Emergency Treatment of Patients with Stroke

Coverdell Stroke Registry – Iowa

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Conflicts of Interest

- I adjudicate events in clinical trials sponsored by Merck and I serve on the DSMB for a clinical study funded by Medtronic. I am a consultant to Pierre Fabre (France)

- I receive grant support from NINDS and St Jude Medical

- I will discuss therapies for treatment of stroke that are not approved by the FDA
Importance of Ischemic Stroke

- A leading cause of death and disability among Americans
  - Approximately 800,000 new strokes annually
  - Affects men, women, and children of all ages
  - More common in Blacks, Hispanics
- A leading cause of long-term disability
- The most common acute neurological illness
  - Leading neurological reason for hospitalization
- The frequency of stroke is increasing
  - Aging of the American population
  - Survival of high-risk patients with heart disease
Stroke in Iowa

- 4th most common cause of death – 1,627 deaths
  - 5 Iowans die from stroke every day
  - 3rd most common cause of death among women
  - 14% of the men dying of stroke are < 65
  - The mortality rate from stroke has been declining
- In 2009, 8140 admissions for stroke in Iowa hospitals
- In 2008, average inpatient costs for stroke were $9282
- Total inpatient hospital costs are $78.2 million
Stroke death rates were defined as those with an underlying cause of death classified by the ICD-10 codes 150-159 for years 2000-2009, and ICD-9 codes 430-434 and 435-438 for years 1989-1998. Beginning in 1999 cause of death is specified with the ICD-10 codes. Therefore, 1999 was excluded.
Number of patients = 14,483
Source of data
- IHA Discharge Data
Rural Stroke Care

- Important issue in Iowa
- Approximately 25% of Americans
  - Rural areas or small communities
- Risk of stroke is 1.34 greater than urban areas
  - Elderly, poor, minorities
- Outcomes among rural patients
  - Relative increase in mortality – 18%
- Many problems not unique to rural America
  - Suburban and non-academic hospitals
  - Non-availability of technology/expertise
Special Problems in Rural Areas

- Large distances to hospitals
- Hospitals – limited resources
  - Critical access hospitals
  - Limited experience with stroke
- Non-availability of stroke specialists
  - Neurology
  - Interventional
- Interventions used in this setting
- Time in transfer to medical center
Iowa: Primary Stroke Center and Stroke Capable Hospital Service Area

94.0% of Iowa residents live within 30 minutes of a Primary Stroke Center or Stroke Capable Hospital.

Drive Time Towards Facility:
- Primary Stroke Center - 14 in Iowa, 6 out of state
- Stroke Capable Hospital - 68 in Iowa
- City population 50,000 and over

Prepared by: IDPH CEHI GIS Team
Source: Iowa Heart Disease and Stroke Prevention Program; US Census Bureau - Centers of Population by State, by Census Tract
Created: 2012.11.05
Brain Attack

- Current approach to early treatment of ischemic stroke
- Change attitude of the public and health care system
- Increase the number of persons treated
- Core message
  - Stroke is a life-threatening or life-changing disease
  - Stroke is an emergency
  - Stroke may be successfully treated and outcomes improved
  - Time is brain
- Public education to recognize stroke and best responses
- Organize medical resources to treat stroke
Public Education on Stroke

- Public recognition of symptoms
  - Sudden onset of neurological symptoms
  - May not be recognized by patient, observers are key
  - Family, friends, neighbors, co-workers
- Response – immediately seek medical attention
  - Do not wait for symptoms to resolve
  - Call 911 or brought to the hospital
  - Arriving by EMS expedites early hospital care
  - If not stroke, many be another serious neurological disease
Brain Attack and Heart Attack

- Treatment of stroke modeled on treatment of MI
  - Vascular events secondary to arterial occlusion
  - Need rapid treatment to limit organ injury
  - Treatment centers on reperfusion
  - Best managed in specialized centers
  - Most important early treatment occurs in the community
- Emergency cardiac care system is well-developed
- Need to think of stroke in the same way and add stroke care to the emergency cardiac care system
Current Management of Ischemic Stroke

- Most patients are not treated with reperfusion therapy
- Most patients arrive too late for treatment or their strokes are considered to be mild
- Overall impact of intravenous thrombolysis is limited
- Impact of intra-arterial interventions is very small
Distribution of Use of rtPA in American Hospitals

- 4750 hospitals with 495,000 patients with ischemic stroke
  - 64% of hospitals had not treated a single patient
  - 0.9% of hospitals had treated 10 or more patients
- Low utilization of rtPA
  - Smaller (< 95 beds) hospitals
  - Less densely populated areas in South and Midwest
  - Areas that involve 40% of the American population

Kleindorfer et al, Stroke, 2009; 40: 3580
Ischemic stroke is a common and serious disease
- Potential for death or severe incapacity
- Affects patient and family
An approved therapy of proven value is available
- Intravenous thrombolysis is approved by the FDA
Success is linked to early treatment
Guidelines provide recommendations for care
- Improve safety and efficacy of treatment
- Failure to follow guidelines associated with poorer outcomes
Legal Implications
Treatment of Ischemic Stroke

- Not treating a patient may violate the rule of “doing no harm”
- The primary legal issue is not prescribing rtPA
  - Need a well-documented reason for not treating
  - Clearly state reasons in the medical record
- Medication may be prescribed by any physician
  - Neurological consultation helps comfort levels of primary care or emergency medicine physician
  - Plans for consultation should have these plans in place
- The size of the hospital is not a defense
  - Expected to have a plan for emergency treatment of stroke
Initiatives to Improve Treatment of Stroke

- Organize emergency medical services
- Certification of stroke centers
  - Primary stroke centers
  - Comprehensive stroke centers
- Time goals for emergency treatment
- Development of regional stroke programs
  - Hub-and-spoke system
  - Drip-and-ship strategy
  - Use of technologies to increase availability of neurological expertise
- Get With The Guidelines
First step in stroke management
- The time the stroke is most “acute”
- Meets the need of early intervention
- Matches the approach for MI

More than just assessment – start treatment

Guidelines proved recommendations
- General emergency care
- Hemorrhage or infarction
Current EMS Recommendations

- 100% use of validated pre-hospital screening tools
  - Compare to final diagnoses
  - Use to improve first responder and EMS training
  - Complete minimum of 2 hours of training/year
  - Use stroke history checklists
- Assure that response time is < 9 minutes
- Dispatch time < 1 minute, travel time same as for MI
- Assure pre-arrival notification of hospitals
- Protocols for transfer of patients from non-stroke hospitals to stroke centers

Jauch et al, Stroke 2013
Pre-Hospital Management

- Assess and manage ABCs
  - Do not treat hypertension unless directed by physician
  - Initiate cardiac monitoring
- Provide O₂ to maintain O₂ saturation > 94%
- Establish IV access with saline
  - Do not give excess volume of fluid
  - Do not administer glucose-containing fluids unless patient has hypoglycemia
- Check blood glucose and treat accordingly
- Determine time of onset of stroke
- Obtain family information, preferably a cell phone

Jauch et al, Stroke, 2013
Regional EMS Transport Acute Stroke Systems

- Diversion of patients to hospitals that can treat stroke
  - Emergency medical services
  - Hospitals that are not ready to treat stroke are bypassed
- Regulations that route patients with acute stroke to primary stroke centers or stroke-ready hospitals
  - Initiated in 2000 in Alabama and Texas
  - End of 2010: 16 states and regional areas in 3 additional states
- Covered population
  - 2000 4,471,933 1.5%
  - 2010 164,705,389 53%
- Efforts continue to expand this system
  
Song & Saver, Stroke, 2012; 43: 1975
EMS Educational Programs
Iowa

- Recognize the wide range of EMS programs in the state of Iowa
  - Full-time paramedics
  - Part-time, unpaid volunteers
- Levels of expertise and experience vary
  - Reflect numbers of patients with stroke seen
- Develop programs that will provide core information to EMS directors and personnel
- Key features
  - Recognition of stroke manifestations
  - Early stabilization and obtain key history
  - Prompt notification and transport to stroke-ready hospital
Message for EMS Personnel

- Recognize the common neurological findings
  - FAST – face, arm, speech
- Obtain key historical information
  - FAST – time of onset of symptoms (last normal)
  - Medications or other recent illness
  - Cell phone # of next-of-kin or family member
- Stabilization
  - As with other critically ill people
- Emergency transport
  - Bypass a hospital that cannot treat patient
- Notification of stroke ready hospital – Code Stroke
  
  Jauch et al, Stroke, 2013
Primary Stroke Centers

- Hospitals that have the capability to give emergency stroke care
  - Focus on care in emergency department
  - Communication closely linked to EMS
  - Rapid evaluation and treatment of stroke
  - Administration of intravenous thrombolysis
  - Communities across the United States
- Protocols in place
- Certified by Joint Commission or states
- Another group of hospitals – stroke capable
Development of Regional Stroke Programs

- Integrated between smaller and larger hospitals
  - Hub-and-spoke system
- Increase availability of neurological expertise
  - In person, telephone consultation, telemedicine
- Develop protocols that can be used in community hospitals
  - Emergency evaluation
  - General emergency treatment
  - Administration of intravenous rtPA
- Drip and ship (emergency transfer to larger hospital)
- Increase the number of patients treated with rtPA
Responsibilities – Hub Regional Stroke Network

- Develop stroke care protocols for the network
  - Used at both the hub and spokes
  - Emergency diagnostic studies and therapies
  - Indications for evacuation to the hub
  - Returning the patients back to the community
- Professional educational programs
  - Physicians and hospital personnel
  - Emergency medical services personnel
- Public educational programs
- Coordinate research
Responsibilities – Spokes Regional Stroke Network

- Emergency Medical Services
  - Treat stroke as a level 1 emergency
  - Dispatchers and rescue services
  - Emergency assessment, transportation and notification

- Primary Stroke Centers or Stroke-Ready Hospitals
  - Protocols for emergency management of stroke
  - Potential collaboration with comprehensive center
  - Community outreach programs
    - Public education, health screening and stroke prevention
    - Maintaining continuity of care
Bringing Stroke Expertise to the Community Hospital

- Limited neurological coverage in most small to medium sized communities
  - Non-availability of a neurologist
  - Even less availability of a vascular neurologist
- Develop close links with a comprehensive stroke center
  - Crucial time lost during transfer to center
  - Treatment started locally
- Choices
  - Telephone consultation
  - Teleradiology
  - Telemedicine (telestroke)
Drip-and-Ship
Acute Stroke Treatment in US

- Nationwide inpatient sample
- 22,243 patients treated with IV thrombolysis
- 4,474 patients treated using drip-and-ship approach
  - 81% referred to teaching hospitals
  - 7% had subsequent endovascular treatment
- States using drip-and-ship had higher rates of use of thrombolytic therapy
  - 5.4% vs. 3.3% (p < 0.001)
- Outcomes (home and self care)
  - Drip-and-ship vs. primary emergency department
  - Odds ratio 1.198 (95% CI 1.019-1.409, p = 0.028)

Tekle et al, Stroke, 2012; 43: 1971
Hospital plan to respond to a patient with acute stroke
  - Coordinate emergency assessment and treatment
  - Emergency alerts to the code stroke team
  - Emergency department is usual site for treatment

Development of a code stroke toolbox
  - Initial assessment including orders and laboratory supplies
  - Screening assessment for stroke and rtPA
  - General emergency management
  - Stroke-specific management and availability of rtPA
Joint Commission Time Goals
Treatment of Acute Ischemic Stroke

- Based on Brain Attack Recommendations
  - Door-to-needle time 60 minutes
    - First contact in the emergency department
    - Clinical assessment and diagnosis
    - Results of diagnostic studies
    - Decisions about treatment
    - Starting bolus dose of rtPA
  - Results of diagnostic studies 45 minutes
    - Time of arrival to hospital
    - CT, laboratory, and ECG
Door to Needle Times
Get With The Guidelines

GOAL
50%

DTN in 60 minutes or less
Eligible Get With The Guidelines-Stroke/Target: Stroke
acute ischemic stroke patients January 2012 to December 2012
Emergency Questions

- Are the neurological symptoms due to stroke?
- Is the stroke hemorrhagic or ischemic?
- Are there acute medical or neurological complications that affect early treatment?
- Is the patient eligible for intravenous thrombolytic treatment?
Hemorrhagic stroke

Seizures with post-ictal signs

Migraine (may or may not have headache)

Metabolic disorder
  - Hypoglycemia

Occult trauma

Intracranial mass
  - Subdural hematoma
  - Tumor

Somatization disorder
Clinical Features of Ischemic Stroke

- Sudden onset of focal neurological symptoms
  - Usually maximal at onset
  - May wax and wane or slowly progress
- Signs should fit within a defined vascular territory
  - Cerebral hemisphere – hemiparesis, sensory loss, visual field defect, aphasia, neglect
  - Brainstem/cerebellum – ataxia, cranial nerve palsy, dysarthria, bilateral motor signs, crossed signs
- Rarely associated with loss of consciousness
- Approximately 20% of patients have headache
- Nausea and vomiting occur with brainstem or cerebellar infarction
## NIH Stroke Scale

<table>
<thead>
<tr>
<th>Category</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consciousness</td>
<td>0 - 3</td>
</tr>
<tr>
<td>Commands</td>
<td>0 - 2</td>
</tr>
<tr>
<td>Visual fields</td>
<td>0 - 3</td>
</tr>
<tr>
<td>Arm motor (x2)</td>
<td>0 - 4</td>
</tr>
<tr>
<td>Limb ataxia</td>
<td>0 - 2</td>
</tr>
<tr>
<td>Language</td>
<td>0 - 3</td>
</tr>
<tr>
<td>Inattention</td>
<td>0 - 2</td>
</tr>
<tr>
<td>Orientation</td>
<td>0 - 2</td>
</tr>
<tr>
<td>Gaze</td>
<td>0 - 2</td>
</tr>
<tr>
<td>Facial paresis</td>
<td>0 - 3</td>
</tr>
<tr>
<td>Leg motor (x2)</td>
<td>0 - 4</td>
</tr>
<tr>
<td>Sensory</td>
<td>0 - 2</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>0 - 2</td>
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</tbody>
</table>

Impact of NIHSS Scores on Outcomes

Brain imaging
  - May be either CT or MRI
  - CT generally more readily available in community hospitals
  - Quick, non-invasive, and relatively inexpensive
  - Gives key information for emergency care

Electrocardiogram

Complete blood count and platelet count

INR and aPTT

Cardiac enzymes, renal studies, glucose

Pulse oximetry
Dense Artery Sign
Similar to other acutely and seriously ill patients

**ABC of life support**
- Airway protection if decreased consciousness or brainstem dysfunction
- Oxygen supplementation not needed unless hypoxic

**Monitor vital signs and neurological status**

**Intravenous access with normal saline**

**Treat fever and look for source of fever**

**Treat serious cardiac arrhythmias**

**Symptomatic treatment – pain, nausea, agitation**
Elevations in blood pressure common – underlying risk factor, stress, physiological response for perfusion

Management is controversial because of lack of clinical trial evidence

Aggressive lowering of blood pressure is not recommended because of risk of worsening of stroke

Need to lower blood pressure to treat rtPA

IV administration of short-acting medications

- Labetalol, nicardipine, apresoline, sodium nitroprusside

Jauch et al, Stroke, 2013
Intravenous Thrombolysis

- Approved medical therapy for treatment of carefully selected patients with acute ischemic stroke
- Engine that is driving acute stroke care
- Improve neurological outcomes
- May “cure” patients
- Efficacy is time-linked
- Cannot be given with impunity – does cause bleeding
- Effective therapy of limited usefulness because too few patients are being treated
### Interval from Stroke Onset and Responses to Intravenous rtPA

Pooled analyses of clinical trials

<table>
<thead>
<tr>
<th>Time</th>
<th>Odds of Favorable Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 90 minutes</td>
<td>2.55 (1.44 – 4.52)</td>
</tr>
<tr>
<td>91 – 180 minutes</td>
<td>1.64 (1.12 – 2.40)</td>
</tr>
<tr>
<td>180 – 270 minutes</td>
<td>1.34 (1.06 – 1.68)</td>
</tr>
<tr>
<td>270 – 360 minutes</td>
<td>1.22 (0.92 – 1.61)</td>
</tr>
</tbody>
</table>

Lees et al, Lancet, 2010; 375: 1695
Recommendations for Intravenous Thrombolysis

- IV administration of rtPA is recommended
  - 0.9 mg/Kg (maximum dose is 90 mg)
  - 10% as bolus, remainder infused over 1 hour
- Carefully selected patients < 3 (4.5) hours
- Can be associated with side effects
  - Overall risk of bleeding is 6%, higher with severe strokes
  - Does not increase mortality
  - Uncommon risk of angioedema
- Success in clinical settings is similar to that achieved in trials
- Success is linked to compliance with guidelines

Jauch et al, Stroke, 2013
Intravenous Thrombolysis
3 – 4.5 Hours

- Goal remains to treat as quickly as possible
- Expansion of time window from 3 to 4.5 hours
- This expansion in time not approved by FDA
  - Require a similar study in the US
- Dosage of rtPA and ancillary care similar
- Some differences in criteria for treatment (3 – 4.5 hours)
  - Age less than 81
  - Maximum NIHSS score – 25
  - Diabetes and history of prior stroke
  - Warfarin use (regardless of level of INR)

Impact on the numbers treated is relatively small
- Approved by European Regulatory Authorities
- Not approved by FDA
  - Did not find the data compelling
  - Requested another study in the US
  - Such a study is not likely to be done
- Marketing of the medication for this indication
- Influence CMS decisions about reimbursement for treatment in time window
- Guidelines continue to recommend the administration of rtPA up to 4.5 hours after onset of stroke

Wechsler and Jovin, Stroke, 2012; 43: 2517
Did the stroke happen in the last 3 – 4.5 hours?
- Stroke upon awakening or unwitnessed stroke
- Minor symptoms with subsequent worsening
- TIA followed by a second (new) event
- Remember the difference in criteria for those treated < 3 hours and those treated 3 – 4.5 hours
- If the stroke is > 3 hours but < 4.5 hours
  - Age must be < 81 for treatment in 3 – 4.5 hours
  - No age restriction for treatment < 3 hours
Any co-morbid disease or recent illness that could be associated with a high risk of bleeding complications?
- History of prior cerebral hemorrhage
- Recent stroke or myocardial infarction
- Recent major trauma or surgery
- Recent major bleeding

Is the patient taking oral anticoagulants?
- If taking warfarin, do not treat in 3 – 4.5 hours
- If taking warfarin, treat in < 3 hours if INR is < 1.8
- Aspirin, clopidogrel, dipyridamole, ticlopidine
- Safety with use of thrombin or direct Xa inhibitors is not known. Interim plan: not to treat if drug was given < 48 hours
- Are baseline coagulation tests normal?
  - Primary issue is anticoagulant use or a history of bleeding
  - Abnormal coagulation tests preclude treatment
  - Tests take time to perform and may treat in some instances if tests are delayed
  - Finger stick test for INR
  - Prolonged aPTT as a marker for dabigatran effect
- Is the patient a diabetic and has a history of a previous stroke?
  - May treat < 3 hours but not in 3 – 4.5 hour time period
- Is the patient taking an ACE-inhibitor?
  - Not a contraindication
  - May be associated with increased risk of angioedema
What is the score on the NIH Stroke Scale?

- No minimum score for treatment
  - Mild stroke may worsen subsequently
  - Composition of score may influence decision
  - A patient may be disabled despite a low score
- No maximum score for treatment < 3 hours
  - Use caution with very severe stroke
  - Higher risk of bleeding complications
  - No increase risk in mortality
- Maximum score for treatment in 3 – 4.5 hours
  - NIHSS score < 25
What are the findings on brain imaging?
- Presence of a hemorrhage – contraindication
- Stroke appears to be older than 3 – 4.5 hours
- Very large ischemic lesion is detected
- Presence of a dense artery sign – usually a severe stroke

Are the patient/family aware of risks of treatment?
- Overall risk of symptomatic bleeding is approximately 6%
- Hemorrhagic transformation of infarction or hematoma
- Risk of bleeding greater in patients with severe strokes
- FDA approved therapy and guidelines available
A number of variables have identified those patients at the highest risk for bleeding following intravenous thrombolysis:

- Elderly, severe strokes, elevated glucose, serious comorbid diseases, cardioembolism
- None of these variables is an absolute contraindication to treatment
- Many of these variables also portend a poor outcome without treatment
- The presence of multiple “risk factors” for a hemorrhagic complication should lead to a careful discussion with the patient and family about the risks and benefits of treatment
Treatment After Thrombolysis

- Close observation and monitoring during first hours
  - Neurological status
  - Blood pressure and vital signs
- Aggressively treat arterial hypertension
  - If systolic > 180 mm Hg or diastolic > 110 mm Hg
  - Parenterally administered, short-acting medications
- Delay placement of devices associated with bleeding
  - Nasogastric tube
  - Bladder catheter
  - Central venous line
Stroke now is being treated as the emergency it is
Requires coordination and collaboration
- Public
- All components of the health care system
- Government and third-party payers
Need to address hurdles to early treatment
- Each community or region has its own issues to address
- Overcome these hurdles with careful and proactive planning
Future Stroke Treatment

- Likely will have new interventions for treating stroke
- Combinations of interventions
  - Thrombolysis and neuroprotective agents
  - Intravenous and intra-arterial interventions
  - Adjunctive use of antithrombotic agents
- Improved selection of patients for specific therapies
- Treatments that could be started in ambulance or helicopter
- Regardless of advances, the success of future stroke treatment will remain time-linked and time-limited