PANEL DISCUSSION

Trends in Ischemic Stroke Pathways, Interventions, and Outcomes

Experts discuss patient positioning during transport, the rising role of artificial intelligence, and the future of stroke care.

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What are the implications of patient positioning prior to mechanical thrombectomy? How can trials like ZODIAC lead to changes in practice?[1]

Dr. Jovin: The potential implications of the ZODIAC trial are quite significant. I commend Dr. Anne Alexandrov and colleagues for tackling an issue we are confronted with daily, and for which we have intuitively thought that current practice (keeping patients up at 30° or even more elevated) may not be ideal. We see that all the time—patients who are transferred, picked up by emergency medical services (EMS) with suspicion of large vessel occlusion (LVO), and they're not flat, which we feel they should be. Until now, we just didn't have any evidence-based arguments to influence this practice.

There have been concerns regarding aspiration in a flat position, and this study goes a long way in debunking these myths and could have profound effects on outcomes of these patients. At 3 months, there were trends toward a more favorable outcome when patients were kept flat, and I believe that had the sample size been bigger than the 92 patients enrolled in the trial, these differences would likely have been statistically significant. Still, the National Institutes of Health Stroke Scale at 24 hours and at 7 days, which is a strong predictor of 3-month outcomes, was better in patients allocated to the flat position group, supporting the argument that this simple intervention leads to improved long-term outcomes.

I think the efficacy data from ZODIAC are quite clear, but I don't know if it will be enough for a level 1A recommendation in the guidelines, which typically require two randomized trials or other supportive evidence, and more safety data in terms of aspiration are needed. I'd like to see what the guidelines recommend for transport of patients with suspected LVO and hope they will

endorse maintaining patients with suspected LVO in a flat position based on the findings of ZODIAC. This will go a long way toward changing current practice.

Dr. Nour: When it comes to LVOs, we know that sustaining vascular collaterals and sustaining perfusion to the tissue at risk plays a big role in protecting the patient from irreversible ischemia and worsened clinical outcomes. The ZODIAC trial—led by Dr. Anne Alexandrov and presented as a late-breaking science presentation at the 2024 International Stroke Conference (ISC)—sought to investigate whether a 0° head position rather than a traditional 30° head position would better serve patients and would lead to improved clinical outcomes as patients awaited recanalization with mechanical thrombectomy. This gravitational maneuver, aimed at preserving brain function in the 92 patients examined across 12 stroke centers, has been described as a "rescue maneuver," suggesting that it can benefit these typically perfusion-dependent patients. The balance then lies with the potential risk of aspiration among patients who may present with facial muscle weakness and not be able to protect against their own secretions. Neurological worsening may also arise when the patient comes to the angio suite and is intubated and given medications for intubation, which may have blood pressure lowering effects. This can inadvertently challenge vascular collaterals prior to vessel recanalization and could affect patient outcome. As a general protocol that may need to be tailored to each patient presentation, the results of the ZODIAC trial encourage a potential change in clinical practice to advocate for 0° head of bed positioning as a measure for salvaging vascular collaterals and tissue perfusion while en route to mechanical thrombectomy.

How would you convey results of the ZODIAC trial in a real-world sense?

Dr. Jovin: If they translate into high-level guideline endorsement, it will be much easier than it currently is to implement in practice because it will filter down into regional policies/guidelines for EMS providers. Otherwise, if there is consensus on this transport specification from professional organizations and societies, with appropriate education measures, it will eventually become standard. In my opinion, when a patient meets the criteria for a high likelihood of LVO based on prehospital scales, the patients should be placed in this position. Ideally, I would love to see a larger study that confirms these findings based on suspicion of LVO and not necessarily proof of LVO from CTA. I don't know whether that's going to ever happen, but ZODIAC is a great start, and I hope that even this small study can change practice.

What is the current role of artificial intelligence (AI) in diagnosis and outcomes of acute ischemic stroke? How does the recently presented GOLDEN BRIDGE II trial further AI in stroke care?[2,3]

Dr. Nour: The flourishing of AI across all fields of practice (including medicine as well as many other fields) has put AI in the center of growth and future advances. Presented as a late-breaking scientific presentation at the 2024 ISC, Dr. Zixiao Li led his group in showcasing the results of the GOLDEN BRIDGE II trial. This study focused on an AI clinical decision support system aimed at enhancing patient outcomes. This system involved supporting the classification of stroke and performing imaging analysis as well as providing recommendations for clinical care. Although this may have impacted quality of care, no specific impact was seen on patient functional disability.

In the medical field, we are at an interesting intersection of technology integration and its balance with clinician acumen and decision-making. Many stroke centers across the world have adopted elements of what the GOLDEN BRIDGE II trial involved, namely AI imaging assessment. Although many of these AI applications serve very well as a PACS (picture archiving and communication system) in-pocket—allowing clinicians immediate access to patient imaging and thereby improving the speed of decision-making—the accuracy of AI as it relates to "go, no-go" decisions has room for improvement. AI algorithmic technologies play a particularly large role in clinical environments in which immediate access to stroke specialists is limited. As AI develops further to be more inclusive of ambient stroke detection and of other domains, the challenge will be finding the balance between technology and the finesse of clinical knowledge and specialist acumen in stroke care.

Dr. Jovin: The GOLDEN BRIDGE II trial, which in my opinion has the most profound implications for medical practice of all studies presented at ISC 2024, showed that an AI-based algorithm for secondary stroke prevention derived from data generated during index hospitalization is superior to the conventional, physician-based secondary prevention regimen practiced at secondary and tertiary stroke centers in China. The presentation of the trial at ISC 2024 was really a great moment for AI in medicine and in stroke. I'm not aware of any other applications before this trial that have so clearly outlined the power of AI in medical decision-making. It should make us rethink our roles as physicians in the future and prepare us for a shift in

the scope of our activities that will inevitably follow the ever-improving AI-based advances in patient care. In my opinion, AI is going to increasingly take over some of the factual, knowledge-based decisions, leading physicians to reorient toward the humanistic side of our profession, such as more communication with patients and families with emphasis on empathy, compassion and other humanistic traits, which I think we're currently largely neglecting.

In my opinion, the study was very well designed. The investigators were thoughtful about building the AI model, and I think that's a big lesson for the future—you need the right data to input into the machine learning model. This is the beginning, and these systems are just going to get better. AI will help with more knowledge-based medicine such as differential diagnosis and evidence-based treatment options, while physicians will gradually assume more supervisory roles and increasingly focus on the humanistic side of stroke care.

The other lesson from GOLDEN BRIDGE II is that there was a differential in terms of hospital type (secondary and tertiary) and where the results were better with AI versus humans. The tertiary centers did a bit better than the secondary centers, which speaks more toward democratizing stroke care and medicine in general. Where specialized knowledge lags behind is where AI is most impactful, and this is ultimately good for our patients as hopefully geographic and socioeconomic disparities in stroke care will diminish.

What will be some of the hallmarks of stroke care of the future?

Dr. Jovin: As I mentioned, I think that AI will profoundly influence stroke care as well as virtually every other area of medicine. GOLDEN BRIDGE II offered a glimpse into how AI will help us improve in making a diagnosis and formulating treatments for secondary stroke prevention. Focusing more on the acute stroke care side, I believe that it is going to be standard for a stroke to be detected at home. Obviously, we know that the biggest problem we have with early treatment for stroke is that patients don't seek medical attention early enough. I think this problem will be significantly improved by AI. There are several AI-based companies or approaches that are testing this, whether it's through sensors, wearables, or cameras recording patients and AI-based analysis of facial and movement asymmetry, in addition to changes in speech, eye movements, and other features indicative of an acute stroke.

The other big advancement of AI I hope to see is the ability to differentiate between hemorrhagic and ischemic stroke in the field. Right now, we can only do that with the mobile stroke unit (MSU), but I think there is a real possibility of being able to do this in all ambulances by integrating multiple sources of data with the help of AI—in essence, making every ambulance an MSU.

I also think it's very likely that for ischemic stroke, we will be able to give neuroprotectants that will freeze the progression of the ischemic process or slow it down so that most LVO patients will be candidates for reperfusion. With neuroprotectants, lytics, and AI-based ultra-early stroke detection, we're going to be able to treat these patients very early and then get them to the hospital quickly. The knowledge that we gain in the field will translate into time saved in the hospital so that most patients who need an intervention will go directly to the procedure suite and undergo treatment, similar to how patients with myocardial infarctions are triaged directly to the angio suite with minimal delays.

From current average door-to–access site puncture times of 90 minutes and door-in/door-out times from transferring hospitals of 2 hours observed in the United States, the future will see dramatically reduced times to treatment, not only as a result of AI but also with advancing knowledge of simplified pathways to thrombectomy. Fewer patients will be seen at the acute care hospital, and patients will go directly to the angio suite at a thrombectomy-capable hospital.

In terms of aftercare, dramatic advances will be made in the recovery area with neuroprotectant drugs, neuromodulation, and brain-computer interface platforms. Right now, we're seeing the tip of the iceberg in that regard. It's an area of greatest potential for development and can make a real impact on patients' lives, including the effects of stroke that are not well appreciated such as mental health, including cognitive problems, fatigue, and depression, complaints that are very common in the long term among stroke patients.

Dr. Nour: I see the future of stroke care as a bright and flourishing one. In the past 10 years, major changes have come to our field with the advancement of thrombectomy and clinical trials. These have continued to build upon our knowledge base of disease pathogenesis and have challenged paradigms within our field, while continuing to advance our ability to give superior care to our stroke patients. I see two domains in particular that will shine in the next decade. One is in extending the reach of stroke specialists to the prehospital setting. With the advent of MSUs, hyperacute therapy can be delivered to patients in earlier times than we've ever seen before. These prehospital treatment units also provide a unique opportunity to advance neurotherapeutics administered at

earlier time points and develop stroke detection and advanced telemedicine technologies for the greater benefit of our local communities. The second large domain in my opinion will involve development of AI technologies focused on ambient detection of stroke and automated notification of EMS resources. Thought leaders in our field relentlessly continue to push the limits of disease understanding with a mutual, global goal of eliminating disparities in care and reducing stroke-related morbidity and mortality. ■

Disclosures
Dr. Jovin: Unavailable at the time of publication.
Dr. Nour: None.

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