ACUTE STROKE AND EARLY MANAGEMENT
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Relationships with commercial interests:
▶ Not applicable

Potential for conflict(s) of interest:
▶ Not applicable
Mitigating Potential Bias

Not applicable
Objectives

• To review the medical management of the acute stroke patient (ischemic and hemorrhagic stroke) pertaining to antithrombotics, blood pressure control, and investigations
• To review the evidence for acute stroke unit care
• To discuss the role and benefit for non-medical interventions in acute stroke care
STROKE- STATS

• Stroke leading cause of adult disability and hospitalization in Canada (HSF)
• Stroke #3 cause of death in Canada (HSF)
• Ischemic stroke (IS)
  • ~85%
• Hemorrhagic Stroke (ie. Intracranial hemorrhage) (ICH)
  • ~15%
  • ICH –high rates of early mortality
Initial ED Evaluation-Hyperacute

• ABCs
• Is it a stroke?
• Does the patient qualify for acute treatment?
  • TIME IS BRAIN
• Standard Blood work (CBC, lytes, renal function INR, aPTT, Troponin, Glucose)
• Standard Brain Imaging including vascular imaging if possible
• ECG
• Blood Glucose
Goals of early acute stroke management

• Manage imminent complications
  • i.e. neurological deterioration, ABCs
• Prevent early complications
  • i.e. UTI, pneumonia, DVT/PE
• Prevent recurrent events and minimize stroke progression
• Optimize recovery
• Prevent future events
Acute stroke unit care

• “A stroke unit is a specialized, geographically defined hospital unit dedicated to the management of stroke patients and staffed by an experienced inter-professional stroke team”. (CBP 2013)

• Reduces death and disability by up to 30% in patients with mild, moderate and severe stroke (Stroke Unit Trialists collaboration, 2009)

• For all patients with stroke including ICH
What is the evidence for stroke unit care? Cochrane Review: 2013

- Reviewed 28 trials with 5855 patients comparing stroke unit care to standard ward care (21 trials)
- Significant benefit on mortality at 1 year
  - OR 0.81, 95% CI 0.69 to 0.94, P = 0.005
- Significant effect on reduction of death and dependency
  - OR 0.79, 95% CI 0.68 to 0.90, P = 0.0007
- No differences based on age, stroke severity, type of stroke, sex
- Did not lengthen patient stay
What does an acute stroke unit consist of?

• Specialized nursing care and inter-professional team
• Implement and follow stroke best practices
• Co-location of patients in discrete geographical space
Some time has past: on to the acute stroke care

• Swallowing Assessment (Swallow screen) before food, liquid or pills
  • Address nutritional needs
  • Oral care

• Assess for continence: No routine urinary catheters
  • Assess for fluid status and urinary retention

• Temperature
  • Monitor and treat > 37.5°C

• Blood glucose
  • Do not aggressively lower- reasonable to maintain 7.8-10 mmol/L
  • Treat hypoglycemia
Other core Features of Acute Stroke Unit Care

• Functional assessments within 48 h and early mobilization (within 24-48 h) (AVERT trial 2015)
  • PT, OT, SLP
• Assess Cognition and depression
• Patient and family education
• Disposition planning
  • Identification of patients who may require palliative care
• Reintegration into the community
  • Return to work and driving
Case 1
Case 1

- 55 yo M farmer admitted to Bluewater Health with new onset CHF (EF < 30%), rapid AFIB
- PMHX: Left Iliac Occlusion
- Meds: Metoprolol, received one dose of Rivaroxaban 20 mg last night
- Social History: current smoker and ETOH~5-8 drinks per day
• Sudden onset right sided weakness and aphasia at 9 am
• 130/80, 92 irregular, NIHSS-21
• Blood work- INR 1.7
• CT head done
• Telestroke consulted 9:45
CT Head
CT angiogram
1. What is the diagnosis?

- Left MCA ischemic stroke- with proximal MCA (M1) occlusion
MRI- DWI
MRI- GRE
Back to the Patient

• Patient could not receive IV tPA because had received Rivaroxaban the night before
• Transferred to LHSC for thrombectomy
• NIHSS-6 at 24 hours
Work-up and management for this patient

• Cause of stroke ? i.e. stroke etiology and Risk Factors
• Choice of antithrombotic
  • ? What is the etiology does that influence your choice in the first 48 hours
• DVT prophylaxis
  • ? in the setting of hemorrhage
• Functional assessments and Disposition Planning
Stroke Work-up: Etiology

• What is the etiology of the stroke?
  • Cardioembolic
  • Large artery disease
  • Small Vessel Disease
  • Cryptogenic (ESUS)
    • Embolic Strokes Undetermined Source (ESUS)
  • Other cause
Assess: A tailored approach to prevent subsequent stroke

1. What are the risk factors?
2. What is etiology or cause?
3. Medication and interventions
4. Non-pharmacologic: Lifestyle changes
5. Continue to monitor for any new events
Basic Investigations Ischemic Stroke (Canadian Stroke Best Practice Guidelines)

• **Labs**
  • Fasting lipids, fasting glucose, HbA1C,

• **Imaging**
  • Immediate (CT, or MRI if urgently available) [Evidence Level A], and vascular imaging of the brain and neck arteries **within 24 hours if not candidate for acute stroke therapy** [Level B].

• **Cardiac**
  • ECG
  • Transthoracic Echocardiography-(low yield~ 3% abnormal in TIA patients without heart disease) [Level B]
  • Cardiac monitoring: Holter Monitor and consider prolonged monitoring (30 days) in select cases where AFIB is suspected [Level B]

• **Other tests:** tailored to age group and if no other etiology identified
Acute Antiplatelet Therapy

- Acute ASA (within 48 h of onset) reduces risk of early recurrent ischemic stroke (IS) and long term therapy reduces IS, MI and vascular death (Sandercock et al. 2014); (Rothwell et al. 2016)

- No tPA: not on ASA- 160-325 mg x 1 then 81-325 mg daily- *check swallowing*

- tPA- no antithrombotics for 24 h

- Endovascular therapy and no tPA: ? unclear
Effects of aspirin on risk and severity of early recurrent stroke after transient ischaemic attack and ischaemic stroke: time-course analysis of randomised trials

Prof Peter M Rothwell, FMedSci, Prof Ale Algra, MD, Prof Zhengming Chen, MBBS, Prof Hans-Christoph Diener, MD, Prof Bo Norrving, PhD, Ziyah Mehta, DPhil

The Lancet
Volume 388, Issue 10042, Pages 365-375 (July 2016)
DOI: 10.1016/S0140-6736(16)30468-8
Pooled analysis of the early risk of recurrent vascular events in 12 trials of any aspirin versus control
Pooled analysis of the effect of aspirin only versus control in secondary prevention after transient ischaemic attack and ischaemic stroke on the absolute risk of recurrent ischaemic stroke

- Non-disabling ischaemic stroke
- Disabling or fatal ischaemic stroke

Events per 100 person-years

Aspirin only  Control  Aspirin only  Control  Aspirin only  Control
0–6 weeks  6–12 weeks  >12 weeks
Pooled analysis of the effect of aspirin versus control on the severity (mRS score on follow-up) of recurrent IS in the first 6 weeks and the first 12 weeks after randomisation in trials in secondary prevention after TIA and ischaemic stroke.

For the first 6 weeks:
- **Any aspirin versus control**
  - mRS≥2: OR 0.40, 0.23-0.71, p=0.0017
  - Ordinal regression: OR 0.42, 0.26-0.70, p=0.0007

For the first 12 weeks:
- **Any aspirin versus control**
  - mRS≥2: OR 0.48, 0.31-0.76, p=0.0018
  - Ordinal regression: OR 0.50, 0.34-0.75, p=0.0007

For the first 6 weeks:
- **Aspirin only versus control**
  - mRS≥2: OR 0.41, 0.22-0.79, p=0.0076
  - Ordinal regression: OR 0.45, 0.25-0.79, p=0.0057

For the first 12 weeks:
- **Aspirin only versus control**
  - mRS≥2: OR 0.50, 0.30-0.86, p=0.0118
  - Ordinal regression: OR 0.50, 0.31-0.81, p=0.0045
Choice of Antiplatelets

• Choices ASA (81-325 mg), Clopidogrel, Aggrenox, Ticagrelor (Socrates trial NS)

• What Aspirin dose?
  • increasing ASA dose increases GI toxic effects
  • NO evidence for 325 or > mg being superior to 80-81 mg

• Dual antiplatelets:
  • ASA + Plavix for 3 months started at 24 hours in patients with high risk TIA and minor stroke is safe and may reduce risk of recurrent stroke at 90 days (Wang et al. CHANCE 2013)
Primary outcome: stroke

Hazard ratio 0.68 (95% CI, 0.57 to 0.81) P<0.001

Survival free of stroke

Days since Randomization

No. at Risk
Aspirin 2586 2307 2287 1906
Clopidogrel - aspirin 2584 2376 2361 1989

8.2 vs. 11.7 %
### Safety outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Aspirin (N=2586)</th>
<th>Clopidogrel-Aspirin (N=2584)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Event No.</td>
<td>Event Risk</td>
<td>Event No.</td>
<td>Event Risk</td>
<td></td>
</tr>
<tr>
<td>Any Bleeding</td>
<td>41 1.6%</td>
<td>60 2.3%</td>
<td>1.41(0.95-2.10)</td>
<td>0.09</td>
</tr>
<tr>
<td>Severe Bleeding</td>
<td>4 0.2%</td>
<td>4 0.2%</td>
<td>0.94(0.24-3.79)</td>
<td>0.93</td>
</tr>
<tr>
<td>Moderate Bleeding</td>
<td>4 0.2%</td>
<td>3 0.1%</td>
<td>0.73(0.16-3.26)</td>
<td>0.68</td>
</tr>
<tr>
<td>Mild Bleeding</td>
<td>19 0.7%</td>
<td>30 1.2%</td>
<td>1.57(0.88-2.79)</td>
<td>0.13</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>10 0.4%</td>
<td>10 0.4%</td>
<td>0.97(0.40-2.33)</td>
<td>0.94</td>
</tr>
</tbody>
</table>

Rate of hemorrhagic stroke 0.3% in both groups
What do you do if your patient has a stroke on ASA etc.?

- Reconsider etiology
- Optimize other risk factors
- Consider switching to another agent or dual antiplatelets for 21 days in minor ischemic stroke or TIA if started within 24 hours
- Medications reduce risk but do not eliminate risk to 0%
Cochrane Review 2015: acute heparin therapy in ischemic stroke

- Early anticoagulation (within 14 days) in early ischemic stroke (90% within first 48 hours)
- 24 trials involving 23,718 participants
- Unfractionated Heparin, LMWH, heparinoids,
- Anticoagulants reduced recurrent stroke (OR 0.76; 95% CI 0.65 to 0.88), pulmonary embolism (OR 0.60; 95% CI 0.44 to 0.81), but increased intracranial hemorrhages (OR 2.55; 95% CI 1.95 to 3.33) and extracranial hemorrhage (OR 2.99; 95% CI 2.24 to 3.99).
- Early anticoagulant therapy is not associated with net short- or long-term benefit in people with acute ischaemic stroke or mortality benefit.
- Not recommended routinely in acute ischemic stroke
How about in patients with Atrial Fibrillation?

- Cardioembolic strokes often have hemorrhagic transformation “petechial”
- Age of patient and larger lesion size are associated with hemorrhagic transformation
- Lack of evidence to rush in to anticoagulation in patients with ischemic stroke especially with heparin - within first 48 hours
- Risk of early recurrent ischemic stroke is low < 5 % (Berge et al. 2000, IST 1997, TOAST 1998); 0.1-1.3% per day (Paciaroni et al 2016)
- Minor stroke likely can start anticoagulation within 3-5 days, TIA earlier after ICH and large stroke ruled out
- Larger strokes 10-14 days (AHA 2014)
Early initiation of anticoagulation with DOACs is it safer and beneficial in patients with non-valvular AFIB?

- Large DOAC trials did not include patients with early stroke or TIA (7-14 days from event)
- Seiffge et al. 2016
  - SWISS NOACISP registry
  - 204 patients with AIS/TIA with AFIB started on OAC with VKA or a DOAC
  - DOAC≤ 7 days vs. DOAC > 7days
  - 65% DOAC started within 7 days median delay 5 days
  - 1 ICH in VKA group (4 days after index event)
  - Recurrent stroke events 6/204, median time-28 days with only 1 patient having OAC initiated > 7 days
Some scenarios you may anticoagulate earlier

• Left ventricular thrombus
• Mechanical mitral valve
• ?carotid thrombus
• Cerebral venous sinus thrombosis
Case 2
Case 2

• 60 yo F from home
• HPI: presented with acute stroke symptoms including aphasia, and mild right arm weakness
• Received IV tPA and endovascular treatment for left M1 occlusion 1h 30 min from symptom onset
• Past Medical History
  • Right Glomus Tumor
  • Left leg swelling x 6 months- investigated with u/s negative for DVT
  • Generally fatigued x several months

• Medications
  • none

• Social History
  • Smoker: ½ PPD x 40 years
Course in hospital

- Patient develops melena stools and drop in HgB- 95 to 70
- Given history of leg swelling- has u/s bilateral legs- which shows extensive above the knee bilateral DVT
- Transthoracic Echo shows a PFO
- Colonoscopy- large rectal mass adenocarcinoma
- CT Thorax: hepatic mass and PE
• Diagnosis: L MCA Stroke. Metastatic rectal adenocarcinoma with bilateral DVT and PE
• Etiology ??
  • Paradoxical embolization

• ? Treatment of DVT/PE
Venous Thromboembolism prophylaxis and treatment in IS

• ~10% risk of DVT and 1% PE in stroke patients
• Risk of major bleeding with heparin DVT prophylaxis in IS
  • ~1-2% (EXCLAIM study 2013; Turpie et al.)
• Who is most at risk (CBPR 2016)?
  • Patients with inability to move one or both lower limbs
  • Patients who are not independent
  • Patients who are dehydrated
  • Patients with cancer
Prevention Options

• Thigh Length Compression Stockings
  • Alone No benefit (CLOTS1 2009)
• IPC (intermittent Pneumatic Compression Stockings)
  • CLOTS3 trial(2013): effective at preventing DVT in stroke patients but increased skin breakdown
  • Still an option if heparinoids are contra-indicated
• Heparin
  • Low Molecular Weight Heparin (Enoxparin 40 mg SC) and Unfractionated Heparin in patients with renal failure
  • Duration: ?period of immobility; continue if patients are immobile after 30 days (Level C)
• Early mobilization and hydration
How about ICH patients?

• Usually withhold DVT prophylaxis for at least the first 48 hours
• Observe for hematoma expansion
• Use IPCs
• Control BP
• Little to no RCT evidence to guide
In this patient

• She received an IVC filter placed
Case 3
• 53 yo M acute onset collapse- noted to be aphasic. EMS called
• In local ED ? Questionable Seizure
• GCS 13, hemiparetic, globally aphasic BP 200/101
• Past medical history: Possible ETOH abuse, HTN, dyslipidemia
• Home meds: Irbesartan, Fenofibrate, Nifedipine
Lobar hemorrhage with intraventricular extension
Intracranial Hemorrhage

Risk Factors
- Hypertension
- ETOH
- Ethnicity
- Age
- Male sex
- ApoE2 and E4 genotype

Etiology
- Hypertensive Angiopathy
- Structural
  - Vascular malformation
- Iatrogenic
  - Antithrombotics
- Congophilic Angiopathy (CAA)
- Cerebral Venous Thrombosis
- Drugs
- Traumatic
- Systemic disease
- Cryptogenic
Treatment Options

1. Manage conservatively

2. Contact neurosurgery for consultation for hematoma evacuation and possible external ventricular drain insertion

3. Treat blood pressure with blood pressure target of <160 SBP and < 90 DBP and contact neurosurgery

4. Treat blood pressure with BP target of < 200 SBP and < 110 DBP
Early surgery vs. Initial Conservative treatment (STICH 2) (Mendelow et al. 2013)

- 307/601 early surgery (12 hours from symptoms)
- Superficial lobar ICH
- 10-100 ml no IVH
- Non-comatose pts

Results:
- No significant difference in disability at 6 mo.
- Trend in mortality favouring early surgery group (18 vs. 24% at 6mo)
Acute Blood Pressure Management: ICH

- no strong evidence that aggressive blood pressure lowering in ICH acutely affects long term outcome, including disability or mortality
- Evidence suggests that lowering blood pressure to systolic < 140 SBP is safe acutely, but can be challenging to achieve and resource intensive
- Intensive BP lowering may prevent hematoma expansion (Tsivgoulos et al. 2015)
INTERACT-2 (Anderson et al. 2013)

• International multi center RCT
• Intensive BP lowering (SBP <140) vs. standard guideline BP lowering (treat if SBP >180) in patients with ICH within 6 hour of onset
• Goal: achieve BP target within 1 hour of randomization
• Agent use: not specified; majority used urapidil
• Primary Outcome: death or major disability (mRS-3-6) at 90 days
Baseline Characteristics of the Participants.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Intensive Blood-Pressure Lowering (N = 1399)</th>
<th>Guideline-Recommended Blood-Pressure Lowering (N = 1430)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from onset of ICH to randomization — hr</td>
<td>3.7</td>
<td>3.7</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>2.8–4.8</td>
<td>2.9–4.7</td>
</tr>
<tr>
<td>Age — yr</td>
<td>63.0±13.1</td>
<td>64.1±12.6</td>
</tr>
<tr>
<td>Male sex — no. (%)</td>
<td>898 (64.2)</td>
<td>882 (61.7)</td>
</tr>
<tr>
<td>Recruited from China — no. (%)</td>
<td>947 (67.7)</td>
<td>973 (68.0)</td>
</tr>
<tr>
<td>Blood pressure — mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>179±17</td>
<td>179±17</td>
</tr>
<tr>
<td>Diastolic</td>
<td>101±15</td>
<td>101±15</td>
</tr>
<tr>
<td>NIHSS score†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>6–15</td>
<td>6–16</td>
</tr>
<tr>
<td>GCS score‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>12–15</td>
<td>12–15</td>
</tr>
<tr>
<td>History of hypertension — no./total no. (%)</td>
<td>1012/1398 (72.4)</td>
<td>1016/1428 (72.5)</td>
</tr>
<tr>
<td>Current use of antihypertensive drugs — no./total no. (%)</td>
<td>627/1398 (44.8)</td>
<td>647/1428 (45.3)</td>
</tr>
<tr>
<td>Prior intracerebral hemorrhage — no./total no. (%)</td>
<td>115/1398 (8.2)</td>
<td>114/1428 (8.0)</td>
</tr>
<tr>
<td>Prior ischemic or undifferentiated stroke — no./total no. (%)</td>
<td>357/1398 (11.2)</td>
<td>166/1428 (11.6)</td>
</tr>
<tr>
<td>Prior acute coronary event — no./total no. (%)</td>
<td>39/1398 (2.8)</td>
<td>42/1428 (2.9)</td>
</tr>
<tr>
<td>Diabetes mellitus — no./total no. (%)</td>
<td>155/1398 (11.1)</td>
<td>150/1428 (10.5)</td>
</tr>
<tr>
<td>Use of warfarin anticoagulation — no./total no. (%)</td>
<td>50/1398 (3.6)</td>
<td>31/1428 (2.2)</td>
</tr>
<tr>
<td>Use of aspirin or other antiplatelet agent — no./total no. (%)</td>
<td>123/1398 (8.8)</td>
<td>142/1428 (9.9)</td>
</tr>
<tr>
<td>Baseline hematoma volume — ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>6–19</td>
<td>6–20</td>
</tr>
<tr>
<td>Deep location of hematoma — no./total no. (%)‡</td>
<td>1084/1294 (83.8)</td>
<td>1098/1319 (83.2)</td>
</tr>
<tr>
<td>Left hemisphere site of hematoma — no./total no. (%)</td>
<td>644/1294 (49.8)</td>
<td>669/1319 (50.7)</td>
</tr>
<tr>
<td>Intraventricular extension of hemorrhage — no./total no. (%)</td>
<td>371/1294 (28.7)</td>
<td>369/1319 (28.0)</td>
</tr>
</tbody>
</table>
Primary, Secondary, and Safety Outcomes at 90 Days.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intensive Blood Pressure Lowering (N = 1399)</th>
<th>Guideline-Recommended Blood Pressure Lowering (N = 1430)</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome: death or major disability — no./total no. (%)†‡</td>
<td>719/1382 (52.0)</td>
<td>785/1412 (55.6)</td>
<td>0.87 (0.79–1.01)</td>
<td>0.06</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score on the modified Rankin scale — no./total no. (%)‡</td>
<td></td>
<td>0.87 (0.77–1.00)</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>0: No symptoms at all</td>
<td>112/1382 (8.3)</td>
<td>107/1412 (7.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1: No substantive disability despite symptoms</td>
<td>202/1382 (22.1)</td>
<td>254/1412 (18.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2: Slight disability</td>
<td>259/1382 (18.7)</td>
<td>266/1412 (18.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3: Moderate disability requiring some help</td>
<td>220/1382 (15.9)</td>
<td>234/1412 (16.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4: Moderate–severe disability requiring assistance with daily living</td>
<td>250/1382 (18.1)</td>
<td>268/1412 (19.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5: Severe disability, bed-bound and incontinent</td>
<td>83/1382 (6.0)</td>
<td>113/1412 (8.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6: Death by 90 days</td>
<td>166/1382 (12.0)</td>
<td>170/1412 (12.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death — no./total no. (%)</td>
<td>166/1394 (11.9)</td>
<td>170/1412 (12.0)</td>
<td>0.99 (0.79–1.25)</td>
<td>0.96</td>
</tr>
<tr>
<td>Health-related quality of life</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Problems with mobility — no./total no. (%)</td>
<td>767/1200 (63.8)</td>
<td>821/1231 (66.7)</td>
<td>0.88 (0.74–1.04)</td>
<td>0.13</td>
</tr>
<tr>
<td>Problems with self-care — no./total no. (%)</td>
<td>563/1202 (46.8)</td>
<td>635/1230 (51.6)</td>
<td>0.83 (0.70–0.97)</td>
<td>0.02</td>
</tr>
<tr>
<td>Problems with usual activities — no./total no. (%)</td>
<td>731/1200 (60.8)</td>
<td>814/1231 (66.1)</td>
<td>0.79 (0.67–0.94)</td>
<td>0.006</td>
</tr>
<tr>
<td>Problems with pain or discomfort — no./total no. (%)</td>
<td>477/1197 (39.8)</td>
<td>552/1227 (45.0)</td>
<td>0.81 (0.69–0.95)</td>
<td>0.01</td>
</tr>
<tr>
<td>Problems with anxiety or depression — no./total no. (%)</td>
<td>406/1192 (34.1)</td>
<td>463/1220 (38.0)</td>
<td>0.84 (0.72–1.00)</td>
<td>0.03</td>
</tr>
<tr>
<td>Overall health utility score</td>
<td>0.60±0.09</td>
<td>0.55±0.40</td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>Living in residential care facility — no./total no. (%)</td>
<td>108/1222 (8.8)</td>
<td>114/1248 (9.1)</td>
<td>0.96 (0.73–1.27)</td>
<td>0.80</td>
</tr>
<tr>
<td>Duration of initial hospitalization — days</td>
<td></td>
<td></td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>20</td>
<td>19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interquartile range</td>
<td>12–35</td>
<td>11–33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Safety outcomes — no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurologic deterioration in first 24 hr†‡</td>
<td>198/1369 (14.5)</td>
<td>211/1395 (15.1)</td>
<td>0.95 (0.77–1.17)</td>
<td>0.62</td>
</tr>
<tr>
<td>Nonfatal serious adverse events[</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any neurologic deterioration from intracerebral hemorrhage‡</td>
<td>326/1399 (23.3)</td>
<td>338/1430 (23.6)</td>
<td></td>
<td>0.92</td>
</tr>
<tr>
<td>Recurrent intracerebral hemorrhage</td>
<td>47/1399 (3.4)</td>
<td>55/1430 (3.8)</td>
<td></td>
<td>0.49</td>
</tr>
<tr>
<td>Ischemic or undifferentiated stroke</td>
<td>8/1399 (0.6)</td>
<td>8/1430 (0.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute coronary event</td>
<td>5/1399 (0.4)</td>
<td>5/1430 (0.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other cardiovascular disease</td>
<td>22/1399 (1.6)</td>
<td>26/1430 (1.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noncardiovascular disease</td>
<td>160/1399 (11.4)</td>
<td>152/1430 (10.6)</td>
<td></td>
<td>0.49</td>
</tr>
<tr>
<td>Severe hypotension†‡</td>
<td>7/1399 (0.5)</td>
<td>8/1430 (0.6)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Effect of Early Intensive Blood-Pressure–Lowering Treatment on the Primary Outcome According to Prespecified Subgroups.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Intensive Treatment</th>
<th>Guideline-Recommended Treatment</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value for Homogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 yr</td>
<td>340 (41.3)</td>
<td>352 (46.7)</td>
<td>0.87 (0.71–1.06)</td>
<td>0.76</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>379 (63.6)</td>
<td>433 (65.7)</td>
<td>0.91 (0.72–1.15)</td>
<td></td>
</tr>
<tr>
<td><strong>Region</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>431 (45.8)</td>
<td>480 (49.6)</td>
<td>0.86 (0.72–1.03)</td>
<td>0.97</td>
</tr>
<tr>
<td>Other</td>
<td>288 (65.5)</td>
<td>305 (68.7)</td>
<td>0.86 (0.65–1.14)</td>
<td></td>
</tr>
<tr>
<td><strong>Time to randomization</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;4 hr</td>
<td>435 (54.3)</td>
<td>465 (56.7)</td>
<td>0.91 (0.75–1.10)</td>
<td>0.48</td>
</tr>
<tr>
<td>≥4 hr</td>
<td>284 (48.9)</td>
<td>320 (54.1)</td>
<td>0.81 (0.65–1.02)</td>
<td></td>
</tr>
<tr>
<td><strong>Baseline systolic blood pressure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;180 mm Hg</td>
<td>372 (50.0)</td>
<td>400 (53.8)</td>
<td>0.86 (0.70–1.05)</td>
<td>0.90</td>
</tr>
<tr>
<td>≥180 mm Hg</td>
<td>347 (54.4)</td>
<td>385 (57.6)</td>
<td>0.88 (0.70–1.09)</td>
<td></td>
</tr>
<tr>
<td><strong>History of hypertension</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>524 (52.5)</td>
<td>555 (54.3)</td>
<td>0.93 (0.78–1.11)</td>
<td>0.12</td>
</tr>
<tr>
<td>No</td>
<td>194 (50.7)</td>
<td>228 (58.9)</td>
<td>0.72 (0.54–0.95)</td>
<td></td>
</tr>
<tr>
<td><strong>Baseline NIHSS score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;15</td>
<td>393 (39.8)</td>
<td>440 (44.3)</td>
<td>0.83 (0.70–0.99)</td>
<td>0.48</td>
</tr>
<tr>
<td>≥15</td>
<td>324 (82.9)</td>
<td>341 (83.4)</td>
<td>0.96 (0.67–1.40)</td>
<td></td>
</tr>
<tr>
<td><strong>Baseline hematoma volume</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;15 ml</td>
<td>285 (39.3)</td>
<td>309 (42.0)</td>
<td>0.90 (0.73–1.10)</td>
<td>0.57</td>
</tr>
<tr>
<td>≥15 ml</td>
<td>383 (69.1)</td>
<td>416 (73.4)</td>
<td>0.81 (0.63–1.05)</td>
<td></td>
</tr>
<tr>
<td><strong>Baseline hematoma location</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep</td>
<td>568 (53.1)</td>
<td>614 (56.9)</td>
<td>0.86 (0.73–1.02)</td>
<td>0.76</td>
</tr>
<tr>
<td>Others</td>
<td>100 (47.6)</td>
<td>111 (49.8)</td>
<td>0.92 (0.63–1.34)</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>719 (52.0)</td>
<td>785 (55.6)</td>
<td>0.87 (0.75–1.01)</td>
<td></td>
</tr>
</tbody>
</table>

*The New England Journal of Medicine*
Original Article

Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage

Adnan I. Qureshi, M.D., Yuko Y. Palesch, Ph.D., William G. Barsan, M.D., Daniel F. Hanley, M.D., Chung Y. Hsu, M.D., Renee L. Martin, Ph.D., Claudia S. Moy, Ph.D., Robert Silbergleit, M.D., Thorsten Steiner, M.D., Jose I. Suarez, M.D., Kazunori Toyoda, M.D., Ph.D., Yongjun Wang, M.D., Haruko Yamamoto, M.D., Ph.D., Byung-Woo Yoon, M.D., Ph.D., for the ATACH-2 Trial Investigators and the Neurological Emergency Treatment Trials Network

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Volume 375(11):1033-1043
September 15, 2016
Mean Hourly Minimum Systolic Blood Pressure during the First 24 Hours after Randomization, According to Treatment Group.

Distribution of Scores on the Modified Rankin Scale, According to Treatment Group.

## Unadjusted Relative Risk of Death or Disability at 3 Months, According to Subgroup.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>No. of Patients</th>
<th>Relative Risk (95% CI)</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glasgow Coma Scale score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3–11</td>
<td>143</td>
<td>0.90 (0.71–1.14)</td>
<td>0.62</td>
</tr>
<tr>
<td>12–14</td>
<td>278</td>
<td>1.16 (0.90–1.49)</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>540</td>
<td>0.97 (0.73–1.28)</td>
<td></td>
</tr>
<tr>
<td>Intraventricular hemorrhage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>253</td>
<td>1.14 (0.95–1.37)</td>
<td>0.53</td>
</tr>
<tr>
<td>No</td>
<td>697</td>
<td>1.00 (0.79–1.26)</td>
<td></td>
</tr>
<tr>
<td>Baseline hematoma volume</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;30 cm³</td>
<td>91</td>
<td>0.95 (0.73–1.22)</td>
<td>0.73</td>
</tr>
<tr>
<td>≤30 cm³</td>
<td>859</td>
<td>1.04 (0.86–1.25)</td>
<td></td>
</tr>
<tr>
<td>Hematoma location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal ganglia</td>
<td>486</td>
<td>1.06 (0.83–1.35)</td>
<td>0.75</td>
</tr>
<tr>
<td>Cerebral lobe</td>
<td>104</td>
<td>1.16 (0.65–2.06)</td>
<td></td>
</tr>
<tr>
<td>Thalamus</td>
<td>359</td>
<td>0.92 (0.74–1.15)</td>
<td></td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>166</td>
<td>1.09 (0.75–1.59)</td>
<td>0.73</td>
</tr>
<tr>
<td>No</td>
<td>778</td>
<td>1.00 (0.84–1.20)</td>
<td></td>
</tr>
<tr>
<td>Met systolic blood pressure target within 2 hr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>901</td>
<td>1.02 (0.87–1.21)</td>
<td>0.51</td>
</tr>
<tr>
<td>No</td>
<td>60</td>
<td>0.61 (0.26–1.43)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>595</td>
<td>1.15 (0.92–1.44)</td>
<td>0.20</td>
</tr>
<tr>
<td>Female</td>
<td>366</td>
<td>0.88 (0.70–1.10)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>555</td>
<td>0.92 (0.73–1.17)</td>
<td>0.60</td>
</tr>
<tr>
<td>Black</td>
<td>117</td>
<td>1.22 (0.81–1.86)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>269</td>
<td>1.09 (0.84–1.42)</td>
<td></td>
</tr>
<tr>
<td>Hispanic ethnic group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>74</td>
<td>0.96 (0.54–1.69)</td>
<td>0.84</td>
</tr>
<tr>
<td>No</td>
<td>887</td>
<td>1.03 (0.87–1.22)</td>
<td></td>
</tr>
<tr>
<td>Enrolled at Asian site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>532</td>
<td>0.95 (0.74–1.21)</td>
<td>0.49</td>
</tr>
<tr>
<td>No</td>
<td>429</td>
<td>1.09 (0.89–1.34)</td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Primary, Secondary, and Safety Outcomes, According to Treatment Group.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Treatment (N = 500)</th>
<th>Standard Treatment (N = 500)</th>
<th>Unadjusted Analysis</th>
<th>Adjusted Analysis†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Relative Risk or Beta Estimate (95% CI)</td>
<td>P Value</td>
<td>Relative Risk or Beta Estimate (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Primary outcome: death or disability</td>
<td>186/481 (38.7)</td>
<td>181/480 (37.7)</td>
<td>1.02 (0.83 to 1.25)</td>
<td>0.84</td>
</tr>
<tr>
<td>— no. (total no. (%)¶)</td>
<td>585/450 (18.9)</td>
<td>104/426 (24.4)</td>
<td>0.78 (0.59 to 1.04)</td>
<td>0.09</td>
</tr>
<tr>
<td>Hernoma expansion — no. (total no. (%)¶)</td>
<td>55 (11.0)</td>
<td>40 (8.6)</td>
<td>1.38 (0.92 to 2.07)</td>
<td>0.13</td>
</tr>
<tr>
<td>Neurologic deterioration within 24 hr — no. (%)¶</td>
<td>8 (1.5)</td>
<td>6 (1.2)</td>
<td>1.33 (0.46 to 3.84)</td>
<td>0.59</td>
</tr>
<tr>
<td>Treatment-related serious adverse event within 72 hr — no. (%)¶</td>
<td>128 (25.6)</td>
<td>100 (20.0)</td>
<td>1.28 (0.99 to 1.66)</td>
<td>0.06</td>
</tr>
<tr>
<td>Hypothesia within 72 hr — no. (%)</td>
<td>6 (1.2)</td>
<td>3 (0.6)</td>
<td>2.00 (0.50 to 8.00)</td>
<td>0.33</td>
</tr>
<tr>
<td>Death — no. (%)</td>
<td>31 (6.6)</td>
<td>34 (6.8)</td>
<td>0.97 (0.60 to 1.57)</td>
<td>0.90</td>
</tr>
<tr>
<td>EQ-SD utility index score**††</td>
<td>-0.01 (-0.05 to 0.02)</td>
<td>0.47</td>
<td>-0.02 (-0.05 to 0.02)</td>
<td>0.29</td>
</tr>
<tr>
<td>Median</td>
<td>0.7</td>
<td>0.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>-0.1 to 1.0</td>
<td>0 to 1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EQ-SD visual-analogue scale score***‡‡</td>
<td>-1.14 (-5.28 to 2.99)</td>
<td>0.59</td>
<td>-1.32 (-5.25 to 2.60)</td>
<td>0.51</td>
</tr>
<tr>
<td>Median</td>
<td>62.5</td>
<td>70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>0 to 100</td>
<td>0 to 100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* The relative risk or beta estimate with 95% confidence intervals for the modified Rankin scale score, hernoma expansion, European Quality of Life-5 Dimensions (EQ-SD) utility index score, and EQ-SD visual-analogue scale score were based on analyses inclusive of missing data imputed by the multiple-imputation method.†† The analysis was adjusted for age, baseline Glasgow Coma Scale (GCS) score, and the presence or absence of intraventricular hemorrhage at baseline.‡‡ Neurologic deterioration was defined as decrease from baseline of 2 or more points on the GCS score or an increase from baseline of 4 or more points on the NIHSS score that was not related to sedation or hypnotic-agent use and that was sustained for at least 8 hours.§§ Treatment-related serious adverse events were assessed by the site investigator.** Since the EQ-SD utility index and the visual-analogue scale scores are continuous variables, beta is the regression coefficient for the treatment effect (standard-treatment group divided by intensive-treatment group) in the generalized linear model. A beta of 0 indicates there was no effect of the treatment on the outcome.†† The EQ-SD utility index (with scores ranging from 0.109 [least favorable health status] to 1.0 [most favorable health status] with 0 impounded for death) was derived by applying Shaw’s weight to the response combinations of five questions regarding mobility, self-care, usual activities, pain and discomfort, and anxiety and depression. Data were missing for 28 patients in the intensive-treatment group and for 27 in standard-treatment group.*** On the EQ-SD visual-analogue scale, patients were requested to indicate their perception of their own health state on a scale of 0 (worst) to 100 (best). Data were missing for 144 patients in the intensive-treatment group and for 144 in the standard-treatment group.
MR BP

- 65 yo M presents with right sided weakness woke up with symptoms
- History of hypertension, diabetes
- Meds: Candesartan, amlodipine, crestor, metformin and lantus
- BP 190/110
- CT head shows an established left corona radiata stroke
Blood Pressure Management

- Treat acutely lower to <140/90
- Admit to hospital treat BP if <220/110, lower by 15% over the next 24 hours, do not exceed 25%
- Lower blood pressure to <185/110 and give tPA
Acute BP lowering in ischemic stroke

- BP will lower spontaneously in many in 24-72 hours post stroke
- Source of ongoing debate
- Also no clear evidence for benefit in improving functional outcome or reducing mortality in acutely lower BP (CBP 2015)
- May be harmful
- Avoid precipitous lowering of BP
- Consider other acute co-morbidities (i.e. MI, aortic dissection, pregnant)
• Patients eligible for IV tPA: target <185/110 and maintain <180/105 for next 24 hours
• Patients not eligible for IV tPA: treat if SBP >220 or DBP >120 (15% reduction no >25% reduction)
• Reintroduce blood pressure agents slowly if patient on antihypertensive medication after 24-48 hours
Conclusions

• Acute stroke care should start right away after the patient has been stabilized and identified as a stroke/TIA requiring admission to hospital.

• Coordinated care teams with expertise in stroke are necessary and effective in reducing stroke mortality and improving functional outcome from stroke.

• Resources and expertise should be concentrated, if possible, in select hospitals to deliver best stroke care.