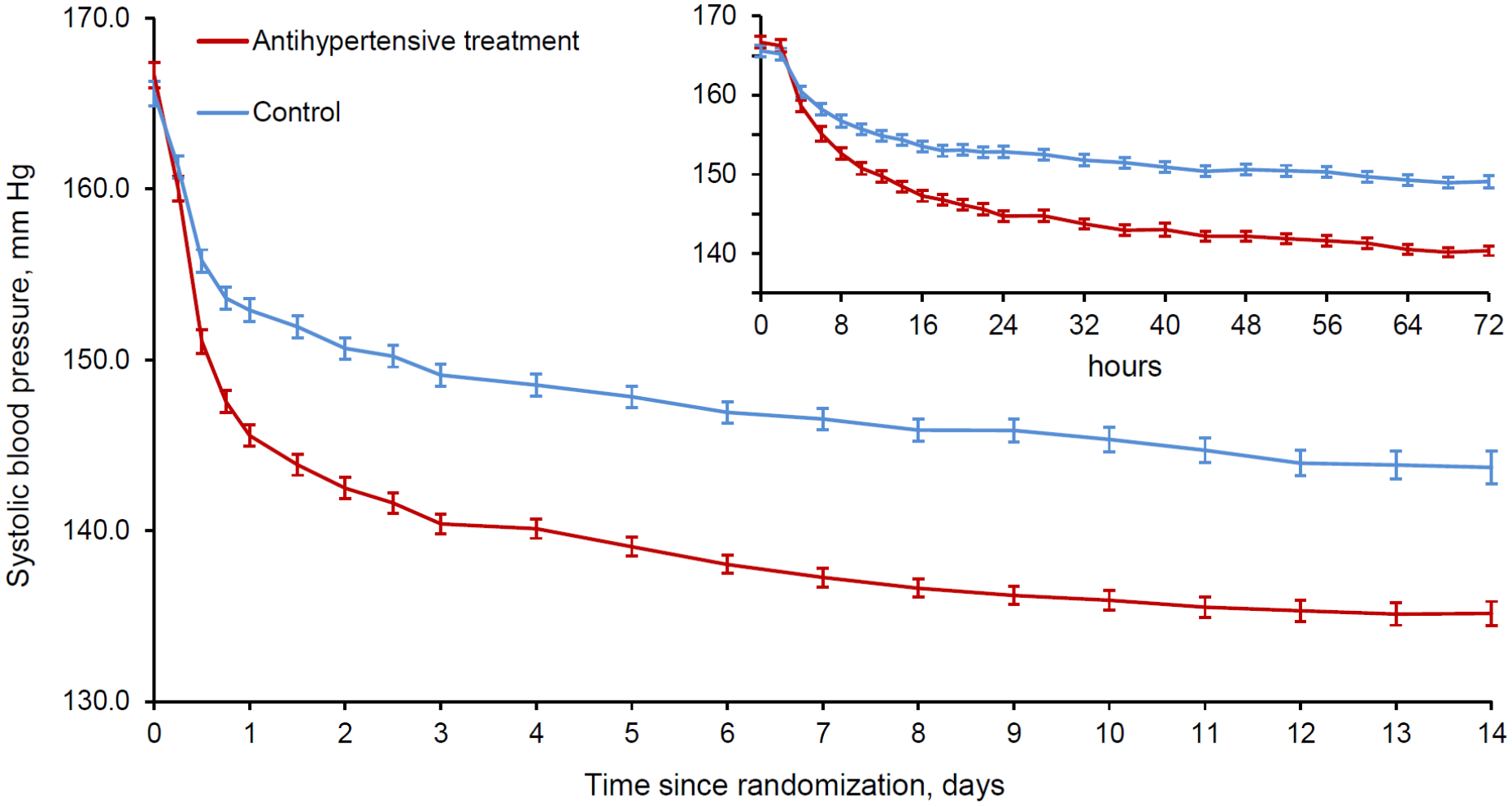
Intervention

- Antihypertensive treatment
  - Lowering systolic BP by 10-25% within the first 24 hours after randomization
  - Achieving a systolic BP <140 and diastolic BP <90 mm Hg within 7 days, and maintaining this level of BP control during the remainder of a patient's hospitalization
- Control
  - Discontinuing all home antihypertensive medications

Baseline Characteristics of Participants

Characteristics	Treatment	Control
Age, years	62.1	61.8
Male, %	64.6	63.3
Time from onset, hours	15.3	14.9
Systolic BP at entry, mm Hg	166.7	165.6
Median NIHSS Score	4.0	4.0
Hypertension, %	79.0	78.7
Use of BP medications, %	49.8	48.4
Subtypes, %		
Thrombotic	77.3	78.5
Embolic	4.9	5.1
Lacunar	20.5	18.9

Systolic BP Since Randomization by Treatment Group



Systolic BP Reduction During Hospitalization

Treatment	Control	Δ (95% CI)	*P* value
Absolute changes within 24 hrs, mm Hg			
-21.8	-12.7	-9.1 (-10.2, -8.1)	<0.001
Proportional changes within 24 hrs, %			
-12.7	-7.2	-5.5 (-4.9, -6.1)	<0.001
Systolic BP at day 7 after randomization, mm Hg			
137.3	146.5	-9.3 (-10.1, -8.4)	<0.001
Systolic BP at day 14 after randomization, mm Hg			
135.2	143.7	-8.6 (-9.7, -7.4)	<0.001

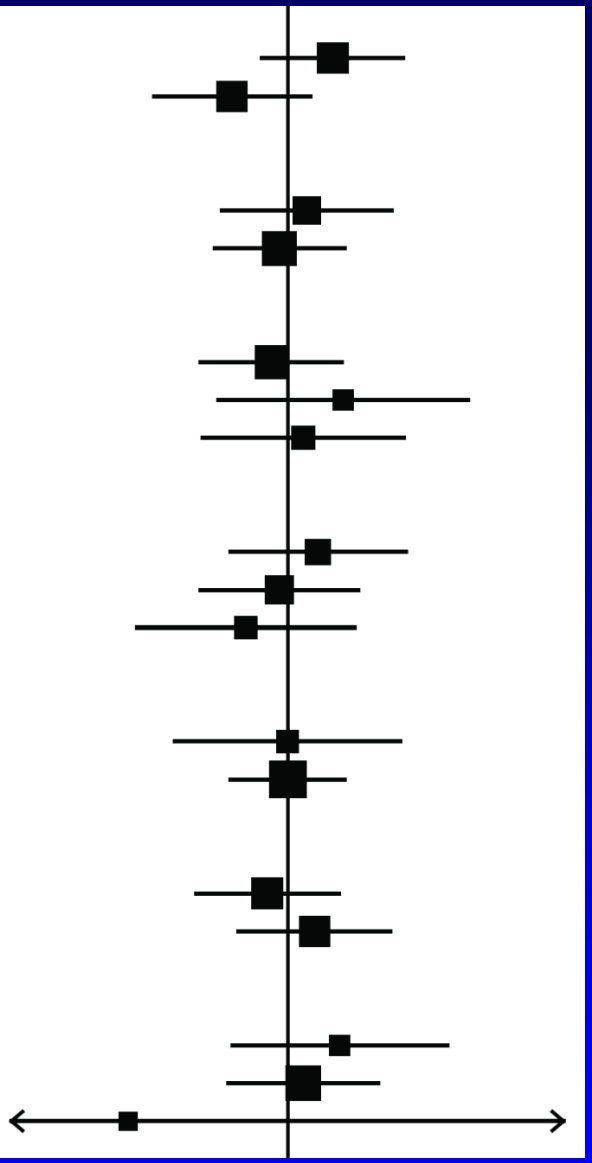
Primary and Secondary Outcomes at 14 Days or Hospital Discharge

	Treatment	Control	Odds Ratio (95% CI)	*P* value
Death or major disability, %	33.6	33.6	1.00 (0.88, 1.14)	0.98
Median modified Rankin score	2.0	2.0		0.70
Death, %	1.2	1.2	1.00 (0.57, 1.74)	0.99
Median time of hospitalization, days	13.0	13.0		0.28

Secondary Outcomes at the 3-Month Post-treatment Follow-up Visit

	Treatment	Control	Odds Ratio (95% CI)	*P* value
Death or major disability, %	25.2	25.3	0.99 (0.86, 1.15)	0.93
Median modified Rankin score	1.0	1.0		0.52
Death, %	3.4	2.7	1.27 (0.88, 1.82)	0.20
Recurrent stroke, %	1.4	2.2	0.65 (0.40, 1.04)	0.07
Vascular events, %	2.4	3.0	0.81 (0.55, 1.19)	0.28
Death or vascular events, %	4.6	4.7	0.98 (0.73, 1.31)	0.88

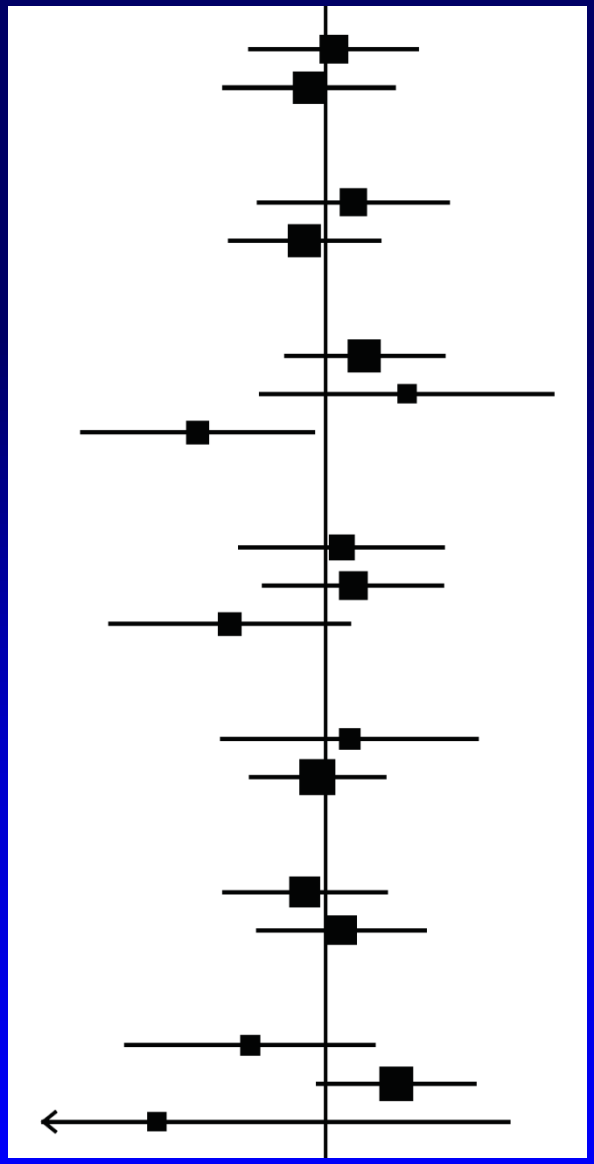
Antihypertensive Treatment Effect on Death or Major Disability at 14 Days According to Prespecified Subgroups



Age, years	<65	1.12 (0.94, 1.34)	0.054
	≥65	0.87 (0.71, 1.05)	
Sex	Women	1.05 (0.85, 1.30)	0.61
	Men	0.98 (0.83, 1.15)	
Time from onset, hours	<12	0.96 (0.80, 1.14)	0.59
	12-23	1.15 (0.84, 1.57)	
	≥24	1.04 (0.81, 1.34)	
Baseline SBP, mm Hg	<160	1.08 (0.87, 1.35)	0.59
	160-179	0.98 (0.80, 1.19)	
	≥180	0.90 (0.69, 1.19)	
History of hypertension	No	1.00 (0.75, 1.32)	0.97
	Yes	1.00 (0.87, 1.16)	
Antihypertensive medications	No	0.95 (0.79, 1.13)	0.36
	Yes	1.07 (0.88, 1.29)	
NIHSS	0-4	1.14 (0.87, 1.49)	0.66
	5-15	1.04 (0.86, 1.25)	
	≥16	0.67 (0.18, 2.44)	

Antihypertensive Treatment Effect on Death or Major Disability at 3 Months According to Prespecified Subgroups

Age, years	<65	1.02 (0.83, 1.25)	0.72
	≥65	0.96 (0.78, 1.18)	
Sex	Women	1.07 (0.85, 1.35)	0.43
	Men	0.95 (0.79, 1.14)	
Time from onset, hours	<12	1.10 (0.91, 1.34)	0.03
	12-23	1.22 (0.85, 1.74)	
	≥24	0.73 (0.55, 0.97)	
Baseline SBP, mm Hg	<160	1.04 (0.81, 1.33)	0.24
	160-179	1.07 (0.86, 1.33)	
	≥180	0.79 (0.59, 1.06)	
History of hypertension	No	1.06 (0.77, 1.44)	0.67
	Yes	0.98 (0.83, 1.15)	
Antihypertensive medications	No	0.95 (0.78, 1.16)	0.53
	Yes	1.04 (0.85, 1.28)	
NIHSS	0-4	0.83 (0.61, 1.12)	0.08
	5-15	1.19 (0.98, 1.44)	
	≥16	0.66 (0.28, 1.58)	

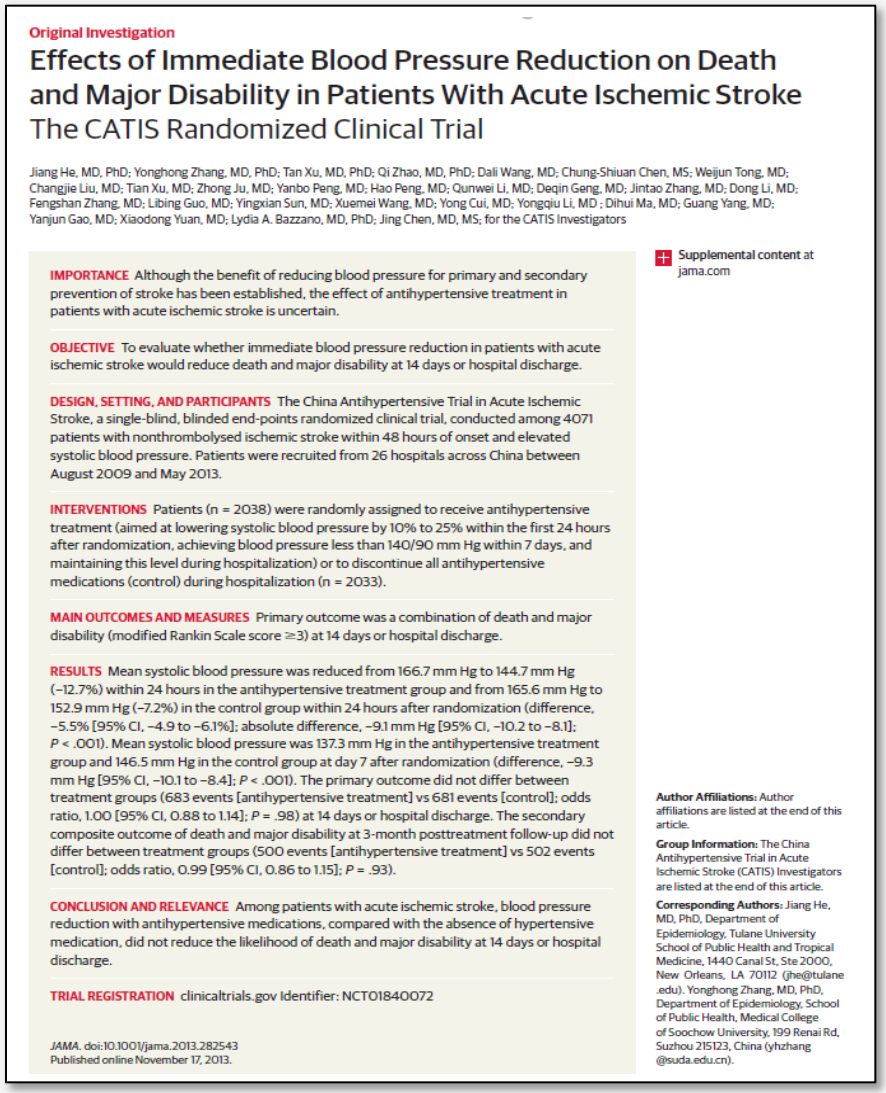


Limitations

- Patients treated with intravenous thrombolytic therapy (i.e., intravenous rtPA) at baseline were excluded from this trial.
- Patients included in this trial had a lower median NIHSS of 4 (interquartile range 2-8) compared with 7 (2-10) in Chinese national registry data.
- This trial was conducted exclusively in Chinese patients.

Conclusion

- Among patients with acute ischemic stroke, BP reduction with antihypertensive medications compared with the absence of antihypertensive medications did not reduce death and major disability at 14 days or hospital discharge.
- These findings suggest that unless a patient's BP ≥220/120 mmHg, the decision to lower BP with antihypertensive treatment in patients with acute ischemic stroke should be based on individual clinical judgment.



Original Investigation

Effects of Immediate Blood Pressure Reduction on Death and Major Disability in Patients With Acute Ischemic Stroke

The CATIS Randomized Clinical Trial

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IMPORTANCE Although the benefit of reducing blood pressure for primary and secondary prevention of stroke has been established, the effect of antihypertensive treatment in patients with acute ischemic stroke is uncertain.

OBJECTIVE To evaluate whether immediate blood pressure reduction in patients with acute ischemic stroke would reduce death and major disability at 14 days or hospital discharge.

DESIGN, SETTING, AND PARTICIPANTS The China Antihypertensive Trial in Acute Ischemic Stroke, a single-blind, blinded end-points randomized clinical trial, conducted among 4071 patients with nonthrombolysed ischemic stroke within 48 hours of onset and elevated systolic blood pressure. Patients were recruited from 26 hospitals across China between August 2009 and May 2013.

INTERVENTIONS Patients (n = 2038) were randomly assigned to receive antihypertensive treatment (aimed at lowering systolic blood pressure by 10% to 25% within the first 24 hours after randomization, achieving blood pressure less than 140/90 mm Hg within 7 days, and maintaining this level during hospitalization) or to discontinue all antihypertensive medications (control) during hospitalization (n = 2033).

MAIN OUTCOMES AND MEASURES Primary outcome was a combination of death and major disability (modified Rankin Scale score ≥3) at 14 days or hospital discharge.

RESULTS Mean systolic blood pressure was reduced from 166.7 mm Hg to 144.7 mm Hg (−12.7%) within 24 hours in the antihypertensive treatment group and from 165.6 mm Hg to 152.9 mm Hg (−7.2%) in the control group within 24 hours after randomization (difference, −5.5% [95% CI, −4.9 to −6.1%]; absolute difference, −9.1 mm Hg [95% CI, −10.2 to −8.1]; $P < .001$). Mean systolic blood pressure was 137.3 mm Hg in the antihypertensive treatment group and 146.5 mm Hg in the control group at day 7 after randomization (difference, −9.3 mm Hg [95% CI, −10.1 to −8.4]; $P < .001$). The primary outcome did not differ between treatment groups (683 events [antihypertensive treatment] vs 681 events [control]; odds ratio, 1.00 [95% CI, 0.88 to 1.14]; $P = .98$) at 14 days or hospital discharge. The secondary composite outcome of death and major disability at 3-month posttreatment follow-up did not differ between treatment groups (500 events [antihypertensive treatment] vs 502 events [control]; odds ratio, 0.99 [95% CI, 0.86 to 1.15]; $P = .93$).

CONCLUSION AND RELEVANCE Among patients with acute ischemic stroke, blood pressure reduction with antihypertensive medications, compared with the absence of hypertensive medication, did not reduce the likelihood of death and major disability at 14 days or hospital discharge.

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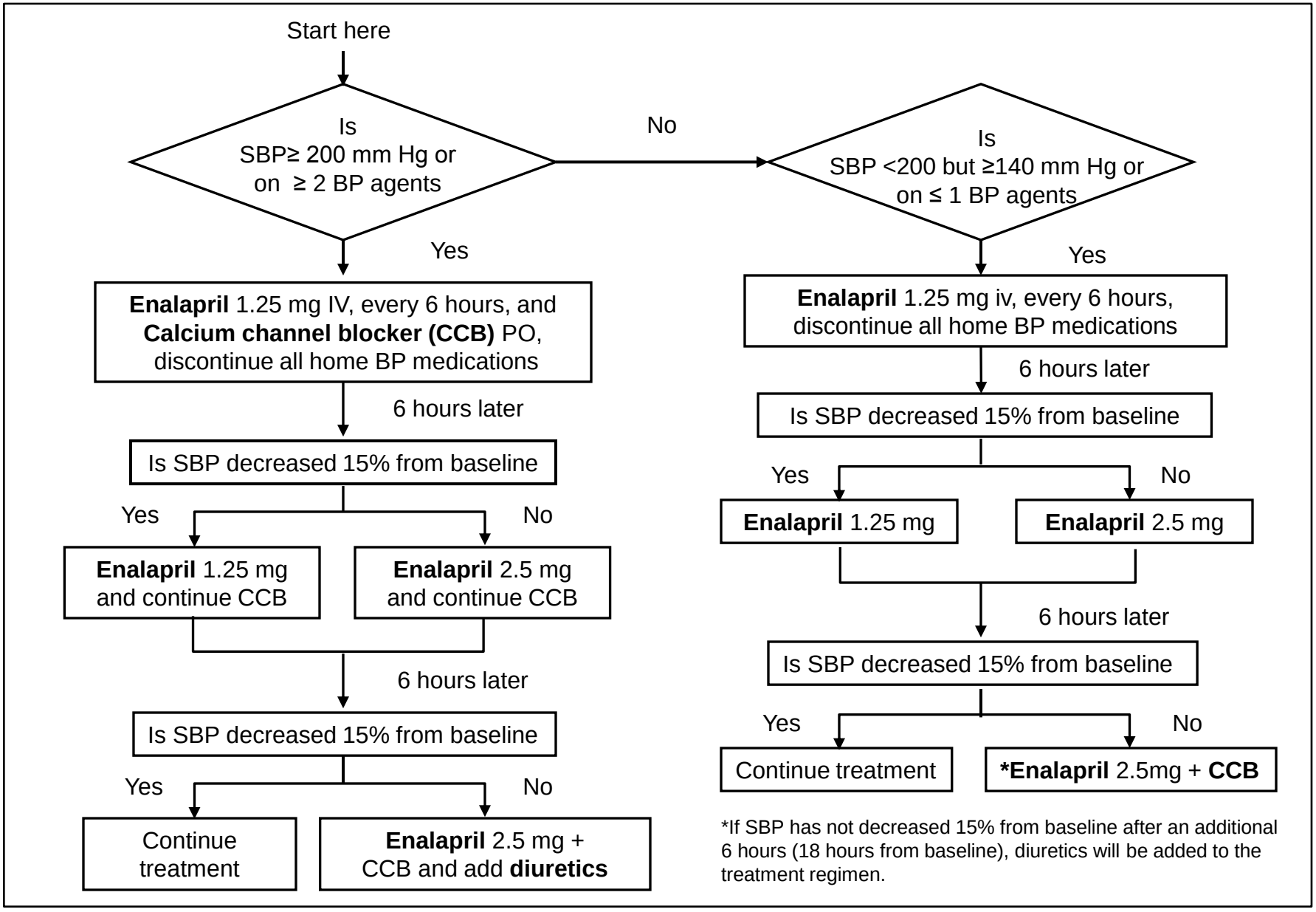
Treatment Algorithm for Blood Pressure Reduction Group



Reasons for Exclusion

A total of 18,159 patients were excluded

- 8,861 BP outside criteria
- 3,821 onset >48 hours
- 1,937 clinical contraindications
- 978 could not be followed-up
- 828 no consent obtained
- 169 refused
- 142 transferred to another hospital
- 82 resistant hypertension
- 1,341 other reasons

Proportions of Patients Achieving Systolic BP of <140 mm Hg

	Treatment	Control
7 days	65.7%	32.2%
14 days	72.0%	39.5%

Treatment of Patients with Acute Ischemic Stroke

Treatment, %	Antihypertensive Treatment	Control	P Value
Anticoagulants	**33.4**	**34.1**	**0.63**
Heparin	12.9	12.7	0.87
LMW Heparin	21.5	21.5	0.97
Antiplatelet agents	**97.8**	**96.5**	**0.01**
Aspirin	83.9	82.2	0.15
Clopidogrel	12.2	12.9	0.52
Ozagrel	47.8	47.4	0.82
Intravenous fibrinolysis	**2.6**	**2.3**	**0.55**
Urokinase	1.4	1.4	0.89
Intravenous rtPA	0.6	0.5	0.67
Dehydrants	**39.8**	**39.6**	**0.91**
Mannitol	31.0	31.3	0.81
Glycerol	11.9	12.1	0.79