Stroke is the fifth leading cause of death and remains one of the leading causes of long-term disability in the United States.1-3 Expeditious treatment of acute ischemic stroke (AIS) after symptom onset is paramount because outcomes improve with faster initiation of treatment.4-6 From a practical perspective, AIS is best classified as either arising from an identifiable large vessel occlusion (LVO) or occurring without any identifiable LVO, as definitive treatment involves mechanical thrombectomy (MT) for the former and intravenous (IV) recombinant tissue plasminogen activator (rtPA) for the latter, each with specific indications and contraindications. Nevertheless, because patient outcomes dramatically improve with faster initiation of both rtPA and MT,4-7 characterizing bottlenecks that delay stroke care and identifying strategies for resolving or mitigating these bottlenecks are essential to ensure the best possible outcomes. This article discusses recent studies that have examined workflow bottlenecks for LVO strokes and identified strategies to overcome them.

PREHOSPITAL BOTTLENECKS

The first barrier to stroke treatment is the accurate and timely recognition of the onset of stroke symptoms; this may represent the greatest delay in some cases.8 For example, the Florida-Puerto Rico Stroke Registry found that the median time between first symptom onset and stroke hospital arrival was 339 minutes.9 Because most patients experience symptoms in the community and not in a medical setting, educating the general population on common stroke presentations and how to effectively activate emergency medical services (EMS) may alleviate this bottleneck.8-10 Implementing strategies to address this bottleneck generally fall within the remit of public health and education, are susceptible to marked local and regional variability, and are outside the scope of this discussion. Once EMS has been notified, strategies and protocols that affect EMS response and coordination of patient presentation to the hospital have been shown to reduce delay times. These include prehospital notification by EMS; activation of a dedicated interdisciplinary “stroke code” team with members from emergency medicine, neurology, and radiology to expedite tests and treatments; and contacting next of kin and collecting necessary information regarding medical history and consent for interventions/procedures while the patient is en route.11 By having the stroke team await the arrival of EMS, already having collected the relevant patient history and other crucial information (eg, consent for interventions), time to evaluation, diagnostics, and treatment can be reduced. The key to efficient workflow is the ability to fulfill multiple tasks while the patient may be otherwise occupied or in transit.11 Other possibilities include bringing imaging or other capacities into the field, such as with use of a mobile stroke unit.12

A clear problem with stroke triage arises with the choice of facility to which the patient is first transported. Depending on local circumstances, patients may be transported to primary stroke centers (PSCs) that do not have the capability for endovascular intervention and therefore may only be able to administer IV rtPA. Patients who are subsequently found to have an LVO within criteria for MT would therefore have
to be transferred to a comprehensive stroke center (CSC), which can lead to a significant treatment delay. This has led to a debate regarding the optimal protocol: the “drip-and-ship” model, which entails bringing any patient with a suspected LVO in the field directly to a CSC, even if transport time is slightly greater, to undergo definitive evaluation and treatment (rtPA, MT, or both). Multiple studies have examined whether the transfer process significantly delays care and affects patient outcomes. In the MR CLEAN trial, interhospital transfer was the most important factor associated with treatment delay. Time from stroke symptom onset to treatment initiation increased by 148 minutes in patients transferred from a PSC, despite improved in-hospital workflow times. Outcomes were also worse in that every hour of delay resulted in an absolute 6.4% decrease in the probability of a good outcome by MT, measured as the risk difference between intervention and control. The ESCAPE trial similarly found that drip-and-ship patients presented to the endovascular-capable center an average of 34 minutes later, a delay of 42%, compared to those who presented directly to the mothership. Furthermore, patients who required transfer experienced additional delays to imaging (8 minutes to diagnostic CT) and intervention (8 minutes to groin puncture). The STRATIS registry echoed these results. Interhospital transfer led to a delay in symptom onset-to-revascularization time of 109.5 minutes, with concomitant worse outcomes. Sixty percent of patients directly admitted to a CSC for MT showed functional independence after discharge, as opposed to 52.2% of those who first required transfer. This has been replicated in a recent meta-analysis of eight published studies, which showed better 90-day outcomes if patients were first taken to a CSC (mothership) rather than transferred (drip and ship).

This growing body of literature supports transporting any patient suspected of having an LVO directly to an MT-capable center or CSC. Patients with symptoms of AIS but not LVO may be initially taken to a PSC (if closer) to undergo stroke evaluation and treatment, with subsequent transfer to a CSC in the rare case that LVO is unexpectedly diagnosed. This will necessitate further education of those in the field who evaluate patients with a potential stroke, perhaps analogous to current systems in place for triage and transport of patients who have undergone trauma. Timely triage of patients to the appropriate stroke center may be a significant bottleneck that health systems must overcome as further data accumulate supporting direct transfer of patients with LVO to CSCs.

**Preprocedural Bottlenecks**

Once the patient arrives at the hospital, a sequence of diagnostic tests, imaging studies, and interventions must be accomplished in an efficient and timely manner. Multiple protocols have been developed to optimize efficiency—the patient is brought to the resuscitation bay in the emergency department where hemodynamics are assessed and stabilized, the patient is evaluated by the neurology team, appropriate IV lines are started, and blood tests are drawn and processed, all in parallel. Point-of-care laboratory testing for international normalized ratio and other relevant assays further reduce wait times. Transport times to CT scanners can also be shortened by direct-to-CT protocols or eliminated by integrating the CT scanner in the resuscitation bay with hybrid CT/emergency department designs. Noncontrast CT and CTA should both be performed to evaluate the aortic arch and intracranial vasculature to identify any possible LVO.

If the patient is a candidate for rtPA, this may represent another potential bottleneck if the patient also has an LVO. Both the ESCAPE and STAR trials showed significant workflow delays to groin puncture associated with rtPA administration. The STAR trial reported that even when patients were directly transported to an MT-capable center, IV rtPA was administered in a dedicated unit and patients were monitored for clinical improvement before being moved to the angiography suite and possibly even before the neurointerventional team was activated. Proponents of this approach had previously argued that patients who clinically improve as a result of IV rtPA represent a wasted mobilization of resources required for emergent angiography and thrombectomy if these resources are then not used. The STAR investigators, however, recommended mobilizing both pathways (IV rtPA and rapid activation of the neurointerventional team) simultaneously, because modern CTA used at baseline can rapidly and accurately identify patients with LVO as valid targets for MT, and any delays in the workflow translate to a risk of worse outcome for the patient. Indeed, current American Heart Association guidelines mandate that “in patients under consideration for [MT], observation after IV alteplase to assess for clinical response should not be performed.”

To overcome this potential bottleneck, multiple teams recommend integrating designated pharmacists as part of the stroke team, premixing the rtPA while the patient is in transit, administering the rtPA in the CT bay while the radiographer is preparing the patient for CTA, and most importantly, transferring the patient to the angiography suite once an LVO has been identified.
without waiting for a clinical response to rtPA. Taken together, a robust, parallel IV rtPA protocol is necessary to overcome any possible bottlenecks to groin puncture that may be encountered at this step.6,10,11,17,18

A potentially controversial bottleneck has been identified by the ESCAPE investigators, who found that induction of general anesthesia was associated with longer CT–to–groin puncture times (on average, by 22 minutes) and prolonged workflow. The investigators concluded that general anesthesia was often unnecessary for MT and was only used in 9% of procedures in their database.10 However, other studies have shown that general anesthesia may reduce procedural time and difficulty and has not shown worse outcomes.21-23

Additionally, integrating anesthesia providers within the interdisciplinary stroke team for monitoring hemodynamic and airway stability, as well as inducing and intubating the unstable patient while the rest of the team carries out other tasks (ie, groin preparation and puncture), may overcome this potential bottleneck and may even improve safety, workflow, and outcomes. Specific techniques used in the procedure itself may also improve reperfusion times. The ESCAPE group reported that use of balloon guide catheters may lead to more efficient and effective recanalization, and other tandem aspiration and stent retriever thrombectomy techniques have shown promising results. A standardized MT approach across neurointerventional practitioners may also reduce overall reperfusion times.

McTaggart and colleagues found that by using a standardized approach to MT in a three-practitioner neurointerventional group, time from groin puncture to first pass was reduced from 39.8 to 20 minutes, and overall time from groin puncture to final recanalization was reduced from 68.2 to 37 minutes.24

CONCLUSION

Effective stroke treatment must be systematically planned to optimize workflow, reduce bottlenecks and delays, and maximize expeditious treatment. Implementing an effective treatment protocol requires coordination of various providers from multiple specialties into interdisciplinary teams, with an emphasis on communication and teamwork. The process itself must undergo iterative quality improvement, with periodic systematic reviews of treatment times, quality metrics, and patient outcomes. An institution-wide culture of active quality improvement should be fostered, and stroke treatment teams should seek out opportunities for continuous improvement. Stroke treatment teams should also be integrated into the wider health care system to identify system-wide improvements and possible bottlenecks or barriers to care external to their specific facilities. Finally, engagement with other institutions should be encouraged to gain knowledge about best practices.

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