

Regional Systems of Care Best Practices Operations Manual

Version 1.1 January 2019



IMplementation of best
PRactices **fO**r acute stroke care —
de**VE**loping and optimizing regional
systems of **Stroke Care**



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INTRODUCTION

Stroke is the 5th leading cause of death in the United States and the leading cause of disability among Americans. On average, every 40 seconds someone in the United States has a stroke, adding up to nearly 800,000 strokes per year. For the past 20 years, the only evidenced based therapy for acute ischemic stroke treatment has been thrombolysis alteplase (recombinant intravenous tissue plasminogen activator- rt-PA). Despite this decades-long standard,

rates of use of alteplase and rates of use within the recommended 60 minutes from arrival to hospital remained low and slow. The American Heart Association/American Stroke Association's Target: Stroke program (launched in 2010 and followed by Phase II in 2014) improve door-to-needle (DTN) times for tPA-eligible patients by advocating for best practice strategies ([Table 1](#)), resulting in significant improvements the hospital reperfusion times.

Table 1. Target: Stroke Key Best Practice Strategies¹

Strategy	Best Practice	Explanation
01	Advance hospital notification by EMS	EMS providers should, if feasible, provide early notification to the receiving hospital when stroke is recognized in the field. Advance notification of patient arrival by EMS can shorten time to CT and improve the timeliness of treatment with thrombolysis.
02	Rapid triage protocol and stroke team notification	Acute triage protocols facilitate the timely recognition of stroke and reduce time to treatment. Acute stroke teams enhance stroke care and should be activated as soon as the stroke patient is identified in the emergency department or after notification from pre-hospital personnel.
03	Single-call activation system	A single-call should activate the entire stroke team. A single-call activation system for the stroke team is defined here as a system in which the emergency department calls a central page operator, who then simultaneously pages the entire stroke team, including notification for stroke protocol imaging.
04	Stroke tools	A stroke toolkit containing clinical decision support, stroke-specific order sets, guidelines, hospital-specific algorithms, critical pathways, NIH Stroke Scale, and other stroke tools should be available and used for each patient.
05	Rapid acquisition and interpretation of brain imaging	It is essential to initiate a CT scan (or MRI) within 25 min of arrival and complete interpretation of the CT scan within 45 min of arrival to exclude intracranial hemorrhage prior to administration of intravenous tPA.
06	Rapid laboratory testing (including point-of-care testing if indicated)	When indicated, laboratories such as platelet count and—for patients in whom coagulation parameters should be assessed due to suspicion of coagulopathy—INR(PT)/PTT results should be available as quickly as possible and no later than 45 min after ED arrival. If standard stat laboratory turnaround times cannot meet this target, point-of care testing in the emergency department can provide the data in the needed timeframe.
07	Mix tPA medication ahead of time	Mix drug and set up the bolus dose and 1-hour infusion pump as soon as a patient is recognized as a possible rtPA candidate, even before brain imaging. Early preparation allows tPA infusion to begin as soon as the medical decision to treat is made. It is the policy of some drug manufacturers to replace, free of charge, medications that are mixed but not used in time-critical emergency situations such as these. Check with your hospital pharmacy for the proper procedures that will allow you to use this strategy to shorten time to treatment without financial risk.
08	Rapid access to intravenous tPA:	Once eligibility has been determined and intracranial hemorrhage has been excluded, intravenous tPA should be promptly administered. tPA should be readily available in the emergency department or CT scanner area (if CT scanner is not located in the ED). Dosing charts and standardized order sets can also facilitate timely administration and minimize dosing errors.
09	Team-based approach	The team approach based on standardized stroke pathways and protocols has proven to be effective in increasing the number of eligible patients treated and reducing time to treatment in stroke. An interdisciplinary collaborative team is also essential for successful stroke performance improvement efforts. The team should meet frequently to review your hospital's processes, care quality, patient safety parameters and clinical outcomes, as well as to make recommendations for improvement.
10	Prompt data feedback	Accurately measuring and tracking your hospital's door-to-needle times, IV tPA treatment rates in eligible patients and performance on other stroke performance/quality measures equip the stroke team to identify areas for improvement and take appropriate action. A data-monitoring and feedback system includes using the Get With The Guidelines-Stroke Patient Management Tool (PMT) and creating a process for providing timely feedback on a case-by-case basis and in hospital aggregate. This system helps identify specific delays, set targets and monitor progress on a case-by-case basis.

EMS indicates emergency medical system; CT, computed tomography; NIH, National Institutes of Health; MRI, magnetic resonance imaging; INR, International Normalized Ratio; PT, Prothrombin Time; PTT, Partial Thromboplastin Time; ED, emergency department; tPA, tissue-type plasminogen activator; IV, intravenous; PMT, patient management tool.



These efforts demonstrated that stroke care can be markedly improved with large scale campaigns to coordinated care and promote evidence based care through simple, uniformly implemented organizational changes.

Optimizing Systems of Stroke Care

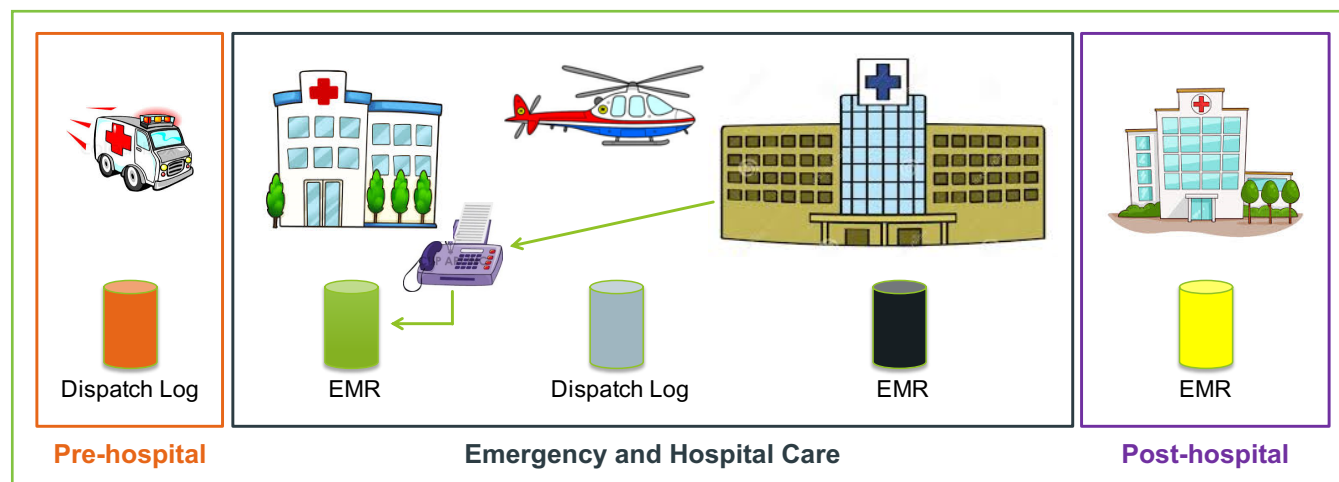
The year 2015 saw the publication of results from 5 large randomized clinical trials showing the efficacy of endovascular thrombectomy (EVT) for treatment of acute ischemic stroke in carefully selected patients, and with a longer treatment window than tPA.⁴⁻⁸ This groundbreaking development in stroke care necessitated a complete paradigm shift in acute management of stroke patients. In 2015, the American Heart Association published new guidelines on the early management of patients with acute ischemic stroke regarding endovascular treatment and recommended treatment for selected patients presenting with acute ischemic stroke with endovascular thrombectomy using newer generation stent retrievers,⁹ making EVT standard of care for large vessel occlusions. Therefore, although thrombolysis with alteplase (t-PA) remains a potential therapy for many patients, the availability of EVT in a timely fashion must now be a consideration in developing stroke systems of care.

Systems of stroke care delivery vary considerably throughout the world, and across the United States. Although there have been regions where coordinated management of patients presenting with acute ischemic stroke occur, a considerable degree of fragmentation of care exists ([Figure 1](#)). There are three broad phases of care; pre-hospital (red box), emergency/hospital care (blue box), and post-hospital (purple box). While data may be captured in various ways in each phase, there is no sharing or pooling of data for any given patient to allow for rapid assessment of efficiency of the processes. In addition, EMS systems across regions and within states vary considerably in terms of training, resources, and level of service provided.

Improving and standardizing systems of care delivery has the potential to improve patient outcomes as much as, if not more than, novel drugs, devices, and new practices. The ideal system of care systematically applies pre-specified and coordinated processes resulting in timely and routine application of evidence based therapies. Integral to the system is the routine collection and timely feedback of relevant data to all providers involved in the care of the stroke patient ([Figure 2](#)).

To effectively expand access to rapid reperfusion (using alteplase and/or EVT), systems of care

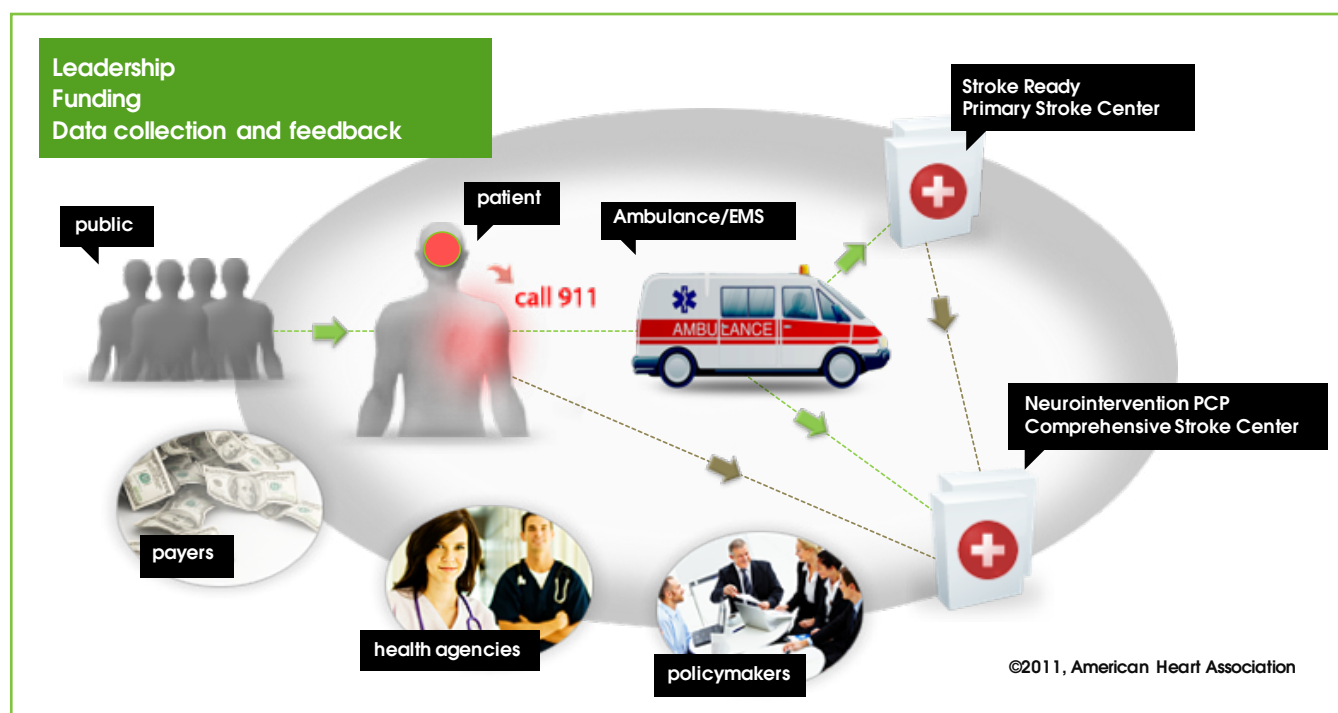
Figure 1. Fragmentation of Care in Current Stroke Systems of Care



There are three broad phases of care to consider in stroke care systems. The prehospital phase (red box), the emergency care and acute hospitalization phase (blue box), and the post hospital rehab or skilled nursing phase (purple box). In addition to the differences in the focus of care and assessment, the records regard the care delivered in each phase also tends to remain isolated from the records within the other phases (colored cylinders).



Fig. 2 The Ideal System of Care



In the above diagram, mobile applications and electronic communication systems are implemented to facilitate care being delivered in each phase and communication between providers within different phases (green arrows to solid green line). The data is captured to a common repository where process times and efficiency can now be assessed on a case-by-case basis. Mobile apps can also be used to automate and capture self-reported outcomes. The post hospitalization phase poses some unique challenges in this concept design and may represent a new opportunity for database contributions such as get with the guidelines.

must be developed at the regional level, leveraging expertise and resources from large centers and the reach and access afforded by numerous community hospitals through hub-and-spoke models. The same strategies and lessons learned from Target: Stroke to reduce DTN times can be extrapolated and expanded to entire regions to reduce reperfusion times. In addition, effectively utilizing the data from a larger regionalized system and rapid feedback of data allows for continual improvement on a large scale, improving outcomes for more patients (Figure 3).

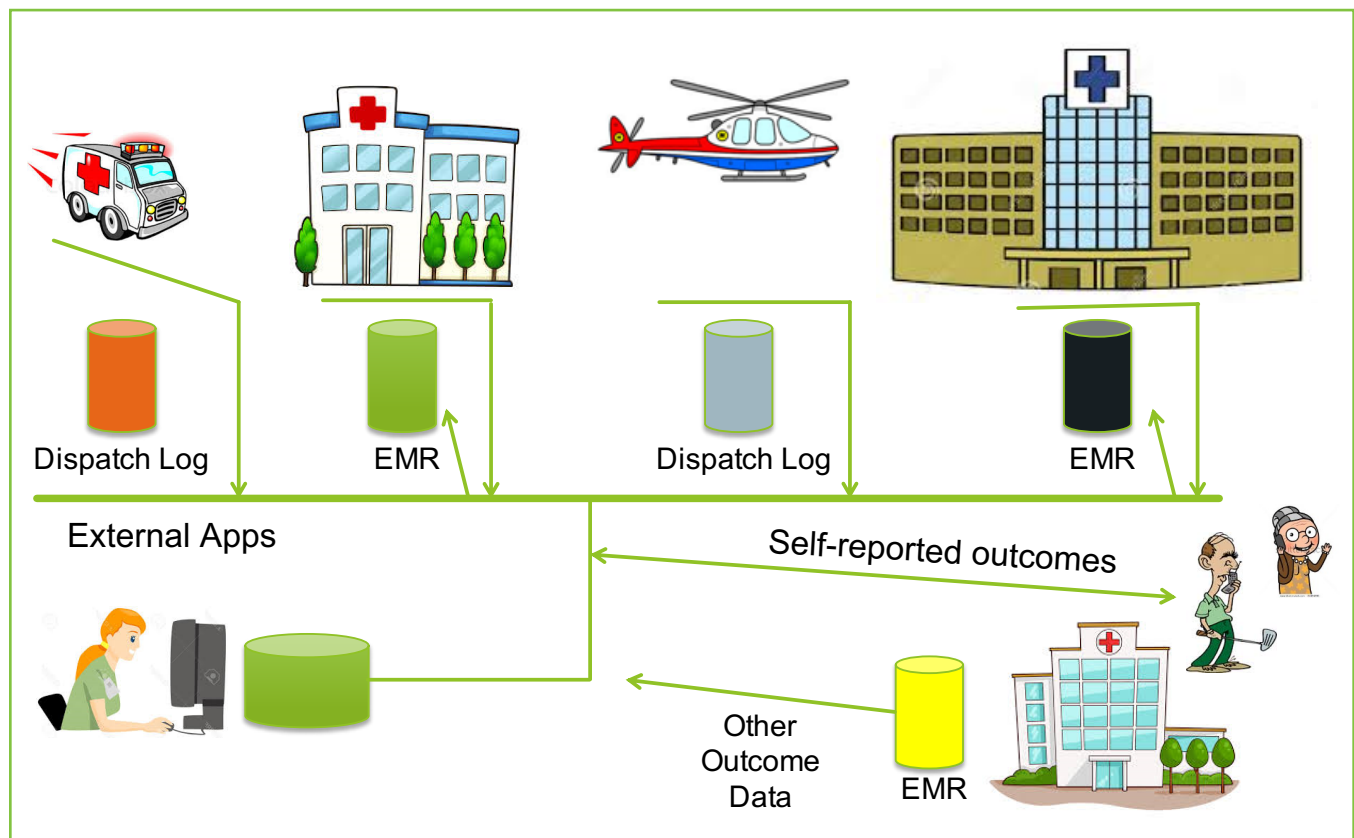
PROJECT OVERVIEW

Incorporating progressive approaches to regional system problems is a key goal of IMROVE Stroke Care. Regional systems will be composed of selected core hospitals (Hubs) and their associated spoke-hospitals, as well as their corresponding emergency medical service providers within a multi-state region

in the heart of the “Stroke Belt” (North Carolina, South Carolina, Georgia, and Tennessee). The IMROVE Stroke Care program will focus on optimizing the prehospital (EMS systems) as well as the acute care in the emergency department and when indicated, the neurointervention suite up to the time of ICU or stepdown admission. Strong evidence based guidelines already exist for the subsequent hospital based care of the acute stroke patient and as such these will be incorporated into the program guidelines. As the majority of patients presenting with acute stroke symptoms have an ischemic etiology as the underlying cause, the main focus of the program will be to optimize reperfusion therapy. However, for those patients presenting with an acute intracerebral hemorrhage, we will focus hyper acute treatment guidelines on the management of hypertension and the reversal of coagulopathy associated with anticoagulant use, as these two areas are the most time sensitive in terms of impact on outcomes.



Figure 3. An integrated System of Care with Web-based Application Functionality



To supplement established guidelines and evidence-based methodology, national and international experts in regional stroke system organizations were surveyed to identify additional effective strategies to accelerate reperfusion therapy delivery. In combination with continual data collection using novel acquisition tools and feedback within networks, systems can identify effective strategies and refine processes to improve care delivery and patient outcomes.

Key Process Objectives

The process for systems optimization will utilize proven implementation science approaches, including provision of standardized clinical care pathways (Stroke Care Manual of Operations), multidisciplinary education, optimization of acute care processes at the local level, improving data captures tools, developing real-time feedback

systems, and disseminating knowledge throughout the consortium to facilitate quality improvement efforts.

1. *Identify and establish regional leadership* in emergency neurovascular in a collaborative fashion—care that includes physician specialists (neurology, radiology, neurointervention, emergency medicine), stroke coordinators, nurses, and hospital administrators from participating institutions, and regional leadership from emergency medical services, the American Heart Association, and pertinent health authorities.
2. *Perform a baseline needs assessment to create an ideal plan* for system improvements, and implement these improvements through ongoing data assessment and feedback on a monthly basis for a minimum of one year.



Project Objectives

The overall objective of the IMPROVE Stroke Care program is *to increase the rate and speed of timely cerebral reperfusion for patients presenting with acute stroke who are eligible for intervention by optimizing systematic and coordinated care with a focus on the initial prehospital and acute phase of care.*

The following treatment and outcome measures will be used to evaluate the optimization of the stroke systems participating in the program.

- A. **Community and patient engagement through targeted education.** The following measures will evaluate the effectiveness of community and patient engagement through public education focusing on stroke recognition and activation of EMS:
 1. Time from symptom onset to first medical contact (ED or 911 activation)
 2. Time from recognition of stroke symptoms (for wake-up stroke) to first medical contact (ED or 911 activation)
 3. Proportion of patients with acute stroke symptoms that present to the ED via EMS vs private vehicle
 4. Proportion of patients presenting with acute ischemic stroke who qualify for acute reperfusion therapy (chemo thrombolysis with alteplase and/or mechanical thrombectomy)
- B. **Optimizing hospital-based processes** involved in the evaluation and treatment of patients with acute stroke from the Emergency Department (ED) and when appropriate to the interventional suite and eventually the ICU or stepdown unit. Key measures of success will be based on the following core metrics of treatment:
 1. **Prehospital evaluation and transfer protocols**
Evaluate current diagnostic modalities for acute stroke identification and establish metrics and methods for time data collection via the following objectives:
 - a. Reliably track the time from first medical contact (EMS) to ED arrival
 - b. Evaluate the accuracy of 911 operators in identifying stroke cases (compared to final discharge diagnosis)
 - c. Evaluate the accuracy of prehospital stroke scales identifying stroke patients (compared against final discharge diagnosis)
 - d. Determine the under and over triage rates for patients transferred for intra-arterial therapy evaluation (compared to initial findings on CTA at destination hospital)
 - e. Establish a predetermined plan for acute stroke identification and timely disposition to the most appropriate hospital, regardless of where the acute stroke patient enters the system.
 2. **Emergency department acute stroke care protocols**
Ischemic stroke acute treatment targets:
 - a. ED arrival to initiation of alteplase (door-to-needle time)
 - b. ED arrival to initiation of mechanical thrombectomy (door-to-groin stick)
 - c. ED arrival to successful reperfusion defined as TICI 2b/3 flow (door-to-successful reperfusion)
 - d. Proportion of patients who are eligible for mechanical thrombectomy and receive it
 - e. Proportion of patients who are eligible for alteplase and receive it
 Intracerebral hemorrhage treatment targets:
 - a. Control of hypertension to target pressure (usually <160 mmHg or less)
 - b. For patients requiring anticoagulation reversal, ED arrival to initiation of acute therapy for reversal of coagulopathy such as prothrombin concentrate, fresh frozen plasma, idarucizumab, and andexanet (when approved) (door to start of coagulopathy reversal agent).



3. Interhospital transfer processes

Inter-hospital transfer times will be monitored in order to evaluate the operational efficiency of a multihospital system of stroke care, which often is composed of a comprehensive stroke center [CSC] or interventional-capable center [ICSC] and a number of referring hospitals [primary stroke centers [PSC] or stroke ready [SR] hospitals. (as defined by The Joint Commission).

The following metrics will be measured:

- Time from presentation at community hospital to contact with CSC or ICSC (tele-stroke activation time) or time to phone connection with CSC or ICSC)
- Time from decision to transfer (by tele-stroke or receiving center consultant) to arrival of transfer team at community hospital
- Time from transfer team arrival at referring hospital to departure of transfer team (door-in-door-out time, at hospital time).
- Time to arrival at CSC/ intervention capable hospital from departure at first hospital
- Time from patient arrival at ED to time of transfer out (Door in Door Out)

4. Clinical outcome measures

Long-term functional outcome after a stroke according to 90-day modified Rankin Scale score.

Participating Hubs; Neurovascular Centers

Comprehensive Stroke Centers (CSC) and Intervention Capable Stroke Centers (ICSC) in a multi-state core region of the “Stroke Belt” (Figure 4) will be invited to join the IMPROVE Stroke Care consortium through a Request for Application (RFA) invitation. Participating centers will be selected according to a number of predefined criteria supporting their commitment to systems improvement both on a clinical and administrative level. The project will initial focus on those

Figure 4. IMPROVE — Southeastern Stroke Care Consortium



centers which that employ stroke telemedicine or “telehealth” services in their stroke system. The participating Hub will choose 2–10 spoke hospitals within its network for participation in the consortium. Spoke hospitals may be either primary stroke centers or stroke ready hospitals (Table 2).

Table 2. Stroke Hospital Types

Type of Hospital	Reperfusion Thrombolysis: Yes	Reperfusion Neurointervention: Yes
Comprehensive Stroke Center	✓	✓
Intervention Capable Stroke Center	✓	✓
Primary Stroke Center	✓	
Acute Stroke Ready	✓	
Other		



Manual of Operations

This IMROVE Stroke Care manual of operations is designed to provide a standardized and structured guideline for care of the stroke patient throughout the ‘Stroke Chain of Survival’, from symptom detection to post-care disposition and follow-up management (Table 3).

Table 3. Stroke Chain of Survival¹⁰

Detection	Patient or bystander recognition of stroke signs and symptoms
Dispatch	Immediate activation of 9-1-1 and priority EMS dispatch
Delivery	Prompt triage and prehospital notification followed by transport to most appropriate stroke hospital
Door	Immediate ED triage to high-acuity area or CT scanner if patient is stable
Data	Prompt ED evaluation, stroke team activation, laboratory studies, and brain imaging if not already done
Decision	Diagnosis and determination of most appropriate therapy: discussion with patient and family
Drug/Device	Administration of appropriate drugs or other interventions
Disposition	Timely disposition to stroke unit, intensive care unit or hospital transfer

ED — Emergency department; EMS — emergency medical services

Throughout the manual, practice recommendations are divided into three major evidence categories ranging from established guidelines as the highest level recommendations, to expert, consensus-based best practices (Figure 5). The manual is intended to be a “living document,” with recommendations being modified as new data becomes available during the process of program implementation (Figure 6).

Figure 5. Categorical Levels of Recommendations in the Manual of Operations

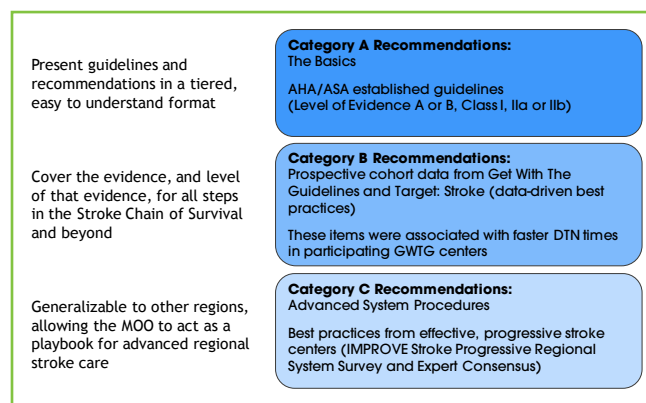
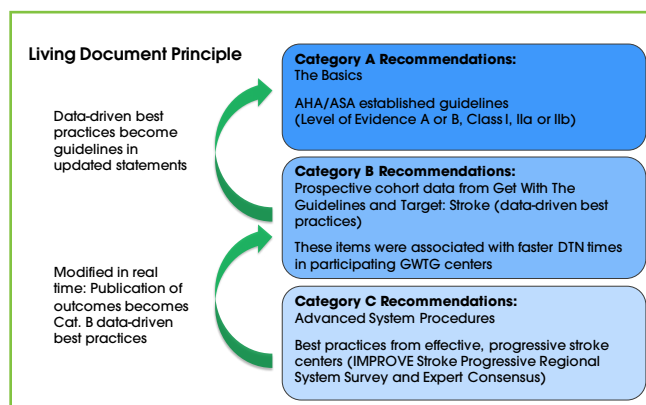


Figure 6. Mechanism for Modification of Stroke Care Recommendations





PREHOSPITAL STROKE CARE

Stroke Recognition and Activation of EMS: Public Engagement through Outreach and Targeted Patient Education

By far the most common reason that a patient with an acute ischemic stroke is disqualified from receiving reperfusion therapy is due to late presentation. Patients and/or their families often fail to recognize the symptoms of acute stroke early-on, and they often do not activate emergency medical dispatch, hindering triage and transport to a medical facility capable of providing appropriate acute stroke care.^{11,12}

Knowledge of stroke symptoms varies considerably across age groups, as well as racial, socioeconomic and ethnic lines. In a national survey conducted in 2009, awareness of 5 stroke warning symptoms and the need to call 911 was highest among whites compared to African Americans and Hispanics (55.9%, 47.1% and 36.5%, respectively). A study conducted among patients admitted to the ED with possible stroke showed that 39% did not know a single sign or symptom of stroke. Overall, almost 40% of patients did not know the signs, symptoms or risk factors for stroke. The median delay time from onset of symptoms to presentation to the ED was 16 hours with only 32% being seen in the ED within 2 hours of symptom onset. Non-use of the 911 system was one of the more significant predictors of delay to presentation within 2 hours. Studies evaluating patterns of emergency medical use and its association with timely stroke treatment have shown that over one third of patients with symptoms of acute stroke still present to the ED having been brought in by private vehicle.¹³ This number is even larger among racial minority populations such as African Americans, Native Americans, and those of Latino origin, as well as in people living in rural communities compared to urban settings.

Recommendations

1. Engage in public education using stroke awareness educational programs such as the AHA's "FAST" campaign. (Category A)
2. Develop targeted educational efforts specifically focusing on high risk groups such as the elderly, African Americans, Latino, and Native Americans and rural based populations by working through faith-based and culturally-based organizations. (Category C) (PSA's and Social Media)
3. Engage local business and corporate partnerships to support public education efforts in the community. (Category C)

Outcome Measures to be Followed

1. Time from last known normal to contact with health system (time to activation of 911 or presentation to the ED).
2. Proportion of patients with stroke symptoms presenting to the ED within 0–3 hours and within 3–4.5 hours of symptom onset. (Longer acceptable time windows may be recommended once the DAWN and DIFUSE studies are published.)
3. Proportion of patients with acute stroke symptoms presenting to the ED via EMS transport.

EMS: Dispatch

Most often, the first point of contact between a patient who is experiencing an acute stroke (or whoever is calling on their behalf) and the health care system is with the 911 operator. Training these individuals to ask the appropriate questions in order to recognize that a person is having an acute stroke is critical. In addition, helping the patient or their family prepare for the arrival of EMS responders in order to avoid loss of time needed to prepare and transport the patient to the closest most appropriate health care facility is of utmost importance. Creating pre-established structured telephone interviews for suspected stroke patients would allow this process



to be consistent and thorough. The following recommendations aim to address these issues:

Basic Recommendations

1. Train 911 operators to recognize acute stroke symptoms and dispatch appropriate EMS resources for stroke care. (Category A)
2. Create protocols for addressing stroke specific questions to be addressed when a suspected stroke case is encountered. (Category C)

Advanced Recommendations

1. Train 911 operators on preparing the family to provide key medical history to EMS personnel including (Category C):
 - a. Last time seen normal (LTSN)
 - b. Concurrent medical problems
 - c. Current medication list and times last taken
 - d. Allergies
 - e. Contact number for legal authorized representative (LAR)

Outcome/Process Measures to be Monitored

1. Time from 911 activation to EMT contact with patient
2. Accuracy of dispatch for a suspected stroke (evaluated against initial diagnosis by stroke team as well as against final discharge diagnosis).
3. Time spent on scene by EMS personnel (on-scene time)

EMS: System Organization

EMT/Paramedic Stroke Training Recommendations (EMS Personnel could include EMTs, AEMT or Paramedics)

1. EMS personnel should all be trained in the use of a prehospital stroke screening scale. (Category A)
2. EMS/ personnel should all be trained in the use of a prehospital stroke severity scale. (Category A)
3. EMS systems should keep records of the initial training and certification of their personnel in the

use of stroke screening and severity scales, as well as ongoing maintenance of stroke knowledge. (Category C)

Basic System Organizational Recommendations

1. Establish a Regional Acute Stroke Plan focused on augment timely diagnosis and treatment through optimal deployment of emergency medical services resources for suspected acute stroke cases. The plan should include a regionally tailored transport algorithm, patient-specific medical factors such as time from symptom onset, and likelihood of presentation being due to stroke (using established prehospital stroke screening and stroke severity scoring tools). (Category A)
2. Establish systems for the routine transfer of identified patient information from emergency medical services to hospitals, and from hospitals to emergency medical systems. These systems should provide for both immediate transfer of information for the acute care providers, and longer term transfer of information for data collection and quality improvement. (Category A)

Advanced System Organization Recommendations

1. EMS systems should adopt the use a prehospital electronic medical record system which allows the prehospital provider to create a document that is imported directly into the patient's medical record. This record would be immediately available to the medical team caring for the patient at the receiving hospital, thus contributing to systems improvement. (Category C)
2. Hospitals receiving patients from these EMS systems should have their electronic medical record system set up in order to be able to incorporate the prehospital EMS record of care for the patient they just received. Ideally the data should be imported as discrete data fields however scanned PDF may be used as initial process. (Category C)
3. EMS systems should adopt the use of telehealth applications and/or communication systems which allow for the direct notification of the acute stroke care team (emergency physicians as well as neurologists and interventional team

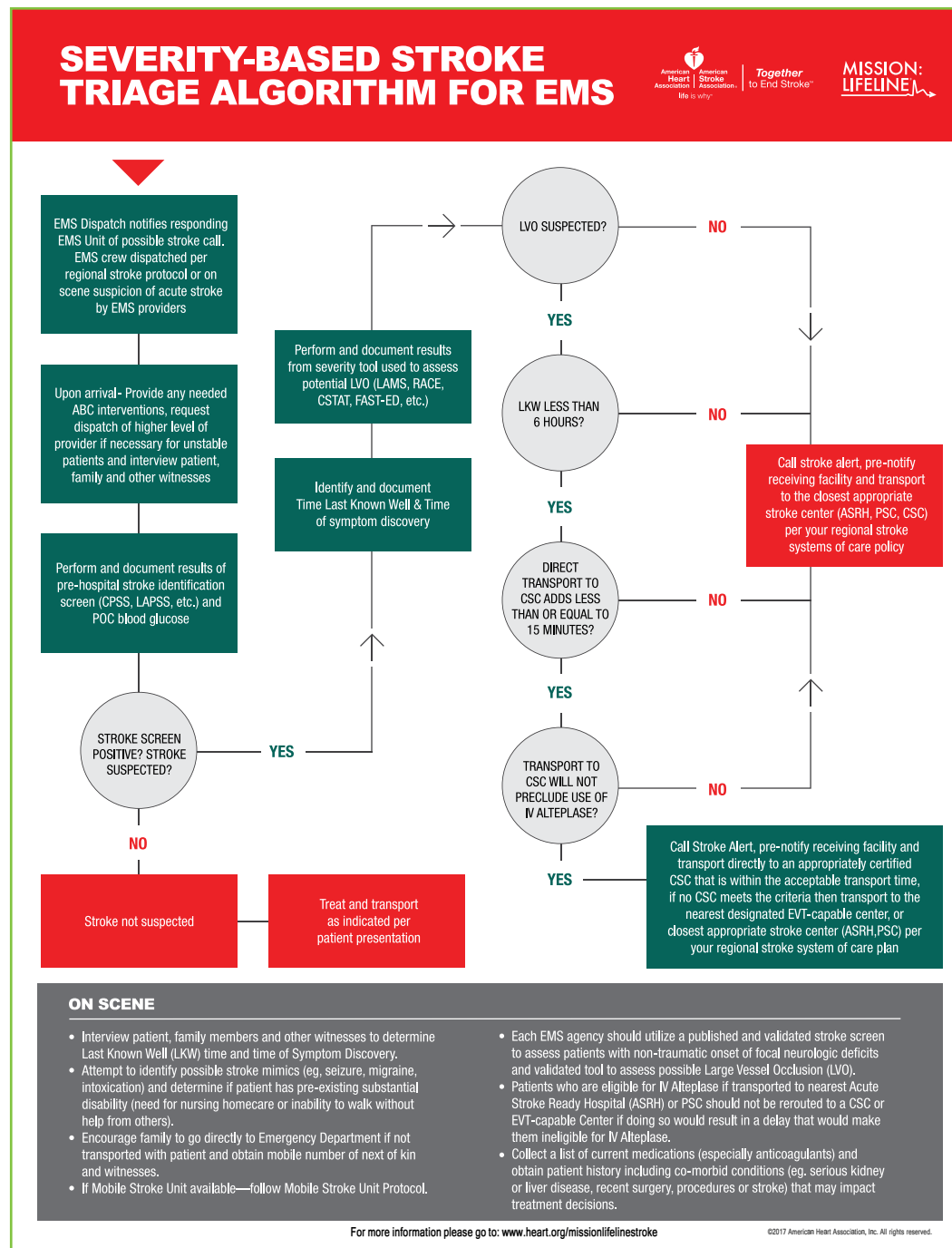


when indicated) when a stroke patient is being transported to a given ED. (Category C)

- EMS systems should implement a standardized destination protocol based on specified clinical

criteria used to select patients with a suspected large vessel occlusion in order to take them directly to intervention capable hospital. (Figure 7). (Category C)

Figure 7. Severity-Based Stroke Destination Algorithm for EMS (Mission Lifeline)





EMT or Paramedic Provider

Initial Contact Recommendations (Category A)

1. Obtain a medical history of the acute symptoms, including last time seen normal (LTSN).
2. Initial evaluation should include immediate assessment and stabilization of airway, breathing, circulation (ABC's) and point of care glucose check.
3. Perform a prehospital stroke screening evaluation
4. Perform stroke severity evaluation if stroke suspected
5. Medication lists should be obtained if feasible, including time last taken (especially if known for anticoagulants).
6. Obtain phone number of legal authorized medical representative (LAR).
7. Target a total on-scene time of 15 minutes or less, from EMS arrival to departure (including conduct of prehospital stroke screening and stroke severity scores).
8. Contact receiving hospital of impending stroke patient being transported, estimated time of arrival, and relay key aspects of medical and medication history, and vital signs, and with stroke severity score.
9. EMS providers should use a standardized hand-off tool at the time of emergency department arrival.

Advanced Recommendations (BLS emergency on scene unless urgent ABC need and ALS performed enroute)

1. EMS providers should consider using advanced telehealth informatics tools (such as smart phone applications) to activate stroke code and notify incoming hospital of history, medical and medication status, and vital signs including stroke screening results (when positive) and stroke severity scores. (Category C)
2. Notify stroke intervention team at CSC/ICSC receiving hospital if LVO is suspected using telehealth tools noted above. (Category C)

3. Establish EMS/ED-triage level protocols to identify patients who should be transported directly to the CT/MRI scanner from the EMS vehicle, bypassing an ED room. (Figure 8) (Category B)
4. Place at least one large bore (at least 18-gauge) IV in forearm above wrist if possible. A second IV is desirable but transfer to hospital should not be delayed if this line cannot be easily placed during transfer (Category C)

Figure 8. Prehospital Checklist of Medical Stability for Direct Transfer to CT Scanner

	YES	NO
Airway		
Is the patient maintaining their own airway?	☐	☐
Are they clearing secretions adequately?	☐	☐
Breathing and Oxygenation		
Are they breathing and saturating over 95%?	☐	☐
Circulation		
Is the systolic blood pressure >220 mmHg?	☐	☐
Is the systolic blood pressure <100 mmHg?	☐	☐
Is the heart rate >120?	☐	☐
Is the heart rate <60?	☐	☐
Is the heart rhythm an unstable one? (i.e., V Tach)	☐	☐
Is the patient actively bleeding?	☐	☐
Neurological		
Is the GCS <10?	☐	☐
Is the patient agitated and uncooperative?	☐	☐
Is or has the patient had a seizure?	☐	☐
Trauma		
Has the patient fallen and is there evidence or concern for trauma?	☐	☐
For Direct to CT patients, a quick pit-stop may occur in the ED to allow for quick registration and handoff of blood draws done by EMS to the ED team for point of care processing. This pit-stop should be no more than 3–5 minutes and should not include transfer of a patient to an ED bed.		
If any of the above are checked as YES, proceed to the Emergency Department for further evaluation and stabilization and do not go to CT scanner.		



5. When allowed by local jurisdiction, create treatment algorithms for management of hypertension in the prehospital setting for patients with stroke symptoms EMS providers should clear this with the emergency physician team at the receiving hospital. Target blood pressure for patients presenting with acute stroke symptoms within 4.5 hours of symptoms onset who meet criteria for thrombolysis or mechanical thrombectomy should be a systolic pressure of <180 mmHg (this would be initial target BP whether stroke was due to an ICH or due to acute ischemia; more aggressive targets can be set if indicated once patient arrived in ED and has initial CT of brain performed). (Category C)

EMT Paramedic: Mobile Stroke Units

Basic Recommendations:

1. Emergency Medical Systems utilizing Mobile Stroke Units should have specific protocols for activation of the Mobile Stroke Unit. (Category C)
2. Systems utilizing Mobile Stroke Units (MSU) should use their specific institutional protocols for the evaluation and treatment of acute stroke patients in the prehospital setting program. (Category C)
3. Clinical outcomes and performance metrics for the prehospital program need to be monitored for quality of care measurements specific to prehospital care. (Category C)
4. The accuracy of prehospital stroke screening and stroke severity scales used to deploy the mobile stroke unit should be compared to the initial diagnosis made by the mobile stroke unit providers as well as the final discharge diagnosis.

EMS: Air Medical Transfer

Air medical helicopter may be activated for transfer of a patient with an acute stroke to a CSC or ICSC for acute medical care if flight logistics such as safe weather and helicopter availability have been met. The following guidelines should be considered in determining the appropriateness for air transport:

Acute Ischemic Stroke with Large Vessel Occlusion (Category C)

1. If total round trip for ground transport would be more than 15 minutes longer than transport by air
2. If ground transport is not available
3. Air medical transport should be considered if the patient has confirmed evidence of LVO or a high probability of LVO (based on predetermined clinical criteria) and the patient would still meet clinical criteria for acute mechanical thrombectomy by the time of arrival to CSC/ ICSC.
4. Air medical transport should be offered if the patient has suffered a stroke and has eminent need of a neurosurgical procedure (such as hemicraniectomy or hematoma evacuation).

Acute Intracerebral Hemorrhage and Subarachnoid Hemorrhage (Category C)

1. If total round trip for ground transport would be more than 15 minutes longer than transport by air.
2. Ground transport is not available.
3. Patient will require acute emergent neurosurgical/ neuro-radiological intervention.
4. Patient requires provision of coagulation reversal agents not available at primary hospital.
5. In the opinion of the receiving medical team, the patient is too unstable to travel by ground.

Air Medical Team Protocols and Communications

1. The Air Medical Team should have protocols for the specific management of each vascular neurology emergency (Ischemic stroke, ICH and SAH).
2. Medical Control should be available by phone to the flight team — this is usually the responsibility of the medical institution where the flight team is based.



HOSPITAL-BASED ACUTE STROKE CARE IN THE EMERGENCY DEPARTMENT AND NEUROINTERVENTIONAL SUITE

Implementation of Stroke Telemedicine (Tele-stroke)

The use of tele-stroke is evidence-based and recommended as a Class 1 intervention by the AHA.¹⁴ Some of the key recommendations are listed below.

Basic Recommendations (Category A)

1. Tele-stroke networks should be deployed whenever a lack of readily available stroke expertise prevents patients in a given community from accessing a primary stroke center (or center of equivalent capability) within a distance or travel time to permit eligibility for intravenous thrombolytic therapy.
2. Organizations providing tele-stroke services should reliably provide access to personnel with an appropriate level of expertise in stroke care and experience with the relevant telemedicine technology; all tele-stroke physician consultants must have training and experience in diagnosing and treating acute cerebrovascular disease, at or above the level expected for primary stroke centers.
3. Organizations providing or requesting tele-stroke services should operate under rules and principles governed by contractual agreements between the facilities
4. Medical advice should be provided during tele-stroke consultation in a manner similar to that which occurs during on-site consultation, and documentation of the recommendations should be made available to the originating site within a reasonable time after completion of the consultation. This should include consideration for IV tPA and endovascular therapy and any contraindications or reasons therapy was not administered.
5. Establish systems for immediate review of computed tomography images by the consulting stroke neurologist.

6. Patients and/or their families should be made aware that the tele-stroke consultation will occur.
7. A copy of the recommendations produced should be kept in the spoke-site medical record in a manner accessible to the tele-stroke consultant at a later date; for patients being transferred to the hub hospital, or other institution, this documentation should be made available to the subsequent receiving facility.
8. The use of tele-stroke should be adopted within all stroke systems of care components to eliminate geographic disparities in care that may occur as a result of limited resources, manpower shortages, and long distances to specially trained providers.
9. Institutions seeking to develop hub-and-spoke tele-stroke networks should attempt to include key stakeholders from the beginning of the process, including multidisciplinary representation from physicians, nurses and allied health professionals from emergency medicine, neurology, neurosurgery, hospitalist medicine, radiology, administration, information technology, and inpatient departments at both the spoke and hub sites.

Advanced Recommendations: Measuring Process and Outcomes¹⁵ (Category C)

1. Tele-stroke networks should monitor process measures for continuous quality improvement including:
 - Time from ED presentation to request for tele-stroke consultation
 - Time from tele-stroke request to response by stroke consultant
 - Time of video connection if different from first response
 - Time from start of consult to intervention decision (recommendation for thrombolysis and/or transfer of patient)
 - Consult to needle time for alteplase (tPA) treated patients
 - Door-to-needle time for alteplase (tPA) treated patients



- Alteplase (tPA) administration rates relative to total consults and total eligible
 - Transfer rates, both for suspected LVO and overall
 - Proportion of patients transferred for suspected LVO who get mechanical thrombectomy
 - Proportion of patients transferred with confirmed LVO who get mechanical thrombectomy
2. Tele-stroke networks should monitor clinical outcomes of the patients that they consult on through regularly scheduled meetings with the spoke to review spoke system performance and hub data on outcomes of patients that were transferred to the hub facility. The tele-stroke consultants as well as the spoke hospital should also be provided with the following clinically significant outcomes metrics:
- Mortality
 - Symptomatic ICH rates
 - Hospital length of stay
 - 90-day functional outcomes (modified Rankin Score) on tPA treated patients (may be obtained via structured phone interview)
 - 90-day outcomes of patients transferred post tPA for supportive care (not LVO patients)
 - 90-day outcomes on patients transferred and treated for mechanical thrombectomy
 - Rates of stroke mimics treated with alteplase or transferred for suspected LVO should be tracked

Acute Stroke Care Hospital-Institutional Support

Basic Institutional Stroke Care Infrastructure

Acute stroke protocols should be clearly defined at an institutional level for standardization of quality care.

1. Institutional protocols for emergency evaluation of suspected stroke patients should be developed and disseminated to all process stakeholders. (Category A)
2. Rapid triage protocols should be established and early stroke team notification, including pre-hospital notification, should occur. (Category B)
3. An Acute Stroke Response Team should be designated including physicians, nurses, radiology, and laboratory personnel. (Category A)
4. The use of a 'single-call' activation system for stroke response team and radiology personnel should be utilized. (Category B)
5. Acute Stroke Ready and Primary Stroke Centers should to provide 24/7 acute neurovascular imaging (CTA) capabilities. (Category C)
6. Facilities without availability of in-house expertise in acute stroke support should have access to a consultation (in-person or by phone if no other option exists) to assist with care of the acute stroke patient. (Category B)

Advanced Institutional Stroke Care Infrastructure

- Facilities without in-house neurological support should have access to a neurological consultation (via tele-stroke) to assist with care of the acute stroke patient. (Category A)
- CT/MRI scanner used in acute stroke assessment should be physically located in or directly connected to the ED. (Category B)
- Comprehensive Stroke Centers should provide 24/7 acute neurovascular perfusion imaging (CT or MR) capabilities. (Category C)
- Comprehensive Stroke Centers / Stroke Interventional Capable Hospitals should provide tele-stroke services to a network of



referring hospitals that lack appropriate and timely access to stroke expertise. (Category C)

- Primary stroke centers and stroke access hospitals should be affiliated with a tele-stroke program from centers that have the capacity to provide acute interventional treatments (thrombectomy or neurosurgical intervention of ICH/SAH patients) and thus reduce requirements for third party involvement in arranging for transfer to CSC or SICH. (Category C)

EMERGENCY DEPARTMENT ACUTE STROKE CARE

The patient management processes should occur in parallel by team members whenever possible to reduce delays. History taking should be brief and concise with collateral sources of information pursued when needed to establish or confirm important facts pertaining to the event. History should be primarily aimed at establishing the needed information for inclusion/exclusion of acute stroke therapies, including pharmacologic thrombolytic administration and mechanical thrombectomy. Physical examination should likewise be concise and targeted in the acute setting.

Acute Stroke Presentation: Arrival by Private Vehicle

Patients with acute strokes may present to the ED either through transport by EMS or brought in via private vehicle. Patients brought in to the ED by private vehicle present unique challenges in terms of rapid triage and evaluation, including mobilization of the acute stroke team. The following guidelines are aimed at reducing delays in diagnosis of probable stroke and activation of the stroke care team.

Basic Recommendations

1. Nurses and advance care providers (physician assistants or nurse practitioners) should receive stroke-specific education and be able to use appropriate screening tools to diagnose suspected stroke. (Category C)

2. Rapid triage protocols should be established and early stroke team notification should occur. (Category B)
3. Any Registered Nurse, Nurse Practitioner/ Physician Assistant or Medical Doctor who initially assess a patient should have the authority to activate the stroke response team via a 'code stroke' system. (Category C)
4. Patients suspected of having an acute stroke should immediately be moved to a high acuity care area of the ED. (Category C)

Advanced Recommendations

1. Door-to-physician evaluation time should be ≤ 10 minutes. (Category A)
2. Door-to-Stroke Team evaluation time should be ≤ 15 minutes. (Category A)
3. Once a patient is considered to be having an acute stroke and the stroke team is notified, follow the algorithm as per patients brought in by EMS (see below).

Acute Stroke Presentation: Arrival by EMS

Basic Recommendations

Clinical Evaluation and Imaging

1. Stroke response team notification should occur as early in this process as possible, with pre-hospital notification recommended. (Category B)
2. Estimated time of arrival should be provided by EMS to the stroke center and further based on to the stroke team.
3. The stroke team should utilize the pre-hospital notification to assemble prior to the patient's arrival.
4. Emergency teams being notified of incoming stroke patients should be made aware of stroke severity using a standardized stroke severity scale. (Category B)
5. The stroke team should utilize the pre-hospital notification to assemble prior to the patient's arrival.



6. EMS providers should use a standardized hand-off tool (**Figure 9**) at the time of ED arrival.

Figure 9. EMS Hand-off Checklist (#FILM)

- # Contact number of EMS crew that transported patient to the ED
- F Family contact numbers
- I Incidents
(surgeries, GI or GU bleeding, prior brain bleeding of any type)
- L Last time seen normal
- M Medications currently being taken
(last time taken in case of anticoagulants)

7. Door-to-physician evaluation time should be ≤ 10 minutes. (Category A)
8. Patients presenting to the ED with suspected acute stroke should be treated with the same priority as serious trauma or acute myocardial infarction, regardless of the symptoms or severity. A similar team approach is imperative. Initial evaluation should mirror that of other critically ill patients including immediate assessment and stabilization of airway, breathing, and circulation (ABCs), followed by rapid neurologic assessment of deficits. (Category A)
9. Emergent brain imaging should be obtained prior to any therapies. Non-contrasted CT head or MRI brain are acceptable imaging modalities to exclude ICH, however non-contrasted CT head provides the necessary information for emergency management decisions regarding the use of alteplase. (Category A)
10. The door to CT initiation should be ≤ 25 minutes. (Category A)
11. Brain imaging studies should be interpreted by an expert physician ≤ 45 minutes of patient arrival to the ED. (Category A)
12. Imaging with radiocontrast should not be delayed for laboratory measurement of renal function. (Category B)
13. Noninvasive head and neck vascular imaging should be obtained during initial evaluation if endovascular therapy is contemplated, but should

not delay IV tPA administration if indicated. IV tPA can be administered immediately after noncontrasted CT results are available, and may be done concurrently while vascular imaging is being carried out. (Category A)

14. Interpretation of brain imaging should be performed immediately by stroke team members present at the time of the imaging study. (Category B)
15. A stroke severity rating scale, preferably the National Institutes of Health Stroke Scale (NIHSS), should be used in initial evaluation. (Category A)
16. Electrocardiogram should be obtained if acute coronary syndrome is expected according to symptoms of ischemic heart disease. This should not delay neurologic evaluation or treatment. (Category A)
17. The Stroke response team (neurologists, neuro-interventionalists, pharmacists, nurses, radiology, etc.) should have clear defined roles and responsibilities and work in parallel.

Advanced Recommendations

- Emergency teams being notified of incoming stroke patients should be made aware of stroke severity using a standardized stroke severity scale. (Category B)
- EMS providers should use a standardized hand-off tool at the time of ED arrival.
- Patients meeting appropriate criteria should be taken from EMS transport vehicle directly to CT scanner (**Figure 8**).

EMERGENCY DEPARTMENT ACUTE ISCHEMIC STROKE CARE; THROMBOLYSIS

Recommendations for Thrombolytic Therapy with Alteplase

General Guidelines

Following initial evaluation, brain imaging should be rapidly obtained, primarily to rule out acute



intracranial hemorrhage (ICH), followed by vascular imaging of the head and neck. Vascular imaging should not be allowed to delay thrombolytic administration when appropriate. Because time is critical, only limited and essential laboratory testing should be obtained, including point of care blood glucose and when indicated in selected patients the following labs may be added, renal function studies, platelet count, prothrombin time (PT), activated partial thromboplastin time (aPTT), international normalized ratio (INR), and cardiac enzymes (troponin). In general, **thrombolytic therapy should not be delayed** for laboratory results unless significant suspicion of therapy-excluding abnormalities exists. Blood draws may be completed by EMS to reduce delays in obtaining labs in cases with suspicion of excluding criteria.

Basic recommendations for thrombolytic therapy using alteplase:

1. IV alteplase benefit is time-dependent and should be initiated as quickly as possible. Door to IV alteplase administration (door-to-needle) should be 60 minutes or less (Category A) and preferably less than 45 minutes. (Category B)
2. IV alteplase (0.9mg/kg, max dose 90mg; 10% push over 1 minute, remaining 90% as infusion over 1 hour) should be administered to selected patients who can be treated within 3 hours of last known normal. Physicians should review inclusion and exclusion criteria (**Figure 10**) to determine eligibility. (Category A)
3. IV alteplase should be administered to eligible patients

Figure 10. Guidelines for Administration of Alteplase in Acute Ischemic Stroke

(Note: These are general guidelines only. It is understood that treatment decisions must be made on a case by case basis)

Inclusion Criteria

1. Ischemic stroke causing clinically significant neurologic deficit (neuroimaging required)
2. Last well known (symptom-free) within 4.5 hours of beginning treatment
3. Age ≥ 18 years

Exclusion Criteria

1. Significant head trauma or prior stroke in previous 3 months
2. Symptoms suggestive of subarachnoid hemorrhage
3. Arterial puncture at an uncompressible site in the previous 7 days
4. History of previous intracranial hemorrhage
5. Intracranial neoplasm, arteriovenous malformation, or aneurysm
6. Recent intracranial or intra-spinal surgery
7. Elevated blood pressure (systolic >185 mmHg or diastolic >110 mmHg)
8. Active internal bleeding
9. Acute bleeding diathesis, including but not limited to:
 - Platelet count $<100,000/\text{mm}^3$
 - Heparin received within 48 hours with aPTT above upper limit of normal**
 - Current use of anticoagulant with INR >1.7 , PT > 15 seconds**
 - Current use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated sensitive laboratory tests (such as a PPT, INR, platelet count, and Ecrin Clot Time; Thrombin time; or appropriate factor Xa activity assays)
 - Blood glucose concentration $<50\text{mg/dL}$ (2.7mmol/L)
 - CT shows multilobar infarction (hypodensity $> 1/3$ cerebral hemisphere)

*Platelet count not required prior to treatment unless history of thrombocytopenia

** PT/INR/PTT not required prior to treatment unless receiving anticoagulant or coagulopathy suspected

Stop infusion if platelet count, PT/INR/PTT outside indicated parameters

Special Considerations

Recent experience suggests that under some circumstances, with careful consideration and weighing of risk-to-benefit, patients may receive fibrinolytic therapy despite 1 or more relative contraindications. Consider risk to benefit of IV-tPA administration carefully if any of these relative contraindications is present:

- Only minor or rapidly improving symptoms (clearing spontaneously)
- Pregnancy
- Seizures at onset with postictal residual neurological impairments
- Major surgery or serious trauma within previous 14 days
- Recent gastrointestinal or urinary tract hemorrhage (within previous 21 days)
- Recent acute myocardial infarction (within previous 3 months)

Additional Considerations (3–4.5 hours of symptoms onset)

- Age >80 years
- Severe Stroke (NIH-SS score >25)
- Taking oral anticoagulants regardless of INR
- History of **both** diabetes and prior stroke

Note: The checklist includes some FDA-approved indications and contraindications for administration of tPA for acute ischemic stroke. Recent guideline revisions have modified the original FDA-approved indications. A physician with expertise in acute stroke care may modify this list.



who can be treated within the period of 3 to 4.5 hours from last known normal with same inclusion criteria as 0- to 3-hour window, with the following special considerations to be made on a case by case basis: those with baseline NIHSS >25, those with imaging evidence of ischemic injury involving >1/3 of the MCA territory, and those with a history of both prior stroke and diabetes mellitus (Figure 8).

4. Strict protocols should be developed regarding IV alteplase administration by initial push followed by pump infusion or by programmed pump alone, and regarding wasting of excess where necessary. A 50-ml bolus of saline following completion of the alteplase infusion is advised in order to assure that the line has fully been cleared of residual alteplase. These can be institution-specific but should be carried out faithfully and designed to best suit the center's work flow. (Category C)
5. Written informed consent is not required before alteplase administration. (Category B)
6. Platelet count results are not required before alteplase administration unless thrombocytopenia is suspected. Unless the patient is known to be, or strongly suspected to be, currently on Coumadin therapy, INR lab results are not required before alteplase administration. (Category B)
7. A limited set of laboratory tests should be obtained; only blood glucose (by point of care method) must be determined prior to initiation of IV alteplase administration. (Category A)
8. Patients who have elevated blood pressure but are otherwise eligible for IV alteplase should have their blood pressure lowered to <185/110 mmHg prior to administration of thrombolytic therapy. Blood pressure should then be maintained following IV alteplase below 180/105 mmHg for the first 24 hours. (Category A)
9. Patients who have elevated blood pressure but are otherwise eligible for IV alteplase should have their blood pressure lowered using IV antihypertensive agents with short duration of action. Labetalol may be used as the first line agent due to its simplicity of use. If these agents

do not sufficiently lower blood pressure within 3–5 minutes, an IV infusion of nicardipine or clevidipine should be started to achieve a target blood pressure as listed below (Figure 11). (Category C)

Figure 11. Guidelines for management of uncontrolled hypertension in acute stroke

General Guidelines

Ischemic stroke patients qualifying for alteplase thrombolytic therapy — controlled rapid reduction of blood pressure is recommended if the patient otherwise meets all other criteria for use of alteplase. It is recommended that one or two doses of shorter acting IV bolus medications be used such as labetalol or metoprolol. If the appropriate reduction of blood pressure is not achieved or maintained with the use of bolus medications, an intravenous infusion using either clevidipine or nicardipine is advised in order to reduce delays in time to treatment. An initial reduction of systolic blood pressure to <185 mmHg is advised. Ischemic stroke patients qualifying for mechanical thrombectomy (with or without alteplase therapy) — these patients should be treated similarly to those undergoing thrombolysis with alteplase. The difference between the two is that the ideal post reperfusion blood pressure is not known. At a minimum, systolic blood pressure should be maintained below 180 mmHg following mechanical thrombectomy. Lower targets may be set by the interventional physician or intensivist as per institutional standards.

Acute intracranial hemorrhage (intracerebral or subarachnoid hemorrhage) — a minimum reduction of systolic blood pressure to <160 mmHg should be targeted. Lower goals may be set at an institutional level, particularly for patients with subarachnoid hemorrhage where there is a lack of clinical trial data supporting specific target goal. Immediate control of blood pressure should follow the same guidelines as per the two sections above.

DRUGS RECOMMENDED FOR HYPERTENSION CONTROL IN THE EMERGENCY DEPARTMENT

Beta blockers

IV Push **Labetalol** — 5–20 mg IVP starting dose

Repeat at increasing doses q 10 min as necessary, max 300 mg

IV drip at 2–8 mg/min, titrate 0.5 mg q 10 min, max 8 mg/min

Vasodilators

IV Push **Hydralazine** — 5–10 mg IV (careful in elderly)

Calcium Channel Blockers

IV **Clevidipine Infusion** — Start 1–2 mg/kg/hr

- Double dose q 90 seconds until near BP goal then increase by smaller increments q 5–10 min
- Max 32 mg/hr, 500 mg/24 hr
- Caution if severe hyperlipidemia, or concurrent propofol use (lipid containing)

IV **Nicardipine Infusion** — Start 5 mg/hr

- Increase by 2.5 mg/hr q 5–15 min, MAX 15 mg/hr
- Slower onset/offset than clevidipine (50% effect in 45 min)
- Less ideal for acute stroke than clevidipine



10. It is generally considered safe if stroke mimics are treated with IV alteplase when acute ischemic stroke cannot be ruled out as the patient's presenting process however rates of stroke mimics should be monitored. (Category C)
 11. IV alteplase is reasonable in patients with seizure at time of onset of stroke symptoms if clinical evidence suggests that residual impairments are secondary to stroke and not postictal phenomenon. (Category A)
 12. In patients with rapidly improving symptoms but with persistent neurological deficits, or mild deficits from stroke onset that in the opinion of the treating physician are still causing significant disability, it is appropriate to treat the patient with alteplase and therefore it should be administered to otherwise eligible patients. (Category B)
 13. In patients taking, or presumed to be taking, direct oral anticoagulant (DOAC) agents (direct thrombin inhibitors or direct factor Xa inhibitors), IV alteplase may be harmful and is not recommended unless the patient has not received a dose within the prior 48 hours. (Category A)
 14. In patients with transient ischemic neurological symptoms which have resolved work up for etiology of the cerebral ischemic event is needed in an expedited manner via admission or observation. Neuroimaging with MRI is recommended within 24 hours; if MRI is unavailable, CT should be obtained. Further, noninvasive vascular imaging of the neck with CTA, MRA, or carotid duplex ultrasonography should be obtained. (Category A)
 15. Patients eligible for IV tPA should receive IV tPA even if endovascular treatment (mechanical thrombectomy) is being considered. (Category A)
 16. For centers without interventional capabilities, EVT eligible patients should be transported rapidly to the closest available high quality, Comprehensive Stroke Center or EVT capable center after determining eligibility or after discussing with the accepting center's Stroke Team. This should not delay IV tPA in eligible patients. (Category A) See section on Transfer of Patients.
- Advanced Recommendations for Thrombolytic Therapy*
1. Transport of suspected stroke patients from EMS vehicle directly to CT or MRI scanner immediately on arrival is associated with faster door-to-needle (DTN) times and is strongly recommended. (Category B)
 2. It is reasonable to establish EMS/ED-triage level protocols to identify those patients that can be transported directly to the CT/MRI scanner from the EMS vehicle, bypassing an ED room (see [Figure 8](#)). (Category B)
 3. A timer or running clock associated with the patient and visible to the treatment team to track elapsed time since onset and arrival is recommended. (Category B)
 4. Point of Care Laboratory — the ability to obtain point of care measurement of PTT, PT and INR are advisable to reduce delay in administering tPA for patients on warfarin that present with acute ischemic stroke. (Category C)
 5. IV tPA benefit is time-dependent and should be initiated as quickly as possible. Door to IV tPA administration (door-to-needle) should be 45 minutes or less. (Category A)
 6. Decision on acute treatments, including IV thrombolytic or endovascular procedure, made by an attending or trainee stroke specialist after in-person evaluation is associated with faster door-to-needle (DTN) times and is strongly recommended. (Category B)
 7. Decision on acute treatments, including IV thrombolytic or endovascular procedure, made by an attending stroke specialist after tele-stroke evaluation is an effective and reasonable alternative for institutions where in-person evaluation is not feasible or not available 24/7. (Category B)



8. IV tPA should be premixed ahead of time when there is reasonable suspicion the patient will be a candidate for thrombolytic therapy. Protocols for this pre-mixing of drug should be established. (Category B)
9. The initiation of the bolus portion of IV tPA should be administered while the patient is still in the brain imaging suite once ICH is ruled out; this is associated with faster door-to-needle (DTN) times and is strongly recommended. (Category B)

EMERGENCY DEPARTMENT ACUTE ISCHEMIC STROKE CARE; MECHANICAL THROMBECTOMY

Recommendations for Mechanical Thrombectomy for Patients Presenting WITHIN 6 HOURS OF SYMPTOM ONSET

The removal of intravascular clots using newer generation mechanical thrombectomy devices has been demonstrated in 6 multicenter clinical trials to be an effective method of treating patients with stroke associated with large vessel occlusion. (Category A)

1. Endovascular therapy (EVT) is time dependent. Reperfusion should be achieved as early as possible within 6 hours of stroke onset. (Category A)
2. Observing patients after IV tPA to assess for clinical response before pursuing EVT is not required and not recommended. (Category A)
3. Patients with acute anterior circulation strokes associated with occlusion of the carotid artery and/or portions of the middle cerebral artery should receive endovascular therapy with a stent retriever if they meet the appropriate inclusion criteria ([Figure 12](#)). (Category A)
4. General anesthesia for EVT procedures is preferred if intubation and induction can be accomplished in a manner which does not delay treatment. Outcomes of patients treated with general anesthesia versus conscious sedation should be monitored. (Category B)

Figure 12. Selection Criteria for Mechanical Thrombectomy

A. Patients should receive endovascular therapy with a stent retriever if they meet all the following criteria (Class I; Level of Evidence A):

1. Pre-stroke mRS score 0 to 1,
2. Acute ischemic stroke receiving intravenous r-tPA within 4.5 hours of onset according to guidelines from professional medical societies,
3. Causative occlusion of the internal carotid artery or proximal MCA (M1),
4. Age ≥ 18 years,
5. NIHSS score of ≥ 6 ,
6. ASPECTS score of ≥ 6
7. Treatment can be initiated (groin puncture) within 6 hours of symptom onset

B. Special considerations should be taken into account when offering mechanical thrombectomy for patients not meeting the above criteria but that may still benefit from this form of treatment on a case by case basis as follows:

1. Contraindications to intravenous r-tPA, endovascular therapy with stent retrievers completed within 6 hours of stroke onset is reasonable (Class IIa; Level of Evidence C).
2. Although the benefits are uncertain, use of endovascular therapy with stent retrievers may be reasonable for carefully selected patients with acute ischemic stroke in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have causative occlusion of the **M2** or **M3** portion of the MCAs, **ACA** (anterior cerebral arteries), **VA** (vertebral arteries), **BA** (basilar artery), or **PCA** (posterior cerebral arteries) (Class IIb; Level of Evidence C).
3. Endovascular therapy with stent retrievers may be reasonable for some patients **<18 years of age with acute ischemic stroke who have demonstrated large vessel occlusion** in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset, but the benefits are not established in this age group (Class IIb; Level of Evidence C).
4. Although the benefits are uncertain, use of endovascular therapy with stent retrievers may be reasonable for patients with acute ischemic stroke in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have **pre-stroke mRS score of >1 , ASPECTS <6 , or NIHSS score <6 and causative occlusion of the internal carotid artery or proximal MCA (M1)** (Class IIb; Level of Evidence B-R).
5. The technical goal of the thrombectomy procedure should be a TICI 2b/3 angiographic result to maximize the probability of a good functional clinical outcome (Class I; Level of Evidence A). Use of salvage technical adjuncts including intra-arterial fibrinolysis may be reasonable to achieve these angiographic results, if completed within 6 hours of symptom onset (Class IIb; Level of Evidence B-R).
6. Patients presenting with stroke from LVO at a time whereby groin access will occur >6 hours post onset of symptoms but who still have large volume of salvageable brain. Specific guidelines for patient selection will be incorporated into the manual as published data become available.



5. Endovascular therapy (EVT) with the suction aspiration devices can be considered as an alternative to, or used in conjunction with, stent retrievers in patients meeting the above criteria. (Category B)
6. The technical goal of EVT procedures is TIC1 grade 2c/3 angiographic result. (Category A)
7. EVT procedures should be carried out by experienced vascular neurosurgeons, vascular neurologists, or interventional radiologists with specialty training in cerebrovascular intervention. (Category C)
8. In patients who have contraindications for IV tPA but meet the above criteria for EVT, EVT should be performed. (Category A)
9. In patients with causative occlusions in the M2 or M3 segment of the MCAs, ACAs, Basilar artery, or PCAs, who otherwise meet the criteria above, EVT may be considered at the discretion of the treating stroke specialist and neuro-interventionalist. (Category B)
10. Angioplasty and/or stenting of proximal cervical vessel stenosis or occlusion at time of thrombectomy to access distal occlusive disease should be considered when technically feasible. (Category C)
3. Patients in category 1 or 2 above with acute anterior circulation strokes associated with occlusion of the carotid artery and/or portions of the middle cerebral artery should receive endovascular therapy with a stent retriever if they meet the appropriate inclusion criteria (Figure 13). (Category A/B)
4. In regards to the methods of clot evacuation (stent vs contact aspiration), use of general anesthesia, reperfusion target goal (TIC1 grade), the same criteria apply for those patients presenting >6

Figure 13. Selection Criteria for Mechanical Thrombectomy

A. Patients should receive endovascular therapy with a stent retriever if they meet all the following criteria: DAWN Criteria

General Inclusion Criteria

1. Pre-stroke mRS score 0 to 1
2. Acute ischemic stroke patients presenting within 6–24 hours from symptom onset
3. Causative occlusion of the internal carotid artery or proximal MCA (M1)
4. Age ≥ 18 years
5. Prestroke mRS of 0 or 1
6. NIHSS score of ≥ 6
7. Brain CT with infarct in $<1/3$ of MCA territory

Group A Patients

1. Age ≥ 80 years
2. NIHSS ≥ 10
3. Infarct volume of <21 mls by CT perfusion or DWI on MRI

Group B Patients

1. Age <80 years
2. NIHSS ≥ 10
3. Infarct volume of 31 to ≤ 51 mls by CT perfusion or DWI on MRI

B. Patients should receive endovascular therapy with a stent retriever if they meet all the following criteria: DEFUSE 3 Criteria

1. Stroke symptoms onset between 6 and 16 hours
2. Age ≥ 18 years
3. Prestroke mRS of 0 or 2
4. NIHSS score of ≥ 6
5. CT Perfusion criteria as follows:
 - a. Brain CT with infarct in $<1/3$ of MCA territory
 - b. Initial infarct core of <70 ml
 - c. Ratio of volume of ischemic tissue to initial infarct volume of 1.8 or more
 - d. Absolute volume of penumbra of 15 mls or more (based on Tmax >6 seconds)

Recommendations for Mechanical Thrombectomy for Patients Presenting 6 TO 24 HOURS FROM SYMPTOM ONSET

The removal of intravascular clots using newer generation mechanical thrombectomy devices has been demonstrated in 6 multicenter clinical trials to be an effective method of treating patients with stroke associated with large vessel occlusion. (Category A)

1. Two recent clinical trials have demonstrated that in selected patients presenting with acute ischemic stroke due to LVO, within 6–16 hours, thrombectomy is effective. (Category A)
2. There is also evidence to recommend performing mechanical thrombectomy for patients with AIS and LVO presenting from 6 to 24 hours. (Category B)



hours from stroke symptom onset as they do for those presenting under 6 hours (see prior section, numbers 3 to 7).

EMERGENCY DEPARTMENT ACUTE INTRACRANIAL HEMORRHAGE ASSOCIATED WITH ANTICOAGULANT USE

Intracranial hemorrhages associated with anticoagulant use represent a special subset of patients as the likelihood of further bleeding and neurological demise is influenced considerably by the ability to reverse the coagulopathy. The guidelines provided below will focus on management of coagulopathy associated with vitamin K antagonists (warfarin) as well as the direct oral anticoagulants (DOAC) including dabigatran, rivaroxaban and apixaban. Edoxaban is not available in the USA. Andexxa (Xa reversal agent) is not approved in the USA for use as a reversal agent for patients taking edoxaban or betrixaban.

Coagulopathy Reversal

Warfarin-Associated Coagulopathy should ideally be treated with prothrombin concentrate containing 4 factors (Kcentra) and dosed as follows:

INR 2.0–4.0: give 25 Units per kilogram body weight

INR 4.0–6.0: give 35 Units per kilogram body weight

INR >6.0: give 50 Units per kilogram body weight

If Kcentra is not available, fresh frozen plasma (FFP) may be used but caution is advised due to the large volume of intravenous fluid that will be infused to meet dosing standard. The recommended adult therapeutic dose of FFP is 12–15 ml/kg with a minimum dose of 10 ml/kg prescribed. A unit of FFP is typically 275 mL and as such the using this calculation, the appropriate number of units may be prescribed. INR based algorithms are also available and may be used in place of the above guidelines¹⁶

Vitamin K should also be provided in order to replenish the missing factors (2, 7, 9, and 10) in patients on warfarin. Recommended doses are 5–10 mg IV or by mouth (if the patient is able to safely swallow) daily for 3 days.

Direct Thrombin Inhibition — dabigatran

associated coagulopathy should be treated with idarucizumab which is a humanized monoclonal antibody capable of neutralizing dabigatran. The recommended dose of idarucizumab is 5 grams IV. If idarucizumab is not available, Kcentra (PCC) may be given at a dose of 50 U/kg although the efficacy of the latter has not been proven in contrast to idarucizumab. Fresh frozen plasma may be given as a last resort although again there is little evidence of its effectiveness.

Direct Factor Xa inhibitor associated coagulopathy (See Appendix A for guidelines on use of Andexxa for DOACs with anti Xa activity.)

INTERHOSPITAL TRANSFERS AND PROCESSES

Endovascular treatment for ischemic stroke can significantly improve outcome of patients with large vessel occlusion if done in timely manner. As expertise to provide endovascular treatment is currently limited to select few centers, this will necessitate interfacility transfer for eligible patients.

The following steps should be taken to improve efficiency and safety of interfacility transportation of acute stroke patients:

1. Develop a written plan to define which patients the hospital will consider transferring to a higher-level center. Following is a suggested list of patients that should be considered for transfer to centers capable of providing higher level of care, i.e. comprehensive stroke centers with 24/7 availability of interventional neuroradiologist and neurosurgical support:
 - Ischemic stroke with last seen normal < 6 hrs. and suspected LVO (in cases where CTA is not available at primary hospital) and clinical suspicion of LVO (the 6-hour timeline is expected to be modified based on the results of clinical trials with selection criteria for patients presenting beyond selection after 6 hours). Patients may be considered for mechanical thrombectomy beyond 6 hours from symptom onset if in the opinion of the



accepting neurovascular team, there is sufficient salvageable brain tissue at risk for infarction that may benefit from thrombectomy. (Category B)

- Patients with basilar artery occlusion
 - Patients with CT brain showing large hemispheric infarct (ASPECTS score <6)
 - Patients not able to receive IV tPA because of elevated INR or history of use of direct oral anticoagulant use within previous 48 hours.
 - Patients with subarachnoid hemorrhage
 - Intracerebral hemorrhage patients with need of neurosurgical intervention such as presence of intraventricular hemorrhage requiring extraventricular drainage (Category C)
2. Identify hospital capabilities and available resources in the surrounding area and establish formal transfer agreements to improve patient access to appropriate care. Transfer agreement should be made to minimize transport time while providing best clinical care. Hospital or corporate affiliations, as well as local and state boundaries, should not interfere with the safe and efficient transport of stroke patients. Such transfer agreements will help establishment of coordinated systems of care between sending and receiving hospitals. (Category C)
 3. Develop interfacility telemedicine to assist with transfer decision making process. (Category A)
 4. Use Trauma system as a model for stroke system development of transport and interfacility transfers. (Category C)
 5. Prior to transfer, ensure compliance with EMTALA requirements by providing a medical screening examination and stabilizing the patient's emergency medical condition to the extent possible given the hospital's capabilities. (Category C)
 6. To address any state or local requirements for interfacility transport, develop community-wide EMS protocols, model pre-established referral processes, and interfacility transport agreements.
- Create easy-to-complete forms that address such requirements that physicians can complete before patient transport. (Category C) Do not delay transfer while waiting to complete paperwork. Establish minimum that must be completed prior to transfer and fax the remaining after the patient has left with the transport team.
7. Prior to transfer, patient or family members should be informed of the benefits and risks of transfer. (Category C)
 8. Alteplase (IV rt-PA) should be initiated to the patients who are candidates for the therapy prior to the transfer and should not be delayed until after transport. The infusion does not need to be completed prior to transfer of the patient. (Category A)
 9. At least two pre-specified plans for urgent inter-facility transfer should be established. Local paramedic staffed emergency medical transport is often the fastest option. Mobile and airborne critical care transport also represent good options. Air transport arrangements requires a ground-based back-up plan when safe flight is not possible. (Category B)
 10. Interfacility transport of stroke patients for stroke intervention should be treated as a high-priority time-critical, similar to a 911 emergency response. A specific term such as "code stroke" should be identified to allow transport dispatcher to recognize this urgency. (Category A)
 11. Once the transport crew has arrived at the transferring hospital, on-scene time should be less than 15 minutes. Procedures should be developed to minimize door-in-door-out time by standardizing equipment such as infusion pumps, streamlining EMTALA documentation, and forwarding copied medical records by fax after the patient has left the facility. If electronic image transfer is not possible between institutions, routinely copying DICOM CT images onto compact discs by the radiology technician in a time frame that allows the images to move with the patient. (Category B)



Data should be collect for process improvement on “on-scene” times or the total time the interfacility team was at the referral hospital. (Make sure alteplase is in the EMS formulary for transport.)

12. Create a checklist of necessary information:

- Last known well
- NIHSS
- Medications prior to admission
- Medications given in the ED
- Vitals
- Lab values
- Result of the imaging
- Family/witness contact information
- IV alteplase given: yes/no. If no: reason (Category C)
- Specific information related to rtPA is necessary: bolus dose and time, drip rate and time started, discard amount if not mixed in pharmacy, total dose to be given, time NS started

13. For an expeditious and safe transfer process, all equipment (i.e. transfusion pump) used should be standardized and transfer personnel should be cross-trained. (Category C)

14. Develop image-sharing capabilities between transferring and receiving facilities. (Category C)

15. Protocols should be designed for strict adherence to blood pressure guidelines, assessment for clinical deterioration and bleeding, and aspiration precautions to ensure safe interhospital transport. (Category C) (Confirm meds are in the EMS Formulary for transfer.)

16. Transport personnel should contact the receiving facility about any change in the patient’s condition en route. (Category C)

17. For interfacility transfers, consider develop a reverse transfer agreement, which returns the stroke patient after the receipt of acute care to the community hospital for subacute care and rehabilitation, as appropriate. (Category C)

Periodic provider education on the transfer process should be completed and feedback systems to institutions and EMS should be created for important process metrics like door-in-door-out time, EMS on-site time, and travel time. (Category C) (Consider quarterly following a case from initial exam, treatment and transfer to hospital discharge with all parties involved.)



GLOSSARY OF TERMS

Contraindication — a specific situation in which a drug or procedure should NOT be used, because it may be more harmful than beneficial to the patient.

Diversion plan — an emergency medical service protocol to divert patients with acute stroke (ischemic or hemorrhagic) from the closest non-comprehensive or stroke interventional capable hospital to a CSD or SICH capable hospital. Diversion protocols are particularly useful when patients have a contraindication to fibrinolysis as well as situations where direct transfer to a CSD/ SICH does not prolonged thrombolysis by more than 15 minutes.

Door-to-Needle Time — the time elapsed from hospital arrival or emergency department registration arrival to the initial infusion of fibrinolytic medication.

Electrocardiogram (ECG) — a recorded tracing of the electrical activity of the heart Emergency medical service (EMS)

EMS Provider (EMT, AMET, Paramedic) — an emergency responder trained to provide pre-hospital care to the critically ill and injured patient.

EMT — Basic Life Support Provider

AEMT — Advanced EMT, basic life support provider with limited ALS abilities

Paramedic — Full advanced life support provider

Emergency medical technician (EMT) — an emergency responder trained to provide pre-hospital emergency medical services (EMS) to the critically ill and injured.

Emergency Medical Treatment and Active Labor Act (EMTALA) — a statute that governs when and how a patient may be (1) refused treatment or (2) transferred from one hospital to another when in unstable condition. The EMTALA was passed as part of the Comprehensive Omnibus Budget Reconciliation Act of 1986, and is sometimes referred to as “the COBRA law.”

Fibrinolysis — the breakdown of fibrin, usually by the enzymatic action of plasmin. Fibrin is a protein necessary for blood clotting that forms a web-like mesh that traps red blood cells and platelets and holds clots together. In the case of acute ischemic stroke, the administration of drugs that facilitate fibrin breakdown is referred to as “fibrinolysis.”

Fibrinolytic — an agent used to facilitate fibrin breakdown by activating plasminogen. Alteplase is the only FDA approved fibrinolytic for treatment of acute ischemic stroke.

First medical contact to device time — the time elapsed from the first medical contact (i.e. EMS scene arrival or ED registration arrival) to the first device deployment in the cerebral vessel.

Reperfusion — the restoration of blood flow to an organ or tissue that has had its blood supply cut off, as after an ischemic stroke and classified by TICI grade.



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APPENDIX A: Coagulation Factor Xa (Recombinant), Inactivated-zhzo (Andexxa) Guidelines for Appropriate Use in Intracranial Hemorrhage

Purpose:

The following guideline for Andexxa has been developed to establish standard recommendations for use in order to ensure that appropriate patients have access to the medication and to avoid unnecessary administrations of this medication due to concerns for safety and cost.

Background:

Andexxa is a recombinant, inactivated coagulation FXa that exerts its procoagulant effect by binding and sequestering FXa inhibitors, rivaroxaban and apixaban. It also binds and inhibits the activity of tissue factor pathway inhibitor, with inhibition leading to an increase in tissue-factor initiated thrombin generation.

Andexxa is currently indicated for patients treated with rivaroxaban or apixaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding.

Andexxa has no contraindications, however, the product does have a Black Box Warning for the association of Andexxa with serious and life-threatening adverse events, including: arterial and venous thromboembolic events, ischemic events, including myocardial infarction and ischemic stroke, cardiac arrest, and sudden deaths. Thromboembolic events were noted in 17.8% of study patients with death occurring in 14% of study patients.

Recommended Guidelines for Patient Selection Prior to Use of Andexxa:

Use of coagulation Factor Xa (recombinant), Inactivated –zhzo [Andexxa] is recommended for use in patients with intracranial hemorrhage meeting the following criteria:

- Patient with known use of rivaroxaban or apixaban
- Expected high quality survival from intracranial hemorrhage (for example but not limited to: Glasgow Coma Score ≥ 7 , ICH Volume < 60 ml)
- No major thromboembolic event within 2 weeks unless in the opinion of the treating physician, the risk of dying from the hemorrhage outweighs the risk of a recurring ischemic event.

Patient Workup:

The following should be determined in order to appropriately assess the severity of the intracranial hemorrhage:

- Intracranial hemorrhage volume according to CT/MRI
- Glasgow Coma Score
- Age
- Origin of hemorrhage

Labs:

In centers with advanced laboratory capabilities that can rapidly turn around an anti-Xa level, the following investigations are recommended:

- Anticoagulant Panel
 - Heparin Anti-Xa Level
 - Will determine if FXa inhibiting drug is present but will not determine how much
 - PT
 - Thrombin Time
- Drug specific (rivaroxaban, apixaban) assay to follow as an add-on lab
 - Order along with Anticoagulation Panel
 - Use to determine drug specific drug level if Anti-Xa activity is detected
 - Order additional lab to be drawn 4 hours after infusion has been stopped
- Additional appropriate labs (e.g. CBC, aPTT, fibrinogen)



Dosing Information—Basic Guidelines for Dosing of Andexxa:

If rapid turnaround (<30 minutes) of anti-factor Xa levels is not available we recommend the following:

Apixaban Reversal

- Last apixaban dose up to 5 mg received <8 hours ago (or timing unknown) — 400 mg IV x1, then 4 mg/min IV infusion for up to 120 min; Max: 480 mg/infusion.
- Last apixaban dose >5 mg (or dose unknown) received <8 hours ago (or timing unknown) — 800 mg IVx1, then 8 mg/min IV infusion for up to 120 min; Max: 960 mg/infusion.
- Any apixaban dose received >8 hours ago — 400 mg IV x1 then 4 mg/min IV infusion for up to 120 min; Max: 480 mg/infusion.

Rivaroxaban reversal

- Last rivaroxaban dose up to 10 mg received <8 hours ago (or timing unknown) — 400 mg IV x1, then 4 mg/min IV infusion for up to 120 min; Max: 480 mg/infusion;
- Last rivaroxaban dose >10 mg (or dose unknown) received <8 hours ago (or timing unknown) — 800 mg IVx1, then 8 mg/min IV infusion for up to 120 min; Max: 960 mg/infusion.
- Any rivaroxaban dose received >8 hours ago — 400 mg IV x1 then 4 mg/min IV infusion for up to 120 min; Max: 480 mg/infusion.

Dosing Information—Advanced Guidelines for Dosing of Andexxa:

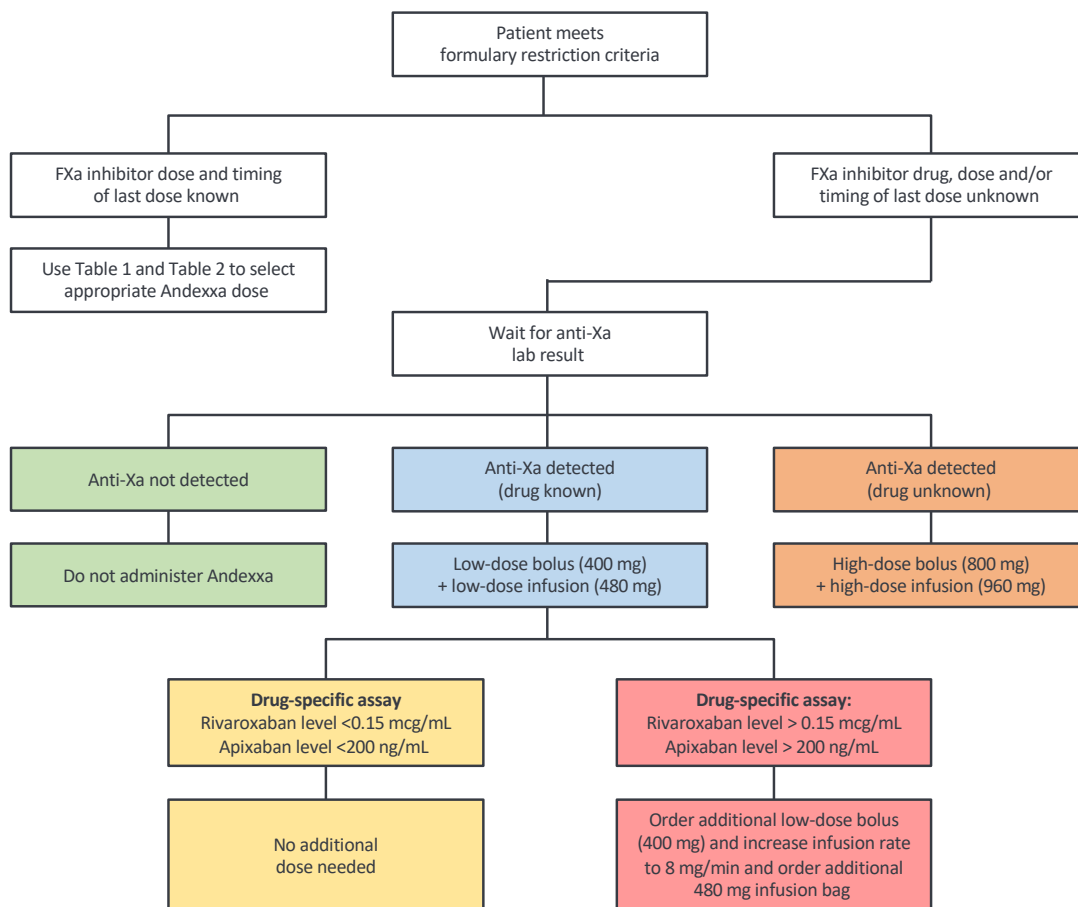



Table 1: Dose Strength and Timing of Last FXa Dose

Medication	Last Dose of Medication	Timing of Medication Last Dose before Andexxa Initiation		
		< 8 hours	≥ 8 hours	>18 hours
Rivaroxaban	≤ 10 mg	Low Dose	Low Dose	Send Rivaroxaban Assay
	> 10 mg	High Dose		
Apixaban	≤ 5 mg	Low Dose		Send Apixaban Assay
	> 5 mg	High Dose		

Table 2: Low Dose and High Dose of Andexxa

Dose of FXa Inhibitor	Initial IV Bolus	Follow-on IV Infusion
Low Dose	400 mg at a target rate of 30 mg/min	4 mg/min for up to 120 mins
High Dose	800 mg at a target rate of 30 mg/min	8 mg/min for up to 120 mins

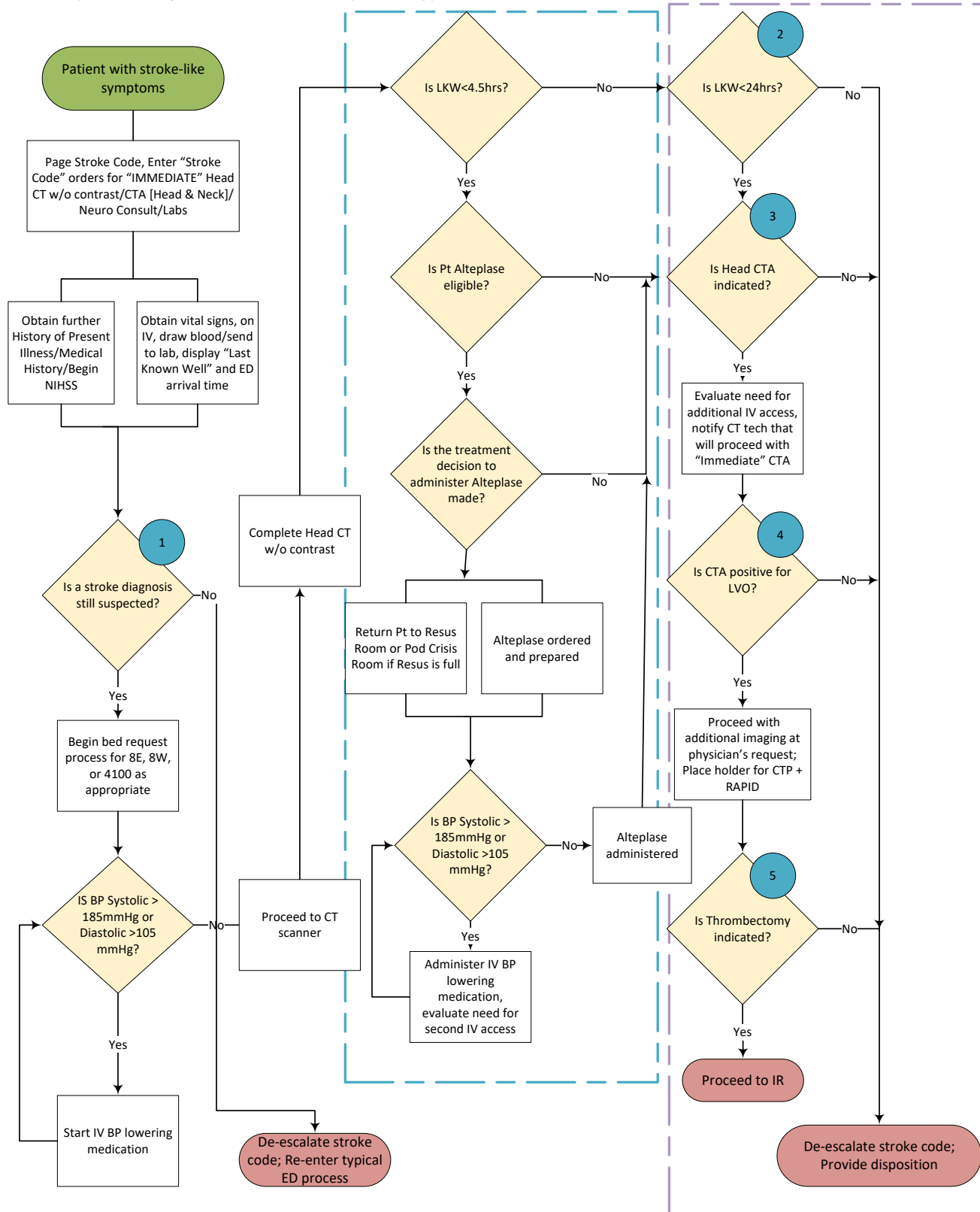
Patient Monitoring:

- Rivaroxaban or apixaban levels should be drawn four hours after end of infusion
 - Rebound to levels >100 for both apixaban and rivaroxaban is likely to occur
 - Redosing with Andexxa at this point has not been studied and FXa activity will decrease at a rate similar to the clearance of the FXa inhibitors.
- Resumption of anticoagulation therapy should be done as soon as is medically appropriate per the care team to avoid potential thromboembolic events



APPENDIX B: DRAFT DUH ED Stroke Code Process

Adapted from original available on the Policy center, approved on 3/2/2017





APPENDIX C: DUH Stroke Code “De-Escalation” Process and Procedure

Purpose: Provide a consistent practice by which **only the most appropriate patients** remain “activated” as stroke codes which require significant resources and effort of the multidisciplinary team (resident physicians, ED team, 1:1 nursing ratio, CT-imaging, etc.)

Background:

- Definition of “Stroke Code” – the coordinated efforts of the multidisciplinary team in the Emergency Department to provide acute management and/or critical care to patients with **any suspected cerebrovascular event within a 22-hour window** from symptom onset of acute neurological deficits.
- If a patient with an activated stroke code is discovered to not require thrombolytics or thrombectomy and is not acutely ill, a stroke code should de-escalated (i.e. cancelled) in an effort to best utilize resources.
- Despite not requiring thrombolytics or thrombectomy, **hemorrhagic strokes remain active stroke codes upon diagnosis** due to the need for continued critical care management of acute neurological illness.

De-Escalation Decision Points:

- Upon initial consultation (prior to non-contrast CT-head)
- Upon indication that LKW time is greater than 22 hours
- Upon consideration whether a CTA is indicated
- Upon indication that CTA is negative for LVO (large vessel occlusion)
- Upon indication that the patient is not a thrombectomy candidate

STROKE CODE DE-ESCALATION PROCEDURE

1. **Communicate clearly to assigned care nurse at bedside that the stroke code is no longer active. (If the care nurse is not immediately available, inform ED charge nurse.)**
2. **Page 115 to cancel stroke code activation via pager notification**
3. **Continue to provide expedient consultation until patient disposition determined**



APPENDIX D: DRAFT Medication Table

DRAFT Drug Treatments for Acute Stroke and Primary and Secondary Prevention

	Drug	Other names	Indication	Dose	Age, renal or hepatic insufficiency considerations
Thrombolysis	Alteplase	recombinant tissue plasminogen activator (rt-PA) Activase Cathflo Activase	Treatment of acute ischemic stroke within 3 hours after onset of symptoms.	The recommended dose is 0.9 mg/kg (not to exceed 90 mg total dose), with 10% of the total dose administered as an initial intravenous bolus over 1 minute and the remainder infused over 60 minutes. Note of Caution: It is extremely important to minimize any delays between the completion of the bolus and the start of the 60 minute infusion.	Higher risk for bleeding in with advanced age and renal disease
			Treatment of acute ischemic stroke within 3 and 4.5 hours of ischemic stroke symptom onset or patient last known well.	IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute). Physicians should review the criteria and updated AHA guidelines in order to determine patient eligibility for treatment between 3 and 4.5 hours as many prior relative contraindications have been removed.	Higher risk for bleeding in with advanced age and renal disease
Acute Emergency Hypertension Management	Labetalol	Normodyne Trandate	Patient otherwise eligible for acute reperfusion therapy except that BP is >185/110 mm Hg:	10–20 mg IV over 1–2 min, may repeat 1 time;	
			If patient presents with a primary intracerebral hemorrhage and systolic BP >160 mm Hg:	10-20 mg IV, may be repeated 1 time; if blood pressure does not remain at target it is advised to begin a continuous infusion of a titratable antihypertensive agent such as labetalol, nicardipine or clevidipine.	
			If blood pressure is control is not achieved to desired target after 2 bolus doses of labetalol, an titratable continuous infusion may be started	Begin an IV infusion 2–8 mg/min;	
	Nicardipine	Cardene	Patient otherwise eligible for acute reperfusion therapy except that BP is >185/110 mm Hg:	5 mg/h IV, titrate up by 2.5 mg/h every 5–15 min, maximum 15 mg/h; when desired BP reached, adjust to maintain proper BP limits;	
			If patient presents with a primary intracerebral hemorrhage and systolic BP >160 mm Hg:	5 mg/h IV, titrate up to desired effect by 2.5 mg/h every 5–15 min, maximum 15 mg/h;	



	Drug	Other names	Indication	Dose	Age, renal or hepatic insufficiency considerations
Acute Emergency Hypertension Management	Clevidipine	Cleviprex	Patient otherwise eligible for acute reperfusion therapy except that BP is >185/110 mm Hg:	1–2 mg/h IV, titrate by doubling the dose every 2–5 min until desired BP reached; maximum 21 mg/h	
			If patient presents with a primary intracerebral hemorrhage and systolic BP >160 mm Hg:	1–2 mg/h IV, titrate by doubling the dose every 2–5 min until desired BP reached; maximum 21 mg/h	
	Hydralazine	Apresoline	If blood pressure has exceeded target range (see above for targets in setting of ischemic stroke needing reperfusion or patients presenting with primary ICH) and labetalol is contraindicated, hydralazine may be given prior to start of a continuous infusion of calcium channel blocker)	10-20 mg IV; repeat PRN	
Coagulopathy Reversal Agents	Vitamin K		Warfarin Reversal Agent	1-10 mg IV/PO (Note of caution: Vitamin K does not rapidly correct coagulopathy and should only be given in addition to IV replacement of Vitamin K factors)	
	Fresh Frozen Plasma	FFP	For treatment of bleeds associated with anticoagulants	10-15 mL/kg	
	Prothrombin Complex Concentrate (4 Factor Complex is the preferred product)	Kcentra	For treatment of bleeds associated with Vitamin K antagonists	25-50 units/kg IV depending on INR (25 U/Kg for INR 2-4; 35 U/Kg for INR 4-6; 50 U/Kg for INR>6)	
	Idarucizumab	Praxbind	Dabigatran Reversal Agent	5 g IV; may consider repeat x 1	
	Andexanet Alfa	Andexxa	Direct oral anticoagulants (Xa inhibitors) Rivaroxaban or apixaban reversal agent	400-800 mg IV bolus and then 4-5mg/min infusion	



	Drug	Other names	Indication	Dose	Age, renal or hepatic insufficiency considerations
Oral anticoagulants for secondary prevention in Atrial Fibrillation	Apixaban	Eliquis	Primary or secondary stroke prevention in patients with Atrial Fibrillation	5 mg twice a day	The recommended dose is 2.5 mg twice daily in patients with at least two of the following characteristics: age greater than or equal to 80 years body weight less than or equal to 60 kg serum creatinine greater than or equal to 1.5 mg/dL
	Dabigatran	Pradaxa		150 mg twice a day	In patients with moderate renal impairment (CrCl 30-50 mL/min), concomitant use of the P-gp inhibitor dronedarone or systemic ketoconazole can be expected to produce dabigatran exposure similar to that observed in severe renal impairment. Reduce the dose of PRADAXA to 75 mg twice daily
	Rivaroxaban	Xarelto		15 mg once a day	XARELTO should not be used in patients with CrCl 15 to <80 mL/min who are receiving concomitant combined P-gp and moderate CYP3A inhibitors (e.g., erythromycin) unless the potential benefit justifies the potential risk
	Edoxaban	Savaysa		60 mg once a day	SAVAYSA should not be used in patients with CrCL > 95 mL/min because of an increased risk of ischemic stroke compared to warfarin
	Warfarin	Coumadin		maintain INR between 2-3	
Antiplatelet agents for secondary stroke prevention	Aspirin		Secondary stroke prevention	Effective doses range from 81 mg/day - 325 mg/day	
	Aspirin Dipyridamole	Aggranox		50/200 mg twice a day	Avoid aspirin in patients with severe renal failure (glomerular filtration rate less than 10 mL/minute)
	Clopidogrel	Plavix		75 mg once a day	Experience is limited in patients with severe and moderate renal impairment

