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Vol. 41, Issue 2, October 2021
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Neurology [ALERT®]

Evidence-based summaries of the latest clinical neurology research

ABSTRACT & COMMENTARY

Surgical Approaches to Decompression in Degenerative Lumbar Spondylolisthesis

By Joshua Weaver, MD

Assistant Professor of Clinical Neurology, Weill Cornell Medical College

SYNOPSIS: A multicenter, randomized, noninferiority trial of people with symptomatic lumbar stenosis and single-level spondylolisthesis who were refractory to conservative treatment found no significant difference between outcomes in those who underwent decompression surgery with instrumented fusion vs. decompression surgery without fusion.

SOURCE: Austevoll IM, Hermansen E, Fagerland MW, et al. Decompression with or without fusion in degenerative lumbar spondylolisthesis. *N Engl J Med* 2021;385:526-538.

Low back pain radiating to the legs often is caused by degenerative lumbar stenosis from disc bulges and overgrowth of the facet joints and ligaments causing compression of the nerve roots. Spondylolisthesis, or misalignment of the spine in which one vertebra has slipped forward from the vertebra below it, also commonly can contribute to stenosis and pain. If this pain does not improve with medication and physical therapy, surgical decompression may be performed to relieve symptoms. Surgical techniques vary widely, with some techniques involving instrumented fusion of the vertebral bodies (e.g., with screws, rods, and/or cages), and other techniques that are less invasive and do not require fusion. Two studies from 2016 compared decompression with or without fusion in lumbar stenosis with slightly different results. Subsequent analyses of these studies led to ambiguous conclusions and persistent questions regarding the superiority of one technique over the other.[1,2]

In this trial, 267 people with low back pain radiating to the legs that was refractory to conservative treatment for three months who had lumbar spinal stenosis and at least 3 mm of spondylolisthesis at the stenotic level were randomized into two groups: decompression-alone and decompression with fusion. The decompression alone group underwent a posterior decompression that was bilateral, ipsilateral, or ipsilateral with crossover to the contralateral side. The fusion group underwent posterior decompression with implantation of various

Financial Disclosure: None of the authors or planners for this educational activity have relevant financial relationships to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

Neurology
[ALERT]

Neurology Alert (ISSN 0741-4234) is published monthly by Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-9468. Periodicals postage paid at Morrisville, NC, and additional mailing offices. POSTMASTER: Send address changes to *Neurology Alert*, Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-9468.

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hardware at the discretion of the surgeon. Demographic characteristics were similar among the two groups. Outcomes were measured at three months, one year, and two years. The primary outcome was a reduction in a disability score (Oswestry Disability Index [ODI]) by 30% or more from baseline by two years. Secondary outcomes included mean change in the ODI score, a claudication scale, functional impairment scale, satisfaction with treatment score, numeric rating scale for leg and back pain, and a quality-of-life scale.

For the primary outcome, 71.4% in the decompression-alone group and 72.9% in the fusion group showed a reduction of at least 30% in the ODI score, showing noninferiority of decompression alone compared to decompression with fusion. Similarly, no significant difference was found in the secondary outcomes of improvement in claudication, functional impairment, leg and back pain, satisfaction, and quality of life. Duration of surgery, length of hospitalization, and blood loss during surgery were significantly less in the decompression-alone group. There was a trend toward the patients in the decompression-alone group needing re-operation by two years compared to the fusion group, although this was not statistically significant.

■ COMMENTARY

Although studies from 2016 have suggested similar outcomes in different surgical techniques for lumbar stenosis (decompression with fusion vs. decompression without fusion), there has remained a debate over which type of surgery is superior. This recent larger study adds to the body of evidence that surgical decompression without fusion is not inferior to surgical decompression with fusion. This is important, since minimally invasive surgery without fusion is less complicated, less invasive, cheaper, and possibly safer than surgery involving fusion.

There are important limitations to this study, however. It is difficult to generalize this study to all patients with lumbar stenosis since it was limited to those patients with spondylolisthesis at one level. Some patients have this degenerative condition at multiple levels, and some have lumbar stenosis without any spondylolisthesis at all. Patients with severe neural foraminal stenosis were excluded in this study, although it is not uncommon for patients to have this condition along with spondylolisthesis. Patients with prior fusion surgeries were excluded in this study. Twenty percent of patients included had dynamic instability of the spondylolisthesis on flexion/extension imaging, but these patients were lumped in with the total group, and subgroup analysis on surgery type (fusion vs. decompression without fusion) in this subgroup could not be done since this study was not powered adequately to do so.

Regardless, this is an important study that highlights the fact that in cases of single-level spondylolisthesis and lumbar stenosis, a less invasive surgical approach has similar outcomes to more invasive fusion surgery. In general, less invasive approaches are favored because of reduced risk of complications and faster recovery.

This is an important discussion neurologists can have both with their patients and their neurosurgical colleagues regarding treatment options. However, it should be noted that surgical treatment options often are quite nuanced and involve many factors, including number of levels of spondylolisthesis, presence of scoliosis, presence of significant neural foraminal stenosis, presence of dynamic instability with various movements of the spine, history of osteoporosis, baseline activity levels, and history of prior surgical fusion, among others.

Many of these conditions may lead a surgeon to choose fusion as an empirically superior alternative to decompression without fusion. Future studies should look at these subgroups for further characterization. Comparison of specific minimally invasive decompression surgical techniques and hardware types for fusion surgeries need to be studied in more detail as well. ■

REFERENCES

1. Försth P, Olafsson G, Carlsson T, et al. A randomized, controlled trial of fusion surgery for lumbar spinal stenosis. *N Engl J Med* 2016;374:1413-1423.
2. Ghogawala Z, Dziura J, Butler WE, et al. Laminectomy plus fusion versus laminectomy alone for lumbar spondylolisthesis. *N Engl J Med* 2016;374:1424-1434.

ABSTRACT & COMMENTARY

Diagnostic Utility of CSF Alpha-Synuclein

By Andrea Lee, MD

Assistant Professor of Clinical Neurology and Assistant Attending Neurologist, New York Presbyterian/Weill Cornell Medical College

SYNOPSIS: This observational study investigated whether the cerebrospinal fluid (CSF) α-synuclein (α-syn) real-time quaking-induced conversion (RT-QuIC) assay, applied to 289 CSF samples, accurately identified patients with mild cognitive impairment (MCI) caused by probable Lewy body (LB) disease. RT-QuIC identified patients with MCI-LB against cognitively unimpaired controls with 95% sensitivity, 97% specificity, and 96% accuracy and showed 98% specificity in neuropathologic controls, indicating that CSF α-syn RT-QuIC is a robust biomarker for prodromal dementia with Lewy bodies.

SOURCE: Rossi M, Baiardi S, Teunissen CE, et al. Diagnostic value of the CSF α-synuclein real-time quaking-induced conversion assay at the prodromal MCI stage of dementia with Lewy bodies. *Neurology* 2021;97:e930-e940.

This retrospective, observational study examined two independent cohorts comprising a total of 231 patients with mild cognitive impairment (MCI) and 58 individuals lacking neurologic signs or cognitive impairment, defined as controls. In both cohorts, MCI was diagnosed according to current diagnostic criteria, which included subjective concerns regarding changes in cognition, objective impairment in cognition, preservation of independence of functional abilities, and absence of dementia. Patients with evidence of non-neurodegenerative causes of cognitive decline, including severe white matter lesions on neuroimaging (Fazekas score 3), were excluded. In both cohorts, parkinsonism was assessed systematically during the neurologic examination and was rated present when the examination showed one or more extrapyramidal signs (rest tremor, bradykinesia, and plastic rigidity). Cognitive fluctuations, visual hallucinations, and rapid eye movement (REM) behavior disorder (RBD) were identified as present or absent.

Clinical features, Alzheimer's disease (AD) core markers, imaging, neurophysiologic data, and evolution at the last follow-up were used to classify the patients into four groups: MCI caused by probable Lewy body (LB) disease (MCI-LB), MCI caused by AD (MCI-AD), MCI caused by other neurodegenerative disorders, and controls. The presence or absence of clinical core features of dementia with Lewy bodies (DLB) was determined according to the definitions and guidelines provided by the DLB Consortium. The application of the "one-year rule" excluded patients with MCI caused by Parkinson disease from the studied cohort. Cerebrospinal fluid was collected at the time of MCI diagnosis in all patient groups and underwent α-synuclein (α-syn) real-time quaking-induced conversion (RT-QuIC) assay, including purification of recombinant wild-type human α-syn. RT-QuIC identified patients with MCI-LB against cognitively unimpaired controls with 95% sensitivity, 97% specificity, and 96% accuracy and showed 98% specificity in neuropathologic controls. The accuracy of the test for MCI-LB was consistent between the two cohorts (97.3% vs. 93.7%). Thirteen percent of patients with MCI-AD also had a positive test; of note, 44% of them developed one core or supportive clinical feature of DLB at follow-up, suggesting an underlying Lewy body copathology.

■ COMMENTARY

There is an urgent need for early and disease-specific biomarkers for neurodegenerative diseases to enable proper patient care and selection in clinical trials. The recent development of ultrasensitive assays that indirectly reveal minute amounts of misfolded amyloid proteins in cerebrospinal fluid, based on a template amplification strategy, has contributed significantly to this goal. Current evidence indicates that RT-QuIC accurately detects misfolded α-syn in the cerebrospinal fluid of patients with Parkinson disease or DLB with an overall sensitivity of 95% and a specificity of 98%. Preliminary data also indicate that the cerebrospinal fluid of patients with pure autonomic failure and isolated RBD, two prodromal syndromes that often evolve to Parkinson disease or DLB, harbors significant α-syn seeding activity. However, no study has yet specifically explored the diagnostic value of α-syn RT-QuIC in patients with MCI, representing a common prodromal clinical manifestation of DLB. The results of the present study demonstrate that the CSF α-syn RT-QuIC assay accurately detects LB disease in patients with MCI. Application of the assay in two large, distinct groups of patients representing the MCI clinical spectrum identified those diagnosed with probable MCI-LB with a 95.1% overall sensitivity. Furthermore, the test demonstrated 96.6% specificity against cognitively unimpaired controls and close to perfect (98.3%) specificity for LB-related pathology in a cohort of 121 pathologic controls lacking LB at postmortem examination. Therefore, the detection of abnormal α-syn species by RT-QuIC not only is very accurate but also represents an early biomarker for LB disease. Thus, its implementation after repeat validation may help the clinical management and recruitment for clinical trials in memory disorder clinics. ■

ABSTRACT & COMMENTARY

Autologous Hematopoietic Stem Cell Transplantation in Multiple Sclerosis

By Jai S. Perumal, MD

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SYNOPSIS: This retrospective study of autologous hematopoietic stem cell transplantation in patients with active relapsing remitting multiple sclerosis or progressive multiple sclerosis showed efficacy in relapse rate reduction and on magnetic resonance imaging and disability outcomes during a median post-transplant follow-up of about two years. There were risks, including death, associated with the treatment.

SOURCE: Nicholas RS, Rhone EE, Mariottini A, et al; London Group on Autologous Hematopoietic Stem Cell Transplantation for Multiple Sclerosis. Autologous hematopoietic stem cell transplantation in active multiple sclerosis: A real-world case series. *Neurology* 2021;97:e890-e901.

Clinical trials of autologous hematopoietic stem cell transplantation in patients with multiple sclerosis have demonstrated efficacy in controlling the disease. Stem cell therapy also is being used increasingly in clinical practice for patients refractory to current immunosuppressive medications. In this study, the authors examined the application of autologous hematopoietic stem cell transplantation (AHSCT) in relapsing remitting multiple sclerosis (RRMS) and progressive MS patients with active disease in a real-world scenario.

The authors reviewed data on consecutive MS patients who underwent AHSCT at two tertiary care hospitals in London, United Kingdom. Data were collected retrospectively. The study included patients who had at least six months of post-transplant follow-up or who died at any time after the transplant. AHSCT was conducted under the standard protocol for the procedure at the respective hospitals, but the procedures were not identical. A total of 120 patients were included in the analysis. Sixty-two (52%) had either primary or secondary progressive MS, and the others had RRMS. Among patients for whom data were available, 90% had evidence of new magnetic resonance imaging (MRI) activity prior to the therapy. The mean age of the patients was 42.3 years, the median Expanded Disability Status Scale (EDSS) score was 6.0, and the mean disease duration was 8.8 years.

The annualized relapse rate decreased from 0.46 ± 0.57 in the two years prior to the procedure to 0.08 ± 0.38 in the four years post-transplant ($P < 0.001$). Ninety-three percent of the patients were relapse-free at two years. There was a significant reduction in the number of new T2 lesions, with 90% of the patients being free of new lesions at two years post-transplant. On analysis of disability, the average EDSS score for the group increased by 0.25 in the 12 months preceding AHSCT and 0.02 in the 12 months post-transplant. In a subgroup analysis, the RRMS cohort showed a mild improvement in EDSS score, while the progressive MS cohort continued to have a worsening of EDSS score. In the RRMS group, the EDSS score had increased by 0.39 prior to AHSCT and decreased by 0.17 after; in the progressive group there was an increase of 0.11 before AHSCT and 0.24 after.

Regarding adverse events, there were three deaths within 100 days of the procedure. Two were the result of cardiac arrest (in the setting of pulmonary edema in one case and electrolyte abnormalities in the other). The third fatality was caused by acute respiratory distress syndrome secondary to pneumonia and sepsis. Other significant adverse events included cytomegalovirus reactivation, which was controlled on antiviral therapy; and seven patients developed secondary autoimmune disorders (six cases of thyroiditis and one case of thrombocytopenia).

The authors concluded that the efficacy in this real-world data analysis matches that demonstrated in clinical trials of AHSCT in MS but stated that risks appeared higher in this study compared to clinical trials. These risks were in the immediate aftermath of the treatment. The investigators pointed out that one should weigh this against any potential long-term complications from continued immunosuppression associated with current aggressive treatments for MS. Limitations of this study also include the relatively short duration of post-transplant follow-up and the retrospective nature of the analysis.

■ COMMENTARY

The efficacy of AHSCT in active MS patients in this real-world data analysis appears comparable to that demonstrated in clinical trials and selected published case series. This study shows impressive efficacy, which will need to be weighed against potential risks. The most concerning adverse effect is the mortality and morbidity in the immediate post-procedure period. Special attention and focus on mitigation strategies and more experience could result in safer protocols that lower this risk.

Another aspect of AHSCT that needs more data is the durability of effect. One would need studies with longer follow-up of patients who have undergone this procedure to assess long-term benefits and risks. With more data and better safety, AHSCT has the potential to grow into a valuable treatment option for a wider spectrum of patients with MS. ■

Neurology [ALERT]

Stroke Alert

By Matthew E. Fink, MD

Pregnancy-Associated Stroke Is Increasing in Frequency

SOURCE: Karjalainen L, Tikkanen M, Ranstanen K, et al. Stroke in pregnancy and puerperium: Validated incidence trends with risk factor analysis in Finland 1987-2016. *Neurology* 2021;96:e2564-e2575.

Stroke during pregnancy or the puerperium is a rare event but accounts for a considerable part of maternal morbidity and mortality. Approximately 15% of maternal deaths are caused by pregnancy-associated stroke. The incidence has been increasing in all countries, particularly in wealthy industrialized countries, where pregnancy is being delayed considerably and other cardiovascular risk factors, such as hypertension, diabetes, cardiovascular disorders, and obesity, have taken on greater importance.

These investigators reviewed a chart-validated data registry in Finland, where all citizens are covered by health insurance, and there is a centralized Medical Birth Register linked to Hospital Discharge Register to identify all women who are pregnant and had incident stroke. The investigators performed a retrospective case-control cohort study in Finland covering the years 1987 through 2016. They identified all women with ischemic stroke, cerebral venous thrombosis, and intracerebral or subarachnoid hemorrhage during pregnancy or the puerperium. Medical records were reviewed to verify the diagnosis. The incidence of pregnancy-associated stroke was calculated over five-year age groups and incidence was calculated per number of deliveries. Three matched controls were selected for each case of pregnancy.

The overall incidence of pregnancy-associated stroke was 14.5 per 100,000 deliveries. It increased from 11.1 to 25.2 per 100,000 deliveries over the years 1987 to 1991 compared to 2012 to 2016 ($P < 0.0001$). Age was an important factor. Stroke incidence increased by age from 9.8 to 29.9 per 100,000 deliveries from 20-24 years of age compared to age > 40 years ($P < 0.0001$). Stroke incidence was fivefold greater in the early postpartum period compared to the first trimester, and overall maternal mortality was 6.6%. The following significant risk factors were found in a multivariable analysis: smoking, migraine, and hypertensive disorders of pregnancy. Greater attention should be paid to modifiable cardiovascular risk factors in women who are pregnant, particularly in older age groups. ■

Intensive Lowering of Blood Pressure Does Not Affect the Progression of Small Vessel Disease

SOURCE: Markus HS, Egle M, Croall ID, et al; PRESERVE study team. PRESERVE: Randomized trial of intensive versus standard blood pressure control in small vessel disease. *Stroke* 2021;52:2484-2493.

Small vessel disease of the brain accounts for 20% to 25% of all ischemic strokes and is a common cause of vascular cognitive impairments. The major risk factor for small vessel disease is hypertension. The precise target blood pressure that is optimal to prevent stroke or long-term cognitive impairment in these patients is undetermined. To prevent other cardiovascular events, targeting a systolic blood pressure of 120 mmHg to 125 mmHg has been recommended, but this has not been confirmed as effective in preventing stroke or long-term cognitive impairment in these patients. Because cerebral autoregulation is impaired in these patients, lowering the blood pressure too much runs the risk of accelerating white matter damage and making outcomes worse.

The investigators in this study performed a randomized, multicenter, controlled, and blinded-to-outcomes clinical trial with 111 patients who had magnetic resonance imaging-confirmed symptomatic lacunar infarcts and extensive white matter hyperintensities. They were randomized into one of two groups: 1) targeting a systolic blood pressure of 130 mmHg to 140 mmHg; or 2) intensive blood pressure lowering, targeting systolic blood pressure of < 125 mmHg. The primary endpoint was a change in diffusion tensor imaging of white matter mean diffusivity between baseline evaluation and 24 months of treatment. Secondary endpoints were imaging markers of recurrent stroke, progression of white matter abnormalities, and cognitive impairments. The mean age of the patients was 60 years and 60% were men. The mean blood pressure reduction was 15.3 mmHg and 23.1 mmHg in the standard and intensive groups, respectively ($P < 0.001$).

There was no difference between the treatment groups in the primary endpoint, and no significant difference between white matter hyperintensities or a decrease in cognition over the 24 months of follow-up. The investigators concluded that intensive blood pressure lowering was not associated with worsening but did not demonstrate any benefit in this population over standard blood pressure management. ■

Telestroke Consultation Increases Rate of Thrombolysis and Reduces Mortality

SOURCE: Wilcock AD, Schwamm LH, Zubizarreta JR, et al. Reperfusion treatment and stroke outcomes in hospitals with telestroke capacity. *JAMA Neurol* 2021;78:527-535.

Real-time video conferencing between the patient, a remotely located stroke specialist, and the bedside healthcare provider in a hospital emergency department is referred to as "telestroke." This modality for evaluation and treatment of acute stroke patients has been in use for more than 20 years and now has been disseminated widely worldwide. However, there are little data comparing its benefit with in-person evaluation and treatment for hospitals that do not have in-hospital stroke specialists 24 hours per day, seven days per week.

The investigators reviewed data from 643 hospitals with telestroke capability and matched them with a similar number from hospitals that did not have telestroke, derived from a Medicare database. The final study sample consisted of 153,272 patients, evenly divided between telestroke hospitals and those that did not have telestroke capability. Of the patients, 57.7% were female and the mean age was 78.8 years.

The primary outcome measure was receipt of reperfusion treatment through intravenous thrombolysis or thrombectomy, mortality at 30 days from admission, cost of care in the first 90 days from admission, and functional status at 90 days as measured by the time spent living in the community after discharge.

Patients who were treated at telestroke hospitals had a higher rate of reperfusion treatment compared to those who were evaluated at the control hospitals (6.8% vs. 6.0%; $P < 0.001$), and a lower 30-day mortality (13.1% vs. 13.6%; $P = 0.003$). There were no significant differences in the time spent living in the community following discharge nor were there any significant differences in costs of care for the first 90 days. The benefits of telestroke were greatest in low-volume hospitals, in rural areas, and among patients who were 85 years of age and older. In conclusion, the availability of telestroke resulted in a higher rate of reperfusion treatment and lower 30-day mortality. ■

Basilar Artery Occlusion: Endovascular Thrombectomy and Medical Therapy Have Similar Outcomes

SOURCE: Langezaal LCM, van der Hoeven EJRJ, Mont'Alverne FJA, et al; BASICS Study Group. Endovascular therapy for stroke due to basilar-artery occlusion. *N Engl J Med* 2021;384:1910-1920.

Basilar artery occlusion is a rare form of ischemic stroke and accounts for about 10% of large vessel occlusions reported in the literature. However, it is associated with a high morbidity and mortality. Studies of endovascular thrombectomy have focused predominantly on occlusions in large vessels of the anterior circulation, and there are very few randomized trials examining the efficacy of thrombectomy in basilar artery occlusion. This is because of the relative rarity of the condition, the difficulty in enrolling patients, and the biases that exist among treating physicians. These investigators conducted a randomized trial, enrolling patients from 2011 through 2019, even though multiple studies published in 2015 demonstrated benefit of endovascular therapy in anterior circulation large vessel occlusions. Efficacy and safety were compared with medical therapy in patients who underwent endovascular therapy within six hours after the estimated time of onset of symptoms. Patients also were treated with intravenous alteplase within four and a half hours.

Randomization was in a 1:1 ratio to receive endovascular therapy or standard medical care. The primary outcome was a favorable neurological outcome as defined by a Rankin scale score of 0 to 3 at 90 days. The primary safety outcomes were symptomatic intracranial hemorrhage within three days of treatment and mortality at 90 days. Three hundred patients were enrolled and divided evenly between the two groups. Intravenous alteplase was administered in 78.6% of the endovascular group and 79.5% in the medical group. Endovascular treatment was initiated at a median of 4.4 hours from onset of stroke symptoms. A favorable outcome, a Rankin scale score of 0 to 3, occurred in 44.2% of the endovascular group and in 37.7% in the medical care group, with a risk ratio of 1.18, 95% confidence interval = 0.92 to 1.50. The wide confidence interval resulted in a lack of statistical significance between the two groups, but it still is possible that endovascular treatment resulted in better outcomes. Symptomatic intracranial hemorrhage occurred in 4.5% of endovascular patients and 0.7% of medical therapy patients, and mortality at 90 days was 38.3% vs. 43.2%. None of the outcomes showed significant differences between the two groups. Because of difficulty in enrollment and the small numbers of patients in each group, many questions remain unanswered. Larger trials will be needed to provide a definitive answer regarding the efficacy of endovascular therapy for basilar artery occlusion. ■

Clinical and Perfusion Mismatch Criteria Both Are Reliable in Identifying Patients Who Will Benefit from Endovascular Therapy

SOURCE: Albers GW, Lansberg MG, Brown S, et al; AURORA Investigators. Assessment of optimal patient selection for endovascular thrombectomy beyond 6 hours after symptom onset: A pooled analysis of the AURORA database. *JAMA Neurol* 2021;78:1064-1071.

Since 2015, when multiple clinical trials were published showing the efficacy of endovascular thrombectomy (EVT) for large vessel occlusion within six hours of stroke onset, additional criteria have been developed to identify those patients who will benefit from EVT beyond six hours. Some studies have used a clinical/imaging mismatch to identify appropriate patients and others have used a target perfusion mismatch profile using magnetic resonance imaging or computed tomography perfusion scans. The AURORA investigators collected patient data from six large clinical trials (DAWN, *N Engl J Med* 2018; DEFUSE3, *N Engl J Med* 2018; REVASCAT, *N Engl J Med* 2015; ESCAPE, *N Engl J Med* 2015; RESILIENT, *N Engl J Med* 2020; and POSITIVE, *J Neurointerv Surg* 2021) and performed a meta-analysis to determine if a clinical mismatch or an imaging mismatch protocol was better at predicting good outcomes in patients treated between six hours and 24 hours after the onset of clinical stroke symptoms. Data were pooled from each study, and analysis was performed using mixed effects modeling.

The primary outcome was reduction in disability as measured by the modified Rankin scale score at 90 days. Outcomes were evaluated to determine whether response to treatment differed based on the imaging profile among patients based on the time of last known well. The benefits of treatment were compared between a clinical mismatch group and the target perfusion mismatch group, and then an undetermined profile subgroup. In the combined studies, there were 505 eligible patients, with a mean age of 68.4 years, and 54.9% were women. A total of 266 patients were assigned to the EVT group and 239 patients were assigned to the control group. In the clinical mismatch subgroup and the target perfusion mismatch group, endovascular therapy was associated with a reduction in disability at 90 days compared to the control group.

Benefits were observed in all of the EVT treatment subgroups, with odds ratios for improvement in outcome of 4.95 and 5.01, respectively, with $P < 0.001$ in both groups. This meta-analysis shows that both criteria, clinical mismatch and target perfusion mismatch, can reliably select patients who will benefit from endovascular therapy between six and 24 hours from onset of stroke symptoms. ■

In Young Adults, Marijuana Use Is Not Associated with Increased Risk of Early Onset Ischemic Stroke

SOURCE: Dutta T, Ryan KA, Thompson O, et al. Marijuana use and the risk of early ischemic stroke: The Stroke Prevention in Young Adults Study. *Stroke* 2021; Jul 16. doi: 10.1161/STROKEAHA.120.032811. [Online ahead of print].

The incidence of ischemic stroke in young adults is increasing, and one of the common modifiable risk factors is drug use. Tobacco smoking and cocaine use are well-known risk factors, but the role of marijuana is unclear. Marijuana use, both recreational and medical, is increasing among young adults, and many states are legalizing its use. A variety of cardiovascular effects have been described, which could increase the risk of cardiovascular complications, including stroke, and some observational studies have suggested an increased stroke risk from marijuana use. But there are few epidemiological studies that have evaluated this association.

The Stroke Prevention in Young Adults Study is a population-based case-control study of young onset ischemic stroke that collected data from 59 acute care hospitals in the greater Baltimore-Washington, DC, area. Exposure information was collected by self-report through a standardized face-to-face interview, and patients were asked specifically to recall use of medications and drugs, whether medical, nonmedical, or recreational. Traditional stroke risk factors also were collected. Current smoking was defined as tobacco smoking within 30 days before the stroke and the amount was based on the average number of cigarettes smoked per day. Subjects were excluded if they were known to have used cocaine or other vasoactive substances. The final study sample consisted of 751 cases and 813 controls. Logistic regression analysis was used to assess the relationship between marijuana use and risk of ischemic stroke, adjusting for other risk factors, including current tobacco smoking, current alcohol use, hypertension, and diabetes.

After adjusting for age, sex, race, and other risk factors, including tobacco smoking, the use of marijuana was not associated with ischemic stroke regardless of the timing of use in relationship to the stroke. There was a trend toward increased stroke risk among those who smoked marijuana at least once a week, but this was not statistically significant.

In this careful epidemiological study, the analysis does not demonstrate an association between marijuana use and increased risk of early onset ischemic stroke. However, no statement can be made regarding heavy users because of the small numbers of subjects considered to be heavy users at the time of data collection. ■

CME INSTRUCTIONS

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CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- discuss current scientific data regarding the diagnosis and treatment of neurological disease;
- discuss the pathogenesis and treatment of pain;
- describe the basic science of brain function;
- discuss new information regarding new drugs for commonly diagnosed neurological conditions and new uses for traditional drugs;
- identify nonclinical issues of importance for the neurologist.

CME QUESTIONS

1. **This study showed that decompressive surgery for lumbar stenosis without fusion was noninferior to decompressive surgery with fusion within which of the following groups?**
   a. Scoliosis
   b. Multilevel spondylolisthesis
   c. Single-level spondylolisthesis
   d. Neural foraminal stenosis
2. **Dementia with Lewy bodies is distinguished from Alzheimer's disease by which of the following biomarkers in cerebrospinal fluid?**
   a. Presence of low beta-amyloid and high total tau
   b. Presence of high beta-amyloid and low total tau
   c. Presence of α-synuclein
   d. Absence of α-synuclein
3. **When compared to clinical trials, the risks associated with stem cell transplantation in this study were which of the following?**
   a. Higher
   b. Lower
   c. Similar
   d. The authors do not make that statement.
4. **Intensive lowering of blood pressure to systolic < 125 mmHg results in a lower risk of recurrent stroke and dementia.**
   a. True
   b. False
5. **Hypertension is the major risk factor for pregnancy-associated ischemic stroke and intracerebral hemorrhage.**
   a. True
   b. False
6. **Telestroke consultations to hospital emergency departments can improve the rate of successful thrombolytic therapies.**
   a. True
   b. False
7. **Endovascular thrombectomy results in better neurological recovery, compared to medical therapy, in patients with basilar artery occlusion.**
   a. True
   b. False
8. **Clinical and imaging mismatch in large vessel occlusion can identify patients who can be successfully reperfused from six to 24 hours after stroke onset.**
   a. True
   b. False
9. **In young adults, marijuana use is a significant risk factor for ischemic stroke.**
   a. True
   b. False