INTRODUCTION

The Neurointerventional Revolution
Past, Present, and Onward

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Abstract

Purpose of the Review
In a short period of time, the field of interventional neurology has been transformed. Supported by strong Class IA evidence, the vascular and interventional neurology community has been empowered to realign systems of care to address the new challenges that have been introduced. Given the recent developments and accelerating pace of the field, the Society of Vascular and Interventional Neurology has collaborated with the American Academy of Neurology to provide an updated supplemental edition of Neurology® focused on endovascular therapy for acute ischemic stroke.

Recent Findings
In this supplemental edition, the authors discuss the unmet need for endovascular therapy, emerging trends in stroke systems of care, the role of imaging in patient selection, prognostication and treatment-related factors, procedural considerations, current top tier guidelines, recent advances in neuroprotection, and future directions of the field.

Summary
The field of interventional neurology continues to grow and advance, particularly since the seminal stroke trials published between 2015 and 2018. Whereas this progress has significantly improved the ability to alter outcomes after acute ischemic stroke due to large vessel occlusion, important new hurdles present themselves to the neurology community.
Cerebral angiography began with the pioneering work of Jean-Athanase Sicard in visualizing and localizing brain tumors in the 1920s, from which Ega Moniz modified the technique and was the first to illuminate arteries of the head and neck by injecting radio-opaque solutions. Cerebral angiography subsequently became the diagnostic mainstay for detecting intracranial parenchymal pathology until CT was introduced in 1975, and the method continues to remain vital to understanding intracranial vessel pathology. More recently, our ability to not only diagnose but also treat cerebrovascular pathology has transformed this imaging-based technique into the unique field of interventional neurology (also termed endovascular neurosurgery or interventional neuroradiology) in which a minimally invasive approach allows detailed understanding of the intracranial and extracranial vasculature and also allows direct access to target injured vessels or downstream affected tissue.

A significant advance in the field was reported by Zeumer et al. in 1982 when they described a 27-year-old woman presenting with a basilar artery occlusion in which a selective vertebral artery angiogram was performed followed by intraarterial infusion of streptokinase with subsequent vessel recanalization. This innovative approach to acute ischemic stroke (AIS) in the setting of a large vessel occlusion (LVO) inaugurated endovascular therapy (EVT) as a revolutionary approach to this devastating stroke subtype.

In 2012, the Society of Vascular and Interventional Neurology (SVIN) published a supplemental edition of Neurology® focused on endovascular AIS treatment. At the time, the first randomized controlled trial (Interventional Management of Stroke III [IMS-III]) comparing medical therapy to medical therapy with EVT had just been halted due to lack of benefit. Indeed, a series of clinical trials were published in 2015 with strong data supporting the use of EVT in select patients in the first few hours after stroke onset followed by a second wave of trials published in 2018 supporting the benefit of EVT in the late time window (up to 24 hours after onset).

This year marks the 6-year anniversary of the positive EVT trials and in a short period of time, the field has transformed. Supported by strong Class IA evidence, the vascular and interventional neurology community has been empowered to realign the systems of care to address the new challenges that have been introduced. Given the recent developments and accelerating pace of the field, SVIN has once again collaborated with the American Academy of Neurology to provide an updated supplemental edition of Neurology focused on endovascular AIS.

**Endovascular Therapy for AIS: Meeting the Needs**

To fully understand the scope and impact of AIS, Saini et al. provide an overview of the incidence of the disease with estimates on the populations that are currently treatment eligible based on the current guidelines. This understanding is helpful in defining the resources that are necessary to provide treatment to all eligible patients. There are significant gaps in utilization of thrombolysis and EVT both in the United States and worldwide with various challenges specific to each region as well as local governmental and political considerations.

After the National Institute of Neurological Disorders and Stroke IV tissue plasminogen activator trial, it became clear that increasing expertise and training was necessary to qualify practitioners in thrombolysis decision-making. Growing the clinical stroke work force continues to be a challenge. As of 2009, there were more than 25,000 practicing cardiologists in the United States, with 800 first-year cardiology fellowship positions every year, in contrast to approximately no more than 80 vascular neurology fellows that graduate each year. Similar shortages are being faced in the endovascular arena; it is estimated that there are approximately 1,000 neurointerventionalists (including specialists from neurology, radiology, and neurosurgery) compared to 5,000 interventional cardiologists. The shortage and need for additional interventional neurologists has to be offset by the importance of rigorous training (i.e., appropriate high volumes of cases to achieve good outcomes) and diversity of skills (e.g., treatment of aneurysms).

Bulwa and Chen explore credentialing beyond the proceduralist as they review the current mechanisms by which hospitals can achieve proper accreditation to receive and care for complex cerebrovascular cases. This is critical to achieving the optimal outcome as the benefit of EVT relies on rapid and experienced workflow from first medical contact to device and beyond. The justification to hospital administrators for dedicating resources, from prehospital care, emergency services, and the angiography team to the intensive care unit, requires an understanding of the relevant financial considerations.

**Getting the Right Patient to the Right Hospital and the Right Part of the Hospital**

While the concept of “time is brain” has been appreciated for decades, the real-life implementation of this dictum in AIS has...
The Role of Imaging in Patient and Treatment Selection

An active area of debate in clinical practice as well as research endeavors is the role of imaging in patient selection and prognosis after AIS. Czap and Sheth\textsuperscript{16} provide a broad overview of techniques currently available with advantages and limitations afforded by several modalities as well as future potential for emerging technologies. Thon and Jovin\textsuperscript{17} review the various strategies for patient selection prior to EVT with emphasis on how pathophysiology may influence the utilization of a simplified vs advanced paradigm. Emerging data suggest that patients can experience infarct growth after an LVO at a variable rate. The underpinning mechanisms driving this heterogeneous ischemic tolerance to LVO, including collateral circulation, are explored by Saber and Liebeskind.\textsuperscript{18}

Beyond the target parenchymal tissue and supplying vasculature, visualization and understanding of the clot itself is increasingly being appreciated as providing valuable insights into treatment responsiveness as well as guiding patient-tailored therapy selection. Joudi and Menu\textsuperscript{19} review the role of various noninvasive approaches in characterizing clot burden, length, and composition. These insights will be critical in informing future modifications of existing reperfusion tactics.

Endovascular Therapy: Prognosis and Treatment

Beyond imaging-based measures, patient-specific features may further factor into the decision to offer EVT as well as influence provider and patient expectations. Raza and Rangaraju\textsuperscript{20} survey the currently utilized pretreatment and posttreatment prognostic scores as well as the various outcome metrics utilized in measuring clinical success. Such information is critical in defining the posttreatment trajectory, directing goals of care as well as tailoring patient-specific features. Procedural approaches are rapidly improving with new devices being introduced to the proceduralists’ toolkit with increasing succession. Familiarity with alternative access site approaches may allow customization of the procedure to individual anatomy. The procedural outcomes and metrics are examined by Ajiboye and Yoo\textsuperscript{21} with attention to current unmet needs in achieving technical success.

Endovascular Therapy: Intraprocedural and Postprocedural Considerations

Given the clinical complexity of the patient with stroke and the technical challenges posed by EVT, multiple factors must be considered in the care of the thrombectomy patient both during and after the procedure. Simonsen et al\textsuperscript{22} focus on periprocedural considerations such as choice of anesthetic and blood pressure measures. Krishnan et al\textsuperscript{23} focus on the postprocedural concerns of reperfusion therapy and access site complications.

Treatment of Patients and Beyond

The majority of randomized controlled trial (RCT) data focus on a select population of patients who meet specific treatment criteria. Jadhav et al\textsuperscript{24} summarize the rationale for the current guidelines and present opportunities for treatment expansions. Among the population of patients undersurveyed in the trials to date include patients with intrinsic disease. Al-Bayati et al\textsuperscript{25} delve into the various extracranial carotid pathologies that accompany and lead to LVO. A major unresolved issue is the decision to acutely stent patients with tandem disease. Even more controversial is the best approach to patients with intracranial atherosclerotic disease (ICAD). Tekle and Hassan\textsuperscript{26} examine the pathophysiology of ICAD and the endovascular options when medical therapy or conventional thrombectomy strategies fail. LVO involving the vertebrobasilar system has been largely excluded from previous RCTs. Symptoms in the posterior circulation may be atypical relative to the symptoms manifested by anterior circulation dysfunction. Novakovic-White et al\textsuperscript{27} probe the manifestations, prognosis, and management of this less common but potentially more fatal stroke subgroup.

IV Treatments: Lytics and Neuroprotection

EVT has been a critical advance in the management of LVO, but there is a continued role for thrombolysis in a subset of patients. Demel et al\textsuperscript{28} investigate the opportunity for novel or adjunctive IV pharmacologic agents to achieve reperfusion. Specifically, safer and more efficacious drugs may allow for faster delivery of therapy (particularly when EVT is not immediately available) as well as facilitate recanalization (particularly of more distal occlusions). Despite EVT, not all patients presenting with LVO achieve favorable outcomes and a majority do not recover to normal. Significant work is needed to further address the disability inflicted by stroke and...
increasing attention has been placed on neuroprotection, especially given the opportunity to deliver medications and biologics to injured tissues after vessel recanalization has been achieved. Desai et al.29 focus on collateral augmentation, neuroprotection, and future therapies.

The Future of the Field

Along with the pace at which the field has progressed, innovations continue to arrive to address the numerous challenges that remain. Jumaa et al.30 provide some insights into the horizon ahead with practice-changing novelties likely soon becoming a reality with integration of technology. Understanding how new data and ideas can be evaluated and translated to improve clinical care is delineated by Gangadhara et al.31

Conclusion

The field of interventional neurology continues to grow and advance, particularly since the seminal stroke trials published between 2015 and 2018. While this progress has significantly improved the ability to alter outcomes after AIS due to LVO, important new hurdles present themselves to the neurology community. This supplemental edition of Neurology serves to provide an update on the current considerations ranging from epidemiology and resource allocation to patient triage, selection, and treatment in both guideline-eligible and ineligible patients. Despite the advances, favorable outcomes plateau at approximately 50% and further research and developments are necessary to improve achieving reperfusion and managing postreperfusion recovery. Continuous technological advances in early prehospital recognition of AIS from LVO, emerging evidence for neuroprotection, and growth of robotic surgery offer new opportunities to provide faster and more effective treatment. It will be exciting to witness what the future brings.

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References

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