Introduction

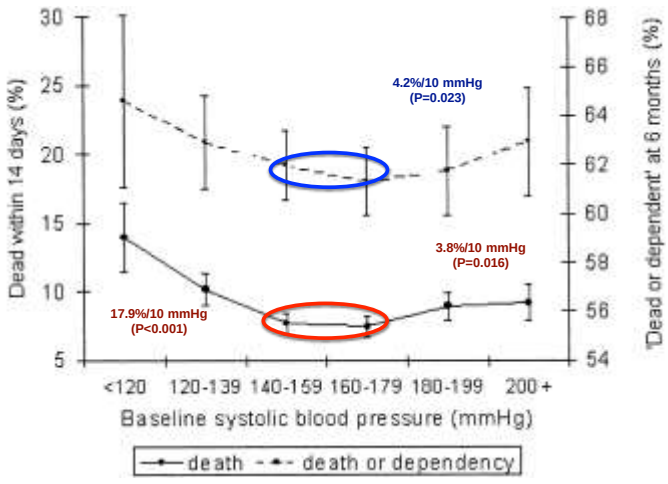
Stroke is the third leading cause of death and is the most common cause of disability

It has a global incidence of 15 million people per year million of these, five million patients die and another five million are left permanently disabled

High BP is the leading modifiable risk factor for both ischemic and hemorrhagic stroke affecting 1 billion people worldwide

In acute stroke, 75% (60-80%) of patients have high BP, only 50% of those have a prior history of hypertension

BP spontaneously falls in 2/3 of patients with an average of 20/10 mmHg within the first 10 days following stroke, 1/3 remain hypertensive and have an increased risk of a poor outcome.



U-shaped relationship between baseline SBP and outcome

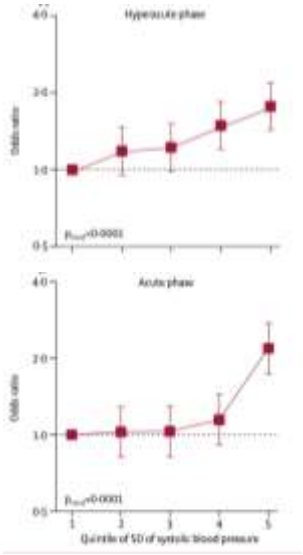
Jo Leonardi-Bee et al. Stroke. 2002;33:1315-1320

Not only increased SBP predicts poor outcome but:

- **Mean arterial pressure (MAP)**
- **Pulse pressure**
- **SBP variability**

2645 participants in the hyperacute phase and 2347 (82·7%) in the acute phase

SD of systolic blood pressure had a significant linear association with the primary outcome

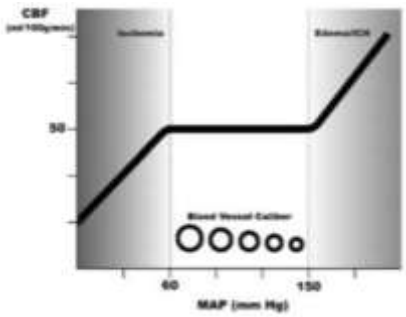


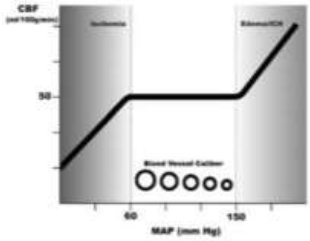
Manning L, et al, Lancet Neurology 2014; 13: 364–73

Cerebral Autoregulation

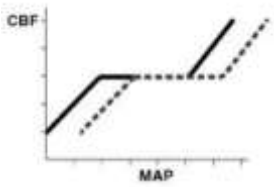
- **Cerebral blood flow (CBF) = CPP/CVR**
- **Cerebral perfusion pressure (CPP) = MAP - ICP**

  "Normally ICP is negligible"
- **CBF is normally held constant at 50 ml/100 g brain tissue per minute, despite fluctuations in CPP between 60 and 150 mmHg**



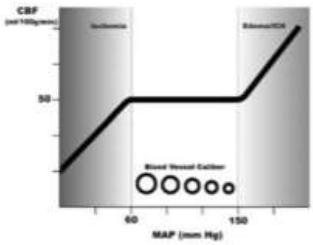


Normal Curve

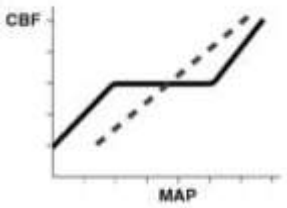


Hypertension

- In **chronic hypertension**, the auto regulatory curve is *shifted to the right,* making brain is relatively intolerant to hypotension



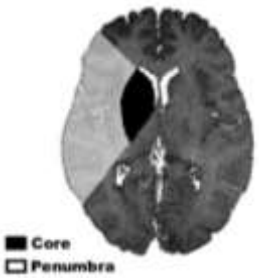
Normal Curve



Acute stroke

- In **acute stroke**, relation between CBF and MAP becomes *linear*

- Rapid, large falls in BP could reduce CBF leading to extension of cerebral infarction, or perihaematomal ischaemia
- Higher BP there is increased risk of haematoma expansion, haemorrhagic transformation in ischaemic stroke and cerebral oedema



Acute Hypertensive Response

It is the elevation of BP above normal and premorbid values within the first 24 hours of symptom onset in patients with stroke

According to ISH statement, acute hypertensive response is defined as "systolic BP 140 mm Hg or diastolic BP of 90 mm Hg demonstrated on 2 recordings taken 5 minutes apart within 24 hours of symptom onset."*

This phenomenon was reported in 60-80% of patients presenting with stroke

- **With 15 million patients experiencing stroke worldwide each year,** the acute hypertensive response may be expected in 10 million patients per year.**

* statement on the management of blood pressure in acute stroke. J Hypertens. 2003;21:665– 672

** International cardiovascular disease statistics (2007 update)

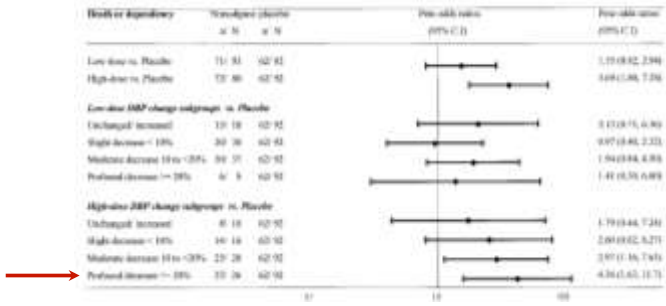
Stroke involves transient or permanent damage to widely spread areas that are involved in the regulation of BP:

- **The parasympathetic and sympathetic nervous systems are lateralized to the left and right cerebral hemispheres**
- **Prefrontal and insular cortices provide inhibitory and excitatory input, respectively, through pathways that connect to the nucleus tractus solitarius and ventrolateral medulla**
- **Further modulation is provided by cingulated cortex, amygdala, and hypothalamus**

- **Increased sympatho-adrenal tone with subsequent release of renin and vasoconstriction of arterioles**
- **An increase in systemic BP secondary to increased ICP [Cushing Reflex], in patients with intracerebral and subarachnoid hemorrhages**
- **Impaired cardiac baroreceptor sensitivity**
- **Infection**
- **Pain, for example, due to urinary retention**
- **Stress related to hospitalisation**

Studies Arguing Against Early Antihypertensive Therapy

The Intravenous Nimaodipine West European Stroke Trial (INWEST)



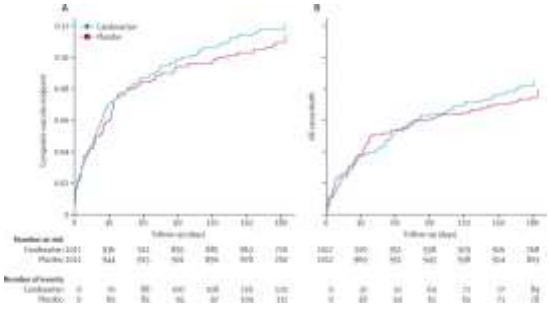
265 patients were enrolled

Effect of IV Nimodipine within 24 hours of an acute ischemic stroke

Patients with a DBP reduction of 20% had a significantly increased adjusted OR for death or dependency compared with placebo patients

Wahlgren NG, et al. Cerebro-vasc Dis. 1994;4:204-210

The Candesartan for treatment of acute stroke trial (SCAST)



2029 patients presenting within 30 hours of an acute stroke

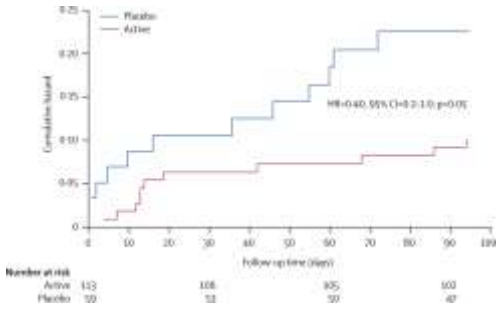
Blood pressures were significantly lower in the Candesartan group within the 7-day treatment

The study concluded BP lowering with Candesartan showed no benefit in patients with acute stroke

Sandset EC, et al. Lancet. 2011 .741-750

Studies Supporting Early Antihypertensive Therapy

Controlling Hypertension and Hypotension Immediately Post-Stroke



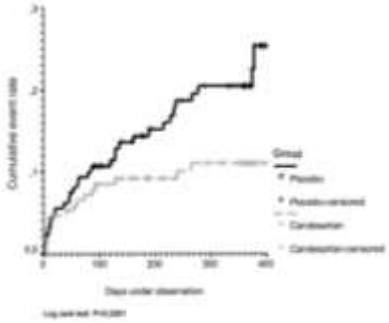
Oral and sublingual Lisinopril and oral and intravenous Labetalol

The primary outcome, death or dependency at 2 weeks, was similar in the active and the placebo group but 3-month mortality was halved

Potter JF, Robinson TG, et al. Lancet Neu- rol. 2009;8(1):48-56

The Acute Candesartan Cilexetil Therapy in Stroke Survivors (ACCESS) study

342 patients



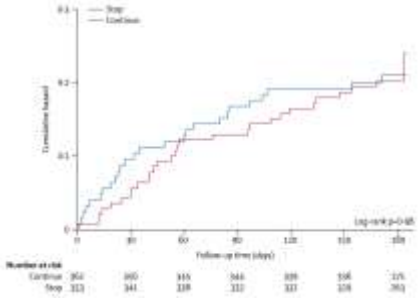
Candesartan treatment for within 24 hours of stroke onset for 7 days.

It reduced the cumulative 12-month mortality rate (7.2% and 2.9% for placebo and candesartan) and vascular events (18.7% and 9.8% for placebo and candesartan)

Schrader J, et al. Stroke. 2003;34(7):1699-1703

Studies with Neutral Results

Continue or Stop Post-Stroke Antihypertensive Collaborative Study (COSSACS)



Patients who were taking antihypertensive drugs were enrolled within 48 hours of stroke

Patients were randomly assigned to either continue or stop pre-existing antihypertensive drugs for 2 weeks

Continuation of antihypertensive drugs did not reduce 2-week death or dependency, cardiovascular event rate, or mortality at 6 months

Robinson T, Bulpitt CJ, et al. J Hypertens. 2010;28:e2

The China Antihypertensive Trial in Acute Ischemic Stroke

4071 patients who presented within 48 hours of onset of stroke and had elevated systolic BP

Randomly assigned to receive antihypertensive treatment or to discontinue all antihypertensive medications during hospitalization

The primary outcome did not differ between treatment groups at 14 days

He J, Zhang Y, Xu T, et al. JAMA. .479-489;2014

Unlike the use of antihypertensive medications in chronic hypertension, the benefit of acutely lowering BP in the setting of ischemic stroke is still unclear

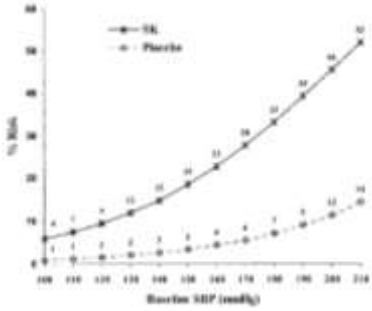
Due to the lack of reliable evidence, the ideal strategy of managing hypertension in acute ischemic stroke remains a matter of debate

Blood Pressure and Fibrinolysis

The acute hypertensive response among patients with ischemic stroke receiving thrombolysis is frequently transient and resolves after recanalization

The NINDS rt-PA stroke treatment trial recommended a BP of <185/110 mmHg before treatment and BP of <180/105 mmHg after treatment

In the Australian streptokinase study, SBP >165 mm Hg was associated with a 25% increased risk of major intracranial haemorrhage



Donnan GA, et al. JAMA. 1996 Sep 25;276(12):961-6

AHA/ASA Guideline

Guidelines for the Early Management of Patients With Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

Endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Not to lower the blood pressure during the initial 24 hours of acute ischemic stroke unless the blood pressure is >220/120 mmHg ***(Class I, Level of Evidence C)*** or there is a concomitant specific medical condition

A reasonable estimate might be to initially lower the SBP by 15%

It is important to monitor BP and neurological status, especially during the first day of stroke

AHA/ASA Recommendations for patients receiving fibrinolytic therapy

Gently bring the BP <185/110 mmHg to qualify for rtPA

(Class I, Level of Evidence B)

Once rtPA is given, the BP blood must be maintained <180/105 mmHg

Prior to Receiving rt-PA

1. If BP is not maintained at or below 185/110 mm Hg, do not administer rtPA.
2. Management of blood pressure could be achieved using:
   a. Labetalol 10 to 20 mg IV over 1 to 2 minutes may repeat 1 time.
   b. Nicardipine 5 mg/h IV, titrate up by 2.5 mg/h every 5 to 15minutes, maximum 15 mg/h.
   c. Hydralazine, enalaprilat, and so on may be considered when appropriate

During and After rt-PA

1. Maintain BP at or below 180/105 mm Hg.
2. Monitor BP every 15 minutes for 2 hours from the start of rtPA therapy, then every 30 minutes for 6 hours, and then every hour for 16 hours.
3. If systolic blood pressure is >180 to 230 mm Hg or diastolic blood pressure >105 to 120 mm Hg: labetalol 10 mg IV followed by continuous IV infusion 2 to 8 mg/min; or nicardipine 5 mg/h IV, titrate up to desired effect by 2.5 mg/h every 5 to 15 minutes, maximum15 mg/h.
4. If BP not controlled or diastolic BP >140 mm Hg, consider IV sodium nitroprusside.

according to the eligibility thresholds for inclusion in the NINDS rtPA efficacy trial

Patients with ICH

The primary rationale for lowering the blood pressure is to avoid hemorhagic expansion

However, the risk of hemorrhagic expansion must be balanced with the the risks of inducing cerebral ischemia in the region that surrounds the hemorrhage

The ASA and European Stroke Initiative guidelines recommend lowering BP in pts. with ICH to maintain systolic BP below 180 mmHg

(Class IIb, Level of Evidence C)

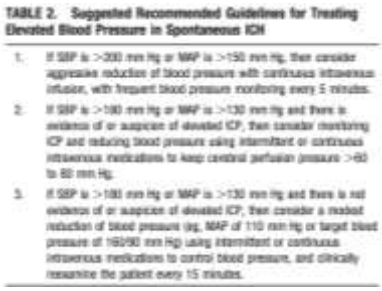


TABLE 2. Suggested Recommended Guidelines for Treating Elevated Blood Pressure in Spontaneous ICH

1. If SBP is >300 mm Hg or MAP is >150 mm Hg, then consider aggressive reduction of blood pressure with continuous intravenous infusion, with frequent blood pressure monitoring every 5 minutes.
2. If SBP is >180 mm Hg or MAP is >130 mm Hg and there is evidence of or suspicion of elevated ICP, then consider monitoring ICP and reducing blood pressure using intermittent or continuous intravenous medications to keep cerebral perfusion pressure >60 to 80 mm Hg.
3. If SBP is >180 mm Hg or MAP is >130 mm Hg and there is not evidence of or suspicion of elevated ICP, then consider a modest reduction of blood pressure (eg, MAP of 110 mm Hg or target blood pressure of 160/90 mm Hg) using intermittent or continuous intravenous medications to control blood pressure, and clinically reexamine the patient every 15 minutes.

Low BP in acute stroke

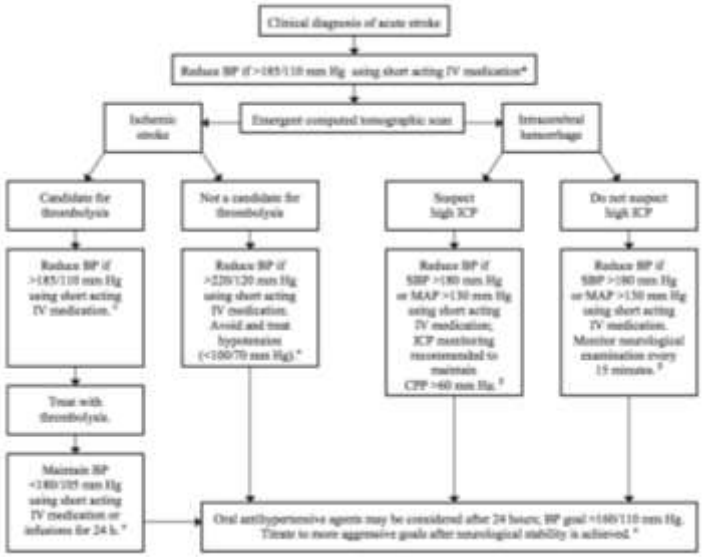
Low BP is far less common in acute stroke, but it is associated with a poorer outcome

Potential causes include sepsis, cardiac arrhythmias, heart failure and ischaemia, hypovolaemia and aortic dissection, If any of these entities are found, they must be treated rapidly.

If there is no correctable cause for hypotension, the patient fails to respond to volume resuscitation, ***induced hypertension*** may be considered.

Studies have shown that induced hypertension may increase CBF and restore perfusion to the penumbra.

Conclusion



Thank You