Surgical Neurology International

OPEN ACCESS

For entire Editorial Board visit : http://www.surgicalneurologyint.com

Editor: **James I. Ausman**, MD, PhD University of California, Los Angeles, CA, USA

Neurosurgery Concepts

Neurosurgery concepts: Key perspectives on embolectomy for stroke with emergent large vessel occlusion (MR CLEAN), endonasal endoscopic craniopharyngioma resection, gamma knife radiosurgery for meningiomas, therapeutic hypothermia for severe traumatic brain injury

Peter Kan, Edward Duckworth, Anand V. Germanwala[1], Panayiotis Pelargos[2], Jin Mo Cho[3], Winward Choy[4], Zachary A. Smith[4], Isaac Yang[2]

Department of Neurosurgery, Baylor College of Medicine, Houston, TX, [1]Department of Neurological Surgery, Stritch School of Medicine, Loyola University Chicago, [4]Department of Neurosurgery, Northwestern University Feinberg School of Medicine, Chicago, IL, [2]Department of Neurosurgery, University of California Los Angeles David Geffen School of Medicine, Los Angeles, CA, USA, [3]Department of Neurosurgery, Catholic Kwandong University School of Medicine, Incheon, South Korea

E-mail: Peter Kan - peter.kan@bcm.edu; Edward Duckworth - duckwort@bcm.edu; Anand V. Germanwala - anand.germanwala@va.gov; Panayiotis Pelargos - ppelargo@uci.edu; Jin Mo Cho - chojinmo@gmail.com; Winward Choy - winward.choy@northwestern.edu; Zachary A. Smith - zsmith@nmff.org; *Isaac Yang - iyang@mednet.ucla.edu
*Corresponding author

Received: 16 June 15 Accepted: 22 June 15 Published: 23 October 15

This article may be cited as:
Kan P, Duckworth E, Germanwala AV, Pelargos P, Cho JM, Choy W, *et al*. Neurosurgery concepts: Key perspectives on embolectomy for stroke with emergent large vessel occlusion (MR CLEAN), endonasal endoscopic craniopharyngioma resection, gamma knife radiosurgery for meningiomas, therapeutic hypothermia for severe traumatic brain injury. Surg Neurol Int 2015;6:165.
http://surgicalneurologyint.com/Neurosurgery-concepts:-Key-perspectives-on-embolectomy-for-stroke-with-emergent-large-vessel-occlusion-(MR-CLEAN),-endonasal-endoscopic-craniopharyngioma-resection,-gamma-knife-radiosurgery-for-meningiomas,-therapeutic-hypothermia-for-severe-traumatic-brain-injury/

Key Words: Craniopharyngiomas, embolectomy, radiosurgery, traumatic brain injury

EMBOLECTOMY FOR STROKE WITH EMERGENT LARGE VESSEL OCCLUSION: REPORT OF THE STANDARDS AND GUIDELINES COMMITTEE OF THE SOCIETY OF NEUROINTERVENTIONAL SURGERY[1]

Study Question: In patients with acute ischemic stroke, large vessel occlusion in the anterior circulation, and limited core infarct, what is the efficacy and safety of rapid revascularization with stent retrievers in conjunction with intravenous (IV) tissue plasminogen activator (tPA) versus IV tPA alone?

In 2013, there were three major trials that were published comparing outcomes of treatment of acute ischemic stroke with IV tPA to interventional methods: IMS III, MR RESCUE, and SYNTHESIS. These trials concurrently failed to show the superiority of endovascular therapy compared to IV tPA for the treatment of acute ischemic stroke. There has been much discussion following the publication of these trials. The three main criticisms were the heavy use of intra-arterial tPA and early-generation devices with limited reperfusion efficacy (use of outdated technology); failure to use vascular imaging to confirm the presence of large vessel occlusion amenable to endovascular therapy, and the slow initiation of endovascular intervention.

Subsequently, in 2015, there are multiple randomized trials which all report-improved outcomes with endovascular therapy for acute ischemic strokes. These

Access this article online	
Quick Response Code:	Website: www.surgicalneurologyint.com
	DOI: 10.4103/2152-7806.168064

trials for the first time showed the efficacy, the safety of a rapid endovascular therapy for the treatment of acute stroke in the anterior circulation with a radiographic proven proximal vessel occlusion.

The Multicenter Randomized Clinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands (MR CLEAN) was a randomized controlled trial comparing endovascular treatment plus usual care to usual care alone. To be included, patients had to have a documented proximal vessel occlusion, and endovascular treatment had to be available within 6 h of stroke onset. Primary outcome was modified rankin scale (mRS) at 90 days. In the study, 502 patients were randomized, and overwhelmingly, stent retrievers were used (82% of patients in the endovascular arm). The primary outcome favored intervention in all mRS scores except death. The absolute difference in treatment effect was 13.5%. All secondary outcomes favored intervention also: NIHSS was on average 2.9 points lower in the intervention group; infarction volume was smaller, and reperfusion was higher in the intervention group. There was no difference in safety between the groups.

The ESCAPE trial was designed to test whether patients with acute ischemic stroke would benefit from rapid endovascular treatment. This multicenter randomized trial enrolled 316 patients up to 12 h after symptom onset. Computed tomography angiogram (CTA) was complete to target patients with proximal vessel occlusion and small infarct core with moderate to good collateral circulation. Retrievable stents were used in 86% of patients who underwent endovascular treatment. The control group received the current standard of care, and both groups received IV tPA within 4.5 h after symptom onset if they met local guidelines. The target time from CT to groin puncture was 60 min or less and to reperfusion was 90 min or less. The primary outcome was assessed using the mRS at 90 days. A median mRS of 0–2 at 90 days was 53% for the intervention group and 29% for the control group. Mortality was also lower, and reperfusion rate higher in the intervention group compared with the control group.

EXTEND-IA was another multicenter randomized trial comparing endovascular therapy in addition to IV tPA and IV tPA alone. Only 70 patients with anterior circulation stroke and documented proximal middle cerebral artery (MCA) or internal carotid artery (ICA) occlusion on CTA were enrolled. These patients also had a salvageable penumbra identified on perfusion imaging and the endovascular therapy was completed within 8 h. The primary outcome was reperfusion and neurologic improvement with a reduction of NIHSS of >8 points. Solitaire stent retrievers were used in all patients. Both primary endpoints favored endovascular therapy with a significant improvement.

SWIFT PRIME is the latest multicenter randomized trial comparing bridging therapy (endovascular therapy plus IV tPA) to IV tPA alone within 6 h of symptoms onset. Patients included had to have a documented proximal MCA or ICA occlusion along with a small to moderate core infarct. Solitaire stent retriever was used exclusively. The primary outcome was means mRS at 90 days. The treatment group reduced disability at 90 days over all mRS scores, and the rate of functional independence (mRS of 2 or less) was 60% in the treatment group compared with 35% in the control group.

Perspective: In the last 10 years, there has been an improvement in outcomes for patients with an acute ischemic stroke caused by proximal vessel occlusion. Advances in technology and standardized stroke care have been the main contributors to the increase in outcome. Although early randomized trials did not show a significant benefit for the endovascular treatment of stroke, they did show that endovascular treatment is safe and patients were not harmed by its use. Later trials improved the presentation to groin puncture time and better-established criteria and protocol for those patients who might benefit from interventional therapy. Together with the use of modern stent retrievers, they showed benefit from endovascular treatment in the treatment of acute ischemic stroke.

Summary Written by: Peter Kan MD, MPH, and Edward Duckworth, MD, MS

LONG-TERM QUALITY OF LIFE AFTER ENDONASAL ENDOSCOPIC RESECTION OF ADULT CRANIOPHARYNGIOMAS[4]

Study Question: What factors influence the quality of life (QOL) for patients with craniopharyngiomas undergoing endoscopic endonasal surgery?

The authors review a prospectively acquired database of consecutive adult patients at a single institution with craniopharyngiomas treated by the endoscopic endonasal approach by the same team over a period of almost 10 years. Data reviewed included preoperative and postoperative QOL forms, Wen class (marker of independence), extent of resection, presence of visual dysfunction or endocrinopathy, tumor recurrence, increase in body mass index (BMI), and the need for adjuvant radiation therapy or reoperation. A contemporaneous group of patients undergoing an endoscopic endonasal resection for nonfunctioning pituitary adenomas was used as a control. QOL forms included the anterior skull base QOL (ASBQ) questionnaire and sinonasal outcome test (SNOT-22). These self-assessment forms evaluate general markers of health and independence, such as sleep patterns, work performance, and physical function, signs of emotional distress and pain, and site-specific severity of symptoms like nasal discharge, loss of smell, and visual disturbance.

A total of 33 procedures were performed in 31 patients with craniopharyngiomas. Average ASBQ and SNOT-22 scores were 3.35 and 19.6, respectively. Increased QOL was associated with gross total resection. Decreased QOL was associated with recurrence, endocrinopathy, long-term visual deficits, BMI increase ≥2.0, and was most strongly correlated with worsening Wen class. Individuals with recurrence had a higher QOL when treated with radiation compared to reoperation. An overall improvement in QOL after surgery was noted but not statistically significant. Furthermore, the results suggested an overall decrease in QOL in patients treated with craniopharyngiomas compared to those with pituitary adenomas.

Perspective: Gross total resections of craniopharyngiomas result in improved QOL, even with the added morbidity of potential hypopituitarism, but should not be pursued at the risk of other overwhelming deficits. The pathophysiology of these tumors is distinct from pituitary adenomas and leads to a decreased QOL. Potential treatment options in the setting of residual tumor include observation, radiation therapy/radiosurgery, and reoperation.

Within neurosurgery, QOL assessments are becoming increasingly popular. Ample literature exists on evaluations within the neuro-oncology and spine realms using questionnaires such as the medical outcomes study short form-36 to measure health status and the Oswestry disability index to quantify disability from back pain. They provide a patient-based metric without observer bias that may serve as a reported measure of success and as a comparative tool between interventions. While limitations include a small sample size, this article is the first to address factors that influence site-specific QOL in patients with craniopharyngiomas. It underscores the importance of acknowledging and prospectively analyzing a focused metric in all patients undergoing neurosurgical intervention.

Summary Written by: Anand V. Germanwala, M.D

GAMMA KNIFE RADIOSURGERY FOR MENINGIOMAS IN PATIENTS WITH NEUROFIBROMATOSIS TYPE 2[2]

Study Question: What is the utility of stereotactic radiosurgery for meningioma in patients with neurofibromatosis type 2 (NF2)?

The authors conducted a retrospective analysis of all patients with NF2 who had undergone gamma knife radiosurgery (GKRS) for meningioma from January 1, 1999, to September 19, 2013, at a single tertiary care center. The indications for treatment of the lesions were symptomatic or growing meningiomas. Twelve consecutive patients with a total of 87 GKRS treated meningiomas were included in the study.

The authors reported that the median age at the first GKRS treatment was 31 years with a median follow-up time in surviving patients of 43 months. The median dose of radiation to the margins of treated tumors was 12 Gy. 5-year local tumor control rate was 92%, which is similar to that for sporadic Grade 1 meningiomas, but 5-year distant treatment failure rate was 77%, which is significantly higher than that for sporadic Grade 1 meningiomas. Multivariate analysis showed that age at distant failure (hazard ratio [HR] 0.91, 95% confidence interval [CI] 0.88–0.95, $P < 0.0001$) and prior number of GKRSs (HR 1.3, 95% CI 1.1–1.5, $P = 0.004$) were significant predictive factors for distant failure. Adverse toxicity events occurred in 25% of treatments though the majority were Grade 1 (alopecia or fatigue) or 2 (treated cerebral edema or seizure). Median overall survival was 110 months. Four patients (33%) died of neurological death with a median time from initial GKRS of 103 months. None of the treated tumors resulted in malignant transformation.

The authors concluded that radiosurgery may be a feasible treatment option for NF2-associated meningiomas given its high local tumor control rates and limited toxicity. They also speculated that a higher radiation dose to the NF2-associated meningiomas may be sensible given the higher rate of high-grade meningiomas in this population and the high distant failure rate seen in their cohort.

Perspective: There are limited data examining the value of radiotherapy for the treatment of NF2-associated meningiomas. In this study, the authors used retrospective analysis to examine the value and outcomes of treating such tumors with GKRS. The authors concluded that radiosurgery for these meningiomas resulted in minimal toxicity and is a feasible modality. While the authors acknowledge the limitations of their study, their findings suggest that radiosurgery must be more closely examined as a possible therapeutic for this population of meningiomas, and further studies are necessary to determine the long-term patterns of treatment failure in these patients.

Summary Written by: Panayiotis Pelargos and Isaac Yang, MD

PROLONGED MILD THERAPEUTIC HYPOTHERMIA VERSUS FEVER CONTROL WITHTIGHT HEMODYNAMIC MONITORING AND SLOW REWARMING IN PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY: A RANDOMIZED CONTROLLED TRIAL[3]

Study Question: Is hypothermia an effective neuroprotective strategy for severe traumatic brain injury (TBI)?

The authors performed a multicenter randomized controlled trial in patients with severe TBI (Glasgow Outcome Scale [GOS] score 4–8) to determine the effectiveness of therapeutic hypothermia. Patients were assigned to two groups: Therapeutic hypothermia (32–34°C, $n = 98$) or fever control (35.5–37°C, $n = 50$). The authors performed rapid cooling, which was maintained for 3 days or more and slow rewarming (<1°C/day) according to a previously published protocol. They compared patients' 6-month scores on the GOS in a blinded fashion. The overall rates of poor neurologic outcomes were 53% (hypothermia group) and 48% (fever control group). There were no significant differences in the likelihood of a poor neurologic outcome. In conclusion, they did not find any clinical benefit of hypothermia in patients with severe TBI.

Perspective: There is much evidence for the beneficial effects of hypothermia in patients with cardiac arrest; however, its benefits for patients with severe TBI are debatable. According to recent guidelines, there is level III evidence for the effectiveness of prophylactic hypothermia; therefore, it could decrease the mortality risk of patients with TBI and could be associated with good clinical recovery. The landmark study of hypothermia in patients with TBI (NABIS, NABIS: H) reported that early hypothermia, young age (<45 years), and focal injury (surgically evacuated mass) could enhance the effect of hypothermia and could be related to good patient outcomes. However, the sample size was too small; therefore, the evidence is a little weak.

In this study, the overall results are not significantly different from the current concepts of hypothermia. The authors conclude that hypothermia cannot improve clinical outcomes or risk of mortality compared with strict body temperature control. Furthermore, there were more complications in the hypothermia group though lacking statistical difference. In contrast to previous studies, there was no clinical improvement, especially in early hypothermia-treated and younger population. There are no data comparing focal versus diffuse injury in this study. Considering the results of this study and those of recent landmark studies, application of hypothermia for severe TBI should be seriously considered only in selective cases because it may cause serious adverse effects rather than clinical improvement. TBI has a heterogeneous pathophysiology; therefore, patients should be treated with an individualized approach based on the injury mechanism, CT findings, and individual clinical settings. Future studies investigating the effectiveness of hypothermia for treatment of severe TBI are warranted.

Summary Written by: Jin Mo Cho, MD. PhD

REFERENCES

1. Jayaraman MV, Hussain MS, Abruzzo T, Albani B, Albuquerque FC, Alexander MJ, *et al.* Embolectomy for stroke with emergent large vessel occlusion (ELVO): Report of the Standards and Guidelines Committee of the Society of NeuroInterventional Surgery. J Neurointerv Surg 2015;7:316-21.
2. Liu A, Kuhn EN, Lucas JT Jr, Laxton AW, Tatter SB, Chan MD. Gamma Knife radiosurgery for meningiomas in patients with neurofibromatosis Type 2. J Neurosurg 2015;122:536-42.
3. Maekawa T, Yamashita S, Nagao S, Hayashi N, Ohashi Y, Brain-Hypothermia Study Group. Prolonged mild therapeutic hypothermia versus fever control with tight hemodynamic monitoring and slow rewarming in patients with severe traumatic brain injury: A randomized controlled trial. J Neurotrauma 2015;32:422-9.
4. Patel KS, Raza SM, McCoul ED, Patrona A, Greenfield JP, Souweidane MM, *et al.* Long-term quality of life after endonasal endoscopic resection of adult craniopharyngiomas. J Neurosurg 2015;123:571-80.