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.

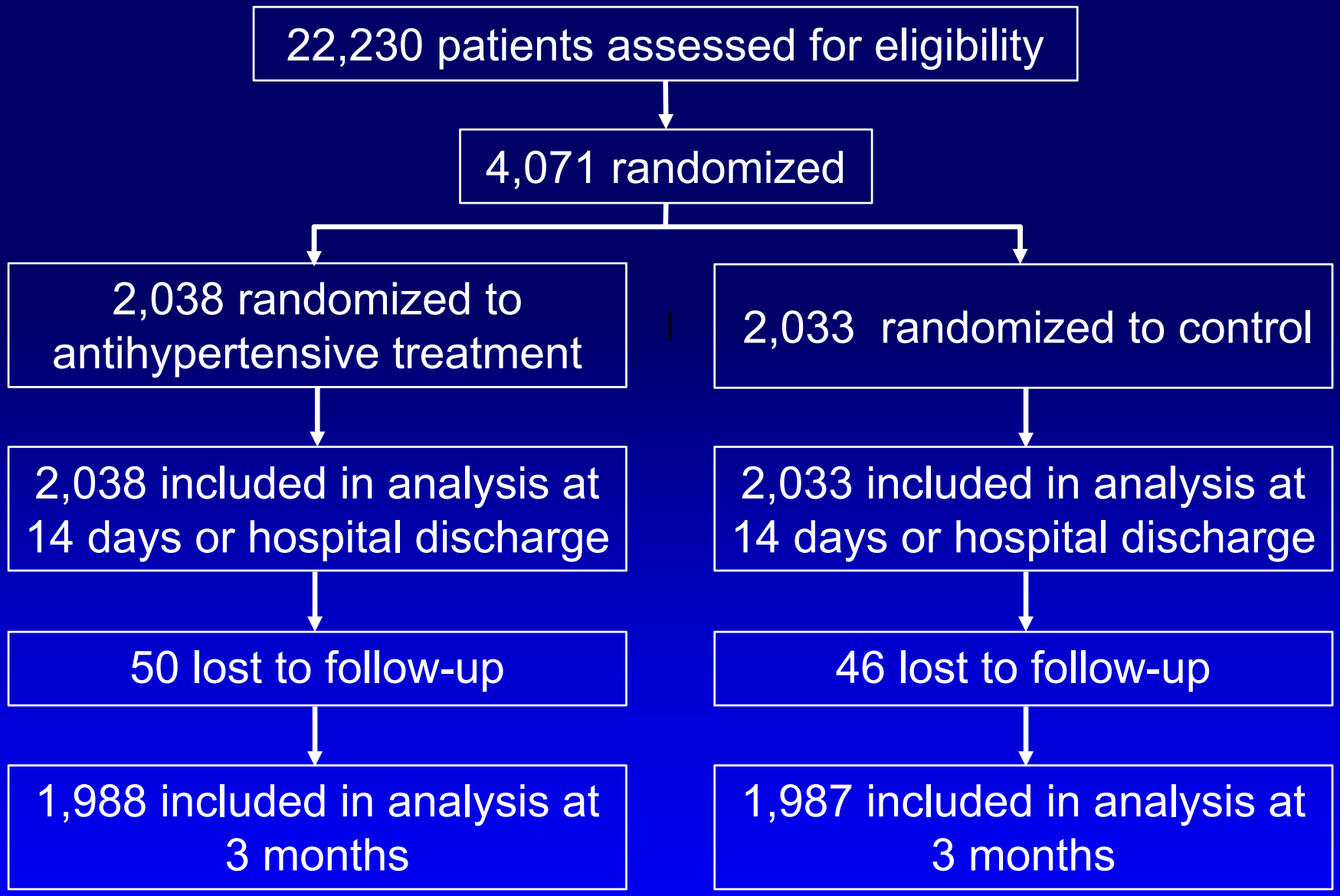
Study Participants

- 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 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



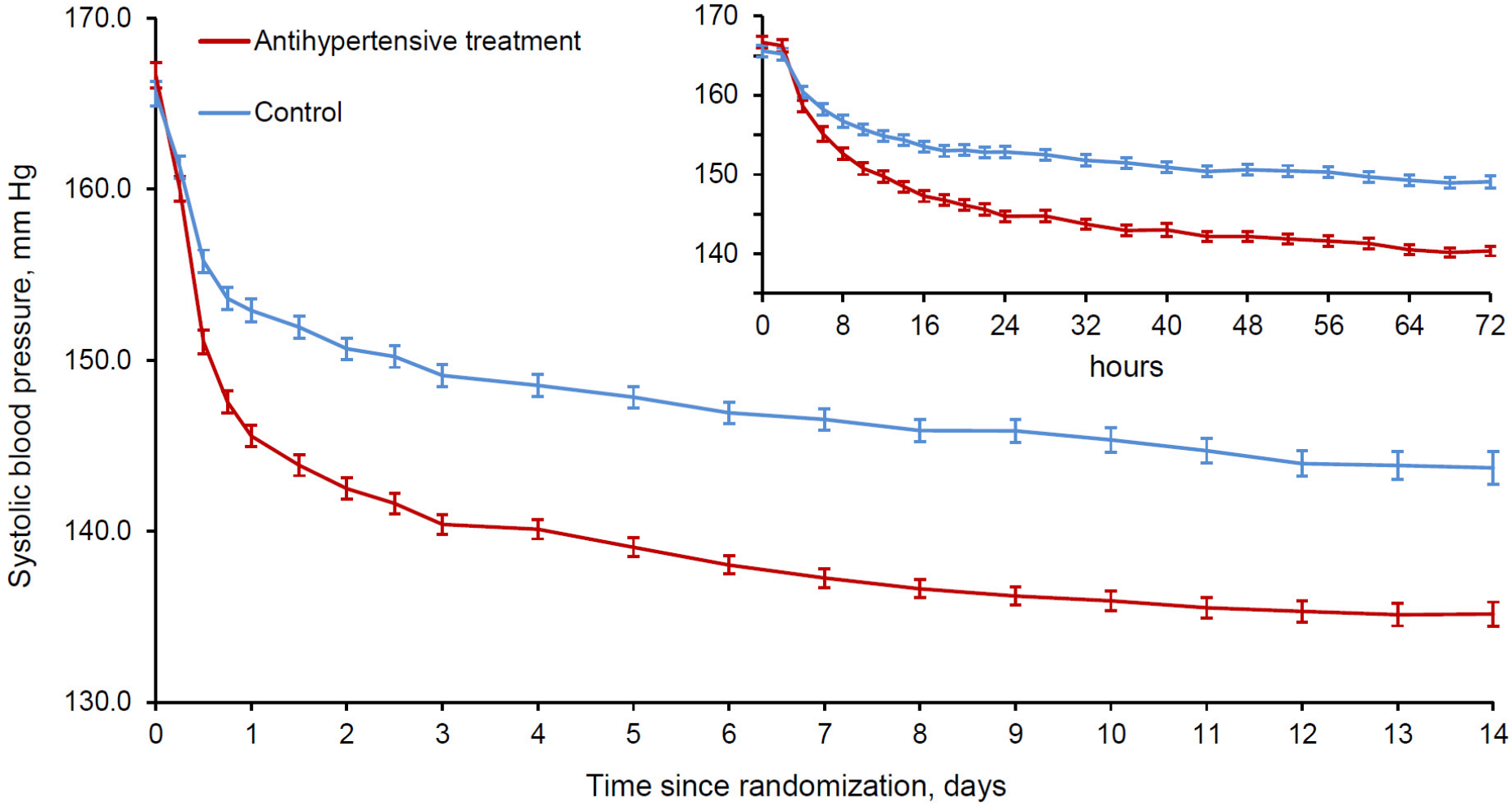
Intervention

- 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 ± 10.8	61.8 ± 11.0
Male sex, %	64.6	63.3
Time from onset, hours	15.3 ± 12.9	14.9 ± 13.0
SBP at entry, mm Hg	166.7 ± 17.3	165.6 ± 16.5
Median NIHSS Score (IQR)	4.0 (2.0 - 7.0)	4.0 (3.0 - 8.0)
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



BP Reduction During Hospitalization

	Treatment	Control	Δ (95% CI)	*P* value
Absolute BP changes within 24 hrs, mm Hg				
Systolic	-21.8 ± 15.9	-12.7 ± 17.3	-9.1 (-10.2, -8.1)	<.001
Diastolic	-11.0 ± 10.5	-6.9 ± 11.0	-4.1 (-4.7, -3.4)	<.001
Proportional BP changes within 24 hrs, %				
Systolic	-12.7 ± 8.7	-7.2 ± 9.8	-5.5 (-4.9, -6.1)	<.001
Diastolic	-10.7 ± 10.1	-6.4 ± 11.1	-4.3 (-3.6, -4.9)	<.001
BP at day 7 after randomization, mm Hg				
Systolic	137.3 ± 11.8	146.5 ± 13.6	-9.3 (-10.1, -8.4)	<.001
Diastolic	82.4 ± 7.2	86.4 ± 8.1	-4.0 (-4.5, -3.5)	<.001
BP at day 14 after randomization, mm Hg				
Systolic	135.2 ± 10.4	143.7 ± 14.0	-8.6 (-9.7, -7.4)	<.001
Diastolic	81.4 ± 7.4	85.3 ± 8.3	-3.9 (-4.6, -3.1)	<.001

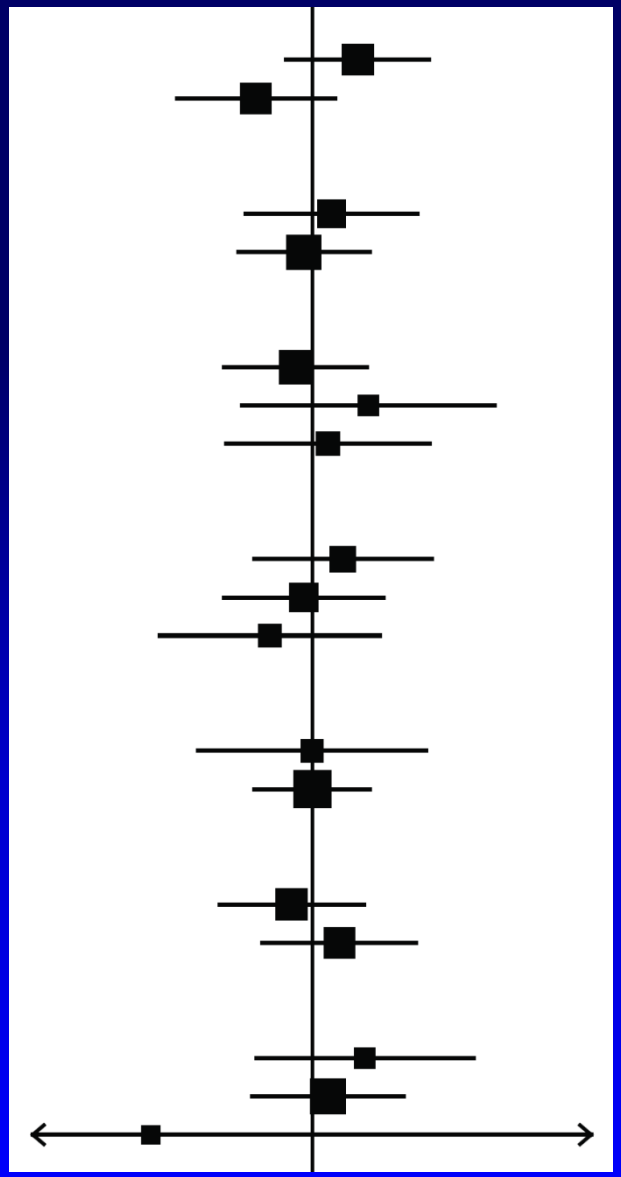
Primary and Secondary Outcomes at 14 Days or Hospital Discharge

	Treatment	Control	Odds Ratio (95% CI)	*P* value
Death or major disability, no. (%)	683 (33.6)	681 (33.6)	1.00 (0.88, 1.14)	.98
Median modified Rankin score (IQR)	2.0 (1.0 - 3.0)	2.0 (1.0 - 3.0)		.70
Death, no. (%)	25 (1.2)	25 (1.2)	1.00 (0.57, 1.74)	.99
Median duration of hospitalization (IQR), days	13.0 (9.0 - 14.0)	13.0 (9.0 - 14.0)		.28

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

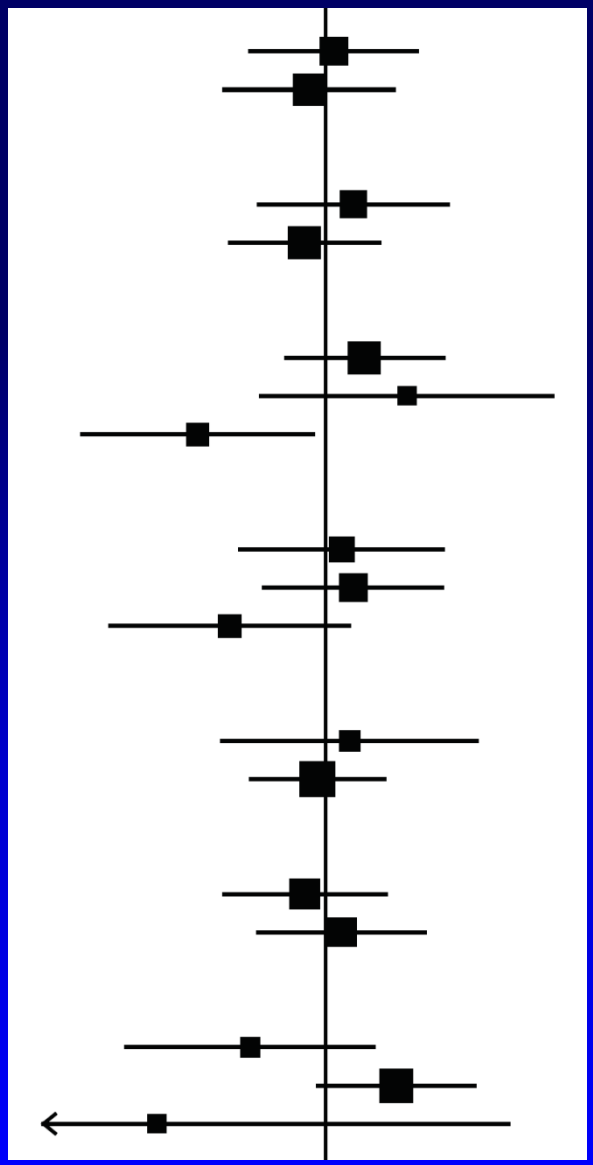
	Treatment	Control	Odds Ratio (95% CI)	*P* value
Death or major disability, no. (%)	500 (25.2)	502 (25.3)	0.99 (0.86, 1.15)	.93
Median modified Rankin score (IQR)	1.0 (1.0 - 3.0)	1.0 (1.0 - 3.0)		.52
Death, no. (%)	68 (3.4)	54 (2.7)	1.27 (0.88, 1.82)	.20
Recurrent stroke, no. (%)	28 (1.4)	43 (2.2)	0.65 (0.40, 1.04)	.07
Vascular events, no. (%)	48 (2.4)	59 (3.0)	0.81 (0.55, 1.19)	.28
Death or vascular events, no. (%)	92 (4.6)	94 (4.7)	0.98 (0.73, 1.31)	.88

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



Age, yrs	<65	1.12 (0.94, 1.34)	.054
	≥65	0.87 (0.71, 1.05)	
Sex	Women	1.05 (0.85, 1.30)	.61
	Men	0.98 (0.83, 1.15)	
Time from onset, hrs	<12	0.96 (0.80, 1.14)	.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)	.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)	.97
	Yes	1.00 (0.87, 1.16)	
Antihypertensive medications	No	0.95 (0.79, 1.13)	.36
	Yes	1.07 (0.88, 1.29)	
NIHSS	0-4	1.14 (0.87, 1.49)	.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, yrs	<65	1.02 (0.83, 1.25)	.72
	≥65	0.96 (0.78, 1.18)	
Sex	Women	1.07 (0.85, 1.35)	.43
	Men	0.95 (0.79, 1.14)	
Time from onset, hrs	<12	1.10 (0.91, 1.34)	.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)	.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)	.67
	Yes	0.98 (0.83, 1.15)	
Antihypertensive medications	No	0.95 (0.78, 1.16)	.53
	Yes	1.04 (0.85, 1.28)	
NIHSS	0-4	0.83 (0.61, 1.12)	.08
	5-15	1.19 (0.98, 1.44)	
	≥16	0.66 (0.28, 1.58)	

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.

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