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RESEARCH ARTICLE

Simple and Swift Acute Ischemic Stroke Therapy based on Cases and Evidence: Possibilities of Cost Reduction and Improving Global Access

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ABSTRACT:
There have been significant improvement in the care of acute ischemic stroke (AIS) resulting in reducing death and improving outcomes. Numerous groundbreaking positive randomized controlled trials have demonstrated that strokes with large vessel occlusion (LVO) treated with endovascular mechanical thrombectomy (EVMT) with standard treatment are associated with much better outcomes compared to those treated only with standard therapy. Additional evidence also revealed that the positive outcomes continue to persists for stroke patients with large vessels occlusion if they are treated with 24 hours of symptoms including those with wake-up stroke. The evidence suggests that for every two-patient treated with EVMT, one patient can be saved, which is the highest evidence in the medicine surpassing acute myocardial infarction and other acute lifesaving therapies. Based on these evidence, the local, National and International organizations have updated the guidelines in the treatment of AIS which have remarkably strengthen the process, pathways and standards for acute ischemic stroke management in the developed countries. However, not much progresses have made in the developing and third-world countries for stroke therapies, because of cost, affordability and there are no third-party payers. Most recent trials have further discovered that stroke patient with LVO and a large core volume treated with endovascular perfusion therapy in conjunction with standard treatment do significantly better comparted to standard treatment alone. New trials have also demonstrated that stroke patients undergoing EVMT with or without thrombolytic have equal functional outcome. Additional evidence suggests that non-disabling stroke patients treated with dual antiplatelet have equal functional outcome with less bleeding risk compared to intravenous thrombolysis. These evolving evidences have provided us with the opportunities to simplify the algorithm and treatment of acute ischemic stroke, which not only will cutdown time by eliminating unnecessary steps and redundant therapies, but also will reduce the healthcare cost and improving global access, specially, countries where patients bear the costs. In this review, author presents real life stroke patients treated based on recent evidence and provides with a simple and swift algorithm, that will reduce time to perfusion therapy and will make treatment affordable globally.

Abbreviations:

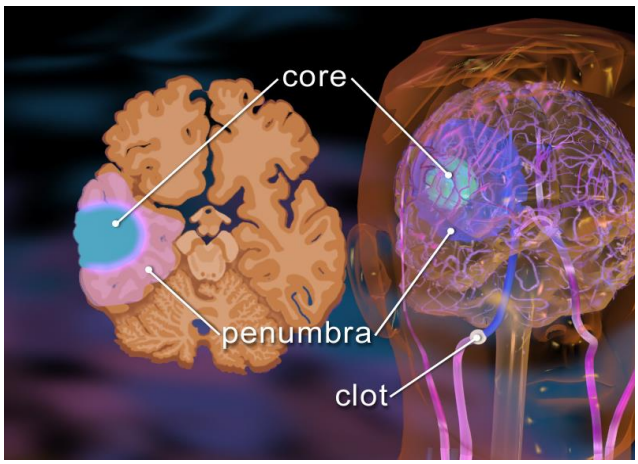
AIS: acute ischemic stroke
AISS: acute ischemic stroke scale
AHA: American Heart Association
ASPECT: Alberta Stroke Program Early CT Score
CPSS: Cincinnati Prehospital Stroke Scale
CIN: contrast-induced nephropathy
CTA: computed tomography angiography
DWI: Diffusion-weighted imaging
ED: emergency department
FAST-ED: Field Assessment Stroke Triage for Emergency Destination (FAST-ED)
GWNS: Gaze Weakness Neglect Speech
IVTPA: Intravenous Tissue Plasminogen Activator
LVO: Large Vessel Occlusion
mRS: Modified Rankin Scale
EVMT: Endovascular Mechanical Thrombectomy
NIHSS: National Institutes of Health Stroke Scale
RACE: Rapid Arterial Occlusion Evaluation Scale

Introduction:

Millions of brain cells are at risk of dying in acute ischemic stroke (AIS) and an ultrafast triage and early perfusion therapy is the key for good function outcomes and preventing disabilities. AIS develops when a blood vessel is occluded by a thrombus from within or by a thrombus travelling from the other part of the body, mainly from the heart impairing the blood flow and oxygen supply to the area of the brain supplied by that particular blood vessel. The center the area of the brain suffering from oxygen is called core where oxygen supply falls below the threshold of brain cells survival. The areas around the core is called the penumbra, where the cells are suffering from impaired oxygen supply, but still salvageable by restoration of blood flow (Figure 1). In AIS, the occluded blood vessel may be a large, medium or small (Figure 2), but all require immediate triage and perfusion treatment for better outcome. The intravenous (IV) thrombolytic (tPA) was first introduced in 1995[1] for AIS patients presenting with disabling stroke with 3 hours of symptoms onset. The tPA was subsequently approved up to 4.5 hours both in the United States and Europe.[2,3] In some instance tPA could be utilized up to 9 hours in specific selected patient based on perfusion imaging when no endovascular mechanical thrombectomy (EVMT) is available.[4] AIS patients with large vessel occlusion (LVO) have disproportionally poor outcomes compared to non-LVO.[5] The positive results of groundbreaking randomized control trials[6-13] of acute ischemic stroke with large vessel occlusion (LVO) allowing patients to receive perfusion therapy within 24 hours of onset, and which is also considered as a standard of care. These novel innovations and initiatives have significantly improved stroke care with the reduction of mortality and morbidity with better outcomes. Presenting stroke symptoms depends on the impaired territory of brain supply a specific blood vessel either in the anterior or in the posterior circulations (Table 1). Available data from these trials also have given us the foundations of clinal signs and symptoms that best correlate with LVO in the anterior circulation. Significant focus has been given for the early identification of AIS with LVO and faster therapy. There are numerous field AIS scales which have been validated in the clinical practice for AIS with LVO.[14-17] Emergency medical service (EMS) uses these field scales of LVO for faster triage and appropriate destination. Subsequently, EMS brings the suspected LVO patients to the designated stroke center capable of EVMT for early perfusion therapy. Unfortunately, in the emergency department (ER) and hospital, neurological examinations are again being repeated using NIHSS, which takes longer time and many of the components of NIHSS do not represent LVO leading to missing the opportunity. Additionally, after the lengthy NIHSS evaluation, patients are sent for multiple images including computed tomographic angiography (CTA) computed tomography (CT) with Alberta stroke program early CT (ASPECT) and computed tomographic perfusion (CTP) leading to further delay in the definitive perfusion therapies with addition of more cost in the triage of the patient, which could be avoided based on the most recent evidence.[18,19] From a healthcare institution prospective, the implementation of such care, the healthcare system must be resourceful and financially sound to process the complex triage process followed by performing series of images with rapid interpretations, which adds addition layers of delays and financial burden. Based on emerging evidence,[18,19] many images such as CTA, CTP, magnetic resonance imaging (MRI), magnetic resonance imaging perfusion (MRP) or steps that are usually taken for the triage may not be necessary to provide early or late perfusion therapy without harm. These additional steps not only cause delays, but also cause redundancy and significantly increase the healthcare cost. In regards to treatment for LVO, these complex processes may create a challenging environment when patients have to pay out-of-pocket, which is the fact for most of the countries in the world, where there are no third parties to pay for these redundant steps including images and combination therapies. Unfortunately, patients have to choose one over other because of affordability as well as availabilities. Recently, author has introduced a new

in hospital/ER acute ischemic stroke with LVO scale for the anterior circulation, which has been validated with CTA, named GWNS stroke scale.[20] The GWNS stroke scale could be easily performed in 3 minutes and would predict LVO better than a lengthy NIHSS. In this review article, authors have presented few AIS patients that were triaged using GWNS acute stroke scale and treated them with most recent evidence, based on the RCT. The latest RCTs for LVO[21] and non-LVO[22,23] may have shaded some lights to guide us to make decisions in those circumstances related to cost, affordability and availability that have global implications without impairing outcome. First objective of this review is to explain the readers that an AIS patient could be triaged and treated as an early or late arrival for perfusion therapy using a simple and economical pathway based on the evidence without sacrifice the outcomes. Secondly, this review clarifies the rationale of choosing a particular triage and treatment option over others on a specific stroke patient of particular clinical scenario. Finally, authors provide their recommendations for faster and affordable acute ischemic stroke therapies using a simple and swift triage and treatment algorithms for possibilities of regional and global access.

Figure 1: Animated representation of a AIS with large vessel occlusion with clot including core and penumbra. Author have published this figure in a previous article in BMANA-Journal.



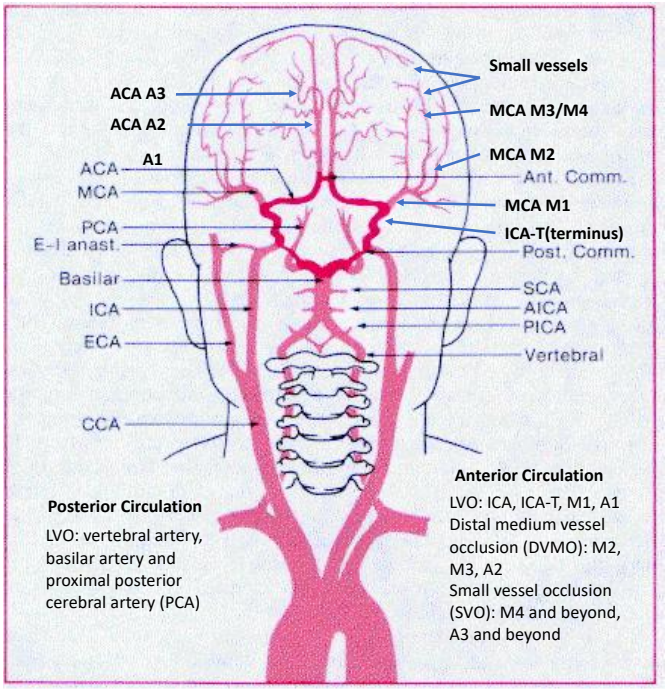


Figure 2: Animated angio-architectures of aortic arch with large blood vessels including anterior and posterior circulations;
CCA; common carotid artery
ICA; internal carotid artery
ECA; external carotid artery
EC-IC; external and internal carotid anastomosis/collateral via ophthalmic artery as as a major collateral.
VA; vertebral artery
BA; basilar artery
PCA; posterior cerebral artery
PComA: posterior communication artery connecting anterior circulation with the posterior circulation as a major collateral
MCA; middle cerebral artery
ACA; anterior cerebral artery
AComA; anterior communication artery connecting right side to the left or vise versa as as a major collateral
Peal collaterals; MCA connecting with ACA through peal connection as a major collateral
Note: collaterals play a vital role to perfuse the penumbra in an event of an occlusion. Therefore, prevention of hypotension and maintaining an acceptable systolic blood is always recommended. The acceptable systolic blood pressure may range from 140 to 185 and if needed, active hydration and vasoactive medication can be used.

Methods:

This is a review article, which has included most of the published randomized control trials of AIS with LVO and non-LVO. The review also has including most recent trials for early and late arrival AIS with LVO that have included patient with large volume stroke and selection of patient was based on CT, ASPECT or perfusion imaging. The review article included studies where simple CT, ASPECT imaging-based selection of patients were compared with advanced imaging modalities including CTP or MRI. For the better understanding of the readers, the review article has presented few index patients who were treated based on the recent evidence and used them as reference in the article for further reviews and discussions.

Review of literature using real cases:

In our review, the first reference patient is an 85 years old man with history of hypertension, hyperlipidemia, who presented to the hospital with NIHSS of 5, GWNS stroke scale 2[20] and last known normal (LKN) 4 1/2 hours ago and his CT Alberta stroke program early CT (ASPECT) was 10.[24] The treatment options were discussed with the patient and the family. Treatment options are; intravenous, tissue plasminogen activator (TPA), intravenous, TNK, and loading doses of aspirin and clopidogrel. Family also wanted to know the natural history of the recovery for a patient with a small NIHSS.[1,3] The natural history was explained to the patient stating that most of the patients with the NIHSS less than 6 do better but there is evidence that may do better with thrombolytic, however there is a chance of intracranial hemorrhage (ICH) among patients receiving thrombolytic. Patient family wanted to explore more about giving aspirin and Plavix based on the most recent trial.[22,23] Patient family was told that this study was performed in China, which has demonstrated that equal benefit with an aspirin and clopidogrel versus intravenous TPA with less asymptomatic hemorrhagic transformation. Patient was loaded with 4 baby aspirin and 300 mg of clopidogrel. Patient remaining management was followed based on the American heart association guideline. Patient symptoms completely resolved and NIHSS became 0. Patient's stroke woke up demonstrated right internal carotid artery (ICA) more than 70% stenosis. Patient was offered ICA revascularization options and underwent successful stenting of the right ICA with embolic protection device (AHA guidelines). Patient was discharged home with NIHSS zero and modified ranking score (mRS) of 1 which is at his baseline. Our next reference patient is a 43 years old woman with history of hypertension, hyperlipidemia presented with left-sided ataxic hemiparesis including sensory symptoms and dysmetria with NIHSS of 5 and LKN 4 hours ago with presenting ASPECT of 10. It was felt to be related to the small vessel disease, and maybe benefited with aspirin clopidogrel, over IV thrombolytics. Patient was offered both treatment options and chosen aspirin and clopidogrel. Patient symptoms resolved, and MRI demonstrated a right subcortical lacunar stroke. Patient stroke work up was negative except for risk factor of hypertension, hyperlipidemia, diabetes and smoking. Patient was counselled on the stroke risk factors including smoking cessation and healthy diet with physical activities options. She was prescribed atorvastatin, antihypertensives and scheduled to have follow up with a stroke specialist. Our third reference patient was last known normal 2 hours ago, presented with right facial droop, right pronator drift with word finding problem and NIHSS of 5 GWNS stroke scale 2.[20] Patient did not have any large vessel occlusion, and we offer thrombolytic. Patient was reluctant; however, we have given the evidence that the patient might be benefited. Patient received the thrombolytic and symptom results in 12 hours. She was in the critical care unit. The cause of the stroke was intermittent arterial fibrillation. Patient was sent home with apixaban 5 mg two times a day with all risk reduction strategies based on AHA guidelines.[25]

In this review, the 4th reference patient is a 65 years old man with history of AF presented with an AIS and his field FAST-ED was 4 by EMS and patient was bought to the hospital. Patient has right gaze with left hemiparesis and neglect with GWNS stroke scale 4[20] and NIHSS 19. Patient's CT ASPECT was 9. Patient immediately received IV TPA[1,3,24] and bought to the interventional suite for mechanical thrombectomy bypassing, CT angiogram and CT perfusion.[18,21] Patient receive full perfusion with 3 hours. Repeat CT head no ICH, but small basal ganglia stroke. His NIHSS became 0 in 48 hours. Patient was started on apixaban 5 mg two times a day with secondary risk factor reduction, including Stroke education. Our 5th patient is a 48-year-old man, educated self-employed and self-pay presented with right sided gaze, left sided of hemiparesis and neglect presented within 11/2 hour of symptoms, GWNS stroke scale 4 indicating AIS with LVO. Patient's wife was also with him. Patient and family made it clear that he has a large medical bill and he would like to choose one best option for his treatment. Patient was offered IV thrombosis followed by mechanical thrombectomy. After reviewing the risk and benefit including cost and most current evidence,[26,27] patient wanted EVMT without

thrombolytic. Additionally, author had a pilot trial[28] of primary EVMT without IV tPA that demonstrated similar results of the most recent RCT.[26,27] Patient was told that the chances of complete perfusion may be less if no tPA is chosen, but, there were no differences in outcomes.[21] However, it was made clear to patient that there is no guarantee of outcomes irrespective of his decisions. Patient received 300 mg rectal aspirin and underwent EVMT with stent retriever device resulting in complete perfusion and became normal in 24 hours. He was discharged home in 48 hours with apixaban 5 mg two times a day with all stroke risk factor modification strategies based on AHAS guidelines.[25] Patient went to work in 7 days and achieved his baseline mRS of 0.

Our next reference patient that we have used for the review of literature is a 78-year-old woman with history of tremors and baseline, mRS of 2 who was last known normal 12 hours ago. Patient was found on the floor with left gaze, right hemiparesis and aphasia; GWNS stroke scale 3.[20] Patient was bought to emergency department where she was found to have NIHSS 25 and GWNS scale of 3, required immediate intubation because of airway. The CTA demonstrates left M2 occlusion and ASPECT score was 9 and underwent immediate EVMT without CT perfusion[18,21] after receiving 300 mg rectal aspirin. Patient achieved TICI3 perfusion (Fig1) and her 24 hours CT head demonstrates no large stroke. Patients was started on apixaban 5 mg two times a day. Patient was extubated ted in 48 hours and NIHSS became 0. She required inpatient rehab and achieved her baseline mRS 2 at 90 day.

Figure 3: 78-year-old woman with baseline mRS 2,last known normal 12 hours ago and found on the floor with left gaze, right hemiparesis and aphasia; GWNS stroke scale 3 and NIHSS 25 , required immediate intubation because of airway and CTA revealed left M2 occlusion and ASPECT score was 9. Underwent immediate EVMT without CT perfusion; achieved TICI3 perfusion, NIHSS became 0 in 48 hours and at 30 day her mRS became 2.

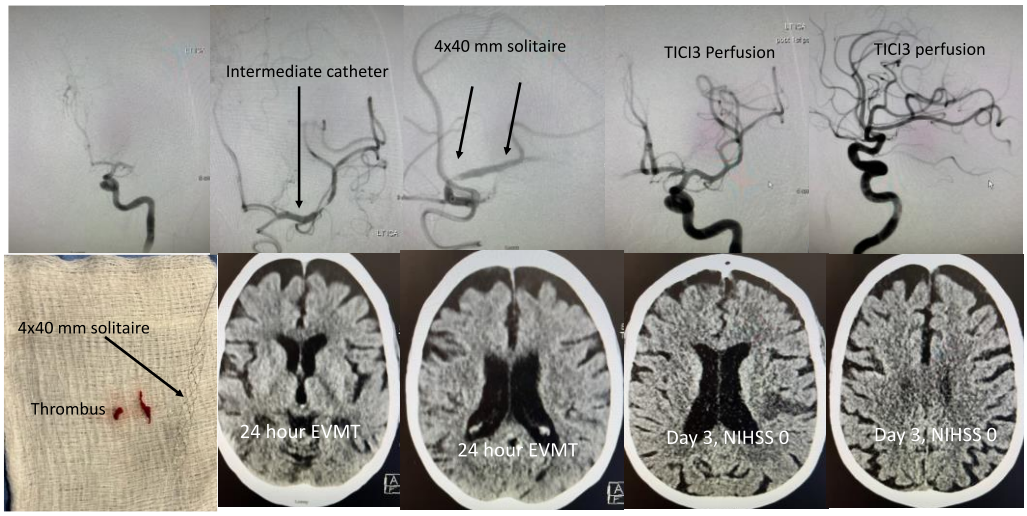


Figure 4: 50 year-old-woman admitted with left MCA non LVO stroke beyond thrombolytic window. NIHSS improved from 9 to 3 on day 3. On day 4, patient was found to have right gaze, left hemiparesis and right neglect (GWNS stroke scale 3), NIHSS 19, ASPECT9 and CTA demonstrated right MCA distal branch occlusion. Patient underwent EVMT with TICI 3 and her NIHSS went to 3 in 24 hours and 1 on day 5 despite density on the CT head.

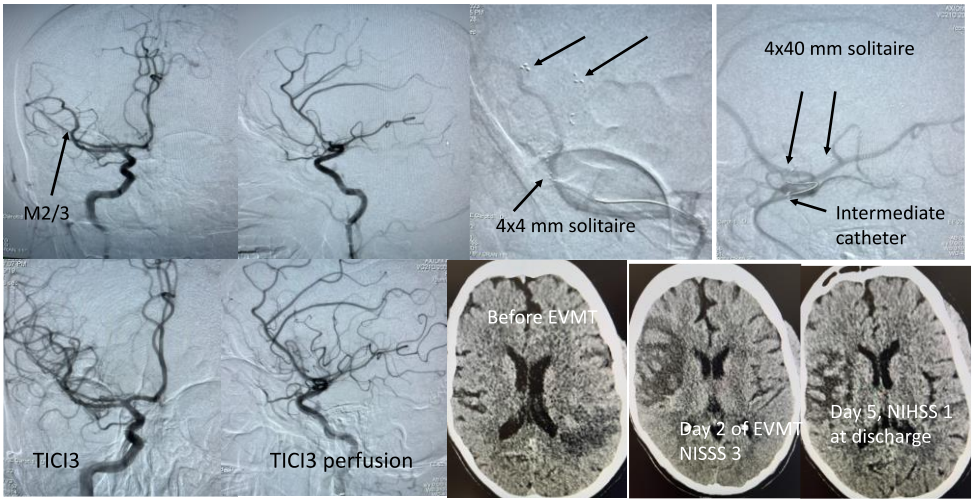


Figure 5A: 55 Y/O women with metabolic syndrome , last known normal 30 minutes ago, transferred from a rural hospital, NIHSS 25 and GWNS, indicative of LVO. CT ASPECT 5, directly went for EVMT without CTA/CTP. Angiogram demonstrated left ICA-T clot, TICI 3 perfusion achieved with stent retriever device, balloon guide and and an intermediate catheter using TRAP technique

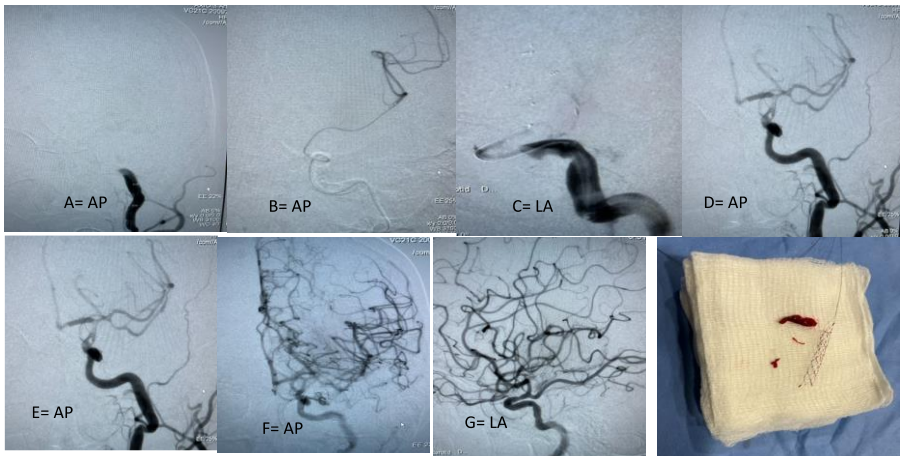
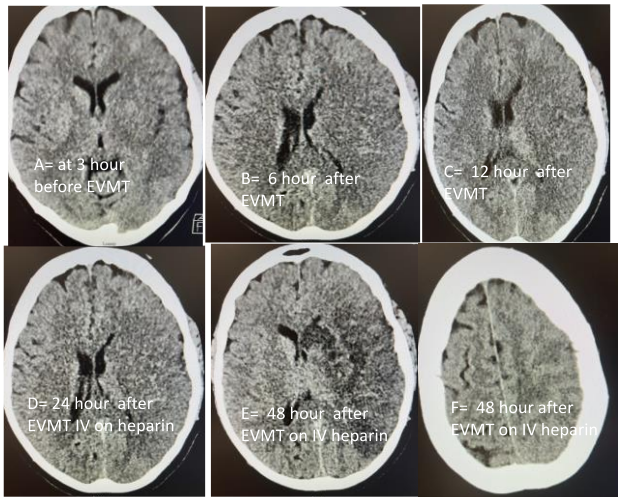


Figure 5B: Initial ASPECT 5 at presentation and, 6, 12, 24 and 48 hours after EVMT



The next index patient we have chosen for the review of literature was a 50 year-old-woman admitted to stroke service with left MCA non LVO stroke beyond thrombolytic window. Patient was placed on both aspiring and clopidogrel and NIHSS improved from 9 to 3 on day 3. On day 4, patient was found to have right gaze, left hemiparesis and right neglect (GWNS stroke scale 3), NIHSS 19, ASPECT9 and CTA demonstrated right MCA distal branch occlusion. Patient underwent EVMT without CTP.[18,21] Patient achieved TICI 3 perfusion (Fig 2) and her NIHSS went to 3 in 24 hours and 1 on day 5, despite density on the CT head (Fig 2). Patient was sent to rehab and her mRS became 2 in 30 days.

The final reference patient used for the review article is a 55-year-old woman, who suddenly developed left gaze deviation, right sided weakness and aphasia in a non-stroke designated rural hospital, LKN 30 minutes ago. Patient was triaged and recommended to bring to stroke hospital. Because of rural ambulance shortage, patient was air lifted and bought to hospital 2 hours after her stroke onset. Upon arrival to endovascular center, patient GWNS stroke scale was 3[20] and NIHSS 25 required immediate endotracheal intubation. Plans was to just perform CT followed by IV TPA based on ASPECT and immediately to NES for faster EVMT. The ASPECT was 5 and was not a candidate for intravenous thrombolytic and underwent EVMT without any advanced imaging.[14,18,21] Angiography demonstrated left ICA-T occlusion and TICI 3 perfusion was achieved with 2 passes using balloon guide, intermediate catheter and 4 mm x 40 mm stent retriever (Figure 3A). It was discovered after thrombectomy that patient was on apixaban (Eliquis) for clots in her kidney and she ran out of her medicine 3 days ago. The follow-up two CT head in 6-hour interval (Fig 3B) didn't demonstrated any perfusion related intracranial hemorrhage. Considering patient history of multiple thrombo-embolic events and prevention of potential subsequent event, it was decided to start intravenous heparin to keep the apparent partial thromboplastin (aPTT) 1.5 to 2 time of her baseline aPTT. Patient baseline aPTT was 28 and the aPTT target was 45 to 55. The 24-hour follow-up CT head after initiation of IV heparin revealed no ICH (Fig 3B). After 5 days, the IV heparin was switched to apixaban. Patient improved and went to inpatient rehabilitation.

Discussion:

Our real time stroke patients chosen for this review article had low to high NIHSS and have presented in the early or the late stage of stroke, and underwent interventions based on the recent trials, guidelines and publications resulting in good outcomes. Additionally, our treatment strategies have not only simplified the stroke triage and treatment algorithms with initiation of early perfusion therapy, but also reduced the health care system resource utilization and providing an option for patient who pays out of pocket. The authors have linked the real stroke patients triage and treatment scenarios with current available publications to make this review interactive and interesting.

In a recent trial,[22] AIS patients with NIHSS 5 or less were randomized to receive IV tPA or loading dose 300 mg clopidogrel and 100 mg aspirin followed 75 mg of clopidogrel and 100 mg daily for 14 days. There was no significant difference[22] in regards to favorable function outcomes (mRS 0-1) between these two arms at 90 days as a primary outcome; aspirin-clopidogrel group (91.6%) achieved a favorable functional outcome at 3-month versus 85 (78.0%) in the alteplase group (OR 4.463, 95%CI 1.708–11.662, $p = .002$). Asymptomatic ICH occurred in 0.8% patients who received aspirin-clopidogrel, as compared with 3.7% patients in alteplase group ($p = .030$); meaning alteplase group had higher incidence of AICH than dual antiplatelet group. Additionally, in the original NINDS and ECASS trills patient with minor disabling stroke patients were excluded. The PRISMS[23] trial (aspirin 325 mg plus IV placebo vs IV tPA and oral placebo) also have demonstrated no significant difference in clinical outcome in regards to 90 days mRS; 78.2%in the alteplase group vs 81.5% in the aspirin group achieved a favorable outcome (adjusted risk difference, −1.1%; 95% CI, −9.4% to 7.3%). In this trial, 5 alteplase-treated patients (3.2%) vs 0 aspirin-treated patients had sICH (risk difference, 3.3%; 95% CI, 0.8%-7.4%). In our reviews, the first reference patient presented with minor non-disabling stroke, NIHSS 5 and older than 85, who have chosen not to receive thrombolytic, but antiplatelets as an alternative option and have achieved good functional outcome. The 2nd reference patient also presented with nondisabling lacunar stroke with NIHSS 5 and have chosen alternative option of acute antiplatelets instead of thrombolytic resulting in good outcome. The alternative option of dual antiplatelets was offered based on the most recent RCT evidence[22,23] with modified dose of aspirin 324 mg instead of 100 mg.

In regards to the cost and resources for developed countries, our both patients have saved significant health care cost and allocation of resources including not requiring critical care stay and potential additional stay in the critical care unit and hospital. If these two patients would have received TPA, they should have required to monitor in the critical care unit as an standard of care after thrombolytic and potentially would have stayed more days in critical care unit or hospital if they would have developed asymptomatic or symptomatic ICH following thrombolytic, occupying the rare resources for those who are still waiting in the ER or transferred out of the community creating significant inconveniences and burden for the patient and their family. Hypothetically, in regard to the individual, regional and global economic impact; where, a patient with out of pocket expenses will have to spent remarkably less if dual antiplatelet are used instead of IV tPA. In many third world countries, tPA is expensive, not available and substituted with alternative thrombolytic may lead to more complications and less benefits. Additionally, dual antiplatelets option would also simplify the stroke system care and access, as the aspiring and clopidogrel are very affordable and readily available all over the world including third world countries.

In this review, the 3rd reference patient received IV thrombolytic despite being a low NIHSS as the patient had disabling stroke symptoms and have achieved good outcome. Additionally, patient had history atrial fibrillation and associated with embolism likely, justifying our decision.[1-3]

The 4th reference patient in our review presented with suspected right sided LVO based on FAST-ED and had high NIHSS with cortical representation; right gaze, left hemiparesis, dysarthria and neglect with GWNS scale of 4.[20] Patient ASPECT was 9 and received tPA and underwent EVMT without advanced imaging. Based on the FAST-ED LVO validation with NIHSS[29] as well as GWNS in hospital stroke scale,[20] this patient has a very high likelihood of having LVO, making it justifiable of taking the patient for definitive perfusion therapy. This strategy simplified the process and avoided the delay and unnecessary intravenous 100 ml contrast and exposure to additional radiation. Additionally, multiple RCTs have demonstrated that IV tPA with EVMT with early perfusion has better outcome.

The 5th reference patient in the review poses a real challenge as he is self-employed and bears the medical cost out of pocket. This patient had similar clinical scenario to our previous case and p with suspected LVO and only had CT with ASPECT 10. Patient has chosen EVMT alone instead of IV tPA plus EVMT after informed consent. The justification and agreeing with patient decision based on the most recent publication in NEJ[26] as well as JAMA.[27] In endovascular therapy with or without IV tPA in acute ischemic stroke[26]; 327 patients assigned to the thrombectomy-alone group and 329 assigned to the combination-therapy group. Endovascular thrombectomy alone was noninferior to combined intravenous alteplase and endovascular thrombectomy with regard to the 90 days mRS (adjusted common odds ratio, 1.07; 95% confidence interval, 0.81 to 1.40; P=0.04 for noninferiority) but was associated with lower percentages of patients with successful reperfusion before thrombectomy (2.4% vs. 7.0%) and overall

successful reperfusion (79.4% vs. 84.5%). Mortality at 90 days was 17.7% in the thrombectomy-alone group and 18.8% in the combination-therapy group. The study concluded that Chinese patients with AIS from LVO, EVMT alone was noninferior with regard to functional outcome, within a 20% margin of confidence, to endovascular thrombectomy preceded by intravenous alteplase administered within 4.5 hours after symptom onset. In Skip randomized clinical trial[27]; Favorable outcome occurred in 60 patients (59.4%) in the mechanical thrombectomy alone group and 59 patients (57.3%) in the combined intravenous thrombolysis plus mechanical thrombectomy group, with no significant difference between-group in regards to 90 day mRS (difference, 2.1% [1-sided 97.5% CI, -11.4% to ∞]; odds ratio, 1.09 [1-sided 97.5% CI, 0.63 to ∞]; P = .18 for noninferiority) with no differences in mortality. Any intracerebral hemorrhage was observed less frequently in the mechanical thrombectomy alone group than in the combined group (34 [33.7%] vs 52 [50.5%]; difference, -16.8% [95% CI, -32.1% to -1.6%]; odds ratio, 0.50 [95% CI, 0.28 to 0.88]; P = .02). Symptomatic ICH was not significantly different between groups (6 [5.9%] vs 8 [7.7%]; difference, -1.8% [95% CI, -9.7% to 6.1%]; odds ratio, 0.75 [95% CI, 0.25 to 2.24]; P = .78). The study concluded that among patients with AIS with LVO, EVMT alone, compared with combined IV tPA plus EVMT, failed to demonstrate noninferiority regarding favorable functional outcome.

In regards to the simplicity and stroke system of care, direct EVMT will simplify the triage and the treatment by cutting extra-steps that would have required in the process and polities of IV tPA administration. Our index patient was taken directly to NES without IV tPA. Additionally, we have not performed any advanced images, such as CTA and CTP leading to much simplicity to the process and significant reduction of precious time. If we look at the cost, this patient has avoided out of pocket cost of tPA and advanced images and still have achieved good outcome. In regards to global implications; in most of the countries, there are no third-party-payers, patients and their family bear the health care cost upfront. Therefore, using direct EVMT without tPA would have made the treatment accessible and affordable. The author would like to emphasis that in AIS with LVO, EVMT is the driver of clinical outcome,[26,27] not IV tPA, but, it is an adjunct. Therefore, unnecessary waiting and loosing time for IV tPA administration prior to EVMT should be avoided; especially, when it is not clear if the patient is or is not a candidate for thrombolytic. The author believes that this strategy will help improve more access for the perfusion therapies in stroke victims with LVO in the countries, where the patient or institution had to pay from their own cutting the cost half without impairing outcomes and do not have to choose between thrombolytic and EVMT.

For the final reference patient of our review article; the presenting GWNS and NIHSS were indicative of an LVO with large territory ischemia. Additionally, patient repeat CT, ASPECT reduced to 5 in 2 hours indication presence of poor collateral or poor cerebral reserve. Because of her rapidly declining ASPECT as well as recent evidence,[14,19] we have avoided advanced imaging including CTA and CTP and initiated early prefusion therapy resulting in complete reperfusion. In support to our simplified strategy, in a recent study,[15] outcome of patients after EVMT selection based on CT/ASPECT, CTA/CTP or MRI/MRI perfusion was evaluated and found to have no significant difference among the groups in regard to the functional outcome or risk of ICH. Patient selected based on MRI/MRI perfusion did poorly compared to ASPECT on CT head. The explanations are very simple; for the initiation, screening and performing MRI/MRP required time resulting in loosing precious penumbra, which is not only impractical but also should be avoided. In regard to CTA/CTP, CTA will need time for the administration 100 ml of contrast as well as its interpretation, requiring additional time. It makes reasonable to bring this patient directly to NES, as the patient already in an endovascular center and surgeon is ready. Therefore, an extra step was avoided. Regarding CTP; CTP requires more time delays in perfusion therapy in addition the exposure to more radiation. The CTP also dependent on the timing of IV admiration of contrast and patient factors including hemodynamic status, which may lead to improper accusation and interpretation. Based on above, performing CTA/CTP may not contribute significantly, but definitely will cost more brain cells and health care burden for the patient and for the health system. In another large cohort study,[14] more than 1 in 5 patients presenting with an ASPECTS of 2 to 5 achieved 90-day functional independence after EVMT. A favorable outcome was nearly 5 times more likely for patients with low ASPECTS who had successful recanalization. The association of a low ASPECTS with 90-day outcomes did not differ for patients presenting in the early vs extended EVMT window. In this study,[19] 213 patients [9.1%] had an ASPECTS of 2-5). At 90 days, 47 of the 213 patients (22.1%) with an ASPECTS of 2 to 5 had a modified Rankin Scale score of 0 to 2 (25.6% [45 of 176] of patients who underwent successful recanalization [modified Thrombolysis in Cerebral

Ischemia score ≥2B] vs 5.4% [2 of 37] of patients who underwent unsuccessful recanalization; P = .007). Therefore, initiated early perfusion therapy and had achieved TICI 3 perfusion.

The most recent SLECT2 trial also shed lights on the outcomes of patient with low ASPECT score. The SELECT2 a prospective, 1:1 ratio to endovascular thrombectomy plus medical care or to medical care alone, open-label, adaptive international trial involving patients with stroke due to occlusion of the ICA-Terminus or the first segment of MCA to assess endovascular thrombectomy within 24 hours after onset. Eligibility criteria was a large ischemic-core volume, defined as an Alberta Stroke Program Early Computed Tomography Score of 3 to 5 or a core volume of at least 50 ml on computed tomography perfusion or diffusion-weighted magnetic resonance imaging. Patient assigned with EVMT plus medical management have significantly better outcome compared to medical management only (20% of the patients in the thrombectomy group and 7% in the medical-care group had functional independence (relative risk, 2.97; 95% CI, 1.60 to 5.51) without any differences in mortality. The generalized odds ratio for a shift in the distribution of modified Rankin scale scores toward better outcomes in favor of thrombectomy was 1.51 (95% confidence interval [CI], 1.20 to 1.89; P<0.001). The SELECT2 trial results will help us to recruit AIS with large volume stroke and LVO for EVMT perfusion therapy, who otherwise would have treated medically only missing the opportunities of achieving good functional outcome.

Conclusions: In conclusions, the evidence suggests that minor non-disabling stroke patients could be treated with loading dose of aspirin and clopidogrel instead of intravenous thrombolytic therapy achieves the same functional outcome with less chance of intracranial hemorrhage. In the review, we have demonstrated that AIS patient could be triaged immediately using an LVO stroke[20] scale and bought directly to the EVMT room after a simple CT with ASPECT without advanced imaging for early perfusion therapy. Emerging data suggest that AIS with LVO within 4.5 hour of symptoms onset achieve similar outcome if treated directly with EVMT compared to intravenous thrombolytic followed by EVMT, which we have demonstrated in our index patients. We have also reviewed that for the early or late selection of patient for perfusion therapy with EVMT, a plain CT with ASPECT score is as good as performing advanced imaging with CTP and MRI with perfusion without harm. Most recent evidence suggests that AIS patient with LVO and a large volume stroke (50 ml and higher) treated with EVMT in conjunction with standard treatment do significantly better comparted to standard medical management. Finally, we have discussed that an AIS patient with LVO and presenting CT ASPECT score as low as 2 benefits from EMVT without increasing chances of symptomatic intracranial hemorrhage. Based on above evidence, we have a simplified the algorithm in the treatment of AIS patents for early perfusion therapy that will make the triage and treatment process swift leading to improving good outcome. Additionally, these strategies will further simplify the global access of AIS therapies affordable by cutting down the cost with redundant triage, imaging and treatment. We are presetting the current complex and comprehensive triage algorithms that are utilized for the treatment of AIS (Table 1). The author is also proposing the most simple and swift algorithm which could be utilized regionally and globally based on the regional and global accessibility and affordability (Table 2). Therefore, the treating stroke team and patient may choose the best option based on the personal, local and regional affordability and availabilities of resources without sacrificing the care and outcomes.

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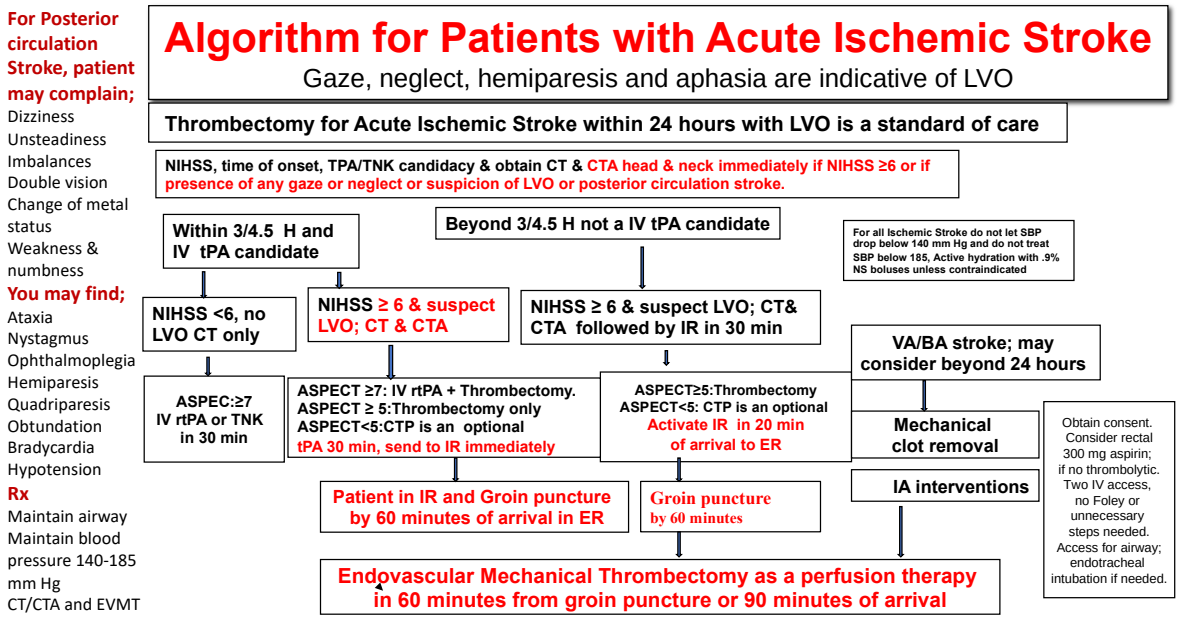
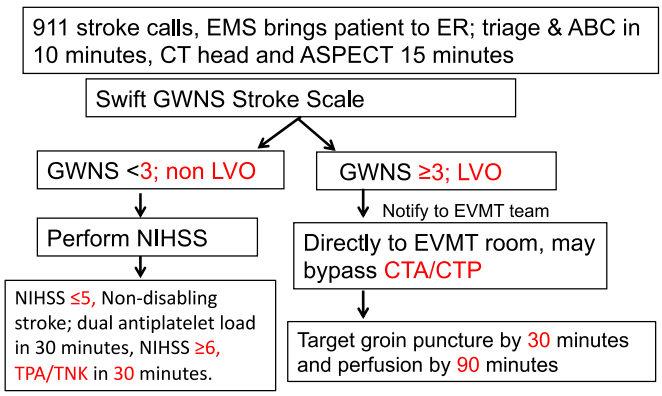


Table 1: Current complex and comprehensive AIS triage algorithm

Gaze, Weakness, Neglect and Speech (GWNS): a stroke scale of large vessel occlusion (LVO) in the emergency department for faster Treatment.



Endovascular Strategies: Airway Breathing Circulation (ABC). Maintain adequate hydration and systolic blood pressure of 140 to 185 mm Hg until endovascular mechanical thrombectomy (EVMT) is initiated. Consider optional IVTPA if a candidate, if not a TPA candidate, consider 300 mg rectal aspirin and bring the patient to EVMT room. Avoid unnecessary steps; Foley catheter, chest x-ray and electrocardiography.

Table 2: Simple and swift AIS triage and treatment algorithm

GWNS Stroke Scale Score

Item	GWNS Score
GAZE deviation or preferences	
Absent	0
Present	1
Any weakness	0
No	1
Drift or complete raralysis	
Neglect/Disregard/Extinction	
Absent	0
Presence	1
Any Speech impairment: aphasia/dysarthria	0
Absent	1
Present	
Total GWNS Score	4

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