Indications and Timing in Ischemic Infarction and Other Disorders

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KEYWORDS

• Ischemic stroke • Malignant cerebral edema • Malignant MCA syndrome
• Decompressive hemicraniectomy • DECIMAL trial • DESTINY trial • HAMLET trial

KEY POINTS

- Malignant cerebral edema can result from a large middle cerebral artery infarction as the result of a complex response to acute tissue ischemia.
- Left untreated, massive hemispheric swelling may lead to transtentorial herniation with a mortality rate approaching 80%.
- Options for medical management are few and have a very limited impact on intracranial pressure control, mortality, and functional outcomes.
- Current guidelines recommend considering surgical decompression in patients $\leq$60 years old who deteriorate neurologically within 48 hours from infarction-associated edema.
- Surgical decompression may also be considered for refractory intracranial hypertension in pathologies such as encephalitis, infection, or venous sinus thrombosis–associated edema and hemorrhage.

INTRODUCTION

Stroke is among the most devastating neurologic disorders worldwide, with ischemic stroke accounting for most cases. It affects hundreds of thousands of individuals annually, and it is consistently ranked as a leading cause of mortality and long-term disability.[1,2] Stroke survivors often live with enduring neurologic deficits, placing a significant burden on patients, families, and health care systems.[3,4] Despite advances in reperfusion therapies such as intravenous thrombolysis and mechanical thrombectomy, large hemispheric infarctions carry high risks of complications, including malignant cerebral edema (MCE).[5]

THE INFLAMMATORY CASCADE AND POSTINFARCT CEREBRAL EDEMA

A complex sequence of molecular events unfolds after a large ischemic stroke, ultimately leading to cerebral edema. This process has been well-described by Liebeskind and colleagues and can be conceptualized as three stages, beginning with cytotoxic edema and progressing to ionic edema and vasogenic edema[6] (**Fig. 1**). The acute obstruction of blood flow compromises the delivery of glucose and oxygen and impairs cellular oxidative phosphorylation. This impaired aerobic metabolism decreases the concentration of intracellular adenosine triphosphate and consequently disrupts the activity of the Na^+/K^+-adenosine triphosphatase

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Abbreviations

ASPECTS	Alberta Stroke Program Early CT Score
CI	confidence interval
DESTINY	decompressive surgery for the treatment of malignant infarction of the middle cerebral artery
HAMLET	Hemicraniectomy after middle cerebral artery infarction with life-threatening edema trial
ICP	intracranial pressure
MCA	middle cerebral artery
MCE	malignant cerebral edema
mRS	Modified Rankin Scale
OR	odds ratio
RCT	randomized controlled trial

pump, which in turn disturbs multiple transport mechanisms that rely on this pump.[7] The resultant high cytosolic concentration of sodium and chloride ions leads to cytotoxic edema, which is characterized by an intact blood–brain barrier and cellular swelling and occurs within minutes to hours of ischemia. Ionic edema, involving endothelial dysfunction, occurs immediately following cytotoxic edema. Solute depletion of the parenchyma creates an ionic gradient between the plasma and interstitial fluid compartments. In this phase, the blood–brain barrier remains intact. The last phase, vasogenic edema, occurs secondary to breakdown of this barrier. This phase occurs when fluid and intravascular proteins extravasate into the extracellular space of the brain parenchyma and peaks approximately 24 to 48 hours after onset.[6]

MALIGNANT CEREBRAL EDEMA

MCE represents the most catastrophic form of poststroke brain swelling. Typically arising after large middle cerebral artery (MCA) territory infarctions, MCE results in massive hemispheric swelling and transtentorial herniation, leading to mortality rates approaching 80% without intervention. Hacke and colleagues first popularized the term *malignant MCA infarction*, describing patients with extreme intracranial hypertension with intracranial pressure (ICP) values exceeding 60 to 80 mm Hg and uniformly poor outcomes.[8]

Previous studies describe an incidence of MCE of approximately 10% in anterior circulation

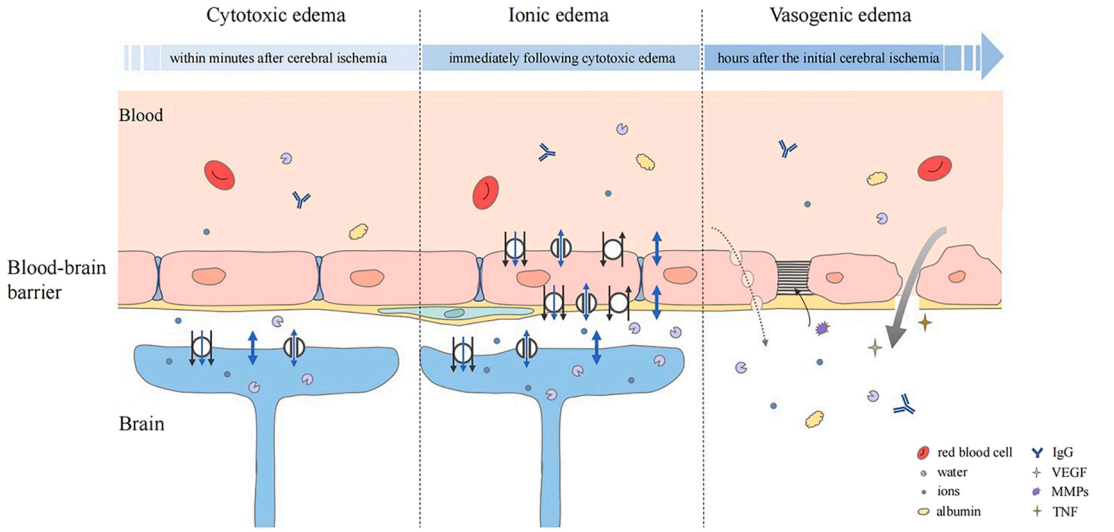

Fig. 1. Status of the blood–brain barrier at 3 phases of cerebral edema. Cytotoxic edema is the initial step and particularly prominent in astrocytes. Cerebral ischemia and hypoxia induced the ion influx (*black arrow*), which leads to osmotic gradient changes. Water may flow into astrocytes in 3 ways, simple diffusion (*thick blue double-headed arrows*), passive transport through transmembrane channels (*thin blue double-headed arrows*), and water cotransport (*blue single-headed arrows*). In ionic edema, ion, and water influx are mediated by plasmalemma channels and transporters of endothelial cells. Upregulation of transporters and ion channels also occurs in astrocytes. Vasogenic edema is characterized by destruction of the blood brain barrier. The transport of ions, water, and serum proteins such as albumin and immunoglobulin G may occur directly (*thick gray arrow*) or via pinocytic vesicles (*dashed gray arrow*). Multiple factors, including vascular endothelial growth factor (VEGF), matrix metalloproteinases (MMPs), and proinflammatory cytokines such as tumor necrosis factor (TNF) are involved. They mediate neuroinflammation and tight junction degradation, aggravating cerebral edema. (Gu Y, Zhou C, Piao Z, Yuan H, Jiang H, Wei H, Zhou Y, Nan G and Ji X (2022) Cerebral edema after ischemic stroke: Pathophysiology and underlying mechanisms. Front. Neurosci. 16:988283. doi: 10.3389/fnins.2022.988283.)

infarcts,[9,10] though this number will likely evolve with the wider application of mechanical thrombectomy. Large-core infarct trials supporting intervention for patients with large core strokes have increased the pool of patients at risk. Recent cohort studies suggest that MCE occurs in 16% to 44% of patients following successful reperfusion in the setting of a large infarction.[11–14]

Based on retrospective series, several parameters have been identified to predict MCE. These include both patient-related factors and imaging-related factors.[15,16] Younger patients are at higher risk of developing MCE, and their reduced intracranial compliance may accelerate the progression to herniation and associated morbidity and mortality.[17] Radiological indicators of mass effect, such as cisternal effacement and midline shift, are also predictive of MCE.[18] Other imaging-based grading scales that attempt to categorize stroke burden and robustness of collateral circulation, including Alberta Stroke Program Early CT Score (ASPECTS) on noncontrast CT and perfusion cerebral blood volume ASPECTS, also predict malignant evolution of cerebral edema.[17,19] In terms of acute management, successful reperfusion lowers the risk of malignant edema.[20,21] The INTEP-AR scale was more recently developed using prospectively collected data and identified the following as predictors of MCE: large infarct size, National Institutes of Health Stroke Scale score, use of thrombolysis, use of endovascular treatment, development of pneumonia, presence of brain atrophy, and recanalization status.[22] The use of such prediction scales could provide a useful tool to identify patients at high risk of MCE and guide management, including potential surgical intervention.

MEDICAL MANAGEMENT OF MALIGNANT CEREBRAL EDEMA

Both medical management and surgical intervention may be used in the management of MCE, however, medical therapies typically only provide temporary relief and rarely alter prognosis. While osmotherapy may effectively lower ICP acutely,[23,24] with hypertonic saline thought to have a more sustained effect compared to mannitol,[25–27] the impact of these agents on outcomes is not as well established. Nontargeted therapies such as sedation, paralysis, and targeted temperature management have also been leveraged to address edema.[28] Nonpharmacologic interventions only have limited benefit. Head of bed elevation can decrease ICP.[29–33] Transient therapeutic hyperventilation to treat acute intracranial hypertension reduces ICP in most patients,[23,24] whereas prophylactic hyperventilation is avoided due to risk of vasoconstriction-associated cerebral ischemia.[34] Cerebrospinal fluid diversion can also be used to lower ICP, but the impact on long-term outcomes is unclear.[35,36] The 2020 Neurocritical Care Society guidelines suggest hyperosmolar therapy for treating elevated ICP and cerebral edema, supplemented as appropriate with head of bed elevation, transient hyperventilation, and cerebrospinal fluid diversion as adjuncts.[23,24,34,37]

SURGICAL MANAGEMENT OF MALIGNANT CEREBRAL EDEMA

Surgical management with decompressive hemicraniectomy was first described in the late 1990s as a life-saving intervention in malignant MCA infarction.[38] Initial systematic reviews[39] and a Cochrane review[40] laid the groundwork for formal randomized controlled trials (RCTs). These RCTs ultimately demonstrated that surgical decompression reduced ICP while creating compensatory space to prevent further herniation and avoid consequent morbidity and mortality.[38]

Indications for Decompressive Hemicraniectomy

Several considerations impact the use and timing of surgical decompression for MCE. Both RCTs and pooled analyses were leveraged to refine the indications. Current guidelines from the American Heart Association/American Stroke Association state that for patients age $\leq$60 who deteriorate neurologically within 48 hours from cerebral edema associated with unilateral MCA infarction, it is reasonable to pursue operative intervention, specifically decompressive craniectomy with dural expansion (Class of Recommendation IIa, Level of Evidence A).[41] Other important considerations include prestroke disability (reflected in premorbid Modified Rankin Scale (mRS) score) and the presence of significant comorbidities, such as terminal illness, that could limit prognosis independent of the patient's acute neurologic injury. In patients greater than 60 years with malignant MCA syndrome with dominant hemispheric infarctions, surgical decompression may be considered (Class of Recommendation IIb, Level of Evidence B-R). Some practitioners consider the following features to be relative contraindications to surgical intervention: bilateral or multiple large territory infarcts, preexisting severe disability (mRS $\geq$ 3), severe comorbidities limiting life expectancy, and late presentation, often defined as greater than 72 hours after stroke onset, with established herniation.[41]

These guidelines were initially developed based on RCTs establishing the positive impact of

decompressive hemicraniectomy for MCE. The 2007 French DECIMAL trial (Sequential-design, multicenter, randomized, controlled trial of early decompressive craniectomy in malignant middle cerebral artery infarction) demonstrated improved mortality in the surgical cohort compared to the medical management group (25% versus 78%), with 25% of patients achieving an mRS of $\leq$3.[42] The 2007 German DESTINY trial (Decompressive surgery for the treatment of malignant infarction of the middle cerebral artery) similarly showed a survival benefit of surgical decompression (27%, versus 53% of patients managed medically).[43] The 2009 HAMLET trial (Hemicraniectomy after middle cerebral artery infarction with life-threatening edema trial) from the Netherlands also demonstrated a survival benefit (22% versus 59%) with surgical intervention within 48 hours of presentation. A pooled analysis demonstrated a reduction in 1-year mortality from 78% to 29% with surgery, with a number needed to treat of 2 to prevent one patient death[44] (**Figs. 2–4**). These studies included patients 18 to 60 year old with infarctions involving at least 50% of the MCA territory randomized within 30 to 96 hours after hospitalization. The data demonstrated a survival benefit, as well as possible improvement in functional status, primarily in those patients treated within 48 hours.

The benefit of surgical decompression may be more limited in the elderly population. The DESTINY II trial extended the inclusion criteria from the original DESTINY study to patients aged 60 or older.[45] The study reaffirmed a significant reduction of mortality in this cohort of patients; however, functional improvement after surgical decompression was limited. No survivors achieved an mRS $\leq$2, and only 7% of patients achieved an mRS of 3. Later studies, including the DECAP trial (2019),[46] confirmed a lack of functional recovery in the elderly population. In contrast, a 2022 Cochrane review incorporating multiple RCTs (DECIMAL, DESTINY I & II, HAMLET, HeADDFIRST,[47] HeMMI,[48] Demitur,[49] Slezins *and colleagues,*[50] Zhao *and colleagues*[51]), some of which enrolled patients of a wider age range, reaffirmed a reduction in death (odds ratio (OR): 0.18; 95% confidence interval (CI): 0.12–0.27), death or severe disability (mRS > 4; OR: 0.22; 95% CI: 0.15–0.32), and death or moderate disability (mRS > 3; OR: 0.34; 95% CI: 0.22–0.52) in patients managed with surgery, but failed to show a difference in outcomes based on age (<60 versus $\geq$60 years old).[52] These data support the role of decompressive hemicraniectomy for MCE to reduce mortality, but the impact on neurologic outcome is less clear.

Timing of Decompressive Hemicraniectomy

The timing of surgical intervention has been examined in several trials, including DECIMAL, DESTINY, and HAMLET, and the data generally suggest that performing decompressive hemicraniectomy within 48 hours of symptom onset results in the best outcomes.[44] Of the 3 trials, only HAMLET permitted randomization after 48 hours. Subgroup analysis demonstrated higher rates of mRS $\leq$4 in those undergoing early surgery, but this benefit was lost in those randomized after 48 hours.[53] While the later HeADDFIRST[47] and HeMMI[48] trials also permitted randomization after 48 hours, with a mean time to surgery of 57.1 hours in HeADDFIRST and 36.6 hours in HeMMI, neither trial performed subgroup analysis based on timing. Using the Nationwide Inpatient Sample, Dasenbrock *and colleagues* found that surgery performed after 72 hours was associated with more discharges to institutional care and a higher rate of poor outcomes.[54] However, this association was only seen in the setting of cerebral herniation, suggesting that timing of surgery may be less important if radiographic signs or clinical symptoms of herniation are absent.

While evidence demonstrates the benefits of therapeutic decompressive hemicraniectomy,

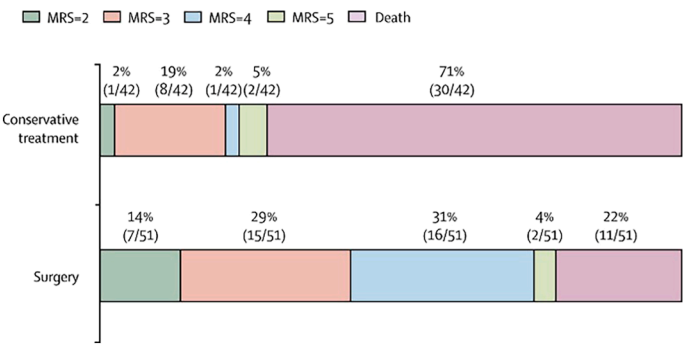

Fig. 2. Distributions of the scores on the mRS and death after 12 months for patients treated with or without decompressive surgery. (*Reprinted with permission from* Elsevier. The Lancet Neurology, 2007, 6(3), 215-222.)

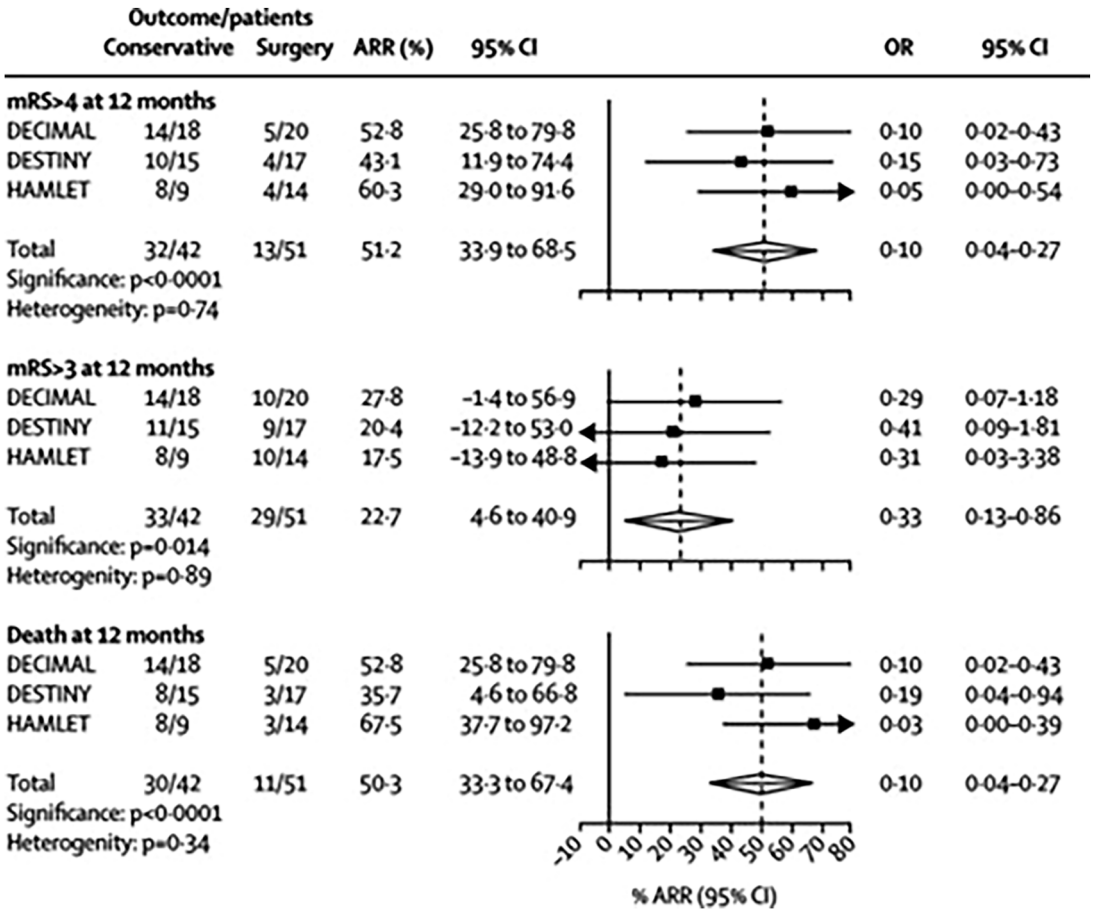

Fig. 3. Absolute risk reductions and ORs for unfavorable outcome at 12 months. (*Reprinted with permission from* Elsevier. The Lancet Neurology, 2007, 6(3), 215-222.)

little data are available regarding the role of prophylactic intervention. Several groups have attempted to identify predictors of the need for decompression and published risk scores such as the Kasner risk index;[55] ASPECTS;[56] DWI ASPECTS, ACA territory involvement, M1 susceptibility vessel sign, hyperglycemia;[57] Enhanced Detection of Edema in Malignant Anterior Circulation Stroke;[18] and Malignant Brain Edema[58] scores. Predictive radiographic features include early computerized tomography scan hypodensity involving greater than half of the MCA territory, poor collateral blood flow, infarct volume greater than 220 mL, and midline shift of 3.7 to 5 mm within 24 to 48 hours after stroke onset.[59,60] MRI findings of an apparent diffusion coefficient less than 80% compared to the contralateral hemisphere with lesion volume $\geq$80 mL within the first 6 hours, or a diffusion weighted imaging infract volume of greater than 145 mL, also predict cerebral edema.[61,62] Pulsatility index derived from transcranial Doppler correlates with increased ICP and may help identify surgical candidates.[63]

Surgical Techniques and Considerations

The approach for surgical decompression involves a large frontal–temporal–parietal hemicraniectomy via a standard reverse question mark incision. An anterior-posterior craniectomy dimension of 15cm with a superoinferior length of approximately 12cm is recommended, with the bone opening carried down to the floor of the middle fossa.[64,65] The dura is opened. Although not routinely performed with the index surgery, patients with particularly large infarcts requiring reoperation may benefit from temporal lobectomy if bony decompression is insufficient.[66,67]

Complications of Decompressive Hemicraniectomy

Both early and late complications may occur after surgical decompression and are reviewed in detail

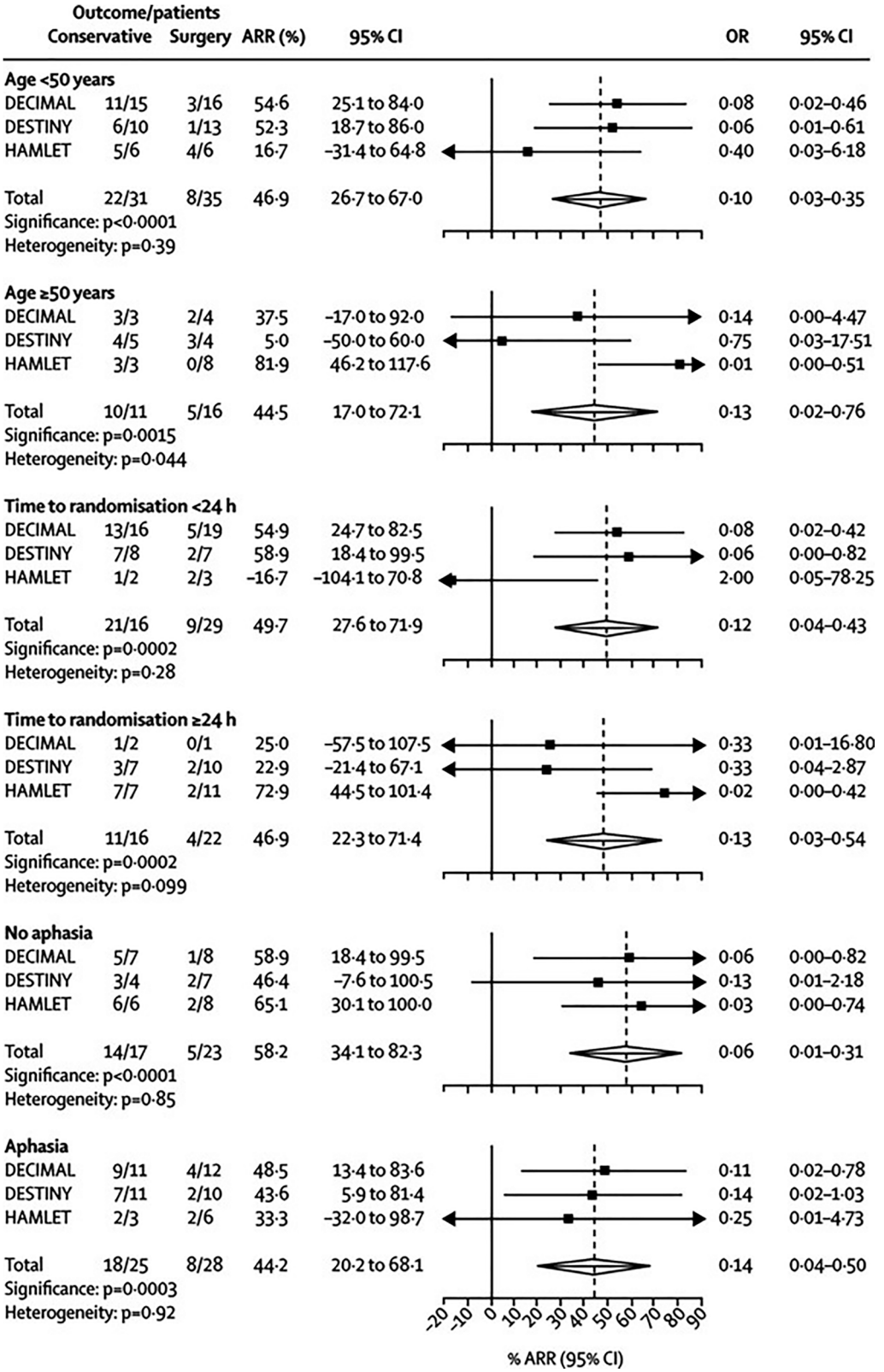

Fig. 4. Subgroup analyses of outcome according to age, timing of randomization, and presence of aphasia. (*Reprinted with permission from* Elsevier. The Lancet Neurology, 2007, 6(3), 215-222.)

elsewhere in this text. Complications somewhat unique to the setting of MCE include inadequate craniotomy size and the impact of surgery on post-infarct seizures. If the bone opening is small relative to the volume of edematous parenchymal tissue, external herniation and hemorrhage may follow due to impingement of the cerebral veins at the bone edges as the brain tissue protrudes through the craniectomy defect.[68] An increase in seizures has been observed following decompression for MCE, with a prevalence up to 61.1% compared to 7.5% to 11.5% in patients who did not undergo surgery.[69–72]

DECISION-MAKING IN PRACTICE

Shared decision-making is crucial, as surgical decompression for MCE dramatically reduces mortality but may leave survivors with significant disability. Several trials attempt to address this complexity and inform the nuanced decision-making required to optimize outcomes for patient and families. Older survivors often retrospectively endorsed desiring surgical decompression despite impaired functional outcomes, emphasizing quality-of-life factors beyond functional independence.[73] In contrast, in a multicenter German study that included patients hospitalized with mild or moderate ischemic stroke, patients and their families mostly reported an mRS of $\geq$4 would be unacceptable,[74] though it is unclear the extent to which cultural differences might have influenced these perspectives. The 2016 ORACLE trial reaffirmed that only a minority of patients initially accepted an mRS of 4 to 5 as acceptable outcomes but did note that perspectives shifted after a discussion of the *disability paradox*—the reporting of quality of life comparable to, or better than, that of an able-bodied individual.[75]

CURRENT GUIDELINE RECOMMENDATIONS REVIEWED

The American Heart Association/American Stroke Association 2019 Guidelines for the Early Management of Patients with Acute Ischemic Stroke recommend early recognition of signs and symptoms of MCE (Class of Recommendation I, Level of Evidence C-EO), and early neurosurgical referral for patients at risk of malignant brain swelling (Class of Recommendation I, Level of Evidence C-LD). In the appropriate clinical context, surgical decompression with dural expansion is reasonable for patients less than 60 years of age who deteriorate within 48 hours from brain swelling (Class of Recommendation IIa, Level of Evidence A) while surgery may be considered for patients older than 60 (Class of Recommendation IIb, Level of Evidence B-R).[41]

The European Stroke Association provides an additional set of recommendations, endorsing that aphasia, additional infarcts, and hemorrhagic transformation are not contraindications for decompression. This group specifies that the craniectomy should be at least 12 cm in diameter and state that surgery beyond 48 hours may be beneficial if death from herniation is imminent.[76]

DECOMPRESSIVE HEMICRANIECTOMY BEYOND ISCHEMIC STROKE

Although surgical decompression is most well established in the setting of malignant ischemic stroke, the principle of relieving ICP by creating additional compensatory space has been extended to other neurologic conditions.

In the setting of hemorrhagic stroke, decompressive craniectomy with or without hematoma evacuation may be pursued. Observational studies suggest a reduction in mortality, but its impact on functional outcomes remain uncertain. Current guidelines recommend consideration of decompressive craniectomy in select young patients with large lobar hemorrhages and impending herniation.[77]

Decompressive surgery outside of stroke-related pathologies is perhaps most thoroughly studied in traumatic brain injury. It has also been evaluated through RCTs and is reviewed in greater detail elsewhere in this volume.

Refractory intracranial hypertension can be a rare complication of acute viral or autoimmune encephalitis leading to diffuse cerebral swelling. Case series and systematic reviews suggest that decompressive hemicraniectomy may be lifesaving in select patients. For example, reports in herpes simplex virus encephalitis describe successful outcomes when decompressive hemicraniectomy was performed for uncontrollable ICP.[78–81] It can be similarly lifesaving in autoimmune encephalitis.[82] While evidence remains limited to observational studies and case reports, surgical intervention could be considered in fulminant encephalitis when medical management fails.

Intracranial abscesses may occasionally cause severe mass effect, particularly when large, multiloculated, or complicated by surrounding vasogenic edema. While the mainstay of treatment remains antibiotics with or without stereotactic aspiration or surgical excision, decompressive craniectomy has been described as a rescue strategy in patients with impending herniation. Isolated case reports describe survival and functional recovery after combined abscess drainage and

decompressive hemicraniectomy.[83–85] Evidence is limited, and no randomized data exist, but expert consensus supports its consideration in catastrophic cases.

Decompressive craniectomy has also been reported in conditions such as cerebral venous sinus thrombosis with massive hemorrhagic infarction, acute hydrocephalus, or malignant edema after aneurysmal subarachnoid hemorrhage. Case series suggests potential benefit when ICP control is otherwise unattainable, but the evidence base remains weak. The results of the recent DECOMPRESS2 trial support decompressive surgery in patients with cerebral venous sinus thrombosis and impending brain herniation.[86–88]

SUMMARY

MCE is a devastating complication of large hemispheric infarctions. Medical management is limited, but decompressive hemicraniectomy has been established as an effective intervention to prevent herniation and reduce mortality. RCTs have confirmed its life-saving role, especially in patients under 60 year old, though functional outcomes may be variable. Beyond ischemic stroke, decompressive hemicraniectomy has also been leveraged as a rescue therapy in select cases of hemorrhagic stroke, encephalitis, abscess, and other neurologic emergencies, though evidence is less robust and often limited to observational studies. Decision-making must balance survival benefits with potential for disability, requiring careful and empathetic discussions with patients and families. Future work may advance the field though refining predictive models, optimizing surgical timing, and integrating patient-centered values into treatment planning, ensuring that outcomes align with clinical evidence and patient goals.

CLINICS CARE POINTS

- Malignant cerebral edema (MCE) complicates up to 10% of anterior circulation infarctions, though rates may be changing in the era of mechanical thrombectomy.
- Left untreated, MCE has a high mortality rate.
- Decompressive craniectomy in the setting of MCE reduces mortality and can improve functional outcomes in a subset of patients.
- Current American Heart Association guidelines suggest considering surgical decompression in patients $\leq$60 year old who deteriorate neurologically within 48 hours from brain swelling associated with unilateral malignant cerebral edema infarctions.

DISCLOSURE

The authors have nothing to disclose.

REFERENCES

1. Li XY, Kong XM, Yang CH, et al. Global, regional, and national burden of ischemic stroke, 1990–2021: an analysis of data from the global burden of disease study 2021. eClinicalMedicine 2024;75. https://doi.org/10.1016/J.ECLINM.2024.102758/ATTACHMENT/C61277E2-358D-4259-B5FE-4B38CD7BD63A/MMC10.DOCX.
2. Feigin VL, Brainin M, Norrving B, et al. World Stroke Organization: global stroke fact sheet 2025. Int J Stroke 2025;20(2):132.
3. Pu L, Wang L, Zhang R, et al. Projected global trends in ischemic stroke incidence, deaths and disability-adjusted life years from 2020 to 2030. Stroke 2023;54(5):1330–9.
4. Gerstl JVE, Blitz SE, Qu QR, et al. Global, regional, and national economic consequences of stroke. Stroke 2023;54(9):2380–9.
5. Ng FC, Yassi N, Sharma G, et al. Cerebral edema in patients with large hemispheric infarct undergoing reperfusion treatment: a HERMES meta-analysis. Stroke 2021;52(11):3450.
6. Liebeskind DS, Jüttler E, Shapovalov Y, et al. Cerebral edema associated with large hemispheric infarction: implications for diagnosis and treatment. Stroke 2019;50(9):2619–25.
7. Przykaza Ł. Understanding the connection between common stroke comorbidities, their associated inflammation, and the course of the cerebral ischemia/reperfusion cascade. Front Immunol 2021;12. https://doi.org/10.3389/FIMMU.2021.782569.
8. Hacke W, Schwab S, Horn M, et al. "Malignant" middle cerebral artery territory infarction: clinical course and prognostic signs. Arch Neurol 1996;53(4):309–15.
9. Heinsius T, Bogousslavsky J, Van Melle G. Large infarcts in the middle cerebral artery territory: etiology and outcome patterns. Neurology 1998;50(2):341–50.
10. Hao Z, Chang X, Zhou H, et al. A cohort study of decompressive craniectomy for malignant middle cerebral artery infarction. Medicine (United States) 2015;94(25):e1039.
11. Huang X, Yang Q, Shi X, et al. Predictors of malignant brain edema after mechanical thrombectomy for acute ischemic stroke. J Neurointerventional Surg 2019;11(10):994–8.
12. Fuhrer H, Schönenberger S, Niesen WD, et al. Endovascular stroke treatment's impact on malignant type of edema (ESTIMATE). J Neurol 2019;266(1):223–31.
13. Zhang L, Li J, Yang B, et al. The risk and outcome of malignant brain edema in post-mechanical thrombectomy: acute ischemic stroke by anterior

circulation occlusion. Eur J Med Res 2023;28(1). https://doi.org/10.1186/S40001-023-01414-X.
14. Nie X, Liu J, Yan B, et al. Cerebral edema progression and outcomes in large infarct patients undergoing endovascular thrombectomy. Ann Neurol 2025; 98(2). https://doi.org/10.1002/ANA.27235.
15. Flores A, Rubiera M, Ribó M, et al. Poor collateral circulation assessed by multiphase computed tomographic angiography predicts malignant middle cerebral artery evolution after reperfusion therapies. Stroke 2015;46(11):3149–53.
16. Broocks G, Kemmling A, Meyer L, et al. Computed tomography angiography collateral profile is directly linked to early edema progression rate in acute ischemic stroke. Stroke 2019;50(12):3424–30.
17. Miao J, Song X, Sun W, et al. Predictors of malignant cerebral edema in cerebral artery infarction: a meta-analysis. J Neurol Sci 2020;409. https://doi.org/10.1016/j.jns.2019.116607.
18. Ong CJ, Gluckstein J, Laurido-Soto O, et al. Enhanced detection of edema in malignant anterior circulation stroke (EDEMA) score. Stroke 2017; 48(7):1969–72.
19. Horsch AD, Dankbaar JW, Stemerdink TA, et al. Imaging findings associated with space-occupying edema in patients with large middle cerebral artery infarcts. Am J Neuroradiol 2016;37(5):831–7.
20. Irvine HJ, Ostwaldt AC, Bevers MB, et al. Reperfusion after ischemic stroke is associated with reduced brain edema. J Cerebr Blood Flow Metabol 2018;38(10):1807–17.
21. Thorén M, Dixit A, Escudero-Martínez I, et al. Effect of recanalization on cerebral edema in ischemic stroke treated with thrombolysis and/or endovascular therapy. Stroke 2020;51(1):216–23.
22. Wu S, Wang Y, Yuan R, et al. Predicting the emergence of malignant brain oedema in acute ischaemic stroke: a prospective multicentre study with development and validation of predictive modelling. eClinicalMedicine 2023;59. https://doi.org/10.1016/j.eclinm.2023.101977.
23. Oertel M, Kelly DF, Lee JH, et al. Efficacy of hyperventilation, blood pressure elevation, and metabolic suppression therapy in controlling intracranial pressure after head injury. J Neurosurg 2002;97(5):1045–53.
24. Fortune JB, Feustel PJ, Graca L, et al. Effect of hyperventilation, mannitol, and ventriculostomy drainage on cerebral blood flow after head injury. J Trauma Inj Infect Crit Care 1995;39(6):1091–9.
25. Harutjunyan L, Holz C, Rieger A, et al. Efficiency of 7.2% hypertonic saline hydroxyethyl starch 200/0.5 versus mannitol 15% in the treatment of increased intracranial pressure in neurosurgical patients - a randomized clinical trial [ISRCTN62699180]. Crit Care 2005;9(5). https://doi.org/10.1186/CC3767.
26. Diringer MN, Scalfani MT, Zazulia AR, et al. Cerebral hemodynamic and metabolic effects of equi-osmolar doses mannitol and 23.4% saline in patients with edema following large ischemic stroke. Neurocritical Care 2011;14(1):11–7.
27. Schwarz S, Schwab S, Bertram M, et al. Effects of hypertonic saline hydroxyethyl starch solution and mannitol in patients with increased intracranial pressure after stroke. Stroke 1998;29(8):1550–5.
28. Halstead MR, Geocadin RG. The medical management of cerebral edema: past, present, and future therapies. Neurotherapeutics 2019;16(4):1133.
29. Moraine JJ, Berré J, Mélot C. Is cerebral perfusion pressure a major determinant of cerebral blood flow during head elevation in comatose patients with severe intracranial lesions? J Neurosurg 2000; 92(4):606–14.
30. Feldman Z, Kanter MJ, Robertson CS, et al. Effect of head elevation on intracranial pressure, cerebral perfusion pressure, and cerebral blood flow in head-injured patients. J Neurosurg 1992;76(2): 207–11.
31. Winkelman C. Effect of backrest position on intracranial and cerebral perfusion pressures in traumatically brain-injured adults. Am J Crit Care 2000; 9(6):373–80 [quiz: 381–82].
32. Durward QJ, Amachier AL, Del Maestro RF, et al. Cerebral and cardiovascular responses to changes in head elevation in patients with intracranial hypertension. J Neurosurg 1983;59(6):938–44.
33. Ng I, Lim J, Wong HB, et al. Effects of head posture on cerebral hemodynamics: its influences on intracranial pressure, cerebral perfusion pressure, and cerebral oxygenation. Neurosurgery 2004;54(3): 593–8.
34. Muizelaar JP, Marmarou A, Ward JD, et al. Adverse effects of prolonged hyperventilation in patients with severe head injury: a randomized clinical trial. J Neurosurg 1991;75(5):731–9.
35. Kerr ME, Marion D, Sereika SM, et al. The effect of cerebrospinal fluid drainage on cerebral perfusion in traumatic brain injured adults. J Neurosurg Anesthesiol 2000;12(4):324–33.
36. Kerr ME, Weber BB, Sereika SM, et al. Dose response to cerebrospinal fluid drainage on cerebral perfusion in traumatic brain-injured adults. Neurosurg Focus 2001;11(4). https://doi.org/10.3171/FOC.2001.11.4.2.
37. Soustiel JF, Mahamid E, Chistyakov A, et al. Comparison of moderate hyperventilation and mannitol for control of intracranial pressure control in patients with severe traumatic brain injury - a study of cerebral blood flow and metabolism. Acta Neurochir 2006;148(8):845–51.
38. Schwab S, Steiner T, Aschoff A, et al. Early hemicraniectomy in patients with complete middle cerebral artery infarction. Stroke 1998;29(9):1888–93.
39. Gupta R, Connolly ES, Mayer S, et al. Hemicraniectomy for massive middle cerebral artery territory

infarction: a systematic review. Stroke 2004;35(2):539–43.
40. Morley NC, Berge E, Cruz-Flores S, et al. Surgical decompression for cerebral oedema in acute ischaemic stroke. Cochrane Database Syst Rev 2002;(3). https://doi.org/10.1002/14651858.CD003435.
41. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2019;50(12):E344–418.
42. Vahedi K, Vicaut E, Mateo J, et al. Sequential-design, multicenter, randomized, controlled trial of early decompressive craniectomy in malignant middle cerebral artery infarction (DECIMAL Trial). Stroke 2007;38(9):2506–17.
43. Jüttler E, Schwab S, Schmiedek P, et al. Decompressive surgery for the treatment of malignant infarction of the middle cerebral artery (DESTINY): a randomized, controlled trial. Stroke 2007;38(9):2518–25.
44. Vahedi K, Hofmeijer J, Juettler E, et al. Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. Lancet Neurol 2007;6(3):215–22.
45. Jüttler E, Unterberg A, Woitzik J, et al. Hemicraniectomy in older patients with extensive middle-cerebral-artery stroke. N Engl J Med 2014;370(12):1091–100.
46. Rahmig J, Wöpking S, Jüttler E, et al. Decompressive hemicraniectomy in elderly patients with space-occupying infarction (DECAP): a prospective observational study. Neurocritical Care 2019;31(1):97–106.
47. Frank JI, Schumm LP, Wroblewski K, et al. Hemicraniectomy and durotomy upon deterioration from infarction-related swelling trial: randomized pilot clinical trial. Stroke 2014;45(3):781–7.
48. Chua AE, Buckley B, Lapitan MC, et al. Hemicraniectomy for Malignant Middle cerebral Infarction (HeMMI): a randomised controlled clinical trial of decompressive surgery with standardized medical care versus standardized medical care alone. Acta Med Philipp 2015;49(1):28–33.
49. Kumral E, Sirin H, Sağduyu A, et al. WITHDRAWN: decompressive surgery in patients with malignant middle cerebral artery infarction: a randomized, controlled trial in a Turkish population (Demitur trial). Int J Stroke 2021. https://doi.org/10.1177/17474930211007671.
50. Slezins J, Keris V, Bricis R, et al. Preliminary results of randomized controlled study on decompressive craniectomy in treatment of malignant middle cerebral artery stroke. Medicina 2012;48:76.
51. Zhao J, Su YY, Zhang Y, et al. Decompressive hemicraniectomy in malignant middle cerebral artery infarct: a randomized controlled trial enrolling patients up to 80 years old. Neurocritical Care 2012;17(2):161–71.
52. Dower A, Mulcahy M, Maharaj M, et al. Surgical decompression for malignant cerebral edema after ischemic stroke: cochrane review. Stroke 2023;54-(12):E500–2.
53. Hofmeijer J, Kappelle LJ, Algra A, et al, HAMLET investigators. Surgical decompression for space-occupying cerebral infarction (the hemicraniectomy after middle cerebral artery infarction with life-threatening edema trial [HAMLET]): a multicentre, open, randomised trial. Lancet Neurol 2009;8(4):326–33.
54. Dasenbrock HH, Robertson FC, Vaitkevicius H, et al. Timing of decompressive hemicraniectomy for stroke: a nationwide inpatient sample analysis. Stroke 2017;48(3):704–11.
55. Kasner SE, Demchuk AM, Berrouschot J, et al. Predictors of fatal brain edema in massive hemispheric ischemic stroke. Stroke 2001;32(9):2117–23.
56. Pexman JH, Barber PA, Hill MD, et al. Use of the Alberta Stroke Program Early CT Score (ASPECTS) for assessing CT scans in patients with acute stroke. AJNR Am J Neuroradiol 2001;22(8):1534–42.
57. Shimoyama T, Kimura K, Uemura J, et al. The DASH score: a simple score to assess risk for development of malignant middle cerebral artery infarction. J Neurol Sci 2014;338(1–2):102–6.
58. Jo KW, Bajgur SS, Kim H, et al. A simple prediction score system for malignant brain edema progression in large hemispheric infarction. PLoS One 2017;12(2). https://doi.org/10.1371/JOURNAL.PONE.0171425.
59. Barber PA, Demchuk AM, Zhang J, et al. Computed tomographic parameters predicting fatal outcome in large middle cerebral artery infarction. Cerebrovasc Dis 2003;16(3):230–5.
60. Park J, Goh DH, Sung JK, et al. Timely assessment of infarct volume and brain atrophy in acute hemispheric infarction for early surgical decompression: strict cutoff criteria with high specificity. Acta Neurochir 2012;154(1):79–85.
61. Oppenheim C, Samson Y, Manai R, et al. Prediction of malignant middle cerebral artery infarction by diffusion-weighted imaging. Stroke 2000;31(9):2175–81.
62. Thomalla GJ, Kucinski T, Schoder V, et al. Prediction of malignant middle cerebral artery infarction by early perfusion- and diffusion-weighted magnetic resonance imaging. Stroke 2003;34(8):1892–9.
63. Asil T, Uzunca I, Utku U, et al. Monitoring of increased intracranial pressure resulting from cerebral edema with transcranial Doppler sonography in patients with middle cerebral artery infarction. J Ultrasound Med 2003;22(10):1049–53.
64. Beez T, Munoz-Bendix C, Steiger HJ, et al. Decompressive craniectomy for acute ischemic stroke. Crit

Care 2019;23(1). https://doi.org/10.1186/S13054-019-2490-X.
65. Curry WT, Sethi MK, Ogilvy CS, et al. Factors associated with outcome after hemicraniectomy for large middle cerebral artery territory infarction. Neurosurgery 2005;56(4):681–91.
66. Lu W, Jia D, Qin Y. Decompressive craniectomy combined with temporal pole resection in the treatment of massive cerebral infarction. BMC Neurol 2022;22(1):167.
67. Bentancourt MV, Romero M, Martinez F. Temporal lobectomy in patients with malignant stroke and raised intracranial pressure after decompressive hemicraniectomy. J Neurol Stroke 2019;9(Issue 2). https://doi.org/10.15406/JNSK.2019.09.00352.
68. Wagner S, Schnippering H, Aschoff A, et al. Suboptimum hemicraniectomy as a cause of additional cerebral lesions in patients with malignant infarction of the middle cerebral artery. J Neurosurg 2001;94(5):693–6.
69. Brondani R, Garcia De Almeida A, Abrahim CP, et al. High risk of seizures and epilepsy after decompressive hemicraniectomy for malignant middle cerebral artery stroke. Cerebrovasc Dis Extra 2017;7(1):51–61.
70. Burn J, Dennis M, Bamford J, et al. Epileptic seizures after a first stroke: the Oxfordshire community stroke project. Br Med J 1997;315(7122):1582–7.
71. Creutzfeldt CJ, Tirschwell DL, Kim LJ, et al. Seizures after decompressive hemicraniectomy for ischaemic stroke. J Neurol Neurosurg Psychiatry 2014;85(7):721–5.
72. So EL, Annegers JF, Hauser WA, et al. Population-based study of seizure disorders after cerebral infarction. Neurology 1996;46(2):350–5.
73. Ragoschke-Schumm A, Junk C, Lesmeister M, et al. Retrospective consent to hemicraniectomy after malignant stroke among the elderly, despite impaired functional outcome. Cerebrovasc Dis 2015;40(5–6):286–92.
74. Neugebauer H, Schnabl M, Lulé D, et al, IGNITE Study Group Initiative of German NeuroIntensive Trial Engagement. Attitudes of patients and relatives toward disability and treatment in malignant MCA infarction. Neurocritical Care 2017;26(2):311–8.
75. Honeybul S, Ho KM, Blacker DW. ORACLE stroke study: opinion regarding acceptable outcome following decompressive hemicraniectomy for ischemic stroke. Neurosurgery 2016;79(2):231–6.
76. van der Worp HB, Hofmeijer J, Jüttler E, et al. European Stroke Organisation (ESO) guidelines on the management of space-occupying brain infarction. Eur Stroke J 2021;6(2):XC–CX.
77. Greenberg SM, Ziai WC, Cordonnier C, et al. Guideline for the management of patients with spontaneous intracerebral hemorrhage: a guideline from the American Heart Association/American Stroke Association. Stroke 2022;53(7):E282–361.
78. Jouan Y, Grammatico-Guillon L, Espitalier F, et al. Long-term outcome of severe herpes simplex encephalitis: a population-based observational study. Crit Care 2015;19(1). https://doi.org/10.1186/S13054-015-1046-Y.
79. Byun YH, Ha EJ, Ko SB, et al. Decompressive craniectomy for herpes simplex encephalitis complicated by frank intracerebral hemorrhage: a case report and review of the literature. BMC Neurol 2018;18(1):176.
80. Abdul Jalal MJ, Fernandez SJ, Varghese P, et al. Decompressive craniectomy in herpes simplex encephalitis. Neurosciences 2015;2:182–6.
81. Adamo MA, Deshaies EM. Emergency decompressive craniectomy for fulminating infectious encephalitis: report of two cases. J Neurosurg 2008;108(1):174–6.
82. Antuña Ramos A, Mayordomo-Colunga J, Blanco Lago R, et al. Decompressive craniectomy in the acute fulminant cerebral edema. Neurocirugía (English Edition) 2024;35(6):329–33.
83. Kunapaisal T, Guo S, Gomez C, et al. Bacterial brain abscess and life-threatening intracranial hypertension requiring emergent decompressive craniectomy after SARS-CoV-2 infection in a healthy adolescent. Cureus 2023;15(3). https://doi.org/10.7759/CUREUS.36258.
84. Jaradat A, et al, Jaradat A, Ba-Shammakh S. Unexpected pathway: delayed idiopathic brain edema following successful stereotactic aspiration of a brain abscess: a case report. Archives of Clinical Infectious Diseases 2024;19(5):e157628.
85. Mork J, Stepanek D, Runt V, Hommerova J, Priban V. Sporadic use of decompressive hemicraniectomy in a patient with brain abscess – a case Report. Ceska a Slovenská neurologie a neurochirurgie. 2014;77(6):765-768.
86. Avanali R, Gopalakrishnan MS, Indira DB, et al. Role of decompressive craniectomy in the management of cerebral venous sinus thrombosis. Front Neurol 2019;10(MAY):511.
87. Elsherbini MM, Badr H, Khalil AF. Efficiency of decompressive craniectomy as a line of management of severe cerebral venous thrombosis. J Cerebrovasc Endovasc Neurosurg 2022;24(2):129.
88. Aaron S, Ferreira JM, Coutinho JM, et al. Outcomes of decompressive surgery for patients with severe cerebral venous thrombosis: DECOMPRESS2 observational study. Stroke 2024;55(5):1218–26.