Negative endovascular therapy trials offer patient mix guidance

Multiple randomized trials of endovascular therapy will be explored during “Negative Randomized Studies in Endovascular Therapy for Acute Stroke: Can Different Study Designs Lead to Different Results” at 8:40–10:10 a.m. Thursday in Ballroom 20BC.

“During this symposium, we’ll discuss if these trials were negative because of the state of the field when conducted and if more positive outcomes are achievable with contemporary knowledge and technology, or if there is a fundamental reason why endovascular therapy will never be superior to IV alteplase,” said Tudor G. Jovin, MD, session co-moderator and associate professor of neurology and chief of the Stroke Division at the University of Pittsburgh.

“One of the benefits of these trials is that they represent an excellent opportunity to learn about who is more and less likely to benefit from endovascular therapy … and develop future directions for endovascular therapy trials,” Jovin said.

Pooja Khatri, MD, professor of neurology at the University of Cincinnati Neuroscience Institute, is co-moderator. The trials have compared endovascular therapies such as intra-arterial thrombolysis, thrombectomy and thromboaspiration with intravenous alteplase and other standard medical therapies in patients with acute stroke. The trials have largely failed to demonstrate that endovascular therapy is superior to conventional therapies, including IV alteplase. The studies also didn’t show that endovascular therapies are inferior.

“Thus, it is uncertain if the negative results are attributable to trial design and execution, outdated technology, lack of proper systems of care and patient selection or to the actual therapies. One key lesson from the trials is the inefficiency of care. Delays occurred between presentation and brain imaging, imaging to angiography and angiography to groin puncture. Streamlining and making the flow of patient care more efficient may lead to shorter treatment times and better outcomes, Jovin said. These issues will be the focus of “State-of-the-Art Endovascular Technology and Faster Reperfusion Times Would Improve Outcomes in Endovascular Treated Patients,” presented by Brian T.

Hypothermia promising therapeutic for stroke

Therapeutic hypothermia is an accepted neuroprotective treatment for cardiac arrest, but the potential for neuroprotection in stroke is less widely recognized. That lack of recognition is about to change.

“Hypothermia is the most promising neuroprotective strategy that we know of,” said Thomas Hemmen, MD, PhD, associate professor of neuroscience and director of the University of California, San Diego Stroke Program in La Jolla. “This is not often appreciated in the neurological community.”

Gregory Zipfel, MD, associate professor of neurosurgery and neurology at Washington University School of Medicine in St. Louis, is co-moderator of the symposium.

“Optimum stroke care is a multidisciplinary effort. The stroke team needs to recognize the factors that are unique to palliative care after stroke, symptom management, roles for palliative care consultants, gaps in evidence and research, and the ways attitudes and beliefs affect quality of life, said Zipfel, associate professor of physical medicine and rehabilitation at Johns Hopkins University School of Medicine in Baltimore.

“Palliative care should be part of a well-coordinated healthcare environment that enables informed patients and caregivers,” he said. “Palliative care must also be responsive to health professionals so they can focus on the disease process and get to know the patient and the family. The ultimate goal is to work with the patient, caregivers and family to make decisions in a collaborative process that is consistent with their values and preferences.”

While feeding is a standard element in palliative care, neurological complications of stroke can affect what might otherwise be a fairly straightforward decision. Aspiration is a common complication of feeding that needs a

Update on palliative care in stroke management

Palliative care in stroke is unlike palliative care in many other disease states. Depending on the patient and the severity of the stroke, palliative care may be end-of-life care or it may be a respite from symptoms that’s part of a longer-term care program. Or care goals may change as the patient’s condition changes.

“Palliative care in stroke is one area that doesn’t have a lot of science to it,” said Richard Zorowitz, MD, co-moderator of “Stroke Palliative Care” at 3:30–5 p.m. Thursday in Ballroom 20A.

“Palliative care clearly has a lot of art in practice. It is important that we have a better understanding of how to provide palliative care and the resources that are needed to implement our decisions.”

Gregory Zipfel, MD, associate professor of neurosurgery and neurology at Washington University School of Medicine in St. Louis, is co-moderator of the symposium.

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Direct thrombin inhibitors offer neuroprotection

Direct thrombin inhibitors are among the newest potential neuroprotective agents to arrive on the clinical trial scene. And while most of these agents are still in clinical development, promising results have left neurologists eager for more data on their safety and efficacy.

“We are still learning about the molecular mechanisms of ischemia and which ones might be targets for treatment,” said Sheryl Martin-Schild, MD, PhD, assistant professor and director of the stroke program at Tulane University Hospital and Clinic, Tulane University School of Medicine in New Orleans. “Thrombin inhibitors are promising because thrombin has recently been demonstrated to play an important role in the ischemic cascade, causing direct injury to the neurovascular bundle.”

Martin-Schild will moderate a symposium on “Direct Thrombin Inhibitors and Neuroprotection: An Unexpected Journey” at 3:30–5 p.m. Thursday in Room 30 A-D. Her co-moderator is Jaroslaw Arnowski, MD, PhD, professor of neurology and vice chair for research at the University of Texas Medical School in Houston.

Thrombin inhibition is not a new concept, but the apparent utility of thrombin inhibition in stroke has been a surprise, Martin-Schild said. Researchers didn’t expect thrombin to play a direct role in instigating injury during ischemia and that thrombin can be targeted to minimize ischemic damage.

Multiple receptors play a role in platelet activation. One of the key families of receptors, protease-activated receptors, is activated in the presence of thrombin.

Direct thrombin inhibitors can prevent microthrombi from occluding smaller vessels downstream from the initial blockage. Thrombin inhibition can also limit the inflammatory component of ischemia.

One of the most promising direct thrombin inhibitors, argatroban, is being studied as an adjunctive treatment to standard thrombolytic therapy. Promising early stage studies showed a significantly higher proportion of patients who achieved a complete and maintained state of recanalization when argatroban was added to standard of care intravenous tissue plasminogen activator treatment compared to patients who got t-PA alone.

Studies in animal models looking at the inflammatory reaction within the ischemic core have found that direct thrombin inhibition reduced inflammation. While results are early, both the rationale and the results to date are positive.

“Hemorrhage is filled with thrombin,” Martin-Schild said. “We already know that at least part of the perihematomal edema is actually related to inflammation. We can reduce inflammation by targeting thrombin with an anti-thrombin agent. Something like argatroban, a direct thrombin inhibitor, has at least theoretical advantages in terms of how much edema develops in the hemorrhagic setting.”

The future for direct thrombin inhibition in stroke is wide open, she said. The question appears to be less about whether direct thrombin inhibitors will enter clinical use than when the first agent will be approved.

“Any area that works on our own natural processes to turn a negative event into a process that can facilitate recovery is exciting,” Martin-Schild said. “We are anticipating that there will be even more studies using these agents to treat not only central occlusions but the actual parenchyma. It is getting close.”

We are still learning about the molecular mechanisms of ischemia and which ones might be targets for treatment. Thrombin inhibitors are promising because thrombin has recently been demonstrated to play an important role in the ischemic cascade, causing direct injury to the neurovascular bundle.
Speakers examine emerging ICH treatment strategies

Blood pressure reduction, minimally invasive surgery and neurosurgical intervention — and other medical and surgical strategies for managing intracerebral hemorrhage — are the focus of “Acute Management of ICH: Blood Pressure Lowering, Surgery and Future Directions” at 1:30–3 p.m. Thursday in Room 30A-D.

“This session will focus on the general pathophysiology of ICH and review blood pressure reduction and other potential management strategies,” said Robert Loch Macdonald, MD, PhD, co-moderator of the symposium from St. Michael’s Hospital University of Toronto. “We’ll discuss pathophysiologic features of ICH that may impact the efficacy of blood pressure reduction, such as whether BP reduction increases the risk of brain injury around the hematoma, as well as comparisons of acute surgical clot removal and medications.”

In the randomized INTERACT-2 trial, researchers found intensive blood pressure lowering was not associated with statistically significant reductions in death or severe disability. However, they found a trend suggesting blood pressure reduction improves secondary endpoints.

“One of the trial’s limitations was that the time needed to reduce patients’ blood pressure to desired levels was too long,” said Joshua Goldstein, MD, PhD, co-moderator of the symposium and associate professor at Harvard Medical School in Boston.

Craig Anderson, MD, PhD, professor of stroke medicine and clinical neuroscience at the University of Sydney, will present “Subgroup Analyses of the INTERACT2 Trial.”

David Mendelow, MD, professor of neurosurgery at Newcastle University, Newcastle in Tyne, England, will present “STICH II: Outcomes from the Surgical Trial of Lobar ICH.” STICH II compared acute surgical hematoma evacuation with medical therapy among patients with superficial lobar stroke.

“Dr. Mendelow’s co-investigator, Barbara Gregson, PhD, is likely to discuss issues in the trial’s execution — such as the large number of patients randomized to medical treatment who crossed over to surgery and delays to treatment — that may have affected results,” Goldstein said.

Gregson, principal research associate at the Institute of Neuroscience, Newcastle University, in Newcastle Upon Tyne, United Kingdom, will discuss “Does Craniotomy Reduce the Volume of ICH-evidence from STICH II.”

Daniel F. Hanley, MD, PhD, professor of neurology, anesthesiology, critical care medicine and neurological surgery at Johns Hopkins University School of Medicine in Baltimore, will present “Innovative Approaches Utilizing Minimally Invasive Surgery plus Pharmacotherapy.”

“Ongoing studies are working on the idea that surgery itself might cause some brain damage,” Macdonald said. “So, if you can do the operation minimally invasively and slowly remove the hematoma with appropriate medications, you might improve outcomes compared to no surgery.”

This session is important to anyone involved in managing ICH patients, including neurointensivists, neurosurgeons and nurses, he said.
Symposium to shed light on pediatric stroke

Heard the latest cutting-edge research and strategies for neuroprotection of the ischemic brain in neonates, children and adolescents is the focus of “Protecting the Ischemic Neonatal Brain: What Can We Do Better?” at 7-8:30 a.m. Thursday in Room 3A.

“Scientists are looking at many strategies for reducing the damage resulting from ischemic injury in the developing brain,” said Rand Askalan, assistant professor of pediatrics at the University of Toronto.

“Hypothermia has been around for decades and is used in adult stroke patients. Only recently have scientists looked at its utility in the developing brain. Interest was stirred by two clinical trials showing benefit in children with diffuse ischemic injury. It is unclear if it will also be beneficial in babies with the focal injuries typical of stroke.”

Jerome Yager, MD, professor and head of the pediatric neurosciences at the University of Alberta in Canada, will focus on hypothermia as a treatment for focal injuries and strategies for improving hypothermia in “Hypothermia: Can We Push the Boundaries?”

Another major area of emerging research is the role of inflammation in stroke.

“As we have always thought that children suffer strokes, they are surprised that children suffer strokes. The ICS has increased the presence of pediatric stroke sessions in the program, and we hope this symposium will help to continue to raise awareness.”

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Session Ideas
Suggested Session Submitter Opened: Monday, Feb. 10, 2014
Suggested Session Submitter Closes: Monday, March 10, 2014

Abstracts
Submission Opens: Wednesday, May 21, 2014
Submission Closes: Tuesday, Aug. 12, 2014

Late-Breaking Science and Ongoing Clinical Trials Abstracts
Submission Opens: Wednesday, Oct. 8, 2014
Submission Closes: Wednesday, Nov. 5, 2014

The link to submit abstracts and/or session ideas can be found at strokeconference.org/submitscience on the appropriate date above. Start planning now for the International Stroke Conference 2015, Feb. 11-13 in Nashville, Tenn.

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ENDOVASCULAR

Jankowitz, MD, assistant professor of neurological surgery and co-director of neuroendovascular therapy at the University of Pittsburgh.

Another controversy surrounding endovascular therapy trials is defining the population of patients mostly likely to benefit. This is the focus of “Better Patient Selection Would Improve Outcomes in Endovascular Treated Patients,” presented by Raul G. Nogueira, MD, director of the Neuroendovascular Division, Marcus Stroke & Neuroscience Center in Atlanta.

Gregory W. Albers, MD, professor of neurology and neurological sciences at Stanford University School of Medicine in Palo Alto, Calif., will present, “Can Endovascular Best IV-tPA? Would Any Other Trial Design Have Led to Different Results?” The session will highlight the fact that contrary to what many believed IV tPA is beneficial for stroke due to middle cerebral artery occlusion. It will analyze what, if any, conditions will need to be satisfied to obtain better outcomes with IA therapy compared to IV tPA.

Antoni Davalos, MD, PhD, professor and head of the Department of Neurosciences at Hospital Universitari Germans Trias i Pujol, in Barcelona, Spain, will discuss “Endovascular Stroke Therapy Outside Clinical Trials: Should We Still Offer It?” The talk will focus on the real-world use of endovascular therapies and the importance of including every eligible patient in clinical trials.

“Although centers are offering endovascular procedures, there is no level I evidence to support its use,” Jovic said. “That is a big problem because if we think that endovascular therapy should become standard of care, we need to generate this type of data. To do that, we need to be able and willing to randomize every eligible patient, and pick and choose patients where the feeling of equipoise is most pronounced. This was a problem in many previous trials. These failed trials provide a good impetus to randomize every eligible patient.”

“To be able to accomplish that, some say that treatment outside of trials should not be offered. This concept is controversial because others contend that under these circumstances, patients who do not meet inclusion criteria will be denied potentially beneficial therapy. How to approach this controversial issue is the focus of Davalos’s talk.”
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**Thursday**
10:11–11 a.m.
AHA/ASA Parts!

11:10–11:30 a.m.
Advocacy — A Year of Advocacy Successes: You’re the Cure
11:35 a.m.–12:15 p.m.
Education On-demand: Learn.Heart.org

Michelle Bruns, AHA Professional Education

12:20–1:00 p.m.
Stroke OnDemand™ Professional Product demonstration
Learn all of the features of this educational tool.

Dane Perrino, Astute Technology

**Check out the many must-see destinations in the Science & Technology Exhibit Hall.**

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**HIS**

11:00 a.m.–12:00 p.m.
**Advocacy — A Year of Advocacy Successes: You’re the Cure**

Michelle Bruns, AHA Professional Education

12:20–1:00 p.m.
**Stroke OnDemand™ Professional Product demonstration**

Learn all of the features of this educational tool.

Dane Perrino, Astute Technology

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**HIS/18**

8:00–8:45 a.m.
**Advocacy — A Year of Advocacy Successes: You’re the Cure**

Michelle Bruns, AHA Professional Education

8:50–9:30 a.m.
**Stroke OnDemand™ Professional Product demonstration**

Learn all of the features of this educational tool.

Dane Perrino, Astute Technology

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**HIS**

9:00 a.m.–10:00 a.m.
**Advocacy — A Year of Advocacy Successes: You’re the Cure**

Michelle Bruns, AHA Professional Education

10:10–11:00 a.m.
**Stroke OnDemand™ Professional Product demonstration**

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for a variety of patients in all stages of stroke designed to facilitate three-dimensional repetitive advanced robotic system for upper limb therapy, guiding wires, the Chaperon® Guiding Catheter System and a full line of access products Embolic Systems, featuring the V-Trak® Delivery System. In addition, the company offers a comprehensive suite of diagnostic and interventional devices to patients suffering from stroke and other medical specialties, using the digital workflow and documentation to overcome the barriers to adoption of telemedicine services.

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HYPOTHERMIA  
continued from page 1

Many neurologists attending ISC 2014 may not be aware of the shift in treatment that has already occurred in cardiac arrest, neonatal asphyxia and other conditions.”

Hemmen will be co-moderator of “Neuroprotection through Therapeutic Hypothermia” at 8:40–10:10 a.m. Thursday in Room 30A-D. His co-moderator is Patrick Lyden, MD, professor and chair of neurology and director of the stroke program at Cedars-Sinai Medical Center in Los Angeles.

“We want to highlight the ongoing research in Europe and in North America on testing the use of hypothermia in ischemic stroke,” Hemmen said. “We have a therapy that works in global hypoxia. Hypothermia is effective in cardiac arrest in adults and in asphyxia in babies, and it should work in focal hypoxia as well. Stroke, in essence, is a focal area of hypoperfusion just as cardiac arrest is a global hypoperfusion in the brain.”

Midori Yenari, MD, professor of neurology at the University of California in San Francisco, will explore the neuroprotective mechanisms of hypothermia in current therapeutic uses as well as in ischemic stroke.

The next presentation will discuss the latest work on hypothermia in ischemic stroke. Guadalupe Angelis Castillo-Abrego, MD, medical director of the Comprehensive Stroke Center at Caja del Seguro Social Hospital in Panama, will describe therapeutic hypothermia for acute spinal cord injury and diffuse axonal injury.

Traumatic brain and spinal cord injuries are the newest areas of research in neuroprotective hypothermia. Work is progressing on plans for a clinical study of therapeutic hypothermia in traumatic spinal cord injury.

Hypothermia offers an elegant therapeutic solution for neuroprotection, but the practice can be complex. The problem with hypothermia is cooling the core temperature without inducing other neurological problems, shivering and associated medical complications, Hemmen said.

Therapeutic hypothermia generally involves either cooling pads on the skin or catheters to remove excess energy. These devices work, but the clinical application of hypothermia is cumbersome. Even minor shivering can generate enough energy and heat to overcome the cooling effect of current technology.

“The exciting news is the possibility of using pharmacologic agents to induce hypothermia,” Hemmen said.

Shan Ping Yu, PhD, professor of anesthesiology at Emory University School of Medicine in Atlanta, will explore the modality of pharmacologic hypothermia to treat ischemic stroke.

Jesper Petersson, PhD, director of research and education in neurology at Malmö University Hospital, Lund University, in Sweden, will explore the overall feasibility of hypothermia.

“This will be an exciting introduction to concepts that could change the way we deal with stroke as dramatically as hypothermia is changing the way our colleagues deal with cardiac arrest,” Hemmen said.

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PALLIATIVE CARE  
continued from page 1

thorough exploration with patients and caregivers.

Pain is a common symptom of stroke that doesn’t always receive the attention it deserves. The initial step is to identify the source of pain, which can be musculoskeletal, neurogenic or a combination.

“The whole idea behind palliative care is to identify symptoms that are making the course of care more difficult for the patient and deal with the symptoms to the extent possible,” Zorowitz said. “And if this is end-of-life care, we need to prevent and relieve suffering as much as possible so that patients can have the best possible quality of life in whatever time remains.”

Quality of life can be a controversial area, he said. Medical evidence may suggest that it’s time to withdraw care, but family members may want to press on.

“Those kinds of attitudes can make a huge difference to the patient,” Zorowitz said. “The patient could be suffering for a long time and maybe unnecessarily. It becomes our job to talk with patients and families about the risks and the benefits of continuing treatment and to come to a consensus about what is best for the patient. Quality of life and the importance of quality of life really comes down to the values and preferences of the patient and the caregivers. We have to make sure they have all the information needed to make their decision.”

PALLIATIVE CARE  
continued from page 1

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Poster Tours, Sessions continue today

SC 2014 offers two types of poster sessions: professor-led poster tours and one-on-one individual Q&A poster presentations. Choose from 10 Professor-Led Poster Tours from 5:15 to 6:15 p.m. Thursday in Hall G. Expert moderators will lead these tours, which are organized by category; they provide a short presentation and Q&A with each of the poster authors in that section. To take part, simply review the Poster Abstracts section of the Final Program (page 72). Decide which section/category of posters you would like to attend. Then, at 5:10 p.m., arrive at the correspondingly numbered “Section” sign for your selected section/category.

During the Regular Poster Sessions, poster presenters will be at their posters for informal Q&As with attendees from 6:15 to 6:45 p.m. Thursday in Hall G. These one-on-one posters are not a part of the earlier Professor-Led Poster Tours. To see the posters featured in Thursday’s Regular Poster Sessions, go to page 79 of the Poster Abstracts section of the Final Program.

Posters also will be available for viewing in the Poster Hall (Hall G) from 8 a.m. to 6:45 p.m. Thursday. Please see page 47 of the Final Program for the Poster Hall map.

Abstract categories

- Acute Endovascular Treatment
- Acute Neuroimaging
- Acute Nonendovascular Treatment
- Aneurysm
- Basic and Preclinical Neuroscience of Stroke Recovery
- Cerebral Large Artery Disease
- Clinical Rehabilitation and Recovery
- Community/Risk Factors
- Diagnosis of Stroke Etiology
- Emergency Care/Systems
- Experimental Mechanisms and Models
- In-hospital Treatment
- Intracerebral Hemorrhage
- Nursing
- Outcomes, Quality and Health Services Research
- Pediatric Stroke
- Preventive Strategies
- SAH and Other Neurocritical Management
- Vascular Biology in Health and Disease
- Vascular Cognitive Impairment
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- Ongoing Clinical Trials

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- Quality Science: JAHA underwent a rigorous evaluation of published content before being accepted by Thomson Reuters.
- Compliance: JAHA became fully compliant with new mandates from Research Councils UK and Wellcome Trust.
- Expanded Reach: Articles are now automatically deposited in PubMed Central (now PMC) on publication as required by the National Institutes of Health. Welcome Trust and other funding agency mandates. This benefits authors and readers alike.

Other highlights and facts about JAHA’s progress

- Original research article submissions have increased by 68 percent from fiscal year 2011–2012 to fiscal year 2012–2013.
- Median time from submission to first decision is 19.5 days.

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