Suspected Large Vessel Occlusion
Should Emergency Medical Services Transport to the Nearest Primary Stroke Center or Bypass to a Comprehensive Stroke Center With Endovascular Capabilities?

Andrew M. Southerland, MD, MSc; Karen C. Johnston, MD, MSc; Carlos A. Molina, MD, PhD; Magdy H. Selim, MD, PhD; Noreen Kamal, MD; Mayank Goyal, MD

The Case
A patient calls 911 for acute onset of stroke-like symptoms. Emergency medical services (EMS) arrives within 2 hours of stroke symptoms onset; National Institutes of Health Stroke Scale score=14.

The Question/Controversy
Should the emergency medical technician (EMT) take the patient to the nearest primary stroke center or should they bypass the primary stroke center to take the patient directly to a comprehensive stroke center with endovascular capabilities?

Yes. EMT Should Take Patients to the Nearest Primary Stroke Center
Andrew M. Southerland and Karen C. Johnston

There is no debate that new data demonstrating significant efficacy of endovascular therapy (EVT) in acute ischemic stroke (AIS) is a paradigm shift. For select patients with anterior circulation stroke, proximal large vessel occlusion (LVO), and supportive brain imaging, timely reperfusion using stent retriever thrombectomy substantially increases the odds of a favorable outcome. However, the suggestion that EMS should bypass primary stroke centers (PSC) to proceed to comprehensive stroke centers (CSC) for patients with suspected moderate/severe AIS is premature.

If you don’t know where you’re going, you might wind up someplace else.

– Yogi Berra

This case highlights the challenge of accurate prehospital diagnosis. In the scenario, an EMT arrives to find the patient with a National Institutes of Health Stroke Scale score=14, but this is misleading. Numerous prehospital stroke scales have been validated for EMS use, but are not measures of stroke severity and lack the requisite sensitivity/specificity for diagnosing anterior circulation LVO. Even more compelling is the discrepancy in number of stroke patients screened compared with the small fraction who are ultimately eligible for EVT (Extend-IA [Extending the Time for Thrombolysis in Emergency Neurological Deficits–Intra-Arterial] trial reported <1%). Using our current tools, selective bypass to a CSC would result in many endovascular ineligible patients triaged to facilities where no additional therapy can be offered, who are subjected to delays in initial intravenous (IV) tissue-type plasminogen activator (tPA) and other standard of care potentially resulting in worse outcomes, and who are unnecessarily uprooted from their local communities and hospitals.

IV-tPA, rapidly administered at PSCs, remains a highly efficacious and proven treatment for AIS. The odds of favorable outcome increases substantially with shorter time to treatment; every 15 minute acceleration in start of IV-tPA results in a 4% increased likelihood of independence. Current guidelines state that delays in IV-tPA and diversion adding >15 to 20 minutes to transport should be avoided.

When you come to a fork in the road, take it.

– Yogi Berra

In a scenario where a PSC and CSC are equidistant or when an absolute contraindication to tPA is known in the field (eg, fully anticoagulated), we would agree that either transport path at the fork is reasonable. However, in rural and underserved areas with greater geographic disparities and time obstacles, selective diversion ultimately delays acute evaluation and treatment. Ambulance telemedicine and mobile stroke units are exciting
new developments to assist with prehospital triage, but are not yet generalizable for clinical practice. Thus, our focus should be on the development of local and regional systems of care to maximize efficient collaboration between providers and stroke centers and to work together, not against, on behalf of our patients.

*The future ain’t what it used to be.*

– Yogi Berra

Truly, we are at a crossroad in the evolution of acute stroke treatment. There is no argument against the impact of EVT to vastly improve outcomes for our stroke patients meeting appropriate eligibility criteria. However, we are not yet ready to bypass our primary responsibility to patients until we have a better idea of where we are going. First, do no harm.

**No. EMT Should Bypass Primary Stroke Centers**

Noreen Kamal and Mayank Goyal

The recent success of 5 endovascular randomized control trials has changed best practice guidelines1 to include EVT for AIS patients with an LVO with effect sizes in some studies as high as 25%. However, EVT is only offered in CSC, which makes access to this highly beneficial therapy difficult for patients who are outside the catchment area of a CSC. Should the EMT bypass a closer PSC to ensure that the patient has access to EVT sooner?

Here are some facts: (1) IV-tPA is not that effective in LVO; (2) time is brain: the faster we can achieve reperfusion, the higher is the likelihood of a good outcome; (3) endovascular treatment is safe and highly effective (number needed to treat of 2.5–7 in recent trials). Also it is quite likely that expertise, efficiency, and workflow are likely related to volume of patients treated and, as such, likely better at the CSC. Most CSCs have better 24/7 service not only for giving tPA but also for imaging, decision-making, and management of complications. It is also important to note that CSCs can administer tPA as needed.

If a patient is to be transported to a PSC to get tPA early before going to a CSC for EVT (ie, drip and ship), they could potentially benefit from early thrombolysis, but result in delayed endovascular treatment. We should keep in mind that the modeled benefits of early tPA is based on the entire stroke population, and LVO typically have a much lower reperfusion rate. This benefit is highly dependent on the distances between the scene of the stroke and the PSC, the scene and the CSC, and the PSC and the CSC. In addition to the distances, the benefit is also highly dependent on the ability for the PSC to administer tPA and get the patient out the door quickly for transport to the CSC.

We can model the benefit of going directly to the CSC versus drip and ship. If we use the Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment (SWIFT-PRIME) trial data and initially look at First Medical Contact to PSC of 30 minutes and assume an onset to First Medical Contact of 90 minutes. Furthermore, we have need to CSC arrival of 110 minutes and door to reperfusion at the CSC of 100 minutes. For the direct transport option, we have a First Medical Contact to CSC of 90 minutes and the same reperfusion time. This results in a total First Medical Contact to endovascular reperfusion for the drip and ship of 260 minutes compared with 180 minutes for the mothership assuming that the door-to-needle time of 30 minutes at the PSC. The model will yield a slight benefit for the drip and ship of 40% compared with 30% for the mothership option. However, this will only happen if the times described above are practically achievable. In reality, the door-to-needle times at PSCs are much longer and the door-in-door-out (DIDO) times are also considerably longer. The median delay of onset to reperfusion as a consequence of drip and ship compared with mothership was ≈2 hours in SWIFT-PRIME (presented at ESOC, Glasgow, 2015). In this scenario (and in most workflow situations), there would be clear benefit of mothership.

Keeping these variables in mind, we argue for bypassing the PSC until we can improve our systems of care to rapidly perform noncontrast head-computed tomography scan followed immediately by a computed tomography angiogram and administer tPA within 30 minutes of arrival; additionally, the PSCs need to get the patient out the door within 45 minutes of arrival. It is possible that there is a slight benefit to early tPA when the distance from the scene to the PSC is small; however, this is based on current data based on tPA response for all comers. It is likely that the curve for decay of tPA response is much shallower in patients with LVO. We will likely have a better understanding of these curves because meta-analysis data from the current trials sheds further light on the subject.

In summary, we argue that we bypass the PSC and transport LVO patients directly to the CSC (in most situations) until we can invest in improving our system of care to ensure rapid DIDO of <40 minutes at the PSC. Further data from ongoing meta-analyses and improvements in endovascular treatment and workflow will continue to refine the model and, in our opinion, continue to tilt the curves in favor of direct to CSC.

**Rebuttal by Drs Southerland and Johnston**

We agree that for AIS patients with known LVO, (1) EVT is safe and effective, (2) EVT+IV-tPA is superior to IV-tPA alone, and (3) the faster we can achieve reperfusion, the higher the likelihood of a good outcome.

However, based on the data, most AIS patients presenting via EMS will not have a retrievable LVO and are ineligible for EVT. Therefore, uniformly bypassing proximate PSCs in favor of CSCs, without more accurate tools for prehospital diagnosis, would be a disservice to the majority of patients with AIS. Additionally, the argument in favor of hospital bypass makes 2 unjustified presumptions: (1) only CSCs can effectively perform EVT (note 17/24 US SWIFT-PRIME sites were not CSCs during study enrollment’); and (2) stroke systems of care can be optimized while concomitantly bypassing PSCs and stroke-ready hospitals. To optimize our stroke systems, we must incorporate all components of the system into the care continuum and not isolate ourselves to a limited number of accessible CSCs.

Thus, once LVO has been accurately determined, we support rapid transport to an EVT-capable center. However, for the majority of AIS patients triaged by EMS, the proper course of action is to the nearest PSC that can offer initial stroke management and identify eligibility for the range of acute therapies.
Rebuttal by Drs Kamal and Goyal

Action Expresses Priorities

—Mahatma Gandhi

We as healthcare professionals should have only one priority in this situation: create systems of care that maximize the chance of this patient who is suffering from a significant stroke to have a good outcome. And with that priority, our actions should correspond to that priority. We agree that although there are limitations of diagnosing in the field and that there cannot be a single solution that would apply to all geographies, however, in the overall picture, we have to acknowledge that (1) IV-tPA has been around for decades. It is unlikely that its efficacy or workflow is going to change in the near future. (2) In light of recent data and the use of modern technology and communication, our ability to better detect patients with LVO in the field will continue to improve. (3) All aspects of endovascular treatment, workflow, quality of reperfusion, complication rate, are likely to continue to improve (because of more experience, better technology, increased resources, and standardization of processes). As such, we respectfully submit that ultimately Yogi Berra is way out of his league to decide priorities on systems of care for an otherwise dismal disease. We believe that our Gandhian action of taking the patient direct to the CSC is a much better reflection of our priority; giving this patient the best chance for independence (pun intended).

Comments by Drs Molina and Selim

The recent overwhelming evidence in favor of EVT in patients with LVO are challenging transfer protocols worldwide, and novel algorithms are being proposed to improve access to EVT for patients living in geographic areas distant from CSC. This is a reperfusion race starting in an island crowded of swimmers that all look the same. We need to pick good swimmers (with LVO), to start a fast and long swim course directly to the CSC shore, from the crowd of regular swimmers (without LVO), who just need a short swim to the nearest stroke center beach. However, some regular are in fact good swimmers, and after a long transition for tPA (DIDO), they need a secondary bike course to the CSC. On the contrary, some good swimmers may suffer the direct transfer and die on the shore because of delay or even deny of tPA at the CSC.

Our opponents agreed that current clinical and imaging tools for diagnosing LVO in the field are inaccurate and poorly implemented, respectively. Moreover, direct transfer by EMS to a distant CSC of some unstable severe strokes, including intracerebral hemorrhage patients, may raise safety concerns. However, transferring severe stroke patients to the nearest stroke center leads to an unacceptable delay for an eventual secondary transfer to CSC for EVT, and a DIDO time <30 minutes seems unrealistic. The benefit of EVT declines dramatically over time, and improving workflows represent a major goal. It seems that there is not a single solution that would apply to different scenarios around the world, including a variety of geographic and resources barriers, health care systems, and reimbursement policies. Direct transfer to CSC bypassing PSC for EVT represents a novel clinical equipoise, and a randomized controlled trial is desperately needed. This trial should define clear processes of care and optimized workflows, use in-ambulance technologies for patient randomization—telemedicine, and establish isochrones to measure the treatment effect. In the meantime, we need to commit ourselves to a continuous development and implementation of reliable tools to optimize the prehospital diagnosis of LVO and improving workflows in stroke center (DIDO), as well as in the CSC!!

Wherever you go, go with all your heart.

—Confucius

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References


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