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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.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01840072

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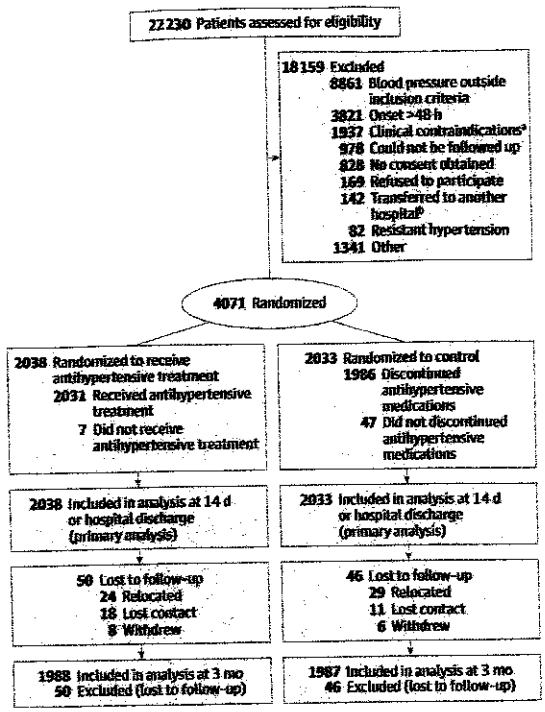
脳卒中治療ガイドライン より (2009)

推奨

1. 脳卒中発症直後の高血圧に対する管理は、高血圧性脳症、クモ膜下出血が強く疑われる場合以外は病型診断が確定してから行って良い。また降圧薬を使用する前に、痛み、嘔気、膀胱の充満などにより血圧が上昇しているのではないかを検討すべきである。一方、著しい低血圧(ショック)は輸液、昇圧薬などで速やかに是正すべきである(グレードC1)。
2. 脳梗塞急性期では、収縮期血圧>220mmHgまたは拡張期血圧>120mmHgの高血圧が持続する場合や、大動脈解離・急性心筋梗塞・心不全・腎不全などを合併している場合に限り、慎重な降圧療法が推奨される(グレードC1)。
3. 血栓溶解療法を予定する患者では、収縮期血圧>185mmHgまたは拡張期血圧>110mmHg以上の場合に、静脈投与による降圧療法が推奨される(グレードB)。

Figure 1. Study Flow



[a] Individuals with severe heart failure (New York Heart Association class III and IV), myocardial infarction, unstable angina, atrial fibrillation, aortic dissection, cerebrovascular stenosis, or in a deep coma.

[b] Eligible at screening visit but transferred to another hospital before randomization.

Inclusion Criteria
- Age ≥22 years
- Ischemic stroke onset within 48 hours confirmed by imaging (CT scan or MRI)
- Systolic blood pressure ≥140 and <220 mm Hg and diastolic blood pressure ≥80 mm Hg
- No contraindications to antihypertensive treatment
- Able and willing to sign informed consent by patients or their direct family members

Exclusion criteria
- Hemorrhagic stroke
- Severe heart failure (NY Heart Association class III and IV), myocardial infarction, unstable angina, atrial fibrillation, aortic dissection and cerebrovascular stenosis (>70%)
- Patients in a deep coma
- Diastolic blood pressure >120 mm Hg
- Resistant hypertension (systolic blood pressure ≥170 mm Hg despite use of ≥4 antihypertensive medications for ≥6 months)
- Intravenous thrombolytic therapy (such as intravenous rtPA)
- Current pregnant women
- Unable to participate in the follow-up examination (i.e., living more than 30 kilometers away from participating hospital)

Table 1. Baseline Characteristics of the Trial Participants

Characteristics	Antihypertensive Treatment (n = 2038)	Control (n = 2033)
Age, mean (SD), y	62.1 (10.8)	61.8 (11.0)
Men, No. (%)	1317 (64.6)	1287 (63.3)
Time from onset to randomization, mean (SD), h	15.3 (12.9)	14.9 (13.0)
Blood pressure at entry, mean (SD), mm Hg		
Systolic	166.7 (17.3)	165.6 (16.5)
Diastolic	96.8 (10.8)	96.5 (11.4)
Body mass index, mean (SD)[a]	24.9 (3.2)	25.0 (3.1)
NIHSS score, median (IQR)[b]	4.0 (2.0-7.0)	4.0 (3.0-8.0)
History of hypertension, No. (%)	1610 (79.0)	1599 (78.7)
Current use of antihypertensive medications, No. (%)	1014 (49.8)	983 (48.4)
Hyperlipidemia, No. (%)	137 (6.7)	140 (6.9)
Diabetes mellitus, No. (%)	369 (18.1)	350 (17.2)
Coronary heart disease, No. (%)	216 (10.6)	228 (11.2)
Current cigarette smoking, No. (%)	725 (35.6)	760 (37.4)
Current alcohol drinking, No. (%)	614 (30.1)	639 (31.4)
Ischemic stroke subtype, No. (%)[c]		
Thrombotic	1575 (77.3)	1595 (78.5)
Embolic	99 (4.9)	103 (5.1)
Lacunar	417 (20.5)	385 (18.9)

Abbreviations: IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale.

[a] Calculated as weight in kilograms divided by height in meters squared.

[b] Scores range from 0 (normal neurologic status) to 42 (coma with quadriplegia).

[c] Twelve patients with both thrombotic and embolic, 93 with thrombotic and lacunar, 6 with embolic and lacunar, and 1 with all 3 subtypes.