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Mini Review

2020 - Limitations of the Current Literature Regarding Anesthesia and Mechanical Thrombectomy for Anterior Ischemic Stroke

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Abbreviation: tPA: Recombinant Tissue- type Plasminogen Activator; AIS: Acute Ischemic Stroke; mTICI: modified Treatment in Cerebral Infarction; mRs: modified Rankin Scale; GA: General Anesthesia; CS: Conscious Sedation; NIHSS: National Institutes of Health Stroke Scale (NIHSS)

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Globally, stroke has grown to become the second leading cause of death and a major cause of disability. The aging of the world's population, as well as a growing epidemic of modifiable stroke risk factors have likely driven this increase over time [1,2]. In the United States, stroke affects 795,000 people each year, making it the leading cause of long-term disability for adults and the fifth leading cause of death [3]. Despite the increase in overall number of stroke events globally, wealthy countries have seen a greater decrease in the incidence of mortality and disability/morbidity, likely due to better prevention, recognition, treatment, and subsequent access to neurorehabilitiation [4].

The first major advance in stroke therapy in the US (1996) and Europe (2002) was the approval of alteplase, a recombinant tissue-type plasminogen activator (tPA), for treatment of an acute ischemic stroke (AIS) [5]. However, large vessel occlusion events were relatively resistant to thrombolysis prompting the development of mechanical thrombectomy devices. Treatment options then expanded to include mechanical thrombectomy to restore blood flow. In 2004, the first mechanical thrombectomy device, a coil-retriever was approved by the FDA (Merci, Stryker Neurovascular, Fremont, CA).

Despite the initial shortcomings of first-generation devices, in 2015, multiple clinical trials (MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, and EXTEND IA) [6-10] demonstrated the benefit of clot-retrieval devices when compared to tPA alone for the treatment of patients with large vessel occlusions [11,12]. The treatment modalities and skill of the Interventionalists has evolved and improved over time, mirroring improvements in patient outcomes. Favorable outcomes measured as successful reperfusion (mTICI 2B-3) and functional independence (mRS 0-2) has fluctuated but steadily improved from 2010 to 2017 [13].

Thus, the evolution of mechanical thrombectomy has revolutionized the treatment of acute ischemic stroke and is now considered the gold standard treatment for acute ischemic stroke caused

by large-vessel occlusion. Subsequently, further clinical trials have expanded the time window for effective treatment with these devices to 16-24 hours in patients determined by CT perfusion to have salvageable brain tissue [12, 14-16].

In combination with these advances, significant efforts are being implemented to optimize emergency medical services, streamline transfers, centralize care, improve rapid imaging, and minimize door-to-needle times. These coordinated improvements in workflow over the past decade have created an opportunity to re-evaluate the impact of anesthetics and physiologic variables on mortality and functional outcome.

Anesthesia support is necessary for the safety and comfort of patients undergoing mechanical thrombectomy; particularly in anticipated complex or difficult cases or in patients with decreased level of consciousness, agitation, airway patency, or aspiration risk. The choice of anesthetic, general anesthesia (GA)/conscious sedation (CS), and its impact on patient outcomes has been studied for the last 20 years. Although the method of anesthesia is thought to have significant implications in outcomes for acute ischemic stroke and mechanical thrombectomy, the understanding of its impact on patient outcomes is unknown. Both techniques have proposed benefits. GA may be perceived as improving procedural safety, while CS allows for real time neurologic monitoring, less alteration of hemodynamics, and a more rapid initiation of therapy [17].

A major limitation of existing prior investigations is they do not account for unmeasured confounding variables that we now know to affect outcomes. Selection of anesthetic technique in many previous retrospective studies is often based on provider comfort and patient characteristics. Administrative databases and early studies lack such detail, which limits the ability for reanalysis of these data while controlling for confounders [18-22]. For example a database analysis of 1,174 patients undergoing mechanical thrombectomy from 2009-2013 concluded that GA was inferior to CS. In this study there was limited information on factors now known to affect outcome (blood pressure, NIHSS) and the only outcome parameters reported were death and length of stay [18]. Similarly, analysis of another quality database of 2,512 patients with similar limitations as the previous study concluded that CS was superior to GA for stroke interventions [23]. Additionally, by including data from the early stages of mechanical thrombectomy intervention, these studies are outdated in comparison to present day conditions. Interventional training/skill, device technology, imaging quality, and inclusion criteria for intervention have all evolved over the last 20 years, which in turn markedly impacted patient outcome.

Much of the published literature has suggested that GA results in poorer clinical outcomes for patients compared to CS [19,21]. These studies have many limitations in that their data are inclusive of cases that are nearly 2 decades old when mechanical thrombectomy was first introduced. In these studies the average NIHSS are not equivalent between the GA vs. CS cases, rather these numbers, for the most part, have been mathematically equalized. Further, patient factors seem to play a role as well in outcome, and these have not been accounted for in the analysis. A post hoc study from North American SOLITAIRE Stent-Retriever Acute Stroke (NASA) registry showed poor clinical outcomes with advancing patient age. This study also looked at the NIHSS score as a predictor of poor outcome. Not surprisingly, higher NIHSS scores predicted poorer outcome [24]. In a univariate analysis after endovascular stroke intervention, good outcomes were associated with a mean NIHSS of 15 +/- 5, whereas poor outcomes were associated with a mean NIHSS of 18 +/- 18 [25]. These studies highlight the possibility that patient factors may play more of a role in interventional outcome compared to anesthetic choice. Further, general anesthesia is frequently selected for patients with a high NIHSS as these patients frequently present with severe neurological dysfunction and an inability to protect their airway [24]. More recent studies, GOLIATH [26], ANSTROKE [27], and SIETSA [28] reported GA and CS to be equally safe. In all three of these randomized trials there was special attention on maintaining systolic blood pressure of >140 mmHg prior to revascularization. However, GA in those studies resulted in a higher incidence of mean arterial pressure decreases of 20% or more [29]. A subsequent analysis of the blood pressure measurements from these three studies revealed that a mean arterial blood pressure less than 70mmHg was associated with a significantly higher modified Rankin score at 90 days [30]. This association in further supported by the work of Fandler et al, who reported outcomes on a retrospective cohort of 115 patients receiving GA for mechanical thrombectomy with stent retrievers [31]. After multi-variate analysis they concluded that any mean arterial pressure less than 60 mmHg was independently associated with worse functional outcome, especially in patients with poor collateral circulation. Thus, the association of GA with worse outcomes after endovascular therapy in many studies may be explained by decreases in blood pressure [17].

In addition to ensuring that future high quality studies and reviews focus on comparability of age, NIHSS, blood pressure management, and outcomes of interest (mortality and functional recovery); future evaluations need to investigate the impact of expanding the time frame from onset to therapy base on CT perfusion imaging results. In the recent randomized trials of GOLIATH [26], ANSTROKE [27], and SIETSA [28] the majority of patients enrolled had intervention within eight hours from the onset of symptoms [29].

In conclusion, endovascular thrombectomy is considered the gold standard treatment for AIS in the large vessels of the anterior circulation. Stent technology and proceduralist experience has expanded rapidly since its first introduction. Debate continues about appropriate anesthetic technique, with more recent studies show-

ing equivocal results between GA and CS. Until more evidence is available, the type of anesthetic should be chosen based on patient presentation with a primary goal of maintaining brain perfusion.

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Conflict of Interest

No conflict of interest.

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