ROUNDTABLE DISCUSSION

Detection, Treatment, and Future Prospects for Distal and Medium Vessel Occlusions

A conversation on data from recent trials, lessons learned for future study, definitions and imaging protocols, how treatment can be refined, and more.

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How do you currently define medium vessel occlusion (MeVO) in your practice?

Dr. Goyal: MeVO is defined based on our publication in *Journal of Neurointerventional Surgery*.[1] The three criteria are: (1) occlusion location (M2, M3, A2, A3, P2, P3), (2) occlusion size of at least 1 mm, and (3) if it is accessible endovascularly.

Dr. Gupta: We define MeVO as patients with an occlusion of a cerebral vessel involving the anterior cerebral

artery (ACA) A1, A2, A3 segments; posterior cerebral artery (PCA) P1, P2, P3 segments; and middle cerebral artery (MCA) M2 mid segment, M2 distal segment, and M3 segment. The proximal M2 segment is not considered MeVO.

Dr. Jumaa: MeVO in my practice is an occlusion in any of the following segments: A2 and A3 segments of the ACA, the P2 and P3 segments of the PCA, distal or nondominant M2 segment, or M3 segment occlusion of the MCA.

Dr. Liebeskind: I define MeVO by arterial segment. I don't believe anyone actually measures vessel size to define "MeVO" in acute ischemic stroke.

Dr. Mistry: I break MeVO down into medium (which are co/nondominant M2s) and distal vessel occlusions (M3, M4, A2, P1, P2). I consider a dominant M2 as essentially a large vessel occlusion (LVO) for clinical decision-making.

What is your strategy for optimizing detection of MeVO on imaging?

Dr. Gupta: Our patients receive a CT, CTA, and CT perfusion (CTP).

Dr. Jumaa: We usually rely on CTA supported by artificial intelligence software (RapidAI) to optimize MeVO detection. We occasionally utilize CTP when CTA in inconclusive.

Dr. Mistry: Usually, I try to look for a MeVO on standard-of-care imaging, which includes CT and CTA at our site. If there is a cortical syndrome but MeVO cannot be readily found on CTA, then I sometimes use CTP to detect a wedge-shaped deficit.

Dr. Liebeskind: We use multimodal CT/MRI, typically using CTA.

Dr. Goyal: We use multiphase CTA. Using CTP maps also works well.

Three recently presented trials (DISTAL, ESCAPE-MeVO, and DISCOUNT) found that mechanical thrombectomy (MT) in distal vessel occlusions/MeVO was not superior or had no added benefit compared to standard of care. What are the primary unanswered questions remaining for you after the presentation of these data?

Dr. Mistry: These were important trials in moving the field of acute treatment for MeVO forward. There are several unanswered questions:

- The trials mostly included mild- and moderate-deficit patients. It remains to be studied whether endovascular treatment (EVT) is beneficial for patients with MeVO who have more severe baseline deficits.
- Results of the ESCAPE-MeVO post hoc analysis were presented at the European Stroke Organization 2025 meeting, which showed that there was a heterogeneity in treatment effect according to time such that patients presenting earlier gained more benefit from EVT compared to those who presented later. This remains to be confirmed.
- Most patients who underwent EVT in these trials had a stent retriever–type device used. It will be important to understand how other endovascular approaches, such as aspiration and intra-arterial lytics compare to medical management for MeVO patients.

Dr. Goyal: We need to better understand why the results are what they are. Other questions include, how can we do things differently? Are there subgroups that will have benefit from EVT? What is the likely effect size? Is modified Rankin Scale (mRS) the best way to measure clinical outcome?

Dr. Liebeskind: All questions remain unanswered.

Dr. Jumaa: Several questions remain unanswered, specifically regarding the fact that there was a high utilization of stentrievers in the three trials. In ESCAPE-MeVO for example, it was mandatory to utilize a stentriever for the first pass. Previous data showed a higher rate of symptomatic intracranial hemorrhage when a stentriever was utilized in MeVO versus LVO. We showed similar findings in a subanalysis of the STRATIS registry several years ago. The most important question in my opinion is: does technique matter? Aspiration technology has seen notable improvement in recent years, with better trackability and navigation of catheters and new aspiration techniques such as cyclical aspiration. Is it possible that MeVOs are more amenable to aspiration or even intra-arterial thrombolytic therapy?

The other unanswered question is whether we should focus on patients with more severe neurologic deficits in the next round of clinical trials. Recent MeVO trials included patients with mild neurologic deficit despite the lack of clear benefit for MT in more proximal occlusions. Pooled patient-level meta-analyses will help answer some those questions.

Dr. Gupta: All of these trials included patients treated with intravenous (IV) tissue plasminogen activator (tPA) or IV tenecteplase (TNK). The question is if treatment of patients with MeVO will benefit from MT if they did not receive TNK or tPA. The one issue that also needs to be

considered is that the mRS of 0 to 2 endpoint is likely not the ideal endpoint to demonstrate efficacy.

What do you think were the strengths and limitations of these studies? How would you describe the differences among the three trials?

Dr. Liebeskind: The trials had limited methodology, mixed populations, and poor arterial segment and size definitions. However, DISCOUNT had the most reliable methods.

Dr. Gupta: The strengths of the trials include the trial size and number of centers involved. All studies included IV TNK and IV tPA patients. Thrombolytics have a good chance of reperfusion for smaller clot burdens, and thus the bar for MT may be too high for distal vessels.

It is important first to demonstrate that MT of a MeVO can be done safely and efficiently. The ongoing DISTALS trial is doing this for patients who did not receive IV TNK or IV tPA. This is a critical study, as the device being used was developed for MeVO. In DISTAL, ESCAPE-MeVO, and DISCOUNT, the tools used were not specifically developed to treat MeVO and may not be the ideal tools. The analogy is similar to the negative result that occurred during the IMS III trial era with the Merci device (Inova Neurosciences). Technologic advances are needed to ensure safety and effectiveness for smaller cerebral vessels.

Dr. Jumaa: The three studies had robust designs and methodologies, with diverse patient populations and comprehensive outcome measures. They were also representative of global practices in the management of ischemic strokes due to MeVO, as they were performed in different geographic areas. Some of the limitations include the high rate of utilization of stentrievers, inclusion of patients with low National Institutes of Health Stroke Scale (NIHSS) score, and the high percentage of patients who received thrombolytics. The results were strikingly similar, but this disease continues to cause significant morbidity and mortality, and further clinical trials—focused on newer MT techniques—with refined inclusion criteria are warranted.

Dr. Goyal: The key strengths include the fact that these are high-quality studies with excellent follow-up done by experienced trialists and centers. There were very few crossovers and very few patients lost to follow-up. The biggest strength, however, is that all three trials showed similar results.

In terms of limitations, relative to the number of sites in each of the trials, there is a concern that the enrollment rate was somewhat low. That raises the possibility of "cherry-picking." Unfortunately, none of the trials kept good records of patients who were eligible but not treated.

There are other aspects of the procedure that have scope for improvement, including faster workflow in the MT arm and/or better reperfusion rates. I hope that future trials are able to accomplish that. There is also a concern that pushing for higher reperfusion rates may increase the complication rate.

Another concern is that MeVO is a heterogeneous population with varying target lesion and clinical presentation. It is not clear how that has played into the overall results. One could think of a solution of limiting this (eg, a trial of only nondominant M2s with an NIHSS > XX). That does create additional issues in terms of enrollment rate and equipoise.

Dr. Mistry: As far as strengths, these are the very first trials of EVT for the MeVO population. The trialists and investigators must be commended for their pragmatic design and for completing the trials with such efficiency. Limitations include lack of screening logs, most patients enrolled had mild-to-moderate presenting deficits, and the device choice was stent retrievers for most patients.

How do you think these results should inform future trials and trial design in this space?

Dr. Gupta: Based on these results, it is important to continue research to determine which populations may benefit. Moreover, technologic advances are required to identify tools that can achieve successful reperfusion without injuring the smaller cerebral vessels where these clots are lodged.

Dr. Mistry: Future trials may focus on more severe deficit patients, protocolize device choices (aspiration-type devices and devices appropriate for the target vessel size), and seek sites that are committed to enrolling consecutive patients and not "cherry-pick" for trial enrollment.

Dr. Jumaa: Future trials should focus on subtypes of MeVOs. It is important to identify the best treatment approach for patients with distal M2 and M3 occlusions who have high NIHSS. PCA occlusions can be studied separately with more refined outcome measures. Future trials should also focus on newer aspiration technology, which can offer a less invasive solutions for this challenging disease.

What do you think are next steps, for the overall trial space and for physicians treating these patients?

Dr. Mistry: I think it is important to understand that in order to move the field of acute treatment of MeVO forward, we must randomize all eligible patients to ongoing

and future clinical trials. There is a reason to believe that treatment of higher deficit patients with EVT outside of the trial (ie, nonconsecutive enrollment) may have been one of the reasons why these original three trials were negative. We must not make the same mistake again. There are many ongoing trials and trials in planning stages that seek to find the best treatment approaches for these patients, ranging from use of existing and novel IV lytics to endovascular approaches. We as a field must commit, just like we did for LVO trials, to randomizing consecutive patients in these trials and not let anecdote supersede evidence generation.

Dr. Goyal: I think we will gain a lot of information and insight from a patient-level meta-analysis and looking at various subgroups. Some are obvious, such as a patient who had substantial mismatch, patients who achieved excellent reperfusion, patients who presented early, or patients who were treated with a particular technique. Once we have that data, we can have a data-driven approach to designing the next trial.

Dr. Gupta: Physicians should consider enrolling patients in the DISTALS trial. If this trial is positive, it can be used as a launching pad for future studies to identify which patients will benefit with regard to clinical outcomes.

Dr. Liebeskind: Physicians should continue to use expert judgement until definitive trials and corresponding data sets are published.

What data would be most transformative for your approach to MeVO? What needs to be further defined to refine treatment?

Dr. Gupta: First, it is crucial to demonstrate MT of MeVO can be done safely and effectively. After this step, efficacy needs to be demonstrated with a larger trial. Finally, development of newer technologies is required with designs specific to the target vessel.

In what scenarios will you still perform MT in these patients? What are your best practices for ensuring the best possible outcome if proceeding with an endovascular approach?

Dr. Goyal: Our approach currently is to treat the more easily accessible, larger MeVOs that have substantial deficit and good imaging.

Dr. Mistry: While some patients with a dominant M2 occlusion were included in these three trials (although all three trials categorized M2 occlusions according to occlusion location [proximal vs mid vs distal] and not dominance), we have ample data from HERMES collaboration that EVT benefits patients with dominant M2 occlusion and a NIHSS ≥ 6. I would likely treat these patients with EVT as standard of care in my practice.

Dr. Jumaa: We continue to provide MT with aspiration for patients with distal M2 and M3 occlusions who have high NIHSS when we believe the occlusion is accessible with a reasonably low risk.

Dr. Gupta: We are only randomizing patients into the DISTALS trial but not performing this procedure outside the trial. Patients with proximal M2 occlusions with large clinical deficits (NIHSS >10) are still being treated with EVT at our institution. Cases that are distal to the proximal M2 MCA segment are being randomized.

What should future technologic innovations for potential use in MeVO focus on?

Dr. Jumaa: There is a huge need for innovation in this space. Ischemic strokes due to MeVO are very common with the majority of patients not achieving complete or near-complete recovery with medical treatment. Similar to how stentrievers provided a breakthrough in the treatment of LVOs, we are now in need of robust aspiration technology or other innovative MT technology to tackle MeVOs. During the evolution of MT for ischemic stroke, we learned to transform lessons from unsuccessful clinical trials into building blocks for future breakthroughs.

Dr. Gupta: Future innovations should focus on developing technologies such as aspiration or stent retrievers, or more novel approaches that target cerebral vessels < 1.5 mm in diameter. Technologies need to be specific to smaller vessels. ■

1. Goyal M, Ospel JM, Menon BK, Hill MD. MeVO: the next frontier?. J Neurointerv Surg. 2020;12:545-547. doi: 10.1136/neurintsurg-2020-015807

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